Cardiovascular Innovations and Applications

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China Heart Society

Beijing Society of Cardiology

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ABSTRACTS

This Supplement contains the selected Abstracts presented at the 30th Great Wall International Congress of Cardiology, China Heart Society, and Beijing Society of Cardiology, held October 10–13, 2019, at the China National Convention Center.

Cardiovascular Innovations and Applications

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BASIC AND TRANSLATIONAL MEDICINE

BASIC RESEARCH OF CARDIOVASCULAR DISEASE

GW30-e0006

Protective effect of sweroside on heart failure induced by excessive isoproterenol in mice

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OBJECTIVES The aim of this study was to evaluate the protective effect of sweroside on excessive isoproterenol induced heart failure in mice and to explore its target and mechanism.

METHODS Heart failure mice model was established by subcutaneous injection of excessive isoprenaline. Mice were randomly divided into four groups including control group, model group, sweroside group and captopril group. Cardiac function was evaluated by echocardiography, myocardial pathological changes were detected by Hematoxylin and eosin staining (HE staining). Drug targets were predicted by BAT-MAN-TCM database, and protein expression was detected by Western blot.

RESULTS Compared with the control group, the left ventricle ejection fraction (LVEF) and left ventricle fractional shortening (LVFS) of the model group decreased by 37.84 and 48.04% respectively. Left ventricular internal systolic diameter (LVIDs) increased to about 3.06±0.51 mm (1.86±0.59 mm in the control group), with an increase of more than 50%. Compared with the model group, EF of sweroside group increased to 71.83±4.82%, which was close to the control group, FS increased by 71.79%, LVIDs decreased by 30.82%. The above data had statistical significance (P<0.01). In Histopathological examination, thinned left ventricular wall, thinned myocardial fiber, scattered necrosis of myocardial cells, as well as aggregation of inflammatory cells were found in model mice. The morphology of myocardial tissue were obtained approximate normal by sweroside. The BAT-MAN-TCM database suggests that sweroside may play a therapeutic role in heart failure through ATPase Na+/K+Transporting Subunit Alpha1(ATP1A1). Western blot results showed that ATP1A1 protein expression was down-regulated in the model group, and the content of ATP1A1 protein was increased in the sweroside group.

CONCLUSIONS Sweroside can significantly improve the heart failure induced by excessive isoproterenol in mice, and the mechanism may be related to the increase of ATP1A1 protein expression and the improvement of myocardial energy metabolism.

GW30-e0011

Age peculiarities of morphological changes in the rats heart at alloxan diabetes

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OBJECTIVES Diabetes mellitus is one of the most common non-communicable diseases. Today, more than 382 million people with diabetes live on the planet. The dynamics of development is increasing every year. Diabetes mellitus is one of the main causes of cardiovascular pathologies. The purpose of our work was to establish the age-old peculiarities of the effect of alloxan diabetes on the heart of rats. The features of changes in internal organs are studied on experimental animal models in order to improve the methods of correction of adverse effects of diabetes mellitus on the body and, in particular, on the heart. One of the inductors of diabetes is alloxan.

METHODS The study was performed on 12 mature and 12 young white male rats, divided into two groups: control and experimental (6 in each). Animal retention and experiments were carried out in accordance with the requirements of the "General Ethical Principles of Animal Experiments", adopted by the First National Congress on Bioethics (Kyiv, 2001). Animals of the experimental group administered once daily alloxan intraperitoneally at a dose of 40 mg/kg. From the 7th to the 10th day after the administration of alloxan, the level of glucose in the blood that was steadily elevated was measured. One month after the induction, the animals were withdrawn from the experiment with an anesthetized lung of decapitation. Hearts were digested according to the method of Avtandilov, separately weighed parts of the heart behind Muller. For histological examination, the ventricles were fixed in a 10% neutral formalin solution over the course of the day, dehydrated in alcohols of increasing concentration, and poured into paraffin. The sections of the myocardium were stained with hematoxylin-eosin and studied using a light microscope Olympus BH-2.

RESULTS Under conditions of alloxan diabetes in mature rats there is an increase in the heart mass by 41.09% (P<0.0001), left ventricle is 56% (P><0.0001), right ventricle is 31.46% (P><0.0001), the left ventricle area was 31.77% (P><0.0001), right ventricle 45.89% (P=0.0008). Atrial weight decreases by 64% (P><0.0001), the ventricular index is 14.94% (P=0.0014), the planimetric index is unreliable. Histologically, the polymorphism of nuclei of cardiomyocytes, local disorientation of muscle fibers and their cytolysis were revealed. Spacing gaps are expanded (stromal edema). Vessels of uneven filling: in some fields, the vessels are empty, in others – the aggregation of erythrocytes in vessels, capillary hyperemia, edema around the vessels. In young rats, an increase in left ventricular mass is observed at 33.48% (P=0.0327), left ventricular area is 18.22% (P=0.0061), right ventricle is 20% (P=0.0287). Atrial weight decreases by 38.78% (P=0.0035), ventricular index is 15.19% (P=0.0036). Other indicators are unreliable. Histologically – the polymorphism of the nuclei of cardiomyocytes, the disorientation of muscle fibers. Unidirectional contents of the vessel: in some fields the vessels are empty, in others the aggregation of red blood cells.

CONCLUSIONS In alloxan diabetes, an increase in the mass of the heart with an overwhelming left ventricular hypertrophy, cardiomyocytes and vascular disorders in the myocardium of experimental animals was detected. The violations of the structural components of the wall of the heart are detected. This indicates a low functional activity of the heart, which leads to cardiovascular pathologies.

GW30-e0029

Apolipoprotein A5 inhibits adipogenesis of human adipose-derived mesenchymal stem cells through modulating CIDEC expression

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OBJECTIVES Obesity is associated with metabolic syndromes. The hallmark of obesity is excessive lipid storage in adipose tissue. As is known, the adipose tissue has such abundant adipose-derived mesenchymal stem cells (AMSCs), which can differentiate into mature adipocytes by imbalance between energy intake and expenditure.

Apolipoprotein A5 (ApoA5) is a novel apolipoprotein. Recently, evidence indicates that lower plasma level of ApoA5 was found in obese subjects and was inversely correlated with BMI. However, the underlying mechanisms are ambiguous. On the other hand, it is noteworthy that ApoA5 could also modulate TG storage in hepatocytes, indicating a crucial intracellular role of ApoA5 in TG metabolism. Since adipocytes provide the largest storage depot for TG, we hypothesized apoA5 might also target to adipocytes and regulate TG storage. The aims of this research were to explore the effect of ApoA5 in AMSCs adipogenesis and the underlying mechanisms.

METHODS We isolated AMSCs from the epigastric adipocyte tissue of the patients underwent abdominal surgery. The pre-adipocytes were treated with adipogenesis medium and human recombinant ApoA5 protein. Then we harvested cells at 7th, 14th, 21st days after adipogenesis. The following tests were performed: (1) effects of ApoA5 on morphological changes of intracellular lipid droplets were observed under microscope; (2) effects of ApoA5 on intracellular TG content were observed by spectrophotometry; (3) effects of ApoA1 on modulating the gene expression levels of the adipogenesis-related markers, such as C/EBPα, C/EBPβ, PPARγ, aP2 and FAS, were detected by PCR; (4) effects of ApoA1 on modulating the gene expression levels of CIDEC were detected by PCR; (5) distribution of ApoA5 and CIDEC were observed by confocal microscope; (6) ApoA5 antibody and CIDEC antibody were used for CO-IP observe whether ApoA5 interacts with CIDEC; (7) we silenced and over-expressed the CIDEC gene in AMSCs. The function of CIDEC in AMSCs adipogenesis was investigated and the effects of ApoA5 on CIDEC expression were detected; (8) the effect of ApoA5 on adipogenesis was further detected in AMSCs with CIDEC-silenced or over-expressed.

RESULTS The main results were listed as follows: (1) ApoA5 could reduce the amount of lipid droplets and decrease the TG content in adipocytes during the adipogenesis; (2) ApoA5 could down-regulate the gene expression level of C/EBPα, C/EBPβ, PPARγ, aP2 and FAS during the adipogenesis; (3) ApoA5 could down-regulate the gene and protein expression level of CIDEC during the adipogenesis; (4) ApoA5 co-localized and had interaction with CIDEC in the surface of lipid droplets; (5) the effect of ApoA5 on inhibiting adipogenesis was attenuated in AMSCs with SORT1 gene over-expression.

CONCLUSIONS In conclusions, our results confirm that CIDEC plays an important role in the adipogenesis of human AMSCs. Furthermore, the results indicate that apoA5 acts as a negative regulator of adipogenesis differentiation in human AMSCs through the inhibition of adipogenesis differentiation-related factors and the promotion the intracellular gene and expression level of CIDEC. The present data provide insight into the mechanisms of the inhibitory effects of ApoA5 and suggest that the inhibitory activity of ApoA5 indicates a potential pharmacological intervention specifically directed toward obesity.

GW30-e0030

Effect and potential mechanisms of apolipoprotein A1 on adipogenesis of human adipose-derived mesenchymal stem cells

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OBJECTIVES Obesity is associated with a series of metabolic syndromes. The hallmark of obesity is excessive lipid storage in adipose tissue. As is known, the adipose tissue has such abundant adipose-derived mesenchymal stem cells (AMSCs), which can differentiate into mature adipocytes by imbalance between energy intake and expenditure.

Apolipoprotein A1 (ApoA1) is the major protein component of HDL. In addition to anti-atherogenic function of ApoA1, recent works focused on ApoA1 in affecting the process of obesity and the lipid metabolism in mature adipocytes, demonstrating that APOA1 gene SNPs were related to obesity and reduced plasma ApoA1 level was associated with increased prevalence of obesity. However, the underlying mechanisms are ambiguous. The aim of this study was to examine the anti-obesity effect of ApoA1 and the potential mechanisms by which ApoA1 influencing human AMSCs adipogenesis.

METHODS We isolated AMSCs from the epigastric adipocyte tissue of the patients underwent abdominal surgery. The pre-adipocytes were treated with adipogenesis medium and ApoA1 protein. Then we harvested cells at 7^{th}, 14^{th} days after adipogenesis. The following tests were performed separately: (1) effects of ApoA1 on the morphological changes of intracellular lipid droplets were observed by Oil red O staining under microscope; (2) effects of ApoA1 on the intracellular TG content were observed by spectrophotometry; (3) effects of ApoA1 on modulating the expression levels of the adipogenesis-related markers, such as C/EBPα, C/EBPβ, FABP4 and FAS, were detected by PCR and Western Blot; (4) by lentiviral transfection technology, we silenced and over-expressed the SORT1 gene in AMSCs. The function of sortilin in AMSCs adipogenesis was investigated and the effects of ApoA1 on sortilin expression were detected by PCR and Western blot; (5) the effect of apoA1 on adipogenesis was further detected in AMSCs with SORT1-silenced or over-expressed.

RESULTS The main results were listed as follows: (1) ApoA1 could reduce the amount of lipid droplets and decrease the TG content synergistically in adipocytes during the adipogenesis; (2) ApoA1 could down-regulate the gene and protein expression level of C/EBPα, C/EBPβ, FABP4 and FAS during the adipogenesis; (3) Sortilin plays an important role in AMSCs adipogenesis. Silencing SORT1 gene could promote excessive adipogenesis of AMSCs, while overexpression of SORT1 gene inhibits the AMSCs adipogenesis; (4) ApoA1 could up-regulate the gene and protein level of sortilin during the adipogenesis; (5) the effect of ApoA1 on inhibiting adipogenesis was attenuated in AMSCs with silencing SORT1 gene; however, there was no significant changes of the effect of ApoA1 on inhibiting adipogenesis in AMSCs with overexpressed SORT1 gene.

CONCLUSIONS In conclusions, our results confirm that sortilin plays an important role in the adipogenesis of human AMSCs. Furthermore, the results indicate that ApoA1 acts as a negative regulator of adipogenesis differentiation in human AMSCs through the inhibition of adipogenesis differentiation-related factors and the promotion the intracellular gene and expression level of sortilin. The present data provide insight into the mechanisms of the inhibitory effects of ApoA1 and suggest that the inhibitory activity of ApoA1 indicates a potential pharmacological intervention specifically directed toward obesity.

GW30-e0038

Echinacoside reduced myocardial apoptosis and improved heart function in heart failure rats induced by isoproterenol via suppressing mitochondrial oxidative stress

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OBJECTIVES Apoptosis of myocardial cells has been shown to be a critical step provoking heart failure. Studies indicated that mitochondrial oxidative stress and excessive production of mitochondrial ROS in heart failure was tightly linked to activation of apoptosis. ECH was used as a traditional Chinese herbal medicine, it has been shown to possess powerful ability of anti-oxidant and anti-apoptosis properties in kinds of cells, but whether it affects myocardial apoptosis in the heart failure remain unknown. The present study investigated the effects of ECH on heart failure and myocardial apoptosis of rats induced by ISO in vivo and on mitochondrial oxidative stress of AC-16 cells induced by ISO and explored the underlying mechanisms in vitro.

METHODS Heart failure rats were induced by ISO, ECH was treated by intraperitoneal injection, echocardiography was performed to evaluate heart function, TUNEL was used to detect myocardial apoptosis in vivo. In vitro AC-16 cells were cultured, mitochondrial oxidative stress was induced by ISO, ECH was pre-treated. Apoptotic cells were detected by flow cytometry, the level of mitochondrial ROS were measured by luminol chemiluminescence, 8-OHdG was used to evaluate the oxidative damage of mitochondrial DNA, mitochondrial membrane potential was detected by JC-1, carbonylation of mitochondrial proteins were measured using Elisa, mitochondrial lipid peroxidation were measured using TBARS assay, intracellular ROS were measured with flow cytometry.

RESULTS The results demonstrated that ECH significantly improved the heart function and reduced myocardial apoptosis of heart failure rats induced by ISO in vivo, and inhibited oxidative damage of mitochondrial DNA, protected mitochondrial membrane potential, reduced intracellular ROS, prevented carbonylation of mitochondrial proteins and mitochondrial lipid peroxidation, suppressed production of mitochondrial ROS, and subsequently inhibited intracellular ROS of AC-16 cells induced by ISO in vitro.

CONCLUSIONS We concluded that ECH significantly inhibited myocardial apoptosis and improved heart function of heart failure rats induced by ISO via suppressing mitochondrial oxidative stress. It was suggested that ECH was a potential drug treatment for heart failure.

GW30-e0051

Hydronephrosis decreases ACE2 and mas receptor expression in the heart

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OBJECTIVES Hydronephrosis is commonly caused by an obstruction of the urine flow from the kidney. The condition involves a dilation and distention of the renal pelvis. Hydronephrosis may be either acute or chronic in nature. It was reported a postnatal infant had hypoplastic left heart with hydronephrosis, indicating that there may be a relationship between hydronephrosis and heart disease. However, whether hydronephrosis causes cardiac damage and affects the RAS in the heart remains unknown. Thus, we assessed BP, heart weight and the expression of components of the RAS in the heart in hydronephrotic mice treated with AT1 receptor blockade and ACE inhibitor.

METHODS Hydronephrosis was induced by left ureteral ligation in Balb/C mice except sham-operated animals. Blood pressure was measured by the tail-cuff method using photoelectric volume oscillometry. At postmortem, heart weight was balanced. The levels of cardiac ACE, ACE2 and Mas receptor were measured by RT-PCR and Western blot after treatment of losartan or enalapril. Plasma renin activity (PRA), Ang I and Ang II were measured by radioimmunoassay using commercial kits.

RESULTS In the normal kidney the tubules were intact while they disappeared in the hydronephrotic kidney. Blood pressure did not significantly change after the left ureteral ligation. Hydronephrosis led to an increase of ACE level and a decreased of ACE2 and Mas receptor in the heart. Losartan decreased cardiac ACE level, but ACE2 and Mas receptor levels significantly increased in hydronephrotic mice ($P<0.01$). Enalapril increased ACE2 levels ($P<0.01$), but did not affect Mas receptor in the heart. PRA decreased in hydronephrotic mice, but significantly increased by losartan or enalapril. Plasma Ang II level decreased in hydronephrotic mice ($P<0.05$). Administration of losartan was accompanied by a rise in plasma Ang I and Ang II concentrations in hydronephrotic animals ($P<0.05$). Enalapril also increased levels of Ang I ($P<0.01$) and Ang II ($P<0.05$) in the circulation.

CONCLUSIONS In this study, we found that Hydronephrosis increased cardiac ACE, suppressed ACE2 and Mas receptor levels. Furthermore, AT1 blockade caused sustained activation of cardiac ACE2 and Mas receptor, but ACE inhibitor had the limitation of such activation of Mas receptor in hydronephrotic animals. These findings may lead to an exciting new area in the clinical administration of AT1 receptor blockade. These results also suggest that activation of cardiac ACE2 by both enalapril and losartan may protect against the adverse effects of activated RAS and renal impairment. Thus, we propose that the change of cardiac ACE2 and Mas receptor expression induced by hydronephrosis can be an important target of strategies for preventing cardiovascular damage. The observations of the different molecular mechanisms of losartan and enalapril could be helpful for better options in the treatment of cardiovascular diseases.

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GW30-e0052

Exosomal miRNA-1915-3p, miRNA-4507, and miRNA-3656 serve as clinical diagnostic biomarkers in acute myocardial infarction patients

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OBJECTIVES MicroRNA (miRNA) can be used as predictive biomarkers for cardiovascular diseases, especially for acute myocardial infarction (AMI). However, few reports have focused on the value of exosomal miRNAs in the mechanism of the pathophysiological process from stable coronary artery disease (SCAD) to AMI.

METHODS Exosomes were isolated via ExoQuick precipitation after serum samples were collected. The exosomes were then identified by transmission electron microscopy (TEM), Western blotting, and nanoparticle-tracking analysis (NTA). The differential expression of miRNAs in exosomes from 6 AMI and 6 matching SCAD patients was screened using Agilent Human miRNA Microarrays. Target genes of the candidate miRNAs were predicted via an online miRNA database, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses. Further validation was conducted through quantitative real-time PCR (qRT-PCR) with 60 exosome (30 AMI and 30 SCAD) samples.

RESULTS The expression of 13 miRNAs (miRNA-4507, miRNA-3656, miRNA-6803-5p, miRNA-7108-5p, miRNA-6850-5p, miRNA-4486, miRNA-6741-5p, miRNA-1227-5p, miRNA-3195, miRNA-4634, miRNA-7975, miRNA-6798-3p, and miRNA-1915-3p) was significantly down-regulated in the AMI samples compared with the SCAD samples. In addition, we identified various target genes that are mainly involved in the pathways of cardiac rehabilitation and remodelling, such as the signalling pathways activated downstream by Nerve Growth Factor (NGF) and Fibroblast growth Factor Receptors (FGFRs). Validation of the expression of candidate miRNAs indicated that exosomal miRNA-1915-3p, miRNA-4507, and miRNA-3656 were significantly less expressed in AMI samples than in SCAD samples, and ROC curve (AUC) analysis showed that the expression of these miRNAs resulted in good predictive accuracy [miRNA-1915-3p (AUC 0.772); miRNA-4507 (AUC: 0.684); and miRNA-3656 (AUC: 0.771)], suggesting that serum exosomal miRNA-1915-3p, miRNA-4507, and miRNA-3656 might be predictive for AMI at an early stage. Correlation analysis revealed that the expression of miRNA-1915-3p was negatively correlated with the PLT (r=–0.479, P=0.038), the expression of miRNA-4507 was negatively correlated with LDL-c (r=–0.5, P=0.029), and the expression of miRNA-3656 was related to the LVEF (r=0.471, P=0.042).

CONCLUSIONS Exosomal miRNA-1915-3p, miRNA-4507, and miRNA-3656 might play an important role in the pathophysiology of acute myocardial infarction and could serve as clinical diagnostic biomarkers.

GW30-e0053

Association of PON1 gene promoter DNA methylation with the risk of clopidogrel poor response in patients with coronary artery disease

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OBJECTIVES The failure of therapeutic response to clopidogrel in platelet inhibition, which is called clopidogrel resistance (CR), is more likely to cause cardiovascular events. We aimed to study the contribution of promoter DNA methylation of paraoxonase 1 (*PON1*) to the risk of clopidogrel poor response.

METHODS Through VerifyNow P2Y12 assay, patient' platelet functions were measured. Among 57 non-CR and 49 CR patients, the levels of DNA methylation in four CpG dinucleotides on the *PON1* promoter were tested using bisulfite pyrosequencing technology. Besides, the relative expression of *PON1* mRNA was analysed by quantitative real-time PCR. Logistic regression was applied to investigate the interatcion of *PON1* methylation and clinical factors in CR.

RESULTS In the subgroup with dyslipidaemia, we discovered that higher CpG4 levels of the *PON1* promoter indicated a poorer clopidogrel response (cases versus controls (%): 51.500±14.742 versus 43.308±10.891, =0.036), and the *PON1* mRNA expression was reduced in CR patients. Additionally, the logistic regression indicated that higher level of albumin and the index of ALT were related with a lower risk of CR, and the index of AST as well as the quantity of stent may be positively associated with CR.

CONCLUSIONS The DNA methylation of CpG4 in the *PON1* promoter would lead to a low expression of *PON1* mRNA, which might induce clopidogrel resistance in the patients with dyslipidaemia, and the number of stents might be a risk for CR.

GW30-e0056

PP2Cm overexpression alleviates MI/R injury mediated by a BCAA catabolism defect and oxidative damagein T2DM mice

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OBJECTIVES Diabetic patients are more sensitive tomyocardial ischemia-reperfusion (MI/R) injury. Branched-chain amino acids (BCAA) catabolism is defective and mitochondrial phosphatase 2C (PP2Cm) expression is reduced in the diabetic state. However, the role of PP2Cm and BCAA in diabetes with MI/R injury remains unclear. This study aims to determine the mechanism of reduced PP2Cm expression and investigate whether PP2Cm and BCAA have a cardioprotective effect in diabetes with MI/R injury.

METHODS C57BL/6 mice were fed a high-fat diet (HFD) and injected intraperitoneally with a dose of streptozotocin (25 mg/kg) twice to generate T2DM model mice. C57BL/6 mice (WT), type 2 diabetes (T2DM), PP2Cm–/– mice, were used in this study. For T2DM mice, PP2Cm-specific adenovirus was delivered to generate diabetic mice with PP2Cm overexpression. The T2DM mice were also treated with with BDK inhibitor BT2, while the PP2Cm–/– mice were treated with MnTBAP (manganese (III) tetrakis (4-benzoic acid)porphyrin chloride). Myocardial infarction/reperfusion (MI/R) was produced simultaneously in all types of mice. Additionally, WT and PP2Cm–/– mice treated with BT2 and expressing adenovirus were analyzed. H9C2 cells were treated with BCAA and BCKA. After H9C2 cells were treated with BCKA and underwent simulated ischemia-reperfusion (SI/R), BT2 and MnTBAP were added. Cardiac function, apoptosis, BCAA metabolism and oxidative damage were assayed.

RESULTS PP2Cm protein levels were significantly decreased in the diabetic heart. Under PP2Cm-overexpressing T2DM mice injury, cardiac function was improved due to a decrease of myocardial infarct size and the increase of LVEF. The Apoptosis rate was decreased as evidenced by Caspase-3 activity and the number of TUNEL positive cardiomyocytes. Cardiac BCAA and BCKA levels, as well as the ratio of p-BCKDE1α/BCKDE1α significantly increased (P<0.01) and BCKD activity significantly decreased (P<0.01) in T2DM mice. After BT2 treatment in T2DM mice with MI/R injury, the BCAA cataboliam defect was alleviated. At the same time, an improvement of Cardiac function and reduction of apoptosis was observed. In PP2Cm–/– mice, aBCAA catabolism defect and MI/R injury was observed. After PP2Cm overexpression and BT2 treatment, BCAA catabolism defect and MI/R injury was obviously alleviated. In PP2Cm–/– mice, oxidative damage was observed evident as an the increases in superoxide concentration, a decrease of MnSOD, complex I and III activities, and ATP levels as well as mitochondrial damage. Supplementation with MnTBAP obviously ameliorated this oxidative damage and MI/R injury in PP2Cm–/– mice. Treatment with BCKA (1.5-3 mM) resulted in significant decreases cell viability, and significant increases in the percentage of LDH release, apoptosis in H9C2 cells with SI/R injury. After BT2 and MnTBAP treatment, these effects were obviously alleviated.

CONCLUSIONS T2DM induced a downregulation of PP2Cm and reduced the defect of BCAA metabolism. PP2Cm directly mediated the defect of BCAA catabolism and oxidative damage. Overexpression PP2Cm alleviated MI/R injury by reducing the catabolism of BCAA and oxidative damage.

GW30-e0060

Protective effect of obeticholic acid on obesity-induced cardiomyopathy

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OBJECTIVES Obesity is a major contributor to myocardial cell apoptosis, fibrosis and ventricle hypertrophy, and associated with the increased risk of hypertrophic cardiomyopathy. Obeticholic acid (OCA), a farnesoid X receptor agonist, is a key regulator of lipid metabolism, inflammatory, fibrosis and metabolic pathways. This study was performed to investigate the effect and mechanism of OCA on obesity-induced myocardial injury.

METHODS C57Bl/6 mice were fed with a 45% high fat diet (HFD) or a standard diet. Biochemical parameters and myocardial pathological changes were examined. Energy metabolism in isolated working heart using radioactive was also tested to reveal the mechanism of myocardial injury. In vitro, 3D cell culture, mitochondria damage and ATP production of C2C12 cells cultured with palmitic acid (PA) in the absence or presence of OCA were tested.

RESULTS The body weight of HFD C57Bl/6 mice has increased by 22.7% compared with mice fed with normal diet. In addition, HFD-induced obese mice developed cardiac hypertrophy, fibrosis, inflammation, apoptosis, oxidative

injury, which was rescued by OCA treatment. There was also a remarkably mitochondria damage in the obese mice and OCA prevented against the mitochondria damage. In vitro, 3D cell culture showed that PA reduced the myocardial contraction and viability. PA also increased the apoptosis rate of C2C12 cells and induced mitochondrial damage identified by the Tom20 level and ATP production assay. OCA showed a protective effect against PA-induced mitochondrial damage and myocardial damage. The results of energy metabolism in isolated working heart further indicated that the contribution of glucose oxidation to ATP production is lower than palmitate oxidation in HFD-induced obese mice heart, and OCA promoted glucose oxidation to protect against PA-induced mitochondrial damage.

CONCLUSIONS The present data suggested that OCA reduced the myocardial cell apoptosis, fibrosis and inflammation in the HFD-induced obese C57Bl/6 mice. OCA also protected cardiomyocytes against PA-induced mitochondria damage through promoting glucose oxidation. Our findings provide evidence for the protective role of OCA in myocardial cells.

GW30-e0072

Pretreatment of diabetic adipose-derived stem cells with mitoTEMPO reverses their defective proangiogenic function in diabetic mice with critical limb ischemia

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OBJECTIVES We hypothesized that pretreatment of dADSCs with mitoTEMPO, a mitochondrial ROS scavenger, may improve their function. We found that pretreatment of dADSCs with mitoTEMPO for three passages enhanced their proangiogenic function and improved their protective effects against critical limb ischemia in streptozotocin (STZ)-induced diabetic mice. This finding suggested that a short-term pretreatment of dADSCs with a mitochondrial ROS scavenger restored their proangiogenic capacity both in vitro and in vivo.

METHODS Animals/Isolation, culture, and characterization of ADSCs/Cell viability assay/Multidifferentiation potential of ADSCs/Scratch and cell migration assays/Proangiogenic analysis of ADSCs/Establishment of a critical limb ischemia model in diabetic mice/Bioluminescence imaging of ADSCs in vivo/Confocal imaging/Western blotting/Statistical analysis.

RESULTS (1) Pretreatment of dADSCs with mitoTEMPO scavenged mitochondrial ROS and improved multidifferentiation potential. (2) Pretreatment of dADSCs with mitoTEMPO improved migration capacity. (3) Pretreatment of dADSCs with mitoTEMPO enhanced proangiogenic capacity. (4) Enhancement of mitochondrial antioxidant capacity contributed to the proangiogenic effects of mitoTEMPO pretreatment on dADSCs. (5) Pretreatment of dADSCs with mitoTEMPO improved their survival in diabetic mice with critical limb ischemia. (6) Pretreatment of dADSCs with mitoTEMPO improved their proangiogenic effects in diabetic mice with critical limb ischemia.

CONCLUSIONS These findings suggested that short-term pretreatment of dADSCs with a mitochondrial ROS scavenger restored their normal functions, which may be an effective strategy for improving the therapeutic effects of ADSC-based therapies in patients with diabetes.

GW30-e0073

Role of (pro)renin receptor and Plc-B3 on cardiac injuries in hypertensive rats

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OBJECTIVES Binding of renin and prorenin to the (pro)renin receptor ((P)RR) increases their enzymatic activity and upregulates the expression of profibrotic genes in vitro. Expression of (P)RR is increased in the heart and kidney of hypertensive and diabetic animals. However, its mechanism in organ damage in the heart remains unclear. To determine whether increased expression of (P)RR is sufficient to induce cardiac injury, we investigated roles of (P)RR and phospholipase C-β3 (PLC-β3) on myocardial injury and myocardial fibrosis, providing a theoretical basis for in-depth understanding of the hypertension pathogenesis.

METHODS Fifty SD rats were randomly divided into five groups (n=10/group). Control: sham operation was done without the aortic ligation; Aortic ligation (AL): abdominal aortic ligation was carried out; U73122 treated (U): AL and PLC-β3 inhibitor, U73122 (40 μg/kg/d) were given; HRP treated (H): AL and (P)RR inhibitor, HRP (4 μg/kg/d) given; Combined group (U+H), AL, U73122 and HRP given as the same doses above. Blood pressure was measured by the tail-cuff method using photoelectric volume oscillometry. Levels of ACE2, Mas, angiotensinogen (AOG), renin, collagen I, collagen III were measured in the heart.

RESULTS Blood pressure significantly rose after aortic ligation surgery. Levels of ACE2 and Mas receptor in the heart was significantly decreased in AL rats than in control (P<0.01). However, ACE2 and Mas in HRP, U and U+H groups increased significantly (P<0.01) following U73122 and HRP administration. AOG and renin levels in AL rats increased significantly (P<0.01). U73122, HRP and the combination treatment lowered AOG and renin expression (P<0.01). In addition, cardiac collagen I and III levels were decreased with U73122 or HRP treatment compared to AL hypertensive rats (P<0.01).

CONCLUSIONS The results showed that aortic ligation led to hypertension. Both U73122 and HRP reduced the activity of renin and AOG and increased expression of protective factors, i.e., cardiac ACE2 and Mas receptor that play an important role in the reduction of risks of hypertension and cardiac injuries. Furthermore, the inhibition of (P)RR and PLC-β3 by HRP and U73122 resulted in a decrease of cardiac collagen I, III levels, and blood pressure as well, demonstrating that activation of (P)RR and PLC-β3 could cause cardiac fibrosis and hypertension in this animal model.

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GW30-e0081

miR-192-5p regulate oxidized LDL induced foam cell formation and atherosclerosis via inhibition of glucagon-like peptide 1 receptor

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OBJECTIVES Atherogenesis initiated by internalization of oxidized low density lipoprotein (ox-LDL) in macrophages via their membrane scavenger receptors that facilitate them transforming into lipid-like foam cells. Recently, glucagon-like peptide-1receptor (GLP-1R) has been shown to mediate this process without fully elucidated mechanism. By bioinformatic prediction, we found GLP-1R is a potential target gene of miR-192-5p, which give the birth to this study that tests their crosstalk in ox-LDL induced atherogenesis.

METHODS Primary human macrophages treated with ox-LDL were transfected with hsa-miR-192-5p mimic or inhibitor to determine the role of miR-192-5p in GLP-1R expression and downstream events. Exendin 9-39, a competitive antagonist of GLP-1R, was used to confirm the effect of GLP-1R in miR-192-5p regulated pathway. Luciferase assay was used to verify direct target gene of miR-192-5p. Gain and loss experiments were used to prove the effect of miR-192-5p in atherosclerotic mouse model.

RESULTS miR-192-5p mimic decreased GLP-1R and increasedLectin-like ox-LDL receptor-1 (LOX-1) and CD36 expression, as well as ROS production and foam cell formation, while its inhibitor showed the opposite effects. Exendin 9-39 almost completely reversed the effect of miR-192-5p inhibitor. Luciferase assay verified that 3′ UTR region of GLP-1R mRNA is a direct target of miR-192-5p. Ablation of miR-192-5p in ApoE−/− mice fed high fat diet increased GLP-1R expression and decreased CD36 and LOX-1 expressions and lipid accumulation in aorta.

CONCLUSIONS Ox-LDL induces foam cell formation by upregulating miR-192-5p that inhibits GLP-1R expression. These findings help to understand the mechanism of atherogenesis.

GW30-e0087

Non-lethal sonodynamic therapy facilitates the M1-to-M2 transition in advanced atherosclerotic plaques via activating AMPK–mTORC1–autophagy pathway

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OBJECTIVES Emerging evidence indicates that macrophage functional polarization is critically involved in the development of atherosclerosis (AS). Herein we sought to examine the role of 5-Aminolaevulinic acid (ALA)-mediated non-lethal sonodynamic therapy (NL-SDT) in macrophage subset polarization and atherosclerotic lesion stability, and explore the potential underlying mechanism.

METHODS Mouse primary bone marrow (BM) derived cells were differentiated into macrophages using granulocyte macrophage colony stimulating factor *in vitro*. Macrophages were then polarized into proinflammatory M1 cells by interferon-γ and lipopolysaccharide. Western blot assay, transmission electron microscopy and GFP-LC3 transfection were used to detect the induction of autophagy by NL-SDT. Levels of intracellular reactive oxygen species (ROS) following NL-SDT were evaluated by staining with the fluorescent probe CellROX® Green Reagent. We performed semi-quantitative detection

of 18 phosphorylated mouse proteins to investigate the molecular mechanism underlying NL-SDT induction of autophagy. Western blot, flow cytometry, arginase assay and ELISA were done to examine the effects of NL-SDT on macrophage polarization. Oil red O staining, cholesterol/cholesteryl ester quantitation assay, RT-PCR and cholesterol efflux fluorometric assay were carried out to determine the effects of cholesterol efflux induced by NL-SDT. We utilized NL-SDT on Western diet-fed *apoE*$^{-/-}$ mice *in vivo*. Hematoxylin and eosin staining and TUNEL assays were performed to evaluate the atherosclerotic plaque size and apoptosis within the atheroma. Histopathology was used to determine percentages of lipid, collagen, macrophages and smooth muscle cells. The macrophage-subset cell numbers within the atheroma were detected by immunofluorescent staining and flow cytometry. To explore the mechanisms of NL-SDT stabilizing atherosclerotic plaques, mice were pretreated with specific pharmacological inhibitors.

RESULTS Using Western diet-fed *apoE*$^{-/-}$ mouse and chimeric $EGFP_{BM}$ *apoE*$^{-/-}$ mouse models, we demonstrated that NL-SDT promoted phenotypic switching of both BM-derived and resident macrophages from M1 to M2 and significantly inhibited the progression of AS. Further mechanistic studies indicated that NL-SDT enhanced macrophage differentiation toward the M2 phenotype by activating the ROS–5′ AMP-activated protein kinase (AMPK)α–mammalian target of rapamycin complex 1 (mTORC1)–autophagy signaling pathway in murine BM-derived M1 macrophages (BMDM1s). Moreover, NL-SDT treatment drastically reduced the lipid droplets, mainly due to the promotion of HDL-mediated cholesterol efflux *in vitro*. Specifically, application of pharmacological inhibitors in animal model had reciprocal effect on macrophage polarization induced by NL-SDT.

CONCLUSIONS These findings highlight that NL-SDT treatment engages a virtuous cycle that enhances M1-to-M2 polarization, cholesterol efflux and anti-inflammatory reactions in advanced plaque *in vivo* and in BMDM1s *in vitro* via activating AMPK–mTORC1–autophagy pathway, a fundamental discovery that might help elucidate the mechanism underlying NL-SDT as a potential treatment to prevent atherothrombotic events.

GW30-e0089

Tetrahydroxystilbene glucoside ameliorates H9c2 cardiomyocytes from doxorubicin-induced toxicity through activation of SIRT1 and AMPK pathway

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OBJECTIVES Doxorubicin (DOX) is an effective anticancer drug, however its clinical application is limited due to its cardiotoxicity. Therefore, identification of effective agents against DOX-induced cardiotoxicity is of critical importance. Tetrahydroxystilbene glucoside (TSG) is extracted from a famous Chinese herbal medicine which is widely used as an antiaging agent in history. This study aimed to determine the beneficial role of TSG in DOX-induced cardiotoxicity in vitro and explored the underlying mechanisms.

METHODS H9c2 cardiomyocytes were pretreated with different concentrations (50, 100 and 200 μM) of TSG prior to DOX exposure. Levels of superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), glutathione (GSH), matrix metalloproteinase (MMP), lactic dehydrogenase (LDH) and caspase-3 were measured by ELISA method, the protein expression of NF-κB, silent mating type information regulation 2 homolog 1 (SIRT1) and adenosine monophosphate-activated protein kinase(AMPK)were detected by Western blot. The mRNA expressions of NADPH oxidase isoforms p^{67phox}, p^{22phox}, and p^{91phox} were detected by qPCR.

RESULTS TSG pretreatment increased cell viability, SOD, catalase, and GPx activities, GSH levels, MMP and the GSH/GSSG ratio; decreased LDH and caspase-3 activities, MDA and ROS levels, mPTP opening and the percentage of apoptotic cells. TSG pretreatment also blunted the mRNA expression of NADPH oxidase isoforms p^{67phox}, p^{22phox}, and p^{91phox}, and abated oxidative stress. TSG pretreatment dramatically restored the decrease of SIRT1, AMPKα and pAMPKα protein expression in doxorubicin-induced cardiotoxicity.

CONCLUSIONS The results showed that TSG pretreatment significantly increased cell viability, inhibited LDH release, and suppressed cell apoptosis induced by DOX. Additionally, TSG pretreatment attenuated the loss of mitochondrial membrane potential and cytochrome c release. These findings also indicate that the protective mechanisms of TSG against doxorubicin-induced cardiotoxicity are involved in the alleviation of energy metabolism.

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GW30-e0096

Apigenin inhibits pyroptosis in macrophages through suppressing AMPK pathway

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OBJECTIVES Atherosclerosis (AS) is considered to be a major underlying cause of cardiovascular disease and a leading cause of cardiac death in developing countries. In addition to a metabolic disease, AS is a complex, long lasting and continuously evolving inflammatory disease characterized by remodeling of the arteries. Cell death and inflammation are inextricably linked with their effectors modulating the process of AS. Pyroptosis is a novel programmed death which is characterized by the formation of inflammasome. And NLRP3 inflammasomes are the most classical and widely studied among numerous forms of inflammasomes. It has been proved that pyroptosis can accelerate progression of AS through promoting the release of inflammatory cytokines such as IL-1β and IL-18. Macrophages are the major inflammatory cells in all stages of AS. The different functional attributes of macrophages influence the initiation of lesions, their progression to advanced atheromata, their complication, and their responses to therapies. What's more, the NLRP3 inflammasomes are highly expressed in macrophages in atherosclerotic plaque. Thus inhibition of pyroptosis in macrophages can be a potential therapy for AS. Apigenin (API) is a natural flavonoid compound and exist in various vegetables, fruits and medicinal plants extensively. Its antioxidant, anticancer and anti-inflammatory effects have been widely studied, and studies have shown that API has anti-atherosclerosis function via up-regulating cholesterol efflux. However, its effects and mechanisms on the pyroptosis in macrophages are still unclear. The purpose of this study was to explore the effects of API on the pyroptosis in macrophages, and discuss the possible mechanisms of it.

METHODS THP-1 was induced into macrophage by treating with 0.5 nM PMA. The cells were divided into the following five groups: control group, LPS+ATP group, 10 nM, 20 nM, and 50 nM API pretreatment group. The solvent or 10 nM, 20 nM, 50 nM API were used as pretreatments before inducing macrophages pyroptosis. One solvent group was used as control group, and the other groups were conducted with lipopolysaccharide (LPS) and ATP to induce pyroptosis. The Apoptosis and Necrosis Assay Kit and fluorescence microscope were used to detect the rate of cell pyroptosis. RT-PCR was conducted to measure the expression levels of NLRP3, Caspase-1, and IL-1β. Western blot was used to evaluate the protein expression of NLRP3, Caspase-1, IL-1β, and AMPK.

RESULTS Compared with LPS+ATP group, API at the concentrations of 10 nM, 20 nM and 50 nM significantly decreased the cell pyroptosis rate ($P<0.05$). The mRNA expression levels of NLRP3, Caspase-1, and IL-1β in API pretreatment groups are lower than control and LPS+ATP group in a concentration-dependent manner ($P<0.001$). The expression levels of key regulatory proteins in cell pyroptosis, including NLRP3 and caspase-1, were obviously lower in API pretreatment groups than LPS+ATP group, especially in 20 nM, and 50 nM API pretreatment groups ($P<0.05$). As a substrate of caspase-1 and a most used imflammatory marker for pyroptosis, API pretreatment reduced the protein expression of IL-1β ($P<0.05$). And the protein expression of AMPK shown the same trend with Caspase-1 ($P<0.05$).

CONCLUSIONS API can inhibit the pyroptosis in macrophages and this effect can be achieved by regulating AMPK signaling pathways. Furthermore, using API to inhibit pyroptosis in macrophages may be a potential therapy for slowing the initiation and progression of AS.

GW30-e0106

Curcumin alleviates atherogenesis via immunomodulatory effect on macrophage polarization

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OBJECTIVES Curcumin is a natural polyphenol with a variety of properties. The aim of our study was to investigate whether curcumin could mitigate the atherosclerosis pathogenesis and explore its immunomodulatory effect on macrophage phenotype together with the underlying molecular mechanisms.

METHODS The apolipoprotein E deficient (ApoE$^{-/-}$) mice were employed to establish atherosclerosis model, alone or combined with curcumin treatment. The aortas were isolated for histological evaluation and gene expression analysis. The RAW 264.7 cells were polarized to M1 cells by lipopolysaccharide (LPS) and treated with different curcumin concentrations. Quantitative real-time polymerase chain reaction (PCR) and Western blot analysis were carried out to examine the effect of curcumin on inflammatory response and the Toll-like receptor 4 (TLR4)-mitogen-activated protein kinases (MAPKs)/nuclear factor (NF)-κB pathway in macrophage.

RESULTS Curcumin significantly alleviated atherosclerotic burden and enhanced plaque stability in experimental AS model. Also, curcumin was capable to suppress M1 phenotype and promote M2 macrophage *in vivo*. Furthermore, the *in vitro* experiment showed that curcumin inhibited the gene expression of pro-inflammatory cytokines TNF-α and IL-6, as well as the phosphorylation of p38, ERK1/2, JNK1/2, IKK, IKBα and p65. With the assistance of specific inhibitors, TLR4-MAPK/NF-κB was verified to be involved in M1 polarization and inflammatory response.

CONCLUSIONS Our findings suggested the anti-atherogenic effect of curcumin could, at least in part, derive from polarizing pro-atherogenic M1 macrophages to repressive M2 phenotypes. These actions may be attributed to the inhibition of TLR4-MAPK/NF-κB signaling pathway. These results may shed some light on the atheroprotective mechanism of curcumin and exhibit the potential of curcumin as a therapeutic approach for the prevention and treatment of AS.

GW30-e0115

Adropin protects against atherosclerosis by regulating endothelial-mesenchymal transition via TGF-β/Smad2/3 signaling pathway

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OBJECTIVES Endothelial-mesenchymal transition (EndMT) was significant for atherosclerosis (AS). Adropin exerts direct effects on the endothelium. This study aims to explore whether adropin can alleviate AS and its molecular mechanism.

METHODS Apolipoprotein E knockout ($ApoE^{-/-}$) mice were fed with high fat for 13 weeks to establish AS mode. $ApoE^{-/-}$ mice were divided in three groups: (i) Normal dieting group; ii) High fat dieting group; iii) High fat dieting+Adropin group: adropin (105 μg/kg×d) was injected intraperitoneally in mice for 13 weeks. We also established EndMT by inducing human umbilical vein endothelial cells (HUVECs) with hydrogen peroxide (H_2O_2) *in vitro* cell culture models. Cells were divided into four groups: i) Control group; ii) H_2O_2 group; iii) H_2O_2+Adropin group; iv) H_2O_2+Adropin+TGF-β plasmid group. Oil red O staining was used to detect the lipid area in AS plaque and HE staining to determine the plaque area in mice. The number of spindle cells transformed from stroma was counted on day 0, 2, 4 and 6 of cell culture. The relative expressions of TGF-β1, TGF-β2, TGF-βR, CD31, VE-cadherin, α-SMA, SM22α, phosphor-Smad2/3 and FSP-1 mRNA were measured by Western-Blot and (or) RT-PCR. The expression of α-SMA and CD31 were also measured by immunofluorescence. Serum total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and triglyceride (TG) were detected by automatic biochemical analysis.

RESULTS *In vivo* animal model, adropin reduced the incidence of AS, inhibited lipid accumulation in atheroselerotic plaque (P<0.05), increased the expression of CD31 and VE-cadherin (P<0.05), and decreased the expression of α-SMA and FSP-1 (P<0.05). The external supplementation of adropin decreased the expression of Adropin (P<0.05). However, adropin did not decrease serum TC, LDL-C, HDL-C, TG levels and body weight. In the experiment of HUVECs *in vitro*, adropin inhibited the morphological changes of endothelial cells and the expression of α-SMA (most obvious on day 6). The expression of CD31, VE-cadherin, α-SMA and SM22α were consistent with those *in vivo* animal experiment. Adropin decreased the expression of TGF-β1 and TGF-β2 (P<0.05), and inhibited the phosphorylation of Smad2/3 which is the downstream signal protein of TGF-β (P<0.05). Transfection of TGF-β plasmid inhibited the effect of adropin on reducing EndMT and inhibiting the TGF-β/Smad2/3 signaling pathway.

CONCLUSIONS Adropin can alleviate AS in $ApoE^{-/-}$ mice that is likely mediated via inhibiting EndMT through TGF-β/Smad2/3 signaling pathway. Adropin represents a novel target to limit AS not directly by regulating lipid levels.

GW30-e0126

Enhancement of high-density lipoproteins quantity and quality to treat dyslipidemia and hypertension by policosanol

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OBJECTIVES Metabolic syndrome is closely associated with higher risk of hypertension, cardiovascular disease, diabetes and stroke. It has been reported that Cuban policosanol improves lipid parameters and HDL functionality in human participants. The aim of the present study was to investigate the long-term effects of policosanol supplementation on blood pressure (BP) and the lipid profile in healthy Korean participants with pre-hypertension.

METHODS This randomized, double-blinded, and placebo-controlled trial included 84 healthy participants who were randomly assigned to three groups receiving 10 mg of policosanol, 20 mg of policosanol, or placebo upto 24 weeks.

RESULTS The BP, lipid profile, and anthropometric factors were measured pre- and post-intervention and then compared. Based on an average of three measurements of brachial BP, the policosanol 20 mg group showed the most significant reduction in average systolic BP (SBP) from 138±12 mmHg at week 0–126±13 mmHg at week 24 (P<0.0001). The policosanol 10 mg group showed a 4% reduction in SBP from 135 mmHg at week 0–128 mmHg at week 24 (P=0.016), whereas the placebo group showed no change in BP between weeks 0 and 24. The policosanol consumption for 12 weeks, the policosanol 20 mg group exhibited the most significant reduction of BP, up to 7.7% reduction of average systolic BP (SBP) from 136.3±6.1 mmHg (week 0) to 125.8±8.7 mmHg (P><0.001). Between group comparisons using repeated measures ANOVA analysis showed that the policosanol 20 mg group had a significant reduction of SBP (P=0.020) and a reduction of DBP (P=0.035). The policosanol 10 mg and 20 mg groups showed significant reductions in aortic SBP of 7.4 and 8.3%, respectively. The policosanol groups showed significant reductions of total cholesterol (TC) of 9.6 and 8.6% for 10 mg and 20 mg of policosanol, respectively. Lipoprotein functionality improved by policosanol to be more anti-atherogenic; LDL showed more anti-oxidant while HDL showed more anti-glycation properties.

CONCLUSIONS Consumption of policosanol resulted in significant reductions of peripheral SBP and DBP, aortic SBP and DBP, and mean arterial pressure (MAP) and serum TC and LDL-C with elevation of %HDL-C.

GW30-e0135

The mobilization of splenic reservoir myeloid-derived suppressor cells in sepsis-induced myocardial injury

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OBJECTIVES Myeloid-derived suppressor cells (MDSCs) play key roles in sepsis, but whether bone marrow is considered the only source remains unclear. The current knowledge about the mechanism of MDSCs leading to myocardial injury in sepsis is poor. The aim of this study is to determine the role of splenic MDSCs in sepsis induced myocardial injury.

METHODS In sepsis patients with cardiac dysfunction, the circulating percentage of $CD14^{-}CD11b^{+}$ and serum concentrations of IL-6 and IL-1β were measured. A mouse sepsis model was established through caecum ligation and puncture (CLP). Animals were divided into four groups: control, sham, CLP and CLP+splenectomy (CLPS). Plasma concentrations of IL-6, IL-1β, TnI and NT-proBNP were measured. $CD11b^{+}Gr\text{-}1^{+}$ cells were detected by immunofluorescence staining and RT-PCR. Myocardial injury was detected by HE, Masson and TUNEL staining. The expression of mTOR, P53 and caspase-3 was measured by Western blot.

RESULTS In sepsis patients, circulating MDSCs were increased, and the plasma concentrations of IL-6 and IL-1β were elevated. The plasma concentrations of IL-6 and IL-1β were correlated with the ratio of circulating MDSCs. In the mouse sepsis model, the spleen was the major source of $CD11b^{+}Gr\text{-}1^{+}$ cells that migrated into circulation and the heart in sepsis. Echocardiography and serum biomarkers showed that cardiomyocyte damage and cardiac hypofunction in sepsis induced myocardial injury. The expression of CD11b, Gr-1 and pro-inflammatory cytokines in the heart was significantly higher in sepsis patients than that in controls. Pathological staining and TUNEL staining showed obvious myocardial damage and cell apoptosis. The Western blot analysis indicated that in the heart, the activation of mTOR was inhibited and that the expression of P53 and caspase-3 was elevated in sepsis-induced myocardial injury.

CONCLUSIONS In sepsis-induced myocardial injury, splenic reservoir $CD11b^{+}Gr\text{-}1^{+}$ cells rapidly migrated into circulation and the heart, further impairing heart function via the high expression of P53 through the inhibition of mTOR.

GW30-e0142

Comprehensive metabolic profiling reveals metabolic dysregulation and identifies potential biomarkers in early stage ischemic heart failure patients

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OBJECTIVES Heart failure (HF) is associated with profound changes in cardiac metabolism. Coronary ischemia is one of the leading cause for heart failure. Yet few studies have discussed metabolic alterations in different stages of heart failure based on global metabolomics profile. In this study, by measuring serum metabolic profile in discovery and validation cohorts, we aim to characterize the metabolic profile and identifies potential biomarkers in heart failure patients at different stages.

METHODS Consecutive patients admitted to hospital for ischemic HF were enrolled in the discovery phase and validation phase. Demographic and biochemical measurements were performed afterwards. Serum samples were obtained after overnight fasting, and coronary angiography was performed afterwards to confirm the diagnosis. Nontargeted metabolomics was applied to demonstrate global metabolic profile in control and different levels of heart failure patients.

RESULTS We have found significant alteration of amino acids and free fatty acids levels, which exhibited prognostic value for severe ischemic HF. Besides, serum amino acids began to change during early stage HF, identified as potential biomarkers for early stage HF. Pathway analyses further shed light on factors underlying amino acids metabolism. Serum amino acid profile exhibited differential correlation pattern to clinical factors in HF patients as compared to control. The dysregulated amino acids profile and enriched pathways were further validated in the secondary cohort.

CONCLUSIONS Using non-targeted metabolic profiling in cohorts based on HF levels, we have successfully identified a group of circulating metabolites that were significantly altered in early stage and late stage HF. The amino acid metabolic signatures shed light on potential new biomarkers and therapeutics for preventing and treating HF.

GW30-e0149

A comprehensive bioinformatics analysis on multiple gene expression omnibus datasets of young-aged coronary heart disease

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OBJECTIVES Try to find out the mechanism leading to the prevalence of YA-CHD through comparing differentially expressed genes (DEGs) among YA-CHD patients and healthy young aged adults, and further investigate the differences through gene oncology analysis (GO analysis), KEGG pathway analysis, protein-protein interaction network analysis (PPI network analysis) and the interaction between important modules.

METHODS Dataset GSE 12288 from Gene Expression Omnibus was imported and performed comprehensive bioinformatics analysis, including gene ontology analysis (GO analysis), pathway analysis, protein-protein interaction network analysis and core network analysis.

RESULTS RAP1A, which regulates platelet integrin activation and has a critical role in platelet production, was significantly up regulated, while TNKS2, which keeps the integrity of the leukocyte telomere structure and shows a significant association with longevity, was significantly downregulated. Biological process analysis showed "phagosome" pathway was mostly significant related to YA-CHD. Innate immune response module and type I interferon signaling module, interacts with IRF1, may major in the regulation of YA-CHD progression and maybe the potential therapeutic target of YA-CHD.

CONCLUSIONS RAP1A and TNKS2 may serve as novel biomarkers in predicting the onset of YA-CHD. Further studies about weather IRF1 influence YA-CHD through regulating innate immune type I interferon signaling pathway was needed.

GW30-e0154

Lack of significant elevation of VE-cadherin-positive endothelial microparticles in cardiac syndrome X

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OBJECTIVES Endothelial microparticles (EMPs), membrane-shed vesicles that are generated from the endothelial cells surface in response to cellular dysfunction and/or damage, has been showed that can be involved in inflammatory process, blood coagulation and endothelial dysfunction. In addition, studies suggest that microvascular coronary dysfunction plays a crucial role in cardiac syndrome X (CSX). The objective of this study was to evaluate the EMP levels in patients with CSX and normal subjects.

METHODS CSX patients (n=40) A were selected from individuals who referred to Department of Cardiology, UMSU, Urmia. Control group (n=19) were selected from healthy subjects without any disease related to endothelial dysfunction. They were matched according gender and BMI. We measured the level of VE-Cadherin by flowcytometery using CD144 monoclonal antibody in the peripheral blood of patients and control subjects.

RESULTS CD144 endothelial microparticles count were 30.79±19.01 counts/μL in CSX patients versus 26.92±11.98 counts/μL in healthy control subjects, P=0.51. CD144 endothelial microparticles percent were 2.13±1.64% in CSX patients versus 1.32±0.93% in healthy control subjects, P=0.10.

CONCLUSIONS Findings indicate that VE-Cadherin CD144 EMP levels increase in CSX patients but VE-Cadherin levels in CSX patients were not significantly higher than healthy control subjects. Endothelial and microparticles may increase risk of thrombosis in CSX.

GW30-e0157

Leptin increases mitochondrial OPA1 via GSK3-mediated OMA1 ubiquitination to enhance therapeutic effects of mesenchymal stem cell transplantation

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OBJECTIVES Accumulating evidence revealed that mesenchymal stem cells (MSCs) confer cardioprotection against myocardial infarction (MI). However, the poor survival and engraftment rate of the transplanted cells limited their therapeutic efficacy in the heart. The enhanced leptin production associated with hypoxia preconditioning contributed to the improved MSCs survival. Mitochondrial integrity determines the cellular fate. Thus, we aimed to investigate whether leptin can enhance mitochondrial integrity of human MSCs (hMSCs) to protect against various stress.

METHODS In vivo, we constructed MI-mouse model and transplantated the leptin-overexpressing hMSCs into the infarcted heart to analyze hMSCs survival and cardiac function. In vitro, we exposed leptin pretreated hMSCs into glucose and serum deprivation under hypoxia (GSDH) stress for an additional 24 h. We detected the mitochondrial microstructure, function and the proteins related to mitochondrial homeostasis.

RESULTS In vivo, transplantation of leptin-overexpressing hMSCs into the infarcted heart resulted in improved cell viability, leading to enhanced angiogenesis and cardiac function. In vitro, pretreatment of hMSCs with recombinant leptin (hMSCs-Leppre) displayed improved cell survival against severe ischemic condition (glucose and serum deprivation under hypoxia), which was associated with increased mitochondrial fusion. Subsequently, Optic atrophy 1 (OPA1), a mitochondrial inner membrane protein that regulates fusion and cristae structure, was significantly elevated in the hMSCs-Leppre group, and the protection of leptin was abrogated by targeting OPA1 with a selective siRNA. Furthermore, OMA1, a mitochondrial protease that cleaves OPA1, decreased in a leptin-dependent manner. Pretreatment of cells with an inhibitor of the proteasome (MG132) prevented leptin-induced OMA1 degradation, implicating the ubiquitination/proteasome system as a part of the protective leptin pathway. In addition, GSK3 inhibitor (SB216763) was also involved in the degradation of OMA1.

CONCLUSIONS In conclusion, in the hostile microenvironment caused by MI, (a) leptin can maintain the mitochondrial integrity and prolong the survival of

hMSCs; (b) leptin-mediated mitochondrial integrity requires phosphorylation of GSK3 as a prerequisite for ubiquitination-depended degradation of OMA1 and attenuation of longOPA1 cleavage. Thus, leptin targeting the GSK3/OMA1/OPA1 signaling pathway can optimize hMSCs therapy for cardiovascular diseases such as MI.

GW30-e0158

Association of CMTM5 Gene expression with the risk of in-stent restenosis in patients with Coronary Artery Disease after drug-eluting stent implantation and the effects and mechanism of CMTM5-stimulated Genes on Human Vascular endothelial proliferation and migration

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OBJECTIVES Although anti-platelet drugs are widely used in clinic, there still exist a small proportion of coronary artery disease (CAD) patients with drug-eluting stent implantation who during regular drug therapy experienced cardiocvascular events, some of them experience in-stent restenosis (ISR). In our study, we try to elucidate the correlation between CMTM5 gene and the risk of ISR, detected the effects and mechanisms of CMTM5-stimulated genes on human vascular endothelial proliferation and migration.

METHODS A total of 131 CAD patients with drug-eluting stent implantation were enrolled in this study, with a mean 36 months' follow up, 39 patients occurred in-stent restenosis event. *CMTM5* gene expression was detected by RT-PCR. DNA methylation levels on *CMTM5* promoter were tested by the bisulfate pyrosequencing technology. Serum CMTM5 level was assessedby Elisa kit. HUVEC were infected by CMTM5 overexpression adenovirus and RNA interference lentivirus. Scrape injury analysis and Transwell migration model were used to investigate effects of *CMTM5* on ECs migration, while cell counting, MTT, Brdu and flow cytometry were performed to detect the ECs proliferation in different groups. Expression of signaling pathway proteins PI3K, p-Akt and CycD1 were detected through immunoblotting in all groups.

RESULTS Low *CMTM5* gene expression and serum CMTM5 level associated with increased restenosis risk in a cohort of 306 patients undergoing coronary angioplasty and stent placement (P<0.05). What's more, high methylation ratio in *CMTM5* promoter was inversely correlated with low expression of *CMTM5*. Overexpression of *CMTM5* attenuated ECs migration and proliferation. a. The scrape injury assay and Transwell migration model suggested that *CMTM5* overexpression attenuated but its suppression promoted migration of ECs compared to the normal and EO-MOCK groups. b. The cell count, MTT, and Flow cytometry assay results showed that proliferation of ECs was attenuated in *CMTM5* overexpression group and enhanced in the *CMTM5* suppression group. Western blot results suggested that protein expressions of PI3K/p-Akt signal pathway decreased in the *CMTM5* overexpression group and increased in *CMTM5* suppression group. Transwell migration model showed that *CMTM5* suppression promoted ECs migration through the PI3K/Akt signal transduction pathway. Flow cytometry indicated that PI3K/Akt signal pathways were involved in the regulation of proliferation of ECs.

CONCLUSIONS The evidence from our study indicates that CMTM5 might be a new biomarker in assessing aspirin clinical efficacy and low *CMTM5* promoter methylation may bring new hints to elaborate the pathogenesis of in-stent restenosis. *CMTM5* suppression facilitates migration and proliferation of ECs through PI3K/Akt signal pathway and contributes to the maintenance of vascular homeostasis. This may provide a promising approach for the prevention and treatment of ISR and late stent thrombosis after PCI.

GW30-e0162

TLR7 attenuates sepsis-induced myocardial dysfunction through enhancing PKC in the sarcoplasmic/endoplasmic reticulum

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OBJECTIVES Our study aimed to determine whether TLR7 is involved in sepsis-induced myocardial dysfunction (SIMD) and, if so, to investigate the underlying molecular mechanisms.

METHODS C57/BL mice (WT) and TLR7–/– mice were subjected to 20 mg/kg lipopolysaccharide (LPS) challenge for 6 h, 12 h, 24 h and 48 h to induce septic cardiomyopathy. Cardiac function was evaluated by echocardiography and hemodynamic. Calcium transients and calcium sparks elicited by electrical stimulation in cardiomyocytes isolated from the indicated mice were observed with confocal microscope. Furthermore, we gathered hearts to detect expression of calcium transients related proteins by Western blot and RT-qPCR. In addition, the hearts were harvested to test the SERCA2a activity and evaluated by HE, Immunohistochemistry and immunofluorescence. To explore the mechanism, WT (Wild-type littermates) mice and cardiac-specific TLR7-transgenic (TLR7-cTG) mice were subjected to PKC specific inhibitor (Go6983) administration for 2 weeks before LPS treatment. Calcium transients and related proteins were evaluated as mentioned above. In the end, we verified the role and mechanisms of TLR7 in septic cardiomyocyte injury by using Ad-GFP-TLR7 and TLR7 siRNA in Neonatal rat cardiomyocyte.

RESULTS After 10 days of intraperitoneal injection of LPS, the total mortality of TLR7 KO mice was 26.4% higher than that of WT mice. Echocardiography and hemodynamic parameters showed that the cardiac function of TLR7–/– mice was significantly deteriorated. The CD68 immunohistochemistry and TUNEL staining showed that inflammatory and apoptosis were enhanced in the TLR7 KO group and the WT group within 24 hours, but there was no difference between the two groups, which was consistent with the results of Western and RT-PCR. Calcium spark and calcium transient detection in cardiomyocytes showed that TLR7 KO mice had the reduced calcium transient amplitude, prolonged time of Ca2+ uptake and the decreased SERCA2a activity, without changing calcium sparks. At the mechanistic level, PKC immunofluorescence staining showed that the expression of PKC in the sarcoplasmic/endoplasmic reticulum was significantly downregulated in TLR7 KO group. Western and qPCR results showed that the expression of PKC, p-PLB (Ser16) was downregulated while the level of PLB was up-regulated. Meanwhile, the expression level of SERCA2a and RyR2 did not change. Therefore, we hypothesized that TLR7 can attenuate LPS-induced sepsis myocardial dysfunction by increasing the recruitment of PKC in the sarcoplasmic reticulum, up-regulating the level of p-PLB (Ser16), increasing the Ca2+-transporting activity of SERCA2a, and maintaining calcium homeostasis in SIMD. In addition, the mice in TLR7-cTg group attenuated LPS-induced sepsis cardiomyopathy, but the cardioprotective effect of TLR7 was abolished after administration of the tail vein PKC-specific inhibitor. Moreover, the utilization of Ad-GFP-TLR7 overexpressing TLR7 in neonatal rat cardiomyocytes alleviated the Calcium homeostasis imbalance and cardiomyocyte injury induced by LPS, while TLR7 siRNA treament has the opposite effect.

CONCLUSIONS TLR7 deficiency aggravates LPS-induced cardiac dysfunction. However, TLR7 overexpression can attenuate LPS-induced cardiac function by enhancing PKC and increasing the Ca2+-transporting activity of SERCA2a in the sarcoplasmic/endoplasmic reticulum. Therefore, retaining the expression of TLR7 may be a potential therapeutic strategy for sepsis-induced myocardial dysfunction (SIMD).

GW30-e0171

Alagebrium targets the miR-27b/TSP-1 signaling pathway to rescue Nε-carboxymethyl-lysine-induced endothelial dysfunction

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OBJECTIVES Nε-carboxymethyl-lysine (CML), a major isoform of advanced glycation end products (AGEs), plays a crucial role in the functional damage of diabetes mellitus. However, it is not clear whether ALT-711 (alagebrium), an inhibitor of AGEs, is capable to rescue CML-induced poor angiogenesis, as well as the underlying mechanism. Here, we tested the hypothesis that alagebrium improves the angiogenic function damage induced by CML via miR-27b/anti-angiogenic protein thrombospondin-1 (TSP-1) signaling.

METHODS Male diabetic mice and normal mice with critical hindlimb ischemia were performed to investigate the impaired angiogenesis in diabetes mellitus and whether miR-27b/TSP-1 signaling is involved in the pathology of it. Then, we used the commercial products CML-BSA and alagebrium on human umbilical cord-derived endothelial cells (HUVECs), in combination with the miR-27b mimic/inhibitor and TSP-1 over-expression plasmids, to determine the effects of alagebrium and miR-27b/TSP-1 on angiogenesis in vitro.

RESULTS Compared with control mice, lower blood flow recovery and less capillary density were appeared in the ischemic lower limb of diabetic mice with the decreased vascular endothelial growth factor (VEGF) and miR-27b expression, whereas the increased TSP-1 expression. Likewise, the tube formation ability of HUVECs in CML-BSA was impaired, which is followed by down-regulated VEGF and miR-27b expression and the up-regulated TSP-1 expression. The trend was reversed by alagebrium, not only on tube network formation, but also on expression of VEGF, miR-27b and TSP-1. MiR-27b mimic contributed to promoted tube formation and positive regulation of VEGF, while decreased TSP-1 expression. And these effects of miR-27b mimic were all abolished when TSP-1 was overexpressed. In addition, miR-27b silencing suppressed the tube formation promotion and VEGF expression improvement induced by alagebrium under CML-BSA treatment, inversely, augmented TSP-1 expression.

CONCLUSIONS These novel findings illustrated that CML exposure severely impairs functional angiogenesis of HUVECs and AGEs inhibitor rescued the damage via miR-27b/TSP-1 signaling cascades, which will provide some new therapeutic strategies to diabetic patients with critical limb ischemia.

GW30-e0172

Distinct roles of myofibroblast-specific Smad2 and Smad3 signaling in repair and remodeling of the infarcted heart

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OBJECTIVES TGF-bs regulate fibroblast responses, by activating Smad2 or Smad3 signaling, or via Smad-independent pathways. We have previously demonstrated that fibroblast-specific Smad3 is critically implicated in repair of the infarcted heart. However, the role of fibroblast Smad2 in myocardial infarction remains unknown. This study investigates the role of fibroblast-specific Smad2 signaling in myocardial infarction, and explores the mechanisms responsible for the distinct effects of Smad2 and Smad3.

METHODS In a mouse model of myocardial infarction, Smad2 activation in infarct myofibroblasts peaked 7 days after coronary occlusion. In vitro, TGF-b1, -b2 and b3, but not angiotensin 2 and bone morphogenetic proteins-2, -4 and -7, activated fibroblast Smad2. Myofibroblast-specific Smad2 and Smad3 knockout mice (FS2KO, FS3KO) and corresponding control littermates underwent non-reperfused infarction.

RESULTS In contrast to the increase in rupture rates and adverse remodeling in FS3KO mice, FS2KO animals had mortality comparable to Smad2 fl/fl controls, and exhibited a modest but transient improvement in dysfunction after 7 days of coronary occlusion. At the 28 day timepoint, FS2KO and Smad2 fl/fl mice had comparable adverse remodeling. Although both FS3KO and FS2KO animals had increased myofibroblast density in the infarct, only FS3KO mice exhibited impaired scar organization, associated with perturbed alignment of infarct myofibroblasts. *In vitro*, Smad3 but not Smad2 knockdown downmodulated fibroblast a2 and a5 integrin expression. Moreover, Smad3 knockdown reduced expression of the GTPase RhoA, whereas Smad2 knockdown markedly increased fibroblast RhoA levels. Smad3-dependent integrin expression may be important for fibroblast activation, whereas RhoA may transduce planar cell polarity pathway signals, essential for fibroblast alignment.

CONCLUSIONS Myofibroblast-specific Smad3, but not Smad2 is required for formation of aligned myofibroblast arrays in the infarct. The distinct in vivo effects of myofibroblast Smad2 and Smad3 may involve Smad3-dependent integrin synthesis, and contrasting effects of Smad2 and Smad3 on RhoA expression.

GW30-e0223

GATA-4-expressing mouse bone marrow mesenchymal stem cells improve cardiac function after myocardial infarction via secreted exosomes

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OBJECTIVES This study aimed to investigate whether exosomes secreted by mouse GATA-4-expressing bone marrow mesenchymal stem cells (BMSCs) could induce BMSC differentiation into myocyte precursors, decrease cardiomyocyte apoptosis, and improve cardiac function following myocardial infarction (MI).

METHODS BMSCs were transduced with a lentivirus carrying a doxycycline (DOX)-inducible GATA-4 or control lentivirus, and secreted exosomes from these BMSCs were collected and co-cultured with BMSCs or cardiomyocytes under hypoxic and serum free conditions. Furthermore, exosomes were injected into mice 48 h after MI. Cardiac function was evaluated by echocardiography at 48, 72, and 96 h after exosome treatment.

RESULTS Quantitative PCR showed that co-culture of BMSCs with GATA-4-BMSC exosomes increased cardiomyocyte-related marker expression. Co-culture of GATA-4-BMSC exosomes with cardiomyocytes in anoxic conditions decreased apoptosis as detected by flow cytometry. Injection of GATA-4-BMSC exosomes in mice 48 h after MI increased cardiac function over the next 96 h; increased cardiac blood vessel density and number of c-kit-positive cells and decreased apoptotic cardiomyocyte cells were also observed. Differential expression of candidate differentiation- and apoptosis-related miRNAs and proteins that may mediate these effects was also identified.

CONCLUSIONS Exosomes isolated from GATA-4-expressing BMSCs induce differentiation of BMSCs into cardiomyocyte-like cells, decrease anoxia-induced cardiomyocyte apoptosis, and improve myocardial function after infarction.

GW30-e0225

Sulfur dioxide maintains the contractile phenotype of vascular smooth muscle cells by promoting the binding of SRF to myocardin

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OBJECTIVES This study aims to explore the regulatory role of SO_2 in vascular smooth muscle cell phenotype transformation and the molecular mechanisms.

METHODS Smooth muscle cells were supplemented with SO_2 donor, and the effects of SO_2 on smooth muscle cell contractile phenotype marker proteins and synthetic phenotypic marker proteins were observed to elucidate the regulation of SO_2 on smooth muscle cell phenotype transformation. By targeting serum response factor/myocardin, the molecular mechanism for SO_2 regulation of smooth muscle cell phenotype transformation was explored.

RESULTS Compared with the control group, the expression of contractile phenotype markers (SMA, SM22α and Smoothelin) was down-regulated and the expression of synthetic phenotypic markers (OPN and PCNA) was up-regulated after the stimulation with PDGF-BB. During this process, the SO_2/AAT pathway was down-regulated, including decreased AAT1 protein expression, decreased AAT activity and decreased SO_2 content. In PDGF-BB-stimulated vascular smooth muscle cells, pre-incubation of SO_2 donor up-regulated the expression of contractile phenotype markers, while the expression of synthetic phenotypic marker molecules was down-regulated, indicating that SO_2 maintained the contractile phenotype of vascular smooth muscle cells. We found that the binding of SRF to myocardin was reduced after vascular smooth muscle cells were stimulated with PDGF-BB, and the pre-incubation with SO_2 increased the binding of SRF to myocardin.

CONCLUSIONS Endogenous SO_2 promotes the expression of contractile phenotype markers in vascular smooth muscle cells by promoting the binding of SRF to myocardin, and maintains the contractile phenotype of vascular smooth muscle cells.

GW30-e0233

MicroRNA-7b attenuates Ischemia/Reperfusion induced H9C2 cardiomyocyte apoptosis via the HIF1a/p-p38 pathway

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OBJECTIVES MicroRNAs (miRNAs) have been shown to play crucial roles in the occurrence, development, and treatment of many cardiovascular diseases. Coronary heart disease (CAD)-related miRNAs are still a growing research area. miR-7b was reported to be downregulated in acute myocardial infarction (AMI) myocardium tissues. However, it remains largely unknown whether miR-7b is involved in the pathogenesis and progression of the AMI ischemia/reperfusion (I/R) injury.

METHODS Male C57BL/6 J mice and H9C2 cells were used as models in this study. Masson staining, real-time polymerase chain reaction, Western blot analysis, and terminal deoxynucleotidyl transferase-mediated dUTP nick-end-labeling immunofluorescence staining assays were performed to detect the related indicators in the study. SPSS 17.0 software was used to calculate the experimental data.

RESULTS The results showed that miR-7b expression is downregulated after I/R in mice, and miR-7b could inhibit apoptosis in I/R-induced H9C2 cells via upregulating hypoxia-inducible factor 1a (HIF1a). The inhibitory effect of miR-7b on I/R-induced apoptosis in H9C2 cells was blocked by HIF1a silencing. In addition, our data suggested that the p-P38 pathway may be involved in the role of miR-7 in I/R-induced H9C2 cell apoptosis.

CONCLUSIONS We confirmed that the overexpression of miR-7b inhibits I/R-induced apoptosis in H9C2 cells by targeting the HIF1a/p-P38 pathway. Our findings not only demonstrate the potential role of miR-7b in attenuating I/R-induced apoptosis but also provide a new insight into the better prevention of the I/R injury by mediating HIF-1 and p-P38.

GW30-e0243

CTRP1 promotes vasodilatory dysfunction by increasing nitric oxide synthase dysfunction through adipo-vascular axis

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OBJECTIVES C1q/TNF-related protein (CTRP) 1 is a newly identified adipokine with identical structural domains of adiponectin but displaying distinct functions. We previously showed that CTRP1 promotes the development of atherosclerosis by increasing vascular inflammation and endothelial dysfunction. We hypothesized that CTRP1 plays a key role in modulating vasodilation through the adipo-vascular axis.

METHODS Vascular dilatory responsiveness was compared by intravital microscopy of cremaster arterioles between obese CTRP1 transgenic (Tg-CTRP1), CTRP1 knockout (CTRP1 KO) and C57 wild type (WT) control mice fed with high-fat diet. Adipose tissue (AT) transplantation was performed to examine the role of CTRP1 on vasodilation via the adipose-vascular axis. The mechanisms by which CTRP1 modulates vasodilation was investigated.

RESULTS We found a marked impairment of endothelium-dependent arteriolar dilation in obese models of Tg-CTRP1 mice, whereas vasodilation

was markedly enhanced in CTRP1 KO mice as compared to WT controls. By performing visceral AT transplantation, we detected that vasodilation was impaired in C57 mice transplanted with AT of Tg-CTRP1 mice but unaffected with that of CTRP1-KO mice. Meanwhile, elevated production of reactive oxygen species (ROS) was detected in the vascular wall of mice transplanted with AT of Tg-CTRP1 animals. In cultured endothelial cells, reduced nitric oxide (NO) bioavailability was observed when incubated with conditioned media of adipocytes or recombinant CTRP1. Furthermore, we found endothelial nitric oxide synthase (eNOS) phosphorylation was inhibited while uncoupling of eNOS dimers was increased by CTPR1 in an arginase-1-dependent pathway. Inhibition of arginase activity by synthetic chemicals markedly improved CTRP1-dependent vasodilatory dysfunction.

CONCLUSIONS These data define the essential role of the AT-derived CTRP1 in mediating vasodilatory dysfunction, as well as propose a novel mechanism that increased arginase activity by CTRP1 leads to eNOS dysfunction, reduced NO biosynthesis and enhanced ROS production.

GW30-e0244

CCDC11 promotes cardiac hypertrophy and dysfunction in response to pressure overload

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OBJECTIVES Mutations in CCDC11, a coiled-coil domain containing protein, are associated with embryonic asymmetry including situs inversus totalis, heterotaxy syndrome, and congenital heart defects. The molecular functions of CCDC11 in adults under different pathophysiological conditions remain totally undetermined. In this study, we sought to investigate the role of CCDC11 in the pathogenesis of adverse cardiac remodeling and dysfunction.

METHODS Animal models of pressure overload-induced cardiac hypertrophy were established either by transverse aortic constriction (TAC) or infusion of angiotensin II through a mini-osmotic pump. Myocardial expression of CCDC11 was enhanced or silenced by intramyocardial injection of adeno-associated virus to delivery CCDC11 short hairpin RNA or complementary DNA, respectively. The role of CCDC11 in cardiac dysfunction and remodeling was then evaluated.

RESULTS Pressure overload resulted in substantially increased expression levels of CCDC11 in mouse myocardium. Immunohistochemistry analysis revealed that increased CCDC1 was abundantly enriched in hypertrophic cardiomyocytes. In isolated mouse adult cardiomyocytes, knockdown of CCDC11 markedly reversed cell enlargement, reorganization of cytoskeleton proteins, oxidative stress, and upregulation of ANP (atrial natriuretic peptide), Col I (collagen type I), Col III (collagen type III), MMP (matrix metalloproteinase)-2 and MMP-9 in response to angiotensin II stimulation. Overexpression of CCDC11 significantly promoted hypertrophic cardiac remodeling and dysfunction, whereas silencing of CCDC11, in turn, remarkably attenuated the development of cardiac hypertrophy, left ventricular dilatation, and dysfunction in pressure overload animal models.

CONCLUSIONS The upregulation of CCDC11 during hypertrophic heart disease facilitates maladaptive cardiac remodeling and left ventricular dysfunction. Pharmacological interventions targeting at CCDC11 may constitute a therapeutic target in the future.

GW30-e0250

Acute local necrosis facilitates electrical conduction in heart

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OBJECTIVES Cardiac necrosis is considered as an electrical barrier that slows the pass by electrical conduction, forming the base of reentry. However, this concept has never been demonstrated in the beating heart.

METHODS We produced a lesion in the left ventricle of rats with absolute ethanol, and the changes of ventricular excitation threshold (VET), ventricular conduction time (VCT) and effective refractory period (ERP) were measured and the arrhythmia score was determined.

RESULTS VET was dramatically reduced after lesion induction. Interestingly, the VCT was shortened along with a shortening of ERP, indicating a facilitation of excitation conduction. With the progressive shortening of pacing interval, the VET and VCT further decreased. A higher arrhythmia score was recorded by induction of ectopic stimulation at the remote peripheral than the boundary of the lesion.

CONCLUSIONS Lesion production did not suppress but rather facilitate impulse induction and propagation in vivo, especially for the ectopic excitations. These alterations facilitate ectopic beats induction and increase the susceptibility to ventricular arrhythmia after cardiac lesion, e.g. myocardial infarction.

GW30-e0252

P21 deletion modulates macrophages differentiation and impair cardiac healing after experimental myocardial infarction

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OBJECTIVES The imbalance resolution of inflammation is the main cause of Adverse remodeling after myocardial infarction (MI). P21 is a central regulator of innate and adaptive immunity, but the role of p21 in MI is unclear. Here, we show that p21 expression increased in heart tissue after MI, and mainly derived from macrophages.

METHODS Induced myocardial infarction using Ligation of the left anterior descending coronary artery. Morphological changes, echocardiographic parameters, histological analyses and markers were used to evaluate cardiac function and healing.

RESULTS P21 deficiency causes less collagen fibril formation in the infarct area which lead to cardiac rupture, characterized by larger LV volumes, worse LV dysfunction, and a worse ejection fraction. P21 deletion decreased expression of M2 macrophage markers, impaired resolution of infarct healing. The overexpression of p21 promotes the transformation of M2 macrophages and fibroblast activation. Depleted of macrophages were unable to further increase LV dysfunction and cardiac rupture in p21 knockout mice. Furthermore, an external supply of macrophages, infected by adenoviral to overexpress constitutively p21, was able to improve catastrophic prognosis in mice post-MI.

CONCLUSIONS We define p21 as an essential molecular switch leading to M2 macrophage activation in post-MI, suggesting that p21 may represent a therapeutic target for the prevention of cardiac rupture after MI.

GW30-e0253

Metabolic reprogramming induces cardiomyocyte proliferation and repair of heart injury

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OBJECTIVES The neonatal mammalian heart has a remarkable regenerative capacity, while the adult heart is difficult to regenerate. A metabolic reprogramming from glycolysis to fatty acid oxidation occurs along with the loss of cardiomyocyte proliferation capacity shortly after birth. In this study, we sought to determine if and how metabolic reprogramming regulates cardiomyocyte proliferation.

METHODS In neonatal mice, we inhibited glucokinase (GCK) to inhibit glycolysis and inhibited carnitine palmityl transferase 1 (CPT1) to inhibit fatty acid oxidation, and observed changes in cardiomyocyte proliferation. Myocardial infarction (MI) models were established in adult mice, and cardiomyocyte proliferation was observed after cardiac specific cpt1a knockout, AAV9 injection or CPT1 inhibitor etomoxir treatment.

RESULTS In neonatal mice, blockade of glycolysis by inhibiting GCK reduced cardiomyocyte proliferation, while blockade of fatty acid oxidation by inhibiting CPT1 delayed the cell cycle arrest in cardiomyocytes. Cardiac-specific *Cpt1a* deletion promoted cardiomyocyte proliferation and improved cardiac function in post-MI mice. This may have clinical significance, because inhibition of CPT1 by AAV9 carrying sh*CPT1*-GFP or etomoxir, an inhibitor of mitochondrial CPT1, replicated the results in mice with MI. CPT1 inhibition stimulated the expression of cell cycle genes including *cyclin A2, cyclin B2*, and *Plk1*, which is probably mediated by inhibition of p38-MAPK and activation of PI3K-Akt signaling pathways, because overexpression of p38-MAPK or inhibition of PI3K or AKT blocked the etomoxir-mediated proliferation of cardiomyocytes.

CONCLUSIONS Inhibition of fatty acid oxidation by targeting CPT1 is a potential therapeutic strategy for stimulating cardiomyocyte proliferation and protection of heart from MI injury. The CPT1 inhibition-induced cardiomyocyte proliferation is through a p38-MAPK and PI3K-Akt-dependent mechanism.

GW30-e0257

A systematic review of immuno-adsorption therapy for improving heart function in patients with Dilated Cardiomyopathy

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OBJECTIVES To systematically evaluate the efficacy of immune-adsorption therapy on the improvement of heart function in dilated cardiomyopathy (DCM) patients.

METHODS Search studies about immune-adsorption therapy for DCM patients in the Cochrane library, Pubmed, Embase, Web of Science, Medline and CNKI database. The retrieval time was from April 22, 2019. The literature was reviewed and screened independently by two investigators according to inclusion and exclusion criteria. Disagreement was discussed by two investigators. Data were extracted and meta-analysis was performed using software Revman5.3.

RESULTS Eight studies and 361 patients were included. Meta-analysis showed that: 1. LVEF significantly improved 3 months after immuno-adsorption therapy compared with before treatment (SMD=–6.02, 95% CI: –7.12~–4.92, P<0.0001). At 6 months after treatment, LVEF improved compared with that before treatment significantly (SMD=–6.7, 95% CI: –6.91~–6.49, P<0.0001). The results also showed that 1 year after treatment, LVEF significantly improved compared than that before treatment (SMD=–7.42, 95% CI: –9.09~–5.39, P<0.0001). 2. at 3 months after treatment, LVEDd reduced compared with that before treatment, and the difference was statistically significant (SMD=3.01, 95% CI: 2.76–3.27, P<0.0001). 3. at 3 months after treatment, the LVEF of the treatment group was higher than that of the control group, with statistical difference (SMD=8.39, 95% CI: 7.75~9.02, P<0.0001). But LVEDd reduction was not statistically significant. (SMD=–3.11, 90% CI: –13.47~7.42, P=0.062).

CONCLUSIONS Immuno-adsorption therapy can improve left ventricular remodeling and heart function in patients with dilated cardiomyopathy. Compared with control group, immune-adsorption therapy can improve LVEF in the treatment group in 3 months after treatment.

GW30-e0265

Effects of LKB1 on cardiomyocyte proliferation through Hippo-Yap signaling

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OBJECTIVES Myocardial infarction (MI) has been a worldwide problem. How to increase to proliferation ability become the main target to treat MI. This study is helpful for us to explore new treatment of cardiomyocyte loss after diseases such as MI.

METHODS LKB1 siRNA treatment and immunofluorescence (IF) was used to evaluate the proliferation rate of cardiomyocytes. Westernblot assay was used to detect the change of protein after LKB1 siRNA treatment. Adult mouse MI model and AAV9 injected to mice heart were used to evaluate the proliferation rate of adult cardiomyocyte.

RESULTS As the proliferation ability is decreased, the expression of LKB1 is increased. LKB1 siRNA treatment and IF shows that the expression of Ki67 and pH3 in cardiomyocytes were increased when LKB1 decreased. Westernblot shows that the expression of YAP and cyclin D were increased, and the level of phospho-YAP was decreased when LKB1 decreased. AAV9-LKB1-shRNA injected to mice heart after MI and the Edu staining shows that after treatment, the proliferation of adult cardiomyocyte was increased.

CONCLUSIONS LKB1 expression is negatively associated with cardiomyocyte proliferation. LKB1 inhibition induces cardiomyocyte proliferation by upregulating YAP and Cyclin D. LKB1 might be a potential treating target for stimulating cardiac regeneration after diseases such as MI.

GW30-e0267

The growth differentiation factor 11 is essential for maintain cardiac function after myocardial injury

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OBJECTIVES Growth differentiation factor 11 (GDF11), a transforming growth factor β superfamily member. The roles of GDF11 in heart diseases and cardiomyocytes (CMs) remain unclear, and little is known about the physiological and pathological functions of GDF11 in cardiomyocytes and heart. Thus, it need to elucidate the cell-specific roles of GDF11 in heart under physiological and pathological conditions.

METHODS Since the GDF11 global knockout in mice resulted in perinatal lethality, we used three cardiac specific Cre line mice (Nkx2.5-Cre, cTnT-Cre, and Myh6-MerCreMer) to identify the cardiac function of GDF11 in embryonic and adult period. Mice were subjected to pressure overload caused by transverse aortic constriction (TAC) and myocardial infarction (MI). Cardiac injury was evaluated using pathological analysis, echocardiograph, haemodynamics, transmission electron microscopy, calcium transient and molecular analysis. In vitro, neonatal and adult CMs of knockout mice were used. Knockdown or overexpression of GDF11 was achieved by siRNA or lentiviral transduction of GDF11 in CMs, respectively. CMs hypertrophy was induced by culturing CMs with phenylephrine (PE) (50 μM) for 24 h. CMs under hypoxia and serum deprivation condition were to mimic the microenvironment of MI. RNA-seq was performed to identify signaling pathway and downstream targets of GDF11 in CMs.

RESULTS GDF11 was mainly derived from CMs in the heart. GDF11 expression increased in patient's heart with dilated cardiomyopathy (DCM) and MI. It also increased in mouse's heart after TAC and MI. Under basal conditions, the knockout mice have normal left ventricular structure and function. In order to identify whether GDF11 deletion at the early stage of CMs development could affect embryonic survival and cardiac morphology, GDF11 floxed mice were crossed with Nkx2.5-Cre and cTnT-Cre Tg. GDF11 deletion in early stage of CMs development does not affect the birth rate at the expected Mendelian ratios, and all mice appeared normal and showed no significant perturbations in the cardiac development. However, deficiency of GDF11 accelerated cardiac dysfunction with left ventricular dilatation, impaired angiogenesis and more fibrosis after TAC and MI.

Moreover, the conditioned medium derived from GDF11 overexpressed CMs had more VEGF expression. It also stimulated tube formation of HUVECs significantly as compared with the null-vector group. The stimulation would be reversed by adding VEGF neutralized antibody into the conditioned medium. In addition to the communication with endothelial cells, CMs overexpressed GDF11 could also influence fibroblast via the secretion of anti-fibrosis mediators.

Furthermore, RNA-seq shown the activation of protein synthesis signaling pathways after overexpressed GDF11 in CMs. We testified that GDF11 enhances Smad2/3 signaling and AKT-mTOR activity in cultured CMs, contributing to VEGF production and anti-fibrosis mediators. In contrast, blockage of TGFβ-Smad pathway and AKT activity by TGF-β receptor inhibitor (SB431542), Smad3 inhibitor (SIS3) and AKT inhibitors (MK-2206) blunted GDF11 overexpression–induced paracrine effect of pro-angiogenesis. GDF11 overexpression in heart with AAV9-GDF11 during TAC rescued the detrimental cardiac function of CKO mice.

CONCLUSIONS GDF11 is necessary for the maintain cardiac function after pathological injury, which actions as an autocrine/paracrine regulatory factor, possibly through the mechanism of activation of TGFβ-Smad and AKT-mTOR signaling axis.

GW30-e0268

DiOHF protects against doxorubicin-induced cardiotoxicity

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OBJECTIVES Doxorubicin (DOX) is an effective anticancer agent. Its clinical use is, however, limited due to its detrimental side effects, especially the cardiotoxicity. 3′,4′-dihydroxyflavonol (DiOHF) is a recently developed potent synthetic flavonoid which has been reported to exert anti- oxidative activity in myocardial ischemia-reperfusion injury and maintain the normal mitochondrial function. The aim of this study was to explore the protective effects of DiOHF on the DOX-induced cardiotoxicity.

METHODS We established DOX-induced cardiotoxicity models in H9C2 cells by incubating them with 1 μM DOX and in BALB/c mice treated with DOX (20 mg/kg, i.p.).

RESULTS DiOHF effectively prevented and reversed the DOX-induced cardiotoxicity, including ROS production, mitochondrial dysfunction, and apoptosis. The cardiotoxicity was accompanied by ERK1/2 activation and abolished by the silence of ERK1, rather than ERK2. Furthermore, treatment with DOX in mice induced an increase in serum CK-MB level and myocardial fibrosis with a reduction in left ventricular (LV) function. These changes were diminished by DiOHF administration.

CONCLUSIONS DiOHF suppresses and reverses the DOX-induced cardiotoxicity by inhibiting ROS release, preserving mitochondrial function and reducing apoptosis through activation of the ERK1 signaling.

GW30-e0269

Transcription factor TBX18 reprograms vascular smooth muscle cells of ascending aorta into pacemaker-like cells

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OBJECTIVES Sinoatrial node (SAN) contains <10,000 genuine pacemaker cells and some mesenchymal cells. Pacemaker cells dysfunction could cause cardiac electrical impulse conduction disorder, which further leads to circulatory collapse and has lethality for patients. Biological pacemaker is aimed to find a replacement for SAN to better treat bradycardia. Transcription factor TBX18 has been successfully applied for constructing biological pacemaker. And vascular smooth muscle cells (VSMCs) of the ascending aorta and SAN

originated from the second heart field. The study explored whether ascending aortic smooth muscle cells in vitro could be reprogrammed into pacemaker-like cells with human TBX18.

METHODS The vascular smooth muscle cells of ascending aorta were cultured by tissue block adherence. After 4–7 days, the cell morphology was observed under light microscope. After passaging, the cells were randomly divided into TBX18 group, GFP group and Null group. TBX18 group was transfected with adenovirus carrying TBX18 transcription factor and green fluorescent protein (GFP), and GFP group was transfected with equal amount of GFP adenovirus as empty virus. And blank group was not transfected with virus as control group (Null group). Three groups of transcription factors TBX3, Shox2, HCN4, NKx2.5 and cardiomyocyte specificity cardiac troponin I (cTnI) were detected by RT-qPCR and Western blot after 4 days. And the expression of HCN4 protein in TBX18 group and GFP group was detected by immunofluorescence. In addition, funny current (I_f current) was detected by the whole cell patch clamp.

RESULTS The purity of vascular smooth muscle cells reached above 90% with α-SMA and MHC antibody. By overexpressing TBX18, the transfected VSMCs expressed high levels of TBX3, Shox2, HCN4 and cTnI and low level of NKx2.5 in both RT-qPCR and Western blot. The result of immunofluorescence showed that HCN4 protein (red fluorescence) in the TBX18 group was expressed and almost consistent with green fluorescent protein and cell nucleus (blue fluorescence), while the GFP group showed barely red fluorescence. I_f current recorded by patch clamp appeared the time and voltage dependence in TBX18 group, which the amplitude of I_f density was from −5.164±0.662 pA/pF to −0.765±0.358 pA/pF (n=14). And I_f current could be blocked Cs^+ (4 mM/L).

CONCLUSIONS Transcription factor TBX18 could reprogram vascular smooth muscle cells of ascending aorta into pacemaker-like cells in vitro.

GW30-e0270

Transcription factor prrx1 promotes brown adipose-derived stem cells differentiation to sinus node-like cells

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OBJECTIVES Biological pacing is the production of a specific gene or cell-induced cell-like cell by genetic engineering to construct a pacing site similar to the atrial junction to replace the original damaged pacing cell, and to obtain the desired heart rate for the patient to be able to meet the normal physiological activity. Transfecting the adenovirus overexpressing prrx1 into BADSCs, our study aimed to investigate whether overexpression of prrx1 can successfully induce the differentiation of BADSCs into sinus nodel cells and construct biological pacing.

METHODS BADSCs of SD rats were isolated and cultured, and the cells were identified by flow cytometry when they were passaged to passages 3–5. The experimental groups were divided into two groups: BADSCs were transfected with empty adenovirus GFP and adenovirus prrx1 (ie, Ad-GFP group, Ad-prrx1 group). Cell morphology and fluorescence intensity were observed under fluorescence microscope. After 5–7 days of virus transfection, sinus node cell-associated pacing protein (HCN4) and ion channel (Cacnalg, encoding T-type calcium channel) as well as the expression levels of transcription factors (TBX18, ISL-1, pitx2, shox2, etc.) were detected by Western blot and RT-qPCR. Then immunofluorescence assay to detect whether cell co-expressed prrx1 with HCN4, TBX18 and ISL-1. Finally, whole-cell patch clamp technique records pacing current If.

RESULTS The newly isolated cells were round, and after being attached to the wall, they were long fusiform and spirally growing. After identification by flow cytological cell surface molecules, the isolated cells showed CD90 positive and almost no CD45, indicating that BADSCs were successfully isolated from rats. Repeated experiments confirmed that the optimal MOI for adenovirus transfection of BADSCs was 100. After 5–7 days of transfection of adenovirus into cells, the biochemical tests showed that the mRNA levels and protein expressions of pacing-related factors (TBX18, ISL-1, HCN4, shox2, Cacnalg) in Ad-prrx1 group were significantly higher than those in Ad-GFP group. However, the expression level of pitx2 was decreased, and there was a statistical difference between the two groups ($P<0.05$). Immunofluorescence showed that prrx1 co-expressed with TBX18, ISL-1 and HCN4 in Ad-prrx1 group, but no expression of pacing-related protein was found in Ad-GFP group. Whole cell patch clamps were able to record the If current in the experimental group and this current was blocked by 4 mmol/L CsCl.

CONCLUSIONS Overexpression of prrx1 can successfully induce the differentiation of BADSCs into sinus node-like cells with biochemical characteristics and electrophysiological characteristics.

GW30-e0284

The study of immune-liposome targeted delivery neuropeptide Y to promote myocardial regeneration after myocardial infarction

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OBJECTIVES The stem cell therapy to treat myocardial infarction (MI) has shown disappointed results largely due to the poor survival of transplanted stem cells in the MI region. We propose a combination therapy by targeted delivery of neuropeptide Y (NPY) to MI region to improve the micro-environment, which may enhance the survival of transplanted stem cells, and further improve the cardiac function.

METHODS In this study, P-selectin conjugated immunoliposomes containing NPY were given to the MI mouse through tail vein injection immediately after surgery. Adipose-derived stem cells (ADSCs) were transplanted to the MI region one week later. Left ventricular percent fractional shortening were measured 1 week and 4 weeks post MI using echocardiography.

RESULTS Results indicate that MI rats with no treatment lost 7% contractility (~40% of its heart function) from 1 week to 4 weeks post-MI. Either targeted NPY or ADSCs treatment alone can slow down the loss by half to 5%. The combination of targeted NPY and ADSCs treatment further decreased the contractility.

CONCLUSIONS So we can use the mature liposomal drug delivery technology to NPY efficient and specific delivery to the myocardial infarction site to improve blood supply and microenvironment, myocardial regeneration, and repair the myocardial infarction to improve the purpose of heart function. Furthermore, the application of immunoliposomal drug loading technology in myocardial tissue repair, which not only provides new possibilities for the clinical treatment of myocardial infarction; but can also use this technology, for other diseases diagnosis and treatment to provide a new idea by combining different disease conditions.

GW30-e0290

Role of Wnt/β-catenin signaling pathway in inducing rat bone marrow mesenchymal stem cells to differentiate into cardiomyocytes

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OBJECTIVES To explore the role of Wnt/β-catenin signaling pathway in the differentiation of rat bone marrow mesenchymal stem cells (BMMSCs) into cardiomyocytes.

METHODS The third generation BMMSCs were divided into two groups: (1) angiotensin II (Ang II) and 5-azacytidine (5-aza) group (final concentration was 0.1 μmol/L and 10 μmol/L respectively); (2) the control group, only choosing basic medium for induction. After induction for 24 hours, the induction medium was abandoned and cultured in complete medium for 4 weeks. Morphological changes, proliferation ability, induction differentiation rate, expression of α-actin and ultrastructure were respectively detected by inverted phase contrast microscopy, MTT, flow cytometry, immunofluorescence staining and transmission electron microscopy. The expression level of Wnt and β-catenin was detected by Western Blotting.

RESULTS BMMSCs showed various morphologies in primary culture. After passage, BMMSCs grew in long shuttle shape and showed uniform growth after induction. MTT assay showed that the growth rate of Ang II combined with 5-aza group was faster than that of control group. Flow cytometry showed that the induction rate of cardiomyocytes in Ang II combined with 5-aza group was (31.2±1.7)% and that in control group was (1.1±0.2)%. Immunofluorescence staining showed BMMSCs after induction expressed α-actin positively. The myofilament and gap junction were observed by transmission electron microscopy. Western Blotting results showed that the expression levels of Wnt and β-catenin in Ang II combined with 5-aza group were significantly higher than those in control group.

CONCLUSIONS Wnt/β-catenin signaling pathway plays an important role in promoting the differentiation of BMMSCs into cardiomyocytes induced by Ang II combined with 5-aza.

GW30-e0295

High-mobility group AT-hook1 promotes cardiac dysfunction in diabetic cardiomyopathy via autophagy inhibition

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OBJECTIVES High-mobility group AT-hook1 (HMGA1, formerly HMG-I/Y), known as an architectural transcription factor, has been involved in a great

many of biological processes. Whereas, its effect on cardiac remodeling in diabetic cardiomyopathy remains vague to a great extent. The aim of this study is to elucidate the functional role of HMGA1 on cardiac remodeling in diabetic cardiomyopathy.

METHODS Adeno-associated virus 9 (AAV9) combined with HMGA1 and shHMGA1 were employed to overexpress or knockdown HMGA1 expression in the streptozotocin induced diabetes mice. Cardiac structure and functions were measured by echocardiography and hemodynamic examinations. Primary cardiomyocytes were used to perform gain/loss-of-function assays in vitro.

RESULTS In this study task, we figured out that HMGA1 was up-regulated in diabetic mice heart and high glucose stimulated cardiomyocytes. Overexpression HGMA1 accelerated high glucose induced cardiomyocytes inflammation and apoptosis, while HMGA1 knockdown relieved inflammation and apoptosis in cardiomyocytes. Overexpression HGMA1 via retro-orbital venous plexus injection of AAV9-HMGA1 caused deteriorated inflammatory response, increased apoptosis and reduced heart function in streptozotocin caused diabetic mice heart. Knockdown of HMGA1 by AAV9-shHMGA1 injection caused ameliorating cardiac remodeling. Mechanismly, we found that HMGA1 regulated autophagy by regulating P27/CDK2/mTOR signaling but not AKT, ERK and AMPKα. Autophagy inhibitor 3-MA, and bafilomycin A1 abrogated the protective effect of HMGA1 silencing. Autophagy inducer rapamycin blocked HMGA1 overexpression induced deteriorating effects in vitro. Moreover, we found that CDK2 silence or P27 overexpression also blocked HMGA1 overexpression induced deteriorating effects in vitro. P27 overexpression in vivo increased autophagy in mice heart and counteracted HMGA1 overexpression induced increased cardiac remodeling in diabetic mice. Furthermore, the regulating effect of HMGA1 on P27 was mediated by miR-222, while was confirm by luciferase reporter. And miR-222 antagomir counteracted HMGA1 overexpression induced deteriorating effects in vitro.

CONCLUSIONS Taken together, our data indicate that HMGA1 aggregates diabetic cardiomyopathy by directly regulating miR-222 promoter activity that inhibits P27/mTOR induced autophagy.

GW30-e0300

miR-324-5p protects against oxidative stress-induced endothelial progenitor cell injury by targeting Mtfr1

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OBJECTIVES This study investigated the related miRNA-324-5p changes of EPCs in peripheral blood of patients with (AMI), and analyzed the molecular mechanism of EPCs injury.

METHODS The peripheral blood of healthy volunteers and patients with ST-segment elevation myocardial infarction (STEMI) was clinically collected. EPCs were transfected by miR-324-5p mimic and simultaneously handled it with hydrogen peroxide (H_2O_2) to inducing EPCs injury. At 24 hrs after H_2O_2 treatment, cell viability, the up-take capacity on DiI-Ac-LDL and carrying ability on FITC-UEA-l and multiplication capacity were analyzed. The mechanism process were carefully researched by valued the characteristics of the mitochondrion morphology, membrane potential, ATP levels and the expressing apoptosis pathways.

RESULTS (1) EPCs derived from peripheral blood were obtained by density gradient centrifugation and cultured in vitro and identified. (2) Small RNA sequencing indicated that the expression level of miR-324-5p in peripheral blood EPCs of patients with STEMI was significantly lower compared to healthy volunteers. The Mtfr1 has been confirmed as a targeted gene of miR-324-5p through miRTarBase software and western blot. (3) The miR-324-5p mimic units could be contributed for the improvement of viability, the up-take capacity on DiI-Ac-LDL and carrying ability on FITC-UEA-l and multiplication capacity on oxidative stress-injured EPCs. (4) miR-324-5p could suppress mitochondrial fragmentation, promote membrane potential and ATP levels, as well as protect against oxidative stress-induced EPCs apoptosis.

CONCLUSIONS Our results suggested that miR-324-5p protects against oxidative stress-induced EPCs injury by regulating Mtfr1.

GW30-e0305

Improvement of mitophagy by RES has protective effects on HG-induced mitochondrial injury in cardiomyocytes

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OBJECTIVES To evaluate the effects of resveratrol (RES) on high glucose (HG)-induced decreased mitophagy level and mitochondrial injury in cardiomyocytes.

METHODS H9c2 rat cardiomyocytes were randomly divided into four groups: control group, HG group, HG+RES group, and HG+RES+cyclosporinea (mitophagy inhibitor) group. The levels of mitophagy, mitochondrial function, including reactive oxygen species (ROS) production, mitochondrial membrane potential (MMP), mitochondrial respiratory chain complex enzyme activities and adenosine triphosphate (ATP) content, and cell activities were measured in each group.

RESULTS RES improved mitophagy suppressed by HG in cardiomyocytes, as the expressions of PINK1 and Parkin increased and the aggregation of LC3 in mitochondria raised. RES inhibited the production of ROS, increased the level of MMP, restored the activities of mitochondrial respiratory chain complex enzymes, increased ATP content, and consequently improved cell activities in cardiomyocytes cultured with HG. However, the above protective effects of RES on cardiomyocytes cultured with HG were attenuated by cyclosporinea.

CONCLUSIONS Improvement of mitophagy by RES has protective effects on HG-induced mitochondrial injury in cardiomyocytes.

GW30-e0311

Knockout of RhoE gene in cardiomycytes based on CRISPR/Cas9 technology and enrichment of its regulatory signaling pathway

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OBJECTIVES To explore the feasibility of the editing RhoE gene in H9C2 cardiomycytes based on CRISPR/Cas9 technology and enrichment of the signaling pathways following RhoE knockout.

METHODS Three rat RhoE knockout lentviral vectors (LV-RhoE-sgRNA-Cas9) and one negative control vector (LV-NC-Cas9) were constructed based on Cas9-containing lentviral vector GV392 (U6-sgRNA-EIF1a-Cas9-FLAG-P2A-puro), and the corresponding lentvirus particles were packaged. Viruses were then infected rat H9C2 cardiomyocytes and Cruiser enzyme digestion was used to screen the effective sgRNA, following western blotting analysis of RhoE expression in puromycin-stressed H9C2 cells. After whole genome expression chips were performed, the ingenuity pathway analysis (IPA) was used to analyze the changes of gene expression profiles and enrich the signal pathways that changed significantly. Finally, quantitative RT-PCR and western blot were used to verify the expression of some differential changes genes.

RESULTS Three sgRNAs targeting RhoE and one non-specific sgRNA were designed. Four lentviral vectors named LV-RhoE-sgRNA1-Cas9, LV-RhoE-sgRNA2-Cas9, LV-RhoE-sgRNA3-Cas9 and LV-NC-Cas9 were constructed, and the associated viral particles with a titer of 3×10^8 TU/mL were successfully obtained. Cruiser digestion confirmed the sgRNA1 displayed the obvious targeting effects against RhoE. With the help of Cas9 protein, sgRNA1 effectively led to editing RhoE gene. Western blot analysis confirmed that the expression of RhoE in mixed H9C2 cell pools was significantly decreased. After infected H9C2 cells with LV-RhoE-sgRNA1-Cas9, 417 genes were up-regulated and 412 genes were down-regulated. IPA analysis indicated that oncostatin M (OSM) signaling, superpathway of cholesterol biosynthesis, interferon signaling, regulation of actin-based motility by Rho and cell proliferation signals were most significantly affected followed RhoE knockout, which was further confirmed by quantitative RT-PCR and western blot analysis of some associated molecules expression. Interesting, cholesterol was predicted to be strongly activated (Z-score=4.423, $P=5.86\times10^{-12}$) and SCAP is predicted to be strongly suppressed (Z-score=−4.617, $P=2.12\times10^{-18}$) after RhoE knockout. And functional analysis indicated that RhoE was involved in cell death and survival, cell movement, tumorigenesis, organism development, gene expression and cardiovascular diseases.

CONCLUSIONS (1) For the first time, we successfully edit the RhoE gene in rat cardiomyocyte H9C2 through CRISPR/Cas9 technology. (2) We obtain the global gene expression profiles of RhoE deficiency in H9C2 cardiomyocytes. (3) IPA analysis suggests that RhoE plays a crucial role in many diseases and functions through mediating multiple signaling pathways, which provides a potential target for future intervention.

GW30-e0312

Decrease of HDL-C is associated with age, household income, and incidence of dementia in adults from Korean national health and nutrition examination survey 2017: correlation analysis of low HDL-C and poverty

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OBJECTIVES Low serum HDL-C is a risk factor of cardiovascular disease and dementia. However, there has been no study to elucidate correlation of household income and HDL-C level in adult population.

METHODS We selected 5535 subjects (20–80 year-old) from Korean national health and nutrition examination survey 2017 (KNHNES, n=2469 men, n=3066 women). They were classified into five level of household income grade from 1 (the lowest) to 5 (the highest). They also classified based on HDL-C level from quintile 1 (.

RESULTS Generally, in both gender, higher HDL-C group showed larger percentage of income grade 5 and the lowest HDL-C group showed the largest percentage of income grade 1. Both group exhibited significant increase of average income grade depends on increase of HDL-C level (men, P=0.03; women, P<0.001). In low HDL-C quintile, the lower income grade is directly associated with the lower HDL-C level, suggesting that the poverty is directly associated with low HDL-C. Women group showed 3.3-fold higher incidence of dementia than men group at age 80's. Sharp decrease of HDL-C after 50's is associated with dramatic increase of dementia incidence in women, while men group showed relatively mild decrease of HDL-C and less dementia incidence than women group.

CONCLUSIONS In conclusion, in both gender, lower income group showed larger percentage of low-HDL-C prevalence. The decline of HDL-C after middle age was strongly associated with explosive increase of dementia in elderly.

GW30-e0338

Intermittent high glucose enhances oxidative stress and apoptosis through RAGE pathway in human coronary artery endothelial cells

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OBJECTIVES RAGE is involved in the progression of atherosclerosis and improves endothelial dysfunction and suppresses vascular inflammation. The aim of this study was to investigate the cellular apoptosis and intracellular level of oxidative stress whether mediated by the receptor of advanced glycation end products (RAGE) in human coronary artery endothelial cells (HCAECs) under constant and intermittent high glucose (IHG) conditions in vitro.

METHODS Cellular viability was evaluated by 3-(4, 5-dimethylthiazol-2-yl) 2, 5-diphenyltetrazolium bromide (MTT) assay. Apoptosis of HCAECs was analyzed by flow cytometry analysis, and the transcript and protein levels of Caspase-3 and RAGE were detected by RT-qPCR and Western blotting respectively. Oxidative stress markers (MDA and GSH) and intracellular ROS level were detected by relevant assay kit. The expression quantity of RAGE was knockdown used the shRNA mediated by lentivirus in HCAECs.

RESULTS The results shown that in the intermittent high glucose group, the cell viability was significantly decreased and the apoptosis rate, the expression level of ROS, MDA, GSH, Caspase-3 and RAGE were significantly increased when compared to control and constant high glucose. Furthermore, these effects can significantly inhibit by the insulin treatment in the intermittent high glucose group. Knockdown the expression level of RAGE can significantly attenuate the badly effects induced by IHG.

CONCLUSIONS These results indicated that intermittent high glucose is more deleterious to HCAECs than constant high glucose, which may be due to the aggravation of cellular apoptosis and oxidative stress, and those effects may mediate by RAGE pathway.

GW30-e0342

Exosomes derived from bone marrow mesenchymal stem cells promote the proliferation and migration of hypoxic-injured endothelial cells by activating the MAPK/Erk1/2 pathway

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OBJECTIVES Endothelial, as a barrier between blood and blood vessels, plays an important role in vascular homeostasis. Endothelial injury can cause the formation of vascular restenosis after percutaneous coronary intervention. Exosomes have been a hot topic in cardiovascular diseases in recent years, but exosomes have not been reported in terms of vascular restenosis. The aim of this study was to investigate the protective effects and potential mechanisms of mesenchymal stem cell derived-exosomes (MSC-Exo) on hypoxic-injured Endothelial cells (HEC).

METHODS In this study, we established a model of HEC under hypoxic conditions. Exosomes were isolated from MSC by using an exosome purification kit. HEC were treated with exosomes to examine their effects on cell proliferation, migration, invasion and apoptosis. The expression of the MAPK/Erk1/2 pathway and its downstream related proteins was then examined.

RESULTS In the model, iNOS was highly expressed and eNOS was lowly expressed compared to the normal group. MSC-Exo were verified through transmission electron microscopy, NTA particle size analysis and western blot and transported to HEC. MSC-Exo could accelerate the proliferation and migration and reduce the apoptosis of HEC. Compared with those in the untreated group, Western blot results showed that the expression levels of PCNA, CyclinD1, MMP9, MMP2, Vimentin and P-Erk1/2 proteins in MSC-Exo group were significantly up-regulated under hypoxic conditions. Importantly, the MAPK/Erk1/2 pathway inhibitor is capable of inhibiting the expression changes of the above related proteins induced by MSC-Exo.

CONCLUSIONS MSC-Exo promote the proliferation and migration of HEC by activating the MAPK/Erk1/2 pathway. Besides, MSC-Exo mediate the expression of PCNA, CyclinD1, MMP9, MMP2, and Vimentin proteins. This study is expected to play a role in the repair of cardiovascular injury and has certain clinical reference value.

GW30-e0352

Attenuating TET2 and transferring endothelial cell-derived exosomes to vascular smooth muscle cell induced by activating CD137 signaling promotes neointimal formation

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OBJECTIVES Activated ECs play an important role in the development of AS which is partly attributed to the formation of neointima resulting from abnormal VSMCs hyperplasia. TET2 was reported as a major regulator of VSMCs phenotypic switch and protect EC from noxious stimulus and to repress inflammation in AS. The purpose of the present study is to determine whether activation of CD137 signaling can regulate VSMCs function by altering endothelial tet2 expression and to explore the potential mechanisms.

METHODS VSMCs were isolated from C57BL/6J mice. The influence of ECs on VSMCs was analyzed using a co-culture system. Western blotting was used to detect the protein expression levels of tet2 and CD9, CD81, CD63 as well as VSMCs phenotypic markers. RT-PCR was performed to detect mRNA levels of tet2. EdU proliferation assay and transwell migration assay were employed to assess VSMCs functions. EXO-spin kits were used to extract and purified exosomes. Transmission electron microscopy, Nanoparticle Tracking Analyzer was applied to characterize exosomes. Tet2 overexpression lentivirus was used to perform gain-of-function experiments.

RESULTS (1) Activation of endothelial CD137 signaling decreased tet2 expression and exosomes tet2. (2) ECs derived exosomes were internalized by VSMCs and inhibited phenotypic switch in vitro and neointimal formation in vivo. (3) Exosomes derived from CD137 activated ECs showed weakened protective effects on VSMCs.

CONCLUSIONS Activation of endothelial CD137 signaling by CD137L attenuated the repressive effects of EC-derived exosomes on PDGF-BB induced VSMCs phenotypic switch and neointimal formation after carotid injury.

GW30-e0362

Prediction of marker genes associated with hypertension by bioinformatics analyses

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OBJECTIVES This study aimed to explore the underlying marker genes associated with hypertension by bioinformatics analyses.

METHODS A gene expression profile (GSE54015) was downloaded. The differentially expressed genes (DEGs) between the normotensive female (NF) and hypertensive female (HF), and between the normotensive male (NM) and hypertensive male (HM) groups were analyzed. Gene Ontology (GO) and pathway enrichment analyses were performed, followed by protein-protein interaction (PPI) network construction. The transcription factors (TFs), and the common DEGs between the HF and HM groups were then analyzed.

RESULTS In total, 411 DEGs were identified between the HF and NF groups, and 418 DEGs were identified between the HM and NM groups. The upregulated DEGs in the HF and HM groups were enriched in 9 GO terms, including oxidation reduction, such as cytochrome P450, family 4, subfamily b, polypeptide 1 (Cyp4b1) and cytochrome P450, family 4, subfamily a, polypeptide 31 Cyp4a31). The downregulated DEGs were mainly enriched in GO terms related to hormone metabolic processes. In the PPI network, cytochrome P450, family 2, subfamily e, polypeptide 1 (Cyp2e1) had the highest degree in all 3 analysis methods in the HF group. Additionally, 4 TFs were identified from the 2 groups of data, including sterol regulatory element binding transcription factor 1 (Srebf1), estrogen receptor 1 (Esr1), retinoid X receptor gamma (Rxrg) and peroxisome proliferator-activated receptor gamma (Pparg). The intersection genes were mainly enriched in GO terms related to the extracellular region.

CONCLUSIONS On the whole, our data indicate that the DEGs, Cyp4b1, Cyp4a31 and Loxl2, and the TFs, Esr1, Pparg and Rxrg, are associated with the progression of hypertension, and may thus serve as potential therapeutic targets in this disease.

GW30-e0366

Palmitate induces myocardial lipotoxic injury via the endoplasmic reticulum stress mediated apoptosis pathway

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OBJECTIVES To explore the role of the endoplasmic reticulum (ER) stress-mediated apoptosis pathway in palmitate (PA)-induced cardiomyocyte lipotoxicity.

METHODS H9c2 cells were treated with various doses (100, 200 and 400 μM) of PA to mimic cardiomyocyte lipotoxicity in vitro. Oil Red O staining was used to determine the accumulation of intracellular lipids. An MTT assay was used to determine the cell viability. Lactate dehydrogenase (LDH) activity was used to measure the injury of H9c2 cells. Flow cytometry analysis was used to detect apoptosis. Western blotting was used to evaluate the expression change of ER stress-mediated apoptosis pathway proteins, including 78 kDa glucose-regulated protein (GRP78), eukaryotic initiation factor 2 α (eIF2α), protein kinase R-like endoplasmic reticulum kinase (PERK), C/EBP homologous protein (CHOP) and cleaved caspase-12.

RESULTS Various doses of PA promoted excessive lipid deposition in cardiomyocytes and resulted in decreased cell viability, and increased the LDH activity and apoptosis rate in a dose-dependent manner. Furthermore, the expression of GRP78, a marker of ER stress, and the phosphorylation of eIF2α and PERK were increased following treatment with PA. Notably, the levels of CHOP and cleaved caspase-12, critical regulators of ER stress-mediated apoptosis pathway, were also elevated, and this effect was reversed by a specific ER stress inhibitor (4-phenyl butyric acid).

CONCLUSIONS The results of the current study demonstrated that PA induces myocardial lipotoxic injury by triggering ER stress and the ER stress-mediated apoptosis pathway.

GW30-e0375

A2A receptor activation mediates Ang II induced aortic remodeling by promoting macrophages retention

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OBJECTIVES Adenosine 2A receptor ($A_{2A}R$) play a crucial role in the pathophysiological process of the cardiovascular diseases. However, the role of $A_{2A}R$ plays in aortic remodeling remains puzzling. This study explored the effects and mechanisms of $A_{2A}R$ on aortic remodeling from the perspective of macrophage migration.

METHODS Dynamic changes in adenosine-$A_{2A}R$ system and proportions of $CD11b^+F4/80^+$ aortic macrophages (AM) in process of aortic remodeling were detected in C57BL/6 mice infused with Ang-II. Next, the role of $A_{2A}R$ in aortic remodeling, the numbers of macrophages mobilized into and out of the aorta and emigrating to iliac lymph node, CC chemokine receptor 7 (CCR7) (CCL19 receptor) expression level and internalization were observed in mice with macrophage knockout of $A_{2A}R$ or receiving $A_{2A}R^{-/-}$ bone marrow transplantation. The roles of CCR7 in mediating $A_{2A}R$ signaling were investigated in Ang II infused *$A_{2A}R$-cKO* mice treated with CCR7 antibody.

RESULTS Adenosine-$A_{2A}R$ in macrophages promotes Ang-II-induced aortic remodeling and macrophages accumulation in the aorta, which is inhibited by $A_{2A}R$ knockout in macrophages. Moreover, macrophage $A_{2A}R$ knockout inhibited macrophage accumulation by inhibiting macrophages retention via promoting macrophages emigration to draining lymph node without affecting macrophages proliferation and apoptosis in the aorta. Effects of macrophage $A_{2A}R$ knockout are correlated with restoring expression and surface content of CCR7. Consistently, $A_{2A}R$ activation inhibited CC-chemokine ligand 19 (CCL19) induced aortic macrophages migration, but has no effect on CC-chemokine ligand 2 (CCL2) induced monocytes migration. The effects of $A_{2A}R$ activation are associated with downregulation and internalization of CCR7. Bone marrow transplantation experiments showed that $A_{2A}R^{-/-}$ bone marrow relieved Ang-II-induced aortic remodeling, macrophages retention, CCR7 downregulation and internalization, which was rescued by $A_{2A}R^{+/+}$ bone marrow transplantation. Furthermore, CCR7 antibody treatment blocked all protective effects observed in *$A_{2A}R$-cKO* mice including attenuation of aortic remodeling and macrophages retention.

CONCLUSIONS $A_{2A}R$ activation in macrophages mediate Ang-II induced macrophages accumulation and subsequent aortic remodeling by inhibiting macrophages emigration to draining lymph node and consequently promoting retention of macrophages through regulating CCR7 expression and internalization.

GW30-e0378

Peroxidasin promotes diabetic vascular endothelial dysfunction induced by advanced glycation end products via NOX2/HOCl/Akt/eNOS pathway

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OBJECTIVES It is widely accepted that reactive oxygen species (ROS) derived from advanced glycation end products (AGEs)-induced activation of NADPH oxidases plays an essential role in the pathological process of diabetic vascular endothelial dysfunction. Peroxidasin (PXDN) is one of family of peroxidases that generates hypochlorous acid (HOCl) from hydrogen peroxide (H_2O_2) and is primarily expressed in cardiovascular tissues. The specific role of PXDN in mediating diabetic vascular endothelial dysfunction has not been reported. Thus, the aim of this present study was to elucidate the role and potential mechanism by which PXDN promotes the pathogenesis of diabetic vascular endothelial dysfunction induced by AGEs.

METHODS Twelve-week-old diabetic experimental mice (db/db) were compared to non-diabetic control mice (db/m). Vasodilatation of aortic rings isolated from db/db and db/m mice were measured by wire myograph. The expression of receptor for advanced glycation end products (RAGE), NADPH oxidase 2 (NOX2), PXDN, and 3-Chlorotyrosine (3-Cl-Tyr) as well as the phosphorylation of Akt (p-Akt) and endothelial nitric oxide synthase (p-eNOS) in aortas was assessed by western blot. The plasma Nitric Oxide (NO) was detected by Griess assay. Expression and location of PXDN, RAGE and 3-Cl-Tyr in mesenteric arteries and aortas were also analyzed by immunofluorescence staining. In vitro experiments were performed in human umbilical vein endothelial cells (HUVECs). HUVECs with PXDN knockdown by siRNA, pretreatment with HOCl or the Akt inhibitor MK2206, or reduction of H_2O_2 production by si-NOX2 and H_2O_2 scavengers were treated with AGEs and the expression of RAGE, NOX2, PXDN, 3-Cl-Tyr, p-Akt, and p-eNOS was measured by western blot, the NO production of cell supernatant was detected by Griess assay.

RESULTS Compared to non-diabetic mice, acetylcholine (Ach)-induced endothelium-dependent relaxation was significantly inhibited in db/db mice. Furthermore, db/db mice had increased expression of RAGE, NOX2, PXDN, 3-Cl-Tyr and lower levels of p-Akt and p-eNOS compared to db/m mice. HUVECs treated with AGEs had significantly elevated expression of RAGE, NOX2, PXDN and 3-Cl-Tyr, while p-Akt, p-eNOS and NO levels were reduced. PXDN silencing attenuated the effect of AGE treatment on 3-Cl-Tyr, p-Akt, p-eNOS and NO levels. Additionally, HOCl treatment alone as well as HOCl in addition to treatment with Akt inhibitor MK2206 blocked phosphorylation of Akt and eNOS, reducing NO production. Furthermore, NOX2 silencing and H_2O_2 inhibitors attenuated AGEs-induced up-regulation of PXDN and generation of HOCl, restored endothelial function.

CONCLUSIONS PXDN promotes AGEs-induced diabetic vascular endothelial dysfunction by attenuating eNOS phosphorylation on Ser1177 via NOX2/PXDN/HOCl/Akt pathway.

GW30-e0386

Knockdown of microRNA-17-5p ameliorates atherosclerotic lesions in ApoE2/2 mice and restores the expression of very low density lipoprotein receptor

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OBJECTIVES To propose and verify a hypothesis that miR-17-5p knockdown may mitigate atherosclerotic lesions using atherosclerotic ApoE−/− mice as serum microRNA-17-5p (miR-17-5p) is elevated in patients with atherosclerosis.

METHODS Peripheral blood leucocytes were obtained from 30 AS patients and 30 healthy controls from April, 2016 to June, 2016. C57BL/6 and ApoE−/− mice (male, 6 weeks of old, 18–22 g) were purchased and were assigned to either a non-AS group (n=6) or the AS groups (n=6 per group).

RESULTS The level of miR-17-5p was higher while the level of very low density lipoprotein receptor (VLDLR), a predicted target of miR-17-5p, was lower in the peripheral blood lymphocytes (PBLs) of atherosclerosis patients as compared with control PBLs. ApoE−/− mice fed with a high-cholesterol diet displayed marked atherosclerotic vascular lesions, which were ameliorated after treatment with antagomiR-17-5p. Moreover, the decreased VLDLR in atherosclerotic mice was partly restored when miR-17-5p was antagonized. Further, luciferase assay confirmed VLDLR as a direct target of miR-17-5p in vascular smooth muscle cells (VSMCs). In addition, the elevated expression of proprotein convertase subtilisin kexin 9 (PCSK9), a secreted protease that binds to and promotes VLDLR degradation, in the atherosclerotic mice was suppressed by antagomiR-17-5p.

CONCLUSIONS A novel interaction between miR-17-5p and VLDLR is revealed and suggests that miR-17-5p may be a potential therapeutic target for AS.

GW30-e0388

Cardioprotective effect of Notch signaling on the development of myocardial infarction complicated by diabetes mellitus

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OBJECTIVES The present study aimed to elucidate the role of Notch signaling in the development of myocardial infarction (MI) concomitant with diabetes in vivo and in vitro and evaluated the therapeutic effect of the Notch signaling in vitro.

METHODS Streptozotocin-induced diabetic rats were subjected to 25 min of ischemia and 2 h of reperfusion. Cardiac troponin T (cTnT) and creatine kinase-MB (CK-MB) isoenzyme levels were detected. Infarct size was measured by 2,3,5-triphenyltetrazolium chloride staining. Myocardial apoptosis and fibrosis were examined by terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling and Masson Trichrome staining, respectively. The mRNA and protein levels of Notch signaling components, including Notch1, Notch4, Delta-like 1, Jagged1, Mastermind-like protein 1 and p300, were quantified by reverse transcription-quantitative polymerase chain reaction and western blotting analyses, respectively. H9c2 cells were treated with/without 33 mM high glucose (HG) and/or subjected to hypoxia in the presence/absence of Jagged1. Cell viability and apoptosis were determined by MTT assay and Annexin V-fluorescein isothiocyanate/propidium iodide assay. Levels of the Notch signaling pathway members were examined.

RESULTS The present findings revealed that diabetes elevated CK-MB and cTnT, increased infarct size, induced myocardial apoptosis and inhibited the Notch signaling pathway in vivo after ischemia/reperfusion. Ischemia/reperfusion augmented the severity of MI in diabetic rats. Furthermore, HG reduced cell viability and induced cell apoptosis in H9c2 cells after hypoxia exposure, which was inhibited by Jagged1. We also found that HG inhibited Notch signaling in H9c2 cells after hypoxia, whereas Jagged1 exerted its cardioprotective effect on hypoxic injury (in HG environments or not) by activating the Notch signaling pathway.

CONCLUSIONS In conclusion, these findings suggest that diabetes promoted the progression of MI in vivo and in vitro via the inhibition of the Notch signaling pathway. Jagged1 may protect against MI in in vitro models by activating Notch signaling.

GW30-e0399

Decreased plasma levels of corin in patients with non-ST segment elevation acute coronary syndrome

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OBJECTIVES Corin was found decreased in coronary heart disease (CHD) recently, which may reflect pathological dysfunction. But there is no data about the plasma corin changing after the onset of Non-ST Segment Elevation Acute Coronary Syndrome (NSTACS). This study is to examine the plasma corin levels in different time points in patients with NSTACS.

METHODS Fifty NSTACS patients without severe heart failure (men 30 and women 20) and 50 healthy individuals were enrolled in this study. Elisa method was used to determine plasma corin levels at 4 time points (admission, 24 h, 48 h, 72 h) respectively in these patients.

RESULTS The decreased plasma corin concentrations were found in both male and female patients when compared with the normal controls on admission. In NSTACS patients, plasma corin levels are significantly decreased than that in the healthy controls (820.354±122.543 versus 1420.123±457.235, P<0.001) on admission and reached the peak level of 989.241±253.717 pg/mL at about 2 days after admission, then the level of plasma corin decreased to 746.161±369.264 pg/mL at the third day after admission. There were more patients with Unstable Angina (UA) than Non-ST Segment Elevation Myocardial Infraction (NSTEMI) (35 versus 15, P<0.001).

CONCLUSIONS Plasma corin levels were found decreased in NSTACS patients compared with normal healthy individuals, which may reflect the dysfunction of the heart in patients with NSTACS.

GW30-e0403

The electrophysiological mechanisms of short QT syndrome induced by sodium channel gene SCN5A mutation

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OBJECTIVES Short QT syndrome (SQTS) is a highly malignant hereditary arrhythmia characterized by shortened QTc, ventricular tachyarrhythmias (ventricular tachycardia and ventricular fibrillation) results in syncope and sudden death. The cardiac sodium channel alpha subunit (Nav1.5) encoded by the SCN5A gene is a key protein that maintains the normal excitability of cardiomyocytes and its mutation causes various congenital arrhythmias. Nav1.5 binds to a variety of proteins which form a multiprotein complex to regulate the sodium channel function. MOG1 protein is a novel sodium channel regulatory protein which promotes Nav1.5 intracellular trafficking to plasma membranes, but its specific regulatory mechanism remains unclear. Our team's previous study screened the sodium channel SCN5A mutation E428G was associated with SQTS, but its role in SQTS and the specific pathogenesis are still unclear. To investigate the effect of E428G on the electrophysiological function of Nav1.5 and the role of MOG1.

METHODS The wild-type (WT) plasmid of Nav1.5 and MOG1 were constructed. At the same time, the mutant (E428G) plasmid was constructed by gene-directed mutagenesis technique using wild-type Nav1.5 as a template. The above plasmids were transfected into human embryonic kidney 293T cells (HEK293T), and the experiment was divided into four groups: WT, E428G, WT+MOG1, E428G+MOG1. Whole cell patch clamp, cell membrane protein separation and immunoblotting technique were used to analyze the electrophysiological properties of sodium ion channels and their expression on cell membranes.

RESULTS Cell electrophysiological studies showed that the E428G mutation resulted in a 70% increase in peak sodium current, and a 30% reduction in late sodium current, steady state activation (SSA) and steady-state inactivation curve (SSA) revealed a hyperpolarization shift compared to the WT group. In the WT group, the peak sodium current was significantly increased 1.5 times after the expression of MOG1, the SSA curve shifted to the negative polarization direction, and the SSI curve did not shift significantly. However, the E428G mutant group overexpressed MOG1 revealed that the peak sodium current decreased by 30% significantly, the SSA curve shifted to the negative polarization direction and the SSI curve has no significant offset. In addition, compared with the WT+MOG1 group, the peak sodium current and the late sodium current of the E428G+MOG1 group were reduced by 50 and 30%, respectively, the SSA curve shifted toward the negative polarization direction, and the SSI curve did not shift significantly. Western blots showed that E4258G increased the sodium channel membrane protein by 1.8-fold compared with the WT group. When overexpressing MOG1, MOG1 increased the sodium channel membrane protein of the WT group by 70%, while MOG1 reduced the expression of sodium channel membrane protein by about 37% in the E428G group. In addition, there was no significant change in cell membrane protein expression of E428G+MOG1 sodium channel compared to WT+MOG1.

CONCLUSIONS The E428G mutation resulted in a significant loss of sodium channel function (late sodium current decreases), which may be the electrophysiological mechanism by which this mutation causes SQTS. MOG1 showed different effects on wild-type and mutant (E428G) Nav1.5: Promoted transport of wild-type Nav1.5 to the membrane and inhibited transport of mutant (E428G) Nav1.5 to the membrane.

GW30-e0440

MircroRNA-10b promotes human embryonic stem cell-derived cardiomyocyte proliferation via a novel target gene LATS1

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OBJECTIVES Human cardiomyocytes (CMs) could not sustain their proliferative activity after birth thus it would be insufficient to compensate for the lost CMs after injury such as myocardial infarction, resulting in nearly irreversible cardiac dysfunction and terminal heart failure. Regulation of the Hippo pathway to promote endogenous CM proliferation has emerged as a promising strategy for heart regeneration. Previous studies have shown that the microRNA cluster miR302–367 negatively regulates the Hippo pathway, promoting CM proliferation. This study aims to determine whether another microRNA, miR-10b has any role in the regulation of cardiomyocyte proliferation and, if so, to explore the underlying mechanisms.

METHODS Human embryonic stem cell-derived cardiomyocytes (hESC-CMs) were produced by standard protocol of small molecules and served as the model to carry out our study. Quantitative PCR (qPCR) was performed to determine the expression pattern of miR-10b during the differentiation process. Gain- and loss-of-function assays were conducted to determine the role of mir-10b in CMs proliferation including immunofluorescent staining and qPCR. Flow cytometry was also used to explore the possible role of miR-10b in protecting CMs against apoptosis. We used bioinformatics analysis to predict the potential targets of miR-10b, luciferase reporter assays and RNA pulldown were used to confirm the relationship between miR-10b and the target genes. Further experiments were performed to explore the underlying mechanisms such as Western blotting, rescue and block assays.

RESULTS We found that the expression of microRNA-10b-5p (miR-10b) decreased during the maturation of human embryonic stem cell-derived

cardiomyocytes (hESC-CMs). In hESC-CMs, overexpression of miR-10b promoted the proliferation capacity, as revealed by both EdU and Ki67 staining. Increased expression of a variety of cell proliferation–associated genes, including PCNA, RACGAP1, NUSAP1, and CCNB, was detected by qRT-PCR as well. Conversely, knockdown of miR-10b suppressed cell cycle re-entry. Disorganized sarcomeres were observed after transfecting miR-10b proving that CMs were in a more dedifferentiated state. Moreover, Flow cytometry analysis showed that miR-10b transfection significantly reduced cell apoptosis compared to NC. qRT-PCR and luciferase assays helped us narrow down the potential targets predicted by bioinformatics screening, which we hypothesized that LAST1 was a major potential target. Overexpression of miR-10b led to decreased luciferase activity of the reporter with WT LATS1-3′UTR, indicating that LATS1 could be the direct target of miR-10b. Western blot analysis further showed that overexpression of miR-10b decreased LATS1 expression at the protein level. Furthermore, we tested the subcellular localization of YAP in hESC-CMs after transfection of miR-10b mimics or si-LATS1. The immunostaining results showed that transfection of miR-10b mimics or si-LATS1 increased the ratio of nuclear- to cytoplasmic-localized YAP.

CONCLUSIONS In summary, our study demonstrated that overexpression of miR-10b can activate hESC-CMs proliferation. Moreover, LATS1 is a direct functional target of miR10b and that miR-10b promotes hESC-CM proliferation, at least in part, by downregulating LATS1. Furthermore, we showed that miR-10b functioned, at least in part, by targeting LATS1. Our study suggests that miR-10b is a promising molecule for heart regeneration.

GW30-e0446

Meta-analysis of genotype-phenotype association between desmosomal genes and arrhythmogenic right ventricular cardiomyopathy

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OBJECTIVES Study the genotype-phenotype correlation between the desmosomal genes and ARVC by meta-analysis, and provide important clinical application basis for genetic testing in ARVC clinical individualized diagnosis and risk stratification.

METHODS This study systematically searched for the relationship between the mutations in desmosomal genes published in the Cochrane Library, PubMed, and Elsevier databases and the clinical phenotype of ARVC. Data was extracted and meta-analysis was performed using Revman 5.3 software. The Cochrane Q test and the I^2 statistic were used to evaluate the consistency of the included studies. The statistical analysis used a random effects model to conduct meta-analysis of common clinical features of ARVC, including patient demographic information and phenotypic characteristics based on diagnostic criterias.

RESULTS *Genotype-phenotype association meta-analysis of desmosomal genes and ARVC:* In total, 15 studies involving 1435 patients were included. The presence of desmosomal gene mutations was associated with a younger onset age of ARVC (32.9±14.7 vs. 41.3±13.1 years; P=0.007), a higher incidence of T wave inversion in V_1–V_3 leads (76.3 vs. 57.5%; P<0.00001) or family history of ARVC (23.4 vs. 8.17%; P=0.008). There was a statistically significant difference in the proportion of patients with a specific diagnosis of ARVC compared with those with a critical or probable diagnosis (RD=0.37; 95% CI, 0.22–0.52; P<0.00001). There was no difference in the proportion of males between desmosomal-positive and desmosomal-negative patients (69.6 vs. 66.8%; P=0.52). The presence of desmosomal gene mutations was not associated with global or regional structural and functional alterations (49.8 vs. 47.2%; P=0.29), epsilon wave (22.4 vs. 22.1%; P=0.43), sustained or non-sustained ventricular tachycardia (54.3 vs. 52.6%; P=0.19) and ventricular tachycardia of left bundle-branch morphology (60.8 vs. 59.0%; P=0.14).

Meta-analysis of genotype-phenotype association between PKP2 and ARVC: A total of 11 articles were included, including 1090 patients with ARVC. Compared with patients with ARVC caused by non-PKP2 gene mutation, the age of onset of PKP2 gene mutation was smaller (32.0±10.3 years vs. 34.7±13.2 years; P=0.03), and the incidence of T-wave inversion in V_1–V_3 lead Higher (78.6 vs. 64.3%; P<0.00001) and a higher probability of family genetic history (19.2 vs. 6.7%, P<0.0001). In male patients, there was no significant difference in the incidence of ARVC between the two (desmosomal group vs. non-desmosomal group) (68.3 vs. 68.9%; P=0.60). In addition, syncope (23.2 vs. 32.2%; P=0.36), ventricular tachycardia (63.5 vs. 60.5%; P=0.34), Epsilon wave (18.1 vs. 20.0%); Left bundle branch block ventricular tachycardia (60.4 vs. 58.8%; P=0.08), late potential and terminal activation duration prolongation in signal averaged electrocardiogram (62.9 vs. 55.2%; P=0.24), 24 h of premature ventricular beats > 500 (42.2 vs. 51.7%; P=0.87), ICD implantation (49.4 vs. 61.6%; P=0.89) there was no statistical difference.

CONCLUSIONS Patients with desmosomal gene mutations are characterized with an earlier onset age, a higher incidence of T wave inversion in V_1–V_3 leads and a strong family history of ARVC; Patients with ARVC who have mutations in the PKP2 gene have clinical features such as younger onset age, higher incidence of T-wave inversion in the chest lead, and more family history.

GW30-e0447

Pantoprazole induces bradyarrhythmia in mice under hypokalemia

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OBJECTIVES To investigate the mechanism of arrhythmia induced by pantoprazole in mice under hypokalemia.

METHODS Mice were randomly divided into control group, pantoprazole group, hypokalemic control group and hypokalemic pantoprazole group, n=20 per group. Pantoprazole 20 mg/(kg×d) was intraperitoneally injected for 5 weeks in pantoprazole group, the same amount of normal saline was given in control group. Hypokalemic control group and hypokalemic pantoprazole group were given intraperitoneal injection of furosemide 30 mg/(kg×d) for 1 week at the end of the fourth week of treatment with normal saline or pantoprazole. After 5 weeks, the ECG parameters (heart rate, PR interval, QRS interval, QTc interval) and spontaneous arrhythmia were monitored by Data Sciences International (DSI). The cardiac structure and functional status were recorded by echocardiography. The blood samples were withdrawn from the inferior vena cava. The changes of the mRNA and protein expression of hyperpolarization-activated and cyclic nucleotide-cation channels 2 and 4 (HCN2 and HCN4), cardiac voltage-gated sodium channel alpha subunit (SCN5A), L-type calcium channel alpha subunit (CACNA1C) and T-type calcium channel alpha subunit (CACNA1G) were analysed by real-time fluorescence quantitative PCR and Western blot technology.

RESULTS In the basal state, compared with the control group, the heart rate was decreased and the PR interval was prolonged in pantoprazole group (P<0.01; P<0.05); in the hypokalemic state, the heart rate and PR interval of hypokalemic pantoprazole group were further decreased and prolonged, respectively (P<0.01; P<0.05), and 4 mice developed sinus arrest while the hypokalemic control group did not appear (P<0.05). However, there was no significant difference in the QRS and QTc interval between pantoprazole group and control group in the basal and hypokalemic states, respectively. In the basal state, the expressions of HCN4 mRNA and protein in pantoprazole group were lower than those in control group (P<0.01), and the expressions in hypokalemic pantoprazole group were lower than those in hypokalemic control group (P<0.01). The expression of HCN2 mRNA in pantoprazole group was lower than that in control group (P<0.05), which was further decreased in hypokalemic pantoprazole group compared with hypokalemic control group (P<0.01).

CONCLUSIONS It is found that pantoprazole may lead to bradyarrhythmia in mice under hypokalemia, which may be related to abnormal expression of HCN2 and HCN4. Clinicians should be aware of adverse cardiovascular effects when using pantoprazole.

GW30-e0453

Activated protein C as an endogenous protease protects heart from ischemic insults in aging

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OBJECTIVES Activated protein C (APC), an activated protease of protein C zymogen, functions as an anticoagulant and a cellular homeostasis modulator with anti-inflammatory activities. Endothelial protein C receptor (EPCR) is crucial for APC signaling pathway. We revealed that APC is also an AMP-activated protein kinase (AMPK) agonist that exhibits cardioprotective effects against ischemic injury. We hypothesized that APC as an endogenous AMPK agonist could rescue an age-related impaired ischemic AMPK activity and improve the resistance of aged hearts to ischemic insults.

METHODS Cardioprotective effects of wild-type APC (APC-WT) and two derivatives, APC-2Cys (no anticoagulant activity) and APC-E170A (no cytoprotective activity) were examined after 45 min of ischemia and 24 h of reperfusion (I/R). APC activity and the expression levels of EPCR were monitored with/without I/R insults.

RESULTS APC treatment showed better beneficial effects on aged versus young hearts I/R injury. Moreover, APC's cardioprotection against I/R insults is independent of its anticoagulant activity. Both APC-WT and APC-2Cys derivative, but not the non-cytoprotective APC-E170A ameliorated cardiac systolic dysfunction and attenuated myocardial infarct size caused by I/R insults. APC-WT activated AMPK and inhibited inflammation in the ischemic heart. Intriguingly, APC-AMPK activation modulated post-ischemic cardiac

metabolism by increasing glucose/fatty acid oxidation ratio. APC generation was impaired in aged versus young hearts during I/R due to excessive shedding of EPCR. Both young and aged hearts exhibited similar protein C zomygen level and APC activity under physiological conditions. However, APC activity was abolished in aged but not young mice during I/R indicating an age-related impaired APC generation. There were significantly decreased cellular EPCR accumulation in aged versus young hearts during I/R linking the causation of the impaired APC generation to exaggerated EPCR shedding.

CONCLUSIONS APC signaling is impaired in aged versus young hearts in responding to I/R stress due to substantial shedding of EPCR, thus APC administration protects aged hearts against I/R insults through activating AMPK and suppressing inflammation.

GW30-e0460

The protective role of miR-199a/214 knockdown in cardiomyocyte hypertrophy and cardiac pathological remodeling

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OBJECTIVES To establish cardiac pathological remodeling models and sequence the possible important regulated microRNA (miRNA) through next-generation microRNA sequencing; To elucidate the possible regulatory mechanism of miR-199a/214 inhibition in neonatal rat ventricular cardiomyocyte hypertrophy model.

METHODS Cardiac pathological remodeling models were established by peritoneal injection of isoproterenol 30 mg/kg/d for seven consecutive days. Cardiac function was detected by using Vevo2100 ultrasound system. HE, Masson staining and biomarkers (ANP/BNP/β-MHC) were used to evaluate the pathological changes of cardiomyocytes. MiRNA expression profile of myocardium in cardiac pathological remodeling group and control group were detected by miRNA sequencing; Established cardiac hypertrophy model of neonatal rat ventricular cardiomyocytes (NRVMs), and transfected cardiomyocytes with miR-199a and miR-214 mimic or inhibitor. The morphology and size changes of cardiomyocytes were detected by confocal microscope through SAA and DAPI staining; Bioinformatics databases were used to predict the target of miR-199a and miR-214. Luciferase recombinant reporter plasmid with 3′-UTR of predicted target gene and the miR-199a/214 mimic was co-transfected into H293T cells to verify the targeting of miR-199a/214.

RESULTS Echocardiography showed that the LVEF, LVFS were significantly decreased, and LVSD was dramatically increased in the cardiac pathological remodeling. HE staining showed obvious ventricular septal hypertrophy, thickened ventricular wall and hypertrophy of cardiomyocytes in cardiac pathological remodeling. Masson staining showed that the collagen fibers in cardiac pathological remodeling were significantly increased. The ANP, BNP and β-MHC were significantly upregulated in cardiac remodeling; According to the analysis of all the 495 miRNAs in rat, we screened 137 miRNA expression with significant changes (fold change >2.0 or <0.5) in terms of TPM (Transcripts per million). Based on the comparison of the expression levels of these 137 miRNAs, we found that compared with the control group, there are 26 dramatic altered miRNAs expression in cardiac remodeling, 16 of which were not reported of cardiac function before; The α-actinin staining and the count of cell surface area of cardiomyocyte showed that the surface area of cardiomyocytes was significantly larger than that of the control group; after miR-199a and miR-214 were overexpressed, the expression of miR-199a and miR-214 were significantly upregulated compared with the control group. And the cardiomyocytes size was significantly reduced by miR-199a and miR-214 inhibition.

CONCLUSIONS MiRNAs are important regulators in cardiac pathological remodeling and the inhibition of miR-199a/214 in NRVM hypertrophy can significantly attenuate cardiomyocyte hypertrophy.

GW30-e0461

KDM3A inhibition modulates macrophage polarization to aggravates post-MI injuring and accelerates adverse ventricular remodeling via IRF4 signaling pathway

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OBJECTIVES Recently, emerging studies have verified that KDM3A involved in an important epigenetic mechanism in cardiovascular diseases. Our previous studies confirmed that KDM3A regulated the function of smooth muscle cells in high glucose environment and vascular remodeling in diabetes mellitus, the underlying mechanism was that KDM3A could regulate the inflammatory response. According to the above findings, we arrive the conclusion that KDM3A may play a central role in the inflammatory response of the cardiovascular system. Meanwhile, owing to macrophages play a key role in inflammatory repair after myocardial infarction, we attempt to explore whether KDM3A could regulate the polarization of macrophages to affect the inflammatory response after myocardial infarction and targeting KDM3A could influence the prognosis of myocardial infarction and adverse left ventricular (LV) remodeling.

METHODS In order to explore whether KDM3A could affect the function of macrophages, our experiment was randomly divided into three groups in vitro: (a) control group: The BMDMs without any treatment; (b) AdshRNA group: The BMDMs were infected by AdshRNA; (c) AdshKDM3A group: The BMDMs were infected by AdshKDM3A. Four groups were divided randomly in vivo: (a) wild-type rat sham operation group (WT-SO); (b) KDM3A knockout rat sham operation group (KO-SO); (c) WT-MI operation group; (d) KO-MI operation group. We analyzed the function of macrophages by phagocytosis and migration assay, and explored the polarization of macrophages. The expression of macrophage inflammation related genes in acute inflammatory phase and surface makers were detected by western blotting and immunofluorescence assay. Echocardiography, Masson's trichrome staining and Hematoxylin & Eosin (H&E) staining were detected the cardiac ventricular function.

RESULTS Inhibition of the expression of KDM3A in BMDMs led to the decrease of phagocytosis and attenuated the migration ability respond to chemokines of myocardial cell necrosis. Further, KDM3A deficiency led to increase in secretion of pro-inflammatory cytokines and more differentiation of macrophages into M1 phenotype under the LPS stimulation, but the ability of macrophages differentiated into M2 phenotype were inhibited under the IL-4 stimulation in vitro. Remarkably, there was a significantly difference in the infiltration of M1 and M2 macrophages between KO-MI and WT-MI groups at 7 days post-MI, we observed that more M1 macrophages ($CD86^+$) infiltration and higher M1/M2 ($CD86^+/CD206^+$) ratio in the myocardial infarction area of KO-MI rats. WT-MI rats, on the other hand, were more infiltrated of M2 macrophages ($CD206^+$). Western blot analysis revealed that the secretion trend of M1 (TNF-α, iNOS, CD86) or M2 (Arg-1, Ym-1, CD206) related phenotypic markers and cytokines in the two groups were consistent in vitro. Importantly, in the post-MI both left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (LVFS) at seven days and one month, fibrosis and cardiac function at 7 days in KO-MI group were worse than those in WT-MI group. Among above all, we confirmed IRF4 as downstream effector of KDM3A-dependent pathway to modulate macrophages polarization by western blot analysis.

CONCLUSIONS KDM3A plays an indispensable role in cardiac repair progress and LV remodeling by modulating macrophages phenotype in the post-MI via IRF4 signaling pathway, therefore suggesting a promising therapy to treat post-MI injuring.

GW30-e0465

Microbiota alteration in hypertension: a systematic review

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OBJECTIVES Hypertension is one of major risk factors to human health and influenced by various factors, including metabolism, immune, etc. Recent studies show gut microbiota can affect many human systems, such as immune, metabolic, and circulation systems; the composition of gut microbiota is altered in many diseases and disorders. However, the association between hypertension or blood pressure and gut microbiota remains unclear. In the present study, we aim to evaluate microbiota alteration in hypertension using a method of systematic review.

METHODS PubMed, EMBASE, and Web of Science databases were searched until March 2019 to identify eligible articles. Additional articles search according to specific authors in this field were also identified. Inclusion criteria were case-control studies based on stool samples with hypertension group and control group written in English or Chinese. Microbiota measures included alpha diversity index, beta diversity comparison, differential taxa, etc. Newcastle-Ottawa quality assessment scale (NOS) was used to assess the quality of the included studies.

RESULTS Six studies, with a total sample size of 590, were enrolled in this systematic review. The average score of NOS was 6.3, which was a score of high-quality category. We found alpha diversity in hypertension decreased significantly compared with control groups. For beta diversity analysis, hypertension cases can separate significantly with controls in both studies based on 16S rRNA sequencing and metagenomic analysis. Additionally, gut microbiota of hypertension showed over-growth of *Prevotella*, *Klebsiella*, *Parabacteroides*, etc.; whereas *Faecalibacterium*, *Roseburia*, etc. were higher in controls. In terms of function prediction analyses, the hypertensive gut microbiota exhibited increased lipid metabolism, including lipopolysaccharide biosynthesis and

steroid degradation, biosynthesis of phenylalanine and phosphatidylethanolamine, etc., and decreased metabolism of amino acid and some hydrolase family. Two gut microbial marker-based model to predict hypertension were developed with the area under the receiver operator characteristic curve (AUC) of 0.81 (95% CI: 0.53–1.00) and 0.78 (95% CI: 0.73–0.82).

CONCLUSIONS Hypertensive gut microbiota shows alterations in alpha diversity, beta diversity, taxa composition, and metabolism. These findings provide new insights for causality study and new gut-based therapies of hypertension. Further validation studies of specific bacteria and function genes in large population are needed.

GW30-e0498

Bisoprolol attenuates cardiomyocyte apoptosis and cardiac function by inhibiting calmodulin kinase II and NF-κB in ischemia-reperfusion injury rats

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OBJECTIVES To investigate the protective effects of bisoprolol (Biso) on cardiomyocyte apoptosis by inhibiting the activity of calmodulin kinase II (CaMKII) and express of NF-κB in ischemic-reperfusion (I/R) injury rats.

METHODS Sixty SD rats were randomly divided into Sham, I/R+Vehicle, I/R+Biso, Sham+Biso groups. The changes of cardiac function were evaluated by ultrasound cardiograph and catheterization. The area at risk (AAR) and infarct size were evaluated by TTC staining, the AAR was expressed as a percentage of the left ventricular area (AAR/LV). The plasma norepinephrine (NE) and the activity of myocardial CaMKII were measured by ELISA, and the expression of NF-κB was detected by Western blot. Cardiomyocyte apoptosis was examined by agarose gel electrophoresis and TUNEL's method. The mRNA levels of bax and bcl-2 were determined by RT-PCR.

RESULTS Compared with I/R+Vehicle, bisoprolol significantly decreased the infarct size and improved cardiac function, decreased plasma NE, and inhibited the activity of myocardial CaMKII and the express of NF-κB. Moreover, bisoprolol decreased the apoptosis index and the mRNA express of bax/bcl-2, and had no obviously DNA ladder.

CONCLUSIONS Biso could improve cardiac function and inhibit cardiomyocyte apoptosis by decreasing NE in plasma and inhibiting the activity of CaMKII and the express of NF-κB in I/R rats.

GW30-e0503

Long non-coding RNA MALAT1 protects epithelial cells from LPS-induced acute lung injury by regulating miRNA-181a-3p/Bcl-2

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OBJECTIVES Long non-coding RNA metastasis-associated lung adenocarcinoma transcript-1 (MALAT1) plays an important role in the pathophysiological process of inflammation. We aimed to investigate MALAT1 and its function in modulating miRNA-181a-3p and Bcl-2 in lipopolysaccharide (LPS)-induced acute lung injury (ALI).

METHODS We analysed MALAT1 in ALI patients, as well as the rat and alveolar epithelial cell models of LPS-induced injury. The expression of MALAT1 and miRNA-181a-3p were evaluated by qRT-PCR, and Bcl-2 was measured by western blot. Inflammatory factors tumor necrosis factor (TNF)-α, Interleukin (IL)-1β and IL-6 mRNA levels were also quantified by qRT-PCR. Luciferase reporter assay was used to verify direct interaction between MALAT1 and miRNA-181a-3p, or miRNA-181a-3p and Bcl-2. Transferase-mediated deoxyuridine triphosphate-biotin nick end labelling (TUNEL) assay was performed to detect alveolar epithelial cell apoptosis.

RESULTS Serum MALAT1 and Bcl-2 levels decreased in ALI patients, whereas miRNA-181a-3p, TNF-α, IL-1β and IL-6 levels increased ($P<0.01$, Figure 1). MALAT1 was inversely correlated to miRNA-181a-3p ($R=-0.508$, $P=0.0031$, Figure 2) in ALI patients. MALAT1 transfection downregulated miRNA-181a-3p level and upregulated Bcl-2 expression, alleviating alveolar epithelial cell apoptosis (Figure 3), whereas siMALAT1 reversed the effect both in rats and alveolar epithelial cells (Figure 4). MiRNA-181a-3p downregulated the Bcl-2 expression both in LPS-induced ALI rats and alveolar epithelial cells, as well as promoted apoptosis (Figure 5). TNF-α, IL-1β and IL-6 levels increased after LPS stimulation and decreased after MALAT1 transfection (Figure 6).

CONCLUSIONS The results demonstrate that LPS-induced ALI decreases lncRNA MALAT1, increases miRNA-181a-3p and inflammatory factor expression, downregulates the Bcl-2 level and promotes alveolar epithelial cell apoptosis. Overexpression of MALAT1 may protect alveolar epithelial cells from LPS-induced ALI via downregulating of miRNA-181a-3p.

GW30-e0521

Experimental confirmation of myocardial hypertrophic preconditioning during pregnancy and role of FoxO3a

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OBJECTIVES A woman's age at final pregnancy is correlated with post-reproductive longevity, and we previously reported a phenomenon termed myocardial hypertrophic preconditioning. Based on these data, we investigated whether myocardial hypertrophic preconditioning during pregnancy created anti-hypertrophic memory and cardiac resistance to subsequent pathological hypertrophic stress, as well slowing progression to heart failure.

METHODS In C57BL/6 mice, cardiac hypertrophy was induced by either transverse aortic constriction (TAC) or infusion of angiotensin II (Ang II). In addition, hypertrophy of cultured neonatal rat ventricular cardiomyocytes (NRVCs) was induced by exposure to Ang II. To assess the influence of preconditioning, mice at 3 weeks postpartum received Ang II infusion or TAC for the same period as the control group, or NRVCs were cultured with Ang II for 12 h and without it for 24 h, followed by re-exposure to Ang II for 48 h like control cultures.

RESULTS In C57BL/6 mice, the heart weight/body weight ratio and expression of fetal genes (ANP and β-MHC) were significantly lower after preconditioning. In addition, the lung weight/body weight ratio was significantly lower in the preconditioned group at 4 weeks after TAC. Consistent results were obtained with cultured NRVCs after Ang II treatment. Activation of FoxO3a was significantly enhanced in the hearts of postpartum mice and in preconditioned NRVCs, and this change persisted after re-exposure to the hypertrophic stimulus. Silencing of FoxO3a attenuated the anti-hypertrophic effect of pregnancy preconditioning in mice with Ang II infusion and increased cardiomyocyte growth and apoptosis, while overexpression of FoxO3a prevented such changes.

CONCLUSIONS Myocardial hypertrophic preconditioning induced by pregnancy confers resistance to subsequent hypertrophic stress and slows progression to heart failure. FoxO3a is involved in cardiac protection by pregnancy hypertrophic preconditioning.

GW30-e0522

The NAD+ precursor nicotinamide riboside alleviates alcoholic cardiomyopathy through Sirt3/PGAM5/FUNDC1-dependent mitophagy

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OBJECTIVES Nicotinamide riboside (NR) is widely used as a NAD+ precursor vitamin. Supplementation with NR has been shown to protect against metabolic disease in mammals. However, the potential effect of NR in alcoholic cardiomyopathy (ACM) has not been well elucidated. This study was designed to examine the effect of NR supplementation on the progression of alcoholic cardiomyopathy.

METHODS Alcoholic cardiomyopathy was established using chronic alcoholic diet containing 36% kcal from ethanol. Echocardiography and IonOptixMyoCam were used to evaluate cardiac contractile function.

RESULTS Our data revealed that NR alleviated alcohol consumption-induced changes in myocardial and cardiomyocyte contractile function as well as cardiac remodeling. To examine the possible involvement of mitophagy in NR-induced beneficial effects, $FUNDC1^{-/-}$ mice with mitophagy deficiency were employed. Interestingly, NR-induced beneficial effect against alcoholic cardiomyopathy was partially attenuated in $FUNDC1^{-/-}$ mice, indicating a role for FUNDC1-mediated mitophagy in NR-offered cardioprotection. *In vitro* study using H9c2 myoblasts suggested that NR regulated mitochondrial homeostasis through induction of FUNDC1-dependent mitophagy, as suggested by mitophagy-related protein expressions and Mitotracker-LC3 dots overlay. NR treatment enhanced cellular NAD^+ level, consequently elevated NAD^+-dependent mitochondrial sirtuin SIRT3 activity. Using mass spectrum assay and Co-IP, PGAM5, which functions to phosphorylate FUNDC1 at serine 13 (Ser13), was found to interact with and deacetylated by SIRT3 following NR administration.

CONCLUSIONS Taken together, our results revealed a protective effect of NR supplementation against alcoholic cardiomyopathy possibly associated with a SIRT3-PGAM5-FUNDC1- dependent regulation of mitophagy. These findings suggested the therapeutic potential of the vitamin B3 precursor of NAD+ in the management of alcoholic cardiomyopathy.

GW30-e0530

Protective effect of luteolin on LPS/ATP-induced pyroptosis in macrophages through suppressing AMPK/SIRT1/NLRP3/GSDMD pathway

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OBJECTIVES The incidence of atherosclerosis has increased dramatically in recent decades and has resulted in serious harm to human health. Atherosclerosis is a leading cause of death in developed countries and is characterized by the deposition of fibrous tissues and lipids in the intima of elastic arteries, leading to thrombus formation and structural damage marked by thickening and hardening of the vessel walls. Cell death and inflammation play critical roles at various stages of atherosclerosis. Pyroptosis is a pro-inflammatory form of regulated cell death and is dependent on the formation of inflammasome including NLRP3 and Caspase-1. In recent years, many studies have found that macrophage pyroptosis may play an important role in the progression of atherosclerosis. Therefore, finding a drug that can inhibit the pyroptosis of macrophages may delay the progression of atherosclerosis. Luteolin is a natural flavone, a subtype of flavonoid, which is abundant in edible plants, including broccoli, green chilies, onion leaf, French beans, carrots, white radish, clover blossom and ragweed pollen. A number of previous studies have reported that luteolin possesses beneficial medicinal properties, including anti-oxidant, anti-inflammatory and anti-aging actions. However, the effect of luteolin on atherosclerosis remains unclear. The aim of this study was to investigate the effects of luteolin on the pyroptosis in macrophages, and discuss the possible mechanisms of it.

METHODS Human THP-1 was induced into macrophages by treating with 0.5 nM PMA and then conducted with lipopolysaccharide (LPS) and ATP to induce pyroptosis. Before induction, we select 10 nM, 20 nM, 50 nM luteolin to pretreat macrophages. The cells were divided into the following five groups: control group, LPS+ATP group, 10 nM, 20 nM, and 50 nM luteolin pretreatment group. The Apoptosis and Necrosis Assay Kit and fluorescence microscope were used to detect the rate of cell pyroptosis. RT-PCR was conducted to measure the expression levels of NLRP3, Caspase-1, IL-1β and GSDMD. Western Blot was used to evaluate the protein expression of NLRP3, Caspase-1, IL-1β, GSDMD, AMPK and SIRT1.

RESULTS After pretreatment with luteolin, the rate of pyroptosis decreased obviously in comparison with that in LPS+ATP group ($P<0.05$). And the mRNA expression levels of NLRP3, Caspase-1, IL-1β and GSDMD in luteolin pretreatment groups are lower than control and LPS+ATP group in a concentration-dependent manner ($P<0.05$), so same as the protein levels. In addition, the protein expression of AMPK and SIRT1 show the downward trend in luteolin pretreatment groups.

CONCLUSIONS The results of the present study suggest that luteolin prevents the progression of atherosclerosis by decreasing macrophage pyroptosis during atherosclerosis, which is mediated by mechanisms including AMPK/SIRT1/NLRP3/GSDMD signaling.

GW30-e0531

Activation of MKKs/p38 signaling participates in ox-LDL induced inflammation in macrophages

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OBJECTIVES This study was aimed to investigate the role and mechanism of MKKs/p38 MAPK signaling in ox-LDL induced inflammation in macrophages.

METHODS ox-LDL at various concentrations were used to stimulate human THP-1 macrophages. specific p38 MAPK inhibitor SB203580 was used to inhibit the phosphorylation of p38 MAPK. Specific siRNA were used to silence MKK3 and MKK6. DCFH-DA fluorescent stain was used to detect the intracellular ROS. Concentrations of IL18 and TNFα in cell culture supernatant was measured by ELISA. Western blotting was used to assess the phosphorylations of MK3, MKK6 and p38 MAPK as well as the expressions of IL18 and TNFα in macrophages.

RESULTS Compared with control, after ox-LDL stimulation, the intracellular ROS level, culture medium supernatant IL18 and TNFα concentrations, the phosphorylations of MKK3, MKK6 and p38 MAPK, the expression of IL18 and TNFα in macrophages were significantly increased ($P<0.05$) in a ox-LDL concentration- dependent manner ($P<0.05$). The TAC was decreased dramatically by ox-LDL stimulation in a concentration- dependent manner ($P<0.05$). SB203580 significantly inhibited phosphorylation of p38 MAPK ($P<0.05$). siRNAs significantly silenced MKK3 and MKK6 respectively ($P<0.05$). SB203580 and siRNAs significantly decreased IL18 and TNFα in both culture medium supernatant and macrophages ($P<0.05$) without significant suppression on ROS level ($P>0.05$).

CONCLUSIONS ox-LDL stimulation increased intracellular ROS which further activated MKKs/p38 MAPK signaling to induce inflammation in macrophages.

GW30-e0532

Advanced glycation end products induces fibrotic responses of vascular smooth muscle cells via activating ASK1/MKKs/p38 signaling

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OBJECTIVES Phenotype shifting of vascular smooth muscle cells (VSMCs) was indicated to play a role at initial stage of atherosclerotic plaque formation by facilitating extracellular matrix deposition. This study was aimed to investigate the involved possible molecular mechanisms of advanced glycation end products (AGEs) induced fibrotic responses in VSMCs.

METHODS Cultured human coronary smooth muscle cells (HCSMCs) were exposed to AGEs. The apoptosis signal- regulating kinase 1 (ASK1) specific inhibitor AGI-1067 and siRNAs silencing *mkk3*, *mkk6* and *p38 mapk* were used to treat the cells respectively. Activations of MKK3, MKK6 and p38 MAPK were assessed by immunoblotting. Fibrotic response was assessed by fluorescence immunohistochemistry staining of collagen I and VIII. Activation of Immunoprecipitation determined the association of ASK1 and its inhibitor thioredoxin. A kinase assay was used to determine the ASK1 activity.

RESULTS AGEs incubation significantly activated ASK1, MKK3 and MKK6 which lead to activation of p38 MAPK, resulting in up-regulated fibrotic response in HCSMCs. However, siRNAs knocking down *mkk3*, *mkk6* and *p38 mapk* impaired this fibrotic response. AGI-1067 administration not only dramatically inhibited the activation of ASK1/MKKs/p38 MAPK, but also suppressed the expression of the down- stream proteins including transforming growth factor-β1 (TGF-β1), connective tissue growth factor (CTGF), collagen I and collagen VIII in HCSMCs exposed to AGEs.

CONCLUSIONS ASK1/MKKs/p38 MAPK pathway was activated by AGEs, leading to fibrotic response in VSMCs.

GW30-e0533

Ryanodine receptor 2 mediated calcium overload is involved in advanced glycation end products induced cardiac dysfunctions

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OBJECTIVES Featured by heart dysfunction, the diabetic cardiomyopathy is causing mortality and morbidity in type 2 diabetes mellitus patients. This study was aimed to investigate the molecular mechanisms of advanced glycation end products (AGEs)-induced cardiac dysfunctions.

METHODS Rats and isolated primary myocytes were exposed to AGEs. Left ventricular hemodynamic parameters were used to assess the cardiac function. Cell apoptosis was detected with TUNEL assay. Calcium indicator was used to determine the intracellular calcium concentration (Ca2+](i)). The molecular coupling between FK506-binding protein 12.6 (FKBP12.6) and ryanodine receptor 2 (RyR2) was evaluated by immunoprecipitation. Apoptotic protein expressions were measured by western blotting. The activity of RyR2 was measured by [H-3]-ryanodine binding assay.

RESULTS AGEs exposure impaired systolic and diastolic functions and induced apoptosis in myocardium. AGEs exposure also elevated [Ca2+](i), decreased mitochondrial membrane potential (MMP) and induced cell apoptosis in myocardium and cultured myocytes. AGEs impaired association between FKBP12.6 and RyR2 and further increased RyR2 activity in vivo and in vitro. The expression levels of cytochrome c and active caspase3 were elevated by AGEs exposure.

CONCLUSIONS AGEs induced cardiac dysfunctions by modulating RyR2-mediated calcium overload- triggered myocardial apoptosis.

GW30-e0550

GDF15 attenuates isoproterenol-induced cardiac energy dysfunction via promoting glycolysis and mitochondrial respiration

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OBJECTIVES The aim of the study is to investigate the effect of GDF15 on energy metabolism in heart failure. To elucidate the mechanism of GDF15 on

the regulation of glycolysis and mitochondrial oxidative respiration in heart failure induced by sympathetic stress.

METHODS The replication-deficient adenoviral vectors were utilized to overexpress or knockdown GDF15 in neonatal rat cardiomyocytes (NRCM). XFe96 Extracellular Flux Analyzer (Seahorse Biosciences) was used to detect the energy phenotype of cardiomyocytes, which were stimulated by ISO (10^{-5} M) or corresponding control. Both mitochondrial oxygen consumption rate (OCR) and rate of extracellular acidification (ECAR) were recorded by Seahorse Analyzer. The direct measurement was recorded as the baseline OCR, followed by the addition of ISO (10^{-5} M) to observe the oxidative respiration level after sympathetic overactivation, and oligomycin (2 μM) to measure the ATP-linked OCR, the oxidative phosphorylation uncoupler FCCP (2 μM) to indicate the maximal respiration. Finally, rotenone (1 μM) and antimycin A (1 μM) were injected to determine non-mitochondrial respiration. In ECAR test, after ECAR-baseline were recorded, ISO (10^{-5} M) were added to observe the effects of sympathetic overactivation on cell oxidative respiration, then glucose (10 mM) was added to measure glycolysis, and oligomycin (2 μM) to measure the glycolytic capacity. Lastly, 2-DG (50 mM) was injected to determine non-glycolytic acidification. In vivo, GDF15−/− and wild type Wistar rats were subcutaneously injected with ISO 10 mg/kg/day or corresponding saline solution for 4 weeks, then the Vevo 2100 Imaging System were utilized to observe the cardiac structure and function. To explore the key mechanisms of GDF15 in regulating glucolysis, differentially expressed genes (DEGs) were analyzed and screened from Gene Expression Omnibus (GEO) datasets (GSE 7033) using a bioinformatics approach.

RESULTS Overexpression of GDF15 increased the glycolysis, glycolytic capacity and glycolytic reserve of cardiomyocytes indicated by ECAR analysis. GDF15 also enhanced the oxidative respiration of mitochondria, including ATP production and maximum respiration in cardiomyocytes. Conversely, knockdown of GDF15 resulted in significantly reduced glycolysis, glycolytic capacity and glycolytic reserve of cardiomyocytes, and slightly reduced mitochondrial oxidative respiration level compared with the control group. We found that compared with the wild type, the incidence and mortality of heart failure in GDF15−/− rats increased significantly. RNA-seq data analyzed by KEGG showed that GDF15 knockout leading to LDHA upregulation by 5.19 times and ALDH1A3 downregulation by 14.96 times.

CONCLUSIONS GDF15 is increased in ISO-induced heart failure rats, GDF15 promotes myocardial cell glycolysis and mitochondrial oxidation to increase the production of ATP. GDF15 makes the energy metabolism of cardiomyocytes tend to a compensatory state and plays a protective role on metabolic failure of cardiac myocytes induced by sympathetic overactivation.

GW30-e0556

Identification of potential miRNA duplexes associated with myocardial infarction

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OBJECTIVES MicroRNAs (miRNAs) have been proved to be involved in myocardial infarction (MI), and they function by targeting 3′-untranslated region (3′-UTR) of specific messenger RNA (mRNA). However, only a small number of miRNAs exert their functions in that way, and we speculated there should be novel mechanisms for miRNAs. It's recently reported that nuclear miR-122 can directly regulate the biogenesis of miR-21 at the posttranscriptional level through forming hybridization between mature miRNAs and primary miRNA (pri-miRNA), which is based on generally accepted miRNA silencing mechanism, but no such mechanisms have been reported in MI yet. Therefore, we conducted this study to determine whether there were such miRNA-miRNA duplexes involved in the pathogenesis of MI.

METHODS We constructed microRNA correlation matrices of circulating miRNAs assessed in the datasets of GSE61741. In this context, we focused on miRNA pairs with negatively correlated expression levels, since negative correlation is a necessary feature of the novel mechanism of action of miRNAs. To determine how MI affected the miRNA correlations, we compared the difference of miRNA correlation coefficients in the two groups by Fisher's Z score. In addition to negative correlation, appropriate complementary binding between one primary microRNA and another mature microRNA is also a prerequisite for this new mechanism, and the site binding to the mature microRNA seed region must be located within 1000 nucleotides away from the 3′ or 5′ ends of premature microRNA transcript, and the minimum free energy of the binding should be lower than −20 kcal/mol. Here, RNAhyrid was used to identify if there were proper binding sites between the miRNA pairs. Those miRNA pairs, which hold appropriate binding sites, were defined as duplexes and may be involved in the pathogenesis of MI through a new mechanism of action of microRNAs. KEGG and Go slim analysis were conducted to reveal the functions of these nominated miRNA pairs. Further, to figure out whether these duplexes could discriminate MI patients from the healthy individuals, we compared the diagnostic value of each single miRNA of the duplex and the union of them by plotting the ROC based on another completely independent dataset GSE31568.

RESULTS (1) By comparing the Z scores, we screened out 444 miRNA pairs in which negative correlation coefficients increased or decreased significantly in MI group compared with healthy group. (2) 9 miRNA pairs out of 444 have at least one binding site between one primary microRNA and another mature microRNA. (3) The nominated 9 miRNA pairs were functionally associated with signaling pathways involved in MI, such as MAPK (FDR, 1.15E-02) and hippo signaling pathways (FDR, 4.70E-06), and cellular nitrogen compound metabolic process (FDR, 5.26E-116). (4) We analyzed diagnostic value of the duplexes for MI, and found that six pairs, which werehsa-miR-516b-3p & hsa-miR-1285-3p, hsa-miR-521 & hsa-miR-1285-3p, hsa-miR-339-5p & hsa-miR-663a, hsa-miR-593-5p & hsa-miR-193a-5p, hsa-miR-362-5p & hsa-miR-767-5p, hsa-let-7a-5p & hsa-miR-142-5p, had larger area under ROC (AUC) when they were combined than separately analyzed.

CONCLUSIONS We found that six pairs of microRNAs were associated with MI by a new mechanism of forming duplexes. Combined application of each pair of microRNAs in the duplex can significantly improve the diagnostic value of MI.

GW30-e0558

The effect of HMGA1 in LPS-induced myocardial inflammation

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OBJECTIVES The High Mobility Group A1 (HMGA1) proteins, serving as a dynamic regulator of gene transcription and chromatin remodeling, plays an influential part in the pathogenesis of a variety of cardiovascular diseases. However, the precise role of HMGA1 in sepsis induced cardiomyopathy (SIC) remains unclear. This study was designed to illustrate the effect of HMGA1 involved in SIC.

METHODS Cardiomyocyte-specific HMGA1 overexpression was obtained using an adeno-associated virus system with intramyocardial injection in mice heart. The model of SIC in mice was constructed via intraperitoneal injection of lipopolysaccharide (LPS) for 6 h. H9c2 rat cardiomyocytes was stimulated with LPS for 12 h. Western blotting was used to detect the expression level of the protein, PCR was applied to exam the transcription level of RNA, and TUNEL staining was utilized to test the apoptosis level of the cells.

RESULTS HMGA1 expression was upregulated in murine inflammatory hearts as well as LPS stimulated H9c2 cardiomyocytes. HMGA1-overexpressing exhibited aggravated cardiac dysfunction, cardiac inflammation as well as cardiac apoptosis following LPS treatment both in vivo and in vitro experiment. Interestingly, HMGA1 knockdown in H9c2 cardiomyocytes attenuated LPS-induced cardiomyocyte inflammation, but aggravated cell apoptosis. Mechanismly, we found that overexpression of HMGA1 induced increased expression of cyclooxygenase-2 (COX-2). COX-2 inhibitor blunted the aggravation of inflammation and apoptosis in HMGA1 overexpressed H9c2 cardiomyocytes. Whereas, HMGA1 knockdown induced a reduction in signal transducer and activators of transcription 3 (STAT3) expression. STAT3 agonist reversed HMGA1 silence induced anti-inflammatory effects, while ameliorated cell apoptosis induced by LPS.

CONCLUSIONS In conclusion, our results suggest that overexpression of HMGA1 aggravated cardiomyocytes inflammation and apoptosis by up-regulating COX-2 expression, while silence of HMGA1 expression attenuated inflammation but aggregated cell apoptosis via down-regulation of STAT3.

GW30-e0564

Long non coding RNA Linc00092 alleviates the activation of cardiac fibroblast via inhibiting glycolysis

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OBJECTIVES Cardiac fibrosis is considered as the key pathophysiology of heart disease. Looking for a target to interfere in cardiac fibrosis exerts great influence. The heart contains a heterogeneous group of cells. Fibroblast is a hot focus for fibrosis research. Recently, several LncRNAs prove to participate. In different physiological functions of different cells by regulating glycolysis. Moreover, it is demonstrated that glycolysis contributes to fibrosis. However, it is still not clear whether lncRNAs exert influence on cardiac fibrosis via regulating glycolysis.

METHODS We use human primary cardiac fibroblast for the vitro test and papillares musculi (PM) from human cardiac valvulectomy (nonfibrotic heart tissue) and ventricular aneurysm tissue (VA) from human ventricular aneurysm resection (fibrotic heart tissue) for vivo tissue detection test. For the knocked down and rescue test, we use siRNA and adenovirus plasmid respectively. Western blog, PCR, Elisa detection and fluorescence in situ hybridization dectection (Fish) were main tools to detect the markers of activation of fibroblast while CCK8 assays, transwell and scratch test are main tests to assess the function of fibroblast.

RESULTS We searched lncRNAs which had reported on Pubmed to be in correlation with glycolysis and detected their expression in cardiac fibroblasts

activation model induced by TGF β1 by RT-qPCR. As a result, 28 lncRNAs were found and detected. Among them, Lincoo092 exhibited the most significant change. To further explore the function of Lincoo092 in cardiac fibrosis, we dectected the expression of Lincoo092 in papillares musculi (PM) from human cardiac valvulectomy (nonfibrotic heart tissue) and ventricular aneurysm tissue (VA) from human ventricular aneurysm resection (fibrotic heart tissue). As a result, the expression of Lincoo092 decreased in VA compared with PM. Furthermore, we demonstrated that Lincoo092 was mainly expressed in fibroblast rather than cardiomyocyte by a fluorescence co-localization test with fluorescence probe of Lincoo092, cardiac troponin T (marker of cardiomyocyte) and vimentin (marker of fibroblast). Then we knocked down Lincoo092 with siRNA and overexpressed it with Lincoo092 adenovirus plasmid. We found that its knocked down could not only increase the expression of α-SMA and COLIA1 but also strengthen the ability of proliferation, migration and the secretion of COLIA1 of cardiac fibroblast together with intensive glycolysis. On the contrary, over-expression of Lincoo092 could exert the opposite effect by decreasing the expression of CTGF and inhibiting the ability of proliferation, migration and the secretion of COLIA1 of cardiac fibroblast together with lessened glycolysis. Besides, we could reverse the increased expression of α-SMA and COLIA1 after knocking down Lincoo092 with the help of 2-deoxyglucose, a glycolysis inhibitor. On the contrary, when we overexpressed PKM2, a key enzyme of glycolysis, the expression of α-SMA and CTGF increased.

CONCLUSIONS Glycolysis contributes to the activation of cardiac fibroblast. Lincoo092 could alleviate the activation of cardiac fibroblast via inhibiting glycolysis.

GW30-e0565

IL-33 inhibits endoplasmic reticulum stress and alleviates cardiac lipotoxicity via promoting autophagy

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OBJECTIVES Prolonged endoplasmic reticulum stress (ER stress) is the key mechanism in cardiac lipotoxicity-induced apoptosis. IL-33 is a potent cardiac protector but the role of IL-33 in cardiac lipotoxicity and ER stress is unknown. Autophagy is essential to maintain homeostasis but its role in cardiomyocytes ER stress also be elusive.

METHODS Effects of IL-33 on lipotoxicity, ER stress and autophagy were assess using db/db mice and palmitic acid (PA) treated cardiomyocytes. The role of ER stress and autophagy in the effects conferred by IL-33 and the mechanism that IL-33 regulates ER stress and autophagy were investigated.

RESULTS db/db mice and PA treatment were associated with enhanced ER stress and apoptosis, which could be reversed by ER stress inhibitor. PA inhibited autophagosome formation and impair autophagic flux. IL-33 and the autophagy inducer, rapamycin, improved cardiac diastolic function, released ER stress, cardiac lipid accumulation and apoptosis. The non-selective autophagy inhibitors, either 3-MA or wortmannin, abolished the effects of IL-33 in reducing ER stress and apoptosis. By gene expression profile analysis, we identified insulin like growth factor binding protein 3 (IGFBP3) as one of the genes mostly distinct between treatments with or without IL-33. siRNA against IGFBP3 mRNA significantly dismissed the effects of IL-33 on ER stress, autophagy and apoptosis.

CONCLUSIONS IL-33 released cardiac lipotoxicity via alleviating ER stress and promoting autophagy. IGFBP3 is essential for IL-33 induced ER stress resolution and autophagy enhancement during cardiac lipotoxicity.

GW30-e0569

cRGD modification improves stem cell homing after myocardial ischemia reperfusion

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OBJECTIVES Poor cell homing limits efficacy of cardiac cellular therapy. The cyclo Arg-Gly-Asp (cRGD) peptide binds with high specificity to platelet which is involved in repair of tissue injury.

METHODS Here, we assessed if cRGD-modified stem cells had enhanced platelet-mediated homing ability resulting in better functional recovery and structural preservation in a rat myocardial injury model. cRGD-modified mesenchymal stem cells (cRGD-MSCs) were obtained via membrane fusion with cRGD-modified liposomes. The cRGD-MSCs targeting ability of platelet was examined both in vitro and in vivo.

RESULTS Under both static and flow conditions in vitro, cRGD peptide significantly enhanced MSCs binding and capture ability to platelet. cRGD-MSCs showed higher accumulation than unmodified MSCs in injured rat myocardium in acute phase after administration, resulting in better structural preservation and functional recovery.

CONCLUSIONS Platelet is therefore a novel target for enhancing homing of transplanted cells to injured myocardium, and the platelet-targeting delivery system maybe a generalizable platform technology for regenerative medicine.

GW30-e0575

Endothelial cell-specific ADAR1 deletion increases vascular permeability and inhibits angiogenesis in mice

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OBJECTIVES Adenosine deaminases that act on RNA (ADARs) catalyze adenosine to inosine conversion in RNA. ADAR1 plays a critical role in the differentiating cells in embryo and adult tissues to support the cell's survival, differentiation and maturation. Previous studies have shown that ADAR1 knockout in mice results in embryonic lethality with impaired vascular development. But the precise roles of ADAR1 in the endothelium remain elusive. We used a mice model to determine the effect of endothelial cell (EC)-specific knockout of ADAR1 on vascular homeostasis.

METHODS Wild-type (WT) mice, $ADAR1^{-/-}$ mice, $ADAR1^{ECKO}$ mice, $ADAR1^{flox/flox}$ mice and Human umbilical vein endothelial cells (HUVECs) were used. Knockdown of ADAR1 was mediated by siRNA carried by Lipofectamine 2000. Tissues were collected for histological observation or transmission electron microscope detection. Vascular permeability was measured by Evans Blue-labeled albumin in vivo and in vitro. Hindlimb ischemia model and aorta ring assay were used in mice and tube formation assay was used in HUVECs. Expression protein was measured by Western blotting or Immunofluorescence.

RESULTS We show that EC-specific disruption of ADAR1 in mice caused partial postnatal lethality and lung defects. Vascular permeability was enhanced in $ADAR1^{ECKO}$ mice, which may be associated with dilated interendothelial junctions and decreased Caveolin-1 expression. Angiogenesis was inhibited by deletion of ADAR1 in vivo and in vitro. Knockdown of ADAR1 in ECs resulted in marked inhibition of VE-Cadherin, which could be recovered by a peptide encoding the caveolin-1 scaffolding domain.

CONCLUSIONS Our findings establish a crucial role of an ADAR1/Caveolin-1 axis in endothelial homeostasis

GW30-e0598

Effect of Shenfuyixin formula on apoptosis of myocardial cells in rats with heart failure following myocardial infarction

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OBJECTIVES This study was designed to determine the effects of Shenfuyixin formula (SFYX) on the myocardial cell apoptosis and apoptosis-related factors in rats with HF induced by myocardial infarction (MI).

METHODS HF was induced by the ligation of left anterior descending coronary artery in adult male Sprague-Dawley rats. Based on the cardiac function at week 4 after MI, all rats were randomly divided into 5 groups: Sham-operated group; HF+vehicle group; routine dose of SFYX group (1.76 g/kg/d) and high dose of SFYX group (8.8 g/kg/d), and lorsartan group (10 mg/kg/d). Equivalent distilled water was given to rats in sham and model groups, and the corresponding drugs dissolved in distilled water were orally gavaged in the drug intervention groups once a day, each group was given medication or water for 4 weeks. The left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), left ventricular ejection fraction (LVEF) and left ventricular fractional shortening (LVFS) were measured by echocardiography at week 4 after the delivery. The apoptotic index of cardiomyocytes was evaluated by TUNEL staining. The protein expressions of apoptosis-related factors Bcl-2, Bax and caspase-3 were determined by Western blot.

RESULTS Compared to HF+vehicle group, SFYX at the dose of 8.8 g/kg/day attenuated the increases in LVEDD (10.21±0.70 vs. 8.77±1.10 mm, P<0.01) and LVESD (8.89±0.55 vs. 6.16±1.53 cm, P<0.01), and the decreases in LVEF (31.64±13.10 vs. 55.20±14.28%, P<0.01) and LVFS (15.54±6.20 vs. 30.72±9.73%, P<0.01) at week 8 after MI. The apoptotic index of cardiomyocytes was decreased in high dose of SFYX rats compared to HF+vehicle rats (8.52±2.70 vs. 16.17±1.41%, P<0.01). In addition, treatment with SFYX at the dose of 8.8 g/kg/day inhibited the expression of Caspase3 and Bax compared to HF+vehicle rats at week 8 after MI (Caspase3: 1.18±0.10 vs. 1.66±0.25% GAPDH arbitrary units, P<0.05; Bax: 0.66±0.19 vs. 1.28±0.13% GAPDH arbitrary units, P<0.01), and increased the ratio of Bcl-2/Bax (1.21±0.23% vs. 0.54±0.06%, P<0.01).

CONCLUSIONS Our studies showed that SFYX administered after HF improved cardiac function, and inhibited left ventricular dilatation and the apoptosis of myocardial cells. The results were associated with the decreased expression of Caspase3 and Bax. Our data suggest that SFYX may inhibit myocardial apoptosis and improve cardiac function, which were associated with

the inhibition of the overexpression of apoptotic factors Bax and caspase-3 in rats with HF following MI.

GW30-e0608

Intermedin1-53 attenuates aging-associated vascular calcification in rats by upregulation of sirt1

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OBJECTIVES Vascular calcification is a very common phenomenon in the elderly. Intermedin (IMD) is a cardiovascular bioactive peptide maintaining vascular homeostasis and inhibiting vascular calcification. In this study, we aimed to investigate whether IMD_{1-53} attenuates aging-associated vascular calcification.

METHODS Aging-associated vascular calcification was induced by vitamin D3 plus nicotine (VDN) in old rats. In vitro, senescence-related calcification of vascular smooth muscle cells (VSMCs) in rats, human and $IMD^{SMC-/-}$ mice were induced using osteogenic media. Rats or VSMCs were treated with IMD_{1-53} peptide.

RESULTS Old rats treated with VDN showed more severe calcification in aortas compared with young control group, and with decreased expression of IMD. Exogenous administration of IMD_{1-53} significantly reduced the calcium deposition, destruction of vascular structure and collagen contents in old VDN rats. IMD_{1-53} also inhibited the transdifferentiation of VSMCs from a contractile to an osteogenic phenotype in old calcified aortas. Moreover, aging-related markers p16, p21 and β-galactosidase were all markedly decreased by IMD_{1-53}. Mechanistically, IMD_{1-53} significantly increased the antiaging factor sirt1 expression and decreased the sirt1 substrate acely-p53/total-p53 level. These results were further confirmed in both rat and human senescent calcified VSMCs in vitro. Furthermore, the inhibitory effects of IMD_{1-53} on calcification and senescence were blocked by sirt1 knockdown. In addition, IMD-deficient VSMCs showed severe senescence features coincided with osteogenic transition, and had significantly decreased expression of sirt1 as compared with VSMCs from wild type mice.

CONCLUSIONS IMD deficient VSMCs are more prone to senescence and calcification, and administration of IMD_{1-53} can attenuate aging-associated vascular calcification by upregulating sirt1.

GW30-e0611

Amphiregulin promotes cardiac fibrosis post myocardial infarction by inducing endothelial-to-mesenchymal shift via EGFR pathway in endothelial cell

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OBJECTIVES *Background:* Endothelial mesenchymal transition (EndMT) plays a key role in the development of cardiac fibrosis (CF) after acute myocardial infarction (AMI). Our previous study has showed that the expression of Amphiregulin (AR) was enhanced after MI and promoted CF by inducing cardiac fibroblast activation. However, the role of AR on EndMT post MI is still unknown. This study aimed to explore the impact of AR on EndMT post MI and related mechanisms.

METHODS HUVECs and MAECs were originated from the umbilical cord of healthy women and the abdominal aorta of C57BL6 mice (8–12 weeks old) respectively. The two types of cells were deposed with different concentrations of AR (0, 10, 100, 1000 pg/mL) and then the cell viability and apoptosis were measured by CCk-8 assay and Annexin V-PE/7-AAD. Western bolt, Real-time PCR, Immunofluorescence were used to detect the cell markers of EndMT at 48 h in endothelial cells after AR stimulation. In vivo, We extracted the myocardium of the border area, the infarct zone and the infarct border zone in the heart of MI mice to detect the expression level of AR at different time points (1, 3, 5, 7, 28 days). Artificially synthesized AR lentivirus (AR-shRNA) was used to knock down the expression of AR in MI mice and then the mice were randomly divided into four groups: Sham group, MI group, MI-shNC group and MI-shAR group. WB, RT-PCR, Immunofluorescence techniques were used to detect the changes of EndMT in the infarct border area, the cardiac ultrasonography was used to detect cardiac function and the Picrosirius Red staining was used to measure CF in those mice. In vitro and vivo Western bolt were used to detect the signaling pathway of AR inducing EndMT in endothelial cells and myocardium in MI mice.

RESULTS In vivo, EndMT which was verified by co-labeling of cells with the myofibroblast and endothelial cell markers was significantly declined after lentivirus-AR-shRNA delivered into the infarct border zone post MI. Moreover, silencing AR ameliorated cardiac function by decreasing the extent of CF of MI mice. In vitro, endothelial cells treatment with AR promoted cell proliferation and anti-apoptotic capacity. In addition, EndMT which was confirmed by detecting the markers of endothelial cells and fibroblast, the expression of epidermal growth factor receptor (EGFR) and the downstream genes such as PI3K/AKT and β-cateninon in endothelial cells was significantly enhanced after stimulation with AR. All these effects could be eliminated by EGFR inhibitor. Furthermore, in vivo, EGFR and the downstream genes in infarct border zone were all significantly decreased in MI mice which were injected with lentivirus-AR-shRNA.

CONCLUSIONS Our results demonstrate that AR induces CF post MI not only by directly activating cardiac fibroblast but also by enhancing EndMT in endothelial cells. All the results show that AR plays a key role in promoting CF post MI. Targeting regulation of AR may provide a new potential therapeutic option for CF after MI.

GW30-e0612

Optogenetics defibrillation of ventricular tachyarrhythmia in myocardial infarction rats in vivo

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OBJECTIVES Optogenetics is a low-invasive, flexible and highly selective intervention. The purpose of our experiment is as follows: (1) explore optogenetic defibrillation and the possible mechanism of continuous illumination defibrillation. (2) explore the effects of optogenetic termination and electric termination of myocardial infarction ventricular tachyarrhythmia (VT) in vivo.

METHODS Systemic delivery via right jugular vein injection of (AAV9-CAG-hChR2(H134R)-mCherry) were performed in juvenile SD rats to achieve the light sensitive protein Channelrhodopsin-2 transfer throughout the whole heart. Ventilation, thoracotomy and recording ECG were performed after anesthesia in rats. Every heart was illuminated by 473 nm laser or electrical stimulated on the right ventricle in a train of 30 pulses at 8 Hz to test the threshold of light intensity or electrical pacing voltage. After that, myocardial infarction was induced by ligation of the left anterior descending coronary artery, and then VT was induced by electrical burst stimulation (10 v, 50 Hz, 2 s). First, we investigated the effects of optogenetic defibrillation and its underlying mechanism by different illumination modes of multiple light intensity (2, 4, 8, 10, 20 times threshold intensity) and pulse duration (20, 50, 200, 500 and 1000 ms). Then, the VT termination process during 20 s after burst stimulation was investigated in different performance: optical termination, 1 s constant illumination repeated in 4 episodes with 1 s interval (470 nm, 20 times threshold intensity); electrical termination, anti-tachycardia pacing (ATP) in 8 pulses of 8 Hz with 2 ms duration in 4 times pacing threshold; natural recovery from VA, without optical or electrical intervention. Recovery time was defined as the time from the end of the burst stimulation to the recovery of sinus rhythm, and the termination rate was the percentage of sinus rhythm recovery after the end of burst stimulation with or without any intervention.

RESULTS (1) We demonstrated that VT could be terminated by illumination of the right ventricle at 20 times threshold intensity in 1 s with the successful defibrillation rate of 95±2.673% (mean±SEM; N=7). Herein, the successful optogenetic defibrillation rate was strongly depending on light intensity (N=5, n=50 episodes, P=0.0118) and duration of illumination (N=5, n=50 episodes, P<0.0001). In regard to mechanism of optogenetic defibrillation, we observed that higher light intensity and longer pulse duration were more conducive to induce an episode of light-triggered focal excitement by ChR2-mediated depolarization. (2) We analyzed the recovery time and the termination rate. The sequence of recovery time was optical termination (7.328±0.3623 s)<electric termination (10.31±0.4482 s)<natural recovery (12.97±0.3834 s). And we confirmed that the termination rate of optical illumination (86.14±4.145%) was higher than those of ATP (63.5±6.371%) and natural recovery (47.71±5.476%).

CONCLUSIONS Optogenetic defibrillation is a highly effective intervention and optogenetic manipulation can shorten recovery time and increased the termination rate in myocardial infarction ventricular arrhythmia. We believe that optogenetic approach is potentially to be translated into more efficient and pain-free clinical termination of ventricular arrhythmia.

GW30-e0613

A mouse model of overwork resulted in heart failure

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OBJECTIVES Overwork is an important cause of cardiovascular diseases such as coronary heart disease, hypertension, arrhythmia. The research on cardiovascular damage caused by overwork stress mainly stays in epidemics and populations, and lacks deep molecular mechanism research. This study aims to construct an animal model of overwork that causes cardiovascular damage and to explore its outcomes and mechanisms.

METHODS Five C57BL/6 mice were placed in a plastic box with a water depth of 0.8 cm and a size of 29 cm×18 cm×15 cm for 8 h/day for 30 days to simulate overworked state caused by stress factors such as fatigue, lack of sleep, fear and anxiety. Then we performed echocardiography to detect functional and structural changes in the mouse heart, and initially explored its mechanism through transcriptome sequencing

RESULTS In the overworked group, the left ventricular ejection fraction (EF) and fractional shortening (FS) were significantly decreased (EF: 36.57 vs. 49.44%, FS: 17.49 vs. 24.57%), while the left ventricular internal diameter both in the systolic phase (LVIDs) and in the diastolic phase (LVIDd) were significantly increased, compared with normal mice. In addition, transcriptome sequencing indicated that a large number of gene expression was significantly up-regulated or down-regulated in the myocardial tissue of the overworked mice. The sequencing cluster analysis revealed that immune system, GPCR signaling, platelet activation and glucose metabolism-related expression were elevated in overworked group.

CONCLUSIONS We have developed an overworked mouse model that leads to dilated cardiomyopathy and heart failure, which is available for molecular mechanisms of cardiovascular diseases caused by overwork-related stress. And this study suggests that immune system, GPCR signaling, platelet activation and glucose metabolism are associated with cardiovascular damage after overwork.

GW30-e0638

The protective effect of geniposide on palmitate-induced H9C2 lipotoxicity injury by inhibiting oxidative stress, inflammation and apoptosis via regulating PK2 pathway

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OBJECTIVES The over consumption of a high-fat diet, which increases the levels of the saturated free fatty acid palmitate in the serum, is one of the contributing factors in overweight or obese. In this study, H9C2 cardiomyocytes treated with palmitic acid (PA) were used as hyperlipidemia model. The protective effect of geniposide (Gen) against PA-induced cardiomyocyte lipotoxicity and its underlying mechanism was investigated.

METHODS The experimental groups were divided as follows: Control group, PA group (200 μM), Gen+PA group (320 μM Gen+200 μM PA) and Gen group (320 μM Gen). The cell viability was measured by CCK-8 kit. Oxidative stress was detected by DHE (ROS) staining and MDA kit. Apoptosis related proteins (Bax, Cleaved-Caspase-3, and Bcl-2), inflammatory proteins (NLRP3) and signal pathway related proteins (AKT, GSK-3β, PICK1, and PKR2) were examined by Western Blot.

RESULTS In H9C2 cardiomyocytes treated with Gen and PA, the fluorescence intensity of DHE (ROS) was significantly decreased, and the content of MDA was decreased. Furthermore, PA treatment increased the expression of Cleaved-Caspase-3 and Bax and decreased the expression of Bcl-2 in H9C2 cardiomyocytes, which were reversed by pretreatment of Gen. Additionally, administration of Gen inhibited the increased expression of NLRP3 protein and enhanced the decreased expressions of p-Akt and p-GSK-3β induced by PA. Finally, treatment with PA induced the decreased expression of PKR2 and PICK1, which were reversed by pretreatment of Gen.

CONCLUSIONS The protective effect of geniposide on palmitate-induced H9C2 lipotoxicity injury is closely related to the inhibition of oxidative stress, inflammation and apoptosis via regulating PK2 pathway. This work was supported by the Foundation from Department of Education of Hubei Province (17Y110), Nature Science Foundation of China (81870576) and the Foundation of Hubei University of Science and Technology (LCZX201515, 2018-19XZY06). Correspondence author: xncf@163.com

GW30-e0640

Flavanone compounds affect exercise capacity and fatigue resistance of rats

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OBJECTIVES Flavanones is a chemical entity nature of this substance has not been found, but a derivative of flavanones present in many foods and plants, these derivatives collectively Flavanones is. If you come up with black tea extract antioxidant substances fatigue, help people learn more about the composition and effectiveness of black tea, research Flavanones developed for a sports drink with Chinese characteristics, sports supplements and health products has important significance.

METHODS Forty male SD rats, first of all before the experiment rats were adaptive swimming practice time a week, once a day. 1.2 days to swim 15 minutes a day; 3rd and 4th day swim 20 minutes a day; first five days to swim 25 minutes a day. After a week feeding adaptation, the rats were randomly divided into four groups: control group, 10, 10 gavage group, the exercise group 10, fed plus exercise group 10. Exercise group and exercise group fed a 12-week swimming training. Sports 7 days a week. Swimming water temperature controlled at about 30°C. Section l, 2 cycles per R swim 15 minutes; 3 and 4 weeks daily swim 20 minutes; daily swim 25 minutes after the first five weeks. Gavage group without any movement, fed seven times a week, the concentration is 150/mg×mg^{-1}. Control group was not fed anything sports and. Four groups of rats were using ordinary food, free access to water. After 12 weeks, once for four groups of rats after exhaustive exercise, exhaustive record time, exhaustive criteria: rats for underwater sports, submerged 10 s are not free floating, uncoordinated limb movement, choking water, remove no turn after J reflective, can be judged as exhaustive. Fish were killed after exhaustive. Remove the blood, measured gastrocnemius indicators.

RESULTS (1) SOD activity: Sports rats fed blood, gastrocnemius high SOD activity than simply fed group and the exercise group. (2) GPX activity: Sports rats fed blood, gastrocnemius GPX activity than simply fed the high group and the exercise group. (3) MDA levels: Sport rats fed blood, gastrocnemius MDA level than mere gavage group and exercise group at the end. (4) During exhaustive exercise length: longer than the mere movement of the head group and administered orally during exercise group rats after exhaustive exercise. (5) Muscle lactate content: Sports rats fed blood lactic acid content than pure gastrocnemius hunger fed group and the exercise group at the end.

CONCLUSIONS (1) Flavanones can effectively improve the body's SOD enzyme activity, thereby clearing the body of oxygen anion radicals generated by the movement to reduce the freedom of machine damage to body cells and increase the body's antioxidant capacity. (2) Flavanones GSH-PX can increase the body's enzyme activity, thus reducing the body's H2O2, reducing peroxide damage to the body, increasing the body's antioxidant capacity. (3) Flavanones MDA can reduce the level of the body, thereby protecting the body's cells and increase the body's antioxidant capacity. (4) Flavanones can effectively clear the muscles of lactic acid, increases the body's athletic ability. (5) Flavanones can effectively improve the exhaustive time in rats, increased exercise capacity.

GW30-e0647

Intermedin1-53 alleviates pathological cardiac remodeling by up-regulating Klotho

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OBJECTIVES Pathological cardiac remodeling involved cardiac hypertrophy, fibrosis and dysfunction. Intermedin (IMD) had a cardiovascular protective effect in previous reports. However, as a paracrine/autocrine peptide, the protective role of endogenous IMD against cardiac remodeling and the underlying mechanism had not been elucidated.

METHODS Pathological remodeling models were induced by abdominal aorta constriction for 4 weeks or angiotensin II (Ang II) infusion for 2 weeks in IMD transgenic, IMD knockout and Klotho knockdown mice. Cultured neonatal rat cardiomyocytes were pre-treated by IMD before Ang II stimulation. Small interfering RNAs were added to knockdown the expression of Klotho in vitro. Western blot, real-time PCR, histological staining, echocardiography and hemodynamics were used to detect the role of IMD in cardiac remodeling.

RESULTS Cardiac hypertrophy, fibrosis and dysfunction were significantly alleviated in IMD transgenic mice compared with wildtype mice, as well as the expression of Klotho was up-regulated. On the contrary, cardiac remodeling was aggravated in IMD knockout mice as expected. Hypertension induced by Ang II infusion rather than abdominal aorta constriction was mitigated by IMD. However, the cardioprotective effect of IMD was blocked in Klotho knockdown mice. The similar results were found in cultured cardiomyocytes. Notably, the benefits of IMD for hypertension were not affected by Klotho. Mechanistically, IMD inhibited phosphorylation of Ca^{2+}/calmodulin dependent protein kinases II and expression of calcineurin to protect against cardiac hypertrophy through up-regulating Klotho. Furthermore, we found that peroxisome proliferators-activated receptor γ (PPARγ) mediated the role of IMD up-regulating Klotho.

CONCLUSIONS In summary, pathological remodeling was inhibited by endogenous IMD, which maintained Ca^{2+} homeostasis by up-regulating Klotho via activating PPARγ pathway.

GW30-e0652

Bioinspired dual-targeting nanoplatform loaded melatonin for ameliorating fibrosis on cardiac hypertrophy

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OBJECTIVES Currently unsatisfactory treatment of cardiac hypertrophy is due to the unbridled myocardial fibrosis. Melatonin have been demonstrated to promote cardiac hypertrophy and accompanied fibrosis in previous studies. But it is not clinically appealing due to its short lasting time against the hostile microenvironment.

METHODS Herein, to overcome these therapeutic hurdles. Magnetic and CHP-based dual targeting melatonin–loaded nanoparticles (CHP-mel@SPIONs) were prepared used for double emusion and carbodiimides, then the general properties were investigated. *Ex vivo* targeting was analyzed by fluorescence imaging in vivo and fluorescence microscopy. For the animal study, we utilized a transverse aortic constriction surgery (TAC) induced cardiac hypertrophy rat model. Animals were treated with either saline, non-targeting mel@SPIONs, targeting CHP-mel@SPIONs, or targeting CHP-mel@SPIONs+M 8 weeks after surgery. Echocardiography was performed after treatment. And then animals were sacrificed, and organs were collected for histological analysis and RT-PCR.

RESULTS The engineered magnetic polymeric nanoparticles CHP-mel@SPIONs are 221±13 nm in size with negative zeta potential of −33.34±0.88 mV and shown to be spherical in shape. The CHP-mel@SPIONs displays the most excellent drug encapsulation capacity of SPIO and melatonin separately, and magnetic properties were characterized by determination of magnetic hysteresis curves and transverse relaxation rates. CHP-mel@SPIONs with external magnetic field (M) group has longer blood circulation and more effective accumulation at heart site than CHP-mel@SPIONs and mel@SPIONs groups, enhanced transfection efficiency with minimized polymer use. As expected, in vivo therapeutic evaluations showed that CHP-mel@SPIONs+M group has augmented anti-hyperthrophy and anti-myocardial fibrosis effect comprehensively compared to other treatments, revealing high efficiency in cardiac-targeted delivery and effective cardioprotection.

CONCLUSIONS Our results demonstrate this simple biocompatible dual-targeting nanoagent can act as a potential candidate for clinical guided therapy of heart disease.

GW30-e0665

Nicotine increases vascular adiponectin resistance in HFD mice

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OBJECTIVES The study aims to determine whether nicotine causes vascular adiponectin resistance in C57 mice with a high-fat diet (HFD).

METHODS Adult male C57 mice were randomly divided into 4 groups, normal diet (ND) group, HFD group, nicotine group, nicotine+HFD group, fed for 12 weeks, the level of total APN and HMW APN in the circulation was measured at different time periods.

RESULTS Compared with the ND group, the total APN of the nicotine+high-fat diet group was significantly increased at 6 weeks, and the HFD group and the nicotine group was significantly increased at 8 weeks, and then decreased rapidly. HMW APN in the nicotine+HFD group was significantly increased at 8 weeks, the HFD group and the nicotine group was significantly increased at 12 weeks, and then decreased rapidly. In the nicotine+HFD group, the HFD group, and the nicotine group, recombinant globular APN (gAPN) induced aortic ring vasodilation was significantly reduced at 12 weeks.

CONCLUSIONS The above experiments indicate that nicotine can cause adiponectin resistance in HFD C57 mice.

GW30-e0688

Ticagrelor alleviate sepsis induced myocardial injury via adenosine-dependent pathway in mice sepsis model

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OBJECTIVES Ticagrelor provided clinical outcomes in patients with acute coronary syndromes not only due to the anti-platelet effect but also the myocardial protection. The aim of this study is to determine if the ticagrelor display the myocardial protecting effect in sepsis induced myocardial injury.

METHODS C57BL6J mice received oral ticagrelor (50 mg/kg) for 7 days and underwent caecum ligation and puncture (CLP) after the last dose of ticagrelor. Adenosine-receptor antagonist (CGS15943) was administered (10 mg/kg, intraperitoneal injection) in some of the CLP mice to block the adenosine pathway 2 h before CLP. After 24 h from CLP, cardiac echocardiography was used to measure the heart function before mice heart and blood was collected. HE staining was used to observe the pathological changes and TUNEL staining was applied to determine the cardiomyocyte apoptosis. ELISA was used to determine the blood concentration of TNF-α and IL-6. qRT-PCR was used to determine the relative expression of TNF-α and IL-6 in myocardial tissue. Western blot was used to determine the expression of signal molecular in myocardial tissue.

RESULTS In ticagrelor group, HE staining showed that less inflammatory cell infiltration and TUNEL showed the less cardiomyocyte apoptosis compared to no ticagrelor group. cardiac echocardiography showed the reserved heart function in ticagrelor group compared to no ticagrelor. The concentration of TNF-α and IL-6 in blood and relative expression of TNF-α and IL-6 in myocardial tissue was significantly lower in ticagrelor group than no ticagrelor. Adenosine-receptor antagonist significantly block the protective effect of ticagrelor. Western blot further showed that ticagrelor activate the phosphorylation of AKT and mTOR. Adenosine-receptor antagonist inhibit the activation of AKT and mTOR.

CONCLUSIONS Ticagrelor reduced the myocardial injury in sepsis mice model. The protective effect was dependent on adenosine-receptor activation with downstream upregulation of phosphorylation of AKT and mTOR.

GW30-e0692

Mechanism of RAGE/gal-3 in diabetic palque calcification patterns mediation

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OBJECTIVES To investigate the mechanism of macro-/micro-calcification transfomation in diabetic vascular calcification.

METHODS Thirty patients with diabetic foot amputation were enrolled from June 2016 to June 2018. Calcium content of each anterior tibial artery was measured and patients were divided into less calcification group (calcium content <5 μmol/mg) and more calcification group (≥5 μmol/mg). Calcification types in plaques was detected and immunohistochemical staining was carried out to show RAGE/gal-3 expression. And then an in vivo and an in vitro diabetic vascular calcification model were established. After silencing RAGE or gal-3, calcification morphology was measured and sortilin expression was determined. Sortilin was further blocked or over-expressed on the base of RAGE/gal-3 silencing to investigate the effect of sortilin on the progression of calcification. Finally, SEM detection and NTA were performed to detect the aggregation of matrix vesicles during the formation of macro-/micro-calcification.

RESULTS Macro- and micro-calcification were both found in human anterior tibial artery plaques. After silencing RAGE, macrocalcification formed. And the blockage of galectin-3 introduced the formation of microcalcification. Sortilin overexpression induced larger calcified nodules formation. Meanwhile, SEM and NTA showed that with the up-regulation of sortilin, the matrix vesicles aggregated earlier.

CONCLUSIONS RAGE transmitted microcalcification signals and gal-3 delivered macrocalcification signals both through sortilin.

GW30-e0705

Identification of hub genes and exploration of their mechanisms in the progression of atherosclerosis based on bioinformatics analysis

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OBJECTIVES Atherosclerosis (AS) is a common disease that seriously endangers human health. This study aims to identify unknown hub genes involved in the progression of atherosclerosis by using the bioinformatic methods so that we can provide evidence to further clarify the molecular biological mechanism of atherosclerosis and to select drug intervention targets in the future.

METHODS Dataset one (GSE43292) and Dataset two (GSE28829) were downloaded from the GEO. Two datasets shared similar grouping scheme (group of early lesion and advanced lesion). Raw probe-level microarray data were preprocessed using the oligo package in R3.5.2 language. Differentially expressed genes (DEGs) were screened by using limma package in R. Weighted gene co-expression network analysis (WGCNA) was performed to screen out disease-related modules and identify hub genes. Functional annotation for the DEGs of each module was carried out by GO, DO analysis with R package. The software cytoscape was used to visualize local regulatory networks associated with the hub genes.

RESULTS For Dataset one, differential expression analysis screened 795 DEGs including 482 upregulated genes and 313 downregulated genes in group of advanced lesion. For Dataset two, there were 903 DEGs including 604 upregulated genes and 299 downregulated genes. WGCNA showed that module "lightgreen" was significantly positively correlated with the progression of atherosclerosis in Dataset one while in Dataset two it was module "brown". GO enrichment analysis showed that DEGs in both modules were mainly involved in activation of immune cells, secretory granule membrane, cytokine activity and so on, which not only indicated biological function of these DEGs, but also suggested that the two modules were exactly similar. DO enrichment analysis showed that DEGs in both modules were significantly enriched in arteriosclerosis. The two modules identified 7 hub genes in common from 208 DEGs shared by two modules including LAIR1, PIK3AP1, HAVCR2, RBM47, HCK, CD53 and TYROBP. Local co-expression networks for these 7 hub genes were constructed through cytoscape and there were 66 highly co-expressed relationships between hub genes and their related candidate genes in each module. The two modules shared 20 highly co-expressed relationships.

CONCLUSIONS In this study, 7 hub genes shared by Dataset one and two were highly expressed in the group of advanced lesion compared to group of early lesion and significantly positively correlated with the progression of atherosclerosis, meaning that these genes were upstream in the regulatory network and might become biomarkers in the progression of atherosclerosis and drug intervention targets in the future. Twenty highly co-expressed relationships between hub genes and their related candidate genes were screened out to further elucidate the underlying molecular pathways and interaction mechanisms of these hub genes in the progression of atherosclerosis, which still need to be verified by a large number of subsequent fundamental and clinical studies.

GW30-e0712

Expression of serum connective tissue growth factor in patients with rheumatic heart disease and its association with myocardial fibrosis

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OBJECTIVES Our previous study indicated that mRNA and protein of connective tissue growth factor (CTGF) was high expression in atrial tissue of the patient with rheumatic heart disease (RHD). The aim of this work was to assess the expression of serum CTGF in RHD patients and its association with myocardial fibrosis.

METHODS Forty patients with rheumatic heart diseases (RHD) and 19 healthy volunteers were enrolled as study group (SG) and control group (CG) in this study. The right atrial muscles samples of SG were obtained during heart valve replacement surgery. Serum CTGF from all participants was detected using a direct high sensitivity sandwich ELISA kit. The mRNA and protein expression of CTGF in right atrial muscles of SG were detected by semiquantitative RT-PCR and immunohistochemistry technique. Masson's trichrome-stained sections was used to evaluate the level of myocardial fibrosis. The area of fibrosis was measured by imaging analysis system, qualified by PU value. SPSS package was used to analyze the relationship between the expression of CTGF and the area of myocardial fibrosis. A P-value<0.05 was considered statistically significant.

RESULTS Serum CTGF concentrations increased significantly in SG compared to CG (85.62±27.61 vs 40.81±19.65, P<0.01). In SG, the expression of serum CTGF was correlated positively with CTGF mRNA, CTGF protein in atrial muscles and the area of myocardial fibrosis (r=0.874; r=0.776; r=0.85, P<0.01). The expression of serum CTGF in SG didn't show correlation with gender, age and case history (r=–0.32; r=0.121; r=0.084, P>0.05), but remarkably correlated with cardiac functional gradings (r=0.484, P<0.05).

CONCLUSIONS Serum CTGF was high expression in RHD patients; it may play an important role in the process of myocardial fibrosis in RHD.

GW30-e0714

The novel Se@SiO_2 nanocomposites improve adverse ventricular remodeling after myocardial infarction through its anti-oxidative stress effect

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OBJECTIVES To investigate whether Se@SiO_2 could improve adverse ventricular remodeling after MI and whether the underlying mechanism is associated with its anti-oxidative effects.

METHODS Sprague Dawley Rats were randomized into the following 5 groups and received the indicated treatment 48 hours after MI induction: (1) Sham control group; (2) Control group; (3) ACEI group; (4) Low-dose Se@SiO_2 group; (5) High-dose Se@SiO_2 group. Cardiac function of rats was assessed by echocardiography. The area of MI size and interstitial fibrosis were assessed by Masson's trichrome staining and sirius red staining, respectively. The expression of TGF-β in myocardium was determined by western blot.

RESULTS After 28 days, both low and high does SeO_2 attenuated the increase in ventricular weight and dimension compared with vehicle group. Compared with vehicle group, low-dose SeO_2 group had higher LVEF (52.45±3.42% vs. 38.21±5.13%, P<0.05), smaller diastolic left ventricular inner diameter (8.32±0.40 mm vs. 9.60±0.42 mm, P<0.05), and smaller systolic left ventricular inner diameter (6.49±0.34 mm vs. 8.17±0.53 mm, P<0.05). Low-dose SeO_2 group also had smaller MI size (27.50±0.39% vs. 45.27±0.72%, P<0.05) and reduced interstitial fibrosis in noninfarct area (2.76±0.14% vs. 5.27±0.21%, P<0.05). Expression of TNF-β was significantly lower in low-dose SeO_2 group than in vehicle group (relative expression: 0.27 vs. 0.55, P<0.05). The above effect was greater in high-dose group. SeO_2 treatment also significantly reduced oxidative stress level and apoptosis in cardiomyocytes treated with H_2O_2.

CONCLUSIONS We found a protective effect of SeO_2 in adverse remodeling post myocardial infarction. The underlying mechanisms may be associated with the anti-oxidative stress effect of SeO_2.

GW30-e0721

Inducible nitric oxide synthase aggravates cardiac dysfunction via mtDNA-cGAS-STING-induced inflammation in the failing heart

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OBJECTIVES Our aim was to investigate the role of inducible nitric oxide synthase (iNOS) in cardiac sterile inflammation and its relationship to mitochondrial damage and cGAS-STING pathway in pressure overload-induced heart failure.

METHODS Transverse aortic constriction (TAC) was used to induce heart failure both in $iNOS^{-/-}$ mutant and wild-type mice. Echocardiography, transmission electron microscopy, RT-PCR and immunohistochemistry were applied to study the role of iNOS and cGAS-STING pathway in the development of heart failure.

RESULTS In wild-type mice, TAC resulted in increased myocardial iNOS expression, cardiac hypertension and dysfunction, whereas iNOS-deficient mice displayed much less cardiac hypertrophy and dysfunction. Consistent with these findings, iNOS deficient attenuated mitochondrial dysfunction and significantly reduce the release of mtDNA in the failing heart. The cGAS–STING pathway, which results in mtDNA-induced inflammatory responses, was highly activated in WT mice 4 weeks after TAC but not in $iNOS^{-/-}$ mice. In vitro, hypoxia can induce the expression of iNOS and active cGAS-STING pathway in neonatal rat cardiomyocytes. Pharmacological blocking iNOS can inhibit the activation of cGAS-STING pathway.

CONCLUSIONS These data demonstrate that iNOS contribute to mtDNA release from damaged mitochondria and trigger cardiac inflammation via cGAS-STING pathway in pressure overload-induced heart failure, which suggests a potential therapeutic target for heart failure.

GW30-e0728

CD137 signaling promotes angiogenesis through regulating macrophage M1/M2 polarization

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OBJECTIVES To investigate whether CD137 signaling can promote angiogenesis via regulating macrophage M1/M2 polarization.

METHODS (1) The primary peritoneal macrophages in mice induced by 3% thiglycollate broth were divided into three groups: control group, CD137 signaling activated group and CD137 signaling inhibited group, detecting various specific markers of M1 and M2 macrophages to observe the phenotype change of macrophages, and the macrophages protein expression of CD137, CD86 and CD206 was detected by flow cytometry (FCM). The mRNA and protein expression of induced nitric oxide synthase (iNOS), arginase-1(Arg-1) was respectively determined by Western blot and RT-PCR determine. The secretion levels of IL-12 and IL-10 in culture supernatant of macrophages was detected by ELISA. (2) Macrophages were co-cultured with the endothelial cells (bEnd.3), and macrophages were implanted in the upper chamber, endothelial cells were implanted in stromal glue of the lower chamber. The experiment was divided into three groups: the control group, CD137 signaling activated group and PPAR-γ(peroxisome proliferator-activated receptor-γ) inhibited group, and test tube formation ability of endothelial cells in each group.

RESULTS (1) The purity of primary peritoneal macrophages in mice was (97.93±1.31)%; The expression of CD137 on the surface of macrophages was (97.40±2.70)%. (2) Compared with control group, the expression levels of Arg-1 mRNA and protein in CD137 signaling activated group were significantly increased (P<0.05), and the expression of iNOS mRNA and protein were significantly decreased (P<0.05); the expression of Arg-1 mRNA and protein in CD137 signaling inhibited group were significantly lower than CD137 signaling activated group (P<0.05), the expression levels of iNOS mRNA and protein were increased (P<0.05). FCM results showed that the average fluorescence intensity of CD206 in CD137 signaling activated group was higher than control group (P<0.05), while the average fluorescence intensity of CD86 was lower than control group (P<0.01); the expression of CD206 in the CD137 signaling inhibited group was significantly lower than CD137 signaling activated group (P<0.05), the expression of CD86 was higher than CD137 signaling activated group (P<0.01). ELISA showed that the secretion of IL-10 in CD137 signaling activated group was higher than control group (P<0.01), and the secretion level of IL-12 was significantly lower than control group (P<0.01); the secretion of IL-10 in CD137 signaling inhibited group was significantly lower than CD137 signaling activated group (P<0.05), and the secretion of IL-12 was significantly increased (P<0.05). (3) Values of the formation of tube length and branch number in CD137 signaling activated group were both longer than control group (P<0.05). The formation of the tube length and branch number in PPAR-γ inhibited group were less than CD137 signaling activated group (P<0.05).

CONCLUSIONS CD137 signaling can promote angiogenesis by regulating macrophage M1/M2 polarization.

GW30-e0736

The biological role of SF3A3 in blood pressure control

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OBJECTIVES A recent genome-wide association study identified a novel gene locus with splicing factor 3a subunit 3 (SF3A3) to be significantly related with blood pressure (BP), we aim to functionally characterize the biological role of SF3A3 in the BP control and hypertension development.

METHODS *Materials and Methods* Bioinformatic tools were utilized to prioritize the investigation. A collection of primary human smooth muscle (SMC) and endothelial (EC) cells were genotyped for SF3A3 BP-related variant. Ang-II induced SMCs and hypertensive mice were constructed as well. Endogenous SF3A3 mRNA and protein levels were assessed by qRT-PCR and western blotting. Mice systolic and diastolic BP were measured with a tail-cuff.

RESULTS The SF3A3 gene risk allele was associated with higher endogenous mRNA and protein levels in human SMCs. No such characteristics were observed in ECs. Elevated levels of SF3A3 were also identified in Ang-II induced SMCs and hypertensive mice arteries.

CONCLUSIONS The findings in this study have suggested a potential role of SF3A3 in the BP control and hypertension development.

GW30-e0743

Co-loading antioxidant N-acetylcysteine attenuates cytotoxicity of iron oxide nanoparticles in hypoxia/reoxygenation cardiomyocytes

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OBJECTIVES Myocardial delivery of magnetic iron oxide nanoparticles (MNPs) might produce iron overload-induced myocardial injury, and the oxidative stress was regarded as the main mechanism. Therefore, we speculated antioxidant modification might be a reasonable strategy to mitigate the toxicity of MNPs.

METHODS Antioxidant N-acetylcysteine (NAC) was loaded into magnetic mesoporous silica coated Fe_3O_4 nanoparticles. Neonatal rat Hypoxia/Reoxygenation (H/R) cardiomyocytes were incubated with nanoparticles for 24 h. The ROS levels of cardiomyocytes were detected by DHE 24 hours after the injection. The lipid peroxidation products (MDA and 8-iso-PGF2 alpha), DNA peroxidation products (8-OHDG), the antioxidant enzyme system (SOD, CAT, GSH-Px) and GSH were detected by ELASA and biochemical methods. The expression levels of endoplasmic reticulum stress protein CHOP and GRP78, autophagy related protein P62, LC3-I and LC3-II were measured by Western Blot. Apoptosis of cardiomyocytes was detected by Annexin V-FITC and PI staining.

RESULTS NAC can effectively mitigate iron-induced oxidative injury of cardiomyocytes, evidenced by reduced production of MDA, 8-iso-PGF2α and 8-OHDG and maintained concentrations of SOD, CAT, GSH-Px and GSH in ELASA and biochemical tests; down-regulated expression of CHOP, GRP78, p62 and LC3-II proteins in Western Blot, and less cardiomyocytes apoptosis in flow cytometric analysis.

CONCLUSIONS NAC modifying could suppress the toxic effects of Fe_3O_4 nanoparticles in H/R cardiomyocytes model *in vitro*, indicating a promising strategy to improve the safety of iron oxide nanoparticles.

GW30-e0744

EP3 blockade uncovers the dilator action of native prostacyclin that adds to the reduced endothelial dilator function in atherosclerotic aorta of TP deficient mice

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OBJECTIVES Endothelial dysfunction, which leads to ischemic events under atherosclerotic conditions, can be attenuated by antagonizing the thromboxane-prostanoid receptor (TP) that mediates the vasoconstrictor effect of prostanoids including prostacyclin (PGI_2). This study aimed to determine whether antagonizing the E prostanoid receptor-3 (EP3; which can also be activated by PGI_2) adds to the effect of TP deficiency ($TP^{-/-}$) under atherosclerotic conditions and if so, the underlying mechanism(s). Endothelial dysfunction, which leads to ischemic events under atherosclerotic conditions, can be attenuated by antagonizing the thromboxane-prostanoid receptor (TP) that mediates the vasoconstrictor effect of prostanoids including prostacyclin (PGI_2). This study aimed to determine whether antagonizing the E prostanoid receptor-3 (EP3; which can also be activated by PGI_2) adds to the effect of TP deficiency ($TP^{-/-}$) under atherosclerotic conditions and if so, the underlying mechanism(s).

METHODS Atherosclerosis was induced in $ApoE^{-/-}$ mice and those with $ApoE^{-/-}$ and $TP^{-/-}$. For functional studies, Rings of the abdominal aorta with plaques were used to study vasomotor reactions of atherosclerotic conditions. COX-1, PGI_2 synthase (PGIS), eNOS, TP, EP3 and IP were detected by Western blot and/or qPCR in abdominal aortas. The PGI_2 metabolite 6-keto-PGF_{1a} produced in abdominal aortas was measured with an EIA kit.

RESULTS Here we show that in the abdominal aortic rings with plaques of $ApoE^{-/-}/TP^{-/-}$ mice, although a biphasic force (which was larger than that of non-atherosclerotic controls) blunting the relaxation evoked by the endothelial muscarinic agonist ACh in $ApoE^{-/-}$ counterparts was largely removed the relaxation was still smaller than that of non-atherosclerotic $TP^{-/-}$ mice. Interestingly, EP3 antagonism not only increased the above relaxation, but also reversed a contraction (which was smaller than that of similar $ApoE^{-/-}$ vessels) evoked by ACh under NO synthase-inhibited conditions of atherosclerotic $ApoE^{-/-}/TP^{-/-}$ rings into a relaxation sensitive to I prostanoid receptor antagonism. Also, in $ApoE^{-/-}$ atherosclerotic vessels the expression of endothelial NO synthase was decreased, yet the production of PGI_2 (which evokes contraction via both TP and EP3) evoked by ACh was unaltered compared to non-atherosclerotic conditions.

CONCLUSIONS Therefore, even after TP-mediated effect was removed, additional EP3 blockade is needed to fully uncover the dilator action of natively produced PGI_2 that can add to the reduced endothelium-mediated dilator function observed under atherosclerotic conditions.

GW30-e0745

Dopamine D5R receptor delivered by degradable hyperbranded polyaminoglycoside as a novel therapy for hypertensive hypertrophic cardiomyopathy

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OBJECTIVES Hypertrophic cardiomyopathy (HCM) is an inherited and ongoing chronic vascular disease which requires timely and effective treatment. Genetic therapy has been shown to ameliorate hypertrophic cardiac damage. However, due to the continuous flow of liquid in the heart chamber, powerful nucleic acid delivery vehicles are essential for effective gene therapy. The gene Drd5 was proved related to HCM in our previous study, Herein, we aimed to test whether one multifunctional delivery polycation (SS-HPT) of tobramycin-based hyperbranded polyaminoglycoside could successfully used for targeted nucleic acid therapy, and investigating the effect of SS-HPT/Drd5 plasmid on hypertensive cardiac damage and regulation mechanism.

METHODS C57 mice were performed transverse aortic constriction (TAC), two weeks later, SS-HPT/Drd5 plasmid or SS-HPT/Drd5 siRNA was given in HCM mouse model for 4 weeks. Cardiac hypertrophy, fibrosis and dysfunction were determined as well as the expression of Drd5

RESULTS It is first reported that D5R expression in left ventricle continuously decreased in the progression of HCM, and seriously degraded in heart

failure patients, which play a crucial role in maintaining cardiac function. D5R plasmid can be effectively delivered by SS-HPT/Drd5 plasmid for the early and precise treatment of HCM in mouse model. Specific targeted D5R in early stage of HCM exhibits impressive performances in attenuated cardiac hypertrophy, fibrosis and dysfunction in via preventing ROS production and autophagy. In contrast, SS-HPT/Drd5 siRNA accelerate the deterioration of myocardial function seriously, which promote the progression of MCH to heart failure. Moreover, SS-HPT, constructed from topamycin, shows excellent biocompatibility and can effective suppress inflammation during HCM development.

CONCLUSIONS Our data emphasize a specific-target and anti-inflammatory role of SS-HPT/Drd5 plasmid and their importance for myocardio healthy. The proposed powerful nucleic acid delivery polycation accurately bombing damaged cardiomyopathy would provide promising precise therapy platforms of cardiovascular diseases.

GW30-e0751

CD137-CD137L signaling promotes calcification in vascular smooth muscle cells by regulating macrophage-derived MMP-9

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OBJECTIVES Vascular calcification is considered as an active process in which vascular smooth muscle cells (VSMCs) plays a critical role. Activation of CD137 in vivo has been reported to promote vascular calcification in mouse atherosclerosis. Matrix metalloproteinase-9 (MMP-9) mainly expressed on macrophages, also known as gelatinase B, is as well as involved in vascular calcification. On the basis of these achievements, we tested the hypothesis that CD137-CD137L signaling regulates VSMC calcification via modulating macrophage production of MMP-9.

METHODS Aortic VSMCs and peritoneal macrophages (PMs) were isolated from C57BL/6J mice, respectively. We used a PM /VSMC co-culture system to investigate the role of MMP-9 in the regulation of CD137-CD137L signaling-induced VSMCs calcification. Gelatin zymography was performed to detect MMP-9 activity. The expression of calcification-related proteins Runt-related transcription factor 2 (RUNX2) and osteopontin (OPN) was determined by western blot. The quantitative colorimetric method was applied to detect calcium ion concentration and alkaline phosphatase (ALP) activity. Von Kossa and alizarin red staining were used to observe the severity of VSMC-calcification.

RESULTS CD137-CD137L signaling induced MMP-9 production from macrophage in a time dependent manner. Treatment with recombinant CD137L protein alone did not stimulate VSMCs calcification. The expression levels of RUNX2 and OPN were significantly higher in VSMCs than that cultured with macrophage without stimulation after recombinant CD137L protein was added to the PM/VSMC co-culture system. Consistent with this finding, CD137-CD137L signaling obviously enhanced calcium deposition and ALP activity in the PM/VSMC co-cultures. Furthermore, SB-3CT, which was a specific inhibitor of gelatinases, alleviated calcification induced by CD137-CD137 axis, accompanied with reduced expression of RUNX2 and OPN.

CONCLUSIONS These data indicate that activated CD137-CD137L signaling contributes to the formation of vascular calcification by upregulating the expression of matrix metalloproteinase-9 (MMP-9) secreted from macrophage. Thus, inhibition of CD137-CD137L signaling pathway and MMP-9 might be a promising strategy to prevent vascular calcification.

GW30-e0752

Exosomes secreted from GATA4 gene engineered cardiosphere-derived cells serve as a reservoir of anti-apoptotic microRNAs for cardioprotection

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OBJECTIVES Exosomes play an important role in intercellular signaling and exert regulatory functions by carrying bioactive molecules. GATA4 is an early cardiac-specific transcription factor, and endogenous GATA4-positive cells play a critical role in cardioprotection after myocardial injury. This study investigated the cardioprotective capabilities of exosomes derived from GATA4-Overexpressing Cardiosphere-Derived Cells (GATA4-Exo) and the underlying mechanisms through the delivery of microRNAs (miRNAs) to regulate target proteins in myocardial infarction.

METHODS Exosomes were harvested from CDCs by ultracentrifugation. The morphology of the CDCs-derived particles was observed under a transmission electron microscope (TEM). miRNA array experiment was used to test the differential expression of the miRNAs between exosomes derived from GATA4-Overexpressing CDCs ($CDCs^{GATA4}$) and control CDCs ($CDCs^{NC}$). Double luciferase reporter assay was applied to confirm that miR221 directly targets the 3′ UTR of the gene of phosphate and tension homology deleted on chromsome ten (PTEN) gene. Echocardiography and Masson trichrome staining were used to determine the extent of cardiac function and myocardial infarct size.

RESULTS Exosomes were isolated and purified from $CDCs^{GATA4}$ and $CDCs^{NC}$. When hypoxia-injured H9C2 were treated with GATA4-Exo vs. NC-Exo, an improved H9C2 survival rate ($P<0.05$) and reduced H9C2 apoptosis were observed with GATA4-Exo compared with NC-Exo. Microarray analysis of the exosomal miRNAs revealed significantly increased expression of miR221 in GATA4-Exo compared with NC-Exo. Direct intramyocardial transplantation of GATA4-Exo at the border of an ischemic region following ligation of the left anterior descending coronary artery significantly restored cardiac contractile function and reduced infarct size. In terms of mechanism, real-time PCR revealed that miR221 levels were higher in H9C2 treated with GATA4-Exo compared with those treated with NC-Exo (317%, $P<0.001$). We then transfected H9C2 with miR221 mimic and miR221 inhibitor. miR221-mimic-transfected vs. miR221-inhibitor-transfected H9C2 demonstrated a significantly increased survival rate ($P<0.01$) following exposure to hypoxic condition. The dual-luciferase reporter gene assay confirmed the PTEN gene as a target of miR221. Western blot analysis showed that H9C2 treated with GATA-4-Exo exhibited lower PTEN protein expression and higher p-Akt expression compared with NC-Exo-treated cells.

CONCLUSIONS Collectively, exosomes derived from GATA4-Overexpressing CDCs protect cardiomyocytes against apoptosis via the miR221-mediated PTEN-PI3K/AKT signaling pathway.

GW30-e0754

Aprotinin promotes atherosclerotic plaque stability by inhibiting up-regulation of ectopic trypsin and inflammatory responses

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OBJECTIVES *Aims* Our previous research has established that ectopic trypsin was expressed in aortic artery and up-regulated in atherosclerotic plaques. Distribution of trypsin was overlapped with that of matrix metalloproteinase-9. As matrix metalloproteinase-9, which could be activated by trypsin, plays trigger roles in the process of plaque rupture. The purpose of this study was to explore the possible roles of trypsin in process of atherosclerotic plaque inflammation and the effects of trypsin inhibitor aprotinin on plaque stability in rabbit models, thus providing a new strategy for stabilizing atherosclerotic plaques.

METHODS Twenty-four New Zealand white rabbits (8-week-old) were randomly assigned to the normal control group, the atherosclerosis experimental group and the trypsin inhibitor aprotinin group, with eight rats in each group. The control group was given standard rabbit chow, while the experimental and aprotinin groups were fed with high-fat diet. At the 13^{th} week of feeding, the rabbits in the aprotinin group were treated with aprotinin via the ear vein at a dose of 5 mg/kg/day for 4 weeks, whereas the experimental group was injected with the same amount of saline. At the end of the 16^{th} week, the rabbits were sacrificed and their heart and aortic tissues were taken for pathological and biochemical examinations.

RESULTS Compared with the experimental group, the lipid deposition in the aortic root cross sections and the aortic wall was significantly reduced in the aprotinin-treated group. Western immunoblotting and immunohistochemical analysis showed that the expression of ectopic trypsin and matrix metalloproteinase-9 in the aortic tissues were significantly up-regulated in the experimental group compared to the control group, and were consistently distributed in atheroma plaques. The high-fat diet also increased the expression of pro-inflammatory cytokines such as IL-6, IL-1β, and TNFα in aortic tissues. Aprotinin treatment significantly inhibited the expression of trypsin and matrix metalloproteinase-9, as well as the production of pro-inflammatory cytokines.

CONCLUSIONS As a potent inhibitor of trypsin, aprotinin can alleviate the inflammatory response of atherosclerotic plaque by inhibiting the expression of ectopic trypsin and matrix metalloproteinase-9 in atherosclerotic plaque tissues, thereby impeding the progression of atherosclerosis.

GW30-e0756

Toll-like receptor 5 deficiency diminishes doxorubicin-induced cardiotoxicity via p38 MAPK signaling pathway

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OBJECTIVES Doxorubicin (DOX) is an effective antineoplastic drug, but its clinical application is limited by cardiovascular toxic effects. Oxidative stress, inflammation and cardiomyocyte apoptosis play critical roles in DOX-induced

cardiotoxicity. Toll-like receptor 5 (TLR5) is a member of TLR family expressed on immune cells and cardiac tissues. However, whether TLR5 is involved in doxorubicin-induced cardiotoxicity and its underlying mechanisms remain unclear.

METHODS Global TLR5-deficient mice and wild-type littermates were subjected to a single intraperitoneal injection of DOX (15 mg/kg) for an acute model. Body weight (BW), heart weight (HW), and tibial length (TL) were measured to reflect cardiac injury. Echocardiographic parameters including ejection fraction (EF) and fractional shortening (FS) were collected to assess heart phenotype.

RESULTS The data in our study demonstrated that DOX resulted in significant weight loss and cardiac atrophy, and these pathological alterations were blocked after TLR5 deficiency. TLR5 deficiency also improved cardiac function in mice with DOX treatment. TLR5 deficiency protected the mice from oxidative stress and apoptosis induced by DOX. TLR5 deficiency cannot affect the acute inflammatory reaction in mice with DOX. Western blotting demonstrated that the activation of p38 in hearts caused by DOX was suppressed in TLR5-deficient mice. CBLB502, an agonist of TLR5, aggravated DOX-related cardiac injury, as indicated by the decreased HW/BW, EF and FS, CBLB502 also further enhanced the phosphorylation of p38 in DOX-treated mice. The rat cardiomyocyte-derived cell line H9c2 was cultured with DOX (1μM). CCK8 assay showed a significant decrease in cell viability after DOX treatment and TLR5 deficiency could largely improve cell viability in vitro. TLR5 deficiency also attenuated DOX-induced oxidative stress in cardiomyocytes.

CONCLUSIONS These findings suggest that TLR5 deficiency attenuated doxorubicin-induced cardiotoxicity in mice.

GW30-e0757

TLR9 deficiency alleviates doxorubicin-induced cardiotoxicity via enhancing autophagy

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OBJECTIVES Doxorubicin, as a representative of anthracycline drugs, is widely used in the clinical treatment. However, cardiotoxicity is a serious and fatal side effect of doxorubicin, which limits its application in cancer treatment. This study aims to explore the effect and mechanism of TLR9 on doxorubicin-induced cardiotoxicity in vivo and in vitro by genetic or pharmacological interference with TLR9.

METHODS Male C57/BL6 and TLR9-KO mice were divided into four groups randomly, WT+ Saline, WT+DOX, KO+ Saline, KO+DOX. DOX groups were injected intraperitoneally with DOX (5 mg/kg, once a week, the total cumulative dose is 15 mg/kg) for 3 times. Body weight and food consumption were monitored. Plasma CK-MB and LDH from tail vein were collected and detected. For further research, another four groups of mice were treated with 3-MA (10 mg/kg/d, i.p.) after each injection of DOX. Four weeks after the first injection, animals were anesthetized and echocardiographic measurements and hemodynamic analysis were performed. Then mice were sacrificed for molecular biology and histopathology use.

H9C2 cells were treated with 1 μm DOX or PBS for 24 hours, alone or with the TLR9 inhibitor ODN2088 (0.2 μM), or with agonist ODN1826 (0.2 μM). For Further research, H9C2 cells treated with DOX or PBS were treated in combination with ODN2088 and 3-MA (10 mM). The cells were collected for western blot analysis and fluorescence staining.

RESULTS The results show that TLR9 deficiency protects against DOX-induced cardiotoxicity both in vivo and in vitro. It alleviates DOX-induced cardiomyocyte apoptosis, oxidative stress, myocardial atrophy, cardiac fibrosis and improved cardiac function. DOX-treated TLR9-KO mice exhibits enhanced autophagy compared with corresponding control group. 3-MA, an inhibitor of autophagy, abrogates the protection of TLR9 deficiency against DOX-induced cardiotoxicity. Collectively, we demonstrate that TLR9 deficiency alleviates doxorubicin-induced cardiotoxicity via enhancing autophagy and it suggests a potential target for clinical treatment of DOX-induced cardiotoxicity.

CONCLUSIONS Our present study implies that TLR9 deficiency protects against doxorubicin-induced cardiotoxicity, accompanied by alleviated cardiomyocyte apoptosis, oxidative stress, myocardial atrophy, cardiac fibrosis and improved cardiac function. However, inhibition of autophagy abrogates the protection of TLR9 deficiency both in vivo and in vitro.

GW30-e0776

rGO/silk fibroin modified nanofibrous patches prevent heart remodeling post-myocardial infarction in rats by Yap/Taz-TGFβ1/Smads signaling pathways

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OBJECTIVES After acute myocardial infarction (AMI), the loss of a large number of cardiomyocytes will be results in the necrotic cardiac tissue, which is eventually replaced by scar formation. Cardiac patches have emerged as a potential regenerative strategy for MI. In this study, we fabricated reduced graphene oxide (rGO)/silk fibroin modified nanofibrous biomaterials as a cardiac patch to improve the heart function and prevent the ventricular remodeling post-MI. Furthermore, we have investigated the effect of rGO on cardiac fibroblasts (CFs) and potential mechanisms.

METHODS We fabricated reduced graphene oxide (rGO)/silk conductive biomaterials through fabricating electrospun silk scaffolds and vacuum filtration. A rat model of acute myocardial infarction was used to investigate the ability of rGO/silk fibroin modified nanofibrous patches to improve heart function in the injured heart in vivo. Echocardiography (ECHO) was used to evaluate heart function 4 weeks after MI. Immunofluorescence staining was used to visualize the expression of cardiac-specific markers. Western blot analysis was used to illustrate the expression of biomarkers for myocardial fibrosis of cardiac tissue. CFs were obtained and treated in different conditions, the secretion levels of type I (Col1) and type III collagen (Col3) in CFs supernatant were measured by ELISA assay. Cellular proliferation of CFs after treatment of rGO was measured by Cell Counting Kit-8 (CCK8). The mRNA expression levels of type I and type III collagen and TGF-β1 were detected by Real-time PCR; the protein expression levels of Yap/Taz-TGFβ1/Smads signaling pathways and type I collagen were also detected by Western blot.

RESULTS Echocardiography demonstrated less ventricular remodeling in rGO/silk fibroin modified nanofibrous group, with an increase in the ejection fraction and fractional shortening compared with the MI group. Histopathological staining demonstrated that cardiac fibrosis was attenuated in rGO/silk fibroin modified nanofibrous group. The expression level of Col1 of myocardial tissues in in rGO/silk fibroin modified nanofibrous group was lower than the MI group. Western blot analysis illustrated that the expression level of Yap/Taz-TGFβ1/Smads signaling pathways was decreased in rGO/silk fibroin modified nanofibrous patches treated hearts.

rGO inhibited proliferation of CFs in a dose-dependent manner ($P<0.05$). The secretion levels of type I (Col1) and type III collagen (Col3) in CFs supernatant induced by Ang II was downregulated by treatment of rGO. Real-time PCR results indicated that the gene expression levels of c Col1, Col3 and TGF-β1 in CFs by exposure to Ang II were significantly increased as compared with those in control group ($P<0.05$). However, Ang II-induced Col1, Col3 and TGF-β1 mRNA upregulation was inhibited by rGO treatment ($P<0.05$). Western blot analysis illustrated that the protein expression of Yap/Taz-TGFβ1/Smads signaling pathways and Col1 was decreased after the treatment of rGO ($P<0.05$).

CONCLUSIONS This study suggests that rGO/silk modified nanofibrous patches improve the heart function and attenuate myocardial fibrosis of infraction area. Reduced graphene oxide inhibits the expressions of type I and type III collagen induced by Ang II in cardiac fibroblasts through regulating the Yap/Taz-TGFβ1/Smads signaling pathways.

GW30-e0796

System-wide construction of lncRNA-miRNA-mRNA ceRNA network of cardiac fibrosis

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OBJECTIVES Cardiac fibrosis is a considerable global health problem that derived from many forms of heart diseases all over the world currently. The aims of this study are to elucidate the interaction between ncRNAs and mRNAs via construction of ceRNA network and validate correlation among genes and correlation between genes and clinical features to further understand molucular mechanisms of cardiac fibrosis.

METHODS The expression profile of mRNA and lncRNA and the miRNA expression profile in human cardiac fibroblast are obtained from NCBI GEO. The different expressed genes (DEGs) were identified using the limma package in R. The Gene Ontology (GO) analysis and KEGG pathway analysis was Performed to idenfity function of DEMs and further indentify enriched signal pathway of DEMs using DAVID. The specific lncRNAs and mRNAs targeted by miRNAs were identified based on starbase, miRcode, miRTarbase, Targetscan databases to construct lncRNA-miRNA-mRNA ceRNA network. We performed WGCNA Using WGCNA package in R to discover the relationship among different genes. Further, the outcome was input into Cytoscape to visualize the gene coexpression network. Different expressed lncRNA and miR were qRT-PCR confirmed. All the statistical analysis were performed using R statistical software package Version 3.5.1. $P<0.05$ was considered to be statistically significant.

RESULTS Total 420 differentially expressed mRNAs (DEMs), 30 different expressed miRNAs (DEMis) and 34 different expressed LncRNAs (DELs) were screened. Depended on GO and KEGG analysis, there are 81 significant

enriched biological processes, 21 significant enriched cellular components, 23 significant Enriched molucular functions and 17 significant enriched pathways among these DEMs. For ceRNA network, the lncRNA-miRNA-mRNA network included 398 mRNA nodes, 30 miRNA nodes and 6 lncRNA nodes and 3256 edges. LncRNA XIST, as a hub lncRNA, was linked with 5 miRNAs, 351 mRNAs and 839 edges in the subnetwork. According to the results of DAVID analysis, these 352 mRNAs were enriched into 64 biological processes like most significant enriched inflammatory response (GO: 0006954). Moreover, the genes can be identified into 4 Network modules and module turquiose is most correlated with cardiac fibrosis phenotype. Most genes in module turquiose are also involved in ceRNA network of cardiac fibrosis.

CONCLUSIONS Three hundred ninety-eight mRNAs are in directly regulated by 6 lncRNA via 30 miRNAs are involved in initiation and development of cardiac fibrosis. More importantly, lncRNA XIST play a critical role in cardiac fibrosis, possibly throughout inflammatory response.

GW30-e0807

Colchicine alleviates cholesterol crystals induced endothelial cells pyroptosis through activating AMPK/SIRT1 pathway

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OBJECTIVES Cholesterol crystals-induced endothelial cell inflammation and pyroptosis plays an important role in the development of cardiovascular diseases, especially in atherosclerosis. As a classical non-specific anti-inflammatory drug, colchicine has been widely used in the treatment of acute gout. However, whether colchicine could alleviate cholesterol crystals-induced endothelial cell injury and the related mechanisms remains to be addressed. Hence, we tested the hypothesis that colchicine limits cholesterol crystals-induced endothelial cell pyroptosis via the activation of AMPK/SIRT1 pathway.

METHODS We synthesized cholesterol crystals in vitro, then treated endothelial cells with cholesterol crystals (0.5 mg/mL) and different concentrations of colchicine (0.1–10 nM) and Si RNA targeting AMPK/SIRT1. We assessed the cell viability using CCK8, and the pyroptotic cell death was evaluated with LDH release assay, Hoechst 33342/PI staining and scanning electron microscopy. We also detected the accumulation of ROS and mitochondrial membrane potential energy using the assay kit. The expression of NLRP3 inflammasome-related proteins (NLRP3, ASC-1, Caspase-1) and AMPK pathway-related proteins (p-AMPKα, AMPKα, SIRT1, SOD-2, SOD-1, HO-1) were assessed by western blotting. Moreover, the mRNA levels of various inflammatory factors such as IL-1β, IL-18, IL-6, IL-8, MCP-1 and GSDMD were examined through quantitative RT-PCR approaches.

RESULTS In this study, the protective effect of colchicine on endothelial cells was confirmed. Our results revealed that after co-treatment with colchicine and cholesterol crystal in endothelial cells, the uptake of cholesterol crystal was reduced, and the expression of intracellular lipoprotein receptor was significantly decreased; the cell viability was obviously increased, the release of LDH and the number of pyroptotic cells decreased significantly; then the expression of NLRP3 inflammasome-related proteins and various inflammatory factors were also visibly suppressed; moreover, as a potent activator of NLRP3 inflammasome, intracellular ROS level was clearly reduced, and the mitochondrial membrane potential energy was significantly improved. However, the above effects of colchicine were completely offset by the treatment of SiRNA targeting AMPK and SIRT1.

CONCLUSIONS Therefore, we conclude that colchicine plays a crucial role in inhibiting the intracellular inflammatory response and NLRP3 inflammation activation, cellular oxidative stress and pyroptosis in endothelial cells via regulating AMPK/SIRT1 signaling, which may be a concrete mechanism for the secondary prevention of cardiovascular diseases.

GW30-e0818

Relaxin mitigates microvascular damage and inflammation following cardiac ischemia-reperfusion

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OBJECTIVES Microvascular obstruction (MVO) and leakage (MVL) forms a pivotal part of microvascular damage following cardiac ischemia-reperfusion (I/R). We tested the effect of relaxin on MVO and MVL in mice following cardiac I/R injury.

METHODS Male mice were subjected to cardiac I/R and then treated with relaxin (50 μg/kg) or vehicle. The severity of MVO and MVL, infarct size, regional inflammation and opening capillaries in the heart were determined. A microvascular permeability tracer, Evans blue (20 mg/kg), was given to allow for identification of myocardial MVL while the tissue Evans blue content was measured chromatographically. Echocardiography was performed to assess cardiac function and remodeling. Using cultured endothelial cell monolayer, effect of relaxin on hyper-permeability induced by simulated I/R conditions was examined.

RESULTS Compared to vehicle group, relaxin treatment reduced both no-reflow area by 38% (43±3% vs. 27±3% of LV) and Evans blue content in jeopardized myocardium by 56% (0.054±0.001 vs. 0.124±0.014 μg/mg, both P<0.05), effects associated with increased opening capillaries (19±1% vs. 38±2%, all P<0.05). Relaxin also decreased leukocyte density (465±33 vs. 696±64 No./mm^2), gene expression of IL-1β and IL-6, and mitigated I/R-induced decrease in protein content of VE-cadherin and relaxin receptor. Infarct size was comparable between the two groups. At 2 weeks post-IR, relaxin treatment partially preserved cardiac contractile function and limited chamber dilatation versus untreated controls by echocardiography. Endothelial cell permeability assay demonstrated that relaxin attenuated leakage induced by hypoxia-reoxygenation, H_2O_2, or cytokines, action that was independent of nitric oxide but associated with preservation of VE-cadherin.

CONCLUSIONS Relaxin therapy attenuates I/R-induced MVO and MVL and endothelial leakage both *in vivo* and *ex vivo*. This protection was associated with reduced regional inflammatory responses and consequently led to alleviated adverse cardiac remodeling.

GW30-e0820

The E3MD G51S variant is associated with high blood cholesterol and increases low-density lipoprotein receptor degradation

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OBJECTIVES The E3MD negatively regulates low-density lipoprotein receptor (LDLR) abundance. The aim of this study was to define the mechanism that how E3MD mutant affected cholesterol level in circulating LDL.

METHODS Using whole-exome sequencing, we identified a nonsynonymous variant in E3MD gene that causes Gly51 to Ser mutation from a Chinese Uygur family.

RESULTS Large cohort analysis revealed +/G51S carriers displayed predominantly higher LDL-C levels. Mechanistically, the Gly51 residue is critical for the maintenance of E3MD protein level. G51S mutant E3MD exhibited reduced dimerization, autoubiquitination and enhanced protein stability. The G51S was more potent to ubiquitinate and degrade LDLR. In vivo hepatic expression of E3MD -G51S mutant in mice caused liver LDLR attenuation and subsequent serum LDL-C elevation.

CONCLUSIONS Our study demonstrates that E3MD (G51S) is a gain-of-function variant responsible for high LDL-C in both humans and mice. These results suggest that E3MD is a key player regulating cholesterol level in humans and required for metabolic homeostasis.

GW30-e0825

Protective effect of HSYA on High ox-LDL induced injury of human coronary artery endothelial cells

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OBJECTIVES To evaluate the protective effects of hydroxysafflor yellow A (HSYA) on the injured human coronary artery endothelial cells (HCAECs) induced by High ox-LDL, and related molecular mechanisms.

METHODS Four groups of HCAECs were cultured individually: the control group, High ox-LDL group, High ox-LDL+HSYA group, and HSYA group. After 24 hours of injury induction, the survival rate of each group was measured by colorimetric method with MTT, and the optimal dose of High ox-LDL and HSYA in the test conditions were selected. NO and LDH released from HCAECs in each group were detected by nitrate reduction and lactate dehydrogenase colorimetry method, respectively; and cell apoptosis was analyzed by flow cytometry. The expression of LOX-1 and eNOS genes in transcription levels were detected by reverse transcription-polymerase chain reaction (RT-PCR), and Western blot (WB) was employed to detect the expression in protein levels of LOX-1, eNOS and Bcl-2/Bax.

RESULTS Compared with the control group, High ox-LDL (20 μg/mL) group behaved lower survival rate (99.39±0.66 vs 67.26±2.68, P<0.05); NO content was decreased, and the expression of eNOS mRNA and protein decreased (P<0.05); conversely, LDH content was increased (P<0.05), either the expression

of LOX-1 mRNA and protein levels (P<0.05); the number of apoptotic cells increased significantly (16.28%, P<0.001), the proportion of Bcl-2/Bax protein decreased similarly (P<0.001). Compared with High ox-LDL (20 μg/mL) group, High ox-LDL (20 μg/mL)+HSYA (0.2 mM) increased the cell viability (67.26±2.68 vs 86.63±3.29, P<0.05), promoted NO release (P<0.05); the mRNA expression of eNOS was restored, and then was upregulated in protein level (P<0.05); besides, suppressed LDH secretion (P<0.05), and the expressions of LOX-1 mRNA and protein were decreased (P<0.05); inhibited the cell apoptosis significantly (12.04%, P<0.001), the Bcl-2/Bax protein expression also increased (P<0.05).

CONCLUSIONS Endothelial damage could be induced by the lipid peroxidation, such as addition of High ox-LDL. HSYA displayed a protective effect through up-regulating the expression of eNOS mRNA and protein and then improvement of NO content. In contrast, it could inhibit LDH releasement by down-regulating the expression of LOX-1 mRNA and protein. Treatment of HSYA restored the apoptosis of HCAECs by up-regulating Bcl-2/Bax expression.

GW30-e0846

Metformin breaks the vicious cycle between atrial fibrillation and epicardial adipose tissue remodeling

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OBJECTIVES Epicardial adipose tissue (EAT) remodeling is important for the pathogenesis of atrial fibrillation (AF). We investigated if metformin (MET) prevents AF-dependent EAT remodeling and AF vulnerability in dogs.

METHODS Eighteen male beagle dogs were randomly divided into three groups: (i) sham-operated (normal diet without pacing, n=6), (ii) RAP (Rapid atrial pacing, n=6), and (iii) RAP+MET (RAP with MET). AF model was induced by rapid atria pacing (RAP) at 400 bpm for 4 weeks with a programmable pacemaker. Daily oral administration of MET (100 mg/kg) was initiated 1 week before surgery and continued throughout the study period. The electrophysiological parameters including effective refractory period (ERP), window of vulnerability induced window (WOV) and AF duration, AF inducibility were measured before and after 6 weeks RAP. The content of ROS, inflammatory factor APN and related signaling pathway protein in LA and EAT were detected. To detect the effect of MET on the interactions between HL-1 atrial myocytes and 3T3-L1 mature adipocytes, HL-1 were indirectly co-cultured with LPS-treated 3T3-L1 via an exchange medium.

RESULTS *In vivo*, MET attenuated the RAP-induced decrease in effective refractory periods (ERP) and increase in ERP dispersion, cumulative window of vulnerability, AF inducibility, and AF duration. RAP increased ROS production and NF-κB phosphorylation, upregulated IL-6, TNF-α, and TGF-β1 levels in LA and EAT, decreased PPARγ and adiponectin (APN) expression in EAT, and were accompanied by atrial fibrosis and adipose infiltration. MET was shown to reverse the alterations described above. *In vitro*, LPS stimulated 3T3-L1 adipocytes inflammatory factor expression and decreased APN expression. Indirect coculture HL-1 cells with LPS-stimulated 3T3-L1 conditioned medium (CM) significantly increased inflammatory response and decreased SERCA2a and p-PLN expression, while LPS+MET CM and APN treatment alleviated the inflammatory factor expression and SR Ca^{2+} handling dysfunction.

CONCLUSIONS MET attenuated RAP-induced increase in AF vulnerability and remodeling of atria and EAT adipokine production profiles and APN may play a key role in MET breaking the vicious "AF begets AF" cycle.

GW30-e0869

Protein expression profiles of extracellular matrix in fibrotic myocardium after myocardial infarction

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OBJECTIVES To analyze the components of ECM proteins and the interaction mechanisms within the differential proteins in fibrotic myocardium of CFMI rats model by label-free proteomics.

METHODS CFMI rats model was established by ligation of the left anterior descending coronary artery, then were randomly divided into four groups: Sham after 2 weeks (Sham 2W), Sham after 4 weeks (Sham 4W), CFMI after 2 weeks (Model 2W) and CFMI after 4 weeks (Model 4W), with 10 rats in each group. ECM proteins were extracted using Mary-three-steps. Changes in ECM differential proteins were analyzed by lable-free proteomics. GO analysis was used to describe the characteristics of cellular component, molecular functions and biological processes of ECM proteins. KEGG analysis was used to find the potential underline pathways in regulating expressions of these ECM differential proteins. Finally, the screened out ECM differential proteins were verified by Western Blot (WB).

RESULTS (1) A total of 243 ECM differential proteins were identified. Compared with Sham 2W, Osteoglycin was up-regulated and Nidogen-1 was down-regulated in Model 2W. Compared with Sham 4W, Lumican and Collagen type VI alpha 2 chain (Collagen 6A2) were up-regulated while Nidogen-1 was down-regulated in Model 4W. Compared with Model 2W, Nidogen-1 and Talin-1 were down-regulated in Model 4W (P<0.05). Bio-informatics analysis showed that the cellular component of ECM differential proteins were significantly enriched in extracellular regions, extracellular matrix and other cell components. Molecular functions such as receptor binding, metal ion binding and Integrin binding were enriched. Biological processes such as immune regulation, protein transportation, membrane organization, intercellular signal transduction and cell adhesion were enriched. KEGG analysis showed that focal adhesion kinase (FAK), phosphatidylinositol-3-hydroxykinase (PI3K)/protein kinase B (Akt) and interaction between Integrin and ECM receptor pathways were significantly regulated.

(2) WB results showed that expressions of Collagen 6A2, Lumican and Talin-1 were up-regulated in Model 2W group when compared with Sham 2W group (P<0.05); Collagen 6A2 and Lumican were significantly increased and Nidogen-1 was significantly decreased in Model 4W group when compared with Sham 4W group (P<0.05). When compared with Model 2W group, the expressions of Nidogen-1, Lumican and Talin-1 were down-regulated in Model 4W group (P<0.05). The results involving Collagen 6A2 and Lumican were up-regulated while Nidogen-1 was down-regulated in Model 4W group when compared with Sham 4W group, Nidogen-1 and Talin-1 were down-regulated in Model 4W group when compared with Model 2W group, were coincident between label-free proteomics and WB detection.

CONCLUSIONS The ECM differential proteins including Collagen 6A2, Nidogen-1, Lumican, Talin-1 and Osteoglycin might be the possible targets of CFMI. The mechanisms of regulation in deposition of these ECM differential proteins may relate to FAK, PI3K/Akt and Integrin signaling pathways.

GW30-e0883

Effects and mechanisms of Hirudin treatment in Cardiac fibrosis after myocardial infraction in vivo and in vitro

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OBJECTIVES To observe the effects and mechanisms of Hirudin intervention on cardiac function and myocardial pathology in Cardiac fibrosis after myocardial infraction (CFMI) rats and Ang II induced neonatal rat cardiac fibroblasts (NRCFs).

METHODS CFMI rats were established by ligating the left anterior descending coronary artery of Wistar rats, which were randomly divided into four groups: Sham group (Sham, normal saline), Model group (Model, normal saline), Valsartan group (Valsartan, 144 mg/kg/d) and Hirudin group (Hirudin, 270 mg/kg/d). Twenty rats in each group were treated once a day for four weeks. Echocardiography parameters, peripheral markers and pathological staining were measured. The expression of AMPK, Integrin β1, FAK, PI3K p110α, PI3K p110β, Akt, TGF-β1 and Smad2/3 in fibrotic signaling pathways were measured by WB. NRCFs were separated, extracted, cultivated and lastly identified via vimentin (+)/vWF (–) immunofluorescence staining in vitro. Then NRCFs were randomly divided into four groups: Control group (Control), Model group (Ang II), Valsartan group (Valsartan) and Hirudin group (Hirudin). After 30 min of pre-intervention with corresponding treatment, 10-6M Ang II was employed to induce fibrotic NRCFs for 24 h. Cell proliferation, phenotypic differentiation, cell migration and cell secretion were measured. The protein expression levels of AMPK α1/α2, Integrin β1, FAK, TGF-β1, and Smad2/3 were detected by WB.

RESULTS (1) Compared with the Model group, IVSTs, LVPWT and LVEF were increased, while LVD, EDV and ESV were decreased in Hirudin group; Serum levels of CK-MB, cTnT, ANP, BNP, Ang II and MDA were decreased, while SOD was increased significantly in Valsartan group and Hirudin group; Infarction area and collagen volume fraction were significantly reduced in Valsartan group and Hirudin group; The protein levels of AMPK, FAK, PI3K p110α and Akt were up-regulated, while Integrin β1, TGF-β1 and Smad2/3 were significantly down-regulated in Valsartan group and Hirudin group (all P<0.05). PI3K p110β protein expression showed no significant difference among groups (P>0.05).

(2) After 24 h culture of NRCFs, the ratio of NRCFs with vimentin (+)/vWF (–) was (98.09±1.03) %. Compared with the Ang II group, the percentage of cells in quiescent GoG1 phase was significantly increased, cells in proliferative S phase was significantly decreased; the number of cells with positive immunofluorescence staining of α-SMA and migrating through the Transwell chamber were significantly reduced, moreover the scratch width was significantly extended; The contents of HYP in supernate was reduced, and protein levels of AMPKα1/α2 and FAK were up-regulated, while Integrin β1 was down-regulated in Valsartan group and Hirudin group (all P<0.05). While expressions of TGF-β1 and Smad2/3 in Hirudin group showed no statistical difference with Ang II group (P>0.05).

CONCLUSIONS Hirudin can relieve left ventricle dilation, improve cardiac function, reduce myocardial injury, decrease infarction area and interstitial collagen deposition in CFMI rats. Meanwhile, Hirudin can inhibit Ang II-induced pro-fibrotic changes in NRCFs, involving cell proliferation, phenotypic differentiation, cell migration and secretion of ECM differential proteins. These mechanisms of optimized abilities in dealing with cardiac fibrogenesis is related to the Hirudin regulation of AMPK/Integrin β1/FAK, PI3K/Akt and TGF-β1/Smad2/3 signaling pathways.

GW30-e0888

Myeloid deletion of ALDH2 increases atherosclerosis plaque vulnerability by weakening efferocytosis

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OBJECTIVES Several studies have confirmed that aldehyde dehydrogenase 2(ALDH2) rs671 polymorphism is a susceptibility gene for atherosclerotic cardiovascular disease, due to its Glu504Lys replacement eliminating ALDH2 activity in both heterozygotes and mutation homozygotes to 1-6%. We hypothesized that deletion of ALDH2 in myeloid cells may affect plaque stability via efferocytosis.

METHODS Irradiated apolipoprotein E knockout mice were transplanted with bone marrow from wild type or ALDH2 knockout mice and fed a high cholesterol Western diet. Atherosclerosis, efferocytosis and inflammatory response is to be characterized. We examined whether ALDH2 deletion could affect efferocytic capacity of peritoneal macrophage by coculturing with apoptotic smooth muscle cells. Lipopolysaccharide and liquid supernatant from apoptotic cells were used to stimulate ALDH2$^{-/-}$ and wild type peritoneal macrophage and expression of MerTK, one kind of surface efferocytosis receptor were analyzed.

RESULTS After coculturing peritoneal macrophage with apoptotic smooth muscle cells, ALDH2$^{-/-}$ macrophage displayed significantly decreased efferocytic capacity comparing to wild type macrophage. Myeloid cells from chimeric mice received ALDH2$^{-/-}$ bone marrow expressed significant less ALDH2 protein compared with those received wild type bone marrow.

CONCLUSIONS Our results demonstrated that ALDH2 may stabilize plaque through regulation of efferocytosis.

GW30-e0910

Mechanism of actions of cardiomyocyte lncRNA-056298 on cardiac intrinsic autonomic nerve remodeling by modulating GAP43 in a canine model with induced atrial fibrillation after ganglionated plexi ablation

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OBJECTIVES Atrial fibrillation is the most common persistent tachyarrhythmia in clinical practice. Radiofrequency ablation has become an important treatment for atrial fibrillation but this therapy has high recurrence rate because of cardic intrinsic autonomic neural remodeling. In this context, this study further explored the molecular mechanisms of neural remodeling after radiofrequency ablation and provided a new explanation for nerve remodeling after cather ablation.

METHODS Twelve adult beagle dogs were divided into 1 month control group,1 month ablation group,6 month control group, 6 month ablation group (n=3 in each group). The control groups only underwent thoracotomy, and the experimental groups ablated the right-sided ganglionated plexi. They were sacrificed after 1 month and 6 months respectively. We defined 1 cm of tissue awat from the ganglionated plexi as the target atrial tissue and these tissues were taken for high-throughput sequencing. The differentially expressed target genes related to neural remodeling were screened. To predict target gene of lncRNA that differentially expressed and choose lncRNA which target gene related to neural remodeling. After analysis, we confirmed that lncRNA-GAP43 is used for subsequent studies. The correlation between lncRNA56298 and GAP43 was verified by interfering with lncRNA56298 by qRT-PCR.

RESULTS KEGG analysis and GO analysis were performed on differentially expressed target genes by high-throughput sequencing, KEGG analysis showed that differentially expressed genes were involved in neural growth and axon formation; GO analysis showed that differentially expressed genes were related to neurodevelopment and cardiovascular disease. Western blot and qRT-PCR for tissues, the result of western blot revealed that the expression level of GAP43 is higher in 6 months ablation group than another groups and the result of qRT-PCR showed that lncRNA56298 and GAP43 of 6 months ablation group is highest in all groups,1 month ablation group is higher than 1 month control group, 6 months control group has no significant difference with 1 month control group. The FISH assay of lncRNA56298 contirmed that its subcellular localization revealed that lncRNA56298 located in the cytoplasm and nucleus. 5′RACE and 3′RACE were conducted to verify the complete nucleotide sequences of lncRNA56298. Isolation and extraction of canine primary cardiomyocytes, interference with lncRNA56298 followed by qRT-PCR and western blot showed that after the decline of lncRNA56298, both the gene and protein levels of GAP43 decreased revealed that the lncRNA56298 and GAP43 were correlated. We further demonstrated lncRNA56298 how to influence GAP43.

CONCLUSIONS The occurrence of neural remodeling after radiofrequency ablation of atrial fibrillation may be related to lncRNAs and lncRNA56298 may influence the level of GAP43 to affect the reccurrence of atrial fibrillation after radiofrequency ablation.

GW30-e0949

Drp1-mediated endothelial mitochondrial fragmentation contributes to vascular dysfunction in hypertension

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OBJECTIVES Epidemiological studies have revealed the potential associations between genetic variations of the mitochondrial dynamics-regulating gene and hypertension. Mitochondrial fission of smooth muscle cells has been demonstrated to be involved in vasoconstriction. However, less information is available about the pathophysiological role of endothelial mitochondrial dynamics in the regulation of vascular tone. The present study was aimed to investigate the alterations of endothelial mitochondrial dynamics and its functional consequences in hypertension.

METHODS Mitochondrial networks in the vascular endothelium of hypertensive human subjects, as well as spontaneously hypertensive rats (SHRs) and AngII-induced hypertensive mice, were assessed using transmission electron microscope. In vitro, mitochondrial morphology in human aortic endothelial cells exposed to AngII (10^{-7} M, 48 h) were evaluated with laser confocal after labeling with MitoTracker Green. Six-week-old SHRs or age-matched WKYs were administrated with Mito-TEMPO or Mdivi-1 by intraperitoneal injection for four weeks. Systolic blood pressure was measured by either tail-cuff or catheterization method, and vasodilatory functions were determined in isolated mesenteric artery rings.

RESULTS Mitochondrial fragmentation and stronger Drp1 staining were observed in the aortic endothelium of AngII-induced hypertensive mice and SHRs. In cultured endothelial cells exposed to AngII, we observed a similar loss of mitochondrial networks and increased Drp1 expression. The observed mitochondrial fragmentation was associated with enhanced mitochondrial ROS production, impaired ACh-stimulated eNOS activation and NO production, all of which were blunted by the Drp1 specific inhibitor Mdivi-1 or Drp1 siRNA treatment. Furthermore, Mdivi-1 pretreatment improved endothelium-dependent vasorelaxation to ACh in isolated mesenteric arteries from SHRs, while four-week intraperitoneal Mdivi-1 administration or six-week swimming training ameliorated endothelial mitochondrial fragmentation, vascular endothelial dysfunction and blood pressure elevation in SHRs. Finally, mitochondrial fragmentation was also observed in the endothelium from mesenteric arteries isolated from human hypertensive subjects.

CONCLUSIONS These findings suggest that Drp1-mediated endothelial mitochondrial fragmentation promotes endothelial dysfunction by increasing mitochondrial ROS production, impairing eNOS activation and nitric oxide bioavilability in hypertension, which implicate increased endothelial mitochondrial fission as a contributing mechanism for hypertension.

GW30-e0952

Isolation of human endothelial cells from patient of thoracic aortic dissection and the effect of angiotensin II on Endothelial-to-mesenchymal transition of human aortic endothelial cells

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OBJECTIVES Thoracic aortic dissection (TAD), which caused by the disruption of the intima and blood entering the tear to extend into the media of the aortic walls, is a life-threatening cardiovascular disease. Although previous studies have reported TAD is associated with hypertension, pathogenesis of TAD is not investigated. Endothelial-to-mesenchymal transition (EndMT) has been showed to be involved in cardiac development and a variety of diseases processes like cardiac fibrosis. We collected aortic specimens from patients underwent surgical repair. More and more findings indicated that angiotensin II (AngII) could induce aortic diseases such as aortic aneurysms and dissection.

However, what role are endothelial cells (ECs) play in and the molecular mechanism(s) underlying aortic dissection remains incompletely understood. Hence, the aim of this experiment is to define a methodology for the isolation of aortic endothelial cells and investigate whether AngII induce aortic endothelial cells to undergo EndMT.

METHODS Aortic specimens were obtained from patients undergoing vascular replacement surgery at the Cardiovascular Surgery Unit of the first affiliated hospital of shantou university medical college. Tissues were collected in saline and processed after surgery, The single primary ECs were isolated from the intima using collagenase and pancreatin, then incubated in a 5% CO 2.37°C incubator. Cell morphology was observed using microscope. Flow cytometry to detect CD31 to identify endothelial cells. Normal human aortic endothelial cells (HAECs) purchased from the company were cultured in complete medium (ECM medium with 5%FBS, 1% ECGS and 1% penicillin and streptomycin). Cells from passages 4-6 were used in experiments. HAECs were divided into two groups: control group, and AngII (10^{-7}, 10^{-6}, 10^{-5}, 10^{-4} mol/L)-treated for 24 h group. The expressions of VE-cadherin, Vimentin, CD31, α-SMA were detected by Western blot.

RESULTS The extracted vascular endothelial cells by this methodology showed a polygonal, cobblestone-like shape. Flow cytometry findings indicated positive expression of CD31. Throughout the culture, after one or two round(s) of expansion, we harvested a population of more than 90% pure ECs. The treatment of HAECs in the AngII group resulted in significant increases in the expressions of Vimentin and angiotensin II in dose-dependent manner. The expressions of Vimentin and α-SMA were significantly increased but Ve-cadherin were markedly decreased in the Ang II group. Thus, treatment with Ang II induced the EndMT, particularly at a dose of 10-4mol/L.

CONCLUSIONS This simple and reproducible isolation method provides pure primary cultures of human aortic endothelial cells, thus allowing us to do further research about aortic diseases. The HAECs with Ang II-treated showed increased expression of the fibroblast marker and decreased expression of the EC marker, manifesting that the ECs underwent EndMT. Further, EndMT was enhanced with the increase of AngII concentration. These findings that angiotensin II could induce endothelial-to-mesenchymal transition in human aortic endothelial cells may help us understand the mechanism of how endothelial cells involved in aortic dissection. And the study of normal HAECs may propose to the study of isolated aortic endothelial cells.

GW30-e0957

A novel sodium channel mutation contributes to short QT syndrome through the loss-of-function of depolarizing late sodium current

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OBJECTIVES We evaluate the role of sodium channel gene (SCN5A) variant in SQTS, and characterize the biophysical properties of this channe mutation to determine whether changes are consistent with cardiac defects.

METHODS A female with recurrent syncope, and electrocardiogram (ECG) characterized by short QT interval (QTc 270 ms) and ventricular tachyarrhythmias was identified. The SCN5A gene and the known disease-causing genes (KCNH2, KCNQ1, KCNJ2, CACNA1C, CACNB2b, CACNA2D1) of SQTS were sequenced. Mutated SCN5A channel (Nav1.5) plasmid was constructed by site-directed mutagenesis system and transfected to Human embryo kidney (HEK) 293 cells. Electrophysiological analysis was evaluated by the whole-cell patch clamp recordings. Both proteins from the whole cell and plasma membrane were extracted to evaluate the expression of mutated and WT Nav1.5 respectively.

RESULTS The patient was completely consistent with the diagnosis of SQTS, according to current guideline. A novel heterozygous missense mutaiton p.E428G (c.1283A>G; p.Glu428Gly) was identified. The patient was completely consistent with the diagnosis of SQTS, according to current guideline. A novel heterozygous missense mutaiton p.E428G (c.1283A>G; p.Glu428Gly) was identified. The mutation was at the highly conservative site and not detected in the 400 healthy control chromosomes of the same ethnic background. Biophysical properties analysis showed that p.E428G significantly decreased depolarizing late sodium current (INaL), compared with WT ($P<0.05$). In addition, both the voltage dependence of steady-state inactivation (SSI) and steady-state activation (SSA) of p.E428G were significantly shifted to the hyperpolarization direction ($P<0.05$). P.E428G displayed increased peak sodium current density (INa), compared with WT ($P<0.05$). There was no significant difference of Nav1.5 expression in the whole cell level between p.E428G and WT. However, p.E428G showed significantly increased expression of Nav1.5 in the plasma membrane ($P<0.01$).

CONCLUSIONS We for the first time report the discovery of a novel *SCN5A* mutation- p.E428G in a strong phentoype of SQTS. The mutation leads to the loss-of-function of I_{NaL}, which may underly the potential basis of SQTS.

GW30-e0964

Upregulation of transient receptor potential canonical type 3 channel via AT1R/TGF-β1/Smad2/3 induces atrial fibrosis in aging and spontaneously hypertensive rats

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OBJECTIVES Fibroblasts proliferation and migration are central in atrial fibrillation (AF) promoting structure remodeling, which is strong associated with aging and Hypertension. Transient receptor potential canonical-3 channel (TRPC3) is a key mediator of cardiac fibrosis and the pathogenesis of AF. Here, we have observed the increased TRPC3 expression that induced atrial fibrosis which possibly either mediated by the aging process or related to hypertensive progression.

METHODS In this study, we measured the pathological structure remodeling by H&E staining, Masson staining and Transmission Electron Microscope (TEM). The protein expression levels of fibrotic biomakers and TRPC3 were measured by Western blotting with atrial tissues from normotensive Wistar-kyoto rats (WKY 4m-o, 4-months old), old WKY (WKY 24m-o, 24-months old), spontaueously hypertensive rat (SHR 4 m-o, 4-months old) and old SHR (SHR 24m-o, 24-months old). To illuminate the molecular mechanism of TRPC3 in atrial fibrosis of aging and SHR rats, we detected the inhibited role of TRPC3 selective blocker Ethyl-1-(4-(2,3,3-trichloroacrylamide) phenyl)-5-(trifluoromethyl) -1H-pyrazole-4-carboxylate, pyrazole 3 (Pyr3) on Angiotensin II (Ang II) induced fibrosis in neonatal rat atrial fibroblasts.

RESULTS The pathological examination showed that the Extracellular matrix (ECM) and intercellular collagen fibrils were markerly increased in aged and hypertensive rats. The proteins of atrial fibrotic biomarkers (collagen I, collagen III, transforming growth factor-β1 (TGF-β1)) were significantly upregulated in atrial tissues from WKY 24m-o group, SHR 4m-o and SHR 24m-o groups compared with WKY 4m-o group. Meanwhile, the expression level of TRPC3 was significantly upregulated in WKY 24m-o and both SHR atrial tissues compared to WKY 4m-o rats. In isolated and cultured neonatal rat atrial fibroblasts, Ang II induced the atrial fibroblast migration and proliferation, upregulated the expression levles of TRPC3 and fibrotic biomarkers. TRPC3 selected blocker Pyr3 attenuated the migration and proliferation in neonatal rat atrial fibroblasts. Furthermore, Pyr3 significantly alleviated Ang II-induced upregulation of TRPC3, Collegen I, Collegen III and TGF-β1 through the molecular mechanism of TGFβ-Smad signaling pathway. And that AT1R is involved in Ang II-induced TRPC3 upregulation.

CONCLUSIONS Hence, upregulation of TRPC3 in aging and Hypertension is involved in atrial fibrosis process. Inhibition the upregulation of TRPC3 contributes to reverse Ang II induced fibrosis. TRPC3 may be a potential therapeutic targets for preventing aging and hypertension caused fibrosis.

GW30-e0969

Notch4 deficiency attenuates pressure overload-induced cardiac remodeling in mice

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OBJECTIVES Previous studies have demonstrated that Notch1 and Notch3 protect against pressure overload-induced cardiac remodeling. However, the effect of Notch4 on cardiac remodeling remains completely unknown. Here, our study aimed to investigate the role of Notch4 in cardiac remodeling and to clarify the underlying mechanism.

METHODS Notch4 gene knockout mice were used. Cardiomyocyte-specific overexpression of the activated form of Notch4, intracellular domain (NICD), was achieved by using adeno-associated virus 9. All the mice were subjected to aortic banding to generate pressure overload-induced cardiac remodeling. Echocardiography and hemodynamics were used to assess the cardiac function. After that, hearts of mice were dissected for further pathological examination and molecular biological detection.

RESULTS Our results showed that the knockout of Notch4 markedly inhibited hypertrophic response induced by pressure overload, as indicated by the ratio of heart weight and tibia length and cross-sectional area of cardiomyocytes. Notch4 deficiency decreased ventricle wall thickness and improved cardiac function in mice with aortic banding. Notch4 deficiency also decreased the mRNA expression of brain natriuretic peptide and β-myosin heavy chain. Further detection demonstrated cardiac fibrosis was also suppressed by Notch4 deficiency. Conversely, overexpression of NICD aggravated cardiac hypertrophy and fibrosis, leading to decreased survival rate. The results of western blot revealed the protective effects of Notch4 knockout were mediated by the suppression of protein kinase B (PKB/AKT) pathway in vivo. Using neonatal rat cardiomyocytes, we found that Notch4 depletion caused a significant decrease

in the cell surface area and the mRNA expression levels of hypertrophic markers, whereas NICD overexpression led to an increase in these hypertrophic phenotypes.

CONCLUSIONS These findings identified that Notch4 promoted cardiac remodeling due to its regulation of the AKT pathway.

GW30-e0973

Toll-like receptor 5 deficiency diminishes doxorubicin-induced cardiotoxicity via attenuating p38 signaling pathway

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OBJECTIVES Doxorubicin (DOX) is an effective anti-neoplastic drug, but its clinical application is limited by cardiovascular toxic effects. Oxidative stress, inflammation and cardiomyocyte apoptosis play critical roles in DOX-induced cardiotoxicity. Toll-like receptor 5 (TLR5) mainly expressed in immune cells and cardiac tissues. However, whether TLR5 is involved in doxorubicin-induced cardiotoxicity and its underlying mechanisms remain unclear.

METHODS Global TLR5-deficient mice and wild-type littermates were subjected to a single intraperitoneal injection of DOX (15 mg/kg) for an acute model. Body weight (BW), heart weight (HW), and tibial length (TL) were measured to reflect cardiac injury. Echocardiographic parameters including ejection fraction (EF) and fractional shortening (FS) were collected to assess heart phenotype.

RESULTS The data in our study demonstrated that DOX resulted in significant weight loss and cardiac atrophy, and these pathological alterations were blocked after TLR5 deficiency. TLR5 deficiency also improved cardiac function in mice with DOX treatment. TLR5 deficiency protected the mice from oxidative stress and apoptosis induced by DOX. TLR5 deficiency cannot affect the acute inflammatory reaction in mice with DOX. Western blotting demonstrated that the activation of p38 in hearts caused by DOX was suppressed in TLR5-deficient mice. CBLB502, an agonist of TLR5, aggravated DOX-related cardiac injury, as indicated by the decreased HW/BW, EF and FS. CBLB502 also further enhanced the phosphorylation of p38 in DOX-treated mice. TLR5 deficiency could largely improve cell viability in DOX-treated H9c2 cells. TLR5 deficiency also attenuated DOX-induced oxidative stress in cardiomyocytes.

CONCLUSIONS These findings suggested that TLR5 deficiency attenuated doxorubicin-induced cardiotoxicity in mice.

GW30-e0975

Berbrine prevents atherosclerosis in Apo$^{-/-}$ mice through mediating microbiota

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OBJECTIVES Coptis Chinensis, a Chinese herbal medicine, has been widely used in traditional Chinese medicine for a long time. Berberine, the main alkaloid of Coptis Chinensis, has shown to possess extensive cardiovascular pharmacological activities. In our research, we examined the effects of Berberine on arotic atherosclerosis in ApoE$^{-/-}$ mice and explored whether the anti-atherosclerotic effect of Berberine is related to gut microbiota modulation.

METHODS Forty-five ApoE$^{-/-}$ mice, fed a high fat diet from 6 weeks of age, were randomized into three groups, model group (ApoE$^{-/-}$ group), Berberine in large dose group and Berberine in large dose group. Fifteen 6-week-old C57BL/6 were treated as the control group, fed a basic diet. After 36 weeks, we sacrificed the mice for various measurements.

RESULTS The results showed that treatment with Berberine significantly reduced the arotic atherosclerosis. Berberine could regulate the level of serum lipid and inflammatory factors. Compared with control group, the abundance of Lachnospiranceae increased. After treatment of Berberine with large dose, the abundance of Allbaculum raised.

CONCLUSIONS Berberine has the effects of anti-atherosclerotic and anti-inflammatory effects, which are related to alterations in gut microbiota compositions, indicating the potential therapeutic value of pharmacological approaches that may modulate the gut microbiota in treating atherosclerosis.

GW30-e0977

Danlou Tablet alleviates myocardial ischemia reperfusion injury via regulation of autophagy

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OBJECTIVES Danlou Tablet, which based on Zhang Zhongjing's classical prescription Gualou Xiebai Baijiu Tang, is the representative prescription of *Phlegm and Blood Stasis Co-treatment*. Previous studies have proved that Danlou Tablet can reduce myocardial ischemia reperfusion injury, while its mechanism is unknown. Therefore, this study is to investigate the effect of Danlou Tablet on autophagy of myocardial cells in mice of ischemia reperfusion injury.

METHODS The mice model of myocardial ischemia reperfusion was induced by left coronary artery ligation (ligation for 30 minutes, reperfusion for 24 hours). Forty male C57BL/6J mice of 8 weeks old were pre-administered for 5 days before modeling. Then randomly divided into 4 groups, 10 in each group, which were sham group, vehicle group, Danlou Tablet group ($3g\times kg^{-1}\times day^{-1}$ gavaged in 5 days) and 3MA group (an autophagy inhibitor, 15 mg/kg intraperitoneal injection twice. the first day and 15 min before surgery). Cardiac function was evaluated by small animals' echocardiography system in 24 hours after reperfusion. Triphenyl Tetrazolium Chloride (TTC) staining method was used to detect myocardial infarct size. The apoptosis of myocardial cells was investigated by TUNEL staining. The protein expression of LC3B and mTOR were analyzed by immunoblotting.

RESULTS Compared to vehicle group, the autophagy related protein expression of LC3B and mTOR were increased after treatment with Danlou Tablet, LVEF and LVFS was improved as well. In addition, the proportion of nucleus in the TUNEL staining positive area and myocardial infarct size was reduced.

CONCLUSIONS Danlou Tablet could improve the heart function of mice with ischemia reperfusion by reducing myocardial cell apoptosis. At the same time, self-degradation of cardiomyocytes was prevented, which may be associated with inhibiting the autophagy of cardiomyocytes.

GW30-e0983

Quercetin inhibits salt-induced renal fibrosis and epithelial-to-mesenchymal transition in Dahl salt-sensitive rats

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OBJECTIVES Accumulating evidence has indicated that salt sensitive individuals on high salt intake are more likely to develop renal fibrosis. Epithelial-to-mesenchymal transition (EMT) participates in the development and progression of renal fibrosis in humans and animals. Our previous study showed that salt intake could induce tubular EMT and renal injury in Dahl salt-sensitive rats. Quercetin, a classic flavonoid with multiple pharmacological effects has been reported to possess therapeutic efficacy in the management and treatment of renal fibrosis. The aim of this study was to determine whether Quercetin would ameliorate salt-induced renal fibrosis and epithelial-to-mesenchymal transition.

METHODS Twenty-four male SS and consomic SS-13BN rats were randomized to a normal diet or a high-salt diet or Quercetin. After 4 weeks, systolic blood pressure (SBP) and albuminuria were analyzed, and renal fibrosis was histopathologically evaluated. Tubular EMT was evaluated using immunohistochemistry and real-time PCR with E-cadherin and alpha smooth muscle actin (a-SMA). The pro-fibrotic transcription factor Snail was aslo evaluated using immunohistochemistry and western blot analysis.

RESULTS After 4 weeks, dietary salt intake induced renal fibrosis and tubular EMT as identified by reduced expression of E-cadherin and enhanced expression of a-SMA in SS rats. The pro-fibrotic transcription factor Snail, a key regulator of epithelial-mesenchymal transition (EMT), was also found to be up-regulated after high salt loading. Furthermore, treatment with quercetin alleviated the decline in renal function, and the elevated expression of snail and a-SMA was inhibited by quercetin.

CONCLUSIONS Our results demonstrate the protective effects of quercetin on salt-induced renal fibrosis and epithelial-to-mesenchymal transition in Dahl salt-sensitive rats, revealing a potential therapeutic agent for salt induced renal impairment treatment.

GW30-e0985

Resveratrol ameliorates cardiac injury via NLRP3 inflammasome modulation in diabetes rats

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OBJECTIVES *Background*: NLRP3 inflammasome plays a pivotal role in the development of diabetic cardiac injury. Resveratrol, a natural phytoalexin, has anti-inflammatory properties via inhibition of oxidation, leukocyte priming, and production of inflammatory mediators. In this study, we aimed to investigate the effect of resveratrol on NLRP3 inflammasome in diabetic cardiac injury.

METHODS We used normal C57BL/6 rat to establish type 2 diabetic cardiac injury model. Cardiac structure was investigated with transmission electron microscopy and pathological examination; and gene expression of markers for oxidative stress and inflammation was detected.

RESULTS Resveratrol treatment alleviated the glucose induced cardiac pathological damage. resveratrol also inhibited the glucose-induced NLRP3, ASC,

caspase-1 mRNA and protein expression, and NLRP3 inflammasome activation. Moreover, resveratrol administration not only suppressed the NF-kappaB p65 nuclear translocation, NF-kappaB activity and ROS production in the diabetic cardiac tissue. Meanwhile, resveratrol obviously induced SIRT1 mRNA and protein expression in the diabetic rats.

CONCLUSIONS We demonstrate that resveratrol had cardioprotective effects in diabetic rats. Resveratrol is a negative regulator of NLRP3 inflammasome activation through the sirt1 signaling pathway and protects cardiomyocyte against diabetic cardiac injury.

GW30-e0989

Vitamin D strengthens the angiogenesis of bone mesenchymal stem cells by regulating the PI3K/AKT pathway

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OBJECTIVES Bone mesenchymal stem cells (BMSCs) are non-haematopoietic stem cells with multi-directional differentiation and self-replication that can promote angiogenesis and directly induce differentiation into various cells types, such as osteoblasts and chondrocytes. This study aimed to explore the mechanisms and effects of Vitamin D on the angiogenesis of BMSCs.

METHODS BMSCs were isolated from the femurs and tibias of rats and characterized by flow cytometry. After treatment with different concentrations of 1,25-(OH)2-VD3 (Vitamin D), Cell Counting Kit-8 (CCK-8) was used to analyse the proliferation of BMSCs. The proliferation and migration of BMSCs were measured by Transwell assays and the cell scratch test, respectively. We observed the ability of cells to form bureaucratic structures on Matrigel. Western blot was used to detect the protein expression of VEGF, MMP2 and MMP9 secreted by BMSCs under the influence of Vitamin D. Meanwhile, the effect of Vitamin D on the activity of MMP2 and MMP9 secreted by BMSCs was detected by gelatine zymography. Finally, the phosphorylation levels of key kinases in the PI3K/AKT pathways were determined by Western blot.

RESULTS Vitamin D can promote the proliferation and migration of BMSCs and the ability of BMSCs to form a bureau-like structure on Matrigel. There was a significant improvement in the protein expression level of VEGF, MMP2 and MMP9 and in the activity of MMP2 and MMP9 secreted by BMSCs treated with Vitamin D. The phosphorylation level of AKT increased with time after Vitamin D treatment, and the specific PI3K inhibitor LY294002 weakened the phosphorylation.

CONCLUSIONS Vitamin D can strengthen the ability of BMSCs to promote angiogenesis in vitro, and its mechanism may be related to activation of the PI3K/AKT signalling pathway.

GW30-e0991

Inhibition of miR-24 expression prevents the hyperlipidemia-induced cardiomyocyte injury

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OBJECTIVES Junctophilin-2 (JP2) is the primary structural protein anchoring the sarcoplasmic reticulum (SR) to T-tubules (TTs), its required for normal excitation-contraction (E-C) coupling. This study aims to identify the effect of hyperlipidemia on the structure of transverse tubule (t-tubule) and expression of junctophilin-2 (JP-2) in mouse cardiomyocytes and to test whether miR-24 suppression can protect the hyperlipidemia-induced cardiomyocytes injury.

METHODS Cardiomyocytes (CMs) were isolated by enzyme digestion and differential adhesion method. CMs were collected and cultured with normal fatty acid or high fatty acid (0.5 mM) medium. The high fatty acid cultured CMs were then divided into two groups; one group was treated with miR-24-ASO (anti-sense oligonucleotide) and the other was treated with miR-24-MM-ASO (control scramble). After 48 hours of culture, miR-24 and JP2 expression analysis, laser confocal microscopy imaging was used to record the calcium sparks and the structure of t-tubule.

RESULTS Hyperlipidemia significantly increased the frequency of spontaneous calcium sparks and the destruction of t-tubules in ventricular myocytes. In addition, hyperlipidemia decreased the expression of JP-2 in t-tubules and miR-24 was up-regulated. The miR-24 inhibitors markedly up-regulated expression of JP-2 mRNA and protein in cardiomyocytes subjected to hyperlipidemia. The frequency of spontaneous calcium sparks were also significantly decreased by miR-24 inhibitors. Moreover, miR-24 suppression protected E-C coupling in cardiomyocytes injury by hyperlipidemia.

CONCLUSIONS Our findings show suppression of MiR-24 up-regulated JP-2 expression, and promotes hyperlipidemia-induced cardiomyocytes injury. Providing a potential strategy for hyperlipidemia-induced heart failure.

GW30-e0992

CTRP9 inhibit high glucose-induced cardiomyocyte hypertrophy by autophagy

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OBJECTIVES This study aimed to investigate the effect of CTRP9 on high glucose-induced cardiomyocyte hypertrophy and the related mechanism.

METHODS A model of high glucose-induced cardiomyocyte hypertrophy was made in vitro. Rat cardiomyocyte were randomly divided into 5 groups: the control group, CTRP9 group, high glucose group, high glucose with CTRP9 (treatment at the same time) group, high glucose with CTRP9 (pretreatment) group. The surface area of cardiomyocyte was determined by professional Image analysis software. The protein expression of ANP, β-MHC, Beclin 1 and Atg 12 in each group was quantified by western blot method. The gene level of Beclin 1 and Atg 12 in each group was determined by real-time PCR.

RESULTS Compared to the high glucose group, the cell surface area and the protein level of ANP and β-MHC decreased significantly than that in high glucose with CTRP9 (treatment at the same time) group and in high glucose with CTRP9 (pretreatment) group, there was significant statistical difference ($P<0.05$). High glucose suppressed the expression of autophagy related protein. compared to the high glucose group, the gene and protein level of autophagy related protein such as Beclin 1 and Atg 12 increased significantly than that in the high glucose with CTRP9 (treatment at the same time) group and in high glucose with CTRP9 (pretreatment) group, there was significant statistical difference ($P<0.05$).

CONCLUSIONS CTRP9 can inhibit high glucose-induced cardiomyocyte hypertrophy, and this effect may be mediated by autophagy.

GW30-e0995

Matrine attenuates pathological cardiac fibrosis via RPS5/P38 in mice

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OBJECTIVES Pathological **c**ardiac fibrosis is the common feature in multiple cardiovascular diseases and is associated with increased ventricular stiffness as well as impaired electrical conduction, that contributing to the occurrence of heart failure and life-threatening arrhythmias. Our previous study demonstrated that matrine could attenuate oxidative stress and cardiomyocyte apoptosis, thereby preventing doxorubicin-induced cardiac dysfunction, however, its effect in cardiac fibrosis remains unclear. Thus, the present study aimed to investigate the effect and underlying mechanism of matrine in pathological cardiac fibrosis.

METHODS Mice were subjected to aortic banding (AB) surgery or isoprenaline (ISO) injection to generate pathological cardiac fibrosis and then were exposed to matrine (200 mg/kg/day, po) or equal volume vehicle as the control. Echocardiography, hemodynamic parameters and molecular markers were used to evaluate the effect of matrine on fibrotic remodeling and cardiac dysfunction. To clarify the involvement of P38 and ribosomal protein S5 (RPS5), constitutively active P38 carried by adenovirus or small hairpin RNA against RPS5 were used. Besides, neonatal rat and human cardiac fibroblasts were cultured to assess the anti-fibrotic effect of matrine in vitro.

RESULTS We found that matrine lavage significantly attenuated AB or ISO-induced cardiac dysfunction and fibrotic remodeling in mice. Besides, we also observed that matrine treatment inhibited the proliferation, migration, collagen production and phenotypic transdifferentiation of cardiac fibroblasts. Mechanistically, matrine suppressed P38 activation, and the overexpression of constitutively active P38 completely abolished the protective effect of matrine in vivo and in vitro. We also demonstrated that RPS5 upregulation was responsible for matrine-mediated inhibition of P38 and fibrogenesis. More importantly, matrine was capable of ameliorating pre-existing cardiac fibrosis in mice.

CONCLUSIONS Matrine treatment attenuates cardiac fibrosis via regulating RPS5/P38 signaling in mice. Matrine might be a promising therapeutic agent for treating pathological cardiac fibrosis.

GW30-e0996

Striatin deficiency in Dahl salt-sensitive rats and protective effects of the flavonoid quercetin

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OBJECTIVES Previous studies report that quercetin, an antioxidant flavonol found in apples, berries, and onions, could lowers both systolic and diastolic blood pressure in the Dahl salt-sensitive rats, However, its pharmacological effects have been rarely reported. Striatin is a scaffolding protein that plays a role in vesicular trafficking in neurons. Striatin deficiency is associated with salt sensitivity of blood pressure. The aim of this study was to determine whether Quercetin would ameliorate Striatin deficiency in Dahl salt-sensitive rats.

METHODS Twenty-four male SS and consomic SS-13BN rats were randomized to a normal diet or a high-salt diet or Quercetin. After 4 weeks, PCR amplification to detect Striatin levels of kidney and aorta vessels was performed with TaqMan gene expression assays. The protein expression of Striatin levels was evaluated using immunohistochemistry and western blot analysis.

RESULTS After 4 weeks, compared to SS-13BN rats, dietary salt intake reduced expression of Striatin levels in the kidney and aorta vessels in SS rats. Furthermore, treatment with quercetin elevated expression of Striatin levels in the kidney and aorta vessels in SS rats.

CONCLUSIONS Our results demonstrate Striatin deficiency was associated with salt sensitivity of blood pressure in Dahl rats, and revealing a potential therapeutic agent for salt sensitive hypertension treatment.

GW30-e1002

A novel signaling complex HIP-55/14-3-3 protect against myocardial infarction

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OBJECTIVES To investigate novel regulatory mechanism of myocardial infarction (MI) injury.

METHODS By microarray analysis, we found a novel signaling protein, HIP-55, associated with myocardial infarction. HIP-55 knockout mice and transgenic mice were constructed by Talent technique. Myocardial infarction model was made by ligating the anterior descending coronary artery. Myocardial infarction area was detected by Evans Blue-TTC double staining method. Apoptosis was detected by TUNEL staining. At cellular level, we performed western blot, Co-IP and GST-pull down to investigate the mechanism of HIP-55 in cell survive.

RESULTS HIP-55 is high expression in heart and increased significantly after myocardial infarction. Genetic deletion of HIP-55 increased cardiomyocyte injury after MI. Cardiac-specific overexpression of HIP-55 alleviated myocardial infarction injury after MI. HIP-55 could inhibit cardiomyocyte apoptosis after myocardial infarction. Mechanism research showed that HIP-55 inhibit HPK1 kinase and its downstream kinase JNK after myocardial infarction. Further studies showed that HIP-55 inhibits HPK1/JNK apoptosis pathway depending on the HIP-55/14-3-3 complex. After the mutation of 14-3-3 binding sites, overexpression of HIP-55 could not inhibit HPK1/JNK pathway. In addition, after the mutation of 14-3-3 binding sites, overexpression of HIP-55 could neither reduce the infarct size after myocardial infarction nor inhibit cardiomyocyte apoptosis after ischemia-hypoxia. We further generated cardiac-specific overexpression of HIP-55 wide-type mouse (interact with 14-3-3) and HIP-55 mutant mouse (not interact with 14-3-3), results showed that HIP-55 wide-type mouse, but not mutant mouse protects against myocardial infarction injury.

CONCLUSIONS The expression of HIP-55 increased significantly after myocardial infarction. Increased HIP-55 recruited 14-3-3 protein to form complex to inhibit HPK1 and its downstream JNK apoptosis signaling pathway, which led to the protective role in myocardial infarction.

GW30-e1005

Study of the role and mechanisms of ERG in cardiac fibrosis

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OBJECTIVES Cardiac fibrosis is the key pathophysiological process for cardiovascular disease progressing to heart failure, which is essentially characterized by excessive proliferation, activation and phenotypic transformation of cardiac fibroblasts, resulting in collagen overproduction and cardiac dysfunction. In addition to fibroblasts, there are also a large number of endothelial cells in cardiac tissues. Previous studies have shown that endothelial cells play an important role in regulating fibroblasts proliferation, activation and phenotypic transformation. ETS-related gene (ERG) is a member of the ETS transcription factor family. It is the most expressed ETS transcription factor in mature endothelial cells and plays an indispensable role in endothelial cell differentiation and vascular maturity. At present, most of the researches on ERG are confined to the field of development and tumor, whereas its role and mechanisms in cardiac fibrosis have not yet been clarified. Therefore, the purpose of this study is to explore the role and possible mechanisms of ERG in cardiac fibrosis.

METHODS Mice were exposed to an intramyocardial injection of adenovirus carrying small hairpin RNA against *Erg* to knock down the endogenous ERG expression, collagen deposition, fibrotic markers and fibrosis-related signal pathways were detected to initially verify the role of ERG in cardiac fibrosis. Next, adult mouse or neonatal rat cardiac fibroblasts as well as human umbilical vein endothelial cells were isolated and cultured to further clarify the role of ERG in vitro. And the possible mechanisms of endothelial ERG in regulating fibroblasts proliferation, activation and phenotypic transformation were studied by using endothelial cells-derived condition medium (ConM). Finally, endothelin-1 (ET-1) neutralizing antibody and its receptor blocker were used to determine the role of ET-1 in ERG-mediated paracrine regulation between endothelial cells and fibroblasts in vivo and in vitro.

RESULTS ERG was mainly expressed in endothelial cells of the adult mouse heart, and its protein level was significantly reduced during cardiac fibrosis. Inhibiting endogenous ERG resulted in the occurrence of spontaneous fibrotic remodeling and cardiac dysfunction, accompanied by the activation of various fibrosis-related signal pathways. ERG knockdown in neonatal rat or adult mouse cardiac fibroblasts made no alteration in α-SMA expression, and the mRNA levels of fibrotic markers were also unaffected. Supernatants from ERG deficient-endothelial cells were collected as the ConM for neonatal rat cardiac fibroblasts. Comparing with the control group ConM, ERG-deficient ConM promoted the proliferation, activation and phenotypic transformation of cardiac fibroblasts, as well as the activation of fibrosis-related signal pathways. Besides, we found that ERG knockdown increased the mRNA level of ET-1 in endothelial cells and enhanced its secretion to the ConM. Application of ET-1 neutralizing antibody and its receptor blocker significantly inhibited the proliferation, activation and phenotypic transformation of cardiac fibroblasts, thereby improving ERG knockdown-induced fibrotic remodeling and cardiac dysfunction.

CONCLUSIONS ERG knockdown leads to increased synthesis and secretion of ET-1, which then promotes the proliferation, activation and collagen production of cardiac fibroblasts through a paracrine manner, triggering the occurrence of fibrotic remodeling and cardiac dysfunction.

GW30-e1008

5-Azacytidine combined with angiotensin II promote the differentiation of bone marrow mesenchymal stem cells into cardiomyocytes

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OBJECTIVES To explore the effect of the differentiation of bone marrow mesenchymal stem cells (BMMSCs) into cardiomyocyte-like cells by inducing with 5-azacytidine (5-aza) and angiotensin II (Ang II).

METHODS BMMSCs were isolated from bone marrow of Sprague-Dawley mouse by density gradient centrifugation. The third passage cells were divided into four groups: 5-aza combined with Ang II group (0.1 μmol/L and 10 μmol/L), 5-aza group (10 μmol/L), Ang II group (0.1 μmol/L) and control group. After induction for 24 h, the medium was changed to complete culture medium without any inductor and the cells were culture for 4 weeks. The phase contrast microscope was used to observe the morphological changes. The methyl thiazolyl tetrazolium (MTT) assay was used to observe the ability of cell proliferation. The immunofluorescence staining was used to identify the cardiomyogenic cells. The flow cytometer was used to examine the cell differentiation ratio. The transmission electron microscope was used to view the ultrastructure of the induced cells.

RESULTS The primary BMMSCs formed cell colonies at 14 days. The passaged cells were larger than those of primary culture. After induction, the cells presented long spindle, aligned in parallel and formed "muscle island"-like structure. MTT assay showed that the cell proliferation in 5-aza combined with Ang II group was higher than that of in Ang II group or 5-aza group. The expression of specific protein of cardiac troponin I (cTnI) in induced BMMSCs was positive. Flow cytometer showed that the cell differentiation ratio in 5-aza combined with Ang II group, 5-aza group and Ang II group were respectively (30.0±1.7) %, (24.6±1.9) % and (25.3±2.2) %, demonstrating that the cell differentiation ratio in 5-aza combined with Ang II group was higher than that of in 5-aza group or Ang II group ($P>0.05$). Transmission electron microscopy showed that the induced cells had myofilaments, Z line-like substances.

CONCLUSIONS 5-aza combined with Ang II can promote the differentiation of BMMSCs into cardiomyocytes.

GW30-e1019

Fat mass and obesity associated gene plays a paradoxical effect on macrophages and vascular smooth muscle cells during ox-LDL stimulation

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OBJECTIVES The frequency of rs9903609 fat mass and obesity associated gene (FTO) variant is about 12% in Chinese population, which means about 156 million Chinese may influence by this FTO variant. There are some studies reveal that this FTO variant is associated with a higher risk of CVD, but much more studies show a negative result. Here we aim to figure out this paradoxical clinical phenomenon by biological methods.

METHODS *In vivo*, expressions of FTO, macrophage marker CD68 and smooth muscle cell marker SM22-α in arteries of normal diet and high fat diet ApoE$^{-/-}$ mice were detected by Immunohistochemical staining, Immunofluorescence staining, western blot and Q-PCR. Human atherosclerosis arteries surgery tissues were detected by Immunohistochemical staining. *In vitro*, relations between stimulating concentrations of ox-LDL, lipid up-take related proteins and FTO expression in macrophages and smooth muscle cells were measured by western blot and Q-PCR. Moreover, Lentivirus and small interference-RNA technique were used to perform FTO gene function gain and loss assay *in vitro*.

RESULTS In atherosclerosis mice model, expressions of FTO were up-regulated in aortic artery of high fat diet ApoE$^{-/-}$ mice by Immunohistochemical staining. Immunofluorescence staining showed that FTO expression was down-regulated in macrophage, but up-regulated in smooth muscle cells. As for human atherosclerosis arteries surgery tissues, FTO expressions were up-regulated compared with non-atherosclerosis artery, same with mice model. *In vitro*, FTO expressions were up-regulated when ox-LDL concentration was increased in smooth muscle cells. However, it was down-regulated in macrophage when ox-LDL concentration was increased. Moreover, function gain assay and function loss assay showed that FTO promotes lipid accumulation and up-regulates lipid up-take related proteins in smooth muscle cells, but performed opposite effects in macrophage.

CONCLUSIONS FTO may play a paradoxical effect on macrophages and vascular smooth muscle cells during ox-LDL stimulation. This phenomenon may help to explain that FTO variant is not always be a risk factor of CVD in different study populations.

GW30-e1021

Zingerone attenuates aortic banding induced cardiac remodelling via activating the eNOS/Nrf2 pathway

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OBJECTIVES To explored the role of zingerone in cardiac remodelling.

METHODS Mice were subjected to aortic banding (AB) or sham surgery and then received intragastric administration of zingerone or saline for 25 days. In vitro, neonatal rat cardiomyocytes (NRCMs) were treated with zingerone (50 and 250 μM) when challenged with phenylephrine (PE).

RESULTS We observed that zingerone effectively suppressed cardiac hypertrophy, fibrosis, oxidative stress and inflammation. Mechanistically, Zingerone enhanced the Nuclear factor (erythroid-derived 2)-like 2 (Nrf2)/antioxidant response element (ARE) activation via increasing the phosphorylation of endothelial nitric oxide synthase (eNOS) and nitric oxide (NO) production. Additionally, we used Nrf2-knockout (KO) and eNOS-KO mice, and found that Nrf2 or eNOS deficiency counteracts these cardioprotective effects of zingerone in vivo.

CONCLUSIONS we concluded that zingerone may be a potent treatment for cardiac remodelling that suppresses oxidative stress via the eNOS/Nrf2 pathway.

GW30-e1025

Down-regulation of microRNA-374 can improve the cardiac function of rats with selenium deficiency

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OBJECTIVES To explore the effect of down-regulation of microRNA-374 on the cardiac function of rats with selenium deficiency.

METHODS Sixty SD rats were randomly divided into control group, selenium deficiency group and down-regulation of microRNA-374 group, with 20 rats in each group. Rats in the control group were fed with standard diet. Rats in the selenium deficiency group were fed with low selenium diet. Rats in the down-regulation of microRNA-374 group were fed with low selenium diet and then injected interference with microRNA-374 by adeno-associated virus 9 through caudal vein. The rats were fed for 17 weeks. Then the blood selenium and BNP level of the rats were measured. The cardiac function of the rats was detected by echocardiography. The expression of microRNA-374 was detected by Real-time Quantitative PCR. The expression level of c-myc and caspase-3 protein were detected by Western Blotting.

RESULTS The blood selenium levels in selenium deficiency group and down-regulation of microRNA-374 group were significantly lower than that of control group. BNP level of down-regulation of microRNA-374 group was lower than that of selenium deficiency group. The echocardiography displayed that the cardiac function of the down-regulation of microRNA-374 group was higher than that of the selenium deficiency group. The expression of microRNA-374 in down-regulation of microRNA-374 group was lower than that of selenium deficiency group. Western Blot displayed lower expression of c-myc and caspase-3 in down-regulation of microRNA-374 group than that of selenium deficiency group.

CONCLUSIONS The down-regulation of microRNA-374 by adeno-associated virus 9 can improve the cardiac function of rats with selenium deficiency.

GW30-e1026

Hyperphosphatemia in chronic kidney disease (CKD) exacerbated atherosclerosis by aberrant activation of α- mannosidase 2A1 and 2A2 promoting a complex-type conversion of SCAP N-glycans

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OBJECTIVES Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of mortality in chronic kidney disease (CKD) patients. Compelling evidence indicates that hyperphosphatemia is linked to cholesterol metabolism and ASCVD. However, the molecular mechanisms underlying hyperphosphatemia accelerated atherosclerosis is unknown.

METHODS We performed a cross-sectional study to examine the correlation between hyperphosphatemia and ASCVD risk in Chinese CKD population. We also produced hyperphosphatemic ApoE−/− mice model with a high-phosphate diet. Finally, we cultured human primary vascular smooth muscle cells.

RESULTS Serum phosphorus levels in Chinese CKD patients correlated positively with increased ASCVD risk. The atheroma burden in the aorta of hyperphosphatemic ApoE−/− mice was increased when compared with control while the severity of atheroma lesion paralleled the serum phosphorus level. Hyperphosphatemia elevated SCAP protein levels and the expression of its downstream signaling molecules in the arteries of ApoE−/− mice. *In vitro*, excessive phosphate increased smooth muscle cell SCAP protein levels and HMGCR expression in a dose and time-dependent manner, aggravating intracellular cholesterol accumulation, which was quenched by phosphonoformic acid (PFA) or SCAP and SREBP2 silencing. Excessive phosphate enhanced a complex-type conversion of SCAP N-glycans, delaying SCAP degradation, which facilitated transactivation of SREBP2. Excessive phosphate raised the activity of α-mannosidase 2A1 and 2A2. Blocking phosphorus uptake by PFA or enzyme gene silencing abrogated the effects of excessive phosphate on α-mannosidase II activity, SCAP degradation, HMGCR expression, and therefore intracellular cholesterol accumulation. Elevated α-mannosidase II activity was observed in the artery of both ApoE−/− mice and uremic patients with hyperphosphatemia.

CONCLUSIONS Hyperphosphatemia increased the activity of both α-mannosidase 2A1 and 2A2, which promoted complex-type conversion of SCAP N-glycans. SCAP with complex glycans degrades slower and over-activates SREBP2, leading to increased de-novo cholesterol synthesis, and thereby intracellular cholesterol accumulation and atherosclerotic foam cell formation, which explains why hyperphosphatemia accelerates atherosclerosis in CKD population.

GW30-e1035

Experimental study on the effect of Yiqi Huoxue recipe on myocardial mitochondrial function in rats with heart failure

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OBJECTIVES To observe the effect of Yiqi Huoxue recipe on heart failure, and to explore the mechanism and target of action based on the change of mitochondrial function.

METHODS The left coronary artery ligator model of SD rats was divided into false operation group, model group, low, middle and high dose groups of Yiqi Huoxue recipe, and the intervention was given for 8 weeks. The cardiac structure and cardiac function, NT-proBNP level, HE, Masson staining, myocardial inflammation, fibrosis and other pathological changes were observed, and the effect of Yiqi Huoxue recipe on heart failure model after myocardial infarction in SD rats was discussed. The structure and morphology of mitochondria in myocardial tissue were observed by transmission electron microscope, and the function of mitochondria was detected. RT-PCR and Western Blotting methods were used to observe the structure and morphology of mitochondria. The expression of autophagy proteins LC3B and PINK1, Parkin genes and proteins were detected by mtDNA fusion, mitotic gene and protein levels.

RESULTS Yiqi Huoxue recipe could significantly improve cardiac contractile function, improve EF and FS, to decrease serum NT-proBNP level, reduce myocardial fiber thickening, breakage and arrangement disorder, and reduce myocardial fibrosis and collagen formation. Yiqi Huoxue recipe can significantly improve the disorder of myocardial mitochondria arrangement, swelling of mitochondria and rupture of mitochondrial crest in rats with heart failure, increase the membrane potential of myocardial mitochondria, decrease the opening degree of mPTP, increase the content of ATP in myocardial energy metabolism, decrease the content of ROS and the further damage of mitochondria caused by myocardial energy metabolism in rats with heart failure. Yiqi Huoxue recipe. It can up-regulate the expression of Mfn1, Mfn2 and Opa1, down-regulate the expression of Drp1, Fis, improve the balance of fusion and division of mitochondria, and up-regulate the expression of LC3B, PINK1, Parkin and regulate the autophagy of mitochondria.

CONCLUSIONS The method of invigorating qi and activating blood circulation can maintain the stability of mitochondrial kinetics, improve the "energy hunger" and "oxidative stress", improve the state of cardiomyocytes and delay the progress of myocardial energy metabolism and remodeling by regulating the classical pathway of mitochondrial autophagy.

GW30-e1041

Resolvin D1, a specialized pro-resolving mediator, protects against sepsis-induced cardiac injury

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OBJECTIVES It has been demonstrated that increased inflammation is the key mechanism that mediates sepsis induced cardiac injury. The resolution of inflammation induced by specialized pro-resolving mediators (SPMs) can attenuate the severity of many inflammatory related diseases. However, the protective role of SPMs in sepsis induced cardiac injury remains unclear.

METHODS Resolvin D1 (RvD1), a member of SPMs, was used to evaluate the protective effects of SPMs in sepsis induced cardiac injury. The mice were randomly divided into three groups: Control group, LPS group and RvD1+LPS group (RvD1 group). LPS (10 mg/kg, i.p.) was used to induce the sepsis induced cardiac injury model. RvD1 (5 μg/kg, i.p.) was injected 30 min before LPS injection. Echocardiography was applied to evaluate the cardiac function 6 h after LPS injection. Then the mice were sacrificed and the heart tissue were harvested for biological experiments.

RESULTS LPS administration significantly deteriorated cardiac contractile function, as evidenced by the decreased left ventricular ejection fraction, which was significantly attenuated by RvD1 injection. TUNEL staining showed that LPS injection results in myocytes apoptosis, while RvD1 injection markedly attenuated the severity of myocytes apoptosis. Increased inflammatory response was found in the heart after LPS injection, as evidenced by the increased expression of inflammatory cytokines and increased infiltration of inflammatory cells in the heart. While these inflammatory responses were significantly attenuated by RvD1injection. In addition, the activated NK-κB signaling and MAPKs signaling induced by LPS injection were significantly attenuated by RvD1 injection.

CONCLUSIONS RvD1 can protect the heart against LPS induced cardiac injuries through attenuating the inflammatory response, highlighting the role of inflammation resolution as a potential therapeutic target in sepsis-induced cardiac injury.

GW30-e1043

Inhibition of long non-coding RNA Linc00312 prevents cardiac fibrosis

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OBJECTIVES Long non-coding RNAs (lncRNAs) were characterized as one of the key causes of cardiovascular diseases. However, our understanding of the importance of lncRNAs in cardiac fibrosis is limited. Here, we aims to identify the role of a novel lncRNA, known as lincoo312, in cardiac fibrosis.

METHODS Global lncRNA profiling revealed that lincoo312 was upregulated in cardiac fibroblasts (CFs) stimulated by TGF-beta 1. In vitro, we identified the function of lincoo312 by loss-of-function approaches. Modified antisense oligonucleotides (ASOs) was used to deplete lincoo312 in both the nucleus and cytoplasm. Western blotting was used to detect the expression level of collagen 1,α-SMA and CTGF. Additionally, Cell Counting Kit-8 (CCK-8) and EdU assays were performed to assess the proliferation of CFs.

RESULTS The expression of lincoo312 was markedly upregualted in CFs treated with TGF-beta1. Knockdown of lincoo312 in CFs inhibited the expression of collagen 1,α-SMA and CTGF, as well as suppressed the proliferation of CFs.

CONCLUSIONS Together, our findings uncover a critical role for lincoo312 in the activation of CFs, which may be a new player in the development of cardiac fibrosis, and offer a new target for the prevention of cardiac remodeling.

GW30-e1055

Involvement of profilin-1 in vascular lesion induced by asymmetric dimethylarginine

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OBJECTIVES Asymmetric dimethylarginine (ADMA), a methylated amino acid derived from L-arginine, is inhibits the production of nitric oxide (NO) synthesis in vivo. It has been shown that plasma ADMA level is significantly elevated in patients with cardiovascular disorders associated with reduction of nitric oxide (NO) synthesis. Exogenous ADMA has been found to stimulate the proliferation of VSMC in a time and concentration-dependent manner as a competitive inhibitor of NO synthase. Profilin-1, a small actin-binding protein, has been documented to be involved in endothelial injury and the proliferation of vascular smooth muscle cells (VSMCs) in hypertension. It has been shown that the knockdown of profilin-1 was protective against endothelial dysfunction in the cultured aortic endothelial cells. Profilin-1 activates hypertrophic signaling cascades which contributes to vascular hypertrophy and hypertension. To investigate the relationship between ADMA and profilin-1 in hypertensive individuals and in cultured VSMCs.

METHODS Twelve male spontaneously hypertensive rats (SHRs) and Wistar Kyoto rats (WKYs) were used four the investigation. Rats were randomly assigned to three groups (n=8). L-Losartan group, SHR were treated with losartan (15 mg/kg/day) orally for 8 weeks. H-Losartan group, SHR were treated with losartan (30 mg/kg/day) orally for 8 weeks. WKYs (n=8) and SHR were treated with saline (1 mL/kg) orally for 8 weeks. Systolic blood pressure (SBP) was measured by tail-cuff sphygmomanometer. RASMCs were treated with different concentrations of ADMA as indicated for 24 h or 30 μM ADMA for different periods of time. RASMCs were transfected with profilin-1 shRNA to interrupt expression of profilin-1 protein. profilin-1 expression in RASMCs was tested through real time-PCR and western blot analysis respectively. RASMCs were treated with ADMA, pretreatment with AG490 (5×10^{-5} M) or rapamycin (10^{-8} M) were used. The level and expression of profilin-1 in RASMCs were tested by real time-PCR and Western blot analysis respectively. Cell proliferation was measured via flow cytometry analysis and MTT assay.

RESULTS Compared with healthy subjects, the levels of ADMA, profilin-1, vWF, interleukin-8 (IL-8) and tumor necrosis factor (TNF-α) were markedly elevated and the levels of nitric oxide (NO) were significantly decreased in hypertensive individuals. ADMA-induced protein expression of profilin-1 in RASMCs in a concentration- and time-dependent manner. Moreover, ADMA induced proliferation of RASCMs in a concentration- and time-dependent manner, which was in keeping with previous study. Profilin-1 siRNA knocked down both profilin-1 mRNA and protein levels in RASCMs successfully. Furthermore, compared with negative group, the stimulation of cell proliferation induced by ADMA (30 μM, 24 h) was blunted profilin-1 siRNA with a remarkable decline in the formazan absorbance and the proportion of cells in the S+G2/M phase of RASCMs. Profilin-1 shRNA successfully declined profilin-1 mRNA and protein expression. Furthermore, pretreatment with AG490 (5×10^{-5} M) or rapamycin (10^{-8} M) suppressed ADMA-mediated profilin-1expression and RASMCs proliferation determined by MTT and flow cytometry. Rapamycin inhibited the proliferation of RASMCs. ADMA-induced proliferation of RASMCs and profilin-1 expression were inhibited by blockade of JAK2/STAT3 pathway.

CONCLUSIONS Profilin-1 may be involved in ADMA-mediated vascular lesion in hypertension.

GW30-e1057

No coronary lesions if no collision between antegrade and retrograde coronary flow

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OBJECTIVES Coronary injuries are hypothesized to be caused by the cavitation phenomenon (explosion of air bubbles) which is seen frequently in domestic or industrial pipes. Following hydraulics principle, with distal negative suctioning in diastole, if the coronary dynamic pressure decreases below the vapor pressure (VP) most likely of nitrogen in the blood, bubbles will form. They explode when the coronary dynamic pressure recovers>the VP during systole. These explosions create jet waves weakening and rupturing the cap of the plaque, triggering acute coronary syndrome (ACS). If because of many reasons, there was only laminar flow, without collision between antegrade and retrograde flow, could the plaques appear?

METHODS Angiograms of patient with stable angina having mild to moderate lesions were selected. The comparisons were the flow between the arteries with and without lesion. (Figure 1A (baseline) and B (flow) The left coronary arteries were recorded in the right anterior oblique caudal view and the right coronary artery in the left anterior oblique view (at 15 frames per second) Then the angiograms were viewed off line frame by frame. The first frame was the angiogram of an artery completely filled with contrast. The following frames showed the blood moving in, seen in white. The flow could be LAMINAR, TURBULENT (mixing of blood in white and contrast in black) (Figure 2A and B) or RETROGRADE (black column traveling backward). The turbulent flow reflects the collision between antegrade and retrograde flow. The LOCATION and the length in TIME of laminar, retrograde and mainly turbulent flow were recorded. The flow of the arteries without lesions was compared with the flow of the arteries with lesion.

RESULTS The results of 50 angiograms with stable CAD showed that after being laminar (85%) at the beginning of diastole, the flow became turbulent with diffuse mixing of black (contrast) and white (blood) at the MID SEGMENT of the LAD, LCX or RCA. This observation matched with the location of 82% of plaques. The length of the time of retrograde flow lasted more than 30 frames encompassing 2 systoles.

CONCLUSIONS This is the first time, the matching of location of plaques and turbulent flow representing the collision between antegrade flow in diastole and retrograde flow in systole was confirmed. These results may help to find the precise measures preventing the genesis of coronary artery disease.

GW30-e1065

Genotypic variations in MYL2 and MYL3 genes in hypertrophic cardiomyopathy patients of Indian origin

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OBJECTIVES Mutations in MYL2 and MYL3 gene are present in <1% of hypertrophic cardiomyopathy and the phenotypic expression may vary with respect to the mutation. Objective of the present study is to investigate the genetic variations in MYL2 and MYL3 genes in hypertrophic cardiomyopathy patients of Indian origin.

METHODS Institutional Human Ethics Committee Savitribai Phule Pune University and Bharti Hospital, Pune approved the present study protocol (DCG1 Reg. no. ECR518). HCM patients were recruited from Cath lab of Bharti Hospital, Pune. 2-D echocardiography and ECG were performed by cardiologists. HCM was determined on the basis of size of interventricular septum (12 mm and above). DNA was extracted by phenol: chloroform: isoamylalchol and PCR optimization was done for all the exons. SSCP was done for study of mutations and mutations were confirmed by Sanger sequencing.

RESULTS Study of all the exons of MYL2 revealed a C>T transition (rs2233260) which is of intron variant at g.7528 located in exon 07 of MYL2 gene. SSCP analysis shows a band shift in exon 7 of proband 16 and no band shift was observed in control and other HCM positive samples. Mutant shows less free energy (−116 Kcal/mol) as compared to control (−118.4 Kcal/mol). This change in free energy results in less stability of mutant as compared to control. Screening of all the exons of MYL3 gene by SSCP technique reveals a band shift in proband 06 of exon 03. Samples were forwarded for Sanger sequencing and bi-directional sequencing reveals a G>C transversion at chromosomal position 46902336. This polymorphism is of "novel status" as confirmed on dbSNP, 1000 genomes and ExAC Browser.

CONCLUSIONS Genotypic variations in MYL2 and MYL3 genes show an effect on phenotypic expression in the probands such as Slit like left ventricular cavity, LV cavity obliteration during systole, LV diastolic dysfunction, sclerotic aortic valve, trivial aortic regurgitation, Minimal and tricuspid mitral regurgitation, Mild pulmonary hypertension, etc.

GW30-e1068

MtFt protects mitochondria and autophagosomes formation against doxorubicin mediated cardiotoxicity

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OBJECTIVES The critical mechanism of doxorubicin (DOX) mediated cardiotoxicity has been previously attributed to a theory of "iron and ROS". Recent study reports which associated with inhibition of autophagic degradation and mitochondrial respiration defection, what's more, defected respiratory chain could inhibit lysosomal hydrolysis. The present study investigates the effect of mitochondrial ferritin (MtFt), a mitochondrial iron-storage protein, on autophagosomes formation in DOX treated cardiomyocytes.

METHODS H9c2 cardiomyoblasts were treated with DOX (0.5–10 μM), with or without pre-treated 10 μM Bay 60–2770, an activator of oxidized and deactivated soluble guanylate cyclase (sGC), which up-regulated the level of MtFt expression significantly in our previous DOX rats model and attenuated DOX induced cardiomyopathy. Cell viability and DCFH-DA were measured. We constructed MtFt knock down (MtFt-KD) cells by using siRNA, subsequently did Cyto-ID autophagy detection. Also, MitoSOX RED and TMRE fluorescence under DOX exposure were examined. Proteins expression levels were examined by western blot analysis.

RESULTS DOX induced mitochondrial ROS increasement significantly, and many autophagosomes formation. DOX decreased TMRE fluorescence in H9c2 cells, induced mitochondrial membrane potential loss. High level MtFt expression associated with decreased intracellular ROS and mitochondrial ROS, and increased TMRE fluorescence with more abundant autophagosomes. But there're no significant on the levels of LC3 II, LC3 I, Becline1 and P62 expression level except for significantly increased autophay-related protein 5 (ATG5). However, siMtFt induced decrease of autophagosomes in DOX H9c2 cells significantly.

CONCLUSIONS MtFt participated in autophagosomes formation. MtFt could protect mitochondrial respiration against DOX cardiotoxicity and improve autophagic degradation process potentially.

TRANSLATIONAL RESEARCH OF CARDIOVASCULAR DISEASE

GW30-e0025

The long non-coding RNA ANRIL regulates endothelial dysfunction by targeting the miR-let-7b/TGFβR1 signalling pathway

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OBJECTIVES The long non-coding RNA antisense non-coding RNA in the INK4 locus (ANRIL) plays a critical role in atherosclerosis development. However, the precise effect of ANRIL on endothelial dysfunction remains unclear. In this study, we investigated the expression of ANRIL in patients with coronary artery disease (CAD) and the regulatory influence of ANRIL on the proliferation, apoptosis, inflammatory activation and tube formation of human umbilical vein endothelial cells (HUVECs) and elucidated the underlying molecular mechanism.

METHODS In this study, 111 CAD patients were included and detected the expression of ANRIL in coronary sinus blood plasma. We analysis the correction between ANRIL and endothelial dysfunction markers. Downregulation the expression of ANRIL in HUVECs and examine the role of ANRIL in regulating endothelial endothelial dysfunction which participates in AS. We also elucidated the underlying molecular mechanism.

RESULTS Levels of ANRIL were elevated in acute coronary syndrome patients. The expression of ANRIL is associate with inflammation cytokines MCP-1 and IL-10 which secreted by endothelial dysfunction. Knockdown of ANRIL significantly promotion the proliferation and tube formation, inhibited of inflammatory activation and apoptosis of HUVECs, significantly increased the levels of TGF-βR1 and p-Smad signalling pathway members and enhanced the expression of let-7b. ANRIL-mediated inhibition of let-7b regulates HUVEC dysfunction by targeting the TGF-βR1 signalling pathway.

CONCLUSIONS We investigated the expression of ANRIL in ACS patients and identified a crucial role of ANRIL in regulating endothelial dysfunction through targeting let-7b-TGFβR1 signalling pathway. This study highlights a new therapeutic strategy for preventing endothelial dysfunction associated with cardiovascular disease.

GW30-e0040

Gene delivery of SERCA2a improves lung and heart function in hypoxia-induced pulmonary arterial hypertension

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OBJECTIVES Sarcoplasmic reticulum Ca2-ATPase 2a (SERCA2a) modulates calcium homeostasis in vascular smooth muscle cells, which is downregulated in pulmonary artery smooth muscle cells isolated from in pulmonary arterial hypertension (PAH) patients and animal models of PAH. The purpose of the study was to evaluate the effects of overexpression of SERCA2a on hypoxia-induced PAH in rats.

METHODS Forty Sprague-Dawley rats weighing 250 to 300 g were randomly divided into normal control (control) group, hypoxia (hypoxia) group, hypoxia+AAV-GFP (hypoxia+GFP) group and hypoxia+AAV-SERCA2a (hypoxia+SERCA2a) group. Adeno-associated virus (AAV-GFP or AAV-SERCA2a) was delivered intratracheally via tracheal catheter in a hypoxia-induced PAH model. The right ventricular systolic pressure (RVSP) and the right ventricular hypertrophy index (RVHI) were detected. The lung tissue sections were stained with van Geison staining. Percentage of wall thickness (WT%) and wall area (WA%) of pulmonary arterioles was measured. Right ventricular wall thickness (RVWT), right ventricular internal diameter (RVID), cardiac output (CO) and pulmonary artery acceleration time (PAAT) were measured by transthoracic echocardiography. The expression of SERCA2a was detected by western blotting.

RESULTS SERCA2a expression was signifcantly decreased in the hypoxia treated rats in comparison with the controls. RVSP and RVHI in the hypoxia group and hypoxia+GFP group were significantly elevated compared with those in the control group. However, overexpression of SERCA2a significantly inhibited the elevation of RVSP and RVHI. Compared with the control group, these parameters of WT%, WA%, RVWT and RVID were significantly increased while CO and PAAT were significantly decreased in the hypoxia and hypoxia+GFP group. Gene transfer of SERCA2a obviously decreased WT%, WA%, RVWT and RVID, restored CO and PAAT to nearly normal level compared with the hypoxia+GFP group.

CONCLUSIONS Our data suggested that overexpression of SERCA2a attenuated pulmonary artery pressure and improves heart function in hypoxia-induced PAH by alleviating lung vascular and right ventricular remodeling.

GW30-e0229

GBGT1, the controversial expression of FS antigen on red blood cell surface, may have an effect on lipid metabolism of human hepatocytes

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OBJECTIVES FORS blood group system, which expresses Fossman antigen on the surface of red blood cells, is newly discovered by human, and its coding gene in human is GBGT1. The mutation c.887G>a [p.arg296gln] in A few ABO subgroup members of does allow FS antigen to be expressed on the surface of red blood cells. However, in recent years, we have also found that most human erythrocytes have negative Fossman antigen expression, and single nucleotide mutations such as c.688G>a, c.887A>G and c.363C>A can explain this conclusion. In addition, our understanding of the function of GBGT1 is limited, so we did this study.

METHODS We compared the expression levels of blood lipidemia and GBGT1 in the peripheral blood of 89 patients with acute myocardial infarction and 89 patients with stable angina pectoris who had no vascular stenosis from May 2016 to October 2016. Meanwhile, gene transfection technology was applied to set the experimental group with GBGT1 gene and the control group with negative vector to compare the triglyceride and cholesterol levels of the two groups. In addition, PT-PCR experiments were conducted to observe whether the experimental group had an effect on the expression of lipid-metabolism-related genes, such as HMGCR and LDLR etc.

RESULTS Clinical experiments showed that the expression level of GBGT1 mRNA in the myocardial infarction group was significantly higher than that in the stable angina pectoris group, and the expression level was represented by, which were 3.180×10^{-3} (2.613×10^{-3}, 4.613×10^{-3}) and 2.794×10^{-3} (1.708×10^{-3}, 4.771×10^{-3}), respectively, with statistically significant differences. At the cellular level, the triglyceride concentration in the GBGT1 group was higher than that in the negative control group, $2.543\times10^{-3}\pm0.037\times10^{-3}$, $2.044\times10^{-3}\pm0.017\times10^{-3}$, respectively. Rt-PCR found that the mRNA levels of SREBP1 and SCAP in GBGT1 group were significantly increased.

CONCLUSIONS GBGT1 gene may affect lipid metabolism by increasing the expressions of SREBP1 and SCAP, and serve as one of the molecular markers for identifying coronary heart disease.

GW30-e0245

C1q/TNF-related protein 5 promotes atherogenesis by enhancing transcytosis and oxidative modification of low-density lipoprotein through increasing 12/15-lipoxygenase

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OBJECTIVES Increased transcytosis of low-density lipoprotein (LDL) across the endothelium and oxidation of LDL deposited within the subendothelial space are crucial early events in atherogenesis. C1q/TNF-related protein (CTRP) 5 is a novel secreted glycoprotein and its biological functions are largely undefined.

METHODS In this study, we analyzed CTRP5 levels in sera of patients with coronary artery disease (CAD, n=288) and non-CAD controls (n=264). In this study, we analyzed CTRP5 levels in sera of patients with coronary artery disease (CAD, n=288) and non-CAD controls (n=264). The role of CTRP5 in LDL transcytosis and oxidative modification was investigated in vivo and in vitro.

RESULTS We found CTRP5 serum levels were higher in patients with than without CAD (247.26±61.71 vs. 167.81±68.08 ng/mL, P<0.001), and were positively correlated to the number of diseased vessels (Spearman's r=0.611, P<0.001). Increased expression of CTRP5 was detected in human coronary endarterectomy specimens as compared to non-atherosclerotic arteries. Immunofluorescence showed that CTRP5 was predominantly localized in endothelium and macrophages in human atherosclerotic lesions. *In vivo* and *in vitro* experiments demonstrated that CTRP5 promoted transcytosis of LDL across endothelial monolayers, as well as the oxidative modification of LDL in endothelial cells. Inhibition of CTRP5 with a neutralizing antibody dramatically attenuated the deposition of oxidized lipids in the aortic wall of $ApoE^{-/-}$ mice. Mechanistically, we found that CTRP5 up-regulated 12/15-lipoxygenase (LOX), a key enzyme in mediating LDL trafficking and oxidation, through STAT6 signaling. Genetic or pharmacological inhibition of 12/15-LOX dramatically attenuated the deposition of oxidized LDL in subendothelial space and the development of atherosclerosis.

CONCLUSIONS These data indicate that CTPR5 is a novel pro-atherogenic cytokine and promotes transcytosis and oxidation of LDL in endothelium through up-regulating 12/15-LOX.

GW30-e0631

Dietary nitrate mediates cardioprotective effect by increasing export of nitric oxide bioactivity from red blood cells

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OBJECTIVES Existing evidences suggest that dietary nitrate improves endothelial function and ischemic tolerance via an NO-dependent mechanism. Recent data indicate that red blood cells (RBCs) are an important source of NO bioactivity that protects the heart from ischemia-reperfusion injury. It is unknown whether dietary nitrate exerts cardioprotection during myocardial ischemia-reperfusion by increasing export of RBC NO bioactivity. Objective: To investigate whether dietary nitrate protects the heart against ischemia-reperfusion injury via a mechanism mediated by RBCs.

METHODS Mice on nitrate-free chow were treated with vehicle or nitrate (1 mM) in the drinking water for 4 weeks. RBCs were collected and isolated by the end of the forth week. Patients with mild hypertension (systolic blood pressure >130, ≤159 mmHg) were randomly assigned to one of three groups after a 2-week run-in period on a diet low in nitrate: group 1 received nitrate-rich vegetables (green leafy, ~150 g/day) plus pill with placebo salt (KCl), group 2 received low nitrate vegetables (cherry tomato, sweet corn, capsicum, carrot, ~150 g/day) and capsules with nitrate salt (KNO_3, 300 mg) and group 3 received low nitrate vegetables and placebo capsules for 5 weeks. The nitrate content of the pills and nitrate-rich vegetables were precisely matched. As a pre-specified substudy, RBCs were collected blindly from 48 subjects before (baseline) and after the 5-week treatment (follow-up). The effect of the RBCs from the mice and human subjects were investigated in isolated Langendorff-perfused mouse and rat hearts, respectively. The hearts were subjected to global

ischemia (mouse hearts 25 min, rat hearts 30 min) followed by reperfusion (60 min). The RBCs were administered into the coronary circulation at the onset of ischemia with and without the soluble guanylyl cyclase (sGC) inhibitor (1H-[1,2,4] Oxadiazolo[4,3-a]quinoxalin-1-one, ODQ). Left ventricular developed pressure (LVDP) was recorded as an indicator of cardiac function.

RESULTS RBCs from nitrate-treated mice improved post-ischemic recovery of LVDP in comparison with RBCs from vehicle-treated mice. The protective effect was abolished by pre-incubation of the RBCs with the sGC inhibitor ODQ (Fig. A). By contrast, pretreatment of the isolated hearts with ODQ failed to block the protective effect of RBCs from nitrate-treated mice (Fig A) indicating that sGC in the RBC but not in the heart is critical for nitrate-induced cardiac protection. The post-ischemic recovery of rat hearts given RBCs collected from the hypertensive patients at baseline was similar in the three groups (Fig. B). Notably, post-ischemic recovery of LVDP was significantly improved by administration of RBCs from patients randomized to high nitrate vegetables or nitrate capsule compared to the group randomized to low nitrate and placebo (Fig. C). There was no difference in LVDP recovery between the groups receiving high nitrate vegetables or nitrate capsule (Fig. B). The nitrate-induced improvement in post-ischemic cardiac recovery was completely abolished by the sGC inhibitor ODQ (Fig. D), indicating that the protective effect induced by RBCs from subjects given nitrate is NO-sGC dependent.

CONCLUSIONS Dietary nitrate induces export of RBC NO activity and protects the heart against ischemia–reperfusion injury via an RBC NO-sGC pathway.

GW30-e0826

Urotensin II gene knock-out ameliorates cardiac fibrosis in type 2 diabetic mice

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OBJECTIVES *Aim:* Urotensin II (UII) is a potent of vasoactive peptides. We previously found that UII was involved in diabetes cardiomyopathy. The aim of this study was to explore whether UII gene knock-out could ameliorate cardiac fibrosis in type 2 diabetic mice.

METHODS Sixteen male six-week-old UII(–/–) C57BL/6J mouse (17–20 g) and 16 age matched male wild type C57BL/6J mouse (17–20 g) were randomly divided into wild type control group (WT), wild type diabetes group (WT+DM), UII(–/–) control group and UII(–/–) diabetes group (UII–/– +DM). UII gene knockout model of mice was established with TALEN. Diabetic mice were induced by feeding high fat diet for six weeks and a one-time intraperitoneal injection of STZ (120 mg/kg), followed by an 8-week of high fat diet. Cardiac function and pathological changes, immunoreactivity of UII/UT (UII receptor), mRNA expression of TGF-β1, IL-6, TGF-βRII, CTGF and Col I, and protein expression of TGF-βRII, CD31, α-SMA were determined by echocardiography, HE staining and Sirius red staining, Real time RT-PCR, immunohistochemistry and Western blotting, respectively.

RESULTS At the 15th weekend, the WT+DM group showed significantly increases of fasting blood glucose and TG, TC and LDL-C levels, lower of Left ventricular ejection fraction and short axis shortening rate, marked myocardial disarray and fibrosis compared with the WT control group. In addition, weaker CD31 immunoreactivity while marked UII/UT, α-SMA immunoreactivity were shown in heart in WT+DM group. Compared with WT control group, the mRNA expression of TGF-β1, TGF-βRII, COLI, CTGF and the protein expression of TGF-βRII, and interstitial cell marker α-SMA were significantly increased while endothelial cell marker CD31 protein expression was significantly decreased in WT+DM group. There were no significant differences about these changes between UII–/– and WT control group except for lower of TGF-β1 and higher of cd31 mRNA expression in the UII–/– control group. Importantly, UII gene knockout can significantly decrease fasting blood glucose and the TG, TC and LDL-C levels, improve Glucose Tolerance and insulin sensitivity by glucose and insulin tolerance tests, and improve cardiac functions in diabetic mice. Compared with the WT+DM group, the degree of myocardial fibrosis in the UII–/– +DM group was significantly alleviated. The immunoreactivity of UII/UT was decreased, CD31 was increased, and the expression of α-SMA was decreased in UII–/– +DM group compared with the WT+DM group. The mRNA expression of TGF-β1, TGFβ-RII, CTGF, IL-6, and the protein expression of TGF-βRII and α-SMA were significantly lower while CD31 protein expression was significantly higher in UII–/– +DM group than that of WT+DM group.

CONCLUSIONS This study suggested that knockout UII gene might reduce fasting blood glucose levels, improve insulin resistance, reduce myocardial fibrosis and improve cardiac function, probably via inhibition of microvascular endothelial mesenchymal transition and inflammation.

GW30-e0842

Single-Cell RNA sequencing reveals classical monocytes promote ventricular remodeling after myocardial infarction through secreting CCL3L3, CCL4L2 and involving the chemokine family inflammatory pathways

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OBJECTIVES Although patients of acute myocardial infarction (AMI) performed primary PCI (PPCI) within 12 hours, 30% still progress to irreversibly ventricular remodeling. The mechanism of this phenomenon is still unclear. The aim of this study was to explore the effects of monocytes cells in peripheral blood on ventricular remodeling by single-cell RNA sequencing.

METHODS We perform scRNA-seq 10X Genomics on 43567 single peripheral blood mononuclear cells (PBMC) from 6 male patients with AMI undergoing PPCI within 12 h and accepted ACEI/ARB, β-Block, and aldosterone standard medicine treatment over 1 year, which including 3 patients with LVEF≥55% as preserved LVEF (Pre-LVEF) group and 3 with LVEF≤40% as reduced LVEF (Re-LVEF) group. Another 3 male healthy people were selected as healthy control. Cell Ranger, Seurat and other R packages are used to normalize data and analyze differentially expressed genes. The scRNA-seq results are verified by flow cytometry and qPCR in PBMC from patients.

RESULTS The clinical marker NT-proBNP and TNT-HS increased significantly in Re-LVEF group compared to Pre-LVEF group and healthy control. Unbiased clustering identified 21 clusters which were singled out with top 20 upregulated markers, including: 8 clusters for T cells, 3 clusters for B cells, 3 clusters for NK cells, 3 clusters for monocytes, 1 cluster for NKT cells, 1 cluster for megakaryocytes, 1 cluster for plasmacytoid dendritic cells, 1 cluster for mixed cells. Compared to the healthy control and Pre-LVEF group, the proportion of classical monocytes, KLRC2+ adaptive NK cells, CD4+ Treg cells and plasmacytoid dendritic cellsare upregulated in Re-LVEF group, which show no significant difference in proportion between healthy control and Pre-LVEF group, and the proportion of CD8+ cytotoxic T cellssubset increases moderately in Pre-LVEF group, and increases significantly in Re-LVEF group, compared to healthy control, respectively. The upregulated genes of different subsets are all involved in several inflammatory pathways through KO and GO enrichment analysis. CCL3L3 and CCL4L2 show similar expression in healthy control and Pre-LVEF group, but significantly upregulated in Re-LVEF group almost in all clusters. Through t-SNE distribution diagram, CCL3L3 and CCL4L2 show extreme enrichment and upregulation in classical monocytes and non-classical monocytes. Cell trajectoryanalysis of monocytes shows S100A family and CCL3L3, CCL4L2 are the key genes in the branch point from classical monocytes to non-classical monocytes. Flow cytometry verified the presence of classical monocytes and non-classical monocytes and show the same proportion compared to the scRNA-seq results.

CONCLUSIONS Classical monocytes, KLRC2+ adaptive NK cells, CD4+ Treg cells, plasmacytoid dendritic cells and CD8+ cytotoxic T cells promote ventricular remodeling after AMI with PPCI through various inflammatory pathways. Classical monocytes promote ventricular remodeling by secreting CCL3L3, CCL4L2 into peripheral blood, meanwhile activating the chemokine family inflammatory pathways and might be a new predict marker of ventricular remodeling in the future. The cell subsets defined by scRNA-seq show the heterogeneous view of peripheral blood immune cells from myocardial infarction after PPCI and provide new therapy targets for ventricular remodeling.

GW30-e0950

Using machine learning to match culprit lesions in acute coronary syndrome with turbulent flow caused by collision of antegrade and retrograde coronary flow

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OBJECTIVES Coronary artery disease (CAD) is hypothesized to be caused by cavitation (explosion of air bubbles) which is seen frequently in domestic or industrial pipes. With distal negative suctioning in diastole, if the coronary dynamic pressure decreases below the vapor pressure (VP), bubbles will form. They explode when the coronary dynamic pressure recovers>the VP in systole and create jet waves weakening, rupturing the cap of plaques, triggering acute coronary syndrome (ACS). How could these events be located and tabulated by Machine Learning of artificial intelligence (AI) program compared to the results of human investigators?

METHODS Angiograms with culprit lesions (recorded at 15 frames/second) were reviewed frame by frame. The first frame was of the artery completely filled with contrast. The following frames showed the (white) blood moving in. The flow could be LAMINAR, TURBULENT (mixing of blood in white and contrast in black) or RETROGRADE (black column traveling backward). The turbulent flow reflects the collision between antegrade and retrograde flow. The investigations included the direction and duration of flows. The intensity of turbulence was measured by (1) length of coronary segment with turbulence (2) length of the stagnant retrograde flow. The AI programs were trained to use the U-Net deep learning for medical image segmentation and then build the UNet model based on the previous dataset (Images, ImageMask).

RESULTS Angiograms of 20 patients showed laminar flow (85%) in diastole. The flow became turbulent at systole with diffuse coarse mixing of black (contrast) and white (blood) at the MID SEGMENT of the left circumflex artery (LCX) or the right coronary artery (RCA). The presence of turbulence matched the location of 86% of ruptured plaques. The time of retrograde flow lasted more than 2 systoles. Special protocols were used successfully to train AI to recognize the lesions, antegrade, retrograde flow, turbulence and the persisting retrograde stagnant area.

CONCLUSIONS This is the first time, the matching of location of ruptured plaques and turbulent flow representing the collision between antegrade flow in diastole and retrograde flow in systole was confirmed and compared between humans and AI These results may help to understand the genesis and offer precise prevention and treatment in ACS.

GW30-e1070

SOX7/WnT4/BMP2 axis modulates endothelial to mesenchymal transition involved in atrioventricular cushion morphogenesis

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OBJECTIVES Disruption in cardiac cushion formation can lead to septal and valvular malformations, which account for the largest proportion in congenital heart defects. The transcription factor Sox7 has critical functions in the differentiation of multiple mesodermal lineages. However, its effect on cardiac cushion development has not been explored. This study aims to clarified the role of Sox7 in cardiac cushion development and the underlying mechanisms.

METHODS Whole exome sequencing was performed in 100 atrioventricular septal defect (AVSD) patients and 100 controls. Sox7 in a patient with 8p23.1 deletion was thought to be the candidate gene of this AVSD patient. Then, Sox7 endocardial lineage specific loss-of-function (Sox7 EnKO) and gain-of-function (Sox7 EnKI), pan-endothelial cells specific and cardiac progenitor cells specific loss-of-function (Sox7 EcKO and Sox7 CpcKO respectively) mice were generated. Transcriptome analysis was performed. Sox7 downstream target genes BMP2 and Wnt4 were confirmed by luciferase, ChIP assays and rescue experiments. Finally, Sox7 EnKI embryos were carefully screened for the changes of EndMT process.

RESULTS Ten rare copy number variants (CNVs) were identified among 100 AVSD patients. Among the 10 rare CNVs, deletion of 8p23.1 had been reported to be associated with congenital heart defects, particularly in the form of AVSD, and we verified the 8p23.1 deletion by qPCR. Interestingly, the known AVSD-related genes were not identified in the patient with 8p23.1 deletion. Sox7 EnKO embryos exhibited delay in fusion of ventricular septum with cardiac cushion and partial AVSD, the cardiac cushion endothelial to mesenchymal transition (EndMT) process of Sox7 EnKO, Sox7 EcKO and Sox7 CpcKO embryos were also severely impaired. To identify altered signaling pathways involved in the impaired EndMT process of Sox7 EnKO, we used AVCs of E9.5 Sox7 EnKO and control embryos to perform RNA-sequencing. Ingenuity pathway analysis identified 15 altered pathways relevant to this study, and BMP signaling pathway was significantly downregulated in Sox7 EnKO embryos. We found that the expressions of BMP2, pSMAD1/5/8 and downstream target gene Tbx2 were significantly reduced in Sox7 EnKO embryo. In addition, endocardial deletion of Sox7 reduced the endocardial Wnt4 expression, which could also downregulated the AVC myocardium BMP2 expression, leading to impaired EndMT process. In vitro, overexpression of Sox7 in mouse embryonic endocardial cells (MEEC) and human umbilical vein endothelial cells (HUVEC) can increase the expression of Wnt4, BMP2, pSMAD1/5/8 and Tbx2. Luciferase and ChIP assays showed that Sox7 could activate Wnt4 and BMP2 by directly bind to Sox7 binding sites in the prompter regions of them. Furthermore, Wnt4 and BMP2 protein can rescue the impaired EndMT process caused by Sox7 deficiency, and the BMP2 signaling inhibitor Noggin can block the effect of Wnt4 protein on Sox7 EnKO AVC explant. Finally, Sox7 EnKI embryos exhibit increased EndMT process in cardiac cushion, and we also found the evidence of ectopic EndMT in the ventricle of Sox7 EnKI embryo.

CONCLUSIONS Sox7 regulates the Wnt4-BMP2 pathway to modulate EndMT process and cardiac cushion formation. Notably, this study identifies a novel gene and clarifies the underlying mechanism involved in cardiac cushion development, provides new strategy for the diagnosis and treatment of congenital heart defect.

CLINICAL RESEARCH ON CARDIOVASCULAR DISEASES

CORONARY HEART DISEASE

GW30-e0012

Relationship of lipoprotein-associated phospholipase A2 and periprocedural myocardial injury in patients undergoing elective percutaneous coronary intervention

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OBJECTIVES Percutaneous coronary intervention (PCI) is one of the dominant methods for revascularization in patients with coronary heart disease (CHD). However, periprocedural myocardial injury (PMI) is a frequent complication following PCI and is known to be a predictor of postprocedural cardiovascular morbidity and mortality. Although several studies try to identify the serum markers to predict the PMI, there is a little information about the role of lipoprotein-associated phospholipase A2 (Lp-PLA2) as a predictor of PMI. Therefore, we aimed to investigate the relationship between lipoprotein-associated phospholipase A2 levels and PMI in patients undergoing elective PCI.

METHODS This study included 265 consecutive patients with normal preprocedural cardiac troponin T (cTNT) who received elective PCI. The samples for cTNT were collected at 8, 16, and 24 hours after PCI to assess perioperative myocardial injury. The Lp-PLA2 and other serum lipid parameters were measured after 12 fasting hours before PCI.

RESULTS The data suggested that the patients with preprocedural high Lp-PLA2 were strongly and independently correlated with the risk of PMI. Pearson correlation analysis showed that preprocedural Lp-PLA2 was significantly positively correlated with postprocedural cTnT elevation ($R=0.549$, $P<0.05$). Logistic regression analysis was used to analyze the risk factors of postprocedural cTnT elevation, we found that smoking, hs-CRP (OR=1.126, $P<0.05$) and Lp-PLA2 (OR=2.348, $P<0.05$) are independent risk factors for postprocedural cTnT elevation.

CONCLUSIONS Our study demonstrated that Lp-PLA2 was associated with postprocedural cTnT elevation, and high Lp-PLA2 levels were the independent risk factor of PMI.

GW30-e0078

The role of AT1 receptor in the instability of atherosclerotic plaque caused by homocysteine

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OBJECTIVES To explore the role of Angiotensin II type 1 receptor (AT1) in the instability of atherosclerotic plaques caused by Homocysteine (HCY).

METHODS Twenty-one 6-week-old male ApoE−/− mice were weighed and divided into three groups according to the random number table: control group (CTL), Hyperhomocysteinemia group (HHCY), HHCY telmisartan treatment (TLM) group (10 mg/kg gavage treatment). Weight and blood pressure were measured before and after 12 weeks of feeding. The blood specimen was retained by removing the eyeball. Plasma HCY was detected by using cyclic enzyme method. Oil red "O" staining was used to measure the area of aortic root plaque, and immunohistochemical SP method was used to detect plaque inflammatory factor interleukin-6 (IL-6), Monocytes chemoprotein-1 (MCP-1), macrophage surface molecules (mac-3), matrix metalloproteinase-9 (MMP-9), and collagen was stained by Masson staining.

RESULTS T The plaque area of HHCY group was significant larger than that of control group. The expression levels of IL-6, MCP-1, mac-3 and MMP-9 in plaque were higher in HHCY group than control group, but collagen content of plaque was reduced in HHCY group. After 12 weeks of treatment, the area of aortic root plaque, the expression levels of IL-6, MCP-1, mac-3 and MMP-9 macrophage infiltration were significantly lower in telmisartan treatment group than in HHCY group, but collagen content of plaque was significantly higher in telmisartan treatment group than in HHCY group. We also noted that the blood pressure and body weight of the telmisartan group were lower than those of the HHCY group.

CONCLUSIONS Homocysteine promotes the development of atherosclerosis and leads to plaque instability, blocking At1 receptor by telmisartan improved atherosclerosis and promoted plaque stabilization, indicating that its mechanism may be through the At1 receptor.

GW30-e0079

Association of serum HMGB2 levels with spontaneous reperfusion of infarct-related artery in patients with ST-segment elevation myocardial infarction

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OBJECTIVES Although the replacement of bare-metal stents with drug-eluting stents has led to a significant reduction in the rate of angiogenic in-stent restenosis (ISR), ISR occurs in 3%–20% of patients with a drug-eluting stent, depending on lesion characteristics and patient risk factors. High-mobility group box 2 (HMGB2) is a novel inflammatory protein that has been positively related to cardiovascular disease. However, information regarding the role of HMGB2 in spontaneous reperfusion (SR) of infarct-related artery in patients with ST-segment elevation myocardial infarction (STEMI) is limited. The present study was designed to evaluate the association of serum HMGB2 levels with SR of infarct-related artery in this high-risk population.

METHODS We measured serum HMGB2 in 1080 consecutive STEMI patients who were recruited between October 2014 and October 2018 using an enzyme-linked immunosorbent assay kit. Blood samples were obtained on admission and before primary percutaneous coronary intervention (pPCI). According to thrombolysis in myocardial infarction (TIMI) results, patients were divided into SR (TIMI 2-3, n=248) and non-SR (TIMI 0-1, n=832) groups. Logistic regression analysis was performed to define the independent predictors of SR.

RESULTS Serum HMGB2 was significantly lower in patients with SR compared to patients with non-SR ([3.01±1.24] ng/mL vs. [6.36±1.32] ng/mL, $P=0.013$). A cut off HMGB2 value of 2.75 ng/mL had a predictive value of 83% to identify patients with SR (sensitivity=87%). Logistic regression analysis showed that serum HMGB2 level is an independent predictor of SR (odds ratio=4.25, 95% confidence interval: 1.58 to 7.69, $P=0.005$) for STEMI patients.

CONCLUSIONS Serum HMGB2 levels were associated with ISR in patients. Lower serum HMGB2 level is an independent and novel predictor of SR for STEMI patients. Detection of serum HMGB2 level is promoted to predict SR in STEMI patients. These findings support the use of HMGB2 as a biomarker of atherosclerosis in this high-risk group.

GW30-e0084

Cystatin C, a reliable and early diagnostic biomarker for acute kidney injury associated with acute myocardial infarction in a Chinese cohort

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OBJECTIVES Patients with acute myocardial infarction (AMI) are at high risk for acute kidney injury (AKI). Studies indicated several biomarkers of early structural kidney injury such as cystatin C, neutrophil gelatinase-associated lipocalin (NGAL) and Klotho have been identified that may predict early AKI before a significant increase in serum creatinine (SCr) level. However, limited researches were executed in AKI after AMI. These novel biomarkers potentially allow timely intervention in high risk patients of AKI when damage is still reversible. Therefore, we performed a prospective study with AMI patients in order to explore early biomarkers for AKI prediction at hospital admission.

METHODS The study included consecutive patients between May 2016 and November 2017 diagnosed with AMI in emergency department of Peking University People's Hospital. Patients with end stage renal disease, septic shock and who died or discharged within 48 h of admission were excluded. AKI were diagnosed according to KDIGO definition. Serum sample for NGAL, cystatin C and Klotho were taken instantly when diagnosed AMI. SCr was measured on the first, third and seven days. All biomarkers were measured in duplicate by a single enzyme-linked immunosorbent assay (ELISA). Baseline characteristics were collected. The primary analysis compared the AKI group with the non-AKI group. $P<0.05$ was considered statistically significant. All variables were tested for a normal distribution through the Kolmogorov-Smirnov test. Continuous variables and normal distribution data were compared using independent sample t tests. Categorical data were tested by the Chi-square test or Fisher's exact test. Discrimination was assessed using the area under a receiver operating characteristic curve (AUROC). The analysis for AUROC was also conducted to estimate the cut-off values, sensitivity and specificity were calculated by determining the best Youden index.

RESULTS Overall, 285 patients were included. In our study, 17.5% (50/285) patients developed AKI. Compared to non-AKI group, the length of hospital stay of the AKI group was obviously longer (17d vs. 11d, $P<0.01$) and mortality was higher either (20.0 vs. 0.4%, $P<0.001$). Clinical data were displayed in Table 1. Cystatin C, NGAL and Klotho both increased significantly in AKI

group (Table 2). The ROC curves of biomarkers and SCr on admission were displayed in predicting development of AKI after AMI in Table 3 and Figure 1, areas showed that serum levels of cystatin C had modest discriminative powers in prediction of AKI than SCr (0.899, 95% confidence interval, 0.855 to 0.944, P<0.001 and 0.734, 95% confidence interval, 0.649 to 0.819, P<0.001, respectively). The cut-off values for cystatin C in predicting AKI were 2362.9 ng/mL, sensitivity and specificity value of cystatin C in predicting AKI in AMI patients was 0.880 and 0.791. NGAL and Klotho didn't display preferable diagnostic values compared with SCr. There was no difference between the discrimination performances of SCr, NGAL and Klotho.

CONCLUSIONS In this cohort of patients with AMI, serum cystatin C maybe a more reliable and earlier diagnostic biomarker for AKI associated with AMI. Meanwhile, serum NGAL and Klotho did not provide additional value regarding AKI prediction compared with baseline creatinine.

GW30-e0090

Angiotensin II type 1 receptor blockers telmisartan reduces plasma trimethylamine oxide level and improves atherosclerosis in apolipoprotein E-deficient mice

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OBJECTIVES Trimethylamine N-oxide (TMAO), a gut microbiota metabolites, has recently been found to promote atherosclerosis. Here, we examined the effect of angiotensin II type 1 receptor blockers (ARB) telmisartan on plasma levels of TMAO in apolipoprotein E-deficient (ApoE−/−) mice.

METHODS Sixteen ApoE−/−mice were randomly divided into two groups: control group and telmisartan (10 mg/kg, intragastric administration) treatment group. All mice were fed a high-fat diet. After 12 weeks, the mice were sacrificed. Venous blood was collected from the retro-orbital sinus to detect TMAO using high performance liquid phase chromatography-tandem mass spectrometry. Severity of atherosclerosis was determined by measuring the area of the plaques. Stability of atherosclerotic plaques were determined by analyzing the expression of inflammatory factors interleukin-6 (IL-6), monocyte chemoattractant protein 1 (MCP-1), matrix metalloproteinase-9 (MMP-9), the infiltration of macrophages and the morphology of plaques at the root of the aorta.

RESULTS Compared with the control group, the plaque area of the telmisartan treatment group decreased significantly, and the expression of IL-6, MCP-1, MMP-9 and the infiltration of macrophages also decreased significantly. The plaque of the telmisartan treatment group had thicker fiber caps, a few foam cells, and a reduced lipid/necrotic core. Plasma TMAO levels were significantly lower in the telmisartan-treated group than in the control group. Meanwhile, the blood pressure and body weight of the mice treated with telmisartan were lower than those of the control group.

CONCLUSIONS That ARB telmisartan lower plasma TMAO levels may be one of the mechanisms by which it improves atherosclerosis, which may indicate a certain intrinsic association between At1 receptor and gut microbiota.

GW30-e0094

Drug-coated balloons for ostial coronary lesions: mid-and long-term clinical and angiographic results from a Chinese institute

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OBJECTIVES The best strategy to treat ostial coronary lesions (OCLs) is controversial. Hypothesis: A drug-coated balloon (DCB)-only strategy for OCLs is safe and efficacious.

METHODS Forty-four patients (55 OCLs) with typical angina symptoms were treated with DCBs. After pre-dilatation, a paclitaxel-eluting balloon was inflated for ≥30 s. Primary outcome was target-lesion revascularization. Secondary endpoints were post-interventional lumen gain and late lumen loss (LLL) at the longest available follow-up.

RESULTS Mean age was 64.35±10.8 years; 25% of patients had diabetes mellitus, and 25.5% presented with in-stent restenosis. We treated OCLs of the left main coronary artery, left anterior descending artery, left circumflex artery, and right coronary artery (first diagonal, marginal, posterior descending and posterolateral branches). Pre-dilatation with a cutting balloon was used in 16.4% of cases. At the longest available clinical follow-up (mean of 15.60±8.7 months), the prevalence of major cardiac adverse events was 14.5%. There was no thrombosis but three OCLs showed total occlusion. LLL was 0.074±0.63 mm.

CONCLUSIONS DCBs are a safe and technically easy therapeutic option, and associated with acceptable long-term clinical outcomes.

GW30-e0095

Comparison of inflammatory status in culprit lesion between plaque erosion and plaque rupture: an optical coherence tomography study

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OBJECTIVES Plaque erosion and plaque rupture are the main pathological mechanisms of acute coronary syndrome (ACS). They have different pathological characteristics. plaque rupture (PR), characteristic with a large necrotic lipid core and thin fibrous cap with discontinued endothelial layer, which accounts for about two-thirds of ACS; Plaque erosion, is rich of smooth muscle cell (SMC) and extracellular matrix, such as hyaluronic acid (HA), but less of macrophage compared to PR, PE accounts about one-thirds of ACS. Because of the different pathological characteristics, The EROSION study (Effective Anti-Thrombotic Therapy Without Stenting: Intravascular Optical Coherence Tomography-Based Management in Plaque Erosion) suggested that in patients with acute coronary syndrome presenting with plaque erosion, conservative treatment with antithrombotic therapy may be a reasonable option instead of stent implantation. And the follow-up results for one month and one year demonstrate that effective anti-thrombotic therapy is safe. Because the different pathological characteristic and clinical treatment. Some researches demonstrated that the mechanism of the two subset maybe different, and some researches claimed that the two subsets have inflammatory status in culprit lesion, Our study is aim to compare the inflammatory status of local white blood cell which is near to culprit lesion between plaque erosion and plaque rupture.

METHODS Fifty-one ST-segment elevation myocardial infarction patients (21 erosion patients and 30 rupture patients) with <6 hours of chest pain were classified as plaque erosion or plaque rupture using optical coherence tomography. During the PCI time, the blood near to culprit lesion was collected, and separated the white blood cell immediately in trizol reagent and kept −80°C in in for RNA extraction. And reversed transcription to cDNA for quantitative real-time polymerase chain reaction (Rt-PCR). We compared the anti-inflammatory cytokine (IL-4, IL-10) and pro-inflammatory factor (IL-1β, TNF-α, IL-8) mRNA expression level in the two groups.

RESULTS Between erosion and rupture patients, there is no significant anti-inflammatory cytokine (IL-4, IL-10) mRNA different expression in the two groups. But erosion patients show elevated mRNA expression of pro-inflammatory factor than rupture patients: IL-1β, (P=0.026), IL-8 (P=0.021), TNF-α, (P=0.028).

CONCLUSIONS These results demonstrate differential pro-inflammatory factor expression in local erosion and rupture culprit lesion. To our surprised, although there is less inflammatory cell in eroded plaque, the local white blood cell in eroded plaque show elevated pro-inflammatory factor (IL-1β, TNF-α, IL-8) mRNA expression than rupture plaque, but no significant different expression anti-inflammatory cytokine (IL-4, IL-10) mRNA expression in the two groups.

GW30-e0104

The effect of the condition of glucose controlment on clopidogrel response in patients with coronary heart disease

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OBJECTIVES The CAD patients with clopidogrel resistance were more likely to get cardiovascular events and the diabetes mellitus may be a risk of clopidogrel resistance.

METHODS The platelet function of CAD patients after PCI was evaluated by VerifyNow P2Y12, and the fasting and 2 h postprandial level of insulin, glucose, and C peptide were tested for examining the glucose control affecting on CR.

RESULTS Compared with NCR patients, incidence rate of CR was higher in DM patients (50.9 vs. 32.4%). Meanwhile, fasting and 2 h postprandial level of insulin and C peptide might affect the clopidogrel response (fasting insulin, CR group vs. NCR group: 56.5±12.2 pmol/L vs. 114.3±42.2 pmol/L; fasting C peptide, CR group vs. NCR group: 10.12±1.89 nmol/L vs. 7.25±2.21 nmol/L). If the glucose could be controlled better, the clopidogrel response would be improved.

CONCLUSIONS The DM and the condition of glucose controlment might be the risks of clopidogrel resistance.

GW30-e0107

Early invasive vs initial conservative strategy in non-ST-segment elevation acute coronary syndromes: 10 most prognostic factors decreasing the hazards to getting the benefits with early invasive strategy

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OBJECTIVES *Aims to:* (1) Review the literature for best initial management approach for Non-ST-Elevated Acute Coronary Syndromes (NSTE-ACS), (2) Minimise the Conflicting Strength with the better understanding of Heterogeneity or Differences between the Trials and Meta-analyses, (3) To collect the relevant Mega-data for a specific topic, our is early invasive strategy or initial conservative strategy; what strategy is best as initial management for NSTE-ACS?, (4) Evaluation of the most Prognostic and Influential factors for the early invasive approach, (5) Posit directions for future research.

METHODS We conducted a computer-based search in representative databases by Medline, Embase, Cochrane database and Google Scholar from 1985 to 2017 using key words of relevant subject headings for randomized controlled trials, meta-analyses and included some standard observational studies that met eligibility criteria for each mentioned topic of our research included 10 influential factors headings. We independently reviewed searches and selected trials that compared early invasive strategy with initial conservative strategy covered many dimensions of our research requirements with prognostic values.

RESULTS We screened more than 500 abstracts, evaluated more than 200 full-text articles. By which included more than 300 Randomised Control Trials and their Meta-Analyses with more than 300 observational but standard studies. As per theme of our type of research, we have collected vast data to cover the almost all aspects of our topic related issues or factors. We corresponded with experts in the field, After focus studying, opinions and discussions with researchers, we extracted and evaluated that there are some influential and prognostic factors regarding early invasive approach for NSTE-ACS patients, which have to be understand, dealing and approach first for the cause of better outcome with early invasive strategy. These most influential factors are: (1) Diagnosis Accuracy, (2) Significance of Early Risk Stratification, (3) Individualised Patient Assessment: Co-Morbidities (Age Factor, DM, CKD, Gender, HTN, etc), (4) Timing of EIS, (5) Radial vs Femoral Approach, (6) Prognostic Value of Peri-Procedural and Long-term Drugs, (7) Peri-Procedural Major Bleeding, (8) Peri-Procedural and Spontaneous MI, (9) Stent Type with two Major Complications: Stent Thrombosis & Stent Re-Stenosis and (10) Peri-Procedural Kidney Injury.

CONCLUSIONS (1) In respect to early invasive strategy for the management of NSTE-ACS, with proper diagnosis, better early risk stratification approach, skilful individualise patient assessment, through proper-site approach, with better understanding of the individualized timing for patients, with administration of proper and recommended pre-and-post procedures, short & long term drugs, and especially the choice and type of stents according to patient co-morbidities, anatomical lesion and clinical condition, we can reduce the mortality hazard complications like peri-procedural major bleeding, peri-procedural & spontaneous MIs, procedural-induced AKI, stent thrombosis and in-stent re-stenosis, all these leads to decreasing mortality indirectly. (2) With the better understanding of some prognostic and influential factors related to the approach of early invasive strategy, for patients with NSTE-ACS, an early invasive strategy should be strongly considered during initial hospitalisation in all-risk-level patients.

GW30-e0108

Obesity is associated with worse long-term outcomes in hypertrophic cardiomyopathy patients with acute myocardial infarction

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OBJECTIVES HCM is associated with poor prognosis. In our previous study, it has been reported that patients with AMI with HCM exhibited worse long-term outcomes than those patients with AMI without HCM and patients with HCM without AMI. In this article, we aimed to assess the impact of BMI on the long-term outcomes of HCM patients with AMI.

METHODS Seventy-eight consecutive patients with HCM and AMI were included. The endpoints were major adverse cardiac events (MACEs) and secondary endpoints.

RESULTS There were no differences in observed in-hospital mortality or 5-year mortality between the two groups of HCM and AMI patients divided by BMI. However, significantly increased incidences of re-PCI and stroke were observed in the group of obesity (re-PCI: 0.0 vs. 21.4%, P=0.007; stroke: 5.6 vs. 28.6%, P=0.042). The 5-year outcomes of MACEs were inferior in the obese group (log-rank P=0.020 and 0.001).

CONCLUSIONS AMI and HCM patients who were obese exhibited worse long-term outcomes than patients without obesity.

GW30-e0109

Relationship between monocyte-to-lymphocyte ratio and coronary plaque vulnerability in patients with acute coronary syndrome: an optical coherence tomography study

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OBJECTIVES To investigate the relationship between monocyte-to-lymphocyte ratio (MLR) and plaque vulnerability assessed by optical coherence tomography in patients with acute coronary syndrome.

METHODS Seventy-two patients with acute coronary syndrome were enrolled in Beijing Anzhen hospital and received coronary angiography and optical coherence tomography test.

RESULTS The coronary plaques in high MLR group exhibited thinner fibrous cap thickness (FCT) (112.37±60.24 vs. 153.49±110.29 μm, P=0.013), greater maximum lipid arc (167.36±62.33 vs. 138.79±56.37°, P=0.010) and longer lipid plaque length (6.34±6.12 vs. 4.50±3.21 mm, P=0.041). Besides, the incidence of vulnerable plaque (TCFA) (44.7 vs. 18.4%, P=0.014) and plaque rupture (36.8 vs. 13.2%, P=0.017) were higher in high MLR group. Meanwhile, MLR was negatively associated with FCT (R=0.225, P=0.005). Furthermore, MLR (OR=3.316, 95% CI: 1.448–7.593, P=0.005) was found to be an independent risk factor of TCFA.

CONCLUSIONS MLR level has potential value in assessing coronary plaque vulnerability in patients with acute coronary syndrome.

GW30-e0113

Efficacy and safety of ticagrelor versus clopidogrel with different dosages in acute coronary syndrome patients with high GRACE and CRUSADE scores

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OBJECTIVES In patients with acute coronary syndrome (ACS), dual antiplatelet therapy (DAPT) has been the cornerstone strategy. Several studies, however, have shown that a clopidogrel loading dose >300 mg resulted in high platelet inhibition, a faster onset of action, and fewer poor responders in both clopidogrel-naïve and clopidogrel-treated patients. Ticagrelor provides faster and more consistent platelet inhibition than that of clopidogrel. Most patients with ACS have comorbidities and risk factors that greatly increase their risk of ischemic or bleeding events. We compared ticagrelor and clopidogrel for the prevention of cardiovascular events and safety in high ischemic and bleeding risk patients who presented with ACS and underwent a percutaneous coronary intervention (PCI).

METHODS One thousand nine hundred and thirty-nine patients with high ischemic and bleeding risk were enrolled into three groups according to their antiplatelet strategy: standard antiplatelet therapy (clopidogrel 75 mg daily plus aspirin 100 mg daily, the Standard group), double-dose clopidogrel (clopidogrel 150 mg daily plus aspirin 100 mg daily, the Double group) and ticagrelor therapy (ticagrelor 90 mg twice daily plus aspirin 100 mg daily, the Ticagrelor group).

RESULTS *Clinical outcomes:* The primary endpoint of MACCE events at 24 months post-PCI occurred in 134 patients (19.5%) in the Standard group, 73 patients (13.7%) in the Double group, and 87 patients (12.0%) in the Ticagrelor group. The difference in the 24-month MACCE rates in the Ticagrelor group was lower than that in the Standard group (hazard ratio [HR]: 0.558, 95% CI: 0.427–0.731), demonstrating the superiority of the ticagrelor strategy over that of standard DAPT. Regarding the Double group, the MACCE rate was lower than that of the Standard group (HR: 0.649, 95% CI: 0.489–0.861). The risks of cardiovascular death and MI did show a significant difference among the three groups. A significantly decreased risk of NACCE could be detected in the Ticagrelor group (HR: 0.646, 95% CI: 0.488–0.856) compared to that of the Standard group.

Subgroup analysis of endpoints: For the efficacy endpoints, we first identified the potential clinical factors associated with MACCE using a COX multivariate analysis; three factors, including renal function, history of MI, and triple vessel artery disease, were revealed to be associated with MACCE. The stratified analyses revealed that participants with an eGFR<90 mL/min/1.73 m^2 had a lower ischemic rate in the Ticagrelor group than that in the Standard group (HR: 0.616, 95% CI: 0.387–0.981, P=0.01). In addition, patients with a previous MI could benefit from stronger antiplatelet treatments (P=0.027). Similar results were also observed in patients with triple vessel artery disease (P=0.019). For the safety endpoints, seven factors were identified to be related with bleeding events, and among these factors, participants aged >70 years accounted for a higher bleeding rate in the Double group than that in the Standard group (HR: 2.264, 95% CI: 1.553–3.30, P<0.001).

CONCLUSIONS In East Asian PCI patients with high ischemic and bleeding risk, the ticagrelor antiplatelet strategy significantly reduced the MACCE rate without increasing the risk of major bleeding. A decreased rate of MACCE was observed in patients with double dosage of clopidogrel, but the bleeding risk was higher than that in the standard group.

GW30-e0125

Influence of different statins on levels of PTX3 and hs-CRP in patients with acute coronary syndrome after PCI

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OBJECTIVES The aims were to investigate the sensitivity of inflammatory factor PTX3 in early forecast of the coronary artery damage in ACS patients accepted PCI by testing the levels of PTX3 and hs-CRP in patients during perioperative period, and to observe the influence of different dose of pitavastatin and atorvastatin on the inflammatory factors, providing theory basis for management of patients with ACS and assessment of the disease prognosis.

METHODS One hundred and twenty-one patients diagnosed as ACS in Cangzhou central hospital were selected from January 2015 to October 2015, and divided into 3 groups randomly: Conventional dose of pitavastatin group (38 cases) took pitavastatin 2 mg before sleep (qn). Conventional atorvastatin group (40 cases) took atorvastatin 20 mg before sleep. Intensive pitavastatin group (43 cases) was given pitavastatin 4 mg before sleep on preoperative and postoperative day, then maintained 2 mg later. Observe all patients: the levels of PTX3 and hs-CRP at preoperative day, 24 h and 72 h after PCI. The major adverse cardiac events (MACE) in 121 patients during 6 months, including cardiac death, target vascular remodeling and nonfatal myocardial infarction.

RESULTS (1) The basic clinical date of 121 patients before PCI showed no statistical difference (P>0.05); (2) There was no statistical difference in levels of hs-CRP among 3 groups in preoperative period (P>0.05); intra-group comparison, the levels of hs-CRP at 24 h, 72 h after PCI showed no statistical difference in each group (P>0.05); compared with preoperative, the levels of hs-CRP at postoperative 24 h, 72 h among 3 groups showed no statistical difference (P>0.05); (3) The levels of PTX3 among 3 groups during preoperative period were no statistical difference (P>0.05); and at 24 h after PCI were higher than preoperative, but at 72 h the levels of PTX3 is decreased compared with 24 h, though the concentrations was still higher than preoperative (P<0.05); comparison between the 2 conventional dose groups, the levels of PTX3 at postoperative 24 h, 72 h was no statistical difference (P>0.05), but the levels of PTX3 in intensive pitavastatin group at 24, 72 h postoperative was lower than conventional groups (P<0.05); (4) There was no cardiac death within 6 months after PCI in 3 groups. In normal dose pitavastatin group, there were 0 MI cases happened, and 4 patients accepted target vessel revascularization; in normal dose atorvastatin group, there was 0 MI cases happened, and 4 patients accepted target vessel revascularization; in intensive pitavastatin group, there was 0 MACE happened; between the 2 conventional dose groups, the total incidence of MACE during 6 months showed no statistical difference (P>0.05); compared with conventional group, the total incidence of MACE in the intensive group was obviously lower (P<0.05).

CONCLUSIONS (1) The sensitivity of PTX3 in early prediction of the blood vessel damage in ACS patients accepted PCI is better than hs-CRP. (2) For ACS patients who accept PCI, PCI itself will damage the vascular wall, cause inflammation and increase the levels of PTX3. (3) There was no significant difference between normal dose pitavastatin and normal dose atorvastatin therapy in reducing inflammation. Intensive pitavastatin therapy can reduce inflammation better than normal dose pitavastatin and atorvastatin therapy. (4) Using intensive pitavastatin therapy at perioperative PCI period can reduce the incidence of MACE within 6 months, improving the prognosis in the near future, and the benefit is superior to conventional therapy.

GW30-e0127

Combining FBG and HbA1c to evaluate the level of inflammation and severe coronary artery lesions in patients with elective PCI

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OBJECTIVES To explore the correlation between fasting blood glucose (FBG) and inflammatory level and severe coronary artery lesions in patients with pre-diabetes (HbA1c 5.7–6.4%) undergoing elective PCI.

METHODS We consecutively enrolled 885 pre-diabetes (HbA1c 5.7–6.4%) undergoing elective PCI in our hospital. Subjects were divided into two groups, one group was IFG group (5.6£FBG<7.0 mmol/L), another was NFG group (FBG<5.6 mmol/L), We recorded and compared the baseline characteristics, inflammation index (white blood cells, hypersensitive c-reactive protein, neutrophil lymphocyte ratio, platelet lymphocyte ratio) and characteristics of coronary artery disease.

RESULTS Compared with the NFG group, the patients in the IFG group had higher BMI (P=0.028), more patients with hypertension (P=0.049), higher TG (P=0.005) and higher LDL-C (P=0.001). After comparing the inflammatory index of the two groups, WBC (P=0.028), NLR (P=0.005), PLR (P=0.013) and hs-CRP (P=0.028) in the IFG group were significantly higher than those in the NFG group. In addition, compared with the NFG group, the proportion of three-vessel disease (P=0.040), the GENSINI score (P=0.014) and the SYNTAX score (P=0.008) were higher in the IFG group.

CONCLUSIONS In patients with elective PCI complicated with pre-diabetes mellitus (HbA1c 5.7–6.4%), IFG patients have higher levels of subclinical inflammation and more severe coronary artery lesions.

GW30-e0139

Serum sclerostin and adverse outcomes in elderly patients with stable coronary artery disease undergoing percutaneous coronary intervention

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OBJECTIVES Recently, sclerostin, a bone-derivedprotein, has been shown to play a key role in the progression of atherosclerosis. However, few studies have investigated the influence of sclerostin on the prognosis of cardiovascular disease. We investigated the relationship betweenserum sclerostin levels and adverse outcomesin elderly patients with stable coronary artery disease (SCAD) who are undergoing percutaneous coronary intervention (PCI).

METHODS A total of 310 elderly SCAD patients who underwent PCI were enrolled in this study, with a follow-up of 3 years. According to the median serum sclerostin levels, subjects were stratified into a low sclerostin (low scl) group (n=144) and a high sclerostin (high scl) group (n=166). Time-to-event analyses were performed by the Kaplan-Meier method. The associations between sclerostin levels and main the adverse cardiovascular and cerebrovascular events (MACCEs) and mortality were evaluated by Cox multivariate regression analysis.

RESULTS Kaplan-Meier curves showed thatthehigh scl group had a significantly higher MACCE-free rate (log rank P<0.001) and better survival (log rank both P<0.05) than the low scl group did. Serum sclerostin was an independent predictor of MACCEs and all-cause mortality. In addition, serum sclerostin levels were significantly associated with N-MID (β=–0.357, P<0.001), β-CTX (β=0.200, P=0.012), and PINP (β=0.207, P=0.006) levels, a lower presence of multivessel disease (β=–0.223, P=0.005) and lower CCS angina class (β=–0.160, P=0.017).

CONCLUSIONS Serum sclerostin is a prognostic parameter for predicting and intervening in the adverse outcomesof elderly SCAD patients undergoing PCI, which may be explained by its potential role in thebone-vascular axis.

GW30-e0140

The expression and clinical significance of interleukin 20 in coronary artery diseases

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OBJECTIVES Previous studies have demonstrated that interleukin 20 (IL-20) is associated with several inflammatory diseases, such as experimental arthritis, osteoporotic bone loss and atherosclerotic plaque formation in mice. However, the expression and clinical significance of IL-20 in coronary artery diseases (CAD) is still unknown.

METHODS Coronary artery tissue samples from normal donors and ischemic cardiomyopathy (ICM) patients who underwent heart transplantation were collected. The expression of IL-20 and its receptors, including IL-20 receptor I (IL-20R I) and IL-20R II, were analyzed in coronary artery tissues. Blood samples were collected from consecutive patients with chest pain who subsequently underwent coronary angiography. Patients were divided into the control group (n=28), stable angina pectoris (SAP) group (n=84) and acute myocardial infarction (AMI) group (n=28). The plasma IL-20 concentrations were evaluated with ELISA kits.

RESULTS The expression levels of IL-20 and its receptors were higher in coronary artery stenosis tissues from ICM patients than in tissues from control patients. Double immunofluorescence showed that $CD3^+$ T lymphocytes were the main source of IL-20. In addition, IL-20 receptors were mainly expressed in T lymphocytes and macrophages in coronary artery tissues. In plasma samples, the plasma IL-20 concentrations were significantly higher in AMI patients than in controls. However, there was no significant difference between the controls and SAP patients. Spearman's correlation analysis showed that plasma IL-20 was positively correlated with cardiac troponin I, cholesterol, LDL cholesterol, systolic blood pressure and diastolic blood pressure. Multiple linear regression revealed that IL-20 was independently associated with the presence of AMI.

CONCLUSIONS Plasma IL-20 levels were significantly increased in AMI patients but not in SAP patients. IL-20 may be involved in the progression of

coronary artery stenosis and plaque vulnerability through regulating CD3+ T lymphocytes and macrophages via binding with its receptors and further participating in the onset of AMI. IL-20 signaling may be a promising biomarker and therapeutic target for AMI.

GW30-e0141

Meta-analysis comparing Non-vitamin K antagonist oral anticoagulants versus warfarin in combination with antiplatelet therapy in atrial fibrillation patients with acute coronary syndrome or undergoing percutaneous coronary intervention

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OBJECTIVES The coexistence of atrial fibrillation and coronary artery disease is commonly found in clinical practice. So far, three RCT trials have evaluated the utilization of non-vitamin K antagonist oral anticoagulants (NOACs) in atrial fibrillation (AF) patients with acute coronary syndrome (ACS) or undergoing percuraneous coronary intervention (PCI). The aim of this meta-analysis is to compare the efficacy and safety of NOACs versus VKA in combination with antiplatelet therapy in AF patients with ACS or undergoing PCI, based on PIONEER AF-PCI, RE-DUAL PCI, and AUGUSTUS trials.

METHODS We included three phase 3 RCT trials comparing the efficacy and safety of NOACs versus VKA, the PIONEER AF-PCI trial, RE-DUAL PCI trial, and the AUGUSTUS trial. The risk ratios (RR) were extracted from each study. Pooled estimates with corresponding 95% confidence intervals were estimated by a fixed or random-effects model.

RESULTS Three studies involving a total of 9532 patients with AF were included in this meta-analysis. 3995 participants received antiplatelet therapy together with VKA and 5537 together with NOACs. The NOACs group was associated with a significantly lower incidence of all bleeding (RR 1.22, P<0.001), TIMI major (RR 1.60, P=0.004), ISTH major (RR 1.63, P<0.001) bleeding events and intracranial hemorrhage events (RR 3.33, P=0.002) but no difference with regard to ischemic vascular events and mortality rate.

CONCLUSIONS NOACs with either a P2Y12 inhibitor or DAPT has significantly reduced the bleeding events, and similar efficacy were observed in terms of outcomes including stroke, myocardial infarction, in-stent thrombosis, all cause and cardiovascular mortality.

GW30-e0144

Clinical characteristics and protective factors in patients with acute myocardial infarction undergoing in-hospital myocardial free wall rupture: a single-center retrospective analysis

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OBJECTIVES Myocardial free wall rupture (MFWR) refers to laceration of heart ventricle or atria, which is a rare but fatal complication of acute myocardial infarction (AMI). In this study, we aim to identify clinical characteristics and protective factors of free wall rupture after myocardial infarction.

METHODS This is a single center, retrospective observational analysis. The study screened all patients admitted to the cardiology department of the First Affiliated Hospital of Xi'an Jiaotong University between January 2013 and April 2018. The biochemical, clinical, angiographic and echocardiographic features of these patients were then collected and analyzed.

RESULTS Among 5946 AMI patients screened, 23 patients with the diagnose of MFWR after AMI were enrolled in the present study. 18 (78.3%) patients were diagnosed with acute ST-segment elevated myocardial infarction (STEMI) and the rest 5 (21.74%) have acute non-ST-segment elevated myocardial infarction (NSTEMI). Early phase MFWR happened in 12 (52.2%) and late phase accounted for 8 (34.8%) in total. Late phase MFWR had lower left ventricle ejection fraction value (45.75±5.55% vs. 63.00±3.81%, P<0.001) as compared to early phase. Patients survived from MFWR has higher ACEI/ARB and β-Blocker coverage in the in-hospital treatment of AMI (ACEI/ARB: 100 vs. 35.3%, P=0.014; β-Blocker: 100 vs. 47.1%, P=0.048).

CONCLUSIONS The present study provides evidence for better understanding of clinical characteristics and protective functions in MFWR after AMI. Reduced cardiac function is correlated to higher incidence of later phase FWR. And higher ACEI/ARB and β-Blocker coverage in the AMI treatment strategy is associated with less MFWR incidence.

GW30-e0146

An observational study of the platelet reactivity in Chinese patients undergoing PCI loading with 600 mg clopidogrel

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OBJECTIVES Although impaired platelet responsiveness to clopidogrel is strong predictors of unfavorable outcome after percutaneous coronary intervention (PCI), the impact of high post-treatment platelet reactivity (HPPR) to 600 mg loading dose clopidogrel in Chinese patients with ACS undergoing PCI is still unknown. We sought to determine whether HPPR to 600 mg loading dose clopidogrel affects outcomes in Chinese patients with the acute coronary syndrome (ACS) following the PCI. To investigate whether there might exist a correlation between platelet reactivity unite (PRU) and the character of the patients such as age, gender, diabetes, hemoglobin, AST, ALT, BUN, Crea, Ccr, BMI.

METHODS We did observational research about 134 unselected patients with ACS undergoing urgent or planned PCI with 600 mg loading dose clopidogrel. The platelet activation expressed as the PRU by VerifyNow assay.

RESULTS Among 134 patients (mean age 60.62±9.13, 60.4% male), there were 46 patients with HPR (34.3%) and 88 patients without HPR (65.7%). The univariate analysis revealed a significant inverse correlation between PRU and hemoglobin (r=−0.291, P<0.05). The multivariate linear analysis identified hemoglobin and gender are independent predictors of PRU ($y=456.355-1.736X_1-31.880X_2$, X_1: Hemoglobin, X_2: male). At a mean follow-up of 6±1 months, cardiac death, unstable angina, and rehospitalization for target lesion revascular (TLR) and bleeding events were higher in the HPPR group (19.5 vs. 6.8%, P=0.026). For the logistic regression model, the only independent variables for the incidence of ischemic events were PRU and angiographic characteristics extent of disease ($Z=-21.135+0.014X_1+2.529X_2$, X_1: PRU, X_2: angiographic characteristics extent of disease). A receiver-operating characteristic curve analysis, PRU values could significantly discriminate between with and without cardiac death, unstable angina, and rehospitalization for TLR (area under the curve [AUC]: 0.758, 95% confidence interval: 0.62–0.85, P<0.001). By ROC analysis the optimum PRU cutoff for definitely-probable was 176, providing a sensitivity 0.933, specificity 0.602.

CONCLUSIONS In patients with ACS following PCI, the presence of HPPR with clopidogrel 600 mg loading dose is associated with worse outcomes after PCI. There is close correlation between the PRU and hemoglobin and gender. The result of PRU can predict the prognosis such as cardiac death, unstable angina, and rehospitalization for TLR.

GW30-e0147

Impact of limb remote ischemic conditioning on serum stromal cell-derived factor-1α level and clinical outcome in patients with acute myocardial infarction

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OBJECTIVES The primary purpose of this study is to evaluate whether RIC participates in myocardial protection by increasing serum stromal cell-derived factor-1α (SDF-1α) levels in patients with acute myocardial infarction (AMI) undergoing percutaneous coronary intervention (PCI)

METHODS Two hundred patients with AMI including acute ST-segment elevation myocardial infarction (STEMI) and acute non-ST-segment elevation myocardial infarction (NSTEMI) were random divided into limb RIC (n=100) group and control group (n=100). AMI patients arrive at the catheterization laboratory, a blood pressure cuff is placed on their right lower limbs by one of the researchers. The limb RIC group underwent 3 cycles of ischemia induced, the control group only underwent PCI. Serum SDF-1α was measured preoperative and postoperative PCI evaluation of during hospitalization and long-term clinical outcomes by echocardiography and major adverse cardiac events (MACE)

RESULTS Compared with the control group, patients in the limb RIC group had a higher postoperative serum SDF-1α (5.04 vs. 8.80%, P=0.006) and left ventricular ejection fraction (LVEF) during hospitalization ((52.48±7.12) vs. (55.74±9.22)%, P=0.007)), whereas long-term MACE was lower (HR=0.45, 95% CI: 0.22–0.87, P=0.020). Postoperative serum SDF-1α levels were negatively correlated with left ventricular end-diastolic diameter (LVDD) (r=−0.346, P=0.006.

CONCLUSIONS This study showed that RIC improved the clinical outcome of patients with AMI undergoing PCI, and that SDF-1α may be involved in the cardioprotective effects of RIC.

GW30-e0156

Cardiac shock wave therapy in elderly patients with coronary artery disease

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OBJECTIVES Coronary artery disease (CAD) is a challenging affliction which has a high annual morbidity rate in China and the worldwide. Some end-stage CAD patients are not beneficial enough from traditional treatments. Cardiac shock wave therapy (CSWT) is a relatively new therapy for severe CAD patients. Many countries run this program, but rare studies to show the efficacy and safety in elderly patients. Our study is to evaluate the efficacy and safety of CSWT in elderly patients with CAD.

METHODS Patients whose age over 65 years old with multiple or diffused coronary artery lesions and refractory angina were enrolled into this study. They were evaluated by myocardial perfusion imaging (MPI), Canadian Cardiovascular Society (CCS) classification, NYHA classification, nitroglycerin (NTG) usage, 6 minutes' walk test (6MWT) and Seattle Angina Questionnaire (SAQ) before and after CSWT. The improvement of MPI score in target segments were collected and analyzed. Manual MPI score was evaluated by two nuclear medicine physicians, while automatic MPI score was given by software. All outcomes were assessed at baseline evaluation and 4 months after the initiation of CSWT. Data were compared using paired t-tests. P<0.05 was considered to indicate a statistically significant difference.

RESULTS A total of 32 elderly CAD patients were enrolled. There were 20 males and 12 females. The mean age was 72.81±6.78 years with a range of 65–88 years. 11 patients underwent CABG previously. CCS classification (2.28–1.18, P=0.003), NYHA classification (2.16–1.90, P=0.003), NTG usage (1.48–0.41 pill/day, P=0.03), physical limitation of SAQ (60.07–66.16, P=0.018), angina frequency of SAQ (76.21–84.63, P=0.04), treatment satisfaction of SAQ (74.14–80.13, P=0.005), manual MPI score in stress (2.68–2.12, P=0.01), automatic MPI score in stress (3.14–2.50, P=0.013) and ischemic area in stress (96.43–64.27%, P=0.000) was shown significantly improved after CSWT. The level of TNT, CKMB and BNP was not different before and after treatment.

CONCLUSIONS CSWT is an effective and safe treatment in elderly patients with severe CAD.

GW30-e0204

Association of prealbumin levels with contrast-induced acute kidney injury in elderly patients with elective percutaneous coronary intervention

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OBJECTIVES Inflammatory factors play a critical role in contrast-induced acute kidney injury (CI-AKI). Prealbumin, a nutritional and inflammatory indicator, is a well-established predictor of short- and long-term outcomes in numerous clinical conditions. The present study investigated the association of pre-procedural prealbumin levels with CI-AKI and long-term outcomes in geriatric patients after elective percutaneous coronary intervention (PCI).

METHODS A total of 558 patients aged ≥75 years, who underwent elective PCI between January 2012 and December 2015, were selected for the present study. Pre-procedural prealbumin levels were measured before PCI. Multivariable logistic regression and Cox proportional hazards regression analyses were performed to identify the independent risk factors for CI-AKI and long- term mortality.

RESULTS 54/558 patients developed CI-AKI. The optimal cutoff value of prealbumin for detecting CI-AKI was 185.5 mg/L with 62.7% sensitivity and 70.4% specificity based on the receiver operating characteristic analysis [C statistic=0.710, 95% confidence interval (CI): 0.673–0.751). Multivariable analysis demonstrated that prealbumin ≤185.5 mg/L was significantly associated with CI-AKI [odds ratio (OR)=0.397; 95% CI: 0.195–0.808; P=0.011). Cox regression analysis demonstrated that prealbumin ≤185.5 mg/L was associated with long-term mortality (adjusted hazard ratio (HR)=0.525; 95% CI: 0.289–0.952; P=0.034) during follow-up.

CONCLUSIONS Pre-procedural levels of prealbumin were independently associated with an increased risk of CI-AKI and long-term mortality in elderly patients undergoing elective PCI.

GW30-e0217

Impact of lesion site remodeling in predicting the long term natural prognosis of intermediate lesions

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OBJECTIVES The management of intermediate coronary lesions remains a daily challenge for interventional cardiologists. Intravascular ultrasound help achieve better vascular profiling of lumen area and plaque burden, which are related to future outcomes. IVUS also provide vascular geological characteristics such as remodeling index. But the impact of lesion site remodeling on clinical outcomes is still poorly understood.

METHODS We consecutively enrolled 162 patients with coronary heart disease who had at least one intermediate lesion without PCI between August 2011 and January 2015. A total of 212 lesions were assessed by IVUS. The intermediate lesions were divided into 3 groups: RI<0.88 as negative remodeling; 0.88≤RI≤1.0 as intermediate remodeling; RI>1.0 as positive remodeling. The IVUS characteristics and MACE events (cardiac death, myocardial infarction, TLR or rehospitalization due to angina) were compared between 3 groups.

RESULTS Negative remodeling group have the smallest MLA (4.16 mm² vs. 5.05 mm²; 4.16 mm² vs. 4.85 mm²; P<0.01) and highest area stenosis rate (59.32±10.15% vs. 54.61±9.09%; 59.32±10.15% vs. 51.67±12.96%; P<0.01) among three groups. During a median follow-up of 5.2 years, the MACE occurred most frequently in the negative remodeling group (41.7 vs. 4.6%; 41.7 vs. 10.5%; P<0.001). After adjusting for multiple covariates, negative remodeling independently predicted future worse clinical outcomes (HR: 4.716; 2.146–10.632; P<0.001).

CONCLUSIONS IVUS derived negative remodeling (RI<0.88) independently predict future MACE of intermediated lesions.

GW30-e0219

Non-acute myocardial infarction patients with chronic kidney disease may not be benefit from percutaneous myocardial revascularization

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OBJECTIVES Percutaneous coronary intervention (PCI) is one of the most commonly performed therapeutic interventions worldwide. However, for relatively stable non-acute myocardial infarction (non-AMI) patients with chronic kidney disease (CKD), the benefits of PCI remain unknown. Therefore we aim to investigate whether myocardial revascularization will lead to decreased mortality in non-AMI patients with CKD.

METHODS A total of 2713 consecutive non-AMI patients with CKD undergoing coronary angiography (CAG) or PCI were divided into a PCI group (n=1604) and a non-PCI group (n=1609) depending on whether they had PCI or not. CKD was defined as estimated glomerular filtration rate (eGFR <90 mL/min/1.73 m²). The endpoint was all cause mortality, which was defined as any death recorded after the date of enrollment. Multivariable logistic regression and Cox proportional hazards regression analyses were performed to identify the association between myocardial revascularization and long-term mortality.

RESULTS Overall, during the mean follow-up of 3.34±0.02 years, mortality was 5.1% (n=49) and 5.7% (n=27) in PCI group and non-PCI group, respectively. Multivariable logistic regression analysis showed that PCI, CKD G4 (eGFR 15–30 mL/min/1.73 m²), age>75 years, pre-procedure hypotension and the use of diuretics were significantly associated with worse long-term mortality [HR of 1.462 (95% CI: 1.035–2.063), HR of 5.488 (95% CI: 3.258–9.245), HR of 1.557 (95% CI: 1.105–2.195), HR of 2.335 (95% CI: 1.153–4.729), and HR of 1.737 (95% CI: 1.239–2.435), respectively]. Log-rank analyses showed that there was no difference in all-cause mortality between PCI group and non-PCI group (P=0.095). Patients with worse renal function were less likely to obtain benefit and may even get harm from PCI. (P<0.05).

CONCLUSIONS Myocardial revascularization is not associated with decreased mortality in non-AMI patients with CKD. Further investigation is needed to evaluate whether such patients will obtain benefit from PCI.

GW30-e0255

Comparative analysis of pharmacodynamics of ticagrelor vs clopidogrel in Chinese patients with acute coronary syndrome: a randomized, open-label, phase IV trial

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OBJECTIVES To explore and compare pharmacodynamic profile of ticagrelor and clopidogrel in Chinese patients with ACS.

METHODS This multicentre, open-label, phase IV, randomized trial was conducted between May, 2013 and March, 2014 in China with 6 weeks follow-up period. Patients with ACS were randomized (1:1) to receive ticagrelor (180 mg loading dose, later 90 mg twice daily) or clopidogrel (600 mg loading dose, later 75 mg once daily [QD]), along with background aspirin therapy (300 mg loading dose, later by 100 mg QD). The primary outcome was P2Y12 reaction unit (PRU) measured by VerifyNow at 2 h post-loading dose. Secondary outcomes included PRU, inhibition of platelet aggregation (IPA%: 100×[PA predosing–PA postdosing/PA predosing]; PA: platelet aggregation) and percentage of patients with.

RESULTS A total of 60 patients (mean age: 58.7±10.3 years; 82.5% males; FAS, n%: 96.55%; PPS, n%: 89.66%) with comparable baseline features were randomized to ticagrelor (n=29) and clopidogrel (n=31) treatment arms. PRU at 2 h after loading dose was significantly better in ticagrelor arm (130.9±111.3 vs. 228.83±74.1; P=0.0002). After 2 h of loading dose, ticagrelor caused rapid and significantly higher IPA% (2 h: 51.6±45.4 vs. 8.4±25; 8 h: 67.9±34.9 vs. 25.4±32.7, 24 h: 79.2±17.9 vs. 28.8±26.9; 6 weeks: 82.8±13.9 vs. 24.22±33.5) and reduced PRU (8 h: 84±87.6 vs. 190.3±86.8; 24 h: 57.2±50.4 vs. 183.7±79.4; 6 weeks: 45.2±42 vs. 187.6±82.8) than clopidogrel (P≤0.0001 for all). Higher proportion of ticagrelor-treated patients had PRU <0.0001; PRU: P=0.0002).

CONCLUSIONS Ticagrelor induced faster and better antiplatelet effect than clopidogrel in Chinese patients with ACS; however, the effect was lower in STEMI patients as compared to that in NSTEACS patients. The safety profiles of both the drugs were comparable.

GW30-e0310

The independent and incremental value of ultrasound carotid plaque length to predict the presence and severity of coronary artery disease: analysis from the CPL prospective registry

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OBJECTIVES Carotid ultrasound has been widely used in the risk assessment of coronary artery disease (CAD). Data regarding the relationship between carotid plaque length (CPL) and CAD are lacking. We evaluated whether CPL had independent and incremental predictive value for the presence or severity of CAD.

METHODS We prospectively enrolled 2149 consecutive patients who underwent both first coronary angiography (CAG) and carotid ultrasound with measurements of mean intima-media thickness (mean-IMT), plaque score (PS), and maximal CPL (max-CPL). The severity of CAD was measured by the Gensini score (GS), and it was divided into tertiles: low, intermediate, and high GS. Ultrasound parameters were tested for their incremental value to predict CAD or high GS over traditional risk factors (TRF). Logistic regression analysis was used to evaluate the association between the three parameters and coronary stenosis. We calculated the area under the curve (AUC) and net reclassification improvement (NRI) to determine the predictive value of different models.

RESULTS The prevalences of CAD and high-GS patients were 65.5% (n=1408) and 33.5% (n=719), respectively. Patients with CAD had longer max-CPL than those without CAD (mean 8.31±6.12 vs. 3.05±4.13 mm, P<0.001). The GS was closely correlated with max-CPL, followed by PS and mean-IMT (P<0.001). Multivariate analysis demonstrated that max-CPL remained independently associated with both CAD (odds ratio: 1.19, P<0.001) and high-GS (odds ratio: 1.23, P<0.001) after adjusting for TRF. Compared with PS or mean-IMT, max-CPL had significantly higher discrimination value for predicting CAD (AUC 0.767 vs. 0.738 vs. 0.642, P<0.001) and high-GS (AUC 0.819 vs. 0.769 vs. 0.634, P<0.001). At a cut-off value for the max-CPL of 6.3 mm, the sensitivity and negative predictive value for high-GS were 84.6 and 89.1%, respectively. Moreover, max-CPL demonstrated significant incremental prediction for high GS over mean-IMT; this was true for both discrimination (AUC 0.821 vs. 0.634, P<0.001) and reclassification (NRI=0.474, P<0.001). When added to TRF, max-CPL showed the highest incremental predictive value for CAD (AUC=0.823, NRI=0.208, P<0.001 for both), and the same was true for high-GS (AUC=0.832, NRI=0.431, P<0.001 for both).

CONCLUSIONS Ultrasound max-CPL had independent and incremental predictive value over TRF for the presence and severity of CAD. And max-CPL had higher incremental value than mean-IMT for detecting CAD and high GS. Furthermore, max-CPL could improve CAD risk prediction when added to mean-IMT. Thus, max-CPL measured by carotid ultrasound seemed to be an effective marker of high-risk patients to refer to CAG.

GW30-e0357

The effect of primary PCI on the recovery of atrioventricular block in inferior STEMI patients with late presentation (>12 h)

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OBJECTIVES There is no definite recommendation of reperfusion time for inferior ST-elevation myocardial infarction (STEMI) patients presenting later than 12 h from symptom onset when complicating new atrioventricular block (AVB) on admission. It is not clear whether the percutaneous coronary intervention (PCI) could facilitate the recovery of AVB or not.

METHODS We conducted a retrospective study including 52 consecutive inferior wall STEMI patients with presenting time >12 h and complicating second or third-degree AVB on admission. All of them underwent PCI. The clinical characteristics, time to PCI after symptom onset, procedural data, and time to AVB improvement were studied.

RESULTS There were 42 males and the mean age was 61±10 yrs. Median presenting time from symptom onset was 36 h (ranging 13–192 h). Median time to PCI after MI was 6.0 days (ranging 1–15 days) and median time course of AVB improvement from symptom onset was 5.0 days (ranging 1–15 days). 24 patients got AVB improvement before PCI procedure (defined as preoperative group) and 28 patients got AVB improvement after PCI procedure (defined as postoperative group). The median time of AVB getting improvement was 5.0 days vs. 5.5 days (P=0.367) in preoperative and postoperative group respectively. In the postoperative group, there was a strong association between time to PCI and time to AVB improvement (r_s=0.869, P=0.000) by Spearman correlation analysis. No adverse PCI procedure-related complications or death occurred and all the patients got complete AVB recovery at discharge.

CONCLUSIONS Early PCI was safe and should be recommended as the priority strategy for late presentation inferior STEMI patients when complicating new onset of AVB. Successful reperfusion of the infarct-related artery was helpful to facilitate AVB improvement in this situation.

GW30-e0359

Mechanism of lycopene in alleviating endoplasmic reticulum stress induced by hypoxia/reoxygenation in H9C2 cardiomyocytes

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OBJECTIVES Mechanism of lycopene in alleviating endoplasmic reticulum stress induced by hypoxia/reoxygenation in H9C2 cardiomyocytes.

METHODS H9C2 cardiomyocytes were randomly divided into control group, lycopene group, H/R group, lycopene+H/R group, 4-phenyl butyric acid (4-PBA)+H/R group, thapsigargin (TG) group, and lycopene+TG group. The apoptosis ratio of H9C2 cardiomyocytes was detected and the expressions of protein of glucoseregulated proteins 78 (GRP78), C/EBP homologous protein (CHOP), c-Jun-N-terminal protein kinase (JNK), phosphorylation of JNK (p-JNK) and caspase-12 were detected by Western blot.

RESULTS The apoptosis ratio and the expressions of protein of GRP78, CHOP, JNK, p-JNK and caspase-12 increased markedly in H/R group and TG group in comparison with those in the control group (P<0.01). They decreased markedly in lycopene+H/R group and 4-PBA+H/R group compared with those in H/R group (P<0.01) and in lycopene+TG group compared with those in TG group (P<0.01). No statistically significant difference was found between lycopene+H/R group and 4-PBA+H/R group. No significant difference was found in the changes of the expression of protein of JNK.

CONCLUSIONS Lycopene may exert its protective effect on H/R H9C2 cardiomyocytes through inhibiting the key signaling pathways of CHOP, p-JNK and caspase-12 to reduce ERS.

GW30-e0360

Protective effect of celastrol on myocardial ischemia–reperfusion injury

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OBJECTIVES Celastrol, a major active constituent of Tripterygium wilfordii, has antioxidant, anti-inflammatory, and anticancer effects. However, whether celastrol can exert protective effect on myocardial ischemia–reperfusion injury (MIRI) is unknown. The aim of this study was to test the protective effect of celastrol on MIRI and elucidate its underlying mechanism.

METHODS Cardiomyocytes (H9C2 cells) were subjected to hypoxia for 8 h followed by reoxygenation for 4 h to create hypoxia/reoxygenation (H/R) model, an in vitro MIRI model. Celastrol was added to the medium 60 min before the H/R process. Cell viability was detected using MTT assay. Myocardial injury was evaluated by measuring lactate dehydrogenase (LDH) and creatine kinase MB isoenzyme (CK-MB) activity. Changes in mRNA and protein expression of TNF-α, IL-1β, and nuclear factor-KB (NF-KB) were measured with RT-qPCR assay and western blot analysis.

RESULTS Results showed that low-dose celastrol (20 and 50 nM) treatment significantly increased cell viability and decreased LDH and CK-MB activity in the condition of H/R, but high-dose celastrol (200 and 400 nM) resulted in extra injury to cardiomyocytes. Moreover, treatment with 50 nM celastrol significantly downregulated mRNA and protein expression of TNF-α and IL-1β. Meanwhile, NF-KB mRNA and protein in the nucleus were also correspondingly reduced.

CONCLUSIONS Our study demonstrated that low-dose celastrol could prevent MIRI in cardiomyocytes by inhibiting the activation of NF-KB, and celastrol may be a potential therapeutic agent for preventing MIRI.

GW30-e0380

PFT-based antiplatelet therapy reduces cardiovascular events in post-AMI patients with left ventricular dysfunction after percutaneous coronary intervention

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OBJECTIVES Dual antiplatelet therapy (DAPT) with aspirin and P2Y12 antagonists has become the standard therapy for preventing adverse cardiovascular events after percutaneous coronary intervention (PCI). Evidence for platelet function testing (PFT)-based antiplatelet therapy is limited for patients with acute myocardial infarction (AMI) and left ventricular dysfunction underwent contemporary PCI.

METHODS We prospectively enrolled 824 consecutive patients subjected to AMI with left ventricular ejection fraction (LVEF) <0.5 undergoing PCI based on the Shanghai East Hospital PCI database since 2012. All these patients received loading dose DAPT with aspirin and a P2Y12 inhibitor (clopidogrel or ticagrelor). Platelet function was assessed more than 72 h post-PCI by vasodilator-stimulated phosphoprotein (VASP) assay. In total, 212 patients (25.73%) were identified with HPR on P2Y12 antagonists, among whom 102 patients (48.11%) adjusted antiplatelet therapy based on PFT. The primary endpoint was major adverse cardiac events (MACE) and the secondary endpoint was major bleeding (BARC grade≥3) 1 year after PCI.

RESULTS Kaplan-Meier survival analysis demonstrated higher mortality in the HPR group during the 1-year follow-up (HR 0.11, 95% CI 0.04–0.28, P<0.01). MACE at 1 year post-PCI was significantly higher in the HPR group (44.81 vs. 21.24%, P<0.01; OR: 3.01, 95% CI: 2.16–4.20), mainly driven by the higher risk of cardiac death, cardiac shock, malignant arrhythmia, stent thrombosis, nonfatal myocardial infarction, target vessel revascularization (TVR) and ischemic stroke (P<0.05). For patients with HPR on P2Y12 antagonists, the intensified antiplatelet strategy by switching from clopidogrel to ticagrelor, but not double-dose clopidogrel, significantly reduce the incidence of MACE when compared with continuing maintenance dose of DAPT (12.00 vs. 60.00%, P<0.01; OR: 0.09, 95% CI: 0.04–0.23). The incidence of major bleeding (BARC grade≥3) was comparable among all groups (P>0.05).

CONCLUSIONS For post-AMI patients with left ventricular dysfunction undergoing PCI, PFT-guided intensified antiplatelet therapy with ticagrelor reduced major cardiovascular events without increasing the risk of bleeding.

GW30-e0381

Investigation of Morphological Characteristics of Coronary Bifurcation Core in Normal Subjects with CCTA

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OBJECTIVES This study aims: (1) to set up a method to detect BFC/POC shape and to its dimension in different bifurcation types and locations; (2) to validate the four models base on the coronary bifurcation measurements from normal population; (3) to investigate potential relevance of the BFC/POC morphology in CBLs interventions.

METHODS Inclusions criteria: (1) subjects with unknown chest discomfort in whom coronary artey disease could be finally excluded clinically, (2) subjects underwent CCTA with normal or negative findings either by CCTA or invasive coronary angiography if obtainable, (3) images of CCTA with high quality.

RESULTS Normal coronary segmentation of a normal case took 20–25 minutes for centerlines and 7 minutes for the mesh computation. Registration time was approximately 40 seconds for the rigid part and 3 minutes for the non rigid on a macbook pro 1-14.3 system with 8 GB of memory and 2.3 GHz intel core i5 processors. Average normal minimum lumen area within the LM were mainly located within POC (51 and 71%). Distal LM proximal to the carina (to include DLM and POC) positively correlated with the normal coronary bifurcation MLA within the POC (r=0.283, P=0.02; BFC within the POC less than 6.1 mm± 2.1 mm (2). The approximate median registration error was 0.29 mm with a median standard deviation of 0.19 mm and a median maximum error of 1.39 mm. Maximum error occurred in areas of high deformation such as large or curved ostium shape. In total where n=330 bifurcations models as follow LMB=100, D1=55, LAD=40, OM1=40, POC=25, LCX=20 and 50 cruxes. Having removed isotropic size (scaling factor), the average model and first three models of variation.

CONCLUSIONS Clinically very important insights and information concluded from normal coronary bifurcation anatomy such as defining normal range and distribution of shape. This method is more like computational which confirms in a quantifiable and computational fashion. This is far superior over a long standing questions of statistically significant shape differences among the major coronary bifurcation in interventional cardiology. The model support and applicable to any collection of shape and can be applied to create a probability model of the major coronary bifurcations. The BFC/POC within the bifurcation was a good surrogate reflecting the overall normal shape of LM bifurcation including ostial LCX and the ability to measure normal distal LM shape as well as final ostial LCX lumen area. Information about the size (and future shape), clinical doctors will have great stent designs and benefits and can span the populations size. According to individual specific patient geometry within the statistical shape, individual stent can be designed or selected, which will reduce the burden of choosing random stent.

GW30-e0410

Prospective study of the biochemical markers of inflammation after angioplasty of bioresorbable scaffolds and everolimus-coated stents in patients with stable coronary artery disease

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OBJECTIVES To carry out a comparative analysis of the dynamics of biochemical markers of vascular wall inflammatory response in patients with stable coronary artery disease (CAD) after angioplasty of BS and stents coated with everolimus.

METHODS Forty-one patients (mean age 62.7±8.6 years) with stable CAD and single-vessel coronary lesion were examined according to coronary angiography and indications for percutaneous coronary intervention (PCI). The study did not include patients who underwent PCI or coronary artery bypass grafting in the previous year, with the presence of restenosis in the stent. Group 1 included 21 patients with an implanted stent coated with everolimus (Xince Prime); group 2 included 20 people with an implanted BS (Absorb). Randomization was carried out by the random number method. All patients received optimal medical treatment that included statins and dual antiplatelet therapy. Endothelial dysfunction markers (endothelin-1, nitrites); inflammatory markers (hs-CRP, TNF-alpha, homocysteine, interleukine 1β, 6, 8, 16; sCD40 L, MMP-9, TIMP-1) were measured. The parameters were evaluated at baseline, 1, 4 days and 1, 6, 12 months after PCI.

RESULTS In the studied groups no undesirable atherothrombotic events were revealed during the follow-up. Initially, the groups did not differ in biochemical parameters before PCI. In both groups, 1 day after PCI, the increase in cytokines was registered, followed by a decrease in 4 days to the initial level and MMP-9, while maintaining a high concentration for 1 month. In both groups, 1 month after PCI, an increase in IL-8 was registered as a response to damage to the vascular wall, followed by an increase to the maximum values in 12 months. In dynamics, the maximum increase in CD40L after 6 months without reaching the initial level after 12 months was observed only in group 2. In the compared groups, after 12 months, the maximum values of endothelin-1 as a marker of vascular endothelial dysfunction were registered in group 1, while in group 2 this figure decreased to the initial level. Both groups maintained a high level of hs-CRP.

CONCLUSIONS Patients with stable CAD after implantation of BS and stents coated with everolimus did not show any differences in the dynamics of the

mediators of the acute phase of inflammation during the 1 month. High levels of pro-inflammatory factors of instability of the atherosclerotic plaque IL-8 and CD40L, as well as a persistent increase in the concentration of hs-CRP within 1 year after PCI suggest a continuing high risk of thrombosis, more pronounced in the group with implanted BS.

GW30-e0426

The independent and incremental value of ultrasound carotid plaque length to predict the presence and severity of coronary artery disease: a prospective registry study

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OBJECTIVES Carotid ultrasound parameters, such as intima-media thickness (IMT) and carotid plaque thickness have been proven to be associated with the prevalence of coronary artery disease (CAD), whereas they are far from optimal for clinical utility, due to small differences among individuals and slight annual changes. So far, data regarding the relationship between carotid plaque length (CPL) and the presence and severity of CAD are lacking. The aim of the study was to evaluate the emerging role of CPL as an effective marker of CAD risk.

METHODS We prospectively enrolled 2149 consecutive patients who underwent both first coronary angiography (CAG) and carotid ultrasonography with measurements of intima-media thickness (IMT), plaque score (PS), and CPL.

RESULTS In total, 1408 (65.5%) had CAD (defined as stenosis ≥50%), and 741 (34.5%) had no CAD. Patients with CAD had longer maximal CPL than those without CAD (mean 8.31±6.12 vs. 3.05±4.13 mm, P<0.001). The severity of CAD, measured by the Gensini score (GS), was closely correlated with max-CPL, followed by PS and mean-IMT. After adjustment for traditional risk factors, max-CPL remained independently associated with CAD and high-GS. Max-CPL, compared with PS or mean-IMT, had significantly higher discrimination value for predicting high-GS (area under the curve 0.819 vs. 0.769 vs. 0.634, P<0.001). At a cut-off value for the max-CPL of 6.3 mm, the sensitivity and negative predictive value for high-GS were 84.6 and 89.1%, respectively. Furthermore, the addition of max-CPL improved the discrimination (AUC 0.821 vs. 0.634, P<0.001) and reclassification (net reclassification improvement [NRI]=0.474, P<0.001) over mean-IMT.

CONCLUSIONS Ultrasound max-CPL has independent and incremental value for predicting the presence and severity of CAD. Max-CPL seems useful to identify high-risk patients to refer to CAG.

GW30-e0472

Characteristics and prognosis of coronary stent fracture

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OBJECTIVES To investigate the clinical, characteristics of lesion procedural characteristics and prognoses of coronary stent fracture (CSF).

METHODS From January 2012 to December 2017, 14,717 patients underwent drug-eluting stents implantation in the Department of Cardiology, the Second Affiliated Hospital of Nanchang University. The angiograms of all 2098 patients who underwent repeat angiography or more advanced imaging examination were studied to identify the presence of stent fracture, then to count the detection rate of coronary stent fracture. The clinical, characteristics of lesion procedural characteristics and prognoses which might predispose to stent fracture were systematically analyzed. The symptoms, vital signs and main adverse cardiac events (MACE) of patients with stent fracture were followed up regularly and analyzed in combination with the relevant literature.

RESULTS The patients of coronary stent fracture was found in 9 patients during the period 2012–2017, with a detection of 0.4%. Open-loop design, alloy material, sirolimus eluting stent, angulated lesions and the right conorary are risk factors that leading to the coronary stent fracture. Follow-up as of December 31, 2018, 2 cases of 9 patients follow-up results in death, more than 3 cases of unstable angina in patients, 2 cases of stable angina, 2 cases of chest has no obvious symptoms such as chest pain. 9 cases of major adverse cardiac events in patients with follow-up, there are 4 cases with routine target-vessel revascularization (TVR). There have no patient with cardiac death, myocardial infarction and in-stent thrombosis, all patients with coronary stent fracture can be found in varying degrees of coronary stent hyperplasia.

CONCLUSIONS There is low detection rate of coronary stent fracture by using the coronary angiography. Predisposing factors of stent fracture may be associated with the open-loop design, alloy material, sirolimus eluting stent, angulated lesions and the right conorary. The main adverse cardiac events that affect coronary stent fracture are target lesion revascularization (TLR).

GW30-e0486

Long-term dual antiplatelet therapy increased adverse events after PCI

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OBJECTIVES The present study aimed to investigate the efficacy and safety of long-term DAPT (>18 months) after PCI.

METHODS A total of 4447 CAD patients after PCI from CORFCHD-PCI, aretrospective cohort study (Identifier: ChiCTR-INR-16010153) were divided into 3 groups (No antiplatelet therapy group [NAPT group, n=1242], Monotherapy of aspirin or clopidogrel group [SAPT group, n=2188], and DAPT group, n=1017) according to antiplatelet therapy situation after administration of 18-month DAPT. All the patients were followed up for at least 24 months and the longest follow-up time is 120 months. The primary endpoint was the mortality and the secondary endpoints were the major adverse cardiac events (MACEs) and bleeding events.

RESULTS The all-cause mortality (ACM) and cardiac mortality (CM) were significantly increased in the NAPT group compared to that in the DAPT group (15.6 vs. 0.6%, P<0.001; and 12.1 vs. 0.3%, P<0.001, respectively) or in the SAPT group (15.6 vs. 0.6%, P<0.001; and 12.1 vs. 0.5%, P<0.001, respectively). We did not found significant difference in mortality (ACM or CM) between the SAPT group and the DAPT group (P=0.611 or P=0.328). The incidence of MACEs was significantly increased in the DAPT group compared to SAPT group (16.3 vs. 9.4%, P<0.001). We also found DAPT increased the bleeding events compared to SAPT (4.6 vs. 2.4%, P<0.001).

CONCLUSIONS The present study suggests that long-term dual antiplatelet therapy longer than 18 months significantly increased the incidence of MACEs and bleeding events after PCI.

GW30-e0487

Physiological serum concentration of gamma-glutamyl transferase reversely associated with long-term mortality in coronary artery disease after percutaneous coronary intervention: Results from a 10-year follow-up of CORFCHD-PCI study

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OBJECTIVES The relation between GGT and outcomes of coronary artery disease (CAD) patients underwent PCI remains controversial. The present study aimed to investigate the association of physiological serum GGT with the long-term up to 10-year follow-up mortality of CAD patient after percutaneous coronary intervention (PCI).

METHODS A total of 6050 CAD patients after PCI from CORFCHD-PCI, a retrospective cohort study (Identifier: ChiCTR-INR-16010153) were evaluated. 412 patients were excluded due to no GGT data available, acute infections, malignancies, hepatobiliary disease or alcohol abuse. 614 patients were further excluded for abnormal high activity of GGT (GGT>60 U/L). Finally, 5024 patients with physiological concentration of GGT were enrolled. The primary outcome was long-term mortality after PCI. The main secondary endpoints were stroke, readmission, and major adverse cardiovascular events (MACEs) defined as the combination of cardiac death, stent thrombosis, recurrent myocardial infarction, and target vessel reconstruction.

RESULTS Patients were divided into 3 groups according to GGT tertiles: 1st tertile (GGT<19.6 U/L; n=1865), 2nd tertile (GGT≥19.6 U/L–32.9 U/L; n=1880) and 3rd tertile (GGT>32.9 U/L; n=1269). Overall, there were 264 all-cause mortality (ACM) during the following up. The incidence of ACM in the 1st tertile is 111 (5.9%), 2nd tertile is 100 (5.3%), and 3rd tertile is 53 (4.2%). The ACM incidence was significantly lower in 3rd tertile compared to that in the 1st tertile (P=0.031). Cardiac mortality (CM) occurred in 212 patients: 92 (4.9%) in the 1st tertile group, 80 (4.3%) in the 2nd tertile and 40 (3.2%) in the 3rd tertile group. There was significant difference in the CM incidence between the 1st tertile group and 3rd tertile group (P=0.016). The multivariate Cox proportional hazards model showed that decreased serum GGT level was independently correlated with the ACM (adjusted HR=1.431 [1.025–1.998], P=0.035) and CM (adjusted HR=1.553[1.064–2.267], P=0.023), We did not found significant difference in the incidence of MACEs, stroke, bleeding events and readmission among these three groups.

CONCLUSIONS The present study indicated that decreased physiological serum GGT concentration was independently associated with long-term mortality in CAD patients underwent PCI.

GW30-e0489

Gamma-glutamyl transferase to albumin ratio (GAR) as a novel predictor of long-term mortality and bleedings in patients after percutaneous coronary intervention: a retrospective cohort study

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OBJECTIVES Both gamma-glutamyl transferase (GGT) and albumin have been reported to be associated the risk and mortality of coronary artery diseased (CAD) with or without percutaneous coronary intervention (PCI). GGT is an important enzyme in glutathione (GSH) metabolism and has been found to be involved in the pathogenesis of CAD. Albumin is the major protein in human plasma and has generally been used as a quantitative measure of nutritional status. Recently, serum albumin concentrations were reported to be associated with increased risk for the development of myocardial infarction (MI), CAD and stroke. Therefore, the ratio of GGT to albumin (GAR) may be a powerful predictor for outcomes in cardiovascular disease. However, the relation between GGT to albumin ratio (GAR) and outcomes in CAD patients after PCI has not been investigated.

METHODS In the present study, we enrolled 5638 CAD patients underwent PCI who were from the Clinical Outcomes and Risk Factors of Patients with Coronary Heart Disease after PCI (CORFCHD-PCI) study. The patients with serious heart failure, rheumatic heart disease, valvular heart disease, congenital heart disease, pulmonary heart disease, and serious dysfunction of liver or kidney were excluded from the present study. 5638 patients were divided into two groups according to GAR (GAR<0.62, n=2712 and GAR≥0.62, n=2926). The primary outcome was long-term mortality including all-cause mortality (ACM) and cardiac mortality (CM) after PCI. The average follow-up time is 35.9±22.6 months.

RESULTS We found there was significant difference between the two groups in the incidence of all-cause mortality (P=0.016) and bleeding events (P=0.010). Multivariate Cox regression analyses suggested that compared to the patients in the lower GAR, the risk of ACM and bleeding events were decreased 23.8% (Hazard risk [HR]=0.762 95% CI: 0.601–0.966, P=0.025), and 39.4% (HR=00.616, 95% CI: 0.446–0.852, P=0.003) in the higher GAR group, respectively, during the long-term follow-up.

CONCLUSIONS The present study indicated that GAR is an independent and novel predictor of mortality and bleeding events in CAD patients underwent PCI.

GW30-e0496

Left ventriculography

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OBJECTIVES Ventriculography done in the catheterization laboratory provides more information than ultrasound ventriculography.

METHODS Catheter based ventriculography vs. Ultrasound ventriculography performed in a single laboratory.

RESULTS One observational study of myocardial infarction patients, prior to PCI/stent revealed an increasing 30-day mortality related to poor LV function determined by cardiac ultrasound Advantages of Catheter Based Ventriculography Catheter base Left Ventriculography provides data on wall motion, volume, ejection fraction, chamber size, valvular regurgitation and helps predict the outcome of patients with coronary artery disease. It is the only method to accurately evaluate LVEDP, and LV Systolic pressure. LV angiography can also identify regional LV wall motion abnormalities consistent with abnormalities found in the epicardial coronaries and coronary microcirculation. LV angiography can also identify regional LV wall motion abnormalities consistent with abnormalities found in the epicardial coronary arteries. Limitations of catheter based LV angiography include: There are no specific guidelines, from ACC, AHA, ESC or SCAI for the performance of left ventriculography at the time of coronary angiography or left heart catheterization. Radiation exposure, contrast-induced AKI and invasive procedure. Advantages of Ultra Sound Readily available, relatively inexpensive, and portable. Can be easily repeated no radiation exposure. Limitations of Ultrasound Studies have shown that quantitative assessment of LV function by 2D TTE is suboptimal in up to 20 percent of patients. Foreshortening of the heart sometimes seen with ultrasound makes interpretation of LV function difficult. Ultrasound may be performed by an experienced sonographer, who does not know the patient's physiology or anatomy and, not by a physician who knows the state of the coronary artery pathology. If Echo is used to assess L V function then the Cath Lab operator should be aware of the quality of the Echo and the findings of ventricular function before the patient enters the catheter laboratory and include in the Cath lab report the reason for not doing an LV angiogram.

CONCLUSIONS All things considered I favor catheter based ventriculography.

GW30-e0497

High expression of SOCS3 genes in peripheral blood leukocytes of patients with acute myocardial infarction and its significance

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OBJECTIVES Suppressor of cytokine signaling 3 (SOCS3) is a member of the suppressor of cytokine signaling (SOCS) family. SOCS regulates cells' responses to external stimuli through a common molecular mechanism. The disorder of SOCS3-mediated cytokine signaling can cause many diseases, including allergies, autoimmune diseases, inflammation and cancer. In addition, the pathogenesis of acute myocardial infarction (AMI) and coronary atherosclerosis is increased vascular responses to inflammation, and a considerable amount of research shows that atherosclerosis is an inflammatory disease. The aim of this study was to evaluate the possibility of using SOCS3 gene expression as a biomarker for predicting the risk of AMI.

METHODS Peripheral white blood cells were collected from 113 patients with AMI and 85 patients with stable coronary artery disease (SCAD). The SOCS3 mRNA expression in peripheral blood was detected by real-time quantitative polymerase chain reaction. Western-blot was used to detect the differences in SOCS3 gene expression at the protein level.

RESULTS The expression level of SOCS3 mRNA in peripheral blood of patients with AMI was 1.33 times higher than that of patients with SCAD, and the expression of SOCS3 genes at the protein level was 1.250 times higher than that of patients with SCAD (both P<0.05). Bivariate logistic regression analysis showed that the high expression of SOCS3 gene was an independent risk factor for AMI, which increased the risk of AMI by 3.197 times. It was also found that there was no correlation between the high expression of SOCS3 genes and fasting blood glucose level, high-density lipoprotein, low-density lipoprotein and cardiac troponin level.

CONCLUSIONS The expression level of SOCS3 genes in patients with AMI was significantly higher than that in patients with SCAD. High expression of SOCS3 genes is an independent risk factor for AMI. It is probable that the high expression of SOCS3 genes increases the risk of AMI by increasing inflammatory responses. High expression of SOCS3 genes may serve as a potential biomarker for predicting the risk of AMI.

GW30-e0518

The impact of anti-hypertension drugs on reduced bleeding events in ACS patients

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OBJECTIVES Anti-hypertension drugs together with DAPT are widely used in ACS patients to reduce the incidence of ischemic events. Bleeding is the most common non-cardiac complication in ACS patients with DAPT. However, the impact of anti-hypertension drugs on bleeding events in ACS patients with DAPT is still unclear. The study is to investigate the association between anti-hypertension drugs and bleeding events in ACS patients with DAPT.

METHODS This retrospective study involved 2017 ACS patients with hypertension in Third XiangYa Hospital of Central South University from April 2007 to July 2017. The patients were divided into two groups: bleeding group (n=154) and non-bleeding group (n=1863). Logistic regression was used to examine the association between anti-hypertension drugs use and bleeding events in ACS patients.

RESULTS *Baseline characteristics between bleeding and non-bleeding groups:* Totally, 2017 patients were included in the study; 154 patients (7.6%) did not have bleeding events (non-bleeding group), 1863 patients (92.4%) had bleeding events (bleeding group).

Demographic data: The SBP, DBP and female people were similar between the two groups (P>0.05). The people were older and the HR was greater in the bleeding group than in the non-bleeding group.

Past history: The number of patients whose Killip grades>1 and the number of smokers were similar between the two groups (P>0.05).

Baseline Laboratory Examination: The Hg, CCr, TP and ALB were lower in the bleeding group than in the non-bleeding group (P<0.05). The AST was higher in the bleeding group than in the non-bleeding group (P<0.05). The RDW, PLT, ALT and Hct were similar between the two groups (P>0.05).

Immediate therapy: The use of β-blocker, ACEI, ARB or CCB in bleeding group was significantly less than that in the non-bleeding group (P<0.05). There were no differences in the number of patients with diuretics, vasodilators, statin, anticoagulant, PPI or PCI between the bleeding group and the non-bleeding group (P>0.05).

The association between anti-hypertension drugs and bleeding events: The incidence of bleeding events was lower in patients with the anti-hypertension drugs of β-blocker, ACEI, ARB and CCB (P<0.05). The incidence of bleeding events was similar in patients with the anti-hypertension drugs of diuretics and vasodilators (P>0.05). After adjustment for covariates, patients with β-blocker, ACEI,

ARB have lower bleeding incidence. ((β-blocker OR 0.48, 95% CI (0.31, 0.72), P<0.001; ACEI OR 0.48, 95% CI (0.31, 0.74), P=0.001; ARB OR 0.54, 95% CI (0.31, 0.95), P=0.020).

Independent predictors of bleeding events: The following baseline characteristics were independent predictors of increased bleeding events: no treatment with β-blocker, ACEI, ARB, greater HR and lower ALB.

CONCLUSIONS We studied the association between bleeding events and the use of anti-hypertension drugs in 2017 ACS patients with hypertension in XiangYa third hospital from April 2007 to July 2017. The use of β-blocker, ACEI and ARB could reduce the incidence of bleeding events among ACS patients with hypertension (P<0.05).

GW30-e0543

ADS score as a novel predictor of long-term outcomes in patients after undergoing percutaneous coronary intervention: results from a 10-year follow-up of the CORFCHD-PCI study

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OBJECTIVES Inflammation-related immune cell and acute phase reactive protein are the bio-markers of systematic inflammation, and the levels of them can reflect the degree of chronic inflammation in the patient. A novel AFR–Alb-derived neutrophil/lymphocyte ratio (dNLR) score (ADS) were reported to associate with clinical outcome in various malignancies, However, the relation between the ADS score and outcomes in CAD patients after percutaneous coronary intervention (PCI) has not been investigated.

METHODS Six thousand fifty patients were divided into 2 groups according to ADS score: Low group (ADS score <2; n=2508) and High group (ADS score ≥2; n=3542). Overall, there were 309 all-cause mortality (ACM) during the following up.

RESULTS The incidence of ACM in the low group is 156 (4.4%) and high group is 153 (6.1%). The ACM incidence was significantly higher in high group compared to that in the low group (P=0.004). Cardiac mortality (CM) occurred in 251 patients: 119 (3.4%) in the low group and 132 (5.3%) in the high group. There was significant difference in the CM incidence between the low group and high group (P<0.001). Major adverse cardiac and cerebrovascular events (MACCE) occurred in 862 patients: 422 (11.9%) in the low group and 398 (15.9%) in the high group. There was significant difference in the MACCE incidence between the low group and high group (P=0.002). Major adverse cardiac and events (MACE) occurred in 785 patients: 422 (11.9%) in the low group and 363 (14.5%) in the high group. There was significant difference in the MACCE incidence between the low group and high group (P=0.004). The multivariate Cox proportional hazards model showed that ADS score was independently correlated with the ACM (adjusted HR=1.520 [1.919–1.204], P<0.001); CM (adjusted HR=1.743 [2.264–1.341], P<0.001); MACCE (adjusted HR=1.296 [1.491–1.127], P<0.001) and MACE (adjusted HR=1.303 [1.509–1.125], P<0.001).

CONCLUSIONS The present study indicated that the ADS score was associated with long-term mortality, the MACCE and the MACE in CAD patients underwent PCI.

GW30-e0548

Creatinine level is an independent predictor of coronary in-stent stenosis for patients with drug eluting stent treatments

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OBJECTIVES The aim of this study was to evaluate the relationship between uric acid, creatinine, glomerular filtration rate and coronary in-stent stenosis (ISR) in patients with drug eluting stent (DES), and provide evidence on management of renal function in patients who receive revascularization with DES.

METHODS A retrospective analysis was made for patients who underwent coronary arteriography after receiving revascularization with drug eluting stent for 12–24 months. Medical history, baseline and follow-up laboratory examination and imaging data was collected. In-stent stenosis (ISR) is defined as more than 50% stenosis of minimum coronary inner diameter in follow up coronary arteriography than that of baseline coronary arteriography. Variance analysis, univariate and multivariate analyses were used to identify the risk factors of renal function for in-stent stenosis.

RESULTS One thousand seven hundred and ninety patients averaged 63.4 years old, with 475 (26.5%) woman, 200 (11.2%) with ISR, with medium coronary arteriography interval 406 days (IQR 378–488 days) were included in this study. There is no significant difference in gender, BMI, history of smoke, diabetes, CKI, hyperlipidemia, baseline and follow-up blood pressure, serum triglyceride, cholesterol, HDL and LDL among ISR and No-ISR group. Independent-samples t-test revealed that there were significant differences between the patients with ISR and No-ISR in baseline creatinine (86.91±60.14 mmol/L vs. 80.11±38.67 mmol/L, P=0.030), follow up creatinine (92.40±92.18 mmol/L vs. 81.29±44.85 mmol/L, P=0.005) and follow up estimated glomerular filtration rate [86.50±25.69 mmol/L vs. 90.70±26.49 mL/(min^{-1}×1.73 m^2), P=0.035]. Binary logistic regression indicated higher baseline creatinine level was the independent and significant risk factor for ISR (OR=1.00240, 95% CI: 1.00047–1.00433, P=0.015).

CONCLUSIONS For patients who receive DES treatment, higher baseline creatinine level could increase the incidence of ISR.

GW30-e0560

Predictive value of combining the SYNTAX score with reactive hyperemia index in patients with acute coronary syndrome undergoing percutaneous coronary intervention

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OBJECTIVES To investigate the predictive value of SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (SS) combined with reactive hyperemia index (RHI) in predicting 2-year major adverse cardiovascular events (MACE) in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI).

METHODS We undertook a prospective study in 401 ACS patients that underwent PCI. The RHI-SYNTAX score (RSS) was calculated by categorizing and summing up the RHI and SS of individual patients. Patients with RHI<1.67 are given 1 point, RHI≥1.67 given 0 points; and those with SS≤22 scored as 0, and >22 as 1 point. Patients were classified into 3 groups: Low RSS (Group 0), moderate RSS (Group 1) and high RSS (Group 2).

RESULTS Among patients in the low, moderate and high groups, the 2-year rates of MACE were 5.50%, 10.66% and 23.33% respectively (P<0.0001). Total revascularization rates were 1.83%, 2.54%, and 8.89% respectively (P=0.015). Ischemic stroke rates were 0.00%, 3.67%, and 5.56% respectively (P=0.031). By multivariate analysis, the RSS was an independent predictor of 2-year MACE (hazard ratio [HR]: 2.09, 95% CI: 1.36 to 3.21, P=0.001). ROC analysis indicated that the area under the curve significantly improved from 0.63 to 0.69 when RHI was added to SS (P<0.0001).

CONCLUSIONS RSS is correlated with 2-year MACE in patients presenting with ACS undergoing PCI.

GW30-e0561

One-year prognosis in patients with obstructive and non-obstructive coronary atherosclerosis and primary myocardial infarction

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OBJECTIVES To study the incidence of long-term cardiac events in patients with acute myocardial infarction (AMI) depending on the type of coronary bed lesion.

METHODS The study comprised 1240 patients admitted to the resuscitation and intensive care unit for patients with myocardial infarction between 2016 and 2017 in S.S. Yudin Moscow city hospital. The diagnosis was established based on the III Universal Definition of MI. All enrolled patients underwent cardioangiography (CAG). CA damage was considered non-obstructive, if a detected CA obstruction was less than 50%, regardless of the number of affected arteries. Following the CAG Results, the patients were divided into 3 groups: group 1 included patients with multivessel obstructive arterial sclerotic disease of the CA according to the CAG data – 664 (53.5%) patients, group 2 included patients with non-obstructive arterial sclerotic disease of the CA – 96 (7.7%) patients, the third comparison group included patients with single-vessel obstructive arterial sclerotic disease with total acute occlusion of the CA – 272 (21.9%) patients. Patients with a hemodynamically relevant disease of the trunk of the left CA – 208 (16.8%) were not enrolled. In one year after discharge, the prospective follow-up was conducted over the phone. The loss in monitoring amounted to 19%.

RESULTS The age of patients in groups 1 and 2 was 66.14±11.8 years and 67.9±11.5 years (P>0.05), the median age of patients in group 3 was 56.59±11.6 years, and was significantly different from the median age of patients in groups 1 and 2 (P<0.001). When analyzing gender distribution between the groups, significant statistical differences were found between groups 1 and 2 (P><0.01) and between groups 2 and 3 (P>0.05), and in the group with single-vessel obstructive arterial sclerotic disease no effort angina was observed in any of the patients.

CONCLUSIONS During the first year after the old MI, patients with non-obstructive coronary atherosclerosis did not develop recurrent coronary events; CAG, XRD and CABG were not performed, as opposed to the patients with obstructive disease of the CA. This bears record to rapid progression of arterial sclerotic disease of the CA in patients with obstructive disease of the CA.

GW30-e0570

Glycyrrhizic acid attenuates balloon induced-vascular injury through inactivation of RAGE signaling pathways

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OBJECTIVES Percutaneous coronary intervention (PCI) is a well-established technique used to treat coronary artery disease (CAD), while the risk of coronary artery in-stent restenosis (ISR) following PCI is still high. Previous study revealed that High-Mobility-Group-Protein B1 (HMGB1) plays critical role in neointimal formation. In this study, we aim to investigate the role of glycyrrhizic acid (GA), a HMGB1 inhibitor, in the process of neointima formation and the potential mechanisms.

METHODS We investigated the role of GA on neointima formation through iliac artery balloon injury model in rabbits. Proliferation, migration and phenotype transformation of vascular smooth muscle cell (hVSMCs) were observed. Besides, inflammation and RAGE/P38/ERK signaling pathways were tested.

RESULTS The results indicated that GA attenuated neointima formation and down-regulated HMGB1 expression in injured artery in rabbits. HMGB1 promoted proliferation, migration and phenotype transformation through the activation of RAGE signaling pathways in VSMCs and blockade of HMGB1 by GA (1, 10 and 100 μM) could attenuate those process and alleviate hVSMCs proliferation.

CONCLUSIONS In conclusion, HMGB1 inhibitor GA might be useful to treat proliferative vascular diseases via down regulating RAGE signaling pathways. Our results indicated a new and promising therapeutic agent for restenosis.

GW30-e0595

Deficiency of adropin in patients with diagonal earlobe crease

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OBJECTIVES The ear lobe crease is a common body surface marker. This simple and easy-to-recovery sign has been closely related to coronary heart disease after extensive screening. However, the mechanism of earlobe creases is not yet clear, and may be related to endothelial dysfunction. This study aimed to investigate the role of Adropin disorder in the formation of earlobe creases and to explore the potential mechanism of coronary heart disease.

METHODS A total of 135 patients ranging from ages 40–68 years who underwent coronary angiography were enrolled. Patients were categorized into three groups based on the presence or absence of coronary artery disease (CAD) and DELC: patients with CAD and DELC (ELC group, n=45); patients without ELC (no-ELC group, n=45); control patients without ELC and CAD (control group, n=45). The Serum Adropin concentration was acquired through enzyme-linked immunosorbnent assay (ELISA).

RESULTS Adropin levels were significantly lower in the earlobe crease-positive group than in the Ear-lobe negative group (168.85±101.25 pg/mL vs. 349.00±189.43 pg/mL). There was a statistically significant difference ($P<0.05$). Coronary heart disease was diagnosed in the positive group of ear lobe creases in this study. In subjects without ear lobes, serum Adropin levels were lower in coronary heart disease patients than in those without coronary heart disease ($P<0.05$); in patients with coronary heart disease, The serum Adropin level in the earlobe crease-positive group was lower than that in the earlobe crease-negative group ($P<0.05$), with statistically significant differences.

CONCLUSIONS The earlobe crease sign is one of the independent risk factors of coronary heart disease; moreover, endothelial dysfunction mediated by the decrease of Adropin level may be one of the reasons for the occurrence of coronary heart disease.

GW30-e0614

New algorithm of 4D strain-stress-echocardiography with adenosine triphosphate in detection of myocardial hidden ischemia

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OBJECTIVES It was demonstrated previously that vasodilatory effects of adenosine triphosphate (ATP) and adenosine are nearly equal. Therefore, ATP is widely utilized in stress-Echo and stress cardiac MRI, CT and PET imaging in the countries of Eastern Asia and Russia instead of adenosine. The recommended algorithm of ATP infusion during stress-test is monotonous intravenous infusion of vasodilator at a dose of 140–160 μg/kg/min without the evaluation of blood pressure level. However, administration of adenosine or ATP in traditional manner in nearly 1/5 of cases did not lead to adequate hemodynamic response systolic blood pressure (SBP) decrease. So in this subgroup of patients submaximal myocardial hyperemia presumably is not achieved. In this study we decided to: 1) develop and test a new algorithm of ATP infusion during stress-Echo with a step-by-step increase in the dosage of vasodilator; 2) analyze if 4D strain-stress-Echo with new algorithm of ATP infusion is helpful in detection of left ventricular (LV) myocardial segments with hidden ischemia in patients with coronary artery disease (CAD).

METHODS Twenty-six patients with CAD (male 24, mean age 63.1±7.5 years, multivessel disease 19) underwent ATP 4D strain-stress-Echo of LV (Vivid E95, AFI technology). Complications and adverse effects registered during modified stress-test were analyzed. 4D Echo data sets of patients were used for detection of myocardial segments with hidden ischemia.

RESULTS The key points of new algorithm of stress Echo with ATP are as follows: 1) Algorithm includes three stages: registration of Echo data sets before, at the time of ATP infusion and after 5 minutes. 2) Registration of Echo data at the second stage should begin only when adequate myocardial hyperemia is generated. Main criterion is stable decrease in SBP by 5 mmHg or more. 3) Initial dose of ATP is 140 μg/kg/min. If after 2 min of ATP infusion SBP do not diminish the infusion rate should be increased at first to 175 and then to 210 μg/kg/min. Using new algorithm of ATP infusion we managed in all cases to achieve effective vasodilation and register interpretable LV 4D Echo data sets for visual analysis of segmental contractility and automatic strain analysis. In 2 (7.6%) patients SBP decreased below 90 mmHg but simple reduction in speed of infusion immediately elevated SBP up to 95 mmHg. In 1 patient drop in SBP was accompanied by appearance of a–v block 2 degree; this conduction disorder was transient and disappeared with increase of SBP. No major complications were registered at all. Visual assessment of LV contractility during ATP stress-test has revealed the expansion of existing hypokinetic zones and the appearance of new ones in 11 patients (42.3%). Application of AFI technology has led to the identification of appearance of new areas of myocardial deformation disturbances in 21 patients (80.7%; $P=0.0044$).

CONCLUSIONS (1) New algorithm of ATP infusion during stress-Echo with a step-by-step increase in the dosage of vasodilator in cases of inadequate myocardial hyperemia was developed. New algorithm is safety and well-tolerated by patients. (2) LV myocardial segments with hidden ischemia can be determined 1.9 times more often using 4D AFI technology with longitudinal strain analysis than traditional technology of myocardial contractility visual assessment.

GW30-e0617

The relation between low expression of FFAR2 in peripheral blood and early diagnosis of acute myocardial infarction

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OBJECTIVES In order to search for molecular marker for diagnosis of acute myocardial infarction (AMI), the relation between FFAR2 gene and AMI is further analyzed in this study by expanding the sample size in accordance with earlier microarray results.

METHODS The leukocytes in peripheral venous blood of 113 patients with AMI and 94 patients with non-coronary artery disease are collected as case group and control group respectively. The relative mRNA expression level of FFAR2 gene is detected by real-time fluorescent quantitative PCR. The clinical data of patients with AMI and patients with non-coronary artery disease are analyzed and compared.

RESULTS The mRNA expression level of FFAR2 gene in peripheral blood shows that the relative mRNA expression level of FFAR2 gene in AMI group is 0.33 (0.04–1.08), while that in control group is 0.62 (0.07–1.86), indicating that there is a statistically significant difference between the two groups. The relative mRNA expression level of FFAR2 gene in peripheral blood of patients with AMI is significantly lower than that in control group, which is 0.53 of the latter. The clinical data of subjects indicate that there is no significant difference between the two groups in the gender, history of hypertension, smoking history, and the level of serum triglyceride, total cholesterol and low density lipoprotein cholesterol ($P>0.05$). However, compared with control group, the patients in AMI group are significantly older, $P<0.01$; the number of patients with type 2 diabetes is larger, $P=0.02$; the fasting blood glucose level is higher, $P<0.01$; the total number of leucocytes is higher, $P<0.01$; and the high density lipoprotein cholesterol level is lower, $P=0.03$. The mRNA expression level of FFAR2 gene has no correlation with age ($P=0.121$), type 2 diabetes ($P=0.836$), fasting blood glucose level ($P=0.339$) and total number of leucocytes ($P=0.502$), while it has a correlation with high density lipoprotein cholesterol level ($P<0.001$). The results of logistic regression analysis show that low expression of FFAR2 gene in peripheral blood is an AMI risk factor which is independent of age, total number of leucocytes, history of diabetes, fasting blood glucose level and high density lipoprotein cholesterol level ($P=0.025$). Compared with high expression of FFAR2, the risk of AMI in low FFAR2 gene expression group

is increased by 6.308 times; high number of leucocytes is an AMI independent risk factor (P=0.014), which increases the AMI risk by 14.316 times; high fasting blood glucose level is also an AMI independent risk factor (P=0.008), which increases the AMI risk by 3.132 times.

CONCLUSIONS The expression level of FFAR2 gene in peripheral blood of patients with AMI is significantly lower than that in control group. Low expression of FFAR2 gene in peripheral blood is an AMI independent risk factor, which may be used as a potential biomarker for predicting the occurrence risk of AMI.

GW30-e0622

The comparison of drug-coated balloon and everolimus-eluting stents in patients with in-stent restenosis: A pair-wise meta-analysis of randomized trials

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OBJECTIVES The efficiency and safety of Drug-coated balloons (DCB) and everolimus-eluting stents (EES) is still unknown for the treatment of in-stent restenosis (ISR). The present pair-wise meta-analysis was to compare DCB with EES for the treatment of ISR.

METHODS A systematic literature search was conducted using the online databases PubMed and EMBASE to identify all relevant studies. Angiographic results and clinical events were separately assessed. Risk ratio (RR) and mean difference (MD) with the 95% confidence interval (CI) were calculated as the effect size for endpoints with categorical and continuous data, respectively. Subgroup meta-analyses were performed according to the type of restenosed stent.

RESULTS Six randomized trials with 1134 patients were included. The overall pooled outcomes indicated that DCB was associated with lower minimum lumen diameter (MD=–0.17, 95% CI=–0.29 to –0.05, P=0.006) and higher target lesion revascularization (RR=2.38, 95% CI=1.36 to 4.18, P=0.002) compared with EES. But subgroup meta-analyses showed DCB was inferior to EES only in patients with DES-ISR, with lower minimum lumen diameter (MD=–0.25, 95% CI=–0.37 to –0.14, P<0.001), higher percent diameter stenosis (MD=5.37, 95% CI=1.33 to 9.42, P=0.009), more binary restenosis (RR=2.01, 95% CI=1.16 to 3.49, P=0.01) and higher incidence of TVR (RR=2.01, 95% CI=1.19 to 3.41, P=0.009) and TLR (RR=2.37, 95% CI=1.24 to 4.52, P=0.009). There were no differences between DCB and EES in patients with BMS-ISR on angiographic results and clinical events.

CONCLUSIONS In patients with DES-ISR, DCB was inferior to EES on angiographic results and clinical events. But for BMS-ISR, the two strategies were comparable. More high-quality randomized trials was needed to further evaluate the role of DCB for the treatment of ISR, especially in patients with DES-ISR. The potential mechanisms of the different efficacy between BMS-ISR and DES-ISR for DCB were also necessary to be explored in the future.

GW30-e0623

Clinical nomogram to predict major adverse cardiac events within one year in acute myocardial infarction patients after percutaneous coronary intervention

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OBJECTIVES The aims of this study was to summarize the clinical characteristics and risk factors of acute myocardial infarction (AMI) patients treated with percutaneous coronary intervention (PCI) developing major adverse cardiovascular events (MACEs) within 1 year. We then build a nomogram and confirmed its utilities using decision curve analysis (DCA).

METHODS One hundred and three AMI subjects (cases) who underwent PCI experienced MACEs within 1 year of their index admission were included in this retrospective study. Cases were matched for age, sex and presentation with 225 controls who did not have MACEs. An analysis was performed to investigate the clinical characteristics and risk factors for MACEs in AMI patients and to subsequently develop a nomogram for MACEs based on multivariate logistic regression. C-index, calibration curves, and DCA were conducted to validate the model.

RESULTS After uni- and multivariate analysis, a nomogram was built based on age, low-density-lipoprotein (LDL)-cholesterol, lipoprotein (a) (Lp(a)), left ventricular ejection fraction (LVEF), serum brain natriuretic peptide (BNP), syntax score, and serum bile acid level. A C-index of 0.819 and the calibration curve demonstrated good concordance. Decision curve analysis demonstrated satisfactory positive net benefits.

CONCLUSIONS The proposed nomogram resulted in more-accurate prognostic prediction for 1-year MACEs in AMI patients treated with PCI. To ensure generalizability, this model needs to be externally validated.

GW30-e0625

Increased serum bile acid level is associated with high-risk coronary artery plaques in an asymptomatic population detected by coronary computed tomography angiography

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OBJECTIVES Bile acid metabolism is reported to be associated with cardiovascular diseases. It is unknown whether serum bile acid level is associated with atherosclerotic plaque. We investigated whether elevated serum bile acid level predict coronary high risk plaque in asymptomatic populations as detected by coronary CT angiography (CTA).

METHODS A total of 194 patients who have suspected coronary artery disease (CAD) and underwent coronary CTA were retrospectively reviewed. Serum bile acid level was quantified by enzyme-linked immunosorbent assay (ELISA). The predictive value of serum bile acid for high risk plaque was determined using multivariate logistic regression model and receiver-operating characteristic (ROC) curves.

RESULTS Serum bile acid level was significantly higher in patients with high risk plaque than in controls (6.18; interquartile range [IQR] 5.29–7.30) vs. 3.16; IQR 2.18–4.01) umol/L, P<0.001). Multivariate regression revealed that serum total bile acid level (OR=6.854, 95% CI: 3.948–11.901, P<0.001) and body mass index (BMI) (OR=1.941, 95% CI: 1.055–3.569, P=0.033) were independently associated with occurrence of high-risk coronary plaque. After adjustment for potential confounding factors, subgroup with high serum total bile acid level was more likely to have high-risk coronary plaque than low bile acid level at multivariate analysis (P for trend <0.001). The area under receiver operating characteristic (ROC) curve for serum total bile acid level was 0.876, with a sensitivity of 87.13% and a specificity of 86.02% for high-risk coronary plaque patients.

CONCLUSIONS We concluded that high level of serum total bile acid appeared to be an independent predictor for the high-risk coronary plaque.

GW30-e0651

Old age is associated with higher risk of short-term bleeding in men who received DAPT post of acute coronary syndromes

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OBJECTIVES Dual antiplatelet therapy (DAPT) with aspirin and a P2Y12 receptor antagonist has been shown to increase the risk of bleeding. It is reported that age and sex are risk factors of long-term outcomes of DAPT-related bleeding. However, whether age and sex affect the short-term bleeding outcomes of DAPT is unclear.

METHODS A total of 3853 subjects were enrolled in the study of the patients who received DAPT after ACS events in the 3rd Xiangya Hospital between April 2007 and July 2017, including 281 patients with bleeding (bleeding group) and 3572 patients without bleeding (nonbleeding group). Bleeding was defined by Thrombolysis In Myocardial Infarction (TIMI) standards and included all four types of non-CABG-related bleeding during hospitalization which equal or less than 30 days. Multivariate regressions were performed to determine age's association with DAPT-related bleeding.

RESULTS There were 2625 men and 1228 in the study. The rate of bleeding was the same in the two groups, 7.3% in men (191 patients occurred bleeding) and 7.3% in women (90 patients occurred bleeding). Old age was associated with increased bleeding outcomes in men (OR=1.778, 95% CI=1.323–2.390, P<0.001), while no difference was found in women (OR=1.446, 95% CI=0.907–2.305, P=0.121). And adjusted for the confounding factors, old age was still associated with increased bleeding outcomes in men (OR=1.712, 95% CI=1.076–2.723, P=0.023).

CONCLUSIONS Old age is associated with increased short-term bleeding events in men who received DAPT post of acute coronary syndromes (ACSs).

GW30-e0675

Coronary injuries triggering acute coronary syndrome was caused by violent collision between antegrade and retrograde coronary flow

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OBJECTIVES Coronary injuries are hypothesized to be caused by the cavitation phenomenon (explosion of air bubbles) which is seen frequently in

domestic or industrial pipes. Following hydraulics principle, with distal negative suctioning in diastole, if the coronary dynamic pressure decreases below the vapor pressure (VP) most likely of nitrogen in the blood, bubbles will form. They explode when the coronary dynamic pressure recovers > the VP during systole. These explosions create jet waves weakening and rupturing the cap of the plaque, triggering acute coronary syndrome (ACS). How could these events be located, recorded and tabulated?

METHODS Angiograms with ACS culprit lesions were selected. The left coronary arteries were recorded in the right anterior oblique caudal view and the right coronary artery in the left anterior oblique view (at 15 frames per second). Then the angiograms were viewed off line frame by frame. The first frame was the angiogram of an artery completely filled with contrast. The following frames showed the blood moving in, seen in white. The flow could be LAMINAR, TURBULENT (mixing of blood in white and contrast in black) or RETROGRADE (black column traveling backward). The turbulent flow reflects the collision between antegrade and retrograde flow. The LOCATION and the length in TIME of laminar, retrograde and mainly turbulent flow were recorded. The intensity of turbulent flow was measured by (1) the length of coronary segment with mixing contrast and blood (2) the length of the stagnant retrograde flow.

RESULTS The results of 50 angiograms with ACS showed that after being laminar (85%) at the beginning of diastole, the flow became turbulent with diffuse mixing of black (contrast) and white (blood) at the MID SEGMENT of the LAD, LCX or RCA. This observation matched with the location of 82% of ruptured plaques. The length of the time of retrograde flow lasted more than 30 frames encompassing 2 systoles.

CONCLUSIONS This is the first time, the matching of location of ruptured plaques and turbulent flow representing the collision between antegrade flow in diastole and retrograde flow in systole was confirmed. These results may help to find the precise measures preventing ACS.

GW30-e0703

CD137 aggravates myocardial ischemia-reperfusion injury through activating the NLRP3 inflammasome and promoting pyroptosis

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OBJECTIVES Myocardial ischemia-reperfusion injury (IRI) after acute myocardial infraction (AMI) is a major cause of worldwide mortality. Various studies have demonstrated that CD137 (4-1BB) promotes atherosclerosis and vascular inflammation via interactions with CD137 ligand (CD137L). However, the exact role of CD137 in myocardial ischemia reperfusion injury remains unknow. In this study, we used a murine model of acute myocardial ischemia reperfusion injury to examine whether the interactions of costimulatory receptor CD137 and its ligand (CD137L) are involved in the early phase of acute myocardial inflammation caused by IRI.

METHODS Myocardial ischemia reperfusion injury murine model was induced with 30 min of left anterior descending (LAD) occlusion followed by 4 h of reperfusion. We analyzed the changes of CD137 expression on heart in the mouse I/R model, as well as alternation of cardiac function, infract size and myocardial inflammatory status after activation or inhibition of the CD137/CD137L pathway using CD137L-Fc or anti-CD137L Monoclonal Antibody. Infract size was detected by Evans Blue and triphenyl tetrazolium chloride (TTC) staining while CCK8 assay was used to analyze the pyroptosis in heart. Meanwhile, the levels of aspartate transaminase (AST), creatine phosphokinase-isoenzyme (CKMB) and lactate dehydrogenase (LDH) in serum were used to analyze the cardiac function. Moreover, the contents of interleukin-1β (IL-1β), interleukin-18 (IL-18) and tumor necrosis factor (TNF-α) were used to analyze the myocardial inflammatory status. Besides, the HL-1 cells were stimulated with H/R protocol in the presence or absence of CD137L-Fc to find the changes of apoptosis-associated speck-like protein containing CARD (ASC), Caspase-1 and NLRP3 inflammasome while the Tunel and CCK8 assay were used to analyze the cardiomyocytes pyroptosis.

RESULTS Firstly, we found that I/R mice showed elevated expression of CD137 in heart tissue during the early phase of acute myocardial inflammation. Remarkably, blockade of the CD137/CD137L pathway ameliorated the myocardial I/R injury and cardiomyocyte H/R as evidenced by Evans blue and TTC staining and CCK8 assay respectively. Secondly, injection of CD137-Fc into I/R mice was founded to increase the level of AST, CKMB and LDH in serum as well as the contents of IL-1β, IL-18 and TNF-α in serum of mice and supernatant of HL-1 cells were increased. In addition, blockade of CD137 signaling remarkably downregulated the expression of toll-like receptor 4 (TLR4) and nuclear factor kappa B (NF-kB). Interestingly, we also found that blockade of CD137 signaling inhibited the upregulations of inflammasome components, such as NLRP3, ASC and Caspase-1 in I/R-induced mice and I/R-induced HL-1 cells with the use of western blot and RT-PCR. In vitro, we also found that blockade of CD137 signaling inhibited inflammasome activation in macrophages, cardiomyocytes, and cardiac fibroblasts via TLR4 and NF-kB signaling.

CONCLUSIONS Our findings indicate that enhanced CD137 costimulation occurs in the early phase of acute myocardial inflammation caused by IRI and promotes the activation of NLRP3 inflammasome, which in turn upregulates cardiac inflammatory response. The CD137 signaling pathway in cardiomyocytes therefore may represent a new target for blocking the initial stage of inflammatory diseases like myocardial IRI.

GW30-e0720

Predictors of different treatment measures in patients with ST-segment elevation myocardial infarction caused by plaque erosion: an one-year follow-up research

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OBJECTIVES ST-segment elevation myocardial infarction (STEMI) is one of the most significant emergency types of acute coronary syndrome (ACS). Stent implantation was the most widely accepted treatment measure in ACS. Three underlying mechanisms for ACS include plaque rupture, plaque erosion, and calcified nodule. Although plaque rupture is the most common cause (60%) of ACS, plaque erosion is responsible for 22–44% of patients. However, at one-year follow-up, partly of the patients with conservative treatment implanted stents in the infarct related arteries. In this study, we retrospectively analysed the baseline clinical and imaging angiography and optical coherence tomography (OCT) data to access which factors may contributed to this phenomenon.

METHODS We assessed plaque characteristics of plaque erosion by OCT in 212 STEMI undergoing emergency procedures and 88 patients were excluded in this research for losing to follow-up. Stent were Implanted in 47 patients immediately, and 77 patients were enrolled in this research finally. All the patients were divided into two groups according to the stent implantation or not: stent implantation (SI) and no stent implantation (nSI).

RESULTS Baseline clinical data didn't show significant difference among two groups expect for the diabetes mellitus. The patients with diabetes mellitus appeared more frequency in SI compared with nSI (25 vs. 3.8%, P=0.01). And the diameter stenosis was similar (65 [41–83] vs. 60% [23%–82%], P=0.259) between SI and nSI. OCT results revealed that the minimum fibrous cap thickness was thinner in SI compared with nSI (50 μm [20 μm–190 μm] vs. 70 μm [20 μm–280 μm], P=0.008). SI had a higher prevalence of thin-cap fibroatheroma (TCFA) (54.2 vs. 26.4%, P=0.018), macrophage accumulation (75.0 vs. 37.7%, P=0.002) and intimal vasculature (41.7 vs. 20.8%, P=0.056) in the culprit lesion compared with nSI.

CONCLUSIONS Despite some studies showed conservative treatment with anti-thrombotic therapy without stenting may be an option for patients with STEMI caused by plaque erosion, the diabetes mellitus and plaque vulnerability were also needed full consideration before selection of treatment strategy.

GW30-e0737

Impact of angiotensin-converting enzyme inhibitors or receptor blockers on long-term mortality in patients with coronary artery disease and contrast-induced nephropathy after angiography

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OBJECTIVES Angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) are widely prescribed drugs for patients with coronary artery disease (CAD), despite their nephrotoxicity in acute setting. It is recommended by the guidelines that ACEI/ARB treatment should be discontinued if serum creatinine (SCr) increase by 30% or more after initiation. However, there is no data on whether patients with CAD and contrast-induced nephropathy (CIN) after angiography should be prescribed ACEI/ARB at discharge. Therefore, we aim to explore the association between prescription of ACEI/ARB at discharge and long-term mortality in patients with CAD and CIN after angiography.

METHODS This prospective observational study included consecutive patients with confirmed CAD and CIN after angiography. CIN was defined as a >25% or 0.5 mg/dL increase in SCr from baseline during the first 48 to 72 hours after contrast exposure. The endpoint was all-cause mortality. Comparison of mortality between groups were conducted, and survival analysis and multivariable cox proportional hazards regression analysis were performed to identify the association between ACEI/ARB and long-term mortality.

RESULTS Overall, 349 patients were divided into ACEI/ARB group (n=312) and non-ACEI/ARB group (n=37). During the mean follow-up of 7.16±1.50 years, mortality was 18.27% (n=57) in ACEI/ARB group and 21.62% (n=8) in non-ACEI/ARB group, respectively. Multivariable cox proportional hazards regression

analyses showed that the prescription of ACEI/ARB at discharge was not associated with long-term mortality HR of 1.02 (95% CI: 0.40–2.56). Survival analyses revealed no difference in long-term mortality between groups (P=0.97).

CONCLUSIONS The ACEI/ARB may not be associated with long-term mortality in patients with CAD and CIN after angiography.

GW30-e0753

Cross-sectional survey of β-blockers usage in hospitalized patients with acute coronary syndrome and stable angina pectoris in China: the COE project

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OBJECTIVES The Coronary artery disease Optimal clinical therapeutic regimen Experience (COE) project aims to improve the understanding and clinical practice of Chinese clinicians on standardized treatment of coronary artery disease (CAD). The present cross-sectional survey was conducted on the application of β-blockers (BB) in hospitalized patients with acute coronary syndrome (ACS) or stable angina pectoris in order to understand the current status of BB use in ACS and stable CAD (SCAD) by cardiovascular specialists in China and to improve patient prognosis.

METHODS The study data are from the COE project, conducted between 11/2017 and 05/2018 in 67 hospitals from 24 cities in China. The frequency of BB use and initial dose within 24 h after admission, transition rate to sustained-release dosage forms, dose titration, patient clinical condition during hospitalization, BB prescription at discharge, and safety of BB were examined in hospitalized patients with ACS or SCAD. The 2013 ACCF/AHA Guideline for the Management of ST-elevation myocardial infarction (STEMI) and 2015 CSC/CMA Guideline for diagnosis and treatment of STEMI were used as references for analysis.

RESULTS There were 13,375 patients with ACS or SCAD, including 1854 with STEMI (14%), 3520 with non-STEMI (NSTEMI; 26%), 3398 with unstable angina (UA; 25%) and 460 with SCAD. The frequency of regular BB use before hospitalization was 17.0%. A total of 12,761 (95.4%) patients received BB within 24 h of admission, with metoprolol tartrate (84.5%) as the most commonly used of all BBs. The overall transition rate of metoprolol tartrate to metoprolol succinate was 68.3% in all patients, with a relatively low rate of 37.0% in patients with SCAD. The heart rates at admission and discharge were 83.9±14.6 vs. 70.7±8.6 bpm for STEMI, 85±16.5 vs. 72.6±11.7 bpm for NSTEMI, 79.9±13.9 vs. 69.9±8.7 bpm for UA, and 81.3±15.1 vs. 71.8±9.5 bpm for SCAD (all P<0.05); the systolic blood pressure were 139.5±20.0 vs. 125.2±13.1 mmHg for STEMI, 139.4±19.7 vs. 124.6±14.1 mmHg for NSTEMI, 140.5±19.6 vs. 127.6±13.4 mmHg for UA, and 138.7±21.2 vs. 126.7±15.3 for mmHg SCAD. The frequencies of BB use at discharge was 35.0, 16.8, 24.9 and 18.9% for STEMI, NSTEMI and UA and SCAD, respectively. At discharge, a total of 39 (1.0%) patients received the target dose of ≥190 mg/day metoprolol and 4419 (33.0%) patients received a high dose of ≥95 mg/day. During hospitalization, 7425 (55.5%) patients had no dose adjustment, 4438 (33.2%) had one dose adjustment, 1076 (8.0%) had two, and 436 (3.3%) had three. A total of 396 (3.0%) events were reported: one patient died, 41 (0.3%) had resting heart rate <45 bpm, 261 (2.0%) had systolic pressure <100 mmHg, 15 (0.1%) had atrioventricular block, 53 (0.4%) had unstable decompensated heart failure, and 26 (0.2%) had cardiogenic shock.

CONCLUSIONS The present study suggests that, despite an adequate initial BB use, the dose form transition rate, time of dose titration and the maintenance dose of BB at discharge were low for hospitalized patients with ACS and SCAD in China. Compared with developed western countries, the BB use in CAD has room for improvement. It is necessary to strengthen the education of Chinese cardiovascular specialists on the application of BB, to gradually narrow the gap between the present situation and the recommended standard by the Chinese and international guidelines and ultimately to improve patient prognosis.

GW30-e0816

Coronary artery dissection: revascularization versus conservative therapy: an analysis of national inpatient sample

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OBJECTIVES Coronary artery dissection is a nonatherosclerotic acute coronary syndrome for which optimal management remains controversial. Our study aimed to compare the inpatient outcomes in coronary artery dissection treated with conservative therapy vs. revascularization (including interventional and surgical).

METHODS We conducted a retrospective cohort analysis of the National Inpatient Sample (HCUP-NIS) 2016 database. Patients hospitalized with a major diagnosis of coronary artery dissection were identified using the ICD-10 codes. Multivariate logistic regression was performed after adjust for patient baseline characteristics, hospital demographics and relevant comorbidities. Inpatient mortality and length of hospital stay (LOS) were compared between the patients who received conservative management and revascularization.

RESULTS A total of 7475 hospitalizations with coronary artery dissection were identified. Of these, 2065 (27.63%) received conservative therapy and 5410 (72.37%) received revascularization. Multivariate logistic regression analysis after adjustment showed that there was no significant difference in in-hospital mortality (conservative 3.16 vs. revascularization 6.96%, OR 95% CI 0.71–3.25, P=0.282) or LOS (5.23 vs. 5.63 days, P=0.717) between the two groups. Further analysis of the revascularization subgroups revealed that 4705 (86.97%) patients received interventional (PCI/PTCA) and 705 (13.03%) patients received surgical revascularization (CABG). Strategies of revascularization had no impact on inpatient mortality (OR 95% CI 0.36–1.32, P=0.263). However, patients who received interventional therapy had shorter LOS compared to those who received CABG (4.96 vs. 10.14 days, P<0.001). Furthermore, patients with cardiogenic shock (OR 3.48, P><0.001), respiratory failure (OR 2.19, P><0.001), or acute kidney failure (OR 1.86, P=0.001) were more likely to receive revascularization.

CONCLUSIONS Methods of treatment (conservative therapy vs. revascularization) and strategies of revascularization (PCI/PTCA vs. CABG) had no impact on inpatient mortality in coronary artery dissection patients.

GW30-e0843

The impact of thrombolysis in patients with STEMI and high thrombus burden in the PCI era

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OBJECTIVES Usage of fibrinolytic therapy is suggested in patients with ST-elevation myocardial infarction (STEMI) upon which a primary percutaneous coronary intervention (PCI) cannot be performed on time or at all. Despite this, the treatment procedure for patients with a high thrombus burden who cannot achieve patency of the infarct-related artery through a primary PCI is not yet clear. In this study, we planned to evaluate the clinical and angiographic findings of patients with a heavy thrombus burden who were firstly given fibrinolytic therapy instead of PCI and according to the findings of the following angiography were performed PCI or not.

METHODS Total of 65 consecutive patients with STEMI, who applied at the emergency room and were subjected to fibrinolytic therapy following heavy thrombus burden detection in coronary angiography, were included in this study. Tissue plasminogen activator (t-PA) was used as a fibrinolytic agent. The fibrinolytic therapy was followed by a control coronary angiography. According to the obstruction degree of the artery affected by the infarction, a PCI procedure was performed. The patients were investigated concerning patency rates for the affected artery, 30-day mortality rates and bleeding-related complications.

RESULTS A total of 65 patients, of which 58 males (89.2%) and seven females (10.8%) were included in the study. The mean age was 56±11. 52 patients (80%) who were subjected to this kind of therapy had a TIMI 3-grade flow at the end of it. The angiographic blood vessel patency rate was 84.6%. The in-hospital mortality rate was found to be 7.7% (5 patients). One of these patients had intracranial bleeding while the others had complications related to the myocardial infarction. Another patient had GI bleeding that required a blood transfusion.

CONCLUSIONS Providing coronary patency through a PCI in STEMI patients with a heavy thrombus burden is a procedure that implies a certain amount of difficulty for the operator. Our study shows that patients presenting with a heavy thrombus burden can also be treated by using fibrinolytic therapy. By lightening the thrombus burden through this procedure, a better angiographic result and a TIMI 3 (Thrombolysis in Myocardial Infarction) grade flow can be obtained while avoiding the development of adverse events.

GW30-e0899

Admission routine clinical parameters improves GRACE scores prediction of long-term MACE events and mortality in myocardial infarction patients with arrhythmia

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OBJECTIVES We sought several parameters on admission to develop the GRACE scoring system for predicting long-term the composite endpoint of all-cause mortality and MACE events for MI patients with arrhythmia.

METHODS A total of 2150 patients treated for MI between 2014 and 2018 were included. Patients were classified into groups according to the new-onset atrial fibrillation (NOAF) or not. We applied multivariate logistic regression model

to select the independent predictors that were added to the GRACE scores to additive prognostic value significantly. The prognostic performance were evaluated by receiver operating characteristic, net reclassification improvement (NRI), and integrated discrimination improvement (IDI).

RESULTS At 3 years follow-up 376 (17.5%) reach the composite endpoint: 274 (14.3%) with Non-NOAF and 102 (44.5%) with NOAF. Eight variables were included in the multivariate logistic regression model: NOAF, Hyperlipidemia, Prior stroke, GRACE scores, hemoglobin (HBA1C), eGFR, left ventricular systolic ejection fraction (LVESD), left ventricular ejection fraction (LVEF). Area under the curve (ROC) of predicting long-term MACE events increased significantly in the extended GRACE score model comparing GRACE score only in both groups. (0.719 vs. 0.798; Z=–6.4085, P<0.001). Furthermore, NRI and IDI improved by new model. (NRI 0.231, 95% CI 0.105 to 0.357, P<0.001; IDI 0.157, 95% CI 0.107–0.207, P<0.001). Though, the AUC of predicting long-term mortality was not be improved in MI patients with NOAF (0.728 vs. 0.773, Z=–1.6779, P=0.093), NRI and IDI were increased significantly. (NRI 0.345, 95% CI 0.150–0.540, P<0.001; IDI 0.122, 95% CI 0.064–0.181, P=0.027).

CONCLUSIONS The several parameters at admission are possible indicators to increase the ability of the GRACE score for detecting MI patients with arrhythmia at high risk for long-term MACE events or mortality.

GW30-e0930

LOW expression of G0S2 gene in peripheral blood may be used as a molecular marker to assess the risk of acute myocardial infarction

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OBJECTIVES The study aimed to assess whether the expression of GoS2 gene in peripheral blood can be used as a biomarker to predict the risk of acute myocardial infarction, and to further investigate the role of GoS2 gene in acute myocardial infarction by analyzing the clinical data of the subjects.

METHODS In this study, 92 patients with acute myocardial infarction (AMI) were enrolled in the case group, and 75 patients with coronary heart disease were enrolled in the control group. The diagnosis of both groups was confirmed by coronary angiography. Clinical data of the two groups were analyzed and compared. Peripheral venous blood was collected, and real-time fluorescence quantitative PCR was adopted to detect the expression level of GoS2 gene mRNA in peripheral blood.

RESULTS After analyzing the relative expression level of GoS2 gene mRNA between patients with acute myocardial infarction and patients with coronary heart disease, the result showed that there was a significant difference in the relative expression level of GoS2 gene mRNA in peripheral blood of AMI patients. The relative expression level of GoS2 gene mRNA in peripheral blood of AMI patients was significantly lower than that of the control group, and its relative expression level was 0.413 times that of the patients with coronary heart disease.

The clinical data analysis results of the study objects indicated that there was no significant difference between the two groups in terms of age, smoking history, triglyceride level, total cholesterol level, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, hypertension diagnosis, type-II diabetes diagnosis.

Further analysis of the clinical data and the expression level of the GoS2 gene suggested that the relative expression level of GoS2 gene mRNA was independent of age (P=0.872), triglyceride level (P=0.525), total cholesterol level (P=0.997), high-density lipoprotein cholesterol level (P=0.823), and low density lipoprotein cholesterol level (P=0.542).

The binary Logistic regression analysis showed that the low expression level of the GoS2 gene was an independent risk factor for the development of coronary heart disease towards acute myocardial infarction. Compared with the group with a high level of GoS2 expression, the group with low expression had a 2.098-fold increased risk in developing AMI.

CONCLUSIONS The expression level of the GoS2 gene is significantly lower in the peripheral blood of patients with acute myocardial infarction, and it is an independent risk factor for acute myocardial infarction. The GoS2 gene could be used as a genetic marker to assess the risk of acute myocardial infarction.

GW30-e0934

Comparison of diabetic versus non-diabetic on the characteristics of coronary culprit lesions in patients with coronary artery disease: optical coherence tomography (OCT) findings

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OBJECTIVES Diabetes mellitus has been acknowledged as a prominent risk factor for coronary artery disease (CAD) and characterized by poor prognosis, which may be due to atherosclerotic plaque characteristics. However, in vivo data are lacking. Optical coherence tomography (OCT) is an intravascular imaging modality that could qualitatively and quantitatively evaluate fibrous cap thickness (FCT), maximum lipid arc and the appearance of microphage. We assessed atherosclerotic plaque characteristics by OCT imaging in coronary heart disease patients with Diabetes mellitus compared with a sex- and age-matched control group. The present study aimed to investigate the effect of diabetes mellitus on the changes of characteristics of coronary culprit lesions measured by OCT.

METHODS We randomly recruited 211 patients with symptomatic or asymptomatic coronary artery disease and objective evidence of myocardial ischaemia who underwent OCT images during coronary angiography (CAG). Patients with incomplete clinical histories or laboratory data were excluded. We divided the population into two groups: One group is DM group (n=45, patients with diabetes) and another group is NDM group (n=166, patients without diabetes). OCT was used to assess FCT, maximum lipid arc and the appearance of microphage of the two groups respectively. FCT of lipid plaque was measured at its thinnest part 3 times, and the average value was calculated. Lipid arc was measured on the cross-section with largest lipid pool. Macrophage accumulation on the OCT images was defined as increased signal intensity within the plaque, accompanied by heterogeneous backward shadows. All OCT images were analyzed using the previously validated criteria for plaque characterization and were then compared between DM and NDM groups. Statistical methods were used to assess the relationship between diabetes mellitus and coronary plaque characteristics.

RESULTS The mean age of the patients was 56.8±10.7, 162 (76.8%) were male. Patients with diabetes showed lower frequency of thrombus (86.7 vs. 95.8%, P=0.024) when compared with NDM group. The maximum lipid arc was comparable in DM group compared with NDM group (322.9±55.5°vs. 293.7±66.2°, P=0.019). However, there is no evident difference of fibrous cap thickness (FCT) between the two groups (54.0±26.0 μm vs. 57.4±28.5 μm, P=0.528). Likewise, no significant distinction in the appearance of microphage can be seen in both groups (91.1 vs. 86.6%, P=0.415).

CONCLUSIONS Diabetes mellitus can affect the maximum lipid arc and the formation of thrombus, but has no significant effect on FCT and the appearance of microphage. Clinically, diabetes and thrombosis may not have a direct relationship, because the impact of diabetes mellitus on atherosclerosis was affected by many factors. Furthermore, in the present study, the small sample size may not objectively reflect the experimental results, which need to be verified in a research with a lot of samples. We cannot determine the occurrence and the treatment of thrombosis based solely on whether we have diabetes or not. However, our research results still provide significant evidence for the diagnosis and treatment of vulnerable plaques in patients with diabetes mellitus complicated with coronary heart disease.

GW30-e0940

Compound of toxicity-removing and blood-activating Chinese herbal medicine treating unstable angina pectoris: a clinical trial

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OBJECTIVES Modern Chinese medical studies indicate that blood stasis caused toxicity is the key pathogenesis of unstable angina pectoris. The combination of traditional Chinese medicine components of toxicity-removing and blood-activating can play an effective role in treating unstable angina pectoris by regulating the balance between pro-inflammatory and anti-inflammatory networks. The purpose of this study is to observe the efficacy of traditional Chinese herbal medicine polygonum cuspidatum and hawthorn for the intervention of unstable angina pectoris with syndrome of toxin and blood stasis, and to explain its mechanism by observing the change of pro and anti-inflammatory network in patients, so as to provide evidence for clinical application.

METHODS Sixty participants with unstable angina pectoris were randomly divided into control group and intervention group. Control group was given conventional basis western medicine treatment, while intervention group was given in addition to conventional basic western medicine treatment with Chinese medical formula of granule polygonum cuspidatum and hawthorn. Each dose of traditional Chinese medicine formula contains 15 g of polygonum cuspidatum and 10 g of hawthorn. Participants were directed to take one dose per day in a course of treatment for 4 weeks. Before and after the treatment, the participants' symptoms were evaluated by scale, and their serum pro-inflammatory factors including Hs-CRP, TNF-alpha, IL-6 and anti-inflammatory factors IL-10 and adiponectin were examined. And the ration of pro-inflammatory factors to anti-inflammatory factors was calculated to observe the difference between the two groups before and after treatment.

RESULTS Compared with the control group, the angina pectoris score, TCM syndrome score, Seattle angina questionnaire score and SF-36 score were significantly improved in intervention group (P<0.05). After treatment, TNF-alpha decreased significantly in both groups (P<0.01). In the intervention group, it was observed that Hs-CRP decreased while IL-10 increased after treatment

(P<0.05), and the serum adiponectin level was much higher than that in the control group (P<0.01). The ratio of pro-inflammatory and anti-inflammatory factors in the two groups are both changed to different degrees after the treatment. Compared with the control group, the IL-6/adiponectin ratio in the intervention group decreased (P<0.05), while the Hs-CRP/adiponectin ratio decreased significantly (P<0.01).

CONCLUSIONS The combination of traditional Chinese medicine components of toxicity-removing and blood-activating can play a therapeutic role in treating unstable angina pectoris by regulating pro-inflammatory/anti-inflammatory balance of patients.

GW30-e0945

Comparison of long-term outcomes of three therapeutic strategies in very elderly coronary artery disease patients with three-vessel disease

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OBJECTIVES The aim of the present study was to compare the long-term outcomes after three different therapeutic strategies for coronary artery disease patients aged ≥75 years with three-vessel disease (3VD).

METHODS A total of 711 coronary artery disease patients aged ≥75 years with 3VD were consecutively enrolled from April 2004 to February 2011 in Fuwai hospital. Patients were followed up for a median of 7.25 years, and were divided into PCI, CABG, or medical therapy (MT) groups according to the treatment they received. The primary endpoint was all-cause death, and the secondary endpoints included cardiac death and major adverse cardiac and cerebrovascular events (MACCE), a composite of death, myocardial infarction, stroke, and unplanned revascularization.

RESULTS Compared with MT group, patients in PCI and CABG group both had lower incidence of all-cause death and cardiac death (all P<0.05). Especially, CABG group also had lower rate of MACCE (41.1 vs. 53.0%, P=0.023) and higher rate of stroke (12.4 vs. 5.7%, P=0.018). Compared with PCI group, patients in CABG group had lower incidence of cardiac death (7.8 vs. 15.7%, P=0.026), myocardial infarction (1.6 vs. 6.3%, P=0.037) and unplanned revascularization (2.3 vs. 8.4%, P=0.020). Kaplan-Meier survival analysis showed similar results. After adjust for confounding factors using multivariate Cox regression analysis, CABG was independently associated with lower risk of cardiac death (HR 0.475, 95% CI: 0.232–0.974, P=0.042), myocardial infarction (HR 0.196, 95% CI: 0.043–0.892, P=0.035) and unplanned revascularization (HR 0.279, 95% CI: 0.079–0.982, P=0.047) compared with PCI group, while MT group was independently associated with higher risk of cardiac death (HR 1.636, 95% CI: 1.092–2.449, P=0.017) compared with PCI group. Subgroup analysis showed that there was a significant interaction between treatment strategy (PCI vs. CABG) and gender for MACCE (P=0.026).

CONCLUSIONS Among 3VD patients aged ≥75 years, patients undergoing PCI or CABG have lower incidence of long-term all-cause and cardiac death compared with patients receiving MT alone. Compared with PCI group, CABG is independently associated with lower risk of long-term cardiac death, myocardial infarction and unplanned revascularization, while MT group had higher risk of long-term cardiac death.

GW30-e0953

Study on balance of pro/anti-inflammatory factors in patients with unstable angina

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OBJECTIVES To observe the balance of pro/anti-inflammatory factors in patients with unstable angina.

METHODS Compared with stable angina and fifty cases of healthy people were included. The serum levels of pro-inflammatory and anti-inflammatory factors including hypertensive c-reactive protein (hs-CRP), tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), interleukin (IL-10) and adiponectin were examined. We calculated the ratio of pro-inflammatory and anti-inflammatory factors.

RESULTS Compared with the healthy group, the serum level of hs-CRP, TNF-α, IL-6, the ratios of pro-inflammatory and anti-inflammatory factors, such as hs-CRP/IL-10, TNF-α/IL-10, IL-6/IL-10, hs-CRP/adiponectin, TNF-α/adiponectin, IL-6/adiponectin, (TNF-α×hs-CRP×IL-6)/(IL-10×adiponectin) significantly elevated in unstable angina group (P is less than 0.05 or 0.01). Compared with the stable angina group. The ratios of pro-inflammatory and anti-inflammatory factors, such as TNF-α/IL-10, IL-6/IL-10 and TNF-α/adiponectin were significantly increased in unstable angina group (P is less than 0.05 or 0.01).

CONCLUSIONS The unstable angina patients have a higher level of pro-inflammatory factors, and a lower level of anti-inflammatory factors. The fluctuation of pro/anti-inflammatory factors is a potential indicator to the severity of coronary heart disease.

GW30-e0956

Studying aggregation activity of platelets in patients with acute myocardial infarction of young age

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OBJECTIVES The study of indicators of platelet aggregation activity in patients with young myocardial infarction.

METHODS Seventy-four patients with acute Q-wave myocardial infarction (AMI) were examined. The patients were divided into 2 groups: 38 young patients with AMI were 1 group and 36 patients with AMI over 60 were 2 group. Evaluated indicators of platelet aggregation activity. ADP was used as an inducer.

RESULTS Analysis of the obtained data showed that in patients of group I and in patients of group II, the initial indicators of platelet aggregation activity (AAT) were significantly higher than in healthy individuals –1.98±0.36 μmol ADP and 1.99±0.41 μmol ADP versus 4.78±0.22 μmol ADP in healthy individuals (P<0.001) and P><0.005). The rates of platelet aggregation (Vagr) in group I were 1.96±0.27 cm/min and group II was 1.83±0.41 cm/min versus 0.34±.5.5 cm/min in healthy individuals, respectively, P><0.001).

CONCLUSIONS The study of platelet aggregation ability depending on age revealed that the rates of aggregation were significantly higher in patients with AMI at a young age.

GW30-e0974

Persistent reversed flow and antegrade slow flow of the right coronary artery with anomalous origin from the left sinus are the mechanisms for chest pain and sudden death

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OBJECTIVES Patient with anomalous coronary origin, such as right coronary artery (RCA) originated from the left sinus, can have chest pain and sudden death. How to identify these patients in the prevention of ischemia and sudden death?

METHODS Patients with the RCA originated from the left sinus were selected. At first, they were interviewed for history of chest pain or no chest pain. Then they underwent bilateral coronary angiogram in order to confirm the origin of the RCA from the left sinus. CT coronary angiograms showing the origin of the RCA from the left sinus were also collected. During coronary angiograms, the left coronary arteries were recorded in the right anterior oblique caudal view and the RCA in the left anterior oblique view (at 15 frames per second). Then the angiograms were viewed off line frame by frame. The first frame was the angiogram of an artery completely filled with contrast. The following frames showed the blood moving in, seen in white. The flow could be LAMINAR, TURBULENT (mixing of blood in white and contrast in black) or ANTEGRADE or RETROGRADE (black column traveling backward). The antegrade flow reflected the normal supply of blood to the myocardium in diastole. The turbulent flow represented the collision between the antegrade and retrograde flow. The retrograde flow represented the flow in reversed direction due to contraction of the left ventricle in systole (Figure 1). The speed and the time of retention of contrast reflected the transit time of blood before it reached the myocardium. A slow speed and a prolonged period of retention increase the possibility of ischemia. The presence and time of persistent ejection of contrast from the ostium into the coronary sinus were evidence of persistent constriction of the proximal RCA squeezed between the aortic root and pulmonary artery (Figure 2).

RESULTS A total of 20 patients with the RCA anomalous origin from the left sinus and patent coronary arteries was selected. The results showed 90% of patient with chest pain had persistent reversed flow with ejection of contrast from the RCA to the right coronary sinus. In these patients, there were significant slow or no flow in the distal coronary segment lasting more than 8 seconds (120 frames) even the arteries were patent. There was also persistent reversed flow in the proximal coronary segment (>90%) and persistent ejection of contrast into the coronary sinus. These 3 above observations (No flow in distal, reversed flow in the proximal coronary arteries and ejection of contrast into the coronary sinus) were the mechanisms of ischemia in patients with RCA having its anomalous ostium originated from the left sinus.

CONCLUSIONS This technique is innovative in the diagnosis (or identification) of patients with possible sudden death due to anomalous origin of the artery crossing between the aorta and pulmonary artery.

GW30-e0978

Association between interleukin-12RB1 and interleukin-12RB2 polymorphisms and coronary heart disease in the Chinese Zhuang population: a case–control

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OBJECTIVES Inflammatory cytokines polymorphism plays an important role in the pathogenesis of cardiovascular disease. So far, few studies had investigated the association between interleukin-12RB1 (IL-12RB1) and interleukin-12RB2 (IL-12RB2) genetic variants and coronary heart disease (CHD). We sought to explore the association between IL-12RB1 and IL-12RB2 polymorphisms and CHD in Chinese Zhuang population.

METHODS Six hundred and twenty CHD patients and 705 age- and sex-frequency match controls were enrolled in our case-control study. Genotypes of the single nucleotide polymorphisms (SNPs) were examined by MassArray (Sequenom) in those subjects. The multivariate logistic regression model was used to evaluate the association between SNPs and CHD risk.

RESULTS Comparing with AA genotype of IL-12RB1 rs11575934, the individuals with GG genotype has 1.62 (95% CI: 1.02–4.12, P=0.042) increasing risk of CHD in Chinese Zhuang population, after adjusting for risk factors, those with GG genotype subjects still had a higher risk of CHD than AA genotype of rs11575934 (OR=1.39, 95% CI: 1.07–5.10, P=0.046). Another SNP of IL-12RB1 rs393548 and all SNPs of IL-12RB2 include rs375947, rs401502, rs3790567 and rs12131065 were not significantly associated with the risk of coronary heart disease.

CONCLUSIONS IL-12RB1 rs11575934 polymorphism was related to the risk of CHD in Chinese Zhuang population.

GW30-e0990

Three year follow-up of patients with left ventricular dysfunction causing ischemia and patent coronary arteries

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OBJECTIVES New onset of heart failure (HF) is an indication for investigation for coronary artery disease (CAD). In many cases, the angiogram results showed mild CAD with normal left ventricular (LV) function or mild to moderate LV dysfunction. Management was to continue medical treatment without percutaneous or surgical interventions. Whether CAD causes HF or HF causes ischemic changes on the EKG as well as the chest pain is not clear. Theoretically an elevation of the left ventricular (LV) end diastolic pressure (LVEDP) representing the systolic and diastolic dysfunction) might cause EKG changes suggestive of ischemia. The aim of this study was to clarify the mechanistic causes of new onset HF associated with ischemic EKG changes, chest pain in patients with patent or minimally diseased coronary arteries

METHODS In group A, 20 patients were consecutively selected using the following criteria: (1) history of new onset of HF on presentation to the emergency room, (2) having chest pain on the index admission, (3) EKG changes indicating ischemia (ST depression (Figure 1) or T wave inversion (Figure 2) and no ST segment elevation), AND (4) negative coronary angiogram. Group B (control) included 15 patients with patent coronary arteries and elevated LVEDP (chronic diastolic HF). The aortic systolic (AOS), aortic diastolic (AOD), aortic mean pressure (AOM), pulse pressure, and ejection fraction (EF) were recorded. CPP using the formula CPP=AOD-LVEDP was calculated in both groups.

RESULTS The results showed that both groups had a similar percentage of chest pain and SOB (P>0.05). All patients had a negative coronary angiogram. The majority of patients in group A had a higher LVEDP than the control group (B) (P<0.05). However, the AO Diastolic (AOD) pressure was lower in group A than in group B (P><0.05). In patients with elevated LVEDP and low AOD, with CPP><20 mmHg, the EKG changes (type 3) with deep T wave inversion were more frequently seen in more chest and limb leads (Figure 2). If the CPP was between 20–30 mmHg, the EKG changes were more of type 2 (mild ST depression) (P><0.5%). If the CPP>30 mmHg, there were normal EKG readings or only type 1 changes (P<0.05%). It was strongly suggested that CPP><20 mmHg was associated with chest pain and ischemia on the EKG. Once the elevated LVEDP was reduced to a lower level or when the OAD pressure improved (no more diastolic hypotension), the ST segment abnormalities improved.

CONCLUSIONS In patients with HF and EKG changes suggestive of ischemia, a lower AOD could aggravate ischemia in patients with elevated LVEDP. The reason is that the coronary perfusion pressure (CPP) is the difference between AOD and LVEDP; the CPP could then decrease and cause ischemia (due to low perfusion pressure) even though the coronary arteries are patent. As result, LV dysfunction could cause ischemia in selected patients, and could be the cause of death in patients with elevated LVEDP (e.g., CAD with LV dysfunction or aortic stenosis) undergoing PCI.

GW30-e0998

Computational fluid dynamic-derived wall shear stress of non-significant left main bifurcation disease may predict acute vessel thrombosis at 3-year follow-up

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OBJECTIVES Wall shear stress (WSS) plays a pivotal role on plaque progression in coronary artery bifurcation disease. Left main (LM) bifurcation is the most clinically relevant bifurcation in humans. To assess the prognostic role of baseline mean WSS in developing a bifurcation-located myocardial infarction (B-MI) over the following three years in angiographically non-significant LM bifurcation disease.

METHODS We reconstructed 32 LM bifurcation with an angiographically non-significant LM bifurcation disease based on the patient-specific geometries derived from the coronary computed tomography angiography (CCTA). A steady flow simulation using the patient-specific diastolic blood pressure assessed during the imaging acquisition was then carried out.

RESULTS Among 32 patients, (20 males, mean age 70.4±12.0 years old, 12 (37.5%) had a B-MI over the following three years after the CCTA; the remaining 20 subjects were used as controls. B-MI patients had a higher significant mean WSS values of the proximal stenotic segments (WSSprox) and of entire lesion (WSSentire—lesion) compared to controls. Both the mean WSSprox and the mean of WSSentire—lesion of each vessel, adjusted for the related mean lesions lengths and 3-dimensional percentage of stenosis (DS%) resulted independent predictors of 3-year B-MI. A mean WSSentire—model ≥5.05 Pa correlated with the risk of B-MI over 3-year follow-up Log-rank (Mantel-Cox analysis) P=0.001). The multivariate Cox-regression analysis confirmed that a baseline means WSSentire—model ≥5.05 Pa (HR 1.98, 95% CI 1.83–2.10, P=0.001) was a predictor of 3-year B-MI independently from the entire mean lesions lengths (HR 1.56. 95% CI 1.43.1.68, P=0.002) and DS% (HR 1.26, 95% CI 1.18–1.37, P=0.03).

CONCLUSIONS In patients with an angiographically non-significant LM 1,1,1 Medina disease, both the mean WSSprox and WSSentire—lesion of each stenotic vessel predicted B- over 3-year follow-up. Moreover, a WSSentire—bifurcation ≥5.05 Pa resulted MI a predictor of 3-year B-MI independently from the DS% and lesions lengths.

GW30-e1015

The expression and role of IL-25 in patients with acute aortic dissection

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OBJECTIVES Acute aortic dissection (AAD) is known as one of the most life-threatening diseases in cardiovascular system which has reported to be associated with inflammatory reaction. But little is known about interleukin (IL) 25 expression and roles in AAD. In present study, we detected levels of IL-25 in serum and aorta and attempted to reveal the potential relationships between inflammatory factor IL-25 and AAD.

METHODS The expression of IL-25 in aorta of AAD was simultaneously measured by immunofluorescence. In addition, we compared and analyzed serum levels of IL-25 in patients including hypertension patients excluded AAD (n=30, we named it NAD group) and AAD patients of Stanford A (n=45) and Stanford B (n=41) by the enzyme-linked immune sorbent assay (ELISA) kits. And the levels of IL-6 and TNF- were also evaluated in those serum samples.

RESULTS Analysis of tissue samples from aorta showed that IL-25 mainly located in macrophages and also up-regulated in tissues of AAD. Furthermore, compared with NAD group, levels of IL-25 in AAD serum were significantly increased. Moreover, both IL-6 and TNF- were markedly elevated in serum of AAD patients. Serum IL-25 levels were positively correlated with IL-6 and TNF- levels in AAD patients. Furthermore, IL-25 was correlated with the occurrence

of AAD which was identified by simple linear regression analysis and binary logistic regression analysis.

CONCLUSIONS Higher levels of IL-25 were found in serum and aorta of AAD patients, which suggested that IL-25 may associated with the occurrence and development of AAD.

GW30-e1017

Association between liver fibrosis score and the risk of mortality among patients with coronary artery disease

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OBJECTIVES Irreversible liver fibrosis in coronary artery disease (CAD) contribute to adverse progression. Whether baseline liver fibrosis scores (LFSs) provide predictive value for long-term mortality among CAD patients requires investigation.

METHODS The analysis was conducted based on a prospective cohort study among 3263 CAD patients, followed to the end of September, 2016. We used Cox models to assess the association of baseline LFSs, including non-alcoholic fatty liver disease fibrosis score (NFS), fibrosis 4 (FIB-4), aspartate aminotransferase to platelet ratio index (APRI), gamma-glutamyltransferase to platelet ratio (GPR) and Forns score, with the risk of all-cause and cardiovascular mortality among patients with CAD. All the LFSs were categorized into low, intermediate and high levels according to their originally developed cut-offs.

RESULTS During a median of 5.63 years follow-up, 357 deaths were identified, 230 of those were cardiovascular-related. Compared with patients in the lowest score levels, multivariable-adjusted hazard ratios (95% CI) for the highest levels of NFS, FIB-4, APRI, GPR and Forns score were 3.19 (2.20–4.64), 3.39 (2.35–4.88), 2.01 (1.43–2.82), 1.60 (1.22–2.09) and 3.34 (1.79–6.26) for all-cause mortality, and 3.74 (2.31–6.06), 3.63 (2.29–5.75), 2.05 (1.36–3.10), 1.86 (1.33–2.60), and 2.48 (1.15–5.35) for cardiovascular mortality, respectively. These associations were consistent when participants were stratified by sex, age (<65 vs. ≥65 years), type of CAD, diabetes status and BMI (<24 vs. ≥24 kg/m^2).

CONCLUSIONS Higher NFS, FIB-4, APRI, GPR and Forns score were associated with increased risks of all-cause and cardiovascular mortality among Chinese patients with CAD. These LFSs might play an important role on prognosis prediction in CAD patients.

GW30-e1018

A simple diagnostic protocol to assess the hemodynamic significance in intermediate coronary lesions: the value of combining visual estimation (VE) and quantitative coronary angiography (QCA)

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OBJECTIVES Angiographic evaluation remains the cornerstone for decision-making regarding revascularization and fractional flow reserve (FFR) is still underutilized in routine clinical care. Thus, we aimed to develop a simple, practical and angiography-based diagnostic protocol to discriminate the intermediate stenosis with functional ischemia.

METHODS Consecutive patients who underwent both invasive coronary angiography and lesion-specific FFR measurement were screened in this retrospective analysis. Percent diameter stenosis (%DS), percent area stenosis (%AS), lesion length (LL), and minimal lumen diameter (MLD) were calculated by the operator-independent software. The ratio of LL to the fourth power of MLD (LL/MLD^4), derived from the Poiseuille equation, was also assessed in the present study. The C statistics of VE and QCA, also known as area under the receiver-operating characteristic curves, were calculated and the Youden index was used to determine the optimal cut-off values. An FFR value ≤0.80 was considered to indicate the physiological significance of stenosis.

RESULTS In total, 351 patients with 366 lesions were included. The positive FFR results were identified in 71 lesions (19%) and the median of FFR values was 0.87. There was a significant but modest correlation between %DS and FFR in VE (ρ=–0.303; P<0.001) and QCA (ρ=–0.245; P<0.001). VE had a greater %DS than QCA with the mean difference (standard deviation) of 21.7% (9.7%). The best cutoff values for predicting FFR≤0.80 were >65% for VE, >48% for %DS by QCA, >73% for %AS, ≤1.66 mm for MLD, >13.53 mm for LL, and >2.42 mm^{-3} for LL/MLD^4. C statistic was revealed as 0.72 for VE, significantly greater than %DS by QCA (0.60; P=0.005), %AS (0.60; P=0.007) and LL (0.58; P=0.009) with comparable to MLD (0.67; P=0.328) and LL/MLD^4 (0.70; P=0.651). In our protocol, any positive of the two parameters (VE>65% or LL/MLD^4>2.42 mm^{-3}) is regarded as a positive result, requiring further FFR measurement. In contrast, the protocol is negative if the two parameters are all negative (VE≤65% and LL/MLD^4 ≤2.42 mm^{-3}). Compared with single variables including VE, %DS by QCA, %AS, LL, MLD, and LL/MLD^4, the protocol yielded a higher sensitivity (88.7%; 95% CI 79.0–95.0; P<0.001 for all) and negative predictive value (94.2%; 95% CI 88.8–97.5), but a lower specificity (43.7%; 95% CI 38.0–49.6; P<0.001 for all besides P=0.001 for LL).

CONCLUSIONS Overall, VE demonstrated a better diagnostic performance than %DS by QCA to predict physiological significance in borderline stenosis. This protocol could be a simple and easy-to-access screening tool to identify those high-risk lesions which need further FFR confirmation, improving risk stratification and clinical outcomes with limited resources.

GW30-e1023

Interleukin-5 levels are decreased in plasma of coronary artery disease patients and inhibits Th1 and Th17 differentiation in vitro

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OBJECTIVES Interleukin (IL)-5 is an anti-inflammatory cytokine which has been demonstrated to be involved in cardiovascular diseases, including aortic aneurysm and heart failure. This study aimed to investigate the involvement of IL-5 in coronary artery disease (CAD) and possible mechanisms.

METHODS The expression of IL-5 in human coronary artery specimens collected from CAD patients and normal donors (we name it Normal) was analyzed. In addition, the plasma IL-5, IL-17, and interferon (IFN)-γ levels in CAD patients were detected using ELISA kits, with samples from chest pain patients (non-CAD, hereafter referred as NCAD) as controls. Mouse CD4+ T helper (Th) cells were separated, and the effect of IL-5 on Th1, Treg and Th17 differentiation and the mRNA levels of their characteristic cytokines were detected using flow cytometry and RT-PCR, respectively.

RESULTS IL-5 was significantly decreased in the coronary plaque of CAD patients when compared with the Normal group, and IL-5 was mainly derived from macrophages in the coronary artery plaque. In addition, compared with the NCAD group, plasma IL-5 levels in the CAD groups were significantly lower, and the sequence from high to low is stable angina pectoris (SAP), unstable angina pectoris (UAP), and acute myocardial infarction (AMI). Binary linear regression analysis showed that IL-5 was independently correlated with the occurrence of CAD. In addition, the recombinant mouse IL-5 (rIL-5) treatment decreased Th1, Th17 levels and the mRNA expression of their characteristic cytokines in oxidized low-density lipoprotein (OX-LDL)-treated CD4+ Th cells.

CONCLUSIONS The IL-5 levels were decreased in CAD patients and inhibits ox-LDL-induced Th1 and Th17 differentiation in vitro.

GW30-e1031

Not all types of thrombus are born equal: role of thrombus type in residual thrombus morphology in STEMI patients: an intravascular optical coherence tomography study

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OBJECTIVES Histology studies have illustrated that different thrombus had distinct characteristics and mechanisms. However, there was no in-vivo study to focus on thrombus type and its morphology. Intravascular imaging, especially optical coherence tomography (OCT), enables us to detect and evaluate thrombus in vivo accurately. In this study, we sought to evaluate the relationship between thrombus type and residual thrombus after thrombus aspiration among STEMI patients using intravascular optical coherence tomography (IVOCT).

METHODS A total of 79 consecutive STEMI patients who did pre-PCI OCT were enrolled into this study. According to thrombus type, patients were divided into two groups: red thrombus (erythrocyte-rich, highly backscattering with high attenuation) group and white thrombus (platelet-rich, less backscattering, and homogeneous with low attenuation) group. Manual thrombus aspiration was performed at the operator's discretion. Thrombus was defined as an irregular mass protruding into the lumen. Other characteristics of residual thrombus and the quantitative method for thrombus analysis were defined with established criteria in previous papers.

RESULTS Among all the 79 patients, 31(39.2%) patients had red thrombus and 48 (60.8%) patients had white thrombus. The frequency of thrombus aspiration 51 (100%) vs. 17 (100%), P=1.000 had no significant difference between the two cohorts. When it came to IVOCT vessel morphology analysing, we found that patients with red thrombus showed a bigger vessel when compared with white thrombus group, including proximal reference area [15.28 (11.03–17.33) vs. 10.99 (9.85–14.34), P=0.024], distal reference area [13.35 (10.69–15.12) vs. 9.98 (7.77–11.92), P=0.003], mean lumen area [3.30 (2.45–5.15) vs. 2.41 (1.79–3.14), P=0.003] and mean flow area [2.39 (1.89–3.97) vs. 1.91 (1.45–2.59), P=0.012]. However, red thrombus cohort had significantly bigger residual thrombus than the white thrombus cohort, including mean thrombus area [0.51 (0.36–1.28) vs. 0.34 (0.20–0.67), P=0.002], maximal thrombus area [1.20 (0.59–2.82) vs. 0.73 (0.40–1.44), P=0.011] and thombus volume [2.54 (1.25–8.33) vs. 1.32 (0.58–2.93), P=0.004]. In plaque components, patients with red thrombus had a bigger lipid arc than white thrombus group [204.0 (145.7–236.7) vs. 152.3 (100.7–199.8), P=0.012].

CONCLUSIONS There were distinct differences between the two cohorts. Patients with red thrombus had a more vulnerable plaque phenotype and much more residual thrombus. However, the red thrombus group had a much bigger lumen and flow area than the white. Further studies should be done to illuminate the underlying mechanisms and to access their impact on long-term prognosis.

GW30-e1040

Using machine learning to detect and confirm the location and intensity of collision between antegrade and retrograde coronary flow triggering coronary artery disease in patients with stable angina

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OBJECTIVES Coronary injuries are hypothesized to be caused by the cavitation phenomenon (explosion of air bubbles) which is seen frequently in domestic or industrial pipes. Following hydraulics principle, with distal negative suctioning in diastole, if the coronary dynamic pressure decreases below the vapor pressure (VP) most likely of nitrogen in the blood, bubbles will form. They explode when the coronary dynamic pressure recovers > the VP during systole. These explosions create jet waves damaging the integrity of the endothelium, allowing infiltration of the LDL molecule into the subintimal space, starting the formation of coronary plaques. How could these events be located and tabulated by Machine Learning (artificial intelligence) program?

METHODS Angiograms of patients with stable angina were selected. The left coronary arteries were recorded in the right anterior oblique caudal view and the right coronary artery in the left anterior oblique view (at 15 frames per second). Then the angiograms were viewed off line frame by frame. The first frame was the angiogram of an artery completely filled with contrast. The following frames showed the blood moving in, seen in white. The flow could be LAMINAR (Figure 1), TURBULENT (mixing of blood in white and contrast in black) (Figure 2) or RETROGRADE (black column traveling backward) (Figure 3). The turbulent flow reflects the collision between antegrade and retrograde flow. The LOCATION and the length in TIME of laminar, retrograde and mainly turbulent flow were recorded. The intensity of turbulent flow was measured by (1) the length of coronary segment with mixing contrast and blood (2) the length of the stagnant retrograde flow. The AI programs were trained to Use the U-Net deep learning for medical image segmentation and then build the UNet model based on the previous dataset (Images, ImageMask) (Figure 4).

RESULTS Angiograms of 50 patients showed laminar flow (85%) in diastole. The flow became turbulent at systole with diffuse coarse mixing of black (contrast) and white (blood) at the MID SEGMENT of the left circumflex artery (LCX) or the right coronary artery (RCA). The presence of turbulence matched the location of 86% of ruptured plaques. The time of retrograde flow lasted more than 2 systoles. Special protocols were used successfully to train AI to recognize the lesions, antegrade, retrograde flow, turbulence and the persisting retrograde stagnant area.

CONCLUSIONS In patients with stable angina, the location of plaques and turbulent flow representing the collision between antegrade flow in diastole and retrograde flow in systole was confirmed. These results may help to find the precise measures preventing formation of de nova coronary plaques.

GW30-e1054

Modified ticagrelor loading doses according to vasodilator-stimulated phosphoprotein phosphorylation index improve clinical outcome in ST-elevation myocardial infarction patients with high on-treatment platelet reactivity

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OBJECTIVES In patients with ST-elevation myocardial infarction (STEMI), residual platelet reactivity soon after a loading dose (LD) of clopidogrel or ticagrelor is higher in healthy volunteers than that in patients with stable coronary artery disease, and the majority of primary percutaneous coronary intervention (PCI) procedures with dual anti-platelet therapy (DAPT) are performed without proper platelet inhibition. However, ticagrelor LD (180 mg once) is just the daily dose (90 mg twice per day), whereas clopidogrel LD is 4 or 8-fold the long-term daily dose. We hypothesized that a vasodilator-stimulated phosphoprotein (VASP)-guided ticagrelor LD may achieve platelet inhibition more effectively, and decrease the rate of major adverse cardiac events (MACE) as compared the standard ticagrelor LD.

METHODS This monocenter prospective randomized trial included 374 patients with a low ticagrelor response after a 180 mg ticagrelor LD undergoing PCI. Patients were randomly assigned into a control group (n=186) and a vasodilator-stimulated phosphoprotein (VASP)-guided group (n=188) (Figure 1). In the VASP-guided group, patients received up to 3 different LD of ticagrelor (180 mg, 270 mg, 360 mg) to achieve platelet reaction index (PRI) less than 50% before PCI. The primary endpoint was the MACE at 1 month. Secondary endpoints were Thrombolysis in Myocardial Infarction (TIMI) major and minor bleeding.

RESULTS Demographic data and clinical characteristics were similar in two groups (Table 1). PCI was performed in all patients. The PRI before ticagrelor LD in two groups was not different (85.4±16.2 vs. 79.3%±13.1%; P=0.22). After totally 180 mg, 270 mg and 360 mg LD of ticagrelor, PRI decreased from 79.3±13.1 to 50.5%±9.4%, 36.9±5.8 and 21.0%±6.9%, respectively (P<0.01) and 98.2% of patients reached PRI<50% in the VASP-guided group; whereas in the control group, PRI decreased from 85.4±16.2 to 45.3%±10.0%, 42.8±9.7 and 39.6%±5.5%, respectively (P>0.05) and 62.4% of patients reached PRI<50%. The adenosine concentration in VASP-guided group increased from 94.3±10.5 to 125.6±19.7, 147.2±15.8 and 177.3±21.2 μg/L (P<0.01), whereas in the control group, the adenosine level fluctuated among 92.6±11.7, 98.4±17.5, 108.4±14.1 and 105.6±10.8 μg/L (P>0.05) (Table 2). The rate of MACE was significantly lower in the VASP-guided group compared to the control group (6.9 vs. 14.5%, P=0.007). There was no major hemorrhagic complication in either group (Table 3). The rate of minor bleeding in the VASP-guided group was higher than that in the control group, but the difference was not significant (12.8 vs. 8.6%, P=0.06) (Figure 2).

CONCLUSIONS The individualized ticagrelor loading dose guided by VASP decreases the rate of major adverse cardiovascular events after PCI without increasing major bleeding.

GW30-e1060

Clopidogrel gene polymorphisms in coronary artery disease

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OBJECTIVES Clopidogrel is an antiplatelet medication used to prevent stent re-thrombosis in patients with coronary artery disease (CAD). Despite using of the standard therapy after implanting DES stents in patients with CAD, some patients may suffer from stent thrombus. Aim of the study was to estimate the impact of clopidogrel gene polymorphisms, including those of CYP2C19*1, CYP2C19*2, CYP2C19*3 and CYP2C19*17 on clopidogrel antiplatelet activity in patients CAD after DES implantation.

METHODS Forty-nine patients undergoing percutaneous intervention with DES implantation in patients with CAD were enrolled in the study. All patients were admitted for elective coronary intervention (aged 43–68 years; mean age 53±12.0; male n=29). Blood samples for platelet function testing were collected before clopidogrel administration (baseline) and at the 36 hours after the loading dose. Platelet aggregation (PA) was performed in a two-channel aggregometer and assessed by inhibition of platelet aggregation (IPA). Genetic polymorphisms was performed using polymerase chain reaction (PCR).

RESULTS Among 49 patients, 45% of patients had CYP2C19*1, 22% CYP2C19*2, 7% CYP2C19*3 and 26% CYP2C19*17 genetic polymorphisms. Only 84% of patients had a response to clopidogerel. Most of the non-responders were subjects with CYP2C19*2 and CYP2C19*3 genotypes. IPA

significantly increased in 36 hours after loading dose in CYP2C19*17 genotype with 5 mmol/L and 20 mmol/L ADP (P<0.01), and normal increased in 36 hours after loading dose in CYP2C19*1 genotyping subjects (P><0.05) whereas IPA did not changed significantly in subjects with CYP2C19*2 and CYP2C19*3 genotypes with 5 mmol/L and 20 mmol/L ADP (P>0.05).

CONCLUSIONS CYP2C19*2 and CYP2C19*3 genetic polymorphisms are the predictor of the clopidogrel non-responders whereas CYP2C19*17 polymorphisms are strong responders in the population.

GW30-e1062

Remodeling of the left ventricle and features of the cytokine status in patients with coronary artery disease

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OBJECTIVES Aim of the study was to establish the prognostic value of post-infarction (PI) cardiac remodeling and cytokine imbalance for the development of chronic heart failure (CHF) in patients with coronary artery disease (CAD).

METHODS Fifty-five patients with the history of Q wave myocardial infarction (MI) were enrolled in this study. All laboratory, instrumental and anthropometric data were obtained and the quality of life was assessed by using the University of Minnesota questionnaire.

RESULTS Men prevailed in this group of patients (67.2% of men and 32.7% of women). Analysis of central hemodynamic parameters in patients with various types of myocardial remodeling showed that in all studied groups there was a decrease in the ejection fraction, systolic shortening of left ventricle (LV), end-diastolic LV pressure and high systolic and diastolic myocardial stress. In patients with the history of Q MI, cardiac remodeling is characterized by the formation of eccentric hypertrophy with dilatation of 27.5% and without LV dilatation of 23.5%; normal heart geometry in 25% and concentric hypertrophy in 24% of cases. Multivariate regression analysis revealed that the decrease in EF <40%, eccentric hypertrophy with dilation, systolic and diastolic dysfunction of the LV, increase in TNF α and IL-6 were the most significant prognostic factors for the CHF in patients of FC III (P>0.05).

CONCLUSIONS For of development of CHF in patients with PI myocardial remodeling the clinical picture, cardio hemodynamic indicators and laboratory markers will allow to identify the maladjusted LV model in the early stages of the disease and to develop new pathogenically based treatment methods for this pathology.

GW30-e1064

Influence of aspirin and prasugrel on platelet functional status in patients undergoing percutaneous interventions

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OBJECTIVES Aspiring along with prasugrel widely used in patients undergoing percutaneous interventions (PCI). Aim of the study was to estimate functional platelet recovery and platelet function after the loading dose of prasugrel.

METHODS Thirty-two patients who underwent loading dose of prasugrel with maintenance dose of aspirin were enrolled in the study. Platelet function was assessed by optical aggregation in the presence of collagen, arachidonic acid (aspirin) and ADP (prasugrel). Platelet-leukocyte complex (PLC) level was quantified at each time-point. Before treatment and after the loading dose of prasugrel, bleeding time and fibrinogen plasma concentration were also evaluated.

RESULTS Platelet function was efficiently inhibited by aspirin and prasugrel at baseline and after the loading dose of prasugrel whilst PLC levels were significantly higher after the loading dose of prosugrel than baseline (+4±10%; P=0.016), in line with an effective platelet inhibition. Prasugrel treatment was associated with variable platelet inhibition and its withdrawal led to variable functional recovery. PLC levels were significantly increased five days after prasugrel reintroduction (+12±18%; P=0.02), compared to baseline. There was a reduction in 5-μM ADP-induced platelet aggregation of after 6 (47±33.8%, P<0.05) and 12 weeks (58±38.5%, P><0.05) in patients with coronary artery disease; 35±41% and 29±59% in the cerebral vascular disease group; and 36±36% and 35±49% in the total group (P>0.05). Plasma fibrinogen levels did not vary during treatment (P>0.05). Bleeding time was significantly prolonged in all studied groups.

CONCLUSIONS Prasugrel along with aspirin significantly reduced inhibition of platelet aggregation in patients with coronary artery disease who underwent percutaneous intervention.

GW30-e1067

Inflammatory biomarkers in patients with different forms of stable coronary artery disease

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OBJECTIVES Quantitative and qualitative analyses of the inflammatory biomarkers play a crucial role to prognosis of the ischemic heart disease. Aim of the study was to conduct a comparative analysis of inflammatory markers in patients with coronary heart disease of stable and unstable flow.

METHODS Ninety-two patients with coronary heart disease (CHD) aged 35–79 years were enrolled in this study (mean age 57.4±13.8 years; male=43%). Laboratory and instrumental data were obtained and assessed. IL-6, TNF-α in blood plasma was carried out by the method of enzyme immunoassay on a solid-phase analyzer 'Humareader Single'. Statistical processing of the obtained results was carried out using vibrational statistics methods recommended for biomedical research on the IBM PC AT Pentium IV.

RESULTS In patients with unstable angina (UA), the frequency of elevated levels of C-reactive protein (CRP), TNF-α, and leukocytes was higher than in the group with stable ischemic heart disease (P<0.05). The mean levels of these markers were greater in patients with UA compared with patients with stable form of CHD (P><0.05), CRP (4.4±2.3 and 2.8±2.4 mg/L, P><0.05, respectively), TNF-α (10.7±2.3 and 7.6±3.6 pg/mL, P><0.05) and leukocytes (9.1±2.6 vs. 6.6±2.1×109/L, P><0.05). The level of IL-6 in patients with UA was higher in comparison in patients with stable angina (3.3±1.8 vs. 2.7±0.4 pg/mL), but the difference was not significant (P>0.05). There were no significant differences in the level of fibrinogen and sedimentation rate between patients with UA and stable angina.

CONCLUSIONS It was noted that the inflammatory biomarkers were detected both group of patients with unstable forms and stable form of CHD, but the degree of inflammation in patients with UA (level of TNF-α, CRP and leukocytes) is higher than those patients with stable ischemic heart disease.

HYPERTENSION

GW30-e0013

Relationship between morning blood pressure increasing and uric acid level in hypertensive patients

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OBJECTIVES Among the population of Eastern Europe, hyperuricemia (HU) prevalence is 28% in female and 23% in male. Patients with comorbidity of HU and arterial hypertension more often suffer from metabolic syndrome, chronic kidney disease and diabetes mellitus. Aim: to study the relationship between the rate of the morning blood pressure increasing and hyperuricemia in hypertensive patients.

METHODS Total of the 60 hypertensive persons, 30 with uric acid level (SUA) 400 μmol/L (2nd group), were included in study. The groups were comparable in age and sex. SUA level was measured on a biochemical analyzer RT-9800. A 24-hour ambulatory blood pressure monitoring was performed by using of a 24-hour blood pressure monitor ABMP-50 HEACO. The strength of association between two variables was determined by Spearman's correlation coefficient.

RESULTS At the baseline daytime SBP and DBP was for 1st group: 146±5 mmHg and 92±2 mmHg; for 2nd group: 152±7 mmHg and 96±5 mmHg. The rate of morning increase in SBP and DBP was for 1st group: 22±3 mmHg/h and 14±2 mmHg/h, for 2nd group: 28±4 mmHg/h and 18±3 mmHg/h. The rate of SBP morning increase was higher by 21.4% in the 2nd group, and DBP – by 22.2% compared with the 1st group. Correlation between rate of morning increase in SBP and serum uric acid were discovered in hypertensive patients. The rate of SBP morning increase was correlated with uric acid level: in 1st group r+0.32 and in 2nd group r+0.63 (P<0.05). The rate of DBP morning increase had a low correlation power with SUA level in the 1st group r+0.26 (P>0.05) and in 2nd group r+0.28 (P<0.05).

CONCLUSIONS Higher level of SUA has a stronger effect on rate of morning increase in SBP in hypertensive patients when the level of SUA>400 μmol/L. The rate of morning increase in SBP was correlated with SUA level (r+0.63), but DBP morning increase had low power correlation without statistical significance meaning.

GW30-e0018

Increased PEDF levels are associated with endothelia inflammation in hypertension

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OBJECTIVES To study the plasma level of pigment epithelium-derived factor (PEDF) and endothelial inflammation in patients with essential hypertension (EH).

METHODS A total of 602 EH patients were divided into 3 groups: Grade I group, n=154, Grade II group, n=252 and Grade III group, n=196. There was a Control group containing 150 healthy subjects. Plasma levels of PEDF, MCP-1 and IL-6 level were tested and compared among different groups.

RESULTS The plasma PEDF level and inflammation level were different between Control group and EH patients, P<0.001. With the increased severity of hypertension, the PEDF level and inflammation level were elevated accordingly. The PEDF level with higher inflammation level is higher than that in lower blood pressure group, P<0.001.

CONCLUSIONS Plasma PEDF is closely related to EH development, and PEDF level may reflect the inflammation level in EH patients.

GW30-e0019

Increased PEDF levels are associated with artery stiffness in essential hypertension

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OBJECTIVES To study the plasma level of pigment epithelium-derived factor (PEDF) and artery stiffness in patients with essential hypertension (EH).

METHODS A total of 602 EH patients were divided into 3 groups: Grade I group, n=154, Grade II group, n=252 and Grade III group, n=196. There was a Control group containing 150 healthy subjects. Plasma levels of PEDF were tested by ELISA, artery stiffness level were tested by the brachial-ankle pulse wave velocity (baPWV), and compared among different groups.

RESULTS The plasma PEDF level and artery stiffness were different between Control group and EH patients, P<0.001. With the increased severity of hypertension, the PEDF level and artery stiffness level were changed accordingly. The PEDF level with lower artery stiffness level is higher than that in lower blood pressure group, P<0.001.

CONCLUSIONS Plasma PEDF is closely related to EH development, and PEDF level may reflect the artery stiffness level in EH patients.

GW30-e0036

Effectiveness and safety of acupuncture treatment for patients with hypertension

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OBJECTIVES Previous studies showed that acupuncture may treat hypertension (HT) and reduce the side effects caused by using western medicine. However, the systemic evaluate effectiveness of acupuncture in the treatment of systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) has not been reported.

METHODS Needling or armature or prod or acupuncture or acupuncture therapy and hypertension or HT are retrieved from PubMed, Elsevier science, Cochrane library, China Sino Med, China National Knowledge Infrastructure, China Science Periodical Database and Chinese Evidence-Based Medicine Database. Evaluate according to Cochrane System Evaluation Manual 4.2 standard. Data were extracted by two reviewers, with disagreement resolved by third party examiners either by consensus or by arbitration. Inclusion criteria: (1) adult HT patients. HT was defined as blood pressure SBP >140 mmHg (1 mmHg=0.133 kPa) and/or DBP>90 mmHg measured 3 times not the same day within a week without the use of antihypertensive drugs. Patients with previous history of HT, currently using anti-HT drugs, although lower than 140/90 mmHg blood pressure should also be diagnosed as HT; (2) treatment group on the basis of western medicine to give acupuncture treatment, acupuncture (including acupuncture, electro-acupuncture). Techniques, needle retention time, treatment, TCM syndrome is not limited; (3) clear control group; (4) the effectiveness of treatment of blood pressure, adverse reaction; and (5) randomized controlled study (RCT). Exclusion criteria: (1) reviews, dissertations and republished papers; (2) animal experiments; and 3) dissertation. RevMan5.3 software provided by Cochrane Collaboration was used for data analysis. The risk ratio (RR) and weighted mean differences (MDs) were used in outcome measures between the end of the final intervention. 95% confidence intervals (CIs) were calculated in the meta-analysis. We pooled data using a fixed-effect model (I^2<50%, P>0.05), otherwise we using random effects model (I^2>50%, P<0.05); The result is expressed in the forest plot. Bias analysis applied by the funnel plot. Statistically significant differences was P<0.05.

RESULTS Of the 13 Chinese literatures, there were 1062 cases, including 528 of the experimental group, 534 of the control group. Compare to control group, total effective rate is significant increased (RR=1.18, 95% CI=1.12–1.24, P<0.05), and reduced blood pressure (SBP: MD=–10.59, 95% CI=–13.89 to –7.29; DBP: MD=–6.83, 95% CI=–13.46 to –0.19, all P<0.05), among the most obvious in lowering DBP in experimental group (MD=15.91, 95% CI=9.82 to 21.99), acupuncturing Taichong points has statistically significant difference in reducing DBP (I^2=84.7%, P<0.05). Adverse reactions has no significant difference between two groups (RR=0.60, 95% CI=0.23 to 1.58, P>0.05).

CONCLUSIONS Acupuncture treatment of HT is safe and effective, especially, reducing DBP by acupuncturing Taichong points, which is worthy of clinical promotion.

GW30-e0132

The relationship between diastolic blood pressure and the first ischemic stroke in elderly hypertensive patients

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OBJECTIVES The aim of this retrospective cohort study was to explore the relationship between diastolic blood pressure and first ischemic stroke in community elderly hypertensive patients from China.

METHODS We enrolled 3315 consecutive elderly hypertensive patients including 1475 men and 1840 women from community between January 2010 and December 2011 in China. Patients were divided into four groups according to diastolic blood pressure at 10 mmHg intervals. Multivariate COX regression analysis, subgroup stratified and interaction analysis were preformed to evaluate the relationship between diastolic blood pressure and first ischemic stroke.

RESULTS During a median 5.5 years follow-up perriod, 206 patients were identified as first ischemic stroke. After adjustment for potential confounders, using the first group (diastolic blood pressure less than 70 mmHg) as the reference, the hazard ratio (HR) (95% CI) for the first ischemic stroke of extra three DBP groups were 1.323(95% CI, 0.730–2.397; P=0.35658), 1.519(95% CI, 1.039–2.752; P=0.01678), and 2.348(95% CI, 1.152–4.782; P=0.01875), respectively (P=0.018 for trend). Subgroup and interaction analysis showed there was no interactive effect on diastolic blood pressure and the first ischemic stroke.

CONCLUSIONS Our findings suggested that higher diastolic blood pressure was associated with a higher risk of first ischemic stroke. Diastolic blood pressure was an independent risk factor for the first ischemic stroke among Chinese elderly hypertensive patients.

GW30-e0133

Association of diastolic blood pressure with stroke in community hypertensive patients: a cross-sectional study

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OBJECTIVES We aim to explore the association of diastolic blood pressure and stroke in community hypertensive population.

METHODS This is a cross-sectional study which obtained a total of 8179 hypertensive patients coming from Dongguan Liaobu community from January 2013 to December 2013. We divided these subjects into five groups according to DBP at 10 mmHg intervals and collected information (values) including demographic characteristics, blood pressure and other clinical variables. Univariable and multivariate logistic regression was performed to detect connection between DBP and stroke. Restricted cubic spline and a two-piecewise linear regression model were also used for further exploration.

RESULTS A total of 8139 subjects were recruited and selected and eventually 8130 were left for data analysis. The average age of them is 64.01 years, and male accounted for 48.6%. Among all the participants, 310 suffered from stroke. There is no connection detected in univariate analysis and in different multivariate logistic regression models. Thus, after adjusting for potential confounders (age, sex, BMI, SBP, smoking, drinking, eGFR, heart rate, FBG, TC, TG, LDL-C, HDL-C, DM and antihypertensive drugs), a non-linear relationship was discovered between DBP and stroke, which had an inflection point of 80. The odd ratios and the 95% confidence intervals on the left and right sides of the inflection point were 0.969 (0.948–0.991) and 1.008 (0.991–1.027), respectively.

CONCLUSIONS The relationship between DBP and stroke risk is non-linear. DBP was positively correlated with risk of stroke when less than 80 mmHg.

GW30-e0134

Time point of blood pressure drop in patients with orthostatic hypotension in the emergency room

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OBJECTIVES In spite of the clinical importance of orthostatic hypotension (OH), time point of blood pressure (BP) drop in the diagnosis of OH is still under debate. The purpose of this study was to identify the time of BP drop of OH test, and to propose a realistic and appropriate duration in OH test.

METHODS A total of 879 consecutive patients (61-year old and 44% female) with positive on OH test in the emergency room (ER) were retrospectively reviewed. OH was defined as drop in standing systolic BP of at least 20 mmHg or standing diastolic BP of at least 10 mmHg from their supine values after standing for 5 minutes. BP measurement was performed at 1, 3, and 5 minutes after standing.

RESULTS 684 patients (77.8%) had BP drop at 1 minute, and 152 patients (17.3%) had BP drop at 3 minutes after standing. Only 43 patients (4.9%) had BP drop at 5 minutes. As compared to patients with BP drop at 1 or 3 minute, patients with BP drop at 5 minute were significantly younger (39 vs. 62 years, P<0.001), female dominant (65 vs. 43%, P=0.004), had more syncopal events (61 vs. 41%, P=0.035) and had less cardiovascular risk factors including hypertension (14 vs. 46%, P><0.001), diabetes (7 vs. 23%, P=0.006) and coronary artery disease (0 vs. 12%, P=0.005). In blood tests, estimated glomerular filtration rate (100 vs. 77 mL/min/1.73 m², P><0.001) and albumin (4.2 vs. 4.0 mg/dL, P=0.033) levels were higher, and glucose (114 vs. 141 mg/dL, P><0.001) and blood urea nitrogen (13 vs. 19 mg/dL, P><0.001) level was lower in patients with BP drop at 5 minute as compared to those with BP drop at 1 or 3 minute. Less patients with BP drop at 5 minute took vasoactive medications (14 vs. 45%, P><0.001). In multivariable logistic regression analysis, younger age (>

CONCLUSIONS Most of the patients with OH (95.1%) in ER showed BP drop within 3 minutes of standing. Younger age (

GW30-e0202

Validity of cardiometabolic index, lipid accumulation product, and body adiposity index in predicting the risk of hypertension in Chinese population

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OBJECTIVES Adiposity, defined by higher cardiometabolic index (CMI), lipid accumulation product (LAP), and body adiposity index (BAI), has conferred increased metabolic risk. However, the incremental utility of CMI, LAP, and BAI in association with prevalent hypertension has not been well described in a population-based setting. We hypothesized that CMI, LAP, and BAI would provide important insight into hypertension risk.

METHODS Blood pressure (BP), fasting lipid profiles, and anthropometric parameters were recorded in a cross-sectional study of 11,400 participants (mean age, 54 years; 53% women) from China. Logistic regression models were used to assess associations of CMI, LAP, and BAI with prevalent hypertension. BAI was evaluated according to hip (cm)/[height (m) 1.5]−18; LAP was calculated separately for men [(WC-65)×TG] and women [(WC-58)×TG]; and CMI was defined by TG/HDL-C×waist-to-height ratio.

RESULTS CMI, LAP, and BAI were independently correlated with higher SBP and DBP, with nonstandardized (B) coefficients ranging from 1.827 to 4.590 mmHg and 1.475 to 2.210 mmHg (all P<0.001). After adjustment for hypertension risk factors and potential confounders, CMI, LAP, and BAI, modeled as continuous measures, carried hypertension odds (95% CI) of 1.356 (1.259–1.459), 1.631 (1.501–1.771), and 1.555 (1.454–1.662) in women, respectively, per SD increment. In men, each SD increase in CMI, LAP, and BAI experienced a 31%, 65%, and 53% higher hypertension risk, respectively. Moreover, among women, the odds ratio (95% CI) for hypertension were 2.318 (1.956–2.745), 3.548 (2.985–4.217), and 3.004 (2.537–3.557) in the 4th quartile vs. the first quartile of CMI, LAP, and BAI, respectively. For men, the corresponding figures were 2.200 (1.838–2.635), 3.892 (3.238–4.677), and 3.288 (2.754–3.927), respectively.

CONCLUSIONS: Measurements of CMI, LAP, and BAI provide a more complete understanding of hypertension risk related to variation in body fat distribution and pinpoint hypertensive participants in great risk of cardiovascular disease in the future.

GW30-e0214

Contribution of non-traditional lipid profiles to reduced glomerular filtration rate in H-type hypertension population of rural China

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OBJECTIVES Despite current interest in the unfavourable impact of non-traditional lipid profiles on cardiovascular disease, information regarding its relations to reduced glomerular filtration rate (GFR) in H-type hypertension population has not been systemically elucidated.

METHODS Analyses were based upon a cross-sectional study of 3259 participants with H-type hypertension who underwent assessment of biochemical, anthropometric and blood pressure values. Reduced GFR was considered if meeting estimated GFR <60 mL/min/1.73 m².

RESULTS A stepwise multivariate regression analysis indicated that non-traditional lipid parameters remained as independent determinants of estimated GFR (all P<0.001). In multivariable models, we observed a 50, 51, 31, and 24% higher risk for decreased GFR with each SD increment in TC/HDL-C, TG/HDL-C, LDL-C/HDL-C ratios and non-HDL-C levels, respectively. The highest quartile of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C ratios carried reduced GFR odds (confidence intervals) of 5.50 (2.50–12.09), 6.63 (2.58–17.05) and 2.22 (1.15–4.29), respectively.

CONCLUSIONS Non-traditional lipid profiles has been linked with the occurrence of cardiovascular disease, but none of the studies that address the effect of non-traditional lipid profiles on reduced GFR risk in H-type hypertension population has been specifically established. A greater emphasis of this study resided in the intrinsic value of TC/HDL-C, TG/HDL-C, LDL-C/HDL-C ratios and non-HDL-C that integrate atherogenic and anti-atherogenic lipid molecules to predict the risk of reduced GFR among H-type hypertension population and provide insight into the pathophysiology of subsequent cardiocerebrovascular outcomes. In a large Chinese H-type hypertension adults, the relative independent contribution of non-traditional lipid profiles, as indexed by TC/HDL-C, TG/HDL-C, LDL-C/HDL-C ratios and non-HDL-C, towards reduced GFR putting research evidence at the very heart of lipoprotein-mediated renal injury set a vital example for applying a clinical and public health recommendation for reducing the burden of CKD.

GW30-e0228

Comparison of Peguero-Lo Presti criteria with Sokolow-Lyon for left ventricular hypertrophy defined by echocardiology in a Chinese population: newer may not necessarily be better

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OBJECTIVES ECG is a cost-effective tool for screening left ventricular hypertrophy (LVH). Sokolow-Lyon criterion is one of the most widely used criteria in clinical practice. A newly Peguero-Lo Presti ECG criterion was reported with higher sensitivity but lower specificity in Caucasian. However, its performance in general Chinese population was limited. Our study aimed to validate Peguero-Lo Presti ECG criterion in general Chinese adults who enrolled in a large-scale nationwide population study and compare its diagnostic performance with the classical Sokolow-Lyon criterion.

METHODS A multi-stage, stratified cluster sampling across China during 2012–2013 was performed to select the representative Chinese adults aged 18–85 years. A total of 7405 participants without intraventricular conduction defects (53% females, mean age 48±15 years) were analyzed in the study. ECG was collected by GE MAC 5500 and analyzed automatically by using Marquette 12SL algorithm in MUSE® Cardiology Information System. Left ventricular

mass (LVM) was estimated by transthoracic echocardiography (echo). LVH was defined as LVM indexed by BSA (LVMI)>115 g/m² for male or >95 g/m² for female. Peguero-Lo Presti was defined as the deepest S wave in any single lead (S_D)+SV_4>2.3 mV for women or >2.8 mV for men. Sokolow-Lyon voltage was defined as SV_1+RV_5/V_6≥3.5 mV or R_{aVL}≥1.1 mV. Sensitivity, specificity and other statistical measures for contingency table were compared using Fisher's Exact test. Diagnostic performance of two ECG criteria was compared by receiver operating characteristic (ROC) analysis and Mcnemar test. All continuous single leads for two criteria, including deepest S (S_D), SV_4, RV_5, SV_1, RV_6 and R_{aVL}, were analyzed for linear correlation with LVMI and diagnostic performance for echo-LVH. LVM indexed by height$^{2.7}$ was used for sensitivity analysis.

RESULTS The overall population, among which 32% were hypertensive, had an average LVMI of 80±18 g/m² and a mean blood pressure of 126/82 mmHg. Prevalence of echo-LVH was 11% while ECG-LVH ranged from 11–27% (27% for Peguero-Lo Presti, 11% for Sokolow-Lyon). Both Peguero-Lo Presti and Sokolow-Lyon were associated with the severity of LVH (P<0.0001 for both). Peguero-Lo Presti had higher sensitivity (29 vs. 12%, P<0.0001) but lower specificity (73 vs 89%, P<0.0001) and reduced accuracy (68 vs. 80%, P<0.0001) compared with Sokolow-Lyon in overall population. Both two ECG – LVH showed poor diagnostic performance (AUC: 0.51 vs. 0.51, P>0.05). All continuous single leads had weak correlation (r=0.12–0.18) and poor diagnostic performance (AUC: 0.50–0.60). R_{aVL} had relatively higher linear correlation (r=0.18, P<0.0001) and diagnostic ability (AUC=0.60) among all the single leads. While S_D, the novel predictor in Peguero-Lo Presti criterion, only showed weak correlation (r=0.12, P<0.0001) and poor diagnostic performance (AUC=0.53). Similar results were observed in sensitivity analysis with LVM indexed by height$^{2.7}$.

CONCLUSIONS Though with higher sensitivity, Peguero-Lo Presti did not have better diagnostic performance compared with the traditional Sokolow-Lyon criteria for detecting echo-defined LVH in general Chinese population. RaVL may have better diagnostic ability for echo-LVH.

GW30-e0232

The relevance about HIF1A gene polymorphism and Primary Hypertension Left Ventricular Hypertrophy in Chinese Han nationality

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OBJECTIVES To investigate the gene polymorphism effect of hypoxia inducible factor 1α in left ventricular hypertrophy of the hypertensive patients.

METHODS The 583 hypertensive patients were divided into two groups, with left ventricular hypertrophy (LVH(+), 198 cases) and without left ventricular hypertrophy (LVH(–), 385 cases). The polymerase chain reaction restriction fragmentlength polymorphism was used in the above groups for the detection of the single nucleotide gene polymorphism of rs11549465, rs11549467, and rs1957757 loci in HIF-1α.

RESULTS The distribution difference of gene frequency of rs11549465, rs11549467, and rs1957757 loci in HIF1A single nucleotide gene polymorphism in LVH(+) and LVH(–) was statistically significant (P<0.05). Thereinto, the T allele of rs11549465 loci and the G allele of rs11549467 loci can increase the risk of LVH, which was related to the increased plasma expression of HIF-1α (P<0.05).

CONCLUSIONS The gene polymorphism of HIF-1α was related to the occurrence of primary hypertension left ventricular hypertrophy, and the rs11549467 loci was correlated with the increasing concentration of plasma HIF-1α.

GW30-e0262

Retrospective analysis of endovascular intervention versus medical management in pediatric Takayasu arteritis: an over-15-year overview

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OBJECTIVES Childhood Takayasu's arteritis (c-TA) are scarcely reported but with devastating morbidity and mortality. Our previous study proved revascularization decision at baseline admission as a protective indicator of further clinical outcomes in childhood TA including all cause death, vascular complications and/or disease re-flares. This study aims to investigate the clinical course, endovascular procedure-related outcomes and associated factors of childhood TA undergoing interventions.

METHODS The present study is based on a retrospective analysis of 101 consecutive childhood TA patients fulfilled the 1990 ACR criteria or the 2010 EULAR/PRINTO/PReS criteria and hospitalized in Fuwai Hospital, between 2002 and 2017, including 5 patients prospectively recruited from 2017/01 and 2017/12. Four patients requiring mere open surgery and medications are excluded. Data are compared between patients undergoing endovascular intervention management (n=69) and patients requiring mere medical management (n=28) during the study period.

RESULTS The median ages at c-TA onset and at intervention are 14 (Interquartile range, IQR 13–16) years and 15.8 (IQR, 14–17) years in group undergoing intervention. Male sex accounts for 18.8 vs. 39.3% in medical-management group (P=0.034). Body mass index (BMI) in 31.9% patients under intervention is lower than 18.5 kg/m², vs. 60.7% in medical group (P=0.009). Hypertension (78.3 vs. 57.1%, P=0.035), blood pressure discrepancy (56.5 vs. 21.4%, P=0.37), bruits (52.2 vs. 53.6%, P=0.9) and pulse deficits (37.7 vs. 39.3%, P=0.88) are core baseline presentations and dominating Hata's angiographic type of disease include type IV (47.8 vs. 17.9%, P=0.006), type V (29 vs. 39.3%, P=0.32) and type I (8.7 vs. 21.4%, P=0.1). Immunosuppressive therapy (89.9 vs. 60.7%, P=0.001) and antiplatelet agents (81.2 vs. 57.1%, P=0.014) are majorly administered. After multivariate logistic regression analysis, male sex (OR=0.20, 95% CI 0.05–0.75, P=0.02), dual antiplatelet therapy (OR=6.64, 95% CI 1.22–36.24, P=0.03), immunosuppressive therapy (OR=12.05, 95% CI 2.57–56.52, P=0.002) and type IV disease (OR=10.69, 95% CI 2.39–47.76, P=0.002) are independent associated factors for intervention in c-TA. Clinical presentations at intervention include hypertension (73.9%), heart failure (21.7%), claudication (21.7%), cerebrovascular symptoms (15.9%), blurred version (7.2%), angina pectoris (2.9%) and pulmonary hypertension (4.3%). Major vascular beds under intervention include renal artery (63.8%), mid-aorta (18.8%) and supra-aortic arch artery (23.2%). Retinopathy (P=0.027), dual platelet therapy (P=0.004), descending thoracic aorta involvement (P=0.003) and time of delay in diagnosis (P=0.016) are independent associated factors for stenting in patients undergoing intervention. At a median 3.1 (IQR 1–6.7) years of follow-up, procedure-related complications including restenosis, bleeding, stroke, dissection, thrombosis and others are observed in 39.1% and re-interventions are observed in 24.6%.

CONCLUSIONS This largest study of c-TA reveals 68.3% patients requiring endovascular procedures during a three-year follow-up, particularly female cases with type IV disease. Immunosuppressive therapy and dual antiplatelet agents are associated with intervention, while baseline retinopathy, descending thoracic aorta involvement and longer delay in diagnosis are related to stenting.

GW30-e0288

Mean corpuscular hemoglobin concentration is a risk factor of hypertension in male prehypertensive patients

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OBJECTIVES To explore the gender-dependent association between mean corpuscular hemoglobin concentration (MCHC) and hypertension incidence in prehypertensive patients.

METHODS This was a longitudinal study involving non-elderly prehypertensive adults without any vascular disease such as stroke or diabetes. MCHC, blood pressure, anthropometric data, medical history, and lifestyle were measured or inquired at baseline visit from all patients. Associations between hypertension incidence and M were assessed by a time-dependent, Cox proportional hazard model.

RESULTS During a median follow-up of 5.02 years, 903 male patients and 607 female patients were enrolled in our study, and hypertension incidence was 27.69 and 13.51% respectively. In male patients, MCHC in the fourth quartile (Q4) were significantly related to hypertension incidence. However, such an association was not found in female patients.

CONCLUSIONS There were gender-dependent associations between MCHC and hypertension incidence in the non-elderly prehypertensive population. High MCHC (higher than 338 g/L) were associated with increased risk of hypertension in male prehypertensive patients. Mean corpuscular hemoglobin concentration is a risk factor in prehypertensive male patients.

GW30-e0335

The Aldosterone/Renin Ratio in different postures predicts left ventricular hypertrophy in hypertensive subjects for primary aldosteronism screening

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OBJECTIVES Left ventricular hypertrophy (LVH) has been linked with stroke, heart failure and atrial fibrillation, interactions between the left ventricular and the renin-angiotensin-aldosterone system (RAAS) are key determinants of cardiovascular function. However, the effects of Aldosterone/Renin Ratio (ARR) in different postures on the prevalence of electrocardiographic LVH are unclear. The aim of this study was to examine the relationship between effects of ARR in different postures and LVH in hypertensive subjects for primary aldosteronism screening.

METHODS Baseline data, supine and upright level of RAAS in plasma, 24 h-ABP and electrocardiographic parameters were compared between LVH group and control group, Logistic regression analysis was performed to obtain independent predictor of LVH after adjusting for confounding factors.

RESULTS A total of 328 with hypertensive subjects for primary aldosteronism screening admitted to the Department of Hypertension, Fuwai YunNan Cardiovascular Hospital from June 2018 to June 2019. The LVH correlated with the number of variables including LDL (r=0.215, <0.001), upright ARR (r=0.238, P<0.001), supine ARR (r=0.124, P=0.025), NT-pro BNP (r=0.161, P=0.004). In a logistic regression analysis, after adjusting for age, gender, LDL and NT-pro BNP, the upright ARR was an independent risk factor for LVH OR=1.149 (95% CI:1.057–1.249, P=0.001).

CONCLUSIONS We demonstrated that ARR in different postures are associated with the prevalence of electrocardiographic LVH in hypertensive subjects for primary aldosteronism screening. Based on this evidence, future studies should investigate ARR-lowering therapy in hypertensive individuals.

GW30-e0384

Late age at menarche is associated with hypertension among women in southern China

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OBJECTIVES The association between age at menarche (AAM) and hypertension has been previously been reported with inconsistent results. There are few such studies on the association in underdeveloped areas in China. The aim of this study was to assess the association between AMM an hypertension in southern China.

METHODS Participants in a cross-sectional study were required to complete a standard self-reporting questionnaire and physical measurements, in Jiangxi Province of southern China. Self-reported AMM was assessed from the questionnaire. A history of hypertension was obtained by answering the questionnaire or physical examination. Binary logistic regression analysis was performed to evaluate the association between hypertension and AAM. Multiple linear regression analysis was carried out to evaluate the association between SBP, DBP and AAM, and compute the subgroup analysis for interactions.

RESULTS A total of 5102 women (aged from 15 to 97 years, with a mean±SD of 52.6±17.7 years at enrollment) were included in this study. The mean±SD of AAM (aged from 9 to 24 years) for the total sample was 15.5±2.1 years. After adjustments, continuous AAM was associated with a higher risk of hypertension [OR (95% CI)=1.15 (1.11–1.19)], and ORs (95% CIs) for hypertension across AMM categories (≤13 y, 14–15 y, 16–17 y, ≥18 y) were 1 (referent), 0.95 (0.76, 1.19), 1.68 (1.34, 2.11), 2.01 (1.56, 2.58), respectively (P for trend <0.001). Independently, continuous AAM was positively correlated with SBP [β (95% CI)=0.88 (0.29, 1.46)], as well as DBP [β (95% CI)=0.80 (0.47, 1.13)], and β (95% CIs) for hypertension across AAM categories (≤15 y, 16–17 y, ≥18 y) were respectively 0 (referent), 3.50 (0.72, 6.27), and 5.84 (2.62, 9.05) for SBP (P for trend <0.001), and 0 (referent), 3.35 (1.81, 4.88), and 4.34 (2.53, 6.16) for DBP (P for trend <0.001). ORs for hypertension across AAM in three age subgroups (Tertile 1: 15–44 y, Tertile 2: 45–61 y, Tertile 3: 62–97 y) were respectively 1.37, 1.16 and 1.10, with a decreasing trend (P for interaction <0.05).

CONCLUSIONS The study is the first to report that, in southern China, a late AMM is associated with a high risk of hypertension. Women with a later AMM tend to develop hypertension in younger adulthood. Knowledge of the menarcheal history would be a preventive marker for hypertension.

GW30-e0387

Clinical observation for the relationship between orthostatic hypotension and blood urea nitrogen-to-creatinine ratio in elderly inpatients

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OBJECTIVES To explore association between orthostatic hypotension (OH) and blood urea nitrogen-to-creatinine ratio in elderly inpatients.

METHODS 180 elderly patients (≥60 years old) who hospitalized during March 2017 to November 2017 in geriatric department of Peking University First Hospital were involved. Continuous Non-invasive Arterial Pressure (CNAP) was used to record the blood pressures and heart rates at the moments of supine, immediately after standing and the first, second, third minute after standing. The gender, age, blood urea nitrogen-to-creatinine ratio, proportions of hypertension, diabetes, coronary heart disease, cerebrovascular disease and medication were compared between OH and non-OH groups immediately and within 3 minutes after standing. Multiple linear regression analysis was used to analyze the correlation between the maximum amplitudes of blood pressure and the age, supine blood pressure, supine heart rates, brachial-ankle pulse wave velocity, left ventricular ejection fraction, and urea nitrogen-to-creatinine ratio.

RESULTS In the 180 elderly inpatients, the proportion of male of OH group immediately after standing was significantly lower than non-OH group (P<0.05); no significant difference in age, urea nitrogen-to-creatinine ratio, proportions of hypertension, diabetes, coronary heart disease, cerebrovascular disease and medication. There was no difference in gender, age, urea nitrogen-to-creatinine ratio, proportions of hypertension, diabetes, coronary heart disease, cerebrovascular disease and medication between OH and non-OH group within 3 minutes after standing. The maximum SBP drops (SBP of supine minus the lowest SBP during postural changes) was positively correlated with brachial-ankle pulse wave velocity and urea nitrogen -to-creatinine ratio [β=0.007 (95% CI 0.001–0.014), 0.673 (95% CI 0.186–1.159); P=0.041, 0.007], while there was no significant correlation with age, supine systolic pressure, supine diastolic pressure, supine heart rate and left ventricular ejection fraction.

CONCLUSIONS OH is very common in elderly inpatients. There may be no correlation between the incidence of OH and blood urea nitrogen-to-creatinine ratio, but maximum decrease in systolic blood pressure during postural changes is positively correlated with blood urea nitrogen-to-creatinine ratio.

GW30-e0409

Inflammatory markers in prognosis of vascular damages in case of arterial hypertension and metabolic syndrome

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OBJECTIVES: To estimate the role of inflammatory markers in vascular damages and their prognostic value in case of arterial hypertension (AH) and metabolic syndrome (MS).

METHODS The study enrolled 70 patients with AH I-III stages (40 males and 30 females) with MS signs (abdominal type of obesity, lipid and carbon metabolism). The MS group had 33.07±2.58 kg/m² of body mass index (BMI), 6.47±1.18 mmol/L of total cholesterol (LDLP 3.49±0.84 mmol/L). Males and females average age was 47.9±1.14 years. Arterial stiffness was measured by recording pulse wave velocity (PWV), with registration of cardio-ankle vascular index (CAVI) and ankle-brachial index using sphygmography. Measurement of carotid artery intima-media thickness (IMT) was carried out. The following inflammatory response markers were studied: high sensitive C-reactive protein (hs CRP) and homocysteine. Blood lipids profile testing included total cholesterol, low-density lipoproteins, high density lipoproteins and triglycerides.

RESULTS Increase in arterial stiffness parameters was detected in AH and MS patients (increased PWV (P<0.05), decrease of ankle-brachial index (P><0.05) and increase of hs CRP and homocysteine (P≤0.05) and P≤0.05) along with AH progress. Increase of vascular wall stiffness was positively correlated with systolic BP (P><0.01), level of hs CRP and homocysteine (P><0.01, P><0.05) and IMT level (P><0.05). Along with the growth of AH and obesity degree, patients with AH and MS had negative correlation of CAVI with total cholesterol and triglycerides (P><0.05) and hs CRP (P><0.05). Arterial stiffness parameters (PWV) were positively related to BMI, left ventricular hypertrophy, total cholesterol and triglycerides level in blood (P><0.05). In the conditions of lipid metabolism disorders, a separate study of arterial stiffness and inflammatory markers in case of AH I, II and III stages was performed. A reliable correlation between PWV and hs CRP and homocysteine increasing along with AH progress (I stage – P≤0.05; II stage – P≤0.01; III stage – P≤0.0001) was revealed.

CONCLUSIONS In AH and MS patients in conditions of lipid metabolism disorders more significant rise of arterial stiffness associated with inflammatory response markers were observed. The increase of direct correlation between these markers along with AH progress highlights the important role of the inflammatory markers and their prognostic value in the vascular complications progress in case of this pathology.

GW30-e0413

Formation of congestive heart failure with preserved ejection fraction in the Arctic watch workers

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OBJECTIVES To estimate structural and functional condition of left ventricular (LV) myocardium with the physical working capacity of AH patients in the Arctic.

METHODS Within the period of 2002–2010, 881 males aged 20–59 years were examined at the medical unit «Gazprom dobycha Yamburg». Patients were randomized into Gr.1 consisted of 373 males with AH of 1, 2 stage doing the watch work in the Arctic (71°N) and Gr.2 (control group) consisted of 144 males with AH of 1, 2 stage living in Tyumen (57°N). The groups matched in age: 46.0±6.0 (P=0.445), office systolic blood pressure (SBP) /diastolic blood pressure (DBP): 157.5/153.9 (P=0.322); 106.7/100.3 (P=0.0640). All patients

had 24-hour BP monitoring, echocardiography, treadmill test, and biochemical blood examination performed.

RESULTS Gr.1 had lower values of SBP24 (P<0.001), higher values of DBP24 (P><0.0001) in comparison with Gr.2; 30% of people with AH (Gr.1) had normotension (SBP24/DBP24><0.001) and heart rate 24 (HR24) (P><0.001). Such metabolic changes as overweight (P=0.0002), elevated level of glucose (P=0.0002) and creatinine (P=0.0001) were observed in Gr.1. Myocardial mass of left ventricle (MMLV) and index of MMLV (P=0.0002), (P=0.0024) were higher in Gr.1. Patients of Gr.1 more often had growth of left atrium (P=0.0088) and concentric LV hypertrophy (P=0.0014) due to thickness of interventricular septum (IVS) and LV posterior wall (P><0.0001); however, LV ejection fraction was reliably higher (P><0.0001) in Gr.1. Disorder of LV diastolic function was observed more often (P=0.0475) in Gr.1 due to slow LV relaxation (P=0.0001). Treadmill test in Gr.1 showed that adaptation mechanism level as per adaptation potential coefficient was in the «tension» range and «unsatisfactory» and even «failure» of adaptation (P=0.0001); threshold level of maximum oxygen consumption was lower in Gr.1 (P=0.0001). Patients of Gr.1 had lower value of specific work and duration of exercise test (χ^2=262, P=0.0001). Only 5.7% of patients had positive treadmill test, and 4.8% out of them had positive test according to ECG (with painless myocardial ischemia).

CONCLUSIONS The expressed structural and functional alterations of myocardium in patients with AH and preserved ejection fraction define the risk of unfavorable clinical outcomes in perspective. These results are also an optimal target for medication therapy and confirm the need for a detailed study of pathogenic and prognostic formation of congestive heart failure with preserved ejection fraction in the Arctic watch workers.

GW30-e0415

Formation of congestive heart failure with preserved ejection fraction in the Arctic watch workers

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OBJECTIVES To estimate structural and functional condition of left ventricular (LV) myocardium with the physical working capacity of AH patients in the Arctic.

METHODS Within the period of 2002–2010, 881 males aged 20–59 years were examined at the medical unit «Gazprom dobycha Yamburg». Patients were randomized into Gr.1 consisted of 373 males with AH of 1, 2 stage doing the watch work in the Arctic (71°N) and Gr.2 (control group) consisted of 144 males with AH of 1, 2 stage living in Tyumen (57°N). The groups matched in age: 46.0±6.0 (P=0.445), office systolic blood pressure (SBP)/diastolic blood pressure (DBP): 157.5/153.9 (P=0.322); 106.7/100.3 (P=0.0640). All patients had 24-hour BP monitoring, echocardiography, treadmill test, and biochemical blood examination performed.

RESULTS Gr.1 had lower values of SBP24 (P<0.001), higher values of DBP24 (P><0.0001) in comparison with Gr.2; 30% of people with AH (Gr.1) had normotension (SBP24/DBP24><0.001) and heart rate 24 (HR24) (P><0.001). Such metabolic changes as overweight (P=0.0002), elevated level of glucose (P=0.0002) and creatinine (P=0.0001) were observed in Gr.1. Myocardial mass of left ventricle (MMLV) and index of MMLV (P=0.0002), (P=0.0024) were higher in Gr.1. Patients of Gr.1 more often had growth of left atrium (P=0.0088) and concentric LV hypertrophy (P=0.0014) due to thickness of interventricular septum (IVS) and LV posterior wall (P><0.0001); however, LV ejection fraction was reliably higher (P><0.0001) in Gr.1. Disorder of LV diastolic function was observed more often (P=0.0475) in Gr.1 due to slow LV relaxation (P=0.0001). Treadmill test in Gr.1 showed that adaptation mechanism level as per adaptation potential coefficient was in the «tension» range and «unsatisfactory» and even «failure» of adaptation (P=0.0001); threshold level of maximum oxygen consumption was lower in Gr.1 (P=0.0001). Patients of Gr.1 had lower value of specific work and duration of exercise test (χ^2=262, P=0.0001). Only 5.7% of patients had positive treadmill test, and 4.8% out of them had positive test according to ECG (with painless myocardial ischemia).

CONCLUSIONS The expressed structural and functional alterations of myocardium in patients with AH and preserved ejection fraction define the risk of unfavorable clinical outcomes in perspective. These results are also an optimal target for medication therapy and confirm the need for a detailed study of pathogenic and prognostic formation of congestive heart failure with preserved ejection fraction in the Arctic watch workers.

GW30-e0416

Arterial hypertension in the Arctic: features of target organ damage

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OBJECTIVES To estimate the role of BP in the formation of severe left ventricular (LV) hypertrophy and carotid artery subclinical atherosclerosis (CASA) in patients with AH in conditions of the watch work in the Arctic.

METHODS Within the period of 2002–2010, 715 males were examined at the medical unit «Yamburggasdobycha» (71°N). Patients were randomized into Gr.1 consisted of 373 males with office BP (157.5±13.7/106.7±8.8 mmHg); and Gr.2 consisted of 173 males with office BP (123.4±7.5/80.5±5.5 mmHg), aged 46.0±6.0 years, (P=0.445), with the watch work duration (11.2±3.8 years). The control group (Gr.3) consisted of 169 patients with normal and elevated BP living in Tyumen (57°N) matched in age and BP. All patients underwent echocardiography, carotid arteries ultrasound examination, standard and chronobiological analysis of 24-hour BP monitoring.

RESULTS Gr.1 compared to Gr.3 had lower values of systolic BP24 (SBP24) (P<0.001), higher values of diastolic BP24 (DBP24) (P><0.0001); and Gr.1 had high variability of SBP24, DBP24 (P><0.001) and heart rate24 (HR24) (P><0.001); 30% of people with AH (Gr.1) had normotension (SBP24/DBP24).

CONCLUSIONS Thus, one of the reasons of the formation of severe target organ damage and CASA in patients with AH in the Arctic watch is not the office BP level and average daily BP according to 24-hour BP monitoring, but hypersympathicotonia with violation of the chronostructure of the BP daily rhythm.

GW30-e0567

Anxiety as an independent risk factor for hypertension and relieving anxiety can improve blood pressure control

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OBJECTIVES Numerous studies have shown that anxiety is closely related to the occurrence and development of hypertension. Anxiety is one of the important psychological factors affecting hypertension. This study explores the relationship between anxiety and hypertension and the influence of anxiety on the blood pressure control rate.

METHODS A total of 272 patients were enrolled in Shaanxi Provincial People's Hospital from 2017 to 2018. Exclusion criteria were: age below 30 years or above 80 years, NYHA III or IV, coronary heart disease, atrial fibrillation, frequent arrhythmia, renal failure, serum creatinine above 175 μmol/L, thyroid dysfunction, acute infection, known history of cancer or chronic-immune-mediated disorders, or current use of immunosuppressive agents including corticosteroids.

Hypertension is defined as systolic blood pressure (SBP) higher than 140 mmHg, or a diastolic pressure (DBP) greater than 90 mmHg. The blood pressure goal was SBP lower than 140 mmHg, and a DBP lower than 90 mmHg. All enrolled subjects completed the Hamilton Anxiety Scale (HAMA) which is a rating scale developed to quantify the severity of anxiety. The total score of HAMA ranges from 0 to 56 points. HAM-A score ≥14 was defined as the presence of anxiety. The association between anxiety and hypertension was estimated with univariate and multivariate logistic regression models. Model 1 was unadjusted. Model 2 was adjusted for age, sex, and smoking. Model 3 adjusted for age, sex, smoking, educational level, economic income. Model 4 adjusted for age, sex, smoking, educational level, economic income, family history of hypertension, and hyperlipemia. We also performed psychological or drug interventions and follow-up of patients with hypertension and anxiety.

RESULTS Participants were divided into two groups according to with anxiety or not. Compared with the non-anxiety group, the ratio of hypertension was significantly higher in the anxiety group (69.3 vs. 50.0%, P=0.002). Then, we assessed the association between anxiety scores and blood pressure, anxiety scores levels were significantly positive correlated to the systolic blood pressure (r=0.511, P<0.001).

In univariate logistic regression models (Model 1), compared with patients in non-anxiety group, the odds ratios (OR) for development of hypertension in the anxiety group were 2.33 (95% CI 1.42–3.84, P=0.001). Multivariate analysis showed that anxiety was independently and positively related to the development of hypertension (adjusted OR: 2.22, 95% CI 1.34–3.61, P=0.002, compared with the non-anxiety group) after adjusting for Model 2. With further adjustment for adjusted for Model 3 and Model 4. The OR for the development of hypertension in the anxiety group showed no change (Model 3, OR 2.16, 95% CI 1.29–3.62, P=0.003; Model 4, OR 1.88, 95% CI 1.08–3.28, P=0.026).

In addition, after 2 months follow-up of patients with hypertension and anxiety, We performed the Hamilton Anxiety Scale again. Compared with the control group, the anxiety scores were significantly decreased in the treatment group (P<0.001). The rate of goal blood pressure of treatment group was significantly increased than the control group in patients with hypertension and anxiety (P=0.008) (treatment group: before 60%, after 75%; control group: before 38.9%, after 27.8%).

CONCLUSIONS Our data indicated that anxiety is an independent risk factor for hypertension. Relieving anxiety can increase the rate of goal blood pressure in patients with hypertension and anxiety.

GW30-e0618

The value of nocturnal mean diastolic blood pressure on the diagnosis of severe obstructive sleep apnea syndrome in patients with hypertension

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OBJECTIVES To explore the diagnostic value of nocturnal blood pressure level for severe OSAS, and establish a simple, economical and effective screening method by combining with the existing scale for OSAS in patients with hypertension.

METHODS Clinical data from 144 patients with hypertension ((45.41±11.13) years old, 102 males), who underwent PSG, ABPM in our hospital from September 2018 to November 2018. Anthropometric index, STOP-Bang questionnaire, NoSAS score, No-Apnea model would be also collected. According to AHI, the patients were divided into non-severe group (AHI<30 times/hour) and severe group (AHI≥30 times/h). The receiver operating characteristics (ROC) curve was used to evaluate the value of predicting severe OSAS, and DeLong method judge that whether there is statistical significance in comparing the difference of ROC curve among each index. Sensitivity, specificity, positive predictive value, negative predictive value, Jordan index, Accuracy and Kappa value were also calculated.

RESULTS The diagnostic value of nocturnal mean systolic blood pressure for OSAS was improved with the increasing of AHI as the cutoff point. When the cutoff point was selected as AHI≥30 times/hour, the AUC of nocturnal mean diastolic blood pressure was 0.793, and the best cutoff point was >86 mmHg (Jordan index 0.533). The sensitivity, specificity, positive predictive value and negative predictive value were 75.8, 77.5, 50.0 and 91.5% respectively, and the Accuracy and Kappa value, 77.1% and 0.451 respectively, were better than the three existing scales mentioned above. After being connected with STOP-Bang questionnaire, the sensitivity, specificity, positive predictive value, negative predictive value, Jordan index, Accuracy and Kappa value were 75.8%, 82.9%, 56.8%, 92.0%, 0.587, 81.3 and 0.525 respectively. All the prediction indexes were higher than before except for the sensitivity.

CONCLUSIONS Nocturnal mean diastolic blood pressure has a good diagnostic value for severe OSAS in hypertensive population, and the ability to diagnosis severe OSAS can be improved after being connected with STOP-Bang questionnaire.

GW30-e0655

China study of valsartan/amlodipine based long-term blood pressure management in hypertensive patients (CHINA STATUS III study): a subgroup analysis of elderly patients

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OBJECTIVES There are still limited real-world data for the 1-year treatment efficacy and safety of valsartan/amlodipine in elderly patients in China. This study aimed to evaluate the efficacy and safety of 1-year blood pressure (BP) management using valsartan/amlodipine in Chinese elderly patients, and to compare the efficacy and safety between middle-aged and elderly patients.

METHODS This was an ad-hoc analysis of the CHINA SATATUS III study, which was a 1-year registry study of valsartan/amlodipine in patients who had already received valsartan/amlodipine for at least 4 weeks before enrollment. Patients were grouped as the middle-aged (30–64 years) and elderly (over 65 years) subgroups. The primary efficacy endpoints were BP control rate after 12 months of treatment. Safety was examined.

RESULTS A total of 894 patients were included the present analysis. The office BP control rates significantly improved from baseline at 56.9 to 74.4% at 12 months (P<0.001). Compared with the middle-aged group, the control rate in the elderly at baseline was lower (56.9 vs. 68.6%, P<0.001), but not at 12 months (74.4 vs. 74.0%, P=0.902). Office systolic blood pressure (SBP) and diastolic blood pressure (DBP) both significantly reduced at 12 months in the elderly group (P<0.05), with a more pronounced reduction in SBP (−5.0±15.1 vs. −2.0±14.6 mmHg, P=0.014) observed compared with the middle-aged group. The occurrence of serious adverse events was not associated with the age group (odds ratio=1.3, 95% confidence interval: 0.8–2.4).

CONCLUSIONS Valsartan/amlodipine is effective and safe in the 1-year treatment of elderly patients with elevated BP.

GW30-e0657

Identification of differentially expressed genes and enriched pathways in Kawasaki disease using bioinformatics analysis

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OBJECTIVES DNA microarray and high-throughput sequencing have been widely used to identify the differentially expressed genes (DEGs) in Kawasaki disease (KD). However, the big data from gene microarrays are also challenging to work with in terms of analysis and processing. The presents study combined data from the microarray expression profile (GSE73464) and bioinformatics analysis to identify the key genes and cellular pathways in KD.

METHODS Gene ontology (GO) and cellular pathway enrichment analyses of DEGs were performed to investigate significantly enriched pathways. A protein-protein interaction network was constructed to determine the key genes in the occurrence and development of KD.

RESULTS A total of 418 DEGs were identified in KD, including 418 upregulated genes and 76 downregulated genes. GO analysis revealed that the most significant biological process of DEGs was immune system process. Kyoto Encyclopedia of Genes and Genome pathway analysis showed that these DEGs were enriched in signaling pathways associated with the immune system, including systemic lupus erythematosus, primary immunodeficiency, cell adhesion molecules (CAMs) and T cell receptor signaling pathway. The current study screened the top 3 genes with higher degrees as hub genes, which included G protein-coupled receptor 84, formyl-peptide receptor-2 and complement component 3a receptor 1. Module analysis revealed that these hub genes were also involved in the chemokine signaling pathway, cytokine-cytokine receptor interaction and staphylococcus aureus infection.

CONCLUSIONS Kawasaki disease, differentially expressed genes, pathway enrichment analysis, gene ontology, protein-protein interaction network.

GW30-e0658

Association of circulating resistin and adiponectin levels with Kawasaki disease: a meta-analysis

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OBJECTIVES The purpose of this meta-analysis is to assess the relationship between circulating blood adipokines levels and Kawasaki disease (KD).

METHODS Articles were identified by searching Web of Science, EMBASE, PubMed, Wanfang and CNKI databases. Studies identified were pooled, and the standardized mean difference (SMD) and its corresponding 95% confidence interval (CI) were calculated. Subgroup analyses and publication bias detection were also conducted. Cochrane Q test and I^2 statistic calculated by Review Manager software (version 5.3) to test heterogeneity. To assess publication bias, the STATA software (version 12.0) was used for statistical analysis.

RESULTS The KD group had a higher level of resistin than HC (healthy control) and DC (disease control) (SMD=2.52, 95% CI=1.48–3.56, P<0.001, SMD=1.26, 95% CI=0.49–2.02, P=0.001). Compared with NCAL (non-coronary artery lesions), the CAL (coronary artery lesions) group had higher levels of adiponectin and resistin (SMD=0.29, 95% CI=0.02–0.55, P=0.03, SMD=0.97, 95% CI=0.10–1.85, P=0.03). Compared to the phase, the active group had a higher level of resistin (SMD=2.10, 95% CI=0.77–3.43, P=0.002).

CONCLUSIONS In conclusion, the present meta-analysis indicated that resistin levels were generally elevated in KD patients. Compared with NCAL, the circulating resistin and adiponectin levels in the CAL group were significantly increased. The active group have a higher level of resistin than the inactive group. The results of these meta-analyses suggest that resistin and adiponectin may play an important role in the pathogenesis of KD. Resistin and adiponectin could be used as biomarkers for KD diagnosis.

GW30-e0719

Depression as an independent risk factor for the development of hypertension

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OBJECTIVES Previous studies have shown that depression is closely related to the occurrence and development of hypertension. Depression is one of the important psychological factors affecting hypertension. Thus, we assessed the impact of depression on the development of hypertension.

METHODS A total of 272 patients were enrolled in Shaanxi Provincial People's Hospital from 2017 to 2018. Exclusion criteria were: age below 30 years or above 80 years, NYHA III or IV, coronary heart disease, atrial fibrillation, frequent arrhythmia, renal failure, serum creatinine above 175 μmol/L, thyroid dysfunction, acute infection, known history of cancer or chronic-immune-mediated disorders, or current use of immunosuppressive agents including corticosteroids.

Hypertension is defined as systolic blood pressure (SBP) higher than 140 mmHg, or a diastolic pressure (DBP) greater than 90 mmHg. All enrolled subjects completed the Hamilton depression Scale (HAMD) which is a rating scale developed to quantify the severity of depression. HAMD score ≥20 was defined as the presence of depression. The association between depression and hypertension was estimated with univariate and multivariate logistic regression models. Model 1 was unadjusted. Model 2 was adjusted for age, sex, and smoking. Model 3 adjusted for age, sex, smoking, educational level, economic income. Model 4 adjusted for age, sex, smoking, educational level, economic income, family history of hypertension, and hyperlipemia.

RESULTS Participants were divided into two groups according to with depression or not. Compared with the non-depression group, the rate of hypertension was significantly higher in the depression group (70.5 vs. 54.1%, P=0.008). Then, we assessed the association between depression scores and blood pressure, depression scores levels were significantly positive correlated to the systolic blood pressure (r=0.283, P<0.001).

To further evaluate the effect of depression on development of hypertension, we used univariate and multivariate regression models to reveal whether the depression was an independent risk factor for the development of hypertension.

In univariate logistic regression models (Model 1), compared with patients in non-depression group, the odds ratios (OR) for development of hypertension in the depression group were 2.43 (95% CI 1.45–4.06, P=0.001). Multivariate analysis showed that depression was independently and positively related to the development of hypertension (adjusted OR: 2.35, 95% CI 1.40–3.95, P=0.001, compared with the non-depression group) after adjusting for Model 2. With further adjustment for adjusted for Model 3 and Model 4. The OR for the development of hypertension in the depression group showed no change (Model 3, OR 2.36, 95% CI 1.29–4.01, P=0.001; Model 4, OR 2.52, 95% CI 1.43–4.45, P=0.001).

CONCLUSIONS Our data indicated that depression is an independent risk factor for the development of hypertension.

GW30-e0726

Prevalence, awareness, treatment, and control and related factors of hypertension in multi-ethnic agriculture, stock raising and urban Xinjiang, Northwest China. A Cross-sectional Screening for 47,000 Adults

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OBJECTIVES The aim was to determine prevalence, awareness, treatment, control and risk factors associated with hypertension among multi-ethnic population in northwest China.

METHODS We conducted a hypertension screening project covering a third of adults in Emin Xinjiang, northwest China during 2014–2016. All the participants were selected from the hypertension screening project which included health archives, health check-up records and disease registrations with a solid information security system. Hypertension was defined as systolic blood pressure (BP) ≥140 mmHg, and/or diastolic BP≥90 mmHg and/or taking anti-hypertension drugs. Awareness was defined as whether they had a medical diagnosis of hypertension and treatment as whether they were receiving BP-lowering medications. Control was defined as an average SBP and DBP <140/90 mmHg. We compared prevalence, awareness, treatment and control of hypertension and related factors by different regions (agricultural, stock-raising or urban) and by ethnic groups.

RESULTS Totally 47,040 adults were screened with 48.5% women. A total of 54.9% participants (n=25,850, aged 43.6 years) were enrolled from rural setting, 17.0% (n=7994, aged 42.0 years) from stock-raising setting and 28.1% (n=13,196, aged 45.9 years) were from urban setting. 77.4% subjects in stock-raising setting were Kazakh ethnicity, and 53.4% in urban setting were Han ethnicity and 43.3% in rural setting were Han and 45.5% were Kazakh ethnicity. Overall prevalence of hypertension was 26.5%. Among those with hypertension, 64.6% (95% CI, 61.9–67.1%) were aware of their condition, 44.5% (95% CI, 43.7–45.2%) were taking medications to lower their BP, whereas only 15.3% (95% CI, 14.8–15.9%) achieved BP control. Age-gender-adjusted hypertension prevalence was higher in urban (28.2%) than in other regions and in Kazakh (30.3%) than in others. The awareness and treatment rates were lower in patients from agricultural regions than in those from urban or stock-raising settings (awareness rate: 59.7 vs. 66.5 vs. 76.3%; treatment rate: 41.6 vs. 42.3 vs. 58.4%), whereas the control rate in patients from stock-raising setting was lower than that of those from urban and rural setting (13.8 vs. 15.2 vs. 15.8%, P<0.05). The awareness, treatment and control rates of hypertension were lower in Kazakh subjects than in other ethnic groups (P for all <0.001). After adjusting for age, gender, ethnicity and regions, abdominal obesity (OR 1.30; 95% CI, 1.21–1.41), general obesity (OR 1.94; 95% CI, 1.75–2.15), cigarette consumption (OR 2.49; 95% CI, 2.20–2.81), and alcohol intake (OR 4.90; 95% CI, 4.33–5.53) were significantly associated with the presence of hypertension (P<0.05).

CONCLUSIONS Disparities in hypertension control among regions and ethnic groups suggested inadequate screening and treatment, especially in stock-raising regions and Kazakh populations. Control of alcohol intake, smoking and obesity should be at high priority of health promotion. Even though the current project did not collect data on salt intake, it is should be addressed as sodium consumption is high in the region.

GW30-e0730

Distribution characteristics of circulating homocysteine and folate and the related factors in agriculture, stock raising and urban populations–a cross-sectional survey

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OBJECTIVES The aim was to investigate Hcy and folate levels, prevalence of hyperhomocysteinemia (HHcy) and of folate deficiency in population from urban, agricultural and stock-raising regions.

METHODS Multistage stratified random sampling method was used to obtain study population aged ≥15 years. Surveys on health behavior questionnaires and physical examinations were conducted. Blood samples were collected for Hcy and folate measurement. Study subjects were divided into three groups as urban, agricultural and stock-raising population. HHcy was defined as Hcy ≥10 μmol/L and folate deficiency as <3 ng/mL.

RESULTS 1926 participants with 885 (45.9%) from urban, 861 (44.7%) from agricultural and 180 (9.4%) from stock raising regions were evaluated. Although Hcy concentration in the three region showed no significant difference (14.2 vs. 13.3 vs. 13.2 μmol/L, P=0.202), subgroup analysis showed significantly higher Hcy in women, Kazakh, non-drinking subjects, low education takers from stock-raising region than did other two regions. Folate concentration in stock raising region is significantly lower than in other two regions (3.3 vs. 7.2 vs. 6.5 ng/mL, P<0.001); subgroup analysis showed consistent results. Prevalence of HHcy and folate deficiency in stock raising region is the highest (82.2 and 54.8% respectively), followed by agricultural (69.7%, 8.3%) and urban (68.4%, 2.6%) region with statistical significance (P=0.001 for HHcy and P<0.001 for folate). Folate deficiency, stock raising region, older age, and male gender showed higher ORs for HHcy presence.

CONCLUSIONS Prevalence of HHcy and folate deficiency is unacceptably high in stock raisers. Current results is of important reference for the prevention and control of HHcy to Xinjiang, extending to others with approximate lifestyles and dietary habits by folate supplementation and lifestyle modification.

GW30-e0732

The improvement of STOP-BANG questionnaire in screening severe sleep apnea syndrome in Chinese hypertensive patients

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OBJECTIVES The STOP-BANG questionnaire was used widely for detecting patients with obstructive sleep apnea (OSA). However, considering the lower mean level of body mass index (BMI) and neck circumference (NC) of Chinese population, the cut-off point value of these two questions needs to be verified. This study was to assess the diagnostic efficacy of the STOP-BANG questionnaire and establish a more appropriate BMI and NC cutoff value for Chinese patients with hypertension.

METHODS A retrospective analysis of 284 patients admitted to the Hypertension center of People's Hospital of Xinjiang Uygur Autonomous Region from 2016 to 2017, who underwent 7-hour nighttime polysomnography (PSG) and completed the ESS score, STOP-BANG questionnaire. The diagnostic ability of STOP-Bang questionnaire of severe OSA (AHI≥30 events/h) were assessed and the improved STOP-BANG questionnaire were established.

RESULTS When the BMI cut-off value is set to 28 kg/m^2 and the neck circumference cut-off point is set to 42 cm, the area under the ROC curve of the STOP-BANG scale is the largest (0.81, P<0.001). The sensitivity and specificity of the STOP-BANG questionnaire for predicting severe OSA in hypertensive patients

were (80.58 and 60.69%), respectively, and the area under the ROC curve was (0.755, P<0.001). In the scale, when the neck circumference was kept and the BMI cutoff value is reduced from 35 to 28, the AUC of the scale increased from 0.755 (0.70–0.80) to 0.784 (0.73–0.83), and the difference is statistically significant (P<0.01). When the neck circumference changed from 40 to 42 in the scale, the AUC of the scale changed from 0.755 (0.70–0.80) to 0.785 (0.73–0.83), and the difference was statistically significant (P<0.01). When the BMI and neck circumference cutoff values were both changed, the area under the curve was 0.81 (0.76–0.85). It was 87.77% (81.1–92.7), the specificity was 62.07% (53.6–70.0), and the Youden index was 0.50.

CONCLUSIONS The STOP-BANG questionnaire has high sensitivity and diagnostic efficacy for screening the population. The improved STOP-BANG questionnaire for this population can improve the diagnostic efficacy of screening. We recommend using BMI (28 kg/m^2), neck circumference (42 cm), STOP-BANG score ≥3 is the cut-off value to identify patients with high risk of severe OSA in Chinese patients with hypertension.

GW30-e0733

Effect of diabetes on sleep disorder in menopausal female with hypertension

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OBJECTIVES To investigate the effect of diabetes on sleep parameters in postmenopausal women by comparing the nocturnal sleep parameter in menopausal and non-menopausal female with hypertension.

METHODS A total of 549 female patients who underwent polysomonography in the Hypertension Center of People's Hospital of Xinjiang Autonomous Region were selected from 2005 to 2010. The patients were divided into menopause and non-menopausal group. Differences in sleep parameters between the two groups of patient.

RESULTS 280 menopausal and 269 non-menopausal patients were included in the study. Menopausal women had a higher prevalence of diabetes [23.2 vs. 4.8%], the prevalence of OSA [81.4 vs. 52.4%] and AHI index [13.5 (6.3, 25.8) vs. 6.3 (1.5, 13.4) P<0.001] than non-menopausal women, but the lowest oxygen saturation was lower [77 (70, 82) vs. 79 (74, 83) P=0.008]. The AHI index in patients with diabetes increased compared those without diabetes [11.8 (2.6, 19.1) vs. 8.5 (5.6, 30.2) P=0.008), but the lowest oxygen saturation was lower [79.5 (71.8, 84) vs. 82 (76, 87) P=0.011]. After adjustment, multivariate analysis showed that menopause and poor glycemic control were associated with sleep disturbances and OSA.

CONCLUSIONS Postmenopausal women with diabetes would increase the risk of OSA and the disorder of sleep parameters.

GW30-e0772

Differential expression profiles of long non-coding RNAs in patients with hypertensive left ventricular hypertrophy

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OBJECTIVES LVH is a strong predictor of cardiovascular morbidity and mortality because of the increased risk of heart failure and malignant arrhythmia. In the present study, we compared the expression profile of circulating lncRNAs in patients with primary hypertension and LVH, primary hypertension without LVH (NLVH) and normotensive individuals. Illuminating the role of lncRNAs in hypertension-induced cardiac remodeling may help in understanding the underlying molecular mechanism and suggest potential therapeutic targets.

METHODS In this study, venous blood was collected from patients with essential hypertension with and without LVH and healthy controls in a case–control study. Total RNA was extracted from each sample, microarray analysis was used to detect lncRNA expression profiles. The Level of targeted lncRNAs was Confirmed by quantitative real-time PCR. Coding–non-coding gene co-expression network and functional enrichment analysis of lncRNAs with significantly differential expression was conducted. Multivariate logistic regression analysis was used to evaluate the association between LVH and the lncRNAs RP11-327F22.4 and KHSRPP1 in hypertensive patients.

RESULTS A total of 94 differentially expressed lncRNAs was identified by microarray-based screening. The comparison of LVH patients and controls revealed 17 upregulated and 34 downregulated lncRNAs. Among these differentially regulated lncRNAs, we chose two, upregulated RP11-327F22.4 and downregulated KHSRPP1, which agreed with the pattern we expected. We also used RT-PCR to analysis levels of the lncRNAs RP11-327F22.4 and KHSRPP1 in hypertensive patients with LVH or NLVH and matched healthy controls. The two lncRNAs showed a consistent expression pattern on microarray assay, which indicates high reliability of the analysis.

Multivariate logistic regression analysis results showed that LVH in hypertensive patients was associated with upregulated lncRNA RP11-327F22.4 (OR: 1.030; 95% CI: 1.008–1.052; P=0.008) but not downregulated KHSRPP1 (OR: 1.002; 95% CI: 0.998–1.006; P=0.348).

To further explore the interaction between lncRNAs and mRNAs in essential hypertension with LVH, we created a coding–noncoding gene co-expression network. Overall, 13 coding genes were correlated with RP11-327F22.4 (PCC≥0.8), and 29 with KHSRP11 (PCC≥0.8). Notably, these relationships do not indicate a direct interaction between the two molecules. On bioinformatics analysis, the functions of the coding genes for the two lncRNAs were closely related to cell activation, cell chemotaxis and wound healing at the biological process level. On KEGG pathway analysis, the two lncRNA-related coding genes were mainly involved in neuroactive ligand–receptor interaction, calcium signaling and Rap1 signaling pathways.

CONCLUSIONS In conclusion, we have shown that two lncRNAs, RP11-327F22.4 and KHSRPP1, are significantly dysregulated in patients with hypertensive LVH and may be associated with the pathogenesis of cardiac hypertrophy. Although the molecular mechanism and function of these two lncRNAs are still unclear, they might be closely related to hypertensive LVH pathogenesis. These findings encourage future studies to explore the function and mechanism of lncRNAs in the pathogenesis of cardiac hypertrophy.

GW30-e0847

Comparative characteristics of β-adrenoblockers and their influence on the quality of life in patients with arterial hypertension

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OBJECTIVES Arterial hypertension – one of the most common diseases of the cardiovascular system and its treatment of questions remain urgent problem of preventive cardiology Purpose: To study the comparative characteristics of β-blockers and their impact on the quality of life of patients with arterial hypertension.

METHODS The examination included 130 patients aged 30–59 years with arterial hypertension. Quality of life and compliance to treatment in case of a long-term monotherapy with different β-blockers: propranolol (23 patients), metaprolol (21 patients), nadolol (28 patients), atenolol (18 patients), bioprolol (16 patients) and nebivolol (24 patients) were studied in a comparative aspect. Treatment compliance studied according to the Morisky-Green General questionnaire, and the quality of life according to the General Well Being Questionarie (GWBQ).

RESULTS In general, with monotherapy, all studied β- blockers had a sufficient antihypertensive effect, however, target blood pressure levels were achieved with atenolol, nebivolol and bisoprolol, and a less pronounced antihypertensive effect was observed in propranolol compared with other – β-blockers. The negative chronotron effect was more pronounced in nadolol, the remaining β-adrenoblockers equally reduced the heart rate. A comparative analysis of changes in the quality of life in monotherapy with different β-adrenoblockers showed that the best parameters of the quality of life were found in the treatment with nebivolol (87.5%), then bisoprolol (81.3%), followed by atenolol (72.2%), metaprolol (71.5%), nadolol (67.8) and to a lesser extent, a positive effect the quality of life is observed in propranolol (43.5%).

CONCLUSIONS Summing up the results of long-term, long-term continuous monotherapy with various β-blokers, it can be stated that, along with stable antihypertensive efficacy and good tolerability with a relatively low incidence of side effects, different β-adrenoblockers have different effects on the quality of life and patient adherence to treatment. The greatest compliance and improvement of the quality of life is observed in patients taking nebivolol, the smallest among those treated with propranolol.

GW30-e0897

Concomitant hypertension is associated with higher mortality and morbidity in patients hospitalized for cancer

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OBJECTIVES Hypertension (HTN) is the most common comorbidity in patients with cancer. Meanwhile, chemotherapy and radiotherapy for the cancer treatment were found to be associated with the development or worsening

of HTN. This study aimed to investigate the impact of HTN on the in-hospital outcomes of patients admitted for cancer.

METHODS We conducted a retrospective cohort analysis of the National Inpatient Sample 2016 database. Patients hospitalized with a principal diagnosis of cancer were identified using the ICD-10 codes. Multivariate logistic regression was performed after adjustment for patient and hospital demographics, and relevant comorbidities. Inpatient mortality was compared between the patients with and without HTN.

RESULTS A total of 1,022,625 hospitalizations with cancer were identified. Of these, 565,430 (55.29%) had HTN. Multivariate logistic regression analysis after adjustment showed that patients with both cancer and HTN had lower in-hospital mortality (4.44 vs. 5.18%, OR 0.71, 95% CI 0.68–0.75, P<0.001) but similar length of stay (LOS) (6.69 vs. 6.32 days, P=0.389) when compared to patients with cancer but no HTN. Further study of the cancer subgroups revealed that HTN was associated with lower mortality than non-HTN in lung cancer (OR 0.73, 95% CI 0.65–0.81, P><0.001), colon cancer (OR 0.81, 95% CI 0.66–0.99, P=0.043), liver cancer (OR 0.67, 95% CI 0.52–0.86, P=0.002), pancreatic cancer (OR 0.79, 95% CI 0.63–0.99, P=0.037), prostate cancer (OR 0.45, 95% CI 0.29–0.70, P><0.001), bladder cancer (OR 0.50, 95% CI 0.35–0.71, P><0.001), kidney cancer (OR 0.43, 95% CI 0.28–0.67, P><0.001), and leukemia (OR 0.71, 95% CI 0.60–0.83, P><0.001), While, the in-hospital mortality in esophageal cancer, stomach cancer, rectal cancer, breast cancer, ovary cancer, lymphoma, melanoma, and brain cancer were similar between patients with and without HTN. Patients with cancer and HTN had higher rate of in-hospital morbidities including ventricular fibrillation/tachycardia (OR 1.83, P><0.001), respiratory failure (OR 1.33, P><0.001), acute kidney injury (OR 2.04, P><0.001), stroke/TIA (OR 2.41, P><0.001), intubation (OR 1.22, P><0.001), major bleeding (intracranial bleeding and acute GI bleeding) (OR 1.22, P><0.001), complete heart block (OR 2.09, P><0.001), red blood cell transfusion (OR 1.22, P><0.001), but less likely to have cardiac tamponade (OR 0.90, P=0.012), and platelet transfusion (OR 0.86, P><0.001).

CONCLUSIONS HTN is associated with lower inpatient mortality in patients hospitalized for cancer. This effect might due to anti-hypertensive medications treatment. Further large prospective studies are needed.

GW30-e0922

Association between non-high-density lipoprotein cholesterol levels and new-onset left ventricular hypertrophy in hypertensive patients

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OBJECTIVES Left ventricular hypertrophy (LVH) is a risk factor of cardiovascular and cerebrovascular diseases, especially in hypertensive patients. We designed this study to investigate the unidentified association between non-high-density lipoprotein cholesterol (non-HDL-C) and new-onset LVH.

METHODS In this retrospective cohort study, we enrolled 834 hypertensive participants with normal echocardiographic left ventricular mass index (LVMI) at baseline and a readable echocardiogram at the end of follow-up. We used multivariable logistic regression to estimate the association between non-HDL-C levels and new-onset LVH.

RESULTS Over a 4-year period, 210 (25.2%) participants progressed to LVH. The incidence of new-onset LVH decreased with increases in non-HDL-C levels from baseline, from the lowest (27.2%) to the middle (25.2%) and the highest (22.7%). After adjustment for confounding factors, the odds ratios (95% confidence interval) of non-HDL-C levels for new-onset LVH in the middle tertile group and the highest tertile group were: 0.840 (0.537–1.313), 0.606 (0.396–0.926), respectively (P trend=0.019). And each 1 mmol/L increase in non-HDL-C levels resulted in a 20.3% lower risk of incident LVH.

CONCLUSIONS In our community-based, retrospective cohort study, non-HDL-C level is negatively related to new-onset LVH.

GW30-e0981

The Usefulness of albumin/creatinine ratio and Plaque in Carotid Artery (PCA) as a predictor of subclinical cardiovascular risk factor in hypertensive patients with metabolic syndrome

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OBJECTIVES The aim of this study was to assess if the usefulness of albumin/creatinine ratio (ACR) and plaque in carotid artery (PCA) could be independent from MetS in hypertensive patients

METHODS We identified 100 participants with hypertension with metabolic syndrome. CIMT and PCA were evaluated by ultrasonography. ACR was obtained from first morning urine specimens. MetS was defined according to the National Cholesterol Education Program (USA) Adult Treatment Panel III classification.

RESULTS Hypertensive patients with MetS had a significantly higher prevalence of a CIMT>0.85 mm (P=0.001) and PCA (P<0.001) as compared with participants without MetS. CIMT was significantly correlated with fasting triglycerides and fibrinogen levels both in participants with MetS and in those without MetS (all P<0.01). Univariate linear regression analysis showed a positive relationship between ACR and PCA, Regression models including ACR, showed that only ACR, BMI, hypertension duration and systolic blood pressure (SBP) were independently associated with ACR.

CONCLUSIONS MetS or hypertension are associated with increased risk of subclinical atherosclerosis. Screening for ACR and PCA in hypertensive patients with MetS may identify at high risk subset for cardiac and renal subclinical organ damage.

ARRHYTHMIAS

GW30-e0034

The value of index beat in evaluating left ventricular systolic and diastolic function in patients with atrial fibrillation: a dual pulsed-wave doppler study

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OBJECTIVES Atrial fibrillation (AF) causes turbulence of LV function status and poses challenges for rapid and accurate assessment of myocardial function by echocardiogram. The index beat assessment of LV systolic function has been shown to agree well with the average method. But whether it is applicable to measurement of Doppler LV systolic and diastolic function parameters has not been fully studied. Recently, the dual Doppler technique allows simultaneous demonstration of flow-tissue pulse wave, hence it facilitates the recording of mitral E wave, systolic (s′) and diastolic (e′) mitral annular motion velocity in the same cardiac cycle. Therefore, E/e′ and s′ can be acquired during the same beat in AF patients. The aim of this study was to assess the value of index beat in assessing s′ and E/e′ using dual pulse wave Doppler technique.

METHODS A total of 50 AF patients were prospectively enrolled for a comprehensive echocardiography study. Dual pulse-wave Doppler technique was used to obtain trans-mitral flow and mitral annular motion velocity simultaneously from apical 4-chamber view. Ten beats were acquired for analysis in each patient. The ratio of peak early mitral inflow velocities (E) and septal and lateral mitral annulus velocity (e′), i.e., E/e′, and peak systolic mitral annular motion velocity (s′) were simultaneously acquired at each cardiac cycle. The index beat was determined if the ratio of the preceding RR interval/pre-preceding RR interval equals 1 (0.95~1.06). Difference, correlation and agreement were assessed between the values (s′ and E/e′) at the index beat, the preceding as well as the ensuing beat and the corresponding mean value.

RESULTS The index beat was identified in only 27 patients for septal analysis, and 22 patients for lateral wall analysis. The mean s′ and E/e′ measured by dual Doppler technique showed no significant difference to the value measured by conventional single Doppler average of 5 beats (both P>0.05). The index beat s′ showed the highest correlation (r=0.96 for septal wall and 0.92 for lateral wall, both P=0.000) with the mean value. While E/e′ at the pre-index beat, instead of the index beat initiated cycle had the best correlation with the mean value (r=0.88 for septal wall and 0.97 for lateral wall, both P=0.000). Bland-Altman analysis showed good agreement between index beat s′ and mean s′, and between E/e′ at the pre-index beat and the mean E/e′ across a wide range.

CONCLUSIONS Measurement of LV systolic function in AF patients from the index beat was representative of the mean value from multiple beats. However, it is E/e′ from the pre-index beat, rather than from the index beat, that correlates best with the average value. This finding should improve decision making when choosing a representative beat for assessing LV systolic and diastolic function in patients with AF.

GW30-e0048

Systematic evaluation treatment effect of Fumai Decoction in patients with atrial fibrillation

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OBJECTIVES Recently, some scholars believed that Fumai Decoction (FMD) might cure patients with atrial fibrillation (AF), we systemic evaluated the efficacy and safety of FMD treatment for patients with AF in order to provide the basis for its extensive clinical application.

METHODS "FMD or Integrated traditional Chinese or Fumai Decoction or Chinese herbal medicine" and "atrial fibrillation or AF" were searched from Elsevier Science, Medline, ProQuest, PubMed, VIP, CNKI, Wanfang database. Inclusion criteria: (1) adult AF patients; (2) FMD treatment AF; (3) with definite control groups; (4) total efficacy and drug untoward reaction; and (5) with randomized controlled trials. Exclusion criteria: (1) with one article if the alike literature republished; (2) with animal and basic experimental literature; and (3) conference and essay articles. The extraction and quality assessment was assessed by two reviewers checking independently and crosswise, when differences appears, handle these through discussion or the third party. Evaluate quality according to the 4.2 standard of Cochrane system evaluation manual. The data analysis used for RevMen5.3 software. Dichotomous data were expressed as relative risk (RR) and continuous outcomes as mean differences (MD), while 95% confidence intervals (CI) were calculated for both. The results were shows the forest. Bias analysis applied by the funnel plot. Sensitive maps for sensitivity analysis by stata 15 software. The statistical heterogeneity was presented as significant when the I square (I^2) value exceeded 50% or P<0.05, we used random effect mode. When the absence of statistical heterogeneity (I^2<50% or P>0.05), we pooled data using the fixed effect mode. The differences were considered significant according to P<0.05.

RESULTS 21 Chinese articles of FMD treating AF patients were selected by screening literature, including 1905 patients totally (treatment group: 999, control group: 906). All the 21 articles mentioned "random". Three mentioned single blind method, but all literature did not method concealment and so on. Only 2 patients were withdrawed because of pulmonary infection. Quality grade was lower. Compared with control group, (1) the total efficacy of FMD treatment for AF patients were significantly increased (RR=1.23, 95% CI=1.15–1.33); (2) heart rate was significantly decreased (MD=–5.51, 95% CI=–10.25 to –0.76);3) AF cardioversion rate was enhanced in 14 days (RR=5.81, 95% CI=2.40–14.04) and 21 days (RR=3.05, 95% CI=1.69–5.50);4) the untoward reaction were significantly decreased (RR=0.28, 95% CI=0.17–0.46). Two subgroups were not heterogeneity whether or not combined with antiarrhythmic drugs group, whether or not elderly patients group (each I^2=0%), except for whether or not including paroxysmal AF groups (I^2=87.7%). The experimental results were firm by sensitive analysis. The funnel plot showed little bias.

CONCLUSIONS We believe that FMD has a role in the treatment of AF, It is worth widely using and popularizing in clinic practice.

GW30-e0049

Hydrochloride Guan Fu Base A treatment for cardiac arrhythmias patients – a meta analysis

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OBJECTIVES Our systemic evaluation of Acehytisine Guan Fu Base A (GFA) treatment for cardiac arrhythmia (CA) is to provide further basis for its wide application clinically.

METHODS "GFA" and "CA" were searched from CNKI, Wanfang database, VIP, PubMed, Medline, ProQuest, Elveset Science. Inclusion criteria: (1) adult patients with CA; (2) using GFA treatment of CA; (3) having control group; (4) observation of therapeutic effect; and (5) randomized controlled trial. Exclusion criteria: (1) case repeated; (2) animal and basic experiments; and (3) evidence-based medical experiments. Independent and cross-checked by two evaluators. When confronted with disagreements, the problem can be resolved through discussion or by inviting the third party to assist. Evaluate quality according to Cochrane System Evaluation Manual 4.2 standard. Dichotomous data were expressed as relative risk (RR), Continuous outcomes as mean differences (MDs), while 95% confidence intervals (CI) were calculated for both. The results was showed forest plot. Bias analysis applied by the funnel plot. The data analyzed by RevMen5.3 software. The statistical heterogeneity was presented as significant when the I square (I^2) value exceeded 50% or P<0.05, we used random effect mode. When the absence of statistical heterogeneity (I^2<50% or P>0.05), we pooled data using the fixed effect mode. The differences were considered significant according to P<0.05.

RESULTS 7 Chinese documents were included in this study by removing 74 and 9 from 90 relevant literatures, including 421 CA patients (247 cases of GFA group, 174 cases of control group). 7 articles were referred to as "random", only one article mentioned blindness, but not in other studies, such as blindness, experiment withdrawal and follow-up. One was compared with amiodarone. The others were compared with propafenone. Compared to control group, (1) the total effect of treatment group was significantly increased (RR=1.32, 95% CI=1.16–1.51), which were significant increased in the treatment of supraventricular tachycardia (RR=1.23, 95% CI=1.08–1.40) and ventricular premature beats (RR=2.10, 95% CI=1.22–3.64), they have not homogeneity (I^2=71.4%); (2) the CA recovery time of treatment group was significantly shorten (MD=–1.45, 95% CI=–2.79 to –0.11);3) PR intervals, QRS intervals and QTc intervals of treatment group was no significant difference (MD=–0.08, 95% CI=–17.04 to 16.88; MD=–2.87, 95% CI=–12.07 to 6.33; MD=–3.68, 95% CI=–16.05 to 8.69);4) untoward reactions of treatment group was no significant differences (RR=0.90, 95% CI=0.54–1.49). The funnel plot showed symmetry and roughly funnel form, indicating little bias.

CONCLUSIONS These results indicated that GFA has good therapeutic effect on CA, as supraventricular tachycardia and ventricular premature beats, and less adverse reactions and hence it can be used widely clinically.

GW30-e0088

Obesity is associated with the long-term outcomes of catheter ablation of atrial fibrillation in patients with dilated cardiomyopathy

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OBJECTIVES Patients with atrial fibrillation and dilated cardiomyopathy often exist exhibit cardiac function and poor prognosis. However, the specific reason is unclear. This study aimed to indicate the impact of obesity in patients with AF and DCM.

METHODS 74 consecutive patients with AF and DCM were enrolled in this study and were classified by BMI. The major endpoints were cardiac death, recurrent AF, recurrent atrial tachyarrhythmia (ATa), stroke and secondary endpoints.

RESULTS In multivariate analysis, overweight and obese group presented more incidence of re-AF (0.0 vs. 30.3 vs. 40.0%, log-rank P=0.048) and re-hospitalization (9.1 vs. 36.4 vs. 45.0%, log-rank P=0.035). The five-year outcomes of primary endpoints were inferior in overweight and obese group (18.2 vs. 30.3 vs. 50.0%, log-rank P=0.042). Overweight patients (from 39.1 to 50.0%, P=0.005) exhibited more benefit in LVEF recovery after ablation than normal weight group (from 43.1 to 52.3%, P=0.199) and obese group (from 44.9 to 51.2%, P=0.216).

CONCLUSIONS AF and DCM patients who were overweight or obese exhibited worse long-term outcomes in recurrent AF than patients with normal weight. However, overweight patients benefit most in cardiac function after ablation.

GW30-e0097

New diagnostic markers for identification of the highest risk group of sudden cardiac death in patients with coronary artery disease

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OBJECTIVES Sudden cardiac death (SCD) remains the leading cause of death. Ventricular tachyarrhythmias (VTA) are the main cause of SCD. The incidence of VTA and SCD in coronary artery disease (CAD) patients still is a hot spot in cardiology. The implantable cardioverter-defibrillator (ICD) is the main method of SCD prevention. However, only 15–25% patients after ICD implantation have VTA events. So, it's necessary to find out new predictors of VTA. And aim of our research was to study the diagnostic value of left ventricle ejection fraction (LVEF) assessment, myocardial perfusion (MPS) and cardiac 123I-methaiodobenzylguanidine (123I-MIBG) scintigraphy in the VTA prediction in patients with CAD.

METHODS 51 patients (male – 41, average age 65.4±6.9 year) with CAD were examined. All patients were divided into 2 groups according to the ICD implantation indications (primary and secondary SCD prevention). Before ICD implantation, patients underwent echocardiography, MPS with 99mTc-methoxy-isobutyl-isonitrile (99mTc-MIBI) and cardiac 123I-MIBG scintigraphy. During 6th month follow-up, VTA events were documented in each group. Data of LVEF, MPS and cardiac 123I-MIBG scintigraphy before ICD implantation were compared in each group between patients with and without VTA events.

RESULTS The 1st group consisted of 21 (41.1%) patients with primary prevention indications (male – 19, age 63.2±7.7 years), 18 patients of them have VTA (3 patient have successful ventricular antitachypacing and 15 patients have nonsustained VTA) and 3 patients from this group don't have VTA events. The 2nd group consisted of 30 (58.9%) patients with secondary prevention indications (male – 22, age 6639±8.6 years), 19 patients of them have VTA (1 patient have successful ICD shock therapy, 9 patients have successful ventricular antitachypacing and 9 patients have nonsustained VTA) and 11 patients from this group don't have VTA events. In 1st group there were significant differences between patients with and without VTA before ICD implantation in terms of: average accumulation defect index of 123I-MIBG on early (SSe%) (29.55±14.97 vs. 11.33±6.35% (P=0.006)) and delayed (SSd%) scintigrams (36.77±14.72 vs. 18.66±4.04% (P=0.03)) and accumulation defect of 99mTc-MIBI – 19.16±12.34 vs. 6.01±3.61% (P=0.01), respectively. In 2nd group there were significant differences between patients with and without VTA before ICD implantation in terms of: LVEF – 50.6±9.2 vs. 64.1±7.9% (P=0.0006), average SSe of 123I-MIBG (31.68±17.71 vs. 7.36±2.24% (P=0.0002)) and SSd (33.05±18.08 vs. 9.36±3.93% (P=0.0001)) and accumulation defect of 99mTc-MIBI – 24.57±15.82 vs. 7.48±7.01% (P=0.001), respectively.

CONCLUSIONS Myocardial perfusion and cardiac sympathetic activity radionuclide assessment, as well as LVEF assessment, can be used for identification of the highest risk group of SCD.

GW30-e0105

PR interval prolongation in patients with acute ST-segment elevation myocardial infarction

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OBJECTIVES The relationship between PR interval prolongation and long-term prognosis in patients with acute ST-segment elevation myocardial infarction (ASTEMI) has not been elucidated. This study aimed to evaluate the prevalence, predictors and outcomes of PR interval prolongation in a prospective cohort of post-STEMI patients.

This study aimed to evaluate the prevalence, predictors and outcomes of PR interval prolongation in a prospective cohort of post-STEMI patients.

METHODS We measured the PR interval in 915 patients with ASTEMI and classified them into those with (>200 ms) and without (≤200 ms) PR interval prolongation. Among 915 patients with ASTEMI, 87 (9.5%) patients developed PR interval prolongation.

RESULTS Stepwise logistic regression analysis was used for exploring the potential predictors of PR interval prolongation. The mean level of calcium during hospitalization was strongly correlated with development of PR interval prolongation (Hazard Ratio [HR] 0.13; 95% Confidence Interval [CI] 0.027–0.66; P=0.01). During the mean follow-up period of 31 months (interquartile range: 22–39 months), 64 all-cause mortality (endpoint) were registered. After adjustment for confounding covariates in Cox regression analyses, PR interval prolongation was independently associated with worse outcomes (HR 5.37; 95% CI 1.85–15.62; P=0.002).

CONCLUSIONS Serum calcium obviously predicts the occurrence of PR interval prolongation in patients with ASTEMI and the prolongation of PR interval independently improves the prognostic value of long-term mortality.

GW30-e0112

Dingji Fumai Decoction combined with metoprolol versus metoprolol alone in the treatment of premature ventricular contractions: a randomized, double-blind, placebo-controlled trial

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OBJECTIVES Premature ventricular contractions (PVCs) are very common in clinical practice, and currently there is no evidence-based traditional Chinese medicine for treatment. We tested the efficacy and safety of Dingji Fumai Decoction (DFD) in the treatment of patients with PVCs.

METHODS The treatment group (50 patients) received DFD (1200 mg three times daily) combined with metoprolol (12.5 mg twice daily) and the control group (50 other patients) received metoprolol (12.5 mg twice daily) combined with placebo (1200 mg three times daily) for 4 weeks. At the baseline and endpoint, the clinical symptoms, signs, Holter, adverse events, laboratory examination and physical examination were determined in both groups and compared.

RESULTS The groups did not differ significantly in demographic and baseline clinical characteristics. The treatment group significantly decreased the TCM syndrome score (P=0.005) and the number of PVCs (P=0.047) compared with the control group. No adverse events occurred in this trial.

CONCLUSIONS The DFD seems to be safe and ameliorates the TCM syndrome score and the number of PVCs in the patients with PVCs.

GW30-e0136

Long-term efficacy of radiofrequency ablation with contact force sensing catheter in paroxysmal atrial fibrillation

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OBJECTIVES To compare the long-term efficacy after raidofrequency catheter ablation of paroxysmal atrial fibrillation (PAF) patients with contact force sensing catheter or traditional open- irrigated tip catheter.

METHODS Retrospectively analyze PAF patients who received initial circumferential pulmonary vein isolation (CPVI) in Shanghai General Hospital from January, 2013 to June, 2015. A total of 243 patients were enrolled, of whom 138 patients were divided into contact force sensing open- irrigated tip catheter group (ThermoCool Smarttouch® Catheter, Biosense Webster Inc, CA, USA; ST group) while 105 patients were divided into traditional open- irrigated tip catheter (ThermoCool Navistar; Biosense Webster Inc, CA, USA; TC group). Endpoint of the catheter ablation is bi- directional electrical isolation of left atrium and pulmonary vein. The duration of operation and X-ray exposure, rate of postoperation complications and long-term efficacy remaining in sinus rhythm were compared.

RESULTS Among 243 patients enrolled, the average age was 61.65±10.12 years old, 61.7% were male, 50.6% with hypertension, 12.3% with diabetes, 7.4% had a history of cerebral infarction, and 8.6% with congestive heart failure. There were no statistically significant differences in baseline clinical characteristics between the two groups, including age, gender, comorbidity, left atrial diameter, and left ventricular ejection fraction. All the patients enrolled completed CPVI and were confirmed bi-directional electrical isolation of left atrium and pulmonary vein. Compared ST group with TC group, the duration of operation was shorter and the duration of X-ray exposure was longer, but there was no significantly difference (196.20±52.2 vs. 198.6±36.6 min, P=0.486; 15.81±7.22 vs. 12.50±4.65 min, P=0.231). There were 2 cases of hematoma in the ST group. 1 case of hematoma and 1 case of pericardial tamponade appeared in the TC group. There was no significant difference in the incidence of complications between the two groups (P=0.782). The success rate at 1 year after PVI was significantly higher in the ST group than in the TC group (87.7 vs. 77.1%, P=0.03). After mean 53.0±3.7 follow-up, the success rate in the ST group was significantly higher than that in the TC group (82.6 vs. 71.4%, P=0.038).

CONCLUSIONS Contact force sensing open- irrigated tip catheter is associated with significantly improved long-term success rate after catheter ablation in patients with PAF.

GW30-e0224

Increased blood pressure was associated with prolonged electrocardiographic Tpeak-to-Tend/QT ratio in a general Chinese population

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OBJECTIVES Electrocardiographic Tpeak-to-Tend interval (Tpe), defined as the time interval between complete epicardial and myocardial repolarization, has been reported as a marker of ventricular arrhythmia and sudden cardiac death. More recently, it has been reported that recently diagnosed, untreated hypertensive outpatients had prolonged Tpe interval than those normotensive ones, which indicates that there might be some potential association between Tpe interval and blood pressure. Therefore, we aimed to examine the association between blood pressure (BP) and Tpe as well as Tpe/QT ratio in a general Chinese population.

METHODS A multi-stage, stratified cluster sampling across China during 2012–2013 was performed to select the representative Chinese adults aged 18–85 years old. 12-lead resting ECG was performed by using GE MAC-5500 with a sampling rate of 1000 Hz and analyzed automatically by utilizing Marquette 12SL algorithm in MUSE Cardiology Information System (GE Healthcare, USA). Only data from leads II, V2, V5 were investigated to limit the amount of statistical tests but cover most of the heart over different axes and planes. Participants were divided into five groups according to the latest hypertension guideline: 1. Optimal: Systolic blood pressure (SBP) was less than 120 mmHg and diastolic blood pressure (DBP) was less than 80 mmHg; 2. Normal: SBP was 120–129 mmHg and/or DBP was 80–84 mmHg; 3. High normal: SBP was 130–139 mmHg and/or DBP was 85–89 mmHg; 4. Grade 1 hypertension: SBP was 140–159 mmHg and/or DBP was 90–99 mmHg; 5. Grade 2 to 3 hypertension: SBP was more than 160 mmHg or and/or DBP was more than 100 mmHg. Generalized linear model adjusted for age, gender, center, smoking and body mass index, was used to assess the association between BP and Tpe (or Tpe/QT ratio).

RESULTS After an exclusion of potential ambiguous Tpe interval, 6251 participants with 47% female and a mean age of 47±14 years old were finally included from the nationwide study. Tpe was normally distributed with a mean of 90±14, 112±16 and 96±11 ms in leads II, V2 and V5, respectively. The average SBP was 125 mmHg and the average DBP was 81 mmHg. The aforementioned five groups had 31, 37, 16, 13 and 3% participants, respectively. After adjustment for age, gender, center, smoking and body mass index, Tpe/QT ratio was positively associated with increased SBP and DBP (P<0.01) while Tpe was not. Furthermore, Tpe/QT ratio increased with elevated BP categories (P<0.0001) while Tpe was associated with neither BP nor BP categories.

CONCLUSIONS Increased BP might relate to prolonged Tpe/QT ratio but not Tpe. Further study is warranted for clear definition of Tpe adjustment and pathophysiological mechanisms between BP and Tpe.

GW30-e0231

Genotype and clinical characteristics of congenital long QT syndrome in China

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OBJECTIVES Congenital long QT syndrome (LQTS) is a rare inheritable arrhythmic disorder which is linked to at least 15 genes. The clinical characteristics and genetic mutations may be variable among different population groups and they have not yet been studied in Chinese population.

METHODS Clinical characteristics were retrospectively reviewed from patients with congenital long QT syndrome whose blood samples were sent for genotyping during 1998–2018. Whole exome sequencing was used to identify variants in all other known LQTS genes. Sangers sequencing was used to sequentially identify LQTS-related genetic variants.

RESULTS Of the 87 subjects (60 families), 63% were female, mean QTc was 525.11±77.48 ms and total Schwartz's score was 4.62±1.39 points. Cardiac events occurred in 61 (70%) patients, and the average age when the first symptoms occurred was 18.08±1.86 years. Genetic studies were performed in all patients, and 74 patients had single pathogenic and likely pathogenic genetic variants (KCNQ1 in 13, KCNH2 in 45, SCN5A in 6, KCNJ2 in 3, KCNE1 in 1, AKAP9 in 4 and KCNJ5 in 2) and 14 patients had multiple LQTS-related mutations (LQTM). Totally 63 genetic variants (9 KCNQ1, 27 KCNH2, 3 SCN5A, 3 KCNJ2, 1 KCNE1, 3 AKAP9 and 1 KCNJ5) were confirmed, including 25 novel LQTS-related mutations. LQT1 patients experienced the majority of their events (99%) during exercise or stress, and only 1% occurred during fever. LQT2 patients developed symptoms under diverse conditions, including emotional stress (23%), noise (19%), arousal (16%), fatigue (16%), urination (6%), fever (3%), hunger (3%), posture change (10%), Menstruation (9%), postpartum (4.5%). LQT3 patients developed symptoms at rest (60%), during sleep (40%) or fever (20%). Cardiac event free survival was lowest in patients with LQTM (P=0.007). Treatment strategies included no active therapy in 36 (41%) patients and beta-blockers in 51 (59%) patients, including 15 (17%) patients combined with implantable cardioverter-defibrillators, 2 (2%) patients combined with pacemaker, 8 (9%) patients combined with left cardiac sympathetic denervation, and 5 (2%) patients combined with mexiletine. Over a median follow-up of 7.14±3.12 years, the annual cardiac event burden after treatment decreased significantly compared before treatment (1.29±1.83 vs. 0.16±0.36, P<0.0001).

CONCLUSIONS LQT2 was the most common subtype in Chinese patients and LQTM was the second most. life-threatening arrhythmias in LQTS patients tended to occur under specific circumstances in a gene-specific manner. Risk factors and outcomes in LQTS patients varied by genotype. Beta-blockers were effective in reducing cardiac events in LQTS patients.

GW30-e0242

Prognostic value of heart rate by Holter recording in hospitalized heart failure patients with atrial fibrillation

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OBJECTIVES Currently the predictive evidence of heart rate (HR) in heart failure (HF) with atrial fibrillation (AF) is limited. We attempted to investigate the role of HR in prognosis of HF patients with AF by Holter recording.

METHODS A prospective cohort study was conducted with hospitalized HF subjects with AF from January 2015 to September 2017. Patients were stratified into paroxysmal AF and persistent AF. We followed the patients until December 2017. The all-cause mortality was investigated. Univariate and multivariate logistic regression analysis was performed to explore the relationship of HR with prognosis in HF with paroxysmal and persistent AF. Areas under the curve (AUCs) were calculated to compare the prognostic value of different HR indexes.

RESULTS 267 HF patients with AF were screened for final analysis. It was illustrated that total beats (adjusted odds ratio: 1.37, 95% CI: 1.08–1.73, P=0.009), average HR (adjusted odds ratio: 1.47, 95% CI: 1.04–2.08, P=0.031) and maximum HR (adjusted odds ratio: 1.22, 95% CI: 1.02–1.46, P=0.028) were independently associated with all-cause mortality in HF with paroxysmal AF but not with persistent AF patients. The AUC of maximum HR-based Cox model was superior to that of resting HR for mortality in HF with paroxysmal AF (0.83 vs. 0.65, P=0.029). The best cutoff value of maximum HR was 148 bpm (sensitivity: 82.4%; specificity: 85.5%).

CONCLUSIONS Compared to resting HR, total beats, average HR and maximum HR can be better predictors for all-cause mortality in HF with paroxysmal AF patients. Moreover, the prognostic value for all-cause mortality on the basis of maximum HR in those paroxysmal AF group was significantly better than that of resting HR. Holter recording would be useful for prognosis in HF with paroxysmal AF, which still need to be identified in large randomized studies.

GW30-e0247

Serum gamma-glutamyltranspeptidase and risk of dabigatran-related bleeding in patients with non-valvular atrial fibrillation: a multicentre real-world prospective cohort study

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OBJECTIVES Evidence regarding the relationship between serum gamma-glutamyltranspeptidase (GGT) and risk of dabigatran-related bleeding in patients with non-valvular atrial fibrillation was limited. Therefore, we aimed to assess the association between GGT and bleeding in non-valvular atrial fibrillation patients treated with dabigatran.

METHODS A prospective cohort study was conducted at multicenter in China from February 2015 to December 2017. Participants completed the follow-up at outpatient reviews 3 months. The exposure and outcome variable were the GGT at the baseline and minor bleeding, respectively. Univariate and multivariate Cox proportional hazards models were used to assess the association between GGT and risk of bleeding.

RESULTS Overall 80 subjects occurred minor bleeding. Multivariate Cox proportional hazards models analysis showed that per 1 U/L increase in GGT was associated with a 2% reduced risk of bleeding (P=0.027). A non-linear relationship was detected between GGT and bleeding by using smooth curve fitting. Further, threshold and saturation effect analysis showed that the inflection point of GGT was 32 U/L. The effect sizes and the confidence intervals of the left and right sides of inflection point were 0.95 (0.91–0.98) and 1.00 (0.98–1.02), respectively. The association between GGT and bleeding was consistent in the different subgroups.

CONCLUSIONS The relationship between GGT and bleeding was non-linear. GGT levels less than 32 U/L was related to reduce dabigatran-related bleeding.

GW30-e0249

Relationship between body mass index and the risk of bleeding in Elderly patients with nonvalvular atrial fibrillation treated with dabigatran: a real-word cohort study

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OBJECTIVES Uncertainty remains regarding the relationship between body mass index (BMI) and the risk of bleeding in nonvalvular atrial fibrillation (NVAF), especially in elderly patients. We aimed to investigate the relationship between BMI and the risk of bleeding in elderly patients with NVAF treated with dabigatran.

METHODS A prospective cohort study was conducted at multicenter in China from February 2015 to December 2017. Participants completed the follow-up at outpatient reviews 3 months. The exposure and outcome variable were the BMI at the baseline and 3 months bleeding, respectively.

RESULTS Finally a total of 499 elderly NVAF patients were recruited, 47 participants occurred minor bleeding, the incidence rate was 9.42% (47/499). On multivariate Cox proportional hazards models analysis, for every 1 kg/m² increase in BMI, the risk of bleeding increased by 16% (95% confidence interval [CI]: 1.05, 1.27). When BMI was used as a categorical variable (<24 kg/m²; 24–28 kg/m²; ≥28 kg/m²), BMI ≥28 kg/m² was associated with increased risk of bleeding (hazard ratio [HR] 2.96, 95% CI: 1.15, 7.65 vs. BMI <24 kg/m²). Moreover, the Cox proportional hazards regression with cubic spline functions and smooth curve fitting showed that the relationship between BMI and bleeding was linear. The subgroup analyses was consistent in the different subgroups.

CONCLUSIONS Elevated BMI at baseline was association with the incidence of bleeding in elderly NVAF patient treated with dabigatran.

GW30-e0251

Peripheral leukocyte count and risk of bleeding in nonvalvular atrial fibrillation patients taking dabigatran: a real-world study

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OBJECTIVES The association between peripheral leukocyte count and bleeding events in nonvalvular atrial fibrillation (NVAF) patients treated with dabigatran remains unclear. We aimed to explore the association between leukocyte count and bleeding events after excluding other confounders.

METHODS A total of 851 NVAF patients treated with dabigatran (110 mg bid) were recruited from 12 centers in China from February 2015 to December 2017. Follow-up was completed by May 2018. The exposure and outcome variables were leukocyte count and bleeding. Multivariate Cox proportional hazards models were constructed to analyze independent associations, and a Cox proportional hazards regression with cubic spline functions and smooth curve fitting (penalized spline method) was used to address nonlinearity between leukocyte count and bleeding. The inflection point was calculated using a recursive algorithm, and then a two-piecewise Cox proportional hazards model for both sides of the inflection point was constructed.

RESULTS Bleeding events occurred in 87 participants. For every $1*10^9$/L increase in leukocyte count, the risk of bleeding increased by 11% (hazard ratio [HR] was 1.11, 95% confidence interval [CI]: 0.99–1.25). The inflection point of the leukocyte count was $6.75*10^9$/L. For leukocyte counts $<6.75*10^9$/L, the HR and 95% CI were 0.88 and 0.69–1.13, respectively. For leukocyte counts $\geq 6.75*10^9$/L, the HR and 95% CI were 1.28 and 1.09–1.51, respectively.

CONCLUSIONS A high leukocyte count at baseline was associated with an increased risk of bleeding in a nonlinear pattern. Leukocyte counts greater than $6.75*10^9$/L in NVAF patients treated with dabigatran are associated with an increased risk of bleeding.

GW30-e0254

Relationship between changes of total bilirubin and bleeding events in nonvalvular atrial fibrillation patients taking dabigatran: a real world study

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OBJECTIVES There is still a lack of effective biomarkers for predicting the risk of dabigatran-related bleeding events. Therefore, we aimed to investigate the relationship between changes of total bilirubin (△TBIL) equals the difference of serum total bilirubin at 3-month follow-up from baseline serum total bilirubin and the risk of dabigatran-related bleeding events in patients with nonvalvular atrial fibrillation (NVAF).

METHODS A total of 486 NVAF patients treated with dabigatran (110 mg bid) were recruited from 12 centers in China from February 2015 to December 2017. Everyone was followed 3 months. Cox proportional hazard regression analysis was used to evaluate the association between △TBIL and risk of bleeding.

RESULTS The mean (SD) follow-up duration was 81.2 (20.2) days. 67 patients occurred bleeding events. Smooth curve fitting showed a U-shaped curve between △TBIL and bleeding. We further calculated the inflection point of the △TBIL was 6.63 μmol/L. The effect values and 95% confidence intervals (CI) on the left side and the right side of the inflection point were 0.90 (0.84, 0.96) and 1.35 (1.14, 1.60), respectively.

CONCLUSIONS Our findings showed a U-shaped relationship between △TBIL and dabigatran-related bleeding. The inflection point of △TBIL was 6.63 μmol/L.

GW30-e0263

Atrial arrhythmia of catecholaminergic polymorphic ventricular tachycardia patients in China

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OBJECTIVES Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a lethal autosomal dominant heritable arrhythmia syndrome and it is characterised by a normal baseline electrocardiogram (ECG), the occurrence of bidirectional ventricular tachycardia (bVT) or polymorphic ventricular tachyarrhythmias (pVT) induced by adrenergic stress. However atrial arrhythmia is rarely described in previous studies.

METHODS A retrospective analysis of all 24-hour ambulatory ECG and exercise treadmill test data for 20 patients with CPVT diagonosed in the Department of Cardiology of Beijing Tsinghua Changgung Hospital and Peking University People's Hospital between September 2006 and March 2019.

RESULTS During 24-hour ambulatory ECG test, atrial arrhythmia is common in CPVT patients. Thirteen cases (13/20, 65%) were present with frequent atrial premature contractions, in addtion two patients (2/20, 10%) had paroxysmal atrial tachycardia. Besides ventricular arrhythmias triggered during the treadmill exercise test, the presence of atrial Arrhythmias also may be associated with CPVT patients. Atrial arrhythmia existed in 15 patients (15/20, 75%), in which isolated premature atrial contractions (PACs) only were common (11/15, 73%), one case (1/15, 7%) showed only atrial tachycardia and thiree remaining child (3/15, 20%) was recorded exercise-induced PACs and atrial tachycardia. Referring to twelve cases with PACs, the atrial threshold heart rate was 88.5±25.1 beats/minute, while ventricular premature contractions (PVCs) threshold heart rate of twelve cases was 119.4±19.1 beats/minute, there was a statistically significant difference between them ($P<0.05$), namely atrial arrhythmias threshold heart rate was significantly lower than ventricular arrhythmias. Meanwhile, atrial arrhythmia was not always benign as ventricular fibrillation could be induced by atrial arrhythmia, and he had an operation of atrial tachycardia ablation.

CONCLUSIONS Atrial arrhythmia is common in CPVT patients and was not always benign.

GW30-e0274

Thoracoscopic left atrial appendage excision plus atrial fibrillation ablation as a secondary prevention strategy against stroke: initial experience and two year outcome data

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OBJECTIVES Atrial fibrillation (AF) patients with a previous stroke are often at a high risk of recurrent stroke and bleeding. Anticoagulation therapy in such patients is a challenging dilemma. Currently, thoracoscopic left atrial appendage excision (LAAE) plus AF ablation is an interventional approach offered to some AF patients. We hypothesized that this approach may be suitable as a secondary stroke prevention strategy for these high-risk patients.

METHODS Between January 2013 and December 2016, a total of 44 patients (26 male; mean age 65.0±9.1 years) with nonvalvular AF and a previous stroke or systemic thromboembolic event were enrolled in our study. The patients underwentthoracoscopic LAAE plus AF ablationby experienced operators and were followed up for 2 years (at 1, 3, 6, 9, and 12 months postoperatively and every 6 months thereafter). Thromboembolic and major bleeding events were recorded. Cerebral computed tomography or magnetic resonance imaging and 7-day Holter monitoring were performed annually.

RESULTS Mean CHA2DS2-VASc and HAS-BLED scores were 4.2±1.2 and 3.3±0.7, respectively. All patients discontinued oral anticoagulation (OAC) therapy after the surgical intervention. One patient suffered a periprocedural transient ischemic attack, and another was diagnosed with a new ischemic stroke at 491 days after surgery. The annual rate of total thromboembolism was 2.05%. No deaths or major bleeding events were observed postoperatively. The rate of successful AF ablation with no AF recurrence is 76.3%.

CONCLUSIONS Trans-thoracoscopic LAAE plus AF ablation may be a promising approach for this high-risk population. Thromboembolism prevention in this secondary prevention cohort was low, even without OAC treatment.

GW30-e0276

Nonfluoroscopic radiofrequency catheter ablation of idiopathic outflow tract ventricular arrythmias guided by Carto3 electro-anatomic mapping system

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OBJECTIVES To compare the efficacy and safety of radiofrequency catheter ablation (RFCA) guided by the 3-dimensional electro-anatomic mapping system (Carto3 electro-anatomic mapping) with fluoroscopy or nonfluoroscopy on ventricular outflow tract idiopathic ventricular arrythmias (VOT-IVAs).

METHODS From January 2016 to April 2017, 103 cases of premature ventricular contractions (PVCs) and ventricular tachycardias (VTs) from ventricular outflow tract were treated with radiofrequency catheter ablation under the guidance of Carto3 in the Department of Cardiology, First Affiliated Hospital of the Army Military Medical University: 53 cases underwent radiofrequency ablation under conventional Carto3 mapping (with fluoroscopy group), and 50 cases underwent radiofrequency ablation without radiography under Carto3 mapping (with nonfluoroscopy group). The anatomical construction of the target area, mapping time, ablation time, X-ray exposure time, total procedure time, and complication rate were compared between the two groups; observation and follow-up efficacy.

RESULTS The fluoroscopy group was shorter than the nonfluoroscopy group in the time of anatomical construction of the target area and mapping, ablation time, fluoroscopic time and the total procedure time (P<0.05). The difference was statistically significant. The immediate success rates were both 100% in two groups, the success rates of 3 days after RFCA were similar in both groups, 98.0% (49/50) in the fluoroscopy group and 96.2% (51/53) in the nonfluoroscopy group (P=0.618), the difference between two groups was not statistically significant; At the follow-up of 1 month and 3 months after RFCA, there were no recurrence cases in both groups, and the success rates were both 100%. There were no serious complications in the two groups during and after operation.

CONCLUSIONS The radiofrequency catheter ablation on ventricular outflow tract idiopathic ventricular arrythmias guided by the 3-dimensional electroanatomic mapping system achieved significant success rates in both the nonfluoroscopy group and the fluoroscopy group. Both methods are safe and effective. The radiofrequency catheter ablation under the guidance of Carto3 without X-ray is safe and effective in the treatment of outflow tract idiopathic ventricular arrhythmia, and it can be clinically applied in cardiac centers with extensive experience in the operation of radiofrequency ablation catheters.

GW30-e0383

Serum Chemerin was associated with the left atrial electrical and anatomical remodeling in patients with atrial fibrillation

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OBJECTIVES To investigate the relationship between serum Chemerin levels and left atrial electrical and anatomical remodeling in patients with atrial fibrillation (AF).

METHODS A total of 322 AF patients (109 paroxysmal and 213 persistent) admitted to the Department of Cardiology from January 2016 to May 2019 were enrolled, including 208 males and 114 females. The average age was 66.8±10.2 years. Another 100 gender- and age-matched patients with sinus rhythm were selected as the control group. Serum levels of Chemerin were measured by ELISA and compared between two groups. In addition, AF patients would further receive 12-lead ECG (Patients with persistent AF received ECG after cardioversion or ablation) and echocardiography to determine the P wave dispersion, left atrial diameter, and left atrial volume. Multivariate linear regression was used to analyze the correlation between serum Chemerin levels and the above indicators in AF patients.

RESULTS Serum Chemerin levels were significantly elevated in AF patients when compared to patients with sinus rhythm (20.68±4.22 pg/mL vs. 11.24±3.75 pg/mL, P<0.001). Furthermore, serum Chemerin levels were higher in patients with persistent AF when compared to patients with paroxysmal AF (22.47±5.02 pg/mL vs. 16.48±3.97 ng/nL, P<0.001). For AF patients, after adjusting for age, gender, AF duration, and medication, multivariate linear regression analysis showed that serum Chemerin levels were positively associated with the P wave dispersion [β(SE)=3.808 (0.564), P<0.001], maximum P-wave duration [β(SE)=4.305 (0.615), P<0.001], left atrial diameter [β(SE)=1.764 (0.305), P<0.001], left atrial maximum volume [β(SE)=1.424 (0.244), P<0.001], and left atrial minimum volume[β(SE)=1.158 (0.172), P<0.001].

CONCLUSIONS Serum Chemerin levels are significantly elevated in AF patients, and positively correlated with the left atrial electrical and anatomical remodeling.

GW30-e0450

Sex-related differences in catheter ablation of atrial fibrillation: a systematic review and meta-analysis

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OBJECTIVES The sex-related differences in the clinical outcomes of rhythm and safety after catheter ablation remain unclear. The purpose of this study was to compare the clinical outcomes of catheter ablation for atrial fibrillation (AF) in women and men.

METHODS The Medline and EMBASE databases were searched for published articles up to December 2018. Studies that met our predefined inclusion criteria were included. The primary endpoints were freedom from AF/atrial tachycardia (AT) recurrence, stroke/transient ischemic attack (TIA) and all-cause mortality. Random-effects modeling was used to calculate odds ratio (OR) and 95% confidence interval (CI) for each endpoint.

RESULTS After literature search and detailed assessment, 19 observational studies (151,370 patients; 34% women) were identified. Our analyses showed that the rate of freedom from AF/AT recurrence was lower in women than men at the 2.4-year follow-up (OR: 0.75; 95% CI 0.69–0.81; P<0.0001). Moreover, women had an increased risk of stroke/TIA (OR: 1.42; 95% CI 1.21–1.67; P<0.0001) and all-cause mortality (OR: 1.53; 95% CI 1.02–2.28; P=0.04). Nevertheless, for the endpoint of all-cause mortality, there was no significant difference between the two genders in the subgroup of prospective studies (OR: 1.19; 95% CI 0.69–2.05; P=0.53). Additionally, women were more likely to experience major complications compared with men (pericardial effusion/tamponade, major bleeding requiring transfusion and pacemaker implantation).

CONCLUSIONS Women who underwent catheter ablation of AF might experience lower efficacy and a higher risk of stroke/TIA and major complications than men. The reasons for these sex-related differences need to be further studied.

GW30-e0466

Bioinformatics analysis of circular RNAs expression profiles of atrial fibrillation based on GEO database chip

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OBJECTIVES To perform bioinformatics analysis on the genetic chip data of patients with atrial fibrillation (AF), in order to investigate the expression profiles of circular RNAs (circRNAs) and proposed circRNA–microRNA (miRNA) regulatory network in atrial fibrillation (AF).

METHODS Gene chip data in GEO database was used to screen out AF information chip and differentially expressed circRNAs in AF were selected. Several differentially expressed circRNAs were chosed for MREs. Co-expression networks of circRNA–miRNA were constructed based on the correlation analyses between the differentially expressed RNAs. We used arraystar's home-made target prediction software based on TargetScan, miRDB and miRTarBase to predict mRNA, to further demonstrate microRNA/mRNA interaction. The Gene Ontology (GO) enrichment analysis of mRNAs was performed to predict the potential functions of the differentially expressed genes and for functional annotation of mRNAs. The Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis was performed to explore the signal pathways invovled significantly.

RESULTS Compared with healthy controls, there were 1317 circRNAs differentially expressed in AF through a combination of statistical significance. Among them, 823 were up-regulated, and 494 were down-regulated. We constructed correlated expression networks between circRNAs and miRNAs. Furthermore, hsa—circ—0058792, hsa—circ—0045114, and hsa—circ—0058794 interacted with 3 miRNAs, miR-6077, miRNA-7-5p and miRNA-6079 simultaneously. The GO and KEGG pathway enrichment analysis of target genes in hsa—circ—0006867-miRNA-mRNA axis were executed to determine the principal functions and to investigate the potential signal pathway involved in AF. We found that the most significantly enriched GO terms were ubiquitin-protein transferase activity (GO:0004842) and ubiquitin-like protein transferase activity (GO:0019787). And the significantly enriched KEGG pathways were TGF-beta signaling pathway (hsa04350), MAPK signaling pathway (hsa04010), ubiquitin mediated proteolysis signaling pathway (hsa04120), signaling pathways regulating pluripotency of stem cells (hsa04550), and longevity regulating pathway (hsa04211) and so on.

CONCLUSIONS Our findings provided a novel perspective on circRNAs involved in AF and establish the foundation for future research of the potential roles of circRNAs in AF. Otherwise, we deliveried a novel strategy for research the potential ralationship between different RNAs in circRNA-miRNA-mRNA axis.

GW30-e0478

Left-side heart structures and association with all-cause mortality in patients with hypertrophic cardiomyopathy following pacemaker implantation: results from a single centre

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OBJECTIVES To examine the association between left atrial diameter (LAD), left ventricular end-diastolic diameter (LVEDD), and long-term risk of all-cause mortality in adults with hypertrophic cardiomyopathy (HCM) following pacemaker implantation over 5-year follow-up.

METHODS A total of 103 adult patients with HCM admitted to our Arrhythmia Center for symptomatic bradycardia and received pacemaker implantation from November 2002 to June 2013 were enrolled. During follow-up, 9 were excluded for generator upgrading of an implantable cardiac defibrillator (ICD). We retrospectively evaluated the clinical characteristics in 94 patients (57.0±15.9 years, mean follow-up 7.3±3.4 years).

RESULTS The mean LAD was 41.7±7.8 mm and the mean LVEDD was 45.7±6.6 mm. Overall, 25 died during follow-up, of which 68% were cardiovascular death. Based on the receiver operating characteristic curve, the cut-off value of LAD=43.5 mm was identified to predict all-cause mortality, with sensitivity and specificity of 0.722 and 0.732, respectively. The cut-off value of LVEDD=42.5 mm was identified to predict all-cause mortality, with sensitivity and specificity of 0.944 and 0.482, respectively. In the Kaplan-Meier survival, LAD≥43.5 mm and LVEDD≥42.5 mm were both associated with all-cause mortality (log-rank test P<0.05). Cox regression analysis indicated that LAD≥43.5 mm (HR 3.254; 95%CI=1.043–10.158, P=0.042) and LAD as a continuous variable (HR 1.072; 95%CI=1.009–1.139, P=0.025) were significantly independent predictors of all-cause mortality, while LVEDD≥42.5 mm was not significantly associated with all-cause mortality in the multivariate model but in the univariate model.

CONCLUSIONS In HCM patients with pacemaker implantation, LAD was an independent predictor for all-cause mortality, especially with a cut-off value of 43.5 mm.

GW30-e0501

Preferential conduction through cavotricuspid isthmus revealed by ultra high resolution mapping in typical flutter

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OBJECTIVES Linear ablation of the cavotricuspid isthmus (CTI) has been recognized as a highly successful and safe technique in the treatment of typical atrial flutter. However, it could be extremely difficult in some patients. The possible explanation would be complex and individual anatomy of the CTI. And the anatomic property could be translated into different activation patterns through the CTI. The purpose of this study was to test the hypothesis that CTI conduction is not in step and preferential conduction could be revealed by ultra high-resolution mapping.

METHODS A total of 28 patients with typical flutter were included between September 2016 to August 2018 (average age: 52 ±16 years, right atrium: 39±5 mm, left ventricular ejection fraction: 60±9%). High-resolution 3D mapping (Rhythmia mapping system, Boston Scientific, Natick, Massachusetts) was performed. Maps were analyzed retrospectively to characterize wave front propagation patterns in CTI region. The length of CTI, the width of preferential conduction area and their ratio were measured. The relationships between the ratio and termination or cycle length prolongation were also evaluated.

RESULTS 16 (57%) patients underwent previous cardiac surgery. 1 (3%) patient has received previous ablation in CTI. There are five different activation patterns through CTI (Figure 1). Type I in 4 patients (14%) was homogenous conduction without preferential wave front though CTI. Type II in 15 patients (53%) was with preferential wave font close to tricuspid annulus. Type III in 1 patients (3%) was with preferential wave front in the middle of CTI. Type IV in 7 patients (25%) was with preferential wave front close to inferior vena cava (IVC). Type V in 1 patients (3%) was with double preferential wave fronts. We found that the termination sites were exactly located at preferential wavefront in 18 of 28 patients (64%). The width of preferential wave front in termination group was shorter than those in non-termination group (16.6±1.0 mm vs. 23.3±3.4 mm, P=0.025). The cycle length (CL) prolongation (20 ms longer than baseline) before termination was noted in 16 of 28 patients (57%). However the width of preferential wave front in CL prolongation group was similar with those in non-prolongation group (18.4±1.5 mm vs. 19.8±3.0 mm, P=0.655). the relationship between the ablation reaction and the ratio (the width of preferential wave front and CTI) were showed in table 1.

CONCLUSIONS Activation conduction through CTI is heterogeneous. The preferential conduction was common and the majority was close to tricuspid annulus. If the preferential conduction is more apparent, it is more likely to terminate atrial flutter during ablation exactly at the preferential wave front site.

GW30-e0539

Effectiveness of coenzyme Q10 on arrhythmia in patients with heart disease: a meta-analysis

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OBJECTIVES Arrhythmia, is a common complication in patients with ischemic/non-ischemic heart disease and has been identified as an independent risk factor for increased cardiovascular events. Previous studies have suggested that coenzyme Q10 can reduce the incidence of arrhythmia in heart disease patients. In this study, we collected the existing evidence to conduct a comprehensive analysis on whether coenzyme Q10 can reduce arrhythmia of heart disease patients.

METHODS We performed a meta-analysis, searching EMBASE, PubMed, Web of Science and Cochrane Library from 1990 to 2018, for randomized controlled trials (RCTs) on coenzyme Q10 in patients with heart disease. Primary outcome was arrhythmia.

RESULTS We identified 6 RCTs enrolling 750 patients who fulfilled our inclusion criteria. When compared with conventional treatment alone, conventional treatment plus coenzyme Q10 was associated with significant decrease in arrhythmia for all enrolled patients (risk ratio [RR], 0.32; 95% confidence intervals [CI], 0.22–0.48). Furthermore, compared with conventional treatment alone, conventional treatment plus coenzyme Q10 could also reduce the incidence of arrhythmia in ischemic heart disease subgroup (RR, 0.31; 95% CI, 0.20–0.49), heart failure subgroup (RR, 0.36; 95% CI, 0.15–0.88), and coronary artery bypass grafting (CABG) subgroup (RR, 0.29; 95% CI, 0.17–0.50). Adverse events observed in 6 RCTs were not severe and resolved without special treatment.

CONCLUSIONS This meta-analysis indicated that coenzyme Q10 can reduce arrhythmia in patients with heart disease. However, further studies with more subjects, long-term follow-up, and evaluation of systemic adverse events are still required to verify the efficacy and safety of coenzyme Q10 on arrhythmia in heart disease patients.

GW30-e0554

Female sex independently predicts AF recurrence after catheter ablation in young patients: evidence from a large center

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OBJECTIVES We have reported female sex was a risk factor of AF recurrence after ablation in aged patients. It was unknown whether this result was applicable to young patients.

METHODS From November 2012 to November 2017, 185 young AF patients (mean age: 39.4±5.1; 31 females, 16.8%; 87 paroxysmal AF, 47%) were included at our center and underwent catheter ablation.

RESULTS After a median follow-up of 41 months (IQL: 25–56 months) and a mean of 1.2±0.5 (median 1, range 1–4) ablation procedures, 142 (76.8%) patients were in stable SR. A second procedure was performed for 36 patients, a third for 8 patients and a forth for 1 patients. Progression towards persistent AF was observed in 4 patients (4.6%). Survival analysis revealed that the ATa-free survival rate in women was significantly lower than that in men after initial and last ablation (P=0.006 and P=0.002). In multivariate analysis, LAD [HR 1.058 (95% CI 1.008–1.110) P=0.022], RA enlargement [HR 1.911 (95% CI 1.066–3.428) P=0.030], structural heart disease (SHD) [HR 2.022 (95% CI 1.147–3.565) P=0.015] and female sex [HR 2.303 (95% CI 1.299–4.084) P=0.004] independently predicted AF recurrence.

CONCLUSIONS Young AF patients can achieve a satisfactory long-term outcome after catheter ablation. Female sex, LAD, RA enlargement and SHD are predictors of atrial fibrillation recurrence after catheter ablation.

GW30-e0566

Surgical intervention for cardiac tamponade during ablation of AF: who and when? A single center experience

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OBJECTIVES Cardiac tamponade (CT) is the most common potential life threatening complication associated with radio-frequency catheter ablation (RFCA) for atrial fibrillation (AF). Based on current clinical practice, the decision of conservative therapy or surgical intervention remains unclear. The aim of this study is to retrospectively analyze the occurrence and management of CT during RFCA for AF in our experienced medical center.

METHODS All patients with a cardiac tamponade perforation who have undergone radio-frequency catheter ablation for atrial fibrillation in our center were included.

RESULTS Of 2890 procedures performed from 2013 to 2018, 28 (0.97%) patients occurred cardiac tamponade. Among them, the left atrium dimension was 35.5±3.7 mm on average. 22 (78.6%) patients were noted during ablation procedure, 6 (21.4%) patients were noted within 1 hour after the procedure. 25 (89.3%) patients were required to perform pericardiocentesis immediately. Ten patients underwent emergency surgical repairs due to the hemodynamic unstable state among whom the average of drainage was 2250 mL (627.5–3050). The perforation sites could be identified during the surgical repairs: 5

at right superior pulmonary vein, 2 at coronary sinus, 1 at left atrium appendage, 1 at left superior pulmonary vein and 1 at tricuspid isthmus, respectively. During the surgical procedure, Cox maze procedure (4/10) and left atrial appendage excision (2/10) were performed accordingly. The drainage volume was strongly associated with decision of surgical repair (OR: 1.003, P=0.033), the cutoff value was 400 mL (AUC: 0.919, sensitivity: 100%, specificity: 72.22%, P<0.001). No patient died of CT in our cohort.

CONCLUSIONS The incidence of CT (0.97%) was lower than 1% in our center. The annual incidence rate was 0.19%. Latent CT occured in 6 (21.4%) patients. The dimension of left atrium was small (35 mm) in patients with CT. The most common perforation site was RSPV. If the drainage was more than 400 mL during the procedure, emergency surgical repair should be recommended.

GW30-e0755

Electrogram dispersion guided driver ablation adjunctive to high-quality pulmonary vein isolation in atrial fibrillation of varying durations

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OBJECTIVES To investigate the role of driver mechanism at different stages of atrial fibrillation (AF) progression and to evaluate the effect of electrogram dispersion guided driver mapping and ablation in AF.

METHODS Two hundred and fifty-six consecutive AF patients who had undergone PVI plus driver ablation or conventional ablation were divided into 3 groups: paroxysmal AF (PAF, Group A, n=51), persistent AF (PsAF) (Group B, n=38); and long-standing persistent AF (LS-PsAF) (Group C, n=39). PVI was performed with guidance of ablation index. The electrogram dispersion was analyzed for driver mapping (Figure 1).

RESULTS The most prominent driver regions were at roof (28.0%), posterior wall (17.6%) and bottom (21.3%). With AF progression (groups A to C), the complexity of extra-PV drivers including distribution, mean number and area of dispersion region increased significantly (P<0.001) (Figure 2). Procedural AF termination rate showed significant differences between driver and conventional ablation (76.6% vs. 28.1%, P<0.001). With AF progression, the termination rate gradually decreased from group A to C, and the role of PVI in AF termination was also gradually weakened from group A to C (39.6%, 7.4% and 4.3%, P<0.001) in patients with driver ablation. At the end of the follow-up, the rate of SR maintenance was significantly higher in patients with driver ablation than those with conventional ablation (89.1% vs. 70.3%, P<0.001) (Figure 3).

CONCLUSIONS The formation of extra-PV drivers provides an important mechanism for AF maintenance and their complexity of drivers increase with AF progression. Electrogram dispersion guided driver ablation appears to be an efficient adjunctive approach to PVI for AF treatment.

GW30-e0766

Feasibility and efficacy of His-Purkinje conduction system pacing combined with atrioventricular node ablation in patients with persistent atrial fibrillation and implantable cardioverter defibrillator therapy

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OBJECTIVES Persistent atrial fibrillation (AF) may lead to higher probability of inappropriate shocks in heart failure (HF) patients with implantable cardioverter defibrillator (ICD) implantation. The aim of the study was to evaluate the impact of His-Purkinje conduction system pacing (HPSP) combined with atrioventricular node (AVN) ablation in preventing inappropriate shock therapy and improving heart function in these patients.

METHODS Ninety-six consecutive patients with persistent AF and HF who had indications for ICD implantation were enrolled from Jan, 2010 to Mar, 2018. With patients consent, HPSP with dual chamber ICD and AVN ablation was attempted in 62 patients, while the remaining patients underwent single chamber ICD implantation only. Left ventricular ejection fraction (LVEF), left ventricular end-systolic volume (LVESV), New York Heart Association (NYHA) heart failure classification, shock therapies and use of drugs were assessed during follow-up.

RESULTS Thirty-six patients received only ICD therapy, 1 of them failed AVN ablation (Group 1). AVN ablation combined with HPSP was successfully achieved in 62 patients (Group 2), 4 of who had prior single chamber ICD implantation (Figure 1). During follow-up, patients in group 2 had lower incidence of inappropriate shock (P<0.01) and adverse event (P=0.011). Meanwhile, improvements in LVEF (37.89±14.41% to 43.61±14.36% vs. 35.15±11.66% to 48.79±14.39%, P=0.01) and LVESV (138.27±68.37 mL to 127.37±82.86 mL vs. 126.03±67.35 mL to 82.11±58.01 mL, P<0.01) were significant in group 2 (Figure 2). NYHA class improved from a baseline 2.57±0.68 to 1.73±0.74 in group 1, from a baseline 2.73±0.59 to 1.42±0.53 in group 2.

CONCLUSIONS HPSP combined with AVN ablation is feasible and safe with high success rate in persistent AF patients with HF and ICD implantation. It can significantly reduce the incidence of inappropriate shocks and improve left ventricular function.

GW30-e0767

Risk factors of stroke in patients with atrial fibrillation after left atrial appendage (LAA) closure

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OBJECTIVES Left atrial appendage (LAA) closure is an attractive alternative for stroke prevention in patients with atrial fibrillation (AF). The risk of stroke in patients with AF after LAA closure is still lacking of thorough studies. Our objective was to evaluate the potential risk factors of stroke in patients with AF after LAA closure.

METHODS Non-valvular AF patients at high risk of stroke were enrolled in the study and underwent LAA closure. Follow-up was performed at 45 days, 6 months, and 12 months. Univariate Cox regression analysis was computed to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for exploring the potential risks for incidence of stoke after LAA closure. Multivariable Cox proportional hazards regression analysis was performed for exploring independent clinical predictors for stroke.

RESULTS The multivariate Cox proportional hazards regression analyses showed that the peri-device flow (HR=4.584, 95% CI: 1.65–12.739, P=0.004) and continue coagulation (HR=0.272, 95% CI: 0.089–0.829, P=0.022) was association with stroke in patients with AF after LAA closure. The stroke rate for patients in the leak group was significantly higher, compared with the no-leak group (12.3 events/100 patient-years versus 1.9 events/100 patient-years, P<0.001). Furthermore, patients with persistent peri-device flow may have an increased rate of strokes (HR=5.041 (95%CI: 1.668–15.230)).

CONCLUSIONS Peri-device flow was associated with the rate of strokes at short-term follow-up.

GW30-e0768

Efficacy and safety of catheter ablation combined with left atrial appendage occlusion in patients with atrial fibrillation

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OBJECTIVES Catheter ablation is an effective therapy for symptomatic, drug-refractory atrial fibrillation (AF) patients. Left atrial appendage occlusion (LAAO) was an attractive alternative for stroke prevention. The concomitant catheter ablation and LAAO may be a feasible way to relieve symptom, reduce stroke and abolish anticoagulation simultaneously. The aim was to evaluate the feasibility and efficacy of the novel one-stop procedure.

METHODS Patients with AF at high risk of thromboembolic events and bleeding who underwent one-stop combined ablation and LAAO for drug-refractory and high risk of thromboembolic events were included. Follow-up was performed at 45-day, 6- and 12-month. Adverse events were recorded in the hospital's on-line information systems. Transoesophageal echocardiography was utilized to detect device-related thrombus and evaluate the device position and width of residual flow. Holter monitoring was performed to screening the recurrence of AF. Baseline and 1-year brain computed tomography were used to detect symptomatic and silent stroke.

RESULTS Two hundred and thirty-eight patients underwent concomitant catheter ablation and LAAO and were included (mean age 69.4±7.5 years; 145 men). The mean CHA_2DS_2-VASc score was 3.9±1.6. Cryoballoon ablation (CBCA) was used in 99 patients and radiofrequency ablation (RFCA) was used in 139 patients. A mean follow-up of 26.2±10.1 months showed 54 documented atrial arrhythmias recurrence of AF. Two patients died at 10-day and 6-month follow-up respectively. Three patients have major bleeding and 5 patients has stroke (Table). Device thrombus occurred in 3 patients.

CONCLUSIONS The one-stop combined LAAO and catheter ablation may be a feasible and efficacious therapeutic option to relieve symptom and reduce stroke simultaneously in patients with AF at high risk of thromboembolic events and bleeding.

GW30-e0943

Quantitative analysis of serum IgG galactosylation assists to predict postoperative recurrence of atrial fibrillation

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OBJECTIVES Radiofrequency catheter ablation is the most common treatment for atrial fibrillation (AF), but it has been controversial due to its high recurrence rate. Left atrial volume (LAV), as a commonly used indicator for predicting postoperative recurrence of AF, presents poor specificity and sensitivity, and is vulnerable to the subjective judgment of the operator and the error of the machine. Therefore, at present, exploring biomarkers that can assist in predicting postoperative recurrence of AF is urgent, so as to help clinicians to preoperatively evaluate patients with paroxysmal AF effectively, and then choose appropriate treatment for the patients.

METHODS The blood samples of untreated patients with paroxysmal AF were collected and the general data (age, gender, electrocardiogram, color Doppler echocardiography, therapeutic drugs, etc.) were analyzed. The blood samples were centrifuged. After serum was separated, isolation of IgG, glycan release and purification, glycan fluorescence labeling and HILIC-UPLC analysis of labeled glycan were carried out. The data were automatically processed by traditional integration algorithm and manually corrected. The degree of galactosylation of IgG was calculated using the formula G4/((GP8b+GP9)+2·GP14). Moreover, it was planed to record the patients' electrocardiogram at 3, 6, 12 and 18 months after surgery and at the occurrence of symptoms.

RESULTS In the study of 218 patients with elevated left atrial volume index levels (>93 mL/m^2), we found that the quantitative analysis of galactosylation in the relapsed group was significantly lower than in the non-recurrent group (0.72 vs. 1.68; P<0.05). ROC analysis showed that galactosylation increased the specificity of atrial fibrillations' postoperative recurrence from 69.1% (predicted only by left atrial volume index) to 82.7%. However, in the current test, the left atrial volume index combined with quantitative analysis of IgG galactosylation can maintain the sensitivity at 90%.

CONCLUSIONS Left atrial volume combined with quantitatively altered IgG galactosylation may provide a more comprehensive and reliable method for predicting recurrence after paroxysmal atrial fibrillation.

GW30-e0944

Efficacy of Nifekalant in patients with Wolff-Parkinson-White syndrome and atrial fibrillation: electrophysiologic and clinical findings

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OBJECTIVES Patients with Wolff-Parkinson-White (WPW) syndrome and atrial fibrillation (pre-excited AF), are at an increased risk of spontaneous ventricular fibrillation. The objective was to assess efficacy of nifekalant in pre-excited AF.

METHODS The study populations were comprised of patients with sustained pre-excited AF (n=51), paroxysmal supraventricular tachycardia (PSVT, n=201), and persistent AF without accessory pathway (AP) (n=87). Effects of intravenous infusion of nifekalant was assessed on electrophysiologic and clinical parameters.

RESULTS Nifekalant prolonged the shortest pre-excited R-R, average pre-excited R-R, and the average R-R intervals from 290±35 to 333±44 ms, 353±49 to 443±64 ms, and 356±53 to 467±75 ms, respectively, in patients with pre-excited AF (all P-values<0.001). Nifekalant also decreased the percent of pre-excited QRS complexes from 100 (100–100%) to 79% (70–91%) [median (percentiles 25–75)], heart rate from 172±25 to 132±24 beat/min, and increased systolic blood pressure from 84±9 to 99±12 mmHg (all P-values<0.001). Nifekalant infusion terminated AF in 33 of 51 patients (65%), in an average of 11±5 min from the start of infusion. Similar effects were also observed in a subgroup of 12 patients with pre-excited AF and impaired left ventricular function.

In patients with PSVT, nifekalant prolonged effective refractory period (ERP) and the block cycle length (BCL) of antegrade accessory pathway (AP) from 272±52 to 309±59 ms, and from 323±51 to 381±63 ms, respectively (n=78, P<0.001 for both). It also prolonged atrial ERP from 202±25 to 235±33 ms (n=168, P<0.001). Nifekalant had no effect on ERP of antegrade atrioventricular node (AVN) (315±69–321±77 ms, n=102, P=0.06). Finally, in patients with persistent AF without AP, nifekalant did not significantly decrease the ventricular rate of AF. One patient with low serum potassium and sinus bradycardia developed Torsades de pointes (TdP). No other adverse effects were observed.

CONCLUSIONS Nifekalant prolongs the ERP of antegrade AP and atrium, without blocking the antegrade conduction through the AVN, leading to slowing and/or termination of pre-excited AF. Thus, nifekalant might be an effective and a relatively safe drug in patients with pre-excited AF.

GW30-e0963

Interleukin-17A contributes to atrial fibrillation recurrence and left atrial reservoir function after catheter ablation

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OBJECTIVES Increasing evidence indicates that inflammation and atrial fibrosis greatly contribute to atrial fibrillation recurrence (AFR) after catheter ablation (CA). Interleukin-17A (IL-17A) is a newly discovered pro-inflammatory cytokine. In the present study, we assessed the prognostic value of IL-17A in patients with AFR after CA.

METHODS A total of 126 patients who underwent first-time CA for paroxysmal AF were enrolled in the present study over a period of 12 months. Levels of IL-17A, N-terminal pro-type natriuretic peptide (NT-proBNP), matrix metallopeptidase 9 (MMP-9), procollagen type I, procollagen type III and the left atrial emptying fraction (LAEF) were determined at baseline. AFR used as the study endpoint.

RESULTS The level of serum IL-17A was increased in all 126 patients before CA, while it was markedly decreased in 71 patients with no recurrence (NR) at 3-month follow-up. The increased IL-17A level was significantly correlated with the levels of NT-proBNP, MMP-9, procollagen type III and LAEF. Receiver operating characteristic (ROC) revealed that the area under the curve of IL-17A for predicting of AFR was 0.959, (95% CI, 0.911–0.982; P<0.0001).

CONCLUSIONS IL-17A might be a novel predictor of AFR after CA. The profibrotic effect of IL-17A might promote adverse cardiac remodeling and progression to AF.

GW30-e0967

Clinical impact of contact force sensing on atrial fibrillation ablation: a meta-analysis of randomized controlled trials

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OBJECTIVES Impact of CF technology on ablation of atrial fibrillation (AF) is controversial. We sought to perform a meta-analysis of data from eligible studies to evaluate the true clinical impact of CF.

METHODS We systematically searched the literature to identify randomized controlled trials (RCTs) examining the efficacy and safety of CF technology for ablation of AF. The relative risk (RR) of AF recurrence/atrial tachycardia at follow-up was assessed as the primary outcome using a fix-effects meta-analysis.

RESULTS There were 861 subjects in the identified 8 studies. At a median follow-up of 12 months, the RR of recurrent AF/atrial tachycardia was not significantly different with CF guided ablation vs. Non -CF guided ablation (1.02, 95% confidence interval [CI] 0.94–1.12, P=0.61). Procedure time (weighted mean differences [WMD] −20.20, 95% CI −39.80 to −0.60, P=0.04) were significantly reduced in CF-guided catheter ablation. CF was significantly greater in the CF group than in the Non-CF group (WMD 3.23, 95% CI 0.84–5.63, P=0.008). Procedure-related complications (RR 1.01, 95% CI 0.53–1.94, P=0.98), cardiac tamponade/pericardial effusion (RR 1.34, 95% CI 0.43–4.21, P=0.61) and incidence of acute reconnection of pulmonary vein (RR 1.69, 95% CI 0.60–4.76, P=0.32) did not differ significantly.

CONCLUSIONS This meta-analysis of RCTs demonstrates similar long-term outcome, acute procedural efficacy and complications when comparing CF guided ablation to Non -CF guided ablation for AF. Procedure length is shorted when using CF technology.

GW30-e0993

Comparison the value of locating ventricular outflow tract tachycardia origin according to conventional electrocardiogram, dynamic electrocardiogram and multi lead electrocardiogram

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OBJECTIVES To analyze whether conventional electrocardiogram (ECG), Ambulatory electrocardiogram (Holter) and multi lead electrocardiogram (MLE) have different diagnostic value for differentiatingventricular outflow tract tachycardia origin.

METHODS Seventy one patients with ventricular outflow tract tachycardiawho underwent intracardiac electrophysiologicalexamination and radiofrequency ablation in our department of Cardiology from January 2017 to December 2018 were enrolled. ECG, Holter and MLE were collected before operation, and the characteristics of QRS waves in each lead were analyzed. Four different methods, including V2 R wave amplitude index and time index, V2 transition ratio, chest lead transition zone indexand SV2/RV3, were used to analyze and compare the differences in the accuracy of three ECG mapping for location of left and right ventricular outflow tract.

RESULTS The main wave directions of the early QRS waves in the lead chambers of I, V2, V3 and V4 were statistically different among the three electrocardiograms. There were no statistical difference in the diagnostic accuracy of ECG, Holter and MLE in the right ventricular outflow tract, according to V2 R wave amplitude index and time limit index, and the V2 transition index. When the chest lead transitional zone index and SV2/RV3 were used to distinguishing left from right ventricular outflow tract tachycardia origin, the diagnostic accuracy of ECG and MLE are better than Holter.

CONCLUSIONS ECG and MLE are superior to Holter in judging left or right ventricular outflow tract tachycardia origin.

GW30-e1001

The comparison of characteristics of intraseptal pacing with and without left bundle branch capture confirmed by direct recruited proximal or distal conduction system

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OBJECTIVES Recent studies demonstrated that left bundle branch pacing (LBBP) to capture proximal left conduction system (LCS) can optimize physiological LV synchronous activation with a low and stable threshold. However, how to confirm LCS capture and its characteristics are not well established. We aimed to identify LCS capture using anterograde and/or retrograde potentials.

METHODS The intraventricular septal pacing lead was fixed in the left ventricular sub-endocardium around the region of the proximal left conduction system. An additional His lead or multipolar electrodes catheter located at left ventricular septum were used to record anterograde and/or retrograde potentials. The relationship between recorded potential and LCS capture confirmed by our previous criteria was assessed. The characteristics of anterograde and/or retrograde potentials were established in LCS capture during selective and non-selective pacing. And the features of the EKG and Sti-LVAT in intraseptal pacing with and without LCS capture were studied and compared.

RESULTS Five intact His-ventricle (non-LBBB) patients with recorded retrograde His potential from His lead (group 1) and three LBBB patients with anterograde distal left conduction system (LCS) potential from LV multipolar electrodes catheter (group 2) during intraseptal lead pacing were included. In group 1, LBB potential were recorded in all patients with the His to LBB potential interval of 28±5.4 ms. Retrograde His potential was not observed in His lead during only septal myocardium pacing and it occurred when stimulus to peak LVAT shortened abruptly with increasing output at the same site (90.2±7.5 vs. 71.2±4.7 ms), with stimulus to retrograde His potential (Sti-RH) interval of 28.2±5.1 ms. Output dependent selective and non-selective LBBP were achieved at finial site in 3 patients, with the same Sti-RH interval of 28.5±5.7 ms. In group 2, stimulus to LBB potential interval was 19.7±2.4 ms during His corrective pacing (Figure 1B). Anterograde distal LCS potential was not observed in multipolar electrodes catheter during only septal myocardium pacing and it occurred when stimulus to peak LVAT shortened abruptly with increasing output at the same site (105±14.2 vs. 85.7±6.6 ms), with stimulus to anterograde distal LCS potential (Sti-ALCS) interval of 20.3±3.7 ms (Figure 1C). Output dependent selective and non-selective LBBP were achieved at finial site in all these patients, with the Sti-ALCS interval of 20.3±3.4 ms and 21±2.9 ms, respectively (Figure 1D).

CONCLUSIONS In intact His-ventricle patients, when LCS directly captured, LBB potential was recorded in all cases, with Sti-RH interval identical to the intrinsic His to LBB potential interval, and the distal LCS potential recorded in front of the ventricle, which could also be observed in LBBB corrected by HBP. The characteristics of LCS capture could be summarized as: (1) paced QRS as a RBBB pattern; (2) Sti-LVAT abruptly shortening from LVSP to LBB pacing and achieving shortest and constant.

GW30-e1038

Electrocardiographic Tpeak-Tend interval and LV diastolic function: results from the China National Survey of ECG Parameters

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OBJECTIVES Tpeak-to-Tend interval (Tpe) is defined as the interval between the top of T wave to the end of T-wave. It was considered to reflect the dispersion of ventricular repolarization and as a novel risk marker of cardiovascular death. Recently, Bachmann et al. reported U-shaped associations between TpTe and cardiovascular risk. However, research on the association between TpTe and LV diastolic function remains limited. Accordingly, we examined their association in general Chinese population enrolled in a China National Survey of ECG Parameters.

METHODS A multi-stage, stratified cluster sampling across China was performed to select the representative Chinese adults aged 18–85 years old. TpTe were measured using Marquette 12SL algorithm in MUSE Cardiology Information System (GE Healthcare, USA). Only data from lead II, V2, V5 were investigated to limit the amount of statistical tests but cover most of the heart over different axes and planes. LV end-diastolic volume (LVEDV) and E/A as measures for LV diastolic function were collected by echocardiography. The study population was categorized into seven groups according to Tpe, Tpe/□, or Tpe/QT ratio, with cut-offs at 5th, 20th, 40th, 60th, 80th, 95th percentiles and reference group as 0–5th. GLM was used to assess the association between Tpe measures and LVEDD, LVEDV as well as E/A in overall population and each group. All models were adjusted for age, gender, center, history of hypertension and body mass index (BMI).

RESULTS After an exclusion of potential ambiguous Tpe interval, 6251 participants with 47% female and a mean age of 47± 14 years old were finally included from the nationwide study. Tpe was normally distributed with a mean of 90±14, 112±16 and 96±11 ms in lead II, V2 and V5. The median of LVEDD, LVEDV and e/a ratio were of 4.6 (4.3, 4.9) cm, 99 (83, 113) mL and 1.2 (0.9, 1.5), respectively. When treated as continuous variable, Tpe in lead II and V2 showed significant association with LVEDV but not in lead V5 (lead II: β=0.05, 95% CI 0.01, 0.09, P=0.008; lead V2: β=0.04, 95% CI 0.01, 0.08 P=0.008). However, Tpe/□ or Tpe/QT ratio in lead V5 demonstrated negative association with LVEDV (Tpe/□: β=–0.05, 95% CI –0.09, –0.02, P=0.005; Tpe/QT ratio: β=–21, 95% CI –38, –5 P=0.01). Surprisingly, when treated as categorical variable, a U-shape association was illustrated for Tpe groups and LVEDV, where the 20th–40th Tpe group in lead V2 (100–107 ms) and the 5th–20th (68–81 ms) Tpe group in lead II showed the least mean of LVEDV. No clear pattern was observed for the association between E/A and Tpe measures.

CONCLUSIONS There might be association between Tpe and LVEDV, either U-shape or linear. However, results differed by different leads. Further study is warranted for clear definition of Tpe and a possibility of non-linear between Tpe and subclinical outcomes.

GW30-e1051

Diagnostic capability and influence factors for a new electrocardiogram criterion on diagnosing left ventricular hypertrophy in a Chinese population

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OBJECTIVES Based on small sample of patients with hypertension, a few studies have reported that the newly proposed S_D+SV_4 criterion for left ventricular hypertrophy (LVH) is better than traditional criteria. This study was to verify the diagnostic capability of S_D+SV_4 criterion in Chinese population with or without hypertension and analyze the factors affecting diagnostic accuracy of LVH.

METHODS A total of 248 patients with LVH or paroxysmal supraventricular tachycardia (PSVT) discharged from Fuwai Hospital from January 2010 to July 2018 were enrolled. Patients with LVH were diagnosed according to left ventricular mass index (LVMI) calculated by the parameter of echocardiogram as the gold standard in this study. The S_D+SV_4 criterion refers to the sum of the amplitude of the deepest S wave (S_D) in all leads and the amplitude of S wave in V_4 lead (SV_4). As an important comparison criterion, the Cornell standard refers to the amplitude of the R wave in the aVL lead plus the amplitude of the S wave in the V_3 lead, that is, RaVL+SV_3. The Sokolow-Lyon criterion refers to the S-wave amplitude in the V_1 lead plus the R-wave amplitude of the higher one in the V_5 or V_6 leads, that is, SV_1+RV_5/RV6. The ROC curve was performed to assess the diagnostic capability of S_D+SV_4, RavL+SV_3 and SV_1+RV_5/RV_6 criteria for LVH. Then, the multivariate logistic regression analyses were performed to investigate the factors affecting the accuracy of the S_D+SV_4 criterion.

RESULTS There were 170 (68.5%) patients with hypertension and 110 (44.4%) with PSVT. According to LVMI, 107 (43.1%) patients were diagnosed with LVH. The area under curve (AUC) of S_D+SV_4 criterion was the largest compared with RavL+SV_3 and SV_1+RV_5/RV_6 criteria (AUC: 0.765 vs. 0.718 vs. 0.713, respectively). AUC of three criteria were similar (AUC: 0.746 vs. 0.758 vs. 0.730, respectively) in male, while the AUC of S_D+SV_4 criterion were apparently higher than that of RavL+SV_3 and SV_1+RV_5/RV_6 criteria (AUC: 0.842 vs. 0.712 vs. 0.641, respectively) in female (Figure 1). The gender-specific S_D+SV_4 criterion has the highest consistency with gold standard (r=0.532±0.054, P<0.01), accompanied by highest sensitivity (70.1%) and specificity (85.8%). According to the consistency of diagnostic results by the gender-specific S_D+SV_4 criterion and gold standard, patients were divided into a consistent group and an inconsistent group. Univariate analysis showed significant differences in history of PSVT (50.0% vs. 25.0%, P<0.01), Posterior wall thickness (PWT) (10.5±2.3 vs. 11.7±3.5, P<0.05) and LVEF (Left ventricular ejection fraction) (61.6±9.6 vs. 54.1±7.9, P<0.001) between the two groups. Variables with P<0.10 in the univariate analysis were included in multivariate logistic regression analysis. The results showed that after adjusting for hypertension, PSVT history, body surface area, interventricular septum thickness, PWT and left ventricular internal diameter, only LVEF (OR=0.920, 95% CI 0.882~0.959, P<0.001) was significantly different between the two groups (Table 1).

CONCLUSIONS The newly proposed S_D+SV_4 criterion provide improved sensitivity and accuracy for the diagnosis of LVH in Chinese population. The decrease of LVEF is an independent factor affecting diagnostic accuracy of the LVH.

GW30-e1056

Characteristics and feasibility of left bundle branch pacing via a novel intraseptal technique in patients with left bundle branch block

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OBJECTIVES His bundle pacing can correct left bundle branch block (LBBB) but may be limited by suboptimal lead delivery and high thresholds. To assess the feasibility of left bundle branch pacing achieved by capture the left conduction system via a novel intraseptal technique (iLCS) to deliver cardiac resynchronization therapy (CRT).

METHODS Patients with LBBB from multicenters indicated for CRT or pacing therapy were included. iLCSP was performed by fixing 3830 lead into the left ventricular septal sub-endocardium targeting the region of the proximal left conduction system. Pacing characteristics, success rate, threshold and R-wave amplitude were assessed.

RESULTS A total of 94 patients with the native QRS duration of 167.2±17.2 ms were included. In 92 patients, iLCSP was achieved and demonstrated RBBB pattern with the paced QRS duration of 116.4±12.6 ms (Figure 1B, middle panel). Fusion of iLCSP and native conduction via the RBB eliminated RBBB and resulted in an average QRS duration of 103.2±10.1 ms (Figure 1C). In a subgroup that underwent a two-lead implantation technique (n=21), a Purkinje pre-potential was recorded during His corrective pacing from the intraseptal lead (Figure 1B, right panel). Output dependent selective and non-selective iLCSP were demonstrated in 52% patients, with the same stimulus to peak left ventricular activation time of 82 ms (Figure 1B, left and middle panel). Lead parameters remained stable at 1-year (threshold 0.61±0.17V/0.5 ms, R wave 13±5.8 mV, Figure 1D,E). During follow-up, only one patient had an increase in LBB capture threshold to 2.5 V/0.5 ms and there were no other complications such as dislodgment, infections, embolism or stroke associated with the implantation.

CONCLUSIONS Permanent iLCSP is feasible and safe in patients with LBBB.

GW30-e1066

Efficacy and safety of rivaroxaban in patients with atrial fibrillation and metabolic syndrome

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OBJECTIVES Prevalence of atrial fibrillation (AF) and metabolic syndrome (MS) are rising and co-existence of these two conditions will increase related complications. Aim of the study was to assess the efficacy and safety of rivaroxaban in patients with AF and MS.

METHODS We compared the efficacy and safety of rivoraxaban and varfarin in patients with AF and metabolic syndrome. One hundred and twenty-four patients were enrolled in this study dividing into two group by 62 (Aged 42–67 years; mean age 51.2 years; 46% male). First group were treated with rivoraxaban and the second group with varfarin. Mean follow-up period was 1.8 years. Metabolic syndrome was diagnosed by the Harmonized definition of the MS. In both treatment groups for efficacy and safety, primary outcomes were stroke, embolism, major and non-major bleeding.

RESULTS During the follow-up period primary endpoints were similar in both groups (1 stroke event in rivoraxaban vs. 1 stroke event in varfarin). There was no embolism in both groups. However, major and non-major clinically relevant bleeding were observed more in varfarin group when compared rivoraxaban group (HR 1.2; CI 95% 1.06–1.29; P=0.03). Among components of MS hypertension and dyslipidemia were correlated with major and non-major bleeding (HR 1.23; CI 95% 1.08–1.32; P=0.04 and HR 1.09; CI 95% 1.05–1.14; P=0.05). There were no correlations between AO and IR with major and non-major bleeding.

CONCLUSIONS Rivaraxaban is superior than varfarin in AF patients with metabolic syndrome. Among components of MS, hypertension and dyslipidemia are risk factors for major and non-major bleeding. Further studies with large amount of patients are needed to clarify.

HEART FAILURE

GW30-e0047

Six-year change in QT interval duration and risk of cardiovascular disease and all-cause mortality

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OBJECTIVES We aimed to examine the association between temporal change in QT interval and cardiovascular diseases and all-cause mortality in the Atherosclerosis Risk in Communities (ARIC) study.

METHODS We included 10,808 participants (age, 60.1±5.7, 45.2% male and 80.0% white) who obtained the 12-lead Electrocardiography (ECG) in both Visit 1 (1987–1989) and Visit 3 (1993–1995) in the Atherosclerosis Risk in Communities (ARIC) study. QT interval duration was corrected by using Bazett's formula (QTc). The change in corrected QT interval duration (ΔQTc) was calculated by subtracting QTc in Visit 3 from Visit 1. The main outcomes measures included all-cause mortality, incident heart failure (HF), coronary artery disease (CHD), stroke and atrial fibrillation (AF). We used multivariable Cox regression models to assess the association between ΔQTc and these outcomes.

RESULTS During a median follow-up of 19.6 years, 3918 cases (36.3%) of death, 1833 cases (17.8%) of HF, 1110 cases (11.1%) of CHD, 765 cases (7.2%) of stroke and 1789 cases (16.9%) of AF occurred. The hazard ratios for all-cause mortality, HF, CHD, stroke and AF with 10 ms increased in ΔQTc were 1.03 (95% CI, 1.01, 1.05; P=0.002), 1.05 (95% CI, 1.03, 1.08; P<0.001), 1.01 (95% CI, 0.98, 1.05; P=0.636), 1.05 (95% CI, 1.01, 1.09; P=0.026) and 1.03 (95% CI, 1.00, 1.06; P=0.051) separately, after adjusted for traditional cardiovascular risk factor, QTc and QRS duration.

CONCLUSIONS Temporal increases in QTc are independently associated with increased risk of death, HF and stroke.

GW30-e0083

New and definitive marker confirming the optimal status in the treatment of heart failure with preserved ejection fraction

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OBJECTIVES At the present time, there is no criterion to estimate the optimal treatment for heart failure (HF) with preserved ejection fraction (HFpEF). In the past, our group suggested the criteria for diagnosis of HFpEF with normal EF and fluid overload using the size of the femoral vein (FV), measured by ultrasound. Since then, when the patients with HF were treated, we used the size of the femoral vein as a criteria of fluid overload or euvolemic status. Is this criterion the best marker of optimal treatment of HFpEF? Which physical sign could guarantee a best treatment result?

METHODS Patients with HFpEF were enrolled. All patients had echocardiography to confirm EF>50% and also underwent the ultrasound test to assess the size and expansibility of the femoral vein (SEFV). The SEFV is the ultrasound study of femoral vein (FV) examining its size and expansibility with cough. The location of the femoral artery (FA) and FV to be checked is the coronal plane immediately proximal to the bifurcation of the superficial and deep femoral artery. The normal size of FV is a little larger than of the FA (Figure 1). If the size of the FV is twice larger than the FA, the patient has fluid overload in the venous compartment. (Figure 2) Then the patient was asked to cough in order to measure the size of the FV.

RESULTS During the 2 years of treatment, the patients were followed up with detailed physical examination in the office (including weight) and had the SEFV at regular 6 months intervals. Patients also underwent right heart catheterization to measure to the pulmonary capillary wedge pressure (PCWP).

CONCLUSIONS With the SEFV test, we could accurately confirm the presence of fluid overload in patients with HFpEF. However, in the follow-up by physical examination, the loss of cutaneous venous volume was an excellent marker of the euvolemic status of the patients with HFpEF. This marker was as sensitive as the SEFV test which measured the size of the femoral vein. Further randomized trials are needed to confirm the above preliminary results.

GW30-e0102

Serum albumin and incident heart failure: insights from epidemiological and Mendelian randomization studies

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OBJECTIVES Identifying unrecognized potentially modifiable risk factors is essential to improve the outcome of HF. However, the relationship of serum albumin with incident HF is uncertain. We aim to characterize the nature and magnitude of prospective association between serum albumin and incident heart failure (HF), and to investigate any causal relevance to the associationusingMendelian randomization.

METHODS Serum albumin levels were measured at baseline in the Atherosclerosis Risk in Communities (ARIC) prospective study of 15,792 participantswithout HF. Hazard ratios (95% confidence intervals) of serum albumin with incident HF were assessed. Eight single-nucleotide polymorphisms associated with serum albumin at genome-wide significance were used as instrumental variables. Mendelian randomization based on summary-level data was used to estimate the causal influence of the exposure on the outcome.

RESULTS During a median follow-up of 25.1 years, 2446 (19.9%) HF were observed. After multiple adjustment, serum albumin was inversely associated with incidence of HF (HR: 0.54, 95% CI: 0.46–0.64, per 1 g/dL increase; HR: 0.71, 95% CI: 0.63–0.81, Q4 vs. Q1). In MR analysis, no causal relationship was detected between serum albumin level and HF (odds ratio [OR]: 1.00, 95% CI: 0.99–1.01, per 1 g/dL increase of albumin; P=0.38) without evidence of heterogeneity between estimates from individual SNPs ($P_{heterogeneity}$=0.21) and pleiotropy effect ($P_{pleiotropy}$=0.83).

CONCLUSIONS The serum albumin level is independently inverse associated with incident HF in a linear pattern. However, MR analyses did not support a causal role of serum albumin in the etiology of HF.

GW30-e0116

Relationship between the change of diastolic blood pressure and the prognosis of chronic heart failure

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OBJECTIVES To investigate the relationship between the change of diastolic blood pressure (DBP) during hospitalization and the prognosis after discharge with a relatively low DBP (<55 mmHg).

METHODS Three hundred and sixty patients with heart failure from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2012 to December 31, 2018 were selected as the subjects in our study. Patients with chronic heart failure and DBP less than 100 mmHg at admission. The change of DBP during hospitalization (ΔDBP) was calculated by subscribing the admission DBP values from the discharge values. All-cause mortality at 1 year and 5 years were recorded during the follow up period and compared among patients with different ΔDBP levels. Multivariable Cox regression hazard model was used to analyze the association between the ΔDBP level and clinical outcomes.

RESULTS The patients were included and divided into two groups according to the ΔDBP level, including ΔDBP<–10 mmHg group (n=160) (44.4%) and ΔDBP≥–10 mmHg group (n=200) (55.6%). All-cause mortality at 1 year was higher in the ΔDBP<–10 mmHg group than those in the ΔDBP≥–10 mmHg group (31.5 vs. 21%, P<0.01). There was no significant statistical difference in the all-cause mortality at 5 years (39.3 vs. 31.1%, P>0.05) between the two groups. After adjusted the age, gender at discharge, NYHA class in the multivariable Cox regression hazard model, we found the adjusted risk of 1 year all-cause mortality in the ΔDBP<–10 mmHg group was approximate twice higher than those in the ΔDBP≥–10 mmHg group (HR=2.011, 95% CI: 1.501–2.509, P<0.05).

CONCLUSIONS DBP value decrease more than 10 mmHg during hospitalization is associated with adverse outcomes in the post-discharged prognosis.

GW30-e0117

Association between hyperuricemia and prognosis in patients with heart failure of dilated cardiomyopathy

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OBJECTIVES To observe the correlation between hyperuricemia and prognosis in patients with heart failure of dilated cardiomyopathy.

METHODS Three hundred and fifty-two patients with heart failure of dilated cardiomyopathy from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2012 to December 31, 2018 were selected as the subjects in our study. Retrospective analysis of 164 patients with heart failure of dilated cardiomyopathy was the A group. A total of 188 patients with non-heart failure of dilated cardiomyopathy admitted to our hospital during the same period were selected as the B group. The basic diseases, correlation between hyperuricemia and heart failure was analyzed, and the mortality rate was followed up for 3 years.

RESULTS The level of serum uric acid in the A group was significantly higher than that in the B group, and the cardiac function index was significantly lower than that in the B group. The rate of combined basic diseases was 57.43% in the A group, the rate of mortality rate was 7.1% in the follow-up 3 years, 27.13% in the B group and the rate of mortality rate was 1.3%. The difference was statistically significant (P<0.05). Multiple logistic regression analysis showed that log hyperuricemia, was independently and signifcantly associated in a positive manner with heart failure (odds ratio: 7.28, 95% confdence interval: 1.03–16.41, P=0.03).

CONCLUSIONS We found a positive and independent association of serum hyperuricemia with heart failure in dilated cardiomyopathy patients. Hyperuricemia is a common problem in patients with heart failure of dilated cardiomyopathy, and it is a risk factor to induce changes in cardiac function.

GW30-e0119

Association between copper levels and heart failure: a meta-analysis

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OBJECTIVES Copper dyshomeostasis can lead to many diseases, including cardiovascular disease. However, there are conflicting reports on the relationship between serum copper levels and heart failure (HF). To explore the relationship between serum copper levels and HF by performing a meta-analysis.

METHODS The PubMed and ScienceDirect databases until June 2017 were searched for reports on the association between serum copper levels and HF.

RESULTS Thirteen reports with 1504 subjects from 29 case-control studies were chosen for the meta-analysis. The pooled analysis indicated that patients with HF had higher copper levels than the control subjects [standardized mean difference (SMD), 0.982; 95% confidence interval (CI), (0.679, 1.285)]. Subgroup analysis stratified by different geographic locations found that HF patients had higher copper levels than the control subjects in Asia and Europe [Asia: SMD, 0.948 and 95% CI, (0.569, 1.327); Europe: SMD, 1.275 and 95% CI, (0.633, 1.917)], but not in America [America: SMD, 0.637 and 95% CI, (–0.109, 1.383)]. Additionally, subgroup analysis revealed that patients with ischemic cardiomyopathy (ICM) [SMD, 1.171; 95% CI, (0.717, 1.624)], idiopathic dilated cardiomyopathy (IDCM) [SMD, 0.569; 95% CI, (0.097, 1.042)] and other types of HF [SMD, 1.152; 95% CI, (0.594, 1.710)] all had higher copper levels than controls. Further subgroup analysis stratified by NOS scores also found higher serum copper levels in patients with HF than controls within each subgroup.

CONCLUSIONS Our meta-analysis identified a significant association between high copper levels and HF.

GW30-e0120

Relationship between myocardial fibrosis indexes in patients with chronic heart failure

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OBJECTIVES To investigate the changes of myocardial fibrosis indexes in patients with chronic heart failure between different NYHA patients.

METHODS One hundred and three patients with heart failure from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2015 to December 31, 2018 were selected as the subjects in our study, while another 101 healthy subjects were selected as the control group. All the subjects received an electrocardiogram examination. The serum myocardial fibrosis indexes [Laminin (LN), pre-III collagen (PCIII), hyaluronic acid (HA)] in patients with chronic heart failure between different NYHA patients were calculated.

RESULTS Myocardial fibrosis indexes was signifcantly higher in study group [20.8 (15.0–25.1) μg/mL] than in control group [13.1 (10.9–26.8) μg/mL] (P=0.04). One-way ANOVA showed that there was significant difference in serum LN, PCIII, and HA levels between different NYHA patients (P<0.05). After multiple comparisons, serum LN, PCIII, and HA levels were higher in grade IV patients than those of grade II and III (P<0.05). Serum LN, PCIII, and HA levels were higher in grade IV and III patients than in grade II patients (P<0.05), after adjustment for age, smoking status, diabetes mellitus, and other risk factors.

CONCLUSIONS The level of myocardial fibrosis is significantly changed in patients with chronic heart failure and it can predict the severity of chronic heart failure.

GW30-e0121

Association between nutritional screening and prognosis in patients with heart failure

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OBJECTIVES To investigate the association between nutritional status (serum albumin and cholesterol levels) and prognosis in patients with chronic heart failure.

METHODS Three hundred and thirty-one hospitalized patients with heart failure from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2015 to December 31, 2018 were selected as the subjects in our study. These 331 patients were divided into two groups according to their prognosis, the death group (n=141), and the relief discharge group (n=190). Multivariate analysis was used to analyze the association between nutritional status and prognosis in patients with chronic heart failure.

RESULTS The nutritional status scores in relief discharge group was significantly higher than in the death group (P=0.03). Multivariate analysis showed that nutritional status scores was an independent predictor of prognosis in patients with chronic heart failure (P=0.04), after adjustment for age, body mass index, smoking status, hypertension, hemoglobin, and other risk factors.

CONCLUSIONS We found a negative and independent association of nutritional status scores and prognosis in patients with chronic heart failure.

GW30-e0122

Association between total bilirubin level and renal impairment in patients with acute heart failure

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OBJECTIVES To investigate the clinical association between the level of total bilirubin (TBIL) and early renal damage in patients with acute heart failure (AHF).

METHODS Three hundred and fifty-two patients with AHF from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2012 to December 31, 2018 were selected as the subjects in our study. They were divided into high TBIL group and low TBIL group according to TBIL at admission. Logistic regression was used to analyze the relation between TBIL and early renal damage.

RESULTS Left ventricular end diastolic diameter, N terminal brain natriuretic peptide (NT-proBNP), urinary α1-microglobulin and β2-microglobulin were signifcantly higher in high TBIL group than in low TBIL group (all P<0.05). Multiple logistic regression analysis showed that log TBIL, was independently and signifcantly associated in early renal damage in patients with AHF, after adjustment for age, body weight, percentage body fat, hemodialysis duration, smoking status, and other risk factors.

CONCLUSIONS We found a positive and independent association of serum TBIL with early renal damage in patients with AHF.

GW30-e0123

The clinical significance of serum levels of GDF-15 in patients with acute heart failure caused by myocardial infarction

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OBJECTIVES To investigate the clinical association between the serum concentration of growth differentiation factor 15 (GDF-15) and in patients with acute heart failure (AHF) caused by myocardial infarction (MI).

METHODS One hundred and three patients with heart failure from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2012 to December 31, 2018 were selected as the subjects in our study (A group), and 80 healthy subjects who underwent physical examination were selected as B group. The levels of serum GDF-15, creatine kinase isoenzyme (CK-MB), and troponin I (cTN-I) between the two groups were analyzed.

RESULTS The serum levels of GDF-15, CK-MB and cTn-I in A group were significantly higher than those in B control group (P<0.05). Multiple logistic regression analysis showed that log GDF-15, but not log CK-MB and cTn-I, was independently and signifcantly associated with AHF (odds ratio: 15.28, 95% confdence interval: 1.01–29.41, P=0.02), after adjustment for age, body weight, percentage body fat, smoking status, and other risk factors.

CONCLUSIONS We found a positive and independent association of serum concentration of GDF-15 with AHF caused by MI, moreover, serum levels of GDF-15 are related to the degree of AHF and MI area in those patients.

GW30-e0153

Apolipoprotein A1 is associated with SYNTAX score in patients with a non-ST segment elevation myocardial infarction

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OBJECTIVES The study was designed to investigate lipid profile and SYNTAX score in patients with non-ST segment elevation myocardial infarction (NSTEMI).

METHODS Three hundred and eleven patients with NSTEMI were enrolled. The demographic, clinical data, blood samples and SYNTAX score were documented. The Pearson linear correlation was used to detect confounding factors linearly correlated with SYNTAX score. The significantly correlated confounding factors were put into the multiple linear regressions.

RESULTS The Pearson linear correlation showed that high-density lipoprotein- cholesterol (HDL-C) and apolipoprotein A1 (ApoA1) were significantly correlated with Syntax Score (r=–0.119, P=0.044 and r=–0.182, P=0.002, respectively). The multiple linear regressions for Syntax Score were built using HDL-C and ApoA1, respectively. After the adjustment of other significantly correlated confounding factors such as white blood cell count (WBC), myohemoglobin (MB), glutamic-oxalacetic transaminase (AST) and creatinine, the ApoA1 still showed significant association with Syntax Score (β=–0.151, P=0.028). The area under curve was (AUC) 0.624 and the optimal cutoff value is 1.07 g/L when using ApoA1 to predict moderate and severe coronary artery lesions. The patients with ApoA1 ≥1.07 g/L and <1.07 g/L have the Syntax Scores of 12.21±11.58 and 16.33±11.53, respectively (P=0.001).

CONCLUSIONS The ApoA1 is the only lipid factor significantly associated with complexity of coronary artery lesion in patients with NSTEMI, the patients with ApoA1 <1.07 g/L may have more complex coronary artery lesions.

GW30-e0246

Relationship of high-density lipoprotein-associated arylesterase activity to systolic heart failure in patients with and without type 2 diabetes

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OBJECTIVES High-density lipoprotein (HDL) confers protection against cardiovascular disease partly attributable to its robust anti-oxidant activities, which is largely impaired in diabetic conditions.

METHODS In this study, we analyzed the anti-oxidant activity of HDL, as represented by the arylesterase activity of paraoxonase 1 (PON1) in HDL particles, in 216 consecutive HF patients with (n=79) or without (n=137) type 2 diabetes, and age- and gender-matched 112 diabetic and 189 non-diabetic non-HF controls.

RESULTS We found arylesterase activity was significantly decreased in patients with than without HF, and was further decreased when comorbid with diabetes. After adjusting for conventional risk factors and apolipoprotein A-I levels, arylesterase activity remained correlated positively with left ventricular ejection fraction in diabetic (r=0.325, P=0.020) but not non-diabetic patients (r=0.089, P=0.415), and negatively with NT-proBNP and NYHA functional class in both subgroups. In regression analyses, a higher risk of HF was observed in diabetic than non-diabetic patients when having low arylesterase activities.

CONCLUSIONS In conclusion, our data demonstrate that impaired serum arylesterase activity in patients with HF is further reduced when comorbid with diabetes. The relationship of impaired arylesterase activity to HF is especially enhanced in diabetic patients.

GW30-e0271

Relationship between plasma iPTH and thyroid hormones in elderly patients with chronic heart failure

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OBJECTIVES To investigate the values of plasma iPTH, thyroid hormones, and cardiac function in elderly patients with chronic heart failure.

METHODS A total of 150 cases of elderly patients with chronic heart failure from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2012 to December 31, 2018 were selected as the subjects in our study, to examine the relationship of plasma iPTH and thyroid hormones to cardiac function in elderly patients with chronic heart failure, whose plasma iPTH and thyroid hormones were detected. According to the NYHA cardiac function classification standard, these patients were divided into grade II, III, and IV groups, with 50 cases in each. Another 50 healthy elderly patients treated in the same period were selected as the control group.

RESULTS The levels of plasma iPTH in grade II, III and IV groups were significantly higher than those in the control group (P=0.03). The level of FT3 in grade II, III and IV groups was significantly lower than that in the control group (P=0.04). Multiple logistic regression analysis showed that log iPTH, but not log FT3, was independently and signifcantly associated with cardiac function (odds ratio: 4.81, 95% confdence interval: 1.10–8.41, P=0.04), after adjustment for age, body weight, and other risk factors.

CONCLUSIONS Plasma iPTH are strongly correlated with cardiac function grading in elderly patients with chronic heart failure, providing a novel method to evaluate the cardiac function of chronic heart failure patients.

GW30-e0272

The association between Cystatin C and depression in patients with chronical heart failure

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OBJECTIVES To investigate the association between cystatin C and depression in patients with chronic heart failure.

METHODS A total of 180 cases of elderly patients with chronic heart failure from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2013 to December 31, 2018 were selected as the subjects in our study. The patients were divided into Cys C abnormal group and Cys C normal group according to Cys C level. Hamilton depression scale (HAMD) was used to evaluate depression and the related clinical and biochemical indicators were measured.

RESULTS The proportion of depression in Cys C abnormal group was signifcantly higher than in Cys C normal group (P=0.03). Pearson correlation analysis showed that depression scores were positively correlated with Cys C abnormalities (r=0.324, P=0.04). Logistic regression analysis showed that the Cys C abnormality was associated with depression (OR=6.03, P=0.01), after adjustment for age, body mass index, hypertension, hemoglobin, albumin, and other risk factors.

CONCLUSIONS Cys C are strongly correlated with cardiac function with chronic heart failure, providing a novel method to evaluate the cardiac function of chronic heart failure patients.

GW30-e0273

Association between hyperhomocysteinemia and heart failure in uremia patient

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OBJECTIVES To explore the association between serum hyperhomocysteinemia and heart failure in uremia patient, and to provide clinical reference for better control of uremia heart failure.

METHODS A total of 205 cases of elderly patients with uremia from the First Affiliated Hospital of Sun Yat-sen University between January 01, 2013 to December 31, 2018 were selected as the subjects in our study. These 205 patients were divided into two groups according to their serum hyperhomocysteinemia concentration, the high- concentration group (n=101), and the low-concentration group (n=104). We analyzed the association between serum hyperhomocysteinemia and the incidence of heart failure.

RESULTS The proportion of the incidence of heart failure in the high serum hyperhomocysteinemia concentration group was signifcantly higher than in low-concentration group (P=0.01). Logistic regression analysis showed that the high serum hyperhomocysteinemia was associated with the incidence of heart failure (OR=4.27, P=0.01), after adjustment for age, body mass index, hypertension, blood fat, and other risk factors.

CONCLUSIONS Serum hyperhomocysteinemia are strongly correlated with the incidence of heart failure, verify the method to evaluate the cardiac function in uremia patient.

GW30-e0319

Insulin resistance is associated with left ventricular dilation after STEMI in non-diabetic patients

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OBJECTIVES Adverse cardiac remodeling after ST-segment elevation myocardial infarction (STEMI) is a major cause for poor cardiovascular outcomes such as heart failure. The predisposing factors and underlying mechanisms remain not fully understood. This study investigates the association of insulin resistance with left ventricular (LV) remodeling after STEMI in non-diabetic patients.

METHODS A total of 485 non-diabetic subjects with index STEMI who underwent primary percutaneous coronary intervention were consecutively enrolled and followed up for 12 months. Correlation between homeostasis model assessment-estimated insulin resistance (HOMA-IR) and changes in echocardiography parameters was studied. We further analyzed the association between insulin resistance parameters and LV dilation.

RESULTS Left ventricular (LV) dilation was detected in 49.1% of subjects at 12-month follow-up after STEMI, and was more severe in subjects with impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and higher HOMA-IR levels. HOMA-IR remained correlated to changes in LV dimensions after adjusting for confounding risk factors (all P<0.001). Multivariate regression analysis demonstrated that higher HOMA-IR was independently associated with greater LV dilation after STEMI. A significant interaction term was present between HOMA-IR and IGT in the model (P=0.002).

CONCLUSIONS Our study reveals high prevalence of insulin resistance and its predictive role for subsequent LV dilation in non-diabetic patients with STEMI.

GW30-e0417

Expression of serum microRNA-155 and its clinical significance in patients with heart failure after myocardial infarction

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OBJECTIVES To investigate the level of microRNA-155 (miRNA-155) in serum of patients with heart failure after myocardial infarction and its clinical significance.

METHODS Patients with heart failure after old myocardial infarction (OMI) were selected as the heart failure group, those without heart failure after OMI as the myocardial infarction group, heathy volunteers were used as control group. Each group had 126 participants. Serum levels of miRNA-155 were measured using reverse transcription polymerase chain reaction (RT-PCR). Left ventricular ejection fraction (LVEF), left ventricular posterior wall thickness (LVPW) and left ventricular end-diastolic diameter (LVEDD) were measured by echocardiography.

RESULTS The miRNA-155 level in patients with heart failure was significantly higher than that in control and myocardial infarction groups (P<0.05); the miRNA-155 level in patients with myocardial infarction group was significantly higher than that in control group (P<0.05). The area under the ROC curve of serum miRNA-155 in diagnosis of heart failure after myocardial infarction was 0.921 (95% CI: 0.842–0.963, the cutoff value was 1.670, the sensitivity was 88.73% (95% CI; 0.375–0.964), and specificity was 92.14% (95% CI: 0.792–0.976). Age, gender, fasting blood glucose and high density lipoprotein cholesterol, low density lipoprotein cholesterol, creatinine and triglyceride were similar between patients with high and low miRNA-155 levels (P>0.05). The amino-terminal pro-B-type natriuretic peptide (NT-proBNP) level was significantly higher in patients with high than low miRNA-155 levels (P<0.05) than with high miRNA-155 level. LVEF was lower in patients with high miRNA-155 level (P<0.05) and LVEDD was higher in patients with low miRNA-155 level (P<0.05). LVPW was similar betweens patient with high and low miRNA-155 level (P>0.05). There were more patients with grade III and IV cardiac function in patients with high than low miRNA-155 levels (P<0.05).

CONCLUSIONS Patients with heart failure after myocardial infarction have elevated miRNA-155 level, which can be used to assess the severity of the disease.

GW30-e0774

Clinical benefits of left bundle branch pacing in patients with left bundle branch block: a multicenter, prospective study

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OBJECTIVES His bundle pacing (HBP) could correct left bundle branch block (LBBB) and improved the cardiac function, however it often requires high pacing output. To assess the clinical benefis of left bundle branch pacing achieved by capture left conduction system via a novel intraseptal technique (iLCSP) to deliver cardiac resynchronization therapy (CRT).

METHODS Patients with LBBB indicated for CRT or pacing therapy from multicenters were included. iLCSP was performed by advancing the MDT 3830 lead deep into the septum about 1 cm distal to the His bundle region. Left ventricular eject fraction (LVEF), left ventricular end-systolic volume (LVESV) and New York Heart Association (NYHA) functional class were assessed.

RESULTS A total of 94 patients aged 68.3±10.7 years were included. Permanent iLCSP was successfully achieved in 92 patients. In patients who completed 1-year follow-up, LVEF improved from 38±14% to 56±11% (P<0.001). In patients with LVEF>35%, LVEF increased from 51±12% to 60±10% at 1 year (P<0.001). In those with baseline LVEF≤35%, a greater magnitude of LVEF improvement was observed from 28±5% to 48±9% at 6 months (n=42, P<0.001,) and from 29±5% to 53±10% at 1-year follow-up (P<0.001). LVESV decreased significantly (P<0.001). The NYHA functional class improved significantly from 3.1±0.5 to 1.5±0.6 at 6 months follow-up (P<0.001). BNP levels improved from 3.0±0.6 to 2.1±0.7 and cardiothoracic ratios also decreased from 0.62±0.06 to 0.56±0.06 at 6 months (All P<0.001). There were no other complications such as infections, embolism or stroke associated with the implantation and heart failure related rehospitalization.

CONCLUSIONS Permanent iLCSP is effective and safe in patients with LBBB. Permanent iLCSP results in an improved cardiac function in patients with LVEF≤35% and preserve cardiac function in those with LVEF>35%.

GW30-e0775

Depressive and anxiety disorders are not associated with the increased in-hospital mortality of patients with heart failure

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OBJECTIVES Although several studies have suggested that depressive and anxiety disorders are associated with negative outcomes and higher mortality in heart failure (HF) outpatients, their contribution to HF inpatient outcome remains unclear. Our study investigated the impact of depressive and anxiety disorders on the in-hospital outcome of HF patients.

METHODS We conducted a retrospective cohort study using the National Inpatient Sample (NIS) 2016 to identify patients with a principal diagnosis of HF with and without depressive/anxiety disorders. We compared the outcome between depression/anxiety group and non-depression/non-anxiety after propensity score matching for patient demographics, hospital demographics, and relevant cardiovascular comorbidities.

RESULTS A total of 216,259 patients were discharged with the primary diagnosis of HF. Of those, 24, 618 (11.3%) patients with depressive and 24,422 (11.3%) with anxiety disorders. A statistically significant higher percentage of female (depression, 59.9 vs. 46.8%, P<0.001; anxiety, 62.5 vs. 46.5%, P><0.001), white race (depression, 72.1 vs. 62.7%, P><0.001; anxiety, 74.3 vs. 62.4%, P><0.001), current (depression, 15.0 vs. 13.6%, P><0.001; anxiety, 16.6 vs. 13.4%, P><0.001) and history (depression, 28.5 vs. 27.5%, P=0.001; anxiety, 28.5 vs. 27.5%, P><0.001) of smoking, hypertension (depression, 33.0 vs. 30.8%, P><0.001; anxiety, 33.5 vs. 30.7%, P><0.001), hyperlipidemia (depression, 57.7 vs. 49.8%, P><0.001; anxiety, 54.6 vs. 50.2%, P><0.001), was found in both depression and anxiety group when compared with unmatched non-depression/non-anxiety group, respectively. A lower percentage of diabetes was noticed in anxiety (44.9 vs. 47.9%, P><0.001) but not in depression group (50.7 vs. 47.1%, P><0.001). In unmatched cohorts, the depression group had lower incidence of cardiac arrest (0.4 vs. 0.6%, P><0.001), cardiogenic shock (1.6 vs. 2.1%, P><0.001), in-hospital mortality (2.3 vs. 2.8%, P><0.001) and shorter length of stay (LOS) (5.66±5.87 vs. 5.31±5.82, P><0.001); whereas the anxiety group had a lower incidence of cardiac arrest (0.5 vs. 0.6%, P=0.009) and shorter LOS (5.57±5.84 vs. 5.32±5.82, P><0.001). After propensity score matching, the depression group remained lower incidence of cardiac arrest (0.4 vs. 0.7%, P=0.001), cardiogenic shock (1.6 vs. 2.0%, P=0.001) and shorter LOS (5.66±5.87 vs. 5.31±5.52, P><0.001) when compared to the matched non-depression group; whereas the anxiety group demonstrated shorter LOS (5.57±5.84 vs. 5.26±5.51, P><0.001) and lower total cost (12369±20112$ vs. 11835±19543$, P=0.003) compared to the matched non-anxiety group. There were no significant differences in in-hospital mortality in both matched depression and anxiety cohorts.

CONCLUSIONS Depressive and anxiety disorders were not associated with increased in-hospital mortality in HF inpatients. Moreover, a significantly decreased incidence of in-hospital cardiac arrest and cardiogenic shock was found in HF patients who had depressive disorders. Further mechanistic study is warranted to verify these findings.

GW30-e0783

Effect of intrinsic QRS morphology on response to His-Purkinje system pacing in atrial fibrillation patients with atrioventricular node ablation

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OBJECTIVES Studies have demonstrated clinical benefits of His-Purkinje system pacing (HPSP) combined with atrioventricular node (AVN) ablation in atrial fibrillation (AF) patients with narrow QRS. This study aimed to assess effect of different intrinsic QRS morphology on HPSP response

METHODS From Aug 2012 to Dec 2018, AF patients who were screened for AVN ablation and permanent HPSP were included. Intrinsic QRS morphology and pacing parameters were recorded. Echocardiographic left ventricular ejection fraction (LVEF), left ventricular end systolic volume (LVESV), cardiothoracic ratio (CTR) were assess before implantation and during follow-up

RESULTS A total of 259 patients were enrolled (age 70±10 years; ICM 13%; NICM 58%; LVEF 42±15%), of them, 239 (92.3%) patients received permanent HPSP and AVN ablation with a mean 25±19 months follow-up time. We divided the patients with permanent HPSP into three groups according to their intrinsic QRS morphology: group 1 (n=183): intrinsic narrow QRS or RBBB pattern, group 2 (n=36): LBBB pattern and group 3 (n=20): IVCD. In those with reduced

baseline LVEF who had implanted permanent HPSP more than 1-year, LVEF improved from baseline of 31±6% to 48±14% at 1-year follow-up in group 1 (N=46, P<0.001), from 31±5% to 57±10% in group 2 (N=16, P<0.001) and from 31±6% to 38±10% in group 3 (N=11, P=0.049), with the highest improvement in group 2. The similar improvements were observed in LVESV and NYHA function class.

CONCLUSIONS Permanent HPSP combined with AVN ablation significantly improved cardiac function in AF patients with different intrinsic QRS morphology, especially in LBBB.

GW30-e0788

Permanent His-Purkinje system pacing combined with atrioventricular node ablation for symptomatic refractory atrial fibrillation: a large sample and long-term follow-up study

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OBJECTIVES His-Purkinje system pacing (HPSP) has been demonstrated an effective therapy for atrial fibrillation (AF) patients who need atrioventricular node (AVN) ablation in studies with short-term follow-up. We aimed to evaluate the long-term clinical outcomes of HPSP in AF patients with narrow intrinsic QRS duration and HF who underwent AVN ablation in a larger population.

METHODS From August 2012 to April 2018, consecutive AF patients with narrow QRS who underwent AVN ablation and HPSP were enrolled. Echocardiographic left ventricular ejection fraction (LVEF), left ventricular end systolic dimension (LVESV), and pacing parameters were assessed at implant and during follow-up.

RESULTS A total of 143 patients were enrolled (age 69.6±9.9 years; ICM 10.5%; NICM 54.5%; LVEF 44.3±15.4%), with 132 (93.6%) of them received permanent HPSP and AVN ablation with a mean follow-up time of 28±19 months. In the subgroup of patients with reduced LVEF who implanted permanent HPSP more than 1 year, LVEF improved from baseline of 31±6 to 48±14% at 1 year follow-up (N=43, P<0.001) and from baseline of 29±6 to 51±13% at 3 year follow-up (N=13, P<0.001), with a greater improvement in LVESV. In the subgroup of patients with preserved LVEF who implanted permanent HPSP more than 1 year, LVEF improved from baseline of 57±11 to 63±7% at 1 year follow-up (N=55, P=0.001) and from baseline of 57±11 to 63±6% at 3 year follow-up (N=19, P=0.03). The threshold of HPSP was 0.8±0.6 V@ 0.5 ms at implanted and maintained stable during long-term follow-up.

CONCLUSIONS HPSP is feasibility and effectiveness in AF patients with narrow QRS who underwent AVN ablation during long time follow-up.

GW30-e0844

The impact of left atrial mechanics on cardiovascular outcome in HFpEF patients: a single center study

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OBJECTIVES Left atrial (LA) mechanics, particularly conduction time is mostly altered in heart failure (HF), especially in preserved ejection fraction type (HFpEF) due to deterioration in diastolic features (DF), but the impact on outcomes remains unknown. Therefore, we sought to investigate the association of LA conduction by coupling obtained from tissue Doppler imaging (TDI) and HF-related hospitalization in patients with HFpEF.

METHODS We retrospectively included 112 consecutive patients (48 men; mean age 59.9±5 years) with HFpEF. HFpEF was defined as the presence of at least one symptom, diastolic dysfunction with TDI and EF>50% by transthoracic echocardiography. The primary outcome was HF-related hospitalization, and hospitalization data from over 12-month period were retrospectively obtained on all HFpEF patients. The cohort was stratified based on the tertiles of their LA – electromechanical delay (EMD) duration: Tertile 1 (42 ms).

RESULTS Demographic features were similar between all tertile groups, and there were no significant differences in left ventricular (LV) volumes and EF (P>0.05). The patients were followed for 12-month, and a total of 41 events occurred as a primary outcome. LA-EMD duration was significantly longer in patients with cardiac events than in those without. Also, DF parameters were significantly correlated with LA-EMD (r=0.627, P<0.001). Additionally, Kaplan-Meier analysis showed that the highest tertile of LA-EMD duration was associated with hospital admission (P log rank><0.001), and it was found to be an independent risk factor for HF-related hospitalization HR for tertile 3 vs. 1: 18.7, 95% CI: 2.46–61.1, P<0.001; HR for tertile 3 vs. 2: 6.17, 95% CI: 1.78–21.2, P><0.001).

CONCLUSIONS Among HFpEF patients, the LA-EMD may be a feasible non-invasive parameter for predicting HF-related hospitalization.

GW30-e0938

Determination of B-type natriuretic peptide in patients with chronic heart failure

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OBJECTIVES To study the relationship between the indices of neurohumoral factors – B-type natriuretic peptide (BNP) and prognosis in patients with I-III FC chronic heart failure (CHF).

METHODS Fifty-two patients with CHF aged from 45 to 60 years old were examined (whose mean age was 53.3±6.9 years). Patients were randomized to CHF groups according to the classification of the New York Association of Cardiology. Patients of the first FC CHF group – 18, FC II CHF – 21 and FC III – 13 patients. Determination of the level of BNP was carried out on the immunoassay analyzer "HUMAREADER SINGLE".

RESULTS In patients with CHF II FC, there was an increase in the content of BNP by 71.1% (P<0.01), and in patients with FC III by 188.3% (P><0.001) compared with patients with FC I. Accordingly, the level of BNP was 1.7 times with II FC and 2.9 times higher with FC III III CHF compared with the values of patients with FC I. Given the fluctuations of these indicators, the distribution of the examined patients was studied according to the content of the studied neurohormone within lower median values (medium-high level) and large values of the median (high level). In patients with FC II and III, a moderately high level of increase in BNP was observed in 51.7% and 40.1% of patients. At the same time, medium-high levels of neurohumoral factors prevailed in patients with FC II, while with FC III high levels of BNP prevailed. A direct correlation was found between the level of neurohormones and FC CHF: in patients with FC II, which was r=0.54, and with FC III, r=0.67 (P><0.001). Studying the association of MNUP with heart remodeling indices showed a high inverse correlation of neurohumoral factors with EF (r=–0.68, r=–0.61 respectively) and a direct correlation with LV CLR (r=0.66, r=0.58 respectively) and an indicator of the maximum speed of early rapid filling of the left ventricle – E (r=0.64; r=0.51). In patients with CHF, the mortality rate had a strong positive correlation with high and medium-high BNP values (respectively, r=0.71; r=0.64).

CONCLUSIONS Thus, in patients with CHF there is an increase in the content of MNUP correlated with the severity of CHF and prognosis.

GW30-e0971

Chemerin may be a novel biomarker associated with the prognosis of chronic heart failure

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OBJECTIVES Chemerin is a novel adipokine which regulates the inflammatory response and glucolipid metabolism. Recent studies have reported that chemerin is related to cardiovascular disease and metabolic disease. However, the relationship between chemerin and chronic heart failure (CHF) remains uncertain. Therefore, we evaluated the association between chemerin and prognosis of CHF patients.

METHODS We selected 105 CHF patients and 34 persons with normal cardiac function as control group from March 2015 to December 2016. The CHF patients were followed up with composite endpoint of cardiac death and rehospitalization caused by worsening of heart failure. Serum chemerin concentration was measured by using a sandwich enzyme-linked immunosorbent assay (ELISA).

RESULTS Elder and male gender patients were more frequent in CHF group. Besides, CHF group had higher levels of NT-proBNP, hsCRP, creatinine and FFA with lower level of HDL-C. Compared with the control group, the serum chemerin level in CHF group increased significantly (54.4 μg/L vs. 39.1 μg/L, P<0.001). For all 105 CHF patients, they were divided into four groups according to NYHA classification, and there were 7, 15, 43, 40 patients with NYHA grade I, II, III and IV, respectively. The average level of serum chemerin in NYHA II (54.8 μg/L), III (62.6 μg/L) and IV (51.7 μg/L) patients was significantly higher than that in NYHA I subjects (29.2 μg/L), but there was no statistical difference among NYHA II to IV. Furthermore, CHF with NYHA III other than NYHA IV had the highest level of chemerin. Serum chemerin level showed an inverted U-shaped relationship with NYHA classification, which was reflected in the gradual increase of chemerin level in NYHA I-III level, but a partial decrease in NYHA IV level. During a follow-up period of 169±69 days, 3 of 105 CHF patients were lost, and 45 subjects suffered composite endpoint. All the 102 patients were divided into event-free group and event group. Compared to event-free group, event group had higher proportion of NYHA III-IV grade, higher levels of NT-proBNP and chemerin, and lower left ventricular ejection fraction (LVEF). Chemerin was a significant predictor of composite endpoint by multivariate Cox analysis. Kaplan-Meier survival analysis showed that the cumulative survival rate was the lowest when chemerin were less than median level (54.7 μg/L) and NT-proBNP were greater than median level (3753 pg/mL).

CONCLUSIONS The serum chemerin level in CHF patients is significantly higher, and it is associated with a cardiac death and re-admission in CHF patients.

GW30-e0997

Studying ID polymorphism of the angiotenzin-transforming (ace) gene in patients with chronic heart failure

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OBJECTIVES To study ID polymorphism of the angiotensin-converting enzyme gene (ACE) in patients with chronic heart failure (CHF) in people of Uzbek nationality.

METHODS Genotyping of the polymorphism ID of the ACE gene was performed in 114 patients with CHF and 51 healthy donors of Uzbek nationality.

RESULTS When analyzing the frequencies of alleles of the polymorphism ID of the ACE gene, it was noted that in the group of patients with CHF the frequency of the functionally significant allele I is 48.6%, which is lower than in the control group (59.8%), however, there was no significant difference in the statistical processing (χ^2=0.5; P=0.4; OR=0.8; 95% CI 0.4828, 1.399), while the incidence of allele D was significantly higher in the group of patients with CHF (51.4 vs. 40.25% in the control group). It is interesting to note that in the group of patients we revealed a tendency to increase the number of carriers of the homozygous genotype D/D. The frequency of occurrence of this functionally unfavorable genotype was 33.8%. These data further strengthen the position of the D/D genotype of the ACE gene as a marker associated with the formation of CHF.

CONCLUSIONS Thus, the results of the calculation of the functional efficiency of the ACE gene under study as independent markers of CHF. determined statistically insignificant OR values.

GW30-e1010

Non-invasive measurement of the pulmonary artery wedge pressure and the left ventricular end diastolic pressure

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OBJECTIVES At the present time, criteria for diagnosis of left ventricular (LV) dysfunction are non-specific. A measurement of left ventricular end diastolic pressure (LVEDP)>24 mmHg or a pulmonary capillary wedge pressure (PCWP)>24 mmHg is considered LV dysfunction. These measurements require invasive procedure and cannot be repeated frequently. How can we measure the PCWP non-invasively?

METHODS Patients arrived to the cardiac catheterization laboratories for right and left heart catheterization were enrolled. The indications for procedures were aortic stenosis, LV dysfunction or pulmonary hypertension. All patients underwent the ultrasound test to measure the size and expansibility of the femoral vein (FV) (SEFV) at baseline and upon cough. The location of the femoral artery (FA) and FV to be checked is the coronal plane immediately proximal to the bifurcation of the superficial and deep femoral artery. The normal size of FV is a little larger than of the FA (Figure 1). If the size of the FV is twice larger than the FA, the patient has fluid overload in the intravascular compartment. (Figure 2) Then the patient was asked to cough in order to measure the size of the FV. Patient underwent right heart catheterization as usual. The LVEDP and PCWP and PAM were measured and correlated with the size of the FV and the expansion of the FV upon cough. (Figure 3)

RESULTS Twenty patients were enrolled. If there was only enlargement of the FV, the LVEDP was between 20 and 24 mmHg. If the FV was enlarged >2 times the size of the FA and there was no enlargement of the FV with cough, then the LVEDP >24 mmHg (90% sensitivity) and (80% specificity).

CONCLUSIONS The SEFV test was accurate in confirming the presence of elevated LVEDP and PAM (pulmonary HTN). The diagnosis was based on the significant fluid overload in the venous system where the majority of the blood is circulating. Larger studies are needed in order to confirm these preliminary results.

GW30-e1011

Efficiency of eplerenon on neurological parameters in patients with chronic heart failure

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OBJECTIVES To study the efficacy of eplerenone on neurohumoral parameters in patients with chronic heart failure (CHF).

METHODS We examined 100 patients with CHF of ischemic genesis with FCI CHF II and III (men aged 38–60 years, mean age 54.51±6.89 years) initially and after 6 months of treatment. To assess the comparative efficacy of AMRK, patients were divided into 2 groups: the first group (I) consisted of 54 patients with FC II (28) and FC III CHF (23 patients) were taken for 6 months against the background of standard therapy – spirinolactone; the second group (II) –46 patients with FC II (26) and FC III CHF (23 patients) – eplerenone.

RESULTS The results of studying the effect of six-month eplerenone therapy on the content of NA and aldosterone in the blood of patients with CHF FC II and III showed that in this group of patients, the content of neurohormones in the blood of patients with CHF of both FC II and FC III was significantly reduced. As a result of therapy in patients with FC II, there was a significant reduction in Al content by 28.4% (P<0.01), and NA by 24.6% (P><0.01) from baseline. Patients with CHF FC III level reduction of NA was more significant than in FC II. In particular, as a result of the therapy, the Al content decreased by 32.1% (P><0.001), and NA by 19.8% (P><0.05) from the baseline. The results of the comparative efficacy of spirinolactone and eplerenone showed that the effectiveness of complex therapy on the level of neurohormones is almost similar in both groups in patients with FC II. However, in patients with PK III, there is a clear superiority of complex therapy with eplerenone than with spirinolactone. In the group of patients who took eplerenone, the level of Al and HA decreased by 32.1 and 19.8%, respectively, whereas in the spirinolactone group, by 20.2 and 10.9%, respectively, and, moreover, the level of reduction of NA was unreliable from baseline.

CONCLUSIONS Thus, during complex therapy using eplerenone in patients with CHF, there was a significant decrease in the level of neurohormones in patients with II and III FC CHF.

GW30-e1028

Three years follow-up of new technique in the assessment of fluid volume after TAVR or MitraClip

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OBJECTIVES It is difficult to diagnose fluid overload or questionable heart failure (HF) after TAVR or MitraClip especially if these patients had concomitant severe chronic obstructive pulmonary disease (COPD), cirrhosis or chronic kidney disease (CKD) or while on respirator. In a normal person, the amount of blood going down to the leg via the common femoral artery (FA) should be the same amount which returns to the heart via the femoral vein (FV). This is manifested by the similar size of the FA and FV. If the size of the FV is significantly larger, there is fluid overload in the venous system.

METHODS Patients with questionable diagnosis of HF after TAVR or MitraClip while having severe comorbidities (COPD, cirrhosis, CKD or on ventilator) were enrolled. The control group underwent physical exam (PE), CXR and BNP level measured. The study group underwent the same protocol PLUS an ultrasound checking the size and expansion of the FV (SEFV). The image was the coronal plane proximal to the bifurcation of the superficial (SFA) and deep femoral artery (PFA). (Figure 1) The principle of this test is that the volume of blood going through the FA and returning through the common FV should be the same. In normal condition, the FV is a little larger than the FA. (Figure 2) If the size of the FV at baseline is 2 times larger than the FA, the patient has significant fluid overload. (Figure 3) If the FV can expand >1.5 times during cough, the test showed that the venous system can accommodate more fluid if needed. In patients with HF, the FV does not expand with cough. Both groups received treatment according the PE or the SEFV.

RESULTS With the SEFV results, all study (50) patients had accurate confirmation to be overloaded or euvolemic. Compared with control, the patients who were treated according to the SEFV results improved with less medications (2.5 vs. 5, P<0.05), at higher doses of diuretics (60 mg of furosemide vs. 30 mg, P><0.05) without having renal failure (2 vs. 14, P><0.05), shorter ICU (1.5 vs. 3 days, P,0.05) hospital stay (3.4 vs. 5 days).

CONCLUSIONS The SEFV test was more accurate in confirming the fluid status of patient after TAVR or MitraClip with complex co-morbidities (COPD,

ascites, chronic kidney disease (CKD). Under the guidance of SEFV, the patients improved with higher doses of diuretics without causing more renal failure. Shorter time in ICU and hospital. These patients could be discharged on time (early compared with traditional method) without inappropriate readmission. The SEFV is a better test to confirm HF and guide its treatment in complex patients after TAVR or MitraClip.

GW30-e1052

Follow up study: the enlarged size of the femoral vein is more accurate in the prognostication of patients with asymptomatic heart failure

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OBJECTIVES At the present time, the criteria for diagnosis of heart failure (HF) are non-specific. The symptoms or findings of HF are at the end of the disease process and there are many clinical confounders. especially if these patients had concomitant severe chronic obstructive pulmonary disease (COPD), cirrhosis or chronic kidney disease (CKD) or while on respirator. There is a need for a specific test which can detect fluid overload (the precursor of HF) and predict the outcome of near future even the patient is clinically asymptomatic.

METHODS Patients with confirmed diagnosis of HF now in good recovery and asymptomatic were enrolled. The patient might have comorbidities (chronic obstructive lung disease cirrhosis, chronic kidney disease). All patients underwent physical exam (PE), Chest XR PLUS an ultrasound study checking the size and expansion of the femoral vein (FV) (SEFV). The image was the coronal plane proximal to the bifurcation of the superficial (SFA) and deep femoral artery (PFA). The principle of this test is that the volume of blood going through the common femoral artery (CFA) and returning through the common FV should be the same. In normal condition, the FV is a little larger than the FA. (Figure 1) In patient with significant fluid overload, the femoral vein is much larger than the common femoral artery and it does not expand following cough. (Figure 2) As the femoral vein is filled with blood, it takes more of a round shape. These asymptomatic patients were divided into 2 groups: group A: with enlarged FV and group B: without enlarged FV. They were followed up for 12 months for relapse of acute on chronic HF and mortality.

RESULTS Altogether 80 patients were enrolled. Forty asymptomatic patients with enlarged FV and 40 asymptomatic patients without enlarged FV. These patients were followed for one year. Ninety percent of patients group B did not require hospitalization compared to 30% in the group A ($P<0.05$). There was no mortality in group B while it was 20% in group A.

CONCLUSIONS The SEFV test was more accurate in confirming the fluid status and predicting the prognosis of asymptomatic HF patients especially patient with complex co-morbidities. With treatment under the guidance of SEFV, the rate of hospitalization and mortality were much lower. Long term and randomized trials are needed to confirm the above findings.

BLOOD LIPIDS AND ATHEROSCLEROSIS

GW30-e0027

Effects of Krüppel-like factor 4 regulated transcription factor EB on endothelial cell inflammation under laminar flow

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OBJECTIVES Endothelial cell inflammation is the main pathogenesis of atherosclerosis (AS). In recent years, studies on hemodynamic regulation of endothelial cell inflammation have gradually moved from lab-based to more patient-oriented approach. Under laminar flow (LSS) mediated transcription factor EB (TFEB) exerts anti-inflammatory effects in endothelial cells by inhibiting inflammatory pathways, affecting the development of AS. Krüppel-like factor 4 (KLF4) as a shear-related factor, the specific anti-inflammatory mechanism of it in endothelial cells is still unclear. KLF4 silencing in endothelial cell under LSS can decrease the activity of TFEB promoter, activate the downstream inflammatory pathway, and participate in the expression of inflammatory cytokines in endothelial cells.

METHODS Human umbilical vein endothelial cells (HUVECs) were cultured in vitro, KLF4 siRNA and overexpression plasmid were transfected into them respectively. The relationship between KLF4 and TFEB promoter region was detected by luciferase reporter gene assay, and the expression level of TFEB was detected by qRT-PCR and western Blot. HUVECs transfected with siRNA KLF4 exposure in LSS (15 dyn/cm2) for 48 hours, and then they were transfected with empty vector and TFEB overexpression plasmids, the levels of TFEB mRNA and protein were tested by qRT-PCR and western Blot and the expression levels of inflammatory factors such as VCAM1, IL6 and IL1β were detected by ELISA subsequently.

RESULTS Comparing to the control group, KLF4 directly binds to the TFEB promoter to activate TFEB mRNA transcription in the overexpressed KLF4 group, but the binding of KLF4 to the TFEB promoter region was reduced and the expression level of TFEB was decreased in the siRNA KLF4 group. After 48 hours of LSS exposure, HUVEC transfected with siRNA KLF4 abolished the increase in TFEB mRNA and protein levels and the decrease in inflammatory factors such as VCAM1, IL6 and IL1β expression in the LSS-induced empty vector group. However, TFEB overexpression reversed the up-regulation of inflammatory factors such as VCAM1, IL6 and IL1β in siKLF4-induced HUVECs exposed to LSS.

CONCLUSIONS Under laminar flow, KLF4 as a previously unrecognized regulator of TFEB expression in ECs inhibits the activation of downstream inflammatory pathways, which in turn affects the secretion of inflammatory factors involved in the changes of endothelial cell inflammatory state.

GW30-e0080

Association of high serum uric acid and increased arterial stiffness is dependent on cardiovascular risk factors in Chinese coastal female population

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OBJECTIVES An elevated serum uric acid (SUA) level is closely associated with increased arterial stiffness. However, whether this association is independent of conventional cardiovascular risk factors is controversial. This study aimed to investigate whether SUA is independently associated with arterial stiffness as assessed by Brachial-ankle pulse wave velocity (baPWV), and to what extent this association is dependent on cardiovascular risk factors.

METHODS Increased arterial stiffness was defined as baPWV>1400 cm/s. Cardiovascular risk factors were defined as hypertension, diabetes, dyslipidaemia and a BMI ≥24.0 kg/m^2.

RESULTS Three thousand and three hundred and forty-two subjects (1334 men and 2008 women, mean age 53.79 ±13.18 years) were included. SUA levels exhibited a graded elevation with an increasing number of cardiovascular risk factors. In female subjects with more than two cardiovascular risk factors, compared with the first quartile of SUA, higher SUA quartiles were associated with a higher probability of increased baPWV (OR=1.500, 1.478, 1.774 for SUA Q2-Q4). In further stratified association analysis, compared with Q1, SUA quartiles showed a graded association with increased baPWV in subjects with TC≥5.2 mmol/L (OR=1.758, 1.942, 2.354 for Q2, Q3 and Q4 respectively), LDL-C≥3.3 mmol/L (OR=1.510, 2.255 for Q3 and Q4) and FBG≥7.0 mmol/L (OR=1.516, 1.748 for Q3 and Q4).

CONCLUSIONS In the Chinese coastal female population, the association of high SUA and increased arterial stiffness is dependent on the coexistence of at least one cardiovascular risk factor, especially hypercholesterolemia.

GW30-e0131

Long term tracking of fasting blood glucose variability and periphery artery disease in people without diabetes

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OBJECTIVES Long-term tracking of fasting blood glucose (FBG) in people without diabetes in relation to periphery artery disease (PAD) has barely been reported. Our study aimed to investigate the association between FBG variability and the incidence of PAD in people without diabetes. Long-term tracking of fasting blood glucose (FBG) in people without diabetes in relation to periphery artery disease (PAD) has barely been reported. Our study aimed to investigate the association between FBG variability and the incidence of PAD in people without diabetes.

METHODS We included 9437 participants without prior PAD and diabetes from the Atherosclerosis Risk in Communities study in the final analysis. At least two measurements of FBG were required during follow-up. Variability of FBG was identified using standard deviation (SD), CV (coefficient of variation) and variability independent of the mean (VIM) across FBG. PAD was defined as an ankle brachial index less than 0.9, or hospitalization with a PAD diagnosis. Cox regression was used to calculate hazard ratios (HR) for incidence of PAD and FBG variability.

RESULTS During a median follow-up of 25.2 years, 896 (9.5%) PAD events were observed, 55.6% (n=498) were male, and 18% (n=161) were African-American. Participants in the lowest quartile of CV compared with the highest ones were at lower PAD risk (HR 1.16, 95% CI 1.11, 1.22; P<0.0001). HRs for SD and VIM were 1.07 (95% CI 1.02, 1.12; P=0.004), 1.06 (95% CI 1.02, 1.11; P=0.009) for PAD, respectively.

CONCLUSIONS High FBG variability was independently associated with increased prevalence of PAD in people without diabetes.

GW30-e0143

Effects of atorvastatin on metabolic profile and glucose metabolism in non-diabetic patients with dyslipidemia

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OBJECTIVES Statin therapy plays an essential part in preventing cardiovascular disease (CVD). Recent studies showed that statin resulted in an increasing rate of new onset diabetes. Yet few studies have discussed global metabolic profile alterations during statin therapy. In this study, by measuring serum metabolic profile, we aim to characterize the metabolic alteration, especially glucose metabolism after atorvastatin therapy in non-diabetic patients with dyslipidemia.

METHODS Patients diagnosed with dyslipidemia without previous history of diabetes were enrolled in the study. Demographic factors were collected and biochemical measurements were performed during initial enrollment, 1-week, 4-week and 16-week follow-up. Nontargeted metabolomics was applied to demonstrate global metabolic profile alteration during statin therapy.

RESULTS Serum LDL levels began to decrease during 1-week follow-up after statin administration. The fasting glucose remains relatively the same during follow up, while HbA1c levels were significantly lowered upon 16-week follow-up. Meanwhile, metabolites in glucose metabolism were also progressively altered during statin therapy. Pathway analyses further shed light on dysregulated glucose metabolism pathways, indicating statin's function in dysregulating glucose metabolism.

CONCLUSIONS In the present cohort study, statin exhibited its function in dysregulating glucose metabolism after 16-week administration. By utilizing non-target metabolic profile surveys, we have found a number of altered metabolites in glucose metabolism after statin administration. The altered metabolites and metabolism pathways shed light on further mechanism study of statin's function in glucose metabolism.

GW30-e0145

Dysregulated serum lipid profile and its correlation to disease activity in young female adults diagnosed with systemic lupus erythematosus: a single-center cross-sectional analysis

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OBJECTIVES Recent studies showed that dyslipidemia could be a critical factor in the progression of cardiovascular disease in systemic lupus erythematosus (SLE). The aim of the present study was to describe the relationship between serum lipid profile and SLE disease activity in young female adults with SLE

METHODS Seventy-one female subjects diagnosed with SLE and the control aged 20–30 years were enrolled. Serum lipid profile including TC, TG, HDL-C, LDL-C, VLDL-C, Apo A, Apo B, and Apo E were evaluated between control and young female SLE patients. Univariate correlation analyses were performed to explore the correlation between serum lipid levels and SLE disease activity.

RESULTS Our results showed that TG and VLDL-C levels were significantly increased in young female SLE as compared to control, with TC, HDL-C, LDL-C, Apo A, and Apo B significantly reduced. Meanwhile, univariate correlation analyses showed negative correlations between SLE disease activity index and HDL-C, LDL-C, Apo A, and Apo B; with positive correlations between SLE disease activity index and TG and VLDL-C.

CONCLUSIONS Serum lipid profile was significantly dysregulated in young female SLE patients. Moreover, SLE disease activity was correlated to the serum lipid levels, supporting the notion that the young patients with SLE might also have a higher risk of cardiovascular disease.

GW30-e0198

Further insight into 10-year CVD risk evaluation and recommended eligibility for statin therapy in general Chinese population: comparison of cardiovascular risk prediction models and their guidelines

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OBJECTIVES Identification of individuals at risk of cardiovascular diseases (CVD) using recommend absolute cardiovascular risk assessment as a clinically sound guide led to better clinical outcomes and may help policy makers in conscious decision making for community based and national intervention strategies. There was good evidence on the comparability of varying approaches to CVD risk estimation and application of different criteria for therapeutic recommendations at Western populations level. However, available evidence for a direct comparison of the calculated CVD risk and resulting statin eligibility generated by the three sets of guidelines (ACC/AHA guideline, ATP-III and ESC guideline) in Asian population is limited and inconsistent. Our objective was to compare various CVD risk assessment tools and their related guidelines in the estimation of 10 year-CVD risk and preventive recommendations in general Chinese population.

METHODS Using data from Northeast China Rural Cardiovascular Health Study (NCRCHS), we estimated the cardiovascular disease risk and proportion of the Chinese population, aged 40–74 years without cardiovascular disease, who would theoretically be eligible for statin treatment under ACC/AHA guideline, ATP-III and ESC guideline. Ten-year CVD predicted risk was calculated using the ACC/AHA 2013 pooled cohort equations, Framingham general cardiovascular risk score, and two versions of Systematic Coronary Risk Evaluation (SCORE) equations (for low and high risk European countries).

RESULTS Mean cardiovascular risks were 11.89, 17.16, 1.47, and 0.92% in men and 5.02, 8.34, 0.62, and 0.43% in women based on ACC/AHA, Framingham, SCORE equation for high-risk European countries and low-risk European countries, respectively. Statins would be recommended for 57.4% (n=3967) of men and 24.7% (n=4617) of women by the ACC/AHA, 18.8% (n=3664) of men and 18.0% (n=4286) of women by the ATP-III, 31.0% (n=3563) of men and 7.0% (n=4151) of women by the SCORE-high model, and 14.3% of men and 2.2% of women by the SCORE-low model.

CONCLUSIONS Implementing the ACC/AHA lipid treatment guidelines in China would identify more individuals as eligible for consideration of statins therapy, proportions exceeding those with ATP-III or ESC guidelines in the general Chinese population. An opportunity exists to make gains in population cardiovascular health by increasing uptake of statin treatment among intermediate- and higher-risk Canadians, whether that risk is calculated via the modified FRS, SCORE or the pooled cohort equations. The differences for individuals eligible for statin treatment also underscored the urgent need for a specific CVD risk algorithm and guideline, designed for China.

GW30-e0200

The impact of nontraditional lipid profiles on left ventricular geometric abnormalities: insights from a general Chinese population

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OBJECTIVES Despite current interest in the unfavorable impact of nontraditional lipid profiles on cardiovascular disease, information regarding its relations to abnormal left ventricular (LV) geometry has not been systemically elucidated. This study sought to understand predictive implication of nontraditional lipid profiles in specific LV geometric patterns in the general population of rural China.

METHODS Analyses were based upon a cross-sectional study of 10,756 participants (mean age 53.8 years; 54.0% females) who underwent assessment of biochemical, anthropometric, and blood pressure variables in rural areas of China. Participants were classified into four groups of LV morphologic pattern according to left ventricular mass index (LVMI) and relative wall thickness with quantitative echocardiographic data.

RESULTS By multivariable-adjusted linear regression models, nontraditional lipid profiles were positive determinants of concentricity index and LV wall thickness (all $P<0.05$), with modest effects on LVMI. Non-high-density lipoprotein cholesterol (non-HDL-C) emerged as an independent correlate of concentric LV hypertrophy (LVH) (adjusted odds ratio [OR]: 1.174 per 1 SD increment in non-HDL-C, 95% confidence interval [CI]: 1.075–1.281), followed by low-density lipoprotein cholesterol (LDL-C)/HDL-C ratio (1.158 [1.059–1.266]), total cholesterol (TC)/HDL-C ratio (1.150 [1.050–1.260]), and triglyceride (TG)/HDL-C ratio (1.134 [1.030–1.249]). The ORs for concentric LVH by tertiles further provided insight into that excess risk was associated with the highest tertile of nontraditional lipid profiles. The areas under the ROC curves to predict concentric LVH were statistically identical among nontraditional lipid parameters.

CONCLUSIONS Nontraditional lipid profiles, easily measured in the everyday routine examination, were responsible for increased risk of concentric LVH, potentially providing enhanced clinical utility at no additional cost, which emphasized the beneficial effect of these markers to supplement and improve CVD risk stratification.

GW30-e0209

Ultrasound ultrafast imaging of the carotid artery pulse wave velocity: is the surrogate of regional artery stiffness?

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OBJECTIVES Cardiovascular diseases (CVDs) are the leading causes of death in the world and responsible for over 17.7 million deaths annually. Arterial stiffness could be a strongest predictor for coronary heart disease and stroke. Pulsed wave velocity (PWV) is "the most hallowed and still probably the best" measure of arterial stiffness and closely related to the processing of arteriosclerosis. Techniques to measure PWV present limitations. There are based on the mathematical model calculation, or need special instruments and required a fairly high level of technical expertise. A new ultrasound-based technique, Ultrasound Ultrafast imaging could noninvasive assessment of regional carotid artery stiffness. The imaging system has a very high frame rates over than 2000 frames per second, and could quickly obtain the PWV propagate along the carotid artery. The objective is to detect the PWV in elder Humans carotid artery in vivo. Determine the feasibility and accuracy to assess artery stiffness by Ultrasound Ultrafast imaging. Confirm the relationship between the local carotid artery PWV and the stiffness of the systemic vessels.

METHODS Ultrasound Ultrafast imaging was performed and obtain the velocity propagate along the left common carotid arteries of fifty-nine (n=59) healthy volunteers. Including the PWV at the beginning of the systole and at the ending of the systole ($_{BS}$PWV, $_{ES}$PWV), the mean PWV (mPWV) were calculated. E-Tracking technology in measuring artery elasticity modulus (PWVβ) and cardio-ankle vascular index (CAVI) were calculated in all subjects. The correlation between parameters derived from Ultrasound Ultrafast imaging and elastic modulus were analyzed. Indicate artery elasticity and the impact of modifying factors such as BMI, age and hypertension.

RESULTS (1) The success rate of first obtain the $_{BS}$PWV, $_{ES}$PWV were 94.2 and 90.8%, which required a median overall duration of 73 s. (2) mPWV were significant positively correlated with PWVβ and CAVI (r=0.68, P<0.01, r=0.48, P<0.05). BMI, age and hypertension were also positively correlated with PWV. (3) The mPWV have a good repeatability and conformity. Interobserver and intraobserver variabilities were 4.2 and 3.6%, respectively.

CONCLUSIONS The elasticity of carotid artery is an integral part of the global arterial elasticity. Ultrasound Ultrafast imaging is a reliable method to assess the regional carotid artery stiffness. The technique can directly and quickly measure PWV of local vessels, with high repeatability and provides a new method for clinical early assessment artery elasticity.

GW30-e0215

Value of reduced glomerular filtration rate assessment with cardiometabolic index: insights from a population-based Chinese cohort

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OBJECTIVES Recent studies have suggested that cardiometabolic index (CMI), a novel estimate of visceral adipose tissue, could be of use in the evaluation of cardiovascular risk factors. However, the potential utility and clinical significance of CMI in the detection of reduced estimated glomerular filtration rate (eGFR) remains uncertain. The purpose of this study was to investigate the usefulness of CMI in assessing reduced eGFR in the general Chinese population.

METHODS This cross-sectional analysis included 11,578 participants (mean age: 53.8 years, 53.7% females) from Northeast China Rural Cardiovascular Health Study (NCRCHS) of general Chinese population (data collected from January 2013 to August 2013). CMI was calculated by triglyceride to high density lipoprotein cholesterol ratio multiply waist-to-height ratio. Reduced eGFR was defined as eGFR<60 mL/min per 1.73 m2. Multivariate regressions were performed to determine CMI's association with eGFR value and eGFR reduction, ROC analyses were employed to investigate CMI's discriminating ability for decreased eGFR.

RESULTS The prevalence of reduced eGFR was 1.7% in males and 2.5% in females. CMI was notably more adverse in reduced eGFR groups, regardless of genders. In fully adjusted multivariate linear models, each 1 SD increment of CMI caused 3.150 mL/min per 1.73 m2 and 2.411 mL/min per 1.73 m2 loss of eGFR before CMI reached 1.210 and 1.520 in males and females, respectively. In logistic regression analyses, per 1 SD increase of CMI brought 51.6% additional risk of reduced eGFR in males while caused 1.347 times of risk in females. After divided into quartiles, people in the top quartile of CMI had higher adjusted ORs of having reduced eGFR, with ORs of 4.227 (1.681, 10.627) and 3.442 (1.685–7.031) for males and females respectively. AUC of CMI was revealed to be 0.633 (0.620–0.646) in males and 0.684 (0.672–0.695) in females.

CONCLUSIONS Higher CMI was independently associated with greater burden of reduced eGFR, highlighting VAT distribution and dysfunction as a potential mechanism underlying the association of obesity with kidney damage and adverse cardiovascular outcomes. The findings from this study provided important insights regarding the potential usefulness and clinical relevance of CMI in the detection of reduced eGFR among general Chinese population.

GW30-e0226

Adverse effects of stains on muscle in adults: a systematic review and meta-analysis

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OBJECTIVES Statin therapy is the cornerstone therapy of cardiovascular diseases, but its muscular adverse effects could be severe. Previous conclusions on statin's muscular adverse effects didn't reach agreement, especially in some certain populations.

METHODS We systematically searched PubMed, EMBASE, Cochrane Library from the beginning of these databases to 28th February, 2017. After assessment of the literature eligibility, we extracted the outcome data. The quality of each study was assessed using the Cochrane risk of bias assessment. Heterogeneity was estimated by the value of I^2. Overall odds ratios (95% confidence interval) were pooled. The analyses were performed via Stata version 14.0.

RESULTS Thirty-two English-written studies were included in this analysis. All of them were clinical randomized control trials (RCTs). The risk of adverse effects on muscles was increased by 10.4% in the statin group compared to the placebo group (OR 1.104, P=0.004) and most frequent adverse effect appeared to be myalgia (OR 1.212, P<0.001). Subgroup analysis were conducted in different populations.

CONCLUSIONS Statins may be associated with greater risk of muscular adverse effects and the statins mainly increased the risk of myalgia. Elder patients or those with chronic kidney disease may not be suffered from such high risk.

GW30-e0239

Association between calf girth and peripheral artery disease in the Atherosclerosis Risk in Communities Study

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OBJECTIVES The pathogenesis of peripheral artery disease (PAD) is associated with impaired calf muscle. We sought to investigate the association between gender specific calf girth and the prevalent of PAD among participants from a community-based cohort study.

METHODS Thirteen thousand and eight hundred and eight participants in the Atherosclerosis Risk in Communities (ARIC) Study without prior PAD were included in the final analysis. Calf girth was measured at baseline (1985–1987). A hospital diagnosis with an ICD-9 code defined incident PAD during follow up. Cox regression analysis adjusted for demographic variables and other covariates were used to estimate hazard ratios (HR) and 95% confidence interval (CI) for the association between calf girth and PAD.

RESULTS After a medium follow-up of 25.2 years, the overall prevalence of PAD in our study was 5.2% (721/13,808), 335 patients were women and 386 were men. The adjusted HR for PAD with calf girth as continuous variables was 0.99 (95% CI 0.95–1.04) in female and 0.93 (95% CI 0.88–0.99) in male, respectively. Moreover, interaction for gender was statistically significant between calf girth and PAD in overall population (P=0.001).

CONCLUSIONS Our findings revealed a linear association of calf girth with the prevalent of PAD among male participants in ARIC.

GW30-e0278

Risk factors analysis of carotid artery plaque based on pathological type

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OBJECTIVES Carotid plaque is closely related to ASCVD, and the ultrasonographic findings of carotid atherosclerosis correlate with its pathological basis. According to the ultrasound, we divided them into 3 groups according to different echogenic plaques: the thickening of IMT was the lipid striation group;

The strongly echogenic plaques were fibrous plaque. Hypoechoic plaques were in the composite lesion group. We wanted to explore the risk factors of different pathological types of carotid plaque under ultrasound.

METHODS A total of 233 patients were enrolled, in the cardiovascular department of QianFo Mountain hospital, applied to Shandong University. Carotid ultrasound examination was performed during hospitalization. The group with no plaque formation was classified as lipid striation lesion (group 147 cases). Carotid artery plaque formation and only the hard plaque was fiberoptic in the ultrasound group (2 groups, 86 cases). Carotid plaque formation with a soft plaque or mixed plaque on ultrasound was a compound lesion group (3 groups, 100 cases). The diagnosis, blood lipid, blood glucose, uric acid, homocysteine (Hcy), smoking history and drinking history were collected. All data were analyzed by SPSS 24.0 version. P<0.05 was considered a statistically significant difference.

RESULTS The independent sample T-test showed that the Hcy level was different among all groups (P<0.05). Pearson correlation analysis results showed that age (P=0.026), gender (P=0.000), smoking (P=0.000), history of coronary heart disease (P=0.017), and Hcy level (P=0.000) were closely correlated with plaque properties. The results showed that age (P=0.01, OR=0.920, 95%CI=0.875–0.968), Hcy level (P=0.000, OR=0.601, 95%CI=0.467–0.772) and smoking (P=0.01, OR=42.621, 95%CI=4.233–429.191) are risk factors in the lipid striation group. Blood glucose (P=0.021, OR=1.540, 95%CI=1.066–2.225) was a risk factor in the fibroblast lesion group.

CONCLUSIONS Different pathological types of carotid plaque risk factors were different, age, Hcy level, and smoking are risk factors of lipid stripe group. Blood glucose is a risk factor for fibrous plate lesions.

GW30-e0285

Association between height and lipid profile among Korean men: results from the 10-year Korea National Health and Nutrition Examination Survey

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OBJECTIVES Despite extensive epidemiologic evidence for the relationship between adult height and cardiovascular disease (CVD), its underlying mechanism remains unclear. Meanwhile, metabolic disorders precede the occurrence of CVD, and play a role as risk factors for CVD. Thus, it could be hypothesized that height might affect the prevalence of metabolic diseases before overt CVD ensues. We investigated the potential association between stature and metabolic risk factors for CVD in a large population.

METHODS This nationwide cross-sectional study was based on data from 21,425 men over 19 years of age from the Korea National Health and Nutrition Examination Survey (2007–2016). The odds ratios (ORs) and 95% confidence intervals (CIs) for 3 metabolic risk factors (hypertension, diabetes, and dyslipidemia) were calculated across height quartiles using multivariate logistic regression models.

RESULTS Short men had more metabolic risk factors, were older, smoked less, were poorer, and had lower body mass index (BMI) values. Among metabolic disorders, only dyslipidemia was significantly associated with height (P-trend=0.007) after adjusting for age, BMI, health habits, and economic status. Further analysis indicated that ORs were decreased across height in a gradual manner for hypercholesterolemia (P-trend=0.006) and hypertriglyceridemia (P-trend<0.001) but not for decreased high-density lipoprotein cholesterol.

CONCLUSIONS Short stature is correlated with a high prevalence of dyslipidemia and adverse lipid profiles in Korean men without apparent CVD. Our finding suggests lipid disorder serves as a bridge between short stature and occurrence of CVD; and it might help explain the inverse relationship between height and CVD.

GW30-e0302

Attenuation of enhanced inflammatory response by lipoprotein apheresis in patients with familial hypercholesterolemia

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OBJECTIVES The aim of this study was to examine the significance of LPS-NF-κB axis and the impact of lipoprotein apheresis (LA) on this pathway in FH patients.

METHODS A matched case-control study based on the cohort who was genetically diagnosed with FH combined with coronary artery disease (CAD) was implemented. It included 63 cases, 63 CAD controls and 63 non-CAD controls matched with the same sex and the age difference≤4 years respectively. Plasma LPS levels and NF-κB activity were compared among three groups. We studied in vitro LPS-induced interleukin-6 (IL-6) production by mononuclear cells from cases without statin use and compared them with control groups (n=16, respectively). Subsequently, the 16 FH patients underwent LA. Blood samples were taken immediately before and regularly after LA for measuring LPS and NF-κB.

RESULTS FH plus CAD cases had significantly higher LPS levels and NF-κB activity than CAD and non-CAD controls (all P<0.01). LPS-induced IL-6 production by PBMCs of FH plus CAD subjects was much higher compared with control groups (both P<0.01). Moreover, plasma LPS levels (P<0.001) and NF-κB activity (P<0.01) were dramatically reduced after apheresis in FH patients.

CONCLUSIONS This study, firstly, showed that genetically confirmed FH patients had a marked activation of LPS-NF-κB axis, while LA significantly attenuated this key inflammatory pathway, suggesting that inflammation may be an important therapeutic target for FH patients.

GW30-e0303

Association between baseline, achieved, and reduction of C-reactive protein and cardiovascular outcomes after LDL-C lowering with statin or ezetimibe: a systematic review and meta-analysis

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OBJECTIVES Several lipid-lowering therapies, i.e. statins and ezetimibe, reduce C-reactive protein (CRP) independently of their effects on reducing low-density lipoprotein cholesterol (LDL-C), but the association between CRP parameters and benefits from more intensive LDL-C lowering is inconclusive. We aimed to determine if the benefits of more-intensive versus less-intensive LDL-C lowering on cardiovascular events related to baseline, achieved or magnitude of reduction in CRP concentrations.

METHODS PubMed, EMBASE, and Cochrane were searched through July 2, 2018. We included randomized controlled, cardiovascular outcome trials of LDL-C lowering with statins or ezetimibe. Two reviewers independently extracted study data and rated study quality, and data were analyzed using meta-analysis and meta-regression analysis. Rate ratios (RRs) of mortality and cardiovascular outcomes associated with baseline, achieved and the magnitude reduction of CRP concentration.

RESULTS We included 24 trials (171, 250 patients) randomly assigned to more-intensive or less-intensive LDL-C lowering treatments. Median follow-up duration was 4.2 years. More intensive LDL-C lowering resulted in a significant reduction in incidences of all outcomes. Meta-regression and meta-analyses showed more intensive LDL-C lowering (compared with less-intensive LDL-C lowering) was associated with less reductions in myocardial infarction with a higher baseline CRP concentration (change in RRs per 1-mg/L increase in log-transformed CRP, 1.12 [95% CI, 1.04–1.22; P=0.007]), but not other outcomes. Similar risk reductions occurred for more vs. less intensive LDL-C lowering therapy regardless of the magnitude of CRP reduction or the achieved CRP level for all outcomes.

CONCLUSIONS Baseline CRP concentrations might be associated with the benefits of LDL-C lowering on myocardial infarction but no other outcomes, while the achieved and magnitude of reduction in CRP did not seem to have an important association.

GW30-e0313

Prediction of calcification in anterior tibial artery plaque in patients with diabetic foot amputation by matrix vesicle level

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OBJECTIVES To analysis the role of matrix vesicles (MVs) in the formation of calcification in the anterior tibial artery plaque in patients with diabetic foot amputation, we hope to provide new ideas for early intervention and treatment of calcification in diabetic patients.

METHODS Sixty-five patients with diabetic foot amputation were enrolled from October 2015 to January 2018, 40 samples were finalized based on inclusion criteria and exclusion criteria. The calcification of anterior tibial artery was measured by calcium quantification and the patients were divided into a low calcification group (calcium quantification<4 mmol/mg, n=20) and a high calcification group (calcium quantitation>4 mmol/mg, n=20). The patients clinical baseline data was collected and analyzed. The calcification of continuous paraffin section of anterior tibial artery was observed by Von Kossa staining. The tissue was removed from the liquid nitrogen, and the lysate was sufficiently lysed, placed in an aseptic grinder and thoroughly ground on ice, and allowed to stand for 1 hour. MVs were extracted by differential centrifugation, and the MV pellet was diluted with PBS buffer and stored at −20°C. Distribution and morphology of MVs was observed by scanning electron microscopy. Western blot was used to determine the expression of MV marker protein in the two groups. The protein concentration was determined by BCA method. The concentration of MVs was detected by NTA. Correlation between calcium content in anterior tibial artery and MVs was analyzed by Pearson correlation analysis. The sensitivity and specificity of MVs for predicting calcification in plaque were analyzed by ROC curve.

RESULTS Von Kossa staining of the anterior tibial artery tissue in patients with diabetic foot amputation showed that a small amount of black calcium deposits were observed in the plaques of the low calcification group. While a large number of brown and black particles were observed under the intima of the high calcification group, and the focal black calcium salt mass in the plaque was significantly enhanced compared with the low calcification group. Calcium content measurements showed that the calcium content of the high calcification group was 2.39 times that of the low calcification group. Scanning electron microscopy showed that the level of MV in the high calcification group was higher than that in the low calcification group. Western blot and BCA showed that the expression of MV marker protein increased with the increase of calcium content. Pearson correlation analysis showed that the level of MV in the anterior tibial artery was positively correlated with the calcium content in the anterior tibial artery plaque in patients with diabetic foot amputation (r=0.7729, P<0.001). The ROC curve showed the area under the curve to be 0.894 (95% CI: 0.788–0.999, P<0.001).

CONCLUSIONS The level of matrix vesicles is positively correlated with the progression of calcification in diabetic arterial plaques, and its level has certain predictive value for different degrees of plaque calcification.

GW30-e0361

Relationship between neutrophil-lymphocyte ratio and brachial-ankle pulse wave velocity

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OBJECTIVES To analyze the relationship between neutrophil-lymphocyte ratio (NLR) and brachial-ankle pulse wave velocity (baPWV) and explore the influence of inflammation on the peripheral artery elasticity.

METHODS A total of 2652 health check-up subjects were enrolled to measure baPWV from March 2015 to March 2016 in our hospital. Based on the results of baPWV, the subjects were divided into normal group and elevated group. The values of blood routine, body mass index, systolic blood pressure, diastolic blood pressure and other biochemistry index were detected and analyzed using t test, Pearson correlation analysis and Logistic regression analysis.

RESULTS The values of male ratio, age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting plasma glucose (FBG), triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), blood uric acid (UA), white blood cells (WBC), neutrophil, NLR were significantly higher in elevated group than in normal group (P<0.05). After correcting BMI, SBP, DBP, TG, TC, HDL-C, LDL-C, FBG and UA, neutrophil and NLR were positively associated with baPWV (P<0.05). NLR, male, age, SBP, DBP and FBG were independent risk factors of baPWV (P<0.05).

CONCLUSIONS NLR is positively associated with baPWV and is an independent influencing factor of baPWV.

GW30-e0468

Reduction in inflammation is associated with improved lipoprotein profile and decreased arterial stiffness in SLE

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OBJECTIVES As one of the causes of premature atherosclerosis, lipid abnormalities have been reported to be associated with the inflammation and disease activity status in patients with systemic lupus erythematosus (SLE). However, much of the studies were performed in cross-sectional design. This study is the first longitudinal cohort study to evaluate the associations of the reduction in inflammation and disease activity with lipoprotein profile and arterial stiffness in adult female SLE patients.

METHODS Fifty-nine female SLE patients with baseline systemic lupus erythematosus disease activity index (SLEDAI)≥6 and SLEDAI reduction >3 at 1-year follow-up were included in the study. All 59 patients were not treated with statins during the study period or for the preceding 6 months. Neutrophil-to-lymphocyte ratio (NLR), erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hs-CRP), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG) and mean brachial-ankle pulse wave velocity (baPWV) were measured and compared between baseline and 1-year follow-up by paired t-test or Wilcoxon rank-sum test. Correlations between reductions in biomarkers of inflammation, SLEDAI, changes in the mean baPWV and lipoprotein profile were also assessed.

RESULTS The median SLEDAI decrease was 6 (Q1-Q3: 4–10). Compared to baseline, we observed significant decreases of NLR (P=0.0006), ESR (P=0.0024) and mean baPWV (P=0.0173) at 1-year follow-up, while hs-CRP was not significantly changed. Significant decreases of LDL-C (P=0.0168), TG (P=0.0014) and TC to HDL-C ratio (TC/HDL-C, P=0.0002) and increased HDL-C (P=0.0398) were also identified, indicating improved lipoprotein profile with decreased SLEDAI. Further correlation analysis showed significant correlations between the reduction in ESR and decreases in TC/HDL-C (r=0.28, P=0.0499), TG (r=0.48, P=0.0001) and mean baPWV (r=0.38, P=0.0054). In addition, a significant correlation was also detected between the reduction in SLEDAI and decrease in mean baPWV (r=0.30, P=0.0221).

CONCLUSIONS Among SLE patients experiencing reductions in SLEDAI, we observed improvements in their lipoprotein profile and arterial stiffness. These findings may provide further insight into the beneficial effects of reducing inflammation on atherosclerosis risk in SLE.

GW30-e0591

Pharmacodynamics, pharmacokinetics and safety of alirocumab in healthy chinese subjects

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OBJECTIVES *Aim* This randomized, double-blind, placebo-controlled phase I study assessed the pharmacokinetics/pharmacodynamics and safety/tolerability of single doses of alirocumab, a fully human monoclonal antibody to PCSK9, in healthy Chinese subjects.

METHODS Subjects (n=35 [4 non-compliant with Good Clinical Practice were excluded], 74.2% male, aged 21–45 years) with baseline low-density lipoprotein cholesterol (LDL-C) >100 mg/dL (2.59 mmol/L) were randomized to a single subcutaneous injection (1 mL) of alirocumab 75, 150 or 300 mg (2× 150 mg/mL injections), or placebo; study registration: chinadrugtrials.org, CTR20160335.

RESULTS Maximum mean LDL-C reductions from baseline were observed on Day 8, 15, and 22 with alirocumab 75 (–55.32%), 150 (–63.65%), and 300 mg (–73.65%), respectively (**Figure**). Across all doses, mean alirocumab half-life was 5.9 days, with no dose effect (P=0.261). Mean free PCSK9 levels were reduced to below the lower limit of quantification within 4 hours of alirocumab dosing and mean total (free and bound) PCSK9 plateaued over Day 3–28, returning to baseline levels by Day 42–84. Treatment-emergent adverse events were reported in 3/8, 6/8, and 7/8 alirocumab 75, 150, and 300 mg groups, respectively, and 2/7 placebo group; nasal congestion and dry throat were the most frequently reported (3/8 and 2/8, respectively [alirocumab 300 mg]). One alirocumab 300 mg subject had a mild local injection-site reaction, which resolved spontaneously. All alirocumab recipients tested negative for anti-drug antibodies.

CONCLUSIONS Alirocumab 75, 150, and 300 mg reduced LDL-C and was generally safe and well tolerated in Chinese subjects. These results are consistent with data from Japanese and Western populations.

This work was first presented at EAS 2019, the 87th EAS Congress in Maastricht.

GW30-e0654

Atorvastatin effectiveness and safety in cardiology patients in real world setting: a registry study in China

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OBJECTIVES The primary objective was to evaluate the effectiveness of atorvastatin in Chinese cardiology patients in real world setting. The secondary objectives were to assess atorvastatin safety in cardiology patients in real world setting and to analyze patterns of atorvastatin prescription in cardiology patients.

METHODS This was a 12-week, multi-center, prospective, observational study. The cardiology patients aged≥18 years who had been prescribed atorvastatin by physician's judgment under normal clinical care were enrolled in this study. At Baseline, patients' demographic information, medical history, medication records, concomitant drugs and laboratory examination results prior to atorvastatin therapy were collected. At Week 12 and any unplanned visits (if

occurred), the laboratory examination results and medication records were collected. The cardiovascular disease (CVD) risk stratification and lipid control targets were all set according to Chinese Guideline on Dyslipidemia Prevention and Treatment in Adult. The primary endpoint was the achievement rate of LDL-C goals at Week 12 of atorvastatin therapy. Safety and tolerability were evaluated by recording the incidence and severity of adverse event (AE) and abnormal laboratory values through the treatment, especially muscle symptoms and hepatic function indices.

RESULTS Four thousand and five hundred forty-eight patients were enrolled in 54 sites and treated with Atorvastatin. Three thousand and four hundred seventy-two patients completed the study and 1076 patients discontinued from the study. The primary reason for discontinuation was lost to follow up (770 [16.93%] patients). Approximately half of the patients (2261 [49.71%]) were at high risk for CVD and 1416 (31.13%) patients were at very high risk for CVD.

Among the full analysis set (FAS) population, which contains 1650 patients, the overall achievement rate of target LDL-C level was 67% (95% CI: 65.0%, 69.7%). The achievement rate was higher in the low CVD risk group (94% [95% CI: 88.2%, 97.0%]) and moderate CVD risk group (90% [95% CI: 84.2%, 93.8%]), as compared with the high CVD risk group (69% [95% CI: 65.8%, 72.2%]) or very high CVD risk group (48% [95% CI: 43.5%, 52.7%]). In general, decreases from baseline in the mean values of total cholesterol, LDL-C and triglyceride concentrations at Week 12 were observed. A total of 1445 (87.6%) patients in FAS were prescribed 20 mg atorvastatin, and the mean dose at Week 12 was generally unchanged compared to the initial dose within each CVD risk group even for those patients without achieving the LDL-C target.

In the safety analysis population, 304 (6.68%) patients experienced 358 treatment emergent AEs, 133 (2.92%) patients had 149 treatment-related AEs and 85 (1.87%) patients experienced serious AEs. As for elevated abnormal laboratory in CK, ALT and AST, only 1 patient at high risk for CVD in 20 mg dose group had a post-baseline laboratory abnormality meeting the specified criterion of CK≥10 X upper limit of normal. No patient had persistent elevation in alanine aminotransferase and aspartate aminotransferase.

CONCLUSIONS Atorvastatin is a powerful lipid-lowering drug with good safety and tolerability in real world setting in China. Twenty milligram was the most commonly used dose in cardiology patients. However, there was nearly no dose up-titration for patients without achieving LDL-C target, which indicates there is still a gap between guideline and clinical practice in the real world setting.

GW30-e0729

Role of NFATc1 in the orthotopic and heterotopic ossification

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OBJECTIVES Nowadays, orthotopic and heterotopic ossification related diseases have gradually become a research hotspot, among which, their respective representative diseases, osteoporosis and vascular calcification, are severely hazardous to health and living standards, and the two always coexists with each other. The bone-vascular axis calcification paradox serves as a bridge between bone and vascular diseases, which links these two seemingly separate diseases up. Striking ectopic calcification in vessel wall always accompanies the decrease of bone mineral density (BMD) or the disorder of bone metabolism, named as calcification paradox. Based on the influences of bone-vascular calcification paradox, it is evitable to wield an influence on vascular calcification when treat bone disorders, vice versa. The treatment result tends not to strike a balance between the two diseases. How to break through this problem is the concern of both clinical and scientific researchers.

METHODS Nuclear Factor of Activated T cells (NFATc) is a kind of transcription factor which widely exists in vertebrates and take an important role. NFATc1, one of the members of NFATc, apart from in the immune system and morphogenesis of cardiac valves and septum being indispensable, is also vital in osteoclasts and atherosclerotic calcification. It can be viewed as the bridge of bone-vascular axis calcification paradox.

RESULTS Numerous studies have shown that NFATc1 is closely related to bone remodeling. During the process of osteoclast formation, NFATc1 plays as a "switching" to promote the formation and maturation of osteoclasts. The findings of Takayanagi et al. demonstrate this: under the stimulation of RANKL, embryonic stem cells lacking of NFATc1 could not differentiate into osteoclasts, but induced ectopic expression of NFATc1 could even induce osteoclast precursor cells to differentiate without the stimulation of RANKL signal. The regulation of osteoclast formation by NFATc1 involves complex signal transduction processes.

Moreover, current studies have also shown that NFATc1 promotes the formation of vascular calcification in the condition of atherosclerosis and chronic renal failure. *In vitro* studies confirmed that inhibition of NFATc1 with CsA completely blocked oxidised low-density lipoprotein-induced osteogenic differentiation of human coronary artery smooth muscle cells, suggesting that NFATc1 promotes vascular wall smooth muscle cells Osteogenesis. For the calcification of chronic renal failure, which is often characterized by medial calcification, its relationship with NFATc1 has also been studied. *In vitro* and *in vivo* experiments showed that the expression of NFATc1 in VSMCs of vascular calcification group in rats with CKD was significantly higher than that of normal control group, and its possible mechanism was to induce phenotype transformation of VSMCs by up-regulating the expression of Runx2, and finally promote calcification.

CONCLUSIONS In conclusion, NFATc1 acts as a "molecular switch" in the orthotopic and heterotopic ossification. However, to develop future treatment strategies through existing knowledge, there is no doubt a long way to go. By further studying the bridging mechanism of NFATc1 in bone-vascular calcification axis paradox, we believe that both bone and vascular diseases can be treated in the near future.

GW30-e0814

Hyperlipidemia acts as a protective factor in patients hospitalized for cancer: nationwide inpatient database analysis

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OBJECTIVES An association between hyperlipidemia (HLD) and malignancy has been reported but incompletely defined. Previous studies on the relationship between HLD and risk of cancer were controversial. Moreover, the impact of concomitant HLD on the inpatient outcomes in patients hospitalized for cancer remains unclear. The aim of our study is to review this association with hyperlipidemia (HLD) and in-hospital outcomes of patients admitted for cancer.

METHODS We conducted a retrospective cohort analysis of the National Inpatient Sample (HCUP-NIS) 2016 database. Patients hospitalized with a principal diagnosis of cancer were identified using the ICD-10 codes. Multivariate logistic regression was performed after adjust for patient baseline characteristics, hospital demographics and relevant comorbidities. Inpatient mortality was compared between the patients with and without HLD.

RESULTS A total of 1,022,625 hospitalizations with cancer were identified. Of these, 318,609 (31.16%) had HLD. Multivariate logistic regression analysis after adjustment showed that patients with both cancer and HLD had lower in-hospital mortality (3.8 vs. 5.21%, OR 0.74, P<0.001) and shorter length of stay (LOS) (6.31 vs. 6.62 days, P><0.001) when compared to patients with cancer but no HLD. Further analysis of the cancer subgroups revealed that HLD was associated with lower mortality than non-HLD in lung cancer (OR 0.64, 95% CI 0.57–0.71, P><0.001), esophageal cancer (OR 0.64, 95% CI 1.05–1.79, P=0.025), colon cancer (OR 0.74, 95% CI 0.59–0.92, P=0.008), pancreatic cancer (OR 0.70, 95% CI 0.55–0.89, P=0.004), ovary cancer (OR 0.47, 95% CI 0.29–0.76, P=0.002), and lymphoma (OR 0.66, 95% CI 0.50–0.86, P=0.002). We found no differences in in-hospital mortality between patients with and without HLD in stomach cancer, rectal cancer, liver cancer, prostate cancer, breast cancer, bladder cancer, kidney cancer, leukemia, and melanoma. When compared with patients without HLD, patients with cancer and HLD also had lower rate of in-hospital cardiac arrest (OR 0.86, P=0.032), palliative care (OR 0.80, P><0.001), DVT/pulmonary embolism (OR 0.85, P><0.001), cardiac tamponade (OR 0.84, P><0.001), platelet transfusion (OR 0.77, P><0.001), sepsis (OR 0.79, P><0.001) and septic shock (OR 0.69, P><0.001); but higher risk of ventricular fibrillation (OR 1.47, P><0.001), respiratory failure (OR 1.15, P><0.001), acute kidney injury (OR 1.25, P><0.001), and complete heart block (OR 1.68, P><0.001).

CONCLUSIONS Concomitant HLD is associated with shorter LOS, lower inpatient mortality in patients hospitalized for certain types of cancer. This result indicated that strict control of hyperlipidemia might not be warranted in patients with cancer. Further large prospective studies are needed.

GW30-e0972

The association of lipid metabolism relative gene polymorphisms and acute myocardial infarction in population of North China

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OBJECTIVES Acute myocardial infarction (AMI) is the most serious type of coronary heart disease that can be influenced by various environmental and inherited factors. It is well known that dyslipidemia is a definitely predisposing factor of acute myocardial infarction, furthermore, previous studies have found many single nucleotide polymorphisms (SNPs) of lipid metabolism associated with AMI occurrence. However, the results are inconsistent. So we designed this study to investigate three genes of lipid metabolism pathways by analysis of 3 SNPs that have not been reported the association with AMI in population of north China.

METHODS Three hundred thirty-six patients with AMI confirmed by Coronary angiography and 270 normal healthy controls are included. Three single nucleotide polymorphisms (SNPs) rs58542926 (E167K) in TM6SF2, rs11591147 (R46L) in PCSK9, and rs320 in LPL were selected and genotyped via multiplex PCR amplifying followed by NGS (next-generation sequencing). The χ^2 test and haplotype analysis were performed to analyse the associations between the three SNPs and AMI using the SPSS V.22.0 software package.

RESULTS Rs58542926 in TM6SF2 was associated with AMI in in population of north China (OR=1.574, P-value=0.03). No significant association was observed between the other two SNPs and AMI. Stratified association analysis showed that rs11591147 was associated with AMI in non-hypertension group (Odds-ratio=1.234, P-value=0.013).

CONCLUSIONS Single nucleotide polymorphisms of lipid metabolism relative gene were significantly associated with the morbidity of AMI in population of north China. The minor allele of rs58542926 was the risk factor of AMI occurrences.

GW30-e0980

Achievement of guideline directed low-density lipoprotein cholesterol goals: a real-world study from a single Chinese center

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OBJECTIVES Large-scale studies have provided insights into the achievement of LDL-C targets, but largely concerned Western Europe and North America, but little is known from outside these regions. We therefore conducted this study to observe guideline directed risk stratification status and the achievement of low density lipoprotein cholesterol (LDL-C) targets in patients who were diagnosed dyslipidemia in the real world from China.

METHODS This cross-sectional observational study was conducted in a single center (January 2018~December 2018) from China for 12 months. Patients (n=2122) who were diagnosed dyslipidemia were enrolled. And the guideline directed risk stratification status and the achievement of LDL-c goals was analyzed.

RESULTS The mean/SD age was 65.9/11.6 years, 57.3% of patients were men and the mean/SD LDL-C value was 2.27/0.86 mmol/L. 1569 patients (73.9%) were stratified into very high risk group, 168 patients (7.9%) into high risk group and the other 385 patients (18.1%) into moderate-low risk group. At enrolment, 98.9% of patients were receiving a statin (0.8% on high intensity treatment). Only 38.2% of the very high risk patients versus 51.9% of the high risk and 55.7% of the moderate risk patients achieved their LDL-C goals. On multivariable analysis, factors independently associated with not achieving LDL-C goals were no (versus low dose) statin therapy, female sex, age>=65 y–<75 y, level of cardiovascular risk, chronic kidney disease, and current smoking. Diabetes was associated with a lower risk of not achieving LDL-C goals. Diabetes and age>=75 y were associated with a lower risk of not achieving LDL-C goals. Statin dose was not a significant factor to affect the LDL-C goal achievement.

CONCLUSIONS These observational data suggest that the achievement of LDL-C goals is suboptimal. High dose statin use rate was very low, while there was no significant correlation between statin dose and LDL-c goal achievement rate. Efforts are needed to improve the management of LDL-C individually and conduct more relevant studies to define the appropriate target of LDL-c level in Chinese population in the future.

STRUCTURAL HEART DISEASE

GW30-e0137

What does hypertrabeculation bring about to the heart?

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OBJECTIVES Left ventricular hypertrabeculation (LVHT) is a congenital cardiomyopathy, the clinical prognosis of which will be deteriorated if complications such as heart failure, arrhythmia or thromboembolism occur. However, the impact of LVHT to the heart remains unclear. The aim of our investigation is to elucidate alteration of the pathology and function of the heart, and find out the most vulnerable category of patients who suffer from LVHT, hoping to refine the recognition of this rare cadiomyopathy for better treatment.

METHODS We selected five patients (2 females, 3 males) from Shanghai General Hospital. They were candidates for diagnosing LVHT with typical clinical presentations and suspicious CMRI (cardiac magnetic resonance imaging) manifestations.

RESULTS Through analyzing and comparing five patients' echocardiography imagings and electrocardiograms, we discover that the impact of hypertrabeculation to the heart is dilation and hypertrophy of the chamber (dilation is more often). With the hyperplasia of myocardial trabeculum, the mobility of myocardium is reduced. As a result, the function of the heart is deteriorated and arrhythmia (especially premature beats and tachycardia) appears. Moreover, according to the history and CMRI, patients who suffer from heart failure, arrhythmia (especially premature beats and tachycardia) or thromboembolism are more vulnerable to LVHT. In addition, the risk of thrombus formation might be further increased in patients with an NMD (neuromuscular disorders) and depressed mobility of ventricle.

CONCLUSIONS In LVHT patients, the alteration of the pathology of the heart is dilation and hypertrophy of the chamber primarily, and left ventricular hypertrabeculation as well, which lead to the dysfunction of the heart. Clinically, patients who were diagnosed as LVHT usually go through heart failure, arrhythmia (especially premature beats and tachycardia) or thromboembolism at the same time.

GW30-e0148

The role of serum leptin in calcific aortic valve disease

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OBJECTIVES Calcified aortic valve disease (CAVD) is presented in approximately 20–30% in individuals aged over 65 years and 48% in those aged over 85 years. The late stage of CAVD with form of severe aortic stenosis leads to an increased mortality. The pathophysiology of CAVD included degenerated process related to aging and atherosclerosis. Systemic inflammation has been observed in patients with CAVD. Accumulation of lipids together with infiltration of inflammatory cells were found in early aortic valve lesions, active calcification and ossification are also regarded as crucial process in CAVD. Leptin, a product of adipocytes regulated by obese gene, has been shown to have proinflammatory effect leading to cardiovascular disease and even predict adverse cardiovascular events. Interestingly, aortic valve calcification was enhanced after chronic treatment with leptin in an animal study. In human calcific aortic valves, leptin is highly expressed which promotes osteoblastic differentiation of vascular smooth muscle cells and calcification of valvular interstitial cells. These observations suggested that leptin may be involved in the process of CAVD as well. Therefore, we investigated the relationship between serum leptin level and CAVD.

METHODS Among a total of 786 consecutive patients referred for coronary angiography/intervention in the Department of Cardiology Shanghai Rui Jin Hospital, 656 patients underwent standard transthoracic echocardiography and Doppler flow imaging. Serum levels of leptin were measured in 397 consecutive patients. Continuous and categorical variables were compared using independent t-test or nonparametric test and Chi-squared tests, respectively. Spearman correlation analysis was done to explore the relation between leptin and clinical data. Multiple logistic regression analyses were used to assess the association between leptin and CAVD. In addition, restricted cubic spline was used to investigate the possible association between serum leptin and CAVD. The diagnostic values of leptin were calculated by constructing receiver-operating characteristic (ROC) curves.

RESULTS There was a significant increase in serum leptin in patients with CAVD compared with non-CAVD controls (20.07 and 9.03 ng/mL, P<0.0001). Leptin correlated positively with age (P<0.001)) and negatively with estimated glomerular filtration rate (eGFR) (P<0.001). Multivariates analysis indicated elevated leptin was an independent predictor for the presence of CAVD (P<0.0001). ROC curve analysis showed that the area under the curve was 0.741 (P<0.001) for leptin in predicting the presence of CAVD. Further analysis revealed the diagnostic value of leptin for detecting CAVD was higher for younger patients as well as those with at least mildly reduced renal function. Multivariate logistic regression analysis showed that an increased serum leptin provided greater risk in patients with younger age (P<0.0001) and lower eGFR level (P<0.0001). ROC curve analysis showed that the area under the curve was 0.756 and 0.731 (P<0.001) for leptin in predicting the presence of CAVD in younger patients and mildly reduced renal function group respectively.

CONCLUSIONS The study suggests that elevated serum leptin level is significantly correlated with presence of CAVD, especially in younger patients or those with renal dysfunction.

GW30-e0210

Assessment of right ventricular systolic function and the displacement of tricuspid annulus in atrial septal defect patients using real-time three-dimensional echocardiography

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OBJECTIVES Assessment of the right ventricular volume and function in atrial septal defect (ASD) patients using real-time three dimensional echocardiography (RT3DE). Assess the correlation between the right ventricular systolic function and the displacement of tricuspid annulus.

METHODS RT3DE were performed in 36 ASD patients. The end diastolic/systolic volume (RVEDV/RVESV), and right ventricular ejection fraction (RVEF) were measured by four dimensional right ventricular quantification (4D RVQ) method. Display the spatial position of tricuspid annulus of the three dimensional imaging at the end of systole and diastole. Measure the distance of the displacement of tricuspid annulus.

RESULTS RVEDV, RVESV and RVEF were 133.72±31.07 mL, 73.04±22.62 mL and 42.35±5.41% respectively. The displacement of tricuspid annulus was 12.01±5.06 mm. The RVEF obtained from 4D RVQ method have an excellent correlation with the displacement of tricuspid annulus (r=0.91, P<0.01).

CONCLUSIONS RT3DE can evaluate right ventricular volume and function, and the correlation between the right ventricular systolic function and the displacement of tricuspid annulus. The displacement of tricuspid annulus was a reliable index for assessment right ventricular function.

GW30-e0211

Right ventricular volumes and function assessed by three-dimensional speckle tracking echocardiography: comparisons with cardiac magnetic resonance imaging

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OBJECTIVES Given the right ventricular (RV) complex structure, three-dimensional (3D) methods would be more suitable for assessing RV volumes and function than two-dimensional methods. Recently, 3D speckle tracking echocardiography (3D-STE) has been increasingly used to quantify RV function and strain. However, direct comparisons of 3D-STE and cardiac magnetic resonance (CMR) imaging for evaluation of RV function and strain are limited. The aim of this study was to test the feasibility and accuracy of 3D-STE using comparison with CMR imaging.

METHODS We enrolled 142 patients who agreed to undergo both CMR and 3D-STE on the same day. RV end-diastolic volume (RVEDV), RV end-systolic volume (RVESV), ejection fraction (EF) and longitudinal strain of RV free wall were obtained from 3D-STE and CMR. In addition, longitudinal strain of RV free wall was also obtained from 2D-STE. CMR imaging was the reference standard. The Pearson correlation coefficient and Bland-Altman analysis were used to assess inter-technique agreement. The patients were divided two groups: normal RV function or mild RV dysfunction group (CMR-derived RVEF≥30%, n=70) and severe RV dysfunction group (CMR-derived RVEF<30%, n=69). There are two groups divided by the main clinical diagnosis of patients: 51 patients with dilated cardiomyopathy, 21 patients with heart transplantation, 20 patients with coronary artery disease, 18 patients with hypertrophic disease (10 patients with hypertrophic cardiomyopathy and 8 patients with hypertension), 10 patients with valvular disease. All the above parameters were compared between 3D-STE and CMR, 3D-STE technique was used to evaluate the accuracy in different degrees of right ventricular dysfunction and different diseases.

RESULTS 3D-STE was feasible in 139 patients (98%). 3D-STE-determined RV volumes, EF and longitudinal strain, and 2D-STE-derived RV longitudinal strain correlated strongly with CMR values (RVEDV, r=0.94; RVESV, r=0.95; RVEF, r=0.91; RV longitudinal strain, r=0.80, r=0.61; P<0.001 for all). Compared with CMR reference, 3D-STE-derived RVEDV, RVESV, RV longitudinal strain and 2D-STE-derived RV longitudinal strain were underestimated by 6.9±29.3 mL, 13.7±29.4 mL, 2.3±4.8%, 2.6±6.6%, respectively. 3D-STE-derived RVEF was overestimated by 4.2±6.3%. Compared with patients with RVEF≥30%, 3D-STE-determined RV volumes, EF and longitudinal strain had better correlations with CMR values in patients with RVEF<30% (RVEDV, r=0.88 vs. 0.92; RVESV, r=0.85 vs. 0.93; RVEF, r=0.63 vs. 0.76; RV longitudinal strain, r=0.52 vs. 0.74; P<0.001 for all). Compared with other patients, 3D-STE-determined RV volumes, EF had better correlations with CMR values in dilated patients (RVEDV, r=0.94; RVESV, r=0.94; RVEF, r=0.90; P<0.001 for all), 3D-STE-determined RV longitudinal strain had best correlation with CMR values in valvular patients (r=0.88, P<0.001). 3D-STE to measure RV volumes, EF, longitudinal strain were highly reproducible.

CONCLUSIONS 3D-STE is highly feasible and reproducible, and it correlates highly with the CMR method. 3D-STE can accurately evaluate the RV volumes, function and strain in patients with different etiologies, especially in patients with severe RV dysfunction or dilated patients.

GW30-e0256

Diagnostic value of NC/C ratio in different phases in noncompaction cardiomyopathy with combined routine and contrast echocardiographic techniques

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OBJECTIVES To discuss diagnostic value of NC/C ratio in different phases in left ventricular noncompaction (LVNC) with combined routine and contrast echocardiographic techniques (2DE+LVO) and assess proper NC/C ratio in a Chinese adult population.

METHODS 30 patients with suspected LVNC were collected and underwent 2DE and LVO from January, 2018 to January, 2019. The distribution of two-layered segments and noncompaction segments (NC segments), diagnostic accuracy at end-diastole and end-systole (diagnostic criteria: NC/C>2.3 at end-diastole; NC/C>2.0 at end-systole) were analyzed using 2DE+LVO techniques, compared with the results of CMR as the diagnostic standard. NC/C ratios were also measured in both LVNC group and control groups which included 20 hypertrophic cardiomyopathys, 20 enlarged left ventricles, 20 healthy volunteers. The new NC/C ratio at end-diastole for echocardiographic diagnosis was analyzed.

RESULTS Compared with CMR, 213 (89.2%) two-layered segments at end-diastole and 170 (71.8%) at end-systole could be observed by 2DE+LVO, respectively (P<0.017). NC/C ratios were underestimated at end-systole compared with CMR and end-diastole values (P<0.05). No significant difference was observed between CMR and end-diastole values (P>0.05). The NC segments detection rates were significantly increased from 44.7% at end-systole to 85.2% at end-diastole by 2DE+LVO (P<0.017). Measurement at end-diastole had higher diagnostic accuracy than that at end-systole (sensitivity, specificity, accuracy 88.5, 75.0, 87.7% vs. 69.2, 75.0, 70.0%, respectively) (P=0.02). The cut-off value of end-diastolic NC/C ratio was 2.4 which had 92.0% sensitivity, 93.0% specificity, 87.0% positive predictions, 98.0% negative predictions in diagnosis of the LVNC with the area under the ROC curve 0.94.

CONCLUSIONS NC/C ratios were measured at end-diathole had higher diagnostic value than at end-systole using echocardiography. The end-diastolic NC/C ratio of 2.4 was suggested as a new echocardiographic diagnostic criteria for LVNC in a Chinese adult population.

GW30-e0277

Evaluation of left ventricular function in aortic stenosis patients by vector flow mapping

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OBJECTIVES To quantitatively analysis the left ventricular vortex parameters and blood energy loss (EL) in aortic stenosis (AS) patients in different phases of cardiac cycle using ultrasonic vector flow mapping (VFM) and explore the EL clinical application value in assessment of early cardiac function of AS.

METHODS 37 patients with various degrees of AS were divided into subgroups (16 mild to moderate as AS1 group, 21 severe as AS2 group), and 35 age and gender matched healthy subjects were selected as control group. Based on time-flow curve of left ventricular and the open-close of valve, the diastole period of left ventricle was divided into the isovolumic relaxation phase (P1), rapid filling phase (P2), slow filling phase (P3), atria contract period (P4), and total diastolic phase (Po). The systole period of left ventricle was divided into isovolumetric contraction phase (P5), rapid ejecting phase (P6), slow ejecting phase (P7), and total systolic phase (P8). The differences of general parameters, vortex parameters and EL value of three groups were compared. The correlation between EL and the cardiac structure and function parameters of relaxation and contraction, and vortex parameters of left ventricle above the groups were analyzed.

RESULTS The vortex area of AS2 group were increased in P2 and P5 with significant differences (all P<0.05). Three peaks of EL were appeared in one cardiac cycle in P2, P4 and P6 respectively. And the EL in total systole and diastole were equal. Compared with control group, the EL of AS1 group were increased in all phases, but there were statistically differences only in phases of P4, P7 and Po (all P<0.05). For AS group, there were significant positive correlation between Po-EL, P8-EL and MPG (r=0.626, 0.522 respectively, all P<0.01). There were significant positive correlation between P2-EL, P3-EL, P4-EL, P5-EL and circulation ($r_{control}$=0.651, 0.361, r_{AS}=0.469, 0.673 respectively, P<0.01).

CONCLUSIONS Quantitative evaluation of left ventricular energy loss by VFM technique is expected to provide a sensitive indicator for evaluating the cardiac structure and functional status of AS patients.

GW30-e0279

Relationship between systemic lupus erythematosus disease activity index scores and right ventricle function

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OBJECTIVES This study investigated the use of three-dimensional speckle tracking echocardiography (3DSTE) and tissue Doppler imaging (TDI) to assess the systolic and diastolic RV function in patients with SLE, and the relationship of RV dysfunction and SLE Disease Activity Index (SLEDAI).

METHODS Fifty SLE patients and fifty age and gender matched healthy (control group) were conducted on 3DSTE and TDI in 2018. Global longitudinal systolic strain of RV septal wall (GLS sep) and Global longitudinal systolic strain of RV free wall (GLS free), EF, EDV, ESV, FAC were obtained by 3DSTE. Pulmonary hypertension (PH) was defined as peak tricuspid regurgitation velocity (TRV) of ≥2.9 m/s based upon 2015 ESC guideline. SLE disease activity was assessed using the SLE Disease Activity Index (SLEDAI). Medical records, including patient characteristics, age at diagnosis, duration of disease, BSA, heart rate, diagnosis criteria, cumulative organ damage, laboratory data, were evaluated.

RESULTS Compared with controls, the right ventricle's systolic function parameters, including GLS (sep), GLS (free), FAC, RVMPI, were significantly reduced in SLE patients. While assessing the right ventricle's diastolic function, there were no significantly difference between SLE patients and controls. A statistically was found that RVMPI, GLS as an index of right ventricle systolic function parameters impairment had closely relation in the SLEDAI scores. The multivariable regression analysis showed that patients with higher SLEDAI scores had higher rates of PH.

CONCLUSIONS Echocardiography is an useful noninvasive technique for detecting subclinical RV systolic dysfunction in SLE patients. Disease activity may contribute to RV myocardial impairment and PH.

GW30-e0280

Prognostic value of right ventricular three-dimensional speckle-tracking strain in pulmonary hypertension: superiority of longitudinal strain over circumferential and radial strain

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OBJECTIVES Right ventricular (RV) dysfunction is a predictor of adverse outcomes in patients with pulmonary hypertension (PH). Three-dimensional speckle tracking echocardiography (3D-STE) has been increasingly used to quantify RV function, but we do not know which 3D-STE parameters provide the most important clinical information. The purpose of our study was to investigate whether RV longitudinal strain (LS) provided a better estimation of RV systolic performance and prognostic information.

METHODS Sixty patients with PH and 35 normal controls were enrolled in our study. RV LS, circumferential strain (CS), radial strain (RS) were calculated by 3D-STE. RV volumes and ejection fraction (EF) were obtained from cardiac magnetic resonance (CMR) imaging.

RESULTS Patients with moderate and severe PH had decreased RVEF compared with controls. Our findings revealed that LS showed significant reduction in mild PH patients; whereas CS and RS were decreased in moderate and severe PH patients. Patients with severe PH exhibited reduced RV LS, RS and CS compared with patients with mild PH. RV LS had a better correlation with CMR-derived RVEF, and 6-min walking distance, pulmonary vascular resistance and pulmonary artery systolic pressure than CS and RS. Only LS improved 6 months after medical treatment. RV LS (hazard ratio [HR]: 1.186; 95% confidence interval [CI]: 1.017 to 1.383; P=0.029) and RVEF (HR: 0.878; 95% CI: 0.779 to 0.989; P=0.033) were independent predictors of unfavorable clinical outcomes.

CONCLUSIONS Patients with PH show decreased RV strain. LS best correlates with CMR-derived RVEF, hemodynamic parameters and exercise capacity, and provides prognostic information.

GW30-e0283

The Normal biventricular mechanical function in the transplanted heart by three-dimensional speckle-tracking echocardiography

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OBJECTIVES Exploring the specifically normal biventricular mechanical function of heart transplantation (HT) patients is essential during follow-up studies. The studies about the normal biventricular mechanical function assessed by three-dimensional speckle-tracking echocardiography (3DSTE) of HT patients has yet to be reported. The objectives of this study were to (1) testify the feasibility and accuracy of 3DSTE to evaluate the biventricular function in HT patients; (2) explore the normal biventricular mechanical function in HT patients using 3DSTE.

METHODS Protocol 1 enrolled 38 HT patients who experienced 3DSTE and cardiac magnetic resonance (CMR) examination within 24 h. Protocol 2, 3DSTE data were compared between 46 clinically stable patients at 1 year after HT and 46 healthy controls.

RESULTS Protocol 1, the left ventricular (LV) and right ventricular (RV) derived from 3DSTE had an excellent accuracy comparison with the corresponding value of CMR: LVEF (r=0.96, LOA=–0.5±3.7%), RVEF (r=0.95, LOA=0.5±4.5%). LV global longitudinal strain (GLS), LV global circumferential strain (GCS) were significantly correlated with standard CMR-LVEF (r=0.85, r=0.93, respectively, P<0.001). RV free wall longitudinal strain (FWLS) were also correlated well with standard CMR-RVEF (r=0.83, P<0.001). Protocol 2, compared with healthy controls, lower 3D LVEF and RVEF were observed in HT patients (P<0.001), but these two values were still within normal range. 3D LVGLS, LVGCS, RV FWLS and LV twist were significantly reduced in HT patients, whereas LV systolic dyssynchrony index (SDI) was increased. And the LV global performance index (GPI) was also reduced. Moreover, the strain values were good for differentiating between these two groups, the cutoff value of −19.3% for the LVGLS had 94% accuracy and the cutoff value of −21.4% for the RV FWLS had 90% accuracy.

CONCLUSIONS Our study demonstrated that 3DSTE had a high sensitivity and accuracy to evaluate biventricular function in HT patients. For clinically stable HT patients with normal conventional echocardiography parameters of ventricular function, their myocardial mechanical function was impaired. Therefore, exploring the specifically normal biventricular mechanical function of HT patients by 3DSTE is essential during follow-up studies.

GW30-e0304

Transcatheter versus surgical aortic-valve replacement in severe aortic stenosis

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OBJECTIVES Transcatheter aortic-valve replacement (TAVR) has emerged as a promising strategy for treating patients with severe aortic stenosis. We aimed to compare TAVR with surgical aortic-valve replacement (SAVR) and determine the performance of TAVR over time and within several subgroups.

METHODS Randomized controlled trials making head-to-head comparison of a TAVR with SAVR strategy in patients with severe aortic stenosis were included. Data of 30 days, 1 year, 2 years, and long-term follow-up (≥2 years) were analyzed separately.

RESULTS Compared with SAVR, TAVR was associated with a lower rate of all-cause mortality or disabling stroke at 30-day (odds ratio [OR], 0.72; P=0.004), 1-year (OR, 0.83; P=0.01) and 2-year (OR, 0.86; P=0.02), but not at long-term (≥ 2 years) follow-up (rate ratio [RR], 1.02 [CI, 0.92 to 1.13]; P=0.67). Notably, 5-year data showed numerically higher incidence in TAVR (RR, 1.11 [CI, 0.97 to 1.27]; P=0.12). The risks associated with TAVR vs. SAVR increased over time, showing a significant interaction (P for interaction=0.002), as were for new-onset atrial fibrillation and rehospitalization. Incidences of major bleeding, new-onset fibrillation and acute kidney failure were lower in TAVR, whereas transient ischemic attack, major vascular complications, permanent pacemaker implantation, reintervention and paravalvular leak were lower in SAVR. Incidences for all-cause and cardiovascular mortality, myocardial infarction and stroke were not statistically different. TAVR with transfemoral approach and new-generation valve was associated with reduction in all-cause mortality or disabling stroke compared with corresponding comparators.

CONCLUSIONS Compared with SAVR, TAVR was associated with a lower risk for all-cause mortality or disabling stroke within 2 years, but not at long-term follow-up; the risks seems to increase over time. More data are needed to determine longer-term performance of TAVR.

GW30-e0323

Insulin resistance is associated with left ventricular remodeling after acute ST-segment elevation myocardial infarction in non-diabetic patients

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OBJECTIVES Adverse cardiac remodeling after ST-segment elevation myocardial infarction (STEMI) is a major cause for poor cardiovascular outcomes such as heart failure. The predisposing factors and underlying mechanisms remain not fully understood. This study investigates the association of insulin resistance with left ventricular (LV) remodeling after STEMI in non-diabetic patients.

METHODS A total of 485 non-diabetic subjects with index STEMI who underwent primary percutaneous coronary intervention were consecutively enrolled and followed up for 12 months. Correlation between homeostasis model

assessment-estimated insulin resistance (HOMA-IR) and changes in echocardiography parameters was studied. We further analyzed the association between insulin resistance parameters and LV dilation.

RESULTS Left ventricular (LV) dilation was detected in 49.1% of subjects at 12-month follow-up after STEMI, and was more severe in subjects with impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and higher HOMA-IR levels. HOMA-IR remained correlated to changes in LV dimensions after adjusting for confounding risk factors (all P<0.001). Multivariate regression analysis demonstrated that higher HOMA-IR was independently associated with greater LV dilation after STEMI. A significant interaction term was present between HOMA-IR and IGT in the model (P=0.002).

CONCLUSIONS Our study reveals high prevalence of insulin resistance and its predictive role for subsequent LV dilation in non-diabetic patients with STEMI.

GW30-e0451

Impact of aortic bioprosthetic calcification measured by computed tomography on long term survival and reintervention following aortic valve replacement

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OBJECTIVES The prognostic value of aortic valve calcification (AVC) measured by non-contrast multidetector computed tomography (MDCT) has been well validated in native aortic stenosis (AS). There are however few data on the impact of MDCT quantitation of valve leaflet calcification after biological aortic valve replacement. The objective of this study was to analyze the association of bioprosthetic AVC with clinical outcomes.

METHODS From 2008 to 2010, we prospectively enrolled 204 patients who had undergone AVR at an average of 7.6±3.4 years ago. AVC measured by the Agatston method was indexed to the cross-sectional area of the aortic annulus to calculate the AVC density (AVCd). The primary endpoint was mortality or reintervention during subsequent follow-up.

RESULTS No significant sex-related difference was detected regarding the levels of bioprosthetic AVCd or correlations with echocardiographic parameters. During a median follow-up of 5.7 3.9, 8.0 years, there were 134 (65.7%) death or reintervention. The univariate analysis showed a strong association between continuous AVCd and the composite endpoint (P<0.001). On multivariable analysis, AVCd was independently associated with the composite endpoint (adjusted HR: 1.11; 95% CI: 1.06 to 1.2 per 20 unit increase of AVCd, P<0.001). When categorized according to the thresholds (58.24 AU/cm^2) suggested by spline curve, higher AVCd was strongly and independently associated with the excess risk of death or reintervention (adjusted HR: 2.55; 95% CI: 1.63 to 4.0, P<0.001). The inclusion of continuous AVCd into a model including traditional clinical and echocardiographic risk factors improved both the discrimination (IDI=0.07 [0.01, 0.13], P=0.013; NRI=0.58 [0.34, 0.73], P=0.033) and calibration (LR test P<0.001) for prediction of outcome. Decision curve analysis further corroborated the superiority of including AVCd in the model.

CONCLUSIONS AVCd measured by MDCT is strongly and independently associated with increased risk of death or valve re-intervention following AVR and it provides incremental prognostic value beyond traditional clinical and echocardiographic risk factors.

GW30-e0452

NT-proBNP ratio predicts cardiac function and mortality in valvular heart disease

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OBJECTIVES N-terminal pro-B-type natriuretic peptide (NT-proBNP) may reflect early deterioration in valvular heart disease (VHD). We aimed to elaborate its value in elder Chinese VHD patients and its relationship with ventricular function and prognosis.

METHODS From China elDerly Valvular heart Disease (China-DVD) cohort study, elder VHD patients (age ≥65 years; moderate or severe: isolated aortic stenosis [AS], aortic regurgitation [AR], mitral stenosis [MS], mitral regurgitation [MR], tricuspid regurgitation [TR], or multivalvular heart disease [MVHD]) with concomitant echocardiography and NT-proBNP measurements at baseline were included. NT-proBNP ratio was calculated individually according to the upper limit of normal for age, sex. Disease-specific thresholds were defined based on spline curve analysis. The primary endpoint was all-cause mortality.

RESULTS In total, 6025 patients were included in the study (mean age of 71.1±7.6 years, 52.6% male, 78.6% NYHA class >I). The overall NT-proBNP ratio was 13.2 ([IQR]: 4.2 to 40.8). Among various VHD, the highest levels were detected in MVHD (19.5 [IQR: 6.4 to 57.4]) and MR (15.0 [IQR: 4.8 to 46.1), and the lowest levels were observed in AR (5.3 [IQR: 1.6 to 19.2). In general, NT-proBNP ratio correlated well with left ventricular ejection fraction (LVEF, r=–0.47, P<0.001), left ventricular end-diastolic dimension (LVEDD, r=0.33, P<0.001) and left atrial dimension (LA, r=0.13, P<0.001). Correlations were strongest in AR and MR and weakest in MS. Lasso regression showed that NYHA class, creatinine, LVEDD and LVEF were most contributive predictors of NT-proBNP ratio (all P<0.001). Except in patients with MS, spline curve based Cox regression revealed a strong monotonic association of NT-proBNP ratio and mortality in various subsets of VHD. On multivariate analysis, higher NT-proBNP ratio was a powerful, independent, and incremental predictor of mortality (adjusted HR: 2.1 [1.7 to 2.5], P<0.001). Except for MS, other subtypes incurred similar excess mortality with elevated NT-proBNP ratio, especially in AS (HR: 10.8 [2.1 to 37.3], P<0.001). Inclusion of NT-proBNP ratio in the model improved both discrimination (NRI: 0.28 [0.23 to 0.32], P<0.001) and calibration (LR test, P<0.001) properties of the model, which was collectively confirmed by decision curve analysis.

CONCLUSIONS Levels of NT-proBNP ratio significantly differ by diagnosis in VHD patients and correlate with echocardiographic parameters to varying degrees, reflecting different hemodynamic changes. In patients with VHD other than single mitral stenosis, NT-proBNP ratio is a powerful, independent, and incremental predictor of mortality.

GW30-e0619

Outcomes in patients with arterial septal defect and severe pulmonary arterial hypertension treated in "treat-repair" strategy

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OBJECTIVES A therapeutic strategy was proposed in recent years as "treat and repair" strategy (PAH-specific medications and subsequent shunt closure). This study aimed to examine the outcomes in patients with ASD and severe pulmonary arterial hypertension treated in this way.

METHODS In this study, we retrospectively reviewed 17 ASD patients (mean age of 31.06±11.85 years) with severe pulmonary arterial hypertension who received PAH targeted medications for 7.26±4.01 months to decrease pulmonary arterial resistance (PVR) and mean pulmonary arterial pressure (mPAP) and then got shunt closure.

RESULTS 15 patients received right heart catheterization (RHC) before the shunt closure and the results showed the PVR and mPAP decreased significantly (PVR decreased from 8.29±3.07 wood units to 5.89±1.83 wood units, P=0.003; mPAP decreased from 58.19±8.89 mmHg to 51.00±8.95 mmHg, P=0.047). All the patients underwent shunt closure successfully (two by surgical repair and fifteen by trans-catheterization repair). None of the patients died in the follow-up. A total of 17 patients were followed up for an average of 24.7 months (3.5–84 months). Among them, 15 cases continued targeted medical therapy or stopped taking medications under medical guidance, whose mPAP decreased to 28.4±9.23 mmHg (P=0.001), right ventricle dimension decreased from 34.4±6.1 mm to 22.9±2.9 mm (P<0.001) and 6-minute-walk-distance (6MWTD) increased from 536.57±35.7 m to 562.64±44.25 m. And 6 of them were considered as non-PAH (Right Ventricle Systolic Pressure<40 mmHg in echocardiography or mPAP 25 mmHg in RHC) by the time of following up. The rest of two patients come to the hospital for worsened exercise capacity (6MWTD decreased). Both of them stop targeted medical therapy without prescription and the RHC showed they had severe PAH.

CONCLUSIONS The results demonstrated that "treat-repair" strategy may be an effective approach for patients with ASD and sever PAH. However, targeted medial therapy and close follow up are necessary after the shunt closure

GW30-e0632

Incidence, risk factors and outcome of coronary occlusion following transcatheter aortic valve replacement: a systematic review and meta-analysis

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OBJECTIVES We aimed to investigate the incidence, risk factors and outcome of CO following TAVR through a systematic review of the published data.

METHODS Studies including case series, case-control studies, cohort studies, and randomized controlled trials published from January 2002 to June 2019 describing CO following TAVR were identified with a systematic electronic search. Pooled incidences and odds ratios (OR) and mean difference were calculated.

RESULTS A total of 38 publications incorporating 33,473 patients were identified. The mean age was 82.8±7.2 years, and 52.2% were female. Overall quality of these eligible studies was good, and no publication bias was seen in these publications. The pooled overall incidence of CO was 0.61%. Incidence of CO show no difference in both genders (0.59% in female and 0.62% in male, P=0.10). In native valve replacement procedure the incidence was 0.25%, while in valve-in-valve replacement procedure the incidence of CO was significantly higher (1.36%). In prior coronary artery bypass graft (CABG) individuals the

incidence of CO was 0.29, and it was higher in non-CABG patients (0.72%). Valve type did not affect the incidence of CO (0.74% for Balloon-expandable valve and 0.46% for Self-expandable valve, OR=0.41, P=0.11). In order to investigate the predictors of CO, we pooled 3 publications incorporating 47 patients suffering from CO and 2394 patients free from CO using the univariate analysis method. In valve-in-valve replacement procedure, the virtual transcatheter valve to coronary ostium (VTC) distance measured by computed tomography scan was significantly lower in CO group (mean difference −2.86 mm, P<0.0001). Sinus of Valsalva was also narrower in CO group (mean difference −3.80 mm, P<0.0001) in valve-in-valve procedure rather than in native valve replacement individuals (mean difference 0.10 mm, P=0.93). However, as to native valve replacement the coronary height was reported to be shorter in CO group than non-CO group (mean difference −2.20 mm, P=0.0003). The 30-day mortality rate of CO in native valve replacement was 35.3%, and in valve-in-valve replacement procedure the 30-day mortality rate could reach up to 52.9%.

CONCLUSIONS The incidence of CO following TAVR is relatively low but the 30-day mortality rate is high, especially in valve-in-valve replacement procedure. The most powerful predictive clinic situation is valve-in-valve replacement procedure. Prior CABG status seemed to be protective factor of CO. In valve-in-valve replacement procedure, VTC distance and diameter of Sinus of Valsalva are most significant risk factors of CO, while in native valve replacement the only risk factor is coronary height.

GW30-e0738

Regional left ventricular longitudinal myocardial dysfunction in mitral valve prolapse could be primary

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OBJECTIVES Regional left ventricular dysfunction in patients with mitral valve prolapse (MVP) and normal ejection fraction has been described by different Authors, and recent data point to a dysfunction (prevalently longitudinal strain) of the myocardium of the LV base secondary to dilatation of the mitral annulus. Purpose of this study was that to investigate degree and extent of regional LV dysfunction and its mechanisms in patients with MVP, severe regurgitation and normal global systolic function, compared to patients with equivalent degree of regurgitation but functional etiology (FMR).

METHODS Speckle-tracking echocardiography was performed in 30 controls (N), and in severe primary (MVP, n=50) or functional (FMR, n=20) mitral regurgitation, to measure global, regional and segmental longitudinal peak systolic strain (LPSS, %), and time delay of peak maximum strain (TTPd, ms, calculated as time to peak maximum strain – time of aortic valve closure). Maximum and minimum mitral annulus diameters and area were measured with 3D echo. We also evaluated as recommended: LV end-diastolic volume index (EDVi, mL/m^2), ejection fraction (EF, %), and left atrial end-systolic volume index (LAESVi, mL/m^2) with 2D echo; LV stroke volume index, and non-invasive pulmonary systolic (PSP, mmHg) and diastolic pressures (PDP), mmHg) with Doppler echo.

RESULTS Age, heart rate, BSA and systolic blood pressure were similar between groups. Atrial fibrillation was present in 34% of MVP and 71% of FMR patients. LV EF was normal in MVP and reduced in FMR (43±14 % vs. N, P<0.001). LV EDVi (MVP: 77±20 mL/m^2; FMR: 107±35, both P<0.001 vs. N) and LAESVi (MVP: 91±26 mL/m^2; FMR: 80±30, both P<0.001 vs. N) were similarly increased (volume overload) in MVP and FMR, as were PSP (MVP: 42±23 mmHg; FMR: 52±25, both P<0.001 vs. N) and PDP (MVP: 16±6 mmHg; MVP: 15±5, both P<0.001 vs. N).

CONCLUSIONS In patients with MVP, severe regurgitation and normal EF, there is a specific dysfunction pattern of regional LV longitudinal function which appears to be primary and not dependent on the degree of preload increase, mitral annulus dilatation, or localization of the prolapsing scallop.

GW30-e0837

Transcatheter aortic valve replacement versus surgical aortic valve replacement in aortic stenosis with chronic coronary artery disease: nationwide inpatient analysis

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OBJECTIVES Our study aimed to compare the inpatient outcomes of transcatheter aortic valve replacement (TAVR) vs. surgical aortic valve replacement (SAVR) in hospitalized patients with aortic stenosis (AS) and concomitant coronary artery disease (CAD). For patients who also received PCI in TAVR group, we studied whether timing of PCI (before TAVR vs. during/after TAVR) had an impact on in-hospital outcomes.

METHODS We conducted a retrospective cohort analysis of the National Inpatient Sample (HCUP-NIS) 2016 database. Patients hospitalized with diagnosis of both AS and CAD were identified using the ICD-10 codes. Multivariate logistic regression was performed after adjust for patient baseline characteristics, hospital demographics and relevant comorbidities. Inpatient mortality and length of hospital stay (LOS) were compared between the patients who received TAVR and SAVR.

RESULTS A total of 50,710 patients with both AS and CAD were included. Of these, 26,055 (51.38%) received TAVR and 24,655 (48.62%) received SAVR. Patients in TAVR group were older than SAVR group (80.58 vs. 71.47 years old). Multivariate logistic regression analysis after adjustment showed that TAVR group had lower in-hospital mortality (1.22 vs. 2.61%, OR 0.32, 95% CI 0.21–0.49, P<0.001) and shorter LOS (4.80 vs. 9.36 days, P><0.001) when compared to SAVR group. Further study of the patients in SAVR group revealed that 15,650 (63.48%) patients also underwent CABG. On the other hand, 1020 (3.91%) patients in TAVR group underwent PCI during the same hospitalization. Among the patients who received both TAVR and PCI, 375 (36.76%) patients received PCI before TAVR and 645 (63.24%) patients received PCI during/after TAVR. Patients received PCI during/after TAVR had lower inpatient mortality than those received PCI before TAVR but without statistical significance (0.78 vs. 4%, OR 95% CI 0.02–1.89, P=0.156). Furthermore, when compared with patients in SAVR group, patients who received TAVR had lower rate of cardiac arrest (OR 0.48), cardiogenic shock (OR 0.33), respiratory failure (OR 0.37), mechanical ventricular support (OR 0.26), AKI (OR 0.50), RBC transfusion (OR 0.37), platelet transfusion (OR 0.08), sepsis (OR 0.27) and septic shock (OR 0.29) with all P><0.001; but higher risk of complete heart block (OR 1.88) and pacemaker placement (OR 2.01).

CONCLUSIONS Patients with AS and CAD had lower in-hospital mortality and morbidity when treated with TAVR compared to SAVR. Moreover, further prospective study is warranted to determine the optimal timing of PCI in patient undergoing TAVR.

GW30-e0845

The effectiveness of left atrial spontaneous echo contrast grade on cardiovascular outcome in patients with rheumatic mitral stenosis

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OBJECTIVES Systemic thromboembolism is a serious morbidity and mortality cause for patients with rheumatic mitral stenosis (RMS). Previously conducted researches showed that spontaneous echo contrast (SEC) found in the left atrium (LA) can constitute a risk factor for thrombus formation and thromboembolism. Underlying conditions are associated with low blood flow velocities in the LA. We sought to determine to evaluate the role of LA SEC grade on hospitalization for transient ischemic attack (TIA) in patients with moderate-severe RMS.

METHODS This retrospective study includes 104 patients (mean age 67 years, range 31–77) who were diagnosed with moderate–severe RMS and underwent trans-esophageal echocardiography between 2011 and 2014, but without any intra-cardiac mass. RMS was graded using by WILKINS criteria. They were then divided in two groups depending on SEC presence; a SEC negative group and a SEC positive group. Data regarding baseline parameters, treatment and clinical features during follow-up were gained based on hospital and out-patient clinic and telephone interviews. The endpoint of the study at follow-up 12 months was hospitalization for TIA.

RESULTS Of the 104 patients, 71 (68%) patients had LA SEC on echocardiography. Both groups had similar demographic parameters and conventional echo parameters such as LVEF and LV volumes (P>0.05). Total of 27 hospitalizations has been recorded during follow-up (Log Rank P<0.001), besides LA thrombus, was present in 7 patients, all of whom had LA SEC. In linear regression analysis, positive correlations were found between the grade of LA SEC and WILKINS criteria (r=0.770, P><0.001), and LA SEC correlated with a higher probability of TIA (P=0.01). LA SEC and intra-cardiac thrombus were significant risk factors for the development of TIA with univariate analysis. However, LA SEC was the only strong predictor for TIA on multivariate analysis.

CONCLUSIONS In RMS patients, coexisting LA SEC was associated with a higher risk for TIA and was predictive of poor long-term hospitalization outcome.

GW30-e0948

In patients undergoing transcatheter aortic valve implantation, does a relatively younger age at the operation predispose to the occurrence of infectious endocarditis?

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OBJECTIVES The question addressed was whether a younger age at the operation was associated with the risk of infectious endocarditis (IE) following transcatheter aortic valve implantation (TAVI).

METHODS Altogether 206 papers were found using the reported search, of which 6 retrospective cohort studies and 1 cross-sectional study represented the best evidence to answer this clinical question. The authors, journal, date and country of publication, patient group studied, study type, relevant outcomes and results of these papers are tabulated.

RESULTS Seven studies commonly showed that the patients who experienced a post-TAVI IE were significantly younger at the operation than the patients who did not experience a post-TAVI IE. Four of these studies occupying the great proportion of the included patients demonstrated that a younger age at the operation could be an independent risk factor for post-TAVI IE after eliminating the bias risks from other confounding factors.

CONCLUSIONS Currently available evidence supports that the patients who are younger at the operation may be at an increased risk of IE after TAVI. That may be because the younger patients who are considered at high operative risk may exhibit a higher comorbidity burden compared to their older counterparts.

GW30-e0962

No flow in the distal coronary segment and reversed flow at the proximal segment are the mechanisms of chest pain in patients with aortic stenosis and patent coronary arteries

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OBJECTIVES Patients with aortic stenosis and patent coronary arteries present with chest pain. What could explain the chest pain?

METHODS Patients with AS were selected. At first, they were interviewed for history of chest pain or no chest pain. Then they underwent right and left heart catheterization in order to calculate the aortic valve area (AVA). During the coronary angiograms, the left coronary arteries were recorded in the right anterior oblique caudal view and the right coronary artery in the left anterior oblique view (at 15 frames per second). Then the angiograms were viewed off line frame by frame. The first frame was the angiogram of an artery completely filled with contrast. The following frames showed the blood moving in, seen in white. The flow could be LAMINAR, TURBULENT (mixing of blood in white and contrast in black) or ANTEGRADE or RETROGRADE (black column traveling backward). The antegrade flow reflected the normal supply of blood to the myocardium in diastole. The turbulent flow represented the collision between the antegrade and retrograde flow. The retrograde flow represented the flow in reversed direction due to contraction of the left ventricle in systole. The speed and the time of retention of contrast reflected the transit time of blood before it reached the myocardium. A slow speed and a prolonged period of retention increase the possibility of ischemia. The TIME of retention flow, the presence and time of the retrograde flow were recorded.

RESULTS A total of 20 patients with AS and patent coronary arteries was selected. They were divided in 2 groups: Significant AS with aortic valve area (AVA) less or above 0.7 cm^2. The results showed 90% of patient had significant AS with AVA 90%). These 2 above observations (No flow in distal and reversed flow in the proximal coronary arteries) were the mechanisms of ischemia in the AS patients with patent coronary arteries.

CONCLUSIONS In patients with aortic stenosis and patent coronary arteries presented with chest pain, the mechanisms of chest pain are severe and prolonged no flow in the distal segments and reversed flow in the proximal segment.

CARDIOMYOPATHY

GW30-e0282

Accuracy of automated three-dimensional echocardiography in evaluating left ventricular volume and ejection fraction in patients with hypertrophic cardiomyopathy: a comparative study with current clinical two-dimensional echocardiography

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OBJECTIVES Accurate, reproducible, noninvasive determination of left ventricular (LV) volumes and ejection fraction (EF) is important for clinical assessment, risk stratification, selection of therapy, and serial monitoring of patients with cardiovascular disease. Current clinical Two-dimensional echocardiography (2DE) may cause inaccurate measurements in patients with irregular ventricular shape because of geometric assumption. Three-dimensional echocardiography (3DE) have demonstrated significantly greater accuracy. But the clinical utility of 3DE has been limited by the time-consuming workflow. We aim to compare the analysis time and accuracy of a novel automated 3DE system (Heart Model, Philips Healthcare) with 2DE in patients with hypertrophic cardiomyopathy (HCM) using cardiac magnetic resonance (CMR) as gold standard.

METHODS 43 patients with HCM were examined by automated 3DE (3DEA), two-dimensional biplane Simpson's method (2DBP) and CMR, respectively. For patients with poor automated quantification, manual correction was performed. The Pearson correlation coefficient and Bland-Altman analysis and paired Student *t* were used to assess inter-technique agreement.

RESULTS The analysis time of 3DEA was obviously shorter than that of 2DBP (3DEA, 213±30 s; 2DBP, 154±36 s). Interobserver variability was reduced 2-fold with use of 3DEA. There was excellent correlation, without statistically significant differences, between CMR and 3DEA for end-systolic volume (ESV) (r=0.92) and end-diastolic volume (EDV) (r=0.88), and EF (r=0.82). 2DBP consistently underestimated volumes (EDV, P<0.01; ESV, P<0.01; SV, P<0.05); correlations with CMR were r=0.81 for ESV, r=0.76 for EDV and r=0.69 for EF.

CONCLUSIONS The novel automated 3DE system allows shorter analysis time, provides improved accuracy and reproducibility for measurement of left ventricular volume and ejection fraction in patients with hypertrophic cardiomyopathy compared with 2DE. It may facilitate further integration of 3DE quantification in routine clinical practice in patients with asymmetric and irregular ventricles.

GW30-e0485

Predictors of cardiac involvement and survival in patients with primary systemic light-chain (AL) amyloidosis – assessed by three-dimensional speckle tracking echocardiography

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OBJECTIVES Light-chain (AL) amyloidosis is the most common type of systemic amyloidosis and with poor prognosis. Currently, the predictors of early cardiac involvement and prognostic staging systems are primarily based on conventional echocardiography and serological biomarkers. We used three-dimensional speckle tracking echocardiography (3D-STE) measurements of strain, hypothesizing it can detect early cardiac involvement and aid in prediction of mortality.

METHODS We retrospectively enrolled seventy-four consecutive patients with biopsy-proven AL amyloidosis. Among them, 42 showed cardiac involvement and 32 without cardiac involvement. LV global longitudinal strain (GLS), global radial strain (GRS), global circumferential strain (GCS) and global area strain (GAS) were obtained.

RESULTS The GLS and GAS were considered significant predictors of cardiac involvement as well as LV mass index (LVMI). The cut-off values discriminating cardiac involvement from without cardiac involvement were 16.10% for GLS,

32.95% for GAS and 73.35 g/m² for LVMI. For the Cox proportional model survival analysis, heat rate (hazard ratio [HR]: 1.036; 95% confidence interval [CI]: 1.008 to 1.066; P=0.011), LVMI (HR: 1.015;95% CI: 1.005 to 1.025), E/e'(HR: 1.086; 95% CI 1.036 to 1.139), cTnT (HR 8.391; 95% CI: 2.546 to 27.649; P<0.001), NT-proBNP levels (HR 2.929; 95% CI: 1.335 to 6.427, P=0.007), GLS (HR 1.318; 95% CI:1.090 to 1.593, P=0.004) and GAS (HR: 1.150; 95% CI: 1.031 to 1.284, P=0.013) were univariate predictors of death, In a multivariate Cox model showed that GLS ≤14.78% (HR: 1.275; 95% CI: 1.017 to 1.597) were independent predictor of survival.

CONCLUSIONS 3D-STE measurements of LV myocardial mechanics can detect early cardiac involvement in patients with AL amyloidosis, and GLS can provide potential prognostic information for mortality prediction.

GW30-e0717

Retrospective analysis of clinical phenotype and prognosis of hypertrophic cardiomyopathy complicated with hypertension

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OBJECTIVES We tried to study the clinical features, cardiac structural and functional changes and prognosis of hypertrophic cardiomyopathy (HCM) patients with hypertension (HTN).

METHODS 90 HCM patients with HTN and 172 patients without HTN were divided into hypertensive group and non-hypertensive group. Patients with myocardial hypertrophy secondary to amyloidosis, aortic stenosis and hypothyroidism were excluded. The clinical characteristics, cardiac structure and function, and prognosis of the two groups were compared.

RESULTS HCM patients with HTN were older at diagnosis (55 vs. 47, P<0.001) and had fewer history of syncope (8 vs. 22%, P<0.01) and family sudden death (3 vs. 10%, P<0.05). The prevalence of apical hypertrophy (18 vs. 7%, P<0.01) and midventricular obstruction (26 vs. 15%, P<0.05) in HTN group was higher. The comparison of 5-year survival rate showed a trend for a worse prognosis in HCM patients with HTN, but the result was statistically insignificant (P=0.065).

CONCLUSIONS In our study, we found that the clinical phenotypes of HCM patients with HTN were different from that of patients with HCM alone, suggesting that HTN may play a pathogenic role in the pathogenesis of hypertensive hypertrophic cardiomyopathy patients, rather than an auxiliary role.

GW30-e0746

Effects of an extensive echocardiographic biventricular pacemaker optimization protocol on the rate of non-responders after cardiac resynchronization therapy

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OBJECTIVES Cardiac resynchronization therapy (CRT) was shown to be effective in patients with advanced heart failure (NYHA III-IV), both in improving prognosis and quality of life and in triggering reverse remodeling of left ventricular (LV) volumes, geometry and function. Among the factors responsible for lack of clinical improvement or LV reverse remodeling in 30–50% of patients (non-responders to CRT), there is a missing or inadequate biventricular pacemaker (PM-Biv) optimization (OPT) of both the atrio-ventricular (AVd) and inter-ventricular (VVd) time intervals. Purpose of this study was that to compare in an echocardiographic observational study the rate of CRT non-responders between patients with and without echocardiographic OPT (OPTe).

METHODS We compared two groups of patients undergoing CRT (guidelines-based indication): Gr 1, 155 patients with intraprocedural AVd and VVd OPT based on QRS duration, or proprietary PM-Biv automated OPT algorithm; Gr.2, 70 patients sent to the echocardiography laboratory (by the attending physician) to perform post-implant additional echocardiographic optimization (algorithm based on modifications of pulsed Doppler velocities of LV inflow and outflow, and the Tei index of LV contractility) and programmed echocardiographic follow-up. Positive response to CRT was defined as LV end-systolic volume reduction >15% at 6 and 12 months post-implant.

RESULTS Gr.1 and 2 were comparable for age (69±10 vs. 68±11 y.), sex (M=53 vs. 47%), LV biplane end-diastolic volume (107±35 vs. 111±37 mL/m²), ejection fraction (31±8 vs. 31±9 %), and pulmonary systolic pressure (continuous wave Doppler of tricuspid regurgitation) (37±12 vs. 37±20 mmHg). Etiology of dilated cardiopathy was ischemic in 44% of Gr.1 and 56% of Gr.2 patients (P=ns). Echocardiographic follow-up was available at 12 months in 68% of Gr.1 and 73% of Gr.2 patients. In Gr.1, rates of non-responders at 6 and 12 months were 68 and 59%, whereas rates in Gr.2 were 58 and 39% (P=0.039 vs. Gr.1).

CONCLUSIONS Our preliminary data suggest a significant role for OPTe to reduce non-responder rate in CRT, allowing for the logistic burden required by the echocardiographic OPTe. Given the dimensions of heart failure epidemiology, the observed reduction in non-responder rate has a potential significant impact on both patients prognosis and management costs of patients with chronic heart failure.

GW30-e0876

Blood-derived DNA methylation signatures reveals novel epigenetic traits and gene deregulation in human hypertrophic cardiomyopathy

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OBJECTIVES Hypertrophic cardiomyopathy (HCM) is a genetic disorder that is characterized by left ventricular hypertrophy unexplained by secondary causes and a non-dilated left ventricle with preserved or increased ejection fraction. Recently, several clinical researches had shown that different HCM patients could show different clinical phenotypes, even though they had the same causal gene mutations, which highlighted the epigenetic mechanism in HCM. Thus, we conducted DNA methylation and RNA microarray to identify DNA methylation alterations that associated with and might contribute to HCM.

METHODS Blood samples were obtained from 12 HCM patients (average 57.41 years old) and 8 healthy controls (average 53.50 years old). All of the participants enrolled in this study were well informed and signed inform consent. DNA methylation patterns were analyzed in samples collected at time of diagnosis at approximately 850,000 sites. RNA microarray was also conducted to identify changes in relation to DNA methylation patterns in HCM. R tool was used for all bioinformatics analysis in our study.

RESULTS We identified 618 5′-cytosine-phosphate-guanosine-3′ (CpG) sites that were differentially methylated between HCM patients and controls, among which 72 sites were hypermethylated and 546 sites were hypomethylated. Function annotations were enriched to HCM (adjustment-P=0.006), arrhythmogenic right ventricular cardiomyopathy (adjustment-P=0.007), and regulation of cardiac muscle cell contraction (adjustment-P=0.008). By using Bumphunted method, a total of 24 differential methylated regions were identified by comparing HCM patients and healthy controls, corresponding to 24 genes. Subsequent gene and noncoding RNA expression analysis revealed 2 long noncoding RNA (CCDC125 and FER-6) and 1 circular noncoding RNA (LCAT1) with significantly unregulated expression level reversely consistent with the direction of methylation comparing HCM patients and healthy controls.

CONCLUSIONS For the first time blood derived DNA methylation alterations and associated gene expression changes were identified in HCM. The methylation-sensitive and disease-associated genes and noncoding RNA (CCDC125, FER-6, and LCAT1) identified from this study represent a unique cohort of loci that demonstrate a plausible potential as a novel diagnostic and therapeutic target in HCM and warrant further investigation.

GW30-e0994

Three-year follow-up of a new test which correctly predicted which patients with borderline hypotension might develop hypotension within the next 24 hours

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OBJECTIVES Many patients presented with borderline low blood pressure (BP=90–100 mmHg) due to (1) internal bleeding, (2) bleeding in the retroperitoneal space during intervention, (3) sepsis or (4) dehydration. These patients present with borderline low BP (90 mmHg). The question is: Which test can predict accurately which patient will develop significant hypotension in the next 24 hours? This is the follow-up study at 3 years.

METHODS Patients with BP 90–100 mmHg were enrolled. All received an ultrasound study checking the size and expansibility of the femoral vein (FV) (SEFV). The image was the coronal plane proximal to the bifurcation of the superficial and deep femoral artery (FA). The principle of this test is that the volume of blood going through the FA and returning through the common FV should be the same. In normal condition, the FV is a little larger than the FA (Figure 1). If the FV is much larger than the FA, the patient has fluid overload

as in heart failure. If the FV is smaller than the FA, the patient has significant contraction of the intravascular (mainly venous) compartment. It could be due to blood loss if the patient had bleeding (Figure 2). Then the patient was asked to cough: if the FV did not expanded >2 times of the baseline: the venous compartment was significantly contracted because there was not enough blood to expand the veins. All patients were divided according to the size of the FV and its expansibility: Hypovolemia or euvolemia.

RESULTS At the beginning, 25 patients with borderline hypotension were enrolled. Within 2 years, 25 more patients were enrolled. For all of these patients, the SEFV test identified accurately 60% patients had euvolemia and 40% with hypovolemia. All patients were treated with 100 cc/hour of normal saline or positive pressors for sepsis. For all 20 patients with smaller FV size showing hypovolemia, if these patients were not aggressively treated with more fluid (250 cc/hour) these patients developed significant hypotension (BP<85 mmHg) in an average of 4 hours. For the 30 patients with normal FV size, with only IV fluid treatment (100 cc of normal saline per hour) these patients with bleeding or sepsis did not develop further hypotension. In these situations, the SEFV could predict correctly future hypotension in bleeding or septic patients without current hypotension. The SEFV could help the acute management of patients with hypotension.

CONCLUSIONS At 3 years follow-up, the SEFV helped classify correctly the borderline hypotensive patients (with bleeding or sepsis) at risks for further significant hypotension. The SEFV test also helped select and direct the correct strategy with or without fluid and pressor. This SEFV test should be used routinely for patients with hypotension admitted to the emergency room or intensive care unit.

GW30-e0999

DNA methylation changes at HIF3A intron 1 is associated with diabetic cardiomyopathy in Chinese population

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OBJECTIVES Diabetic cardiomyopathy (DCM) is the main cause of morbidity and mortality in diabetic patients. Recent studies revealed that epigenetic modifications, especially DNA methylation, play a key role in the pathogenesis of DCM. Differential hypoxia inducible factor 3 alpha subunit (HIF3A) methylation has been reported to be associated with diabetes. However, little is known about the association between the metabolic and myocardial dysfunction of DCM and HIF3A methylation. Here, we aimed to assess the association of the methylation level of CpG sites in HIF3A intron 1 with HIF3A mRNA expression, the clinical/echocardiographic factors and serum biomarkers of collagen biosynthesis in DCM patients in China.

METHODS We included 55 DCM patients and 68 age and gender matched control subjects for measurement of blood DNA methylation levels of CpG sites in HIF3A intron 1 by using the pyrosequencing and MassARRAY system. HIF3A mRNA and protein expression was detected by real-time PCR and Elisa assay. Clinical status of DCM patients was assessed by the New York Heart Association (NYHA) functional class. Myocardial function was assessed via standard echocardiography. Serum biomarkers of collagen biosynthesis such as procollagen N-terminal and carboxy-terminal propeptides (PINP, PIIINP and PICP) were measured in serum by radioimmunoassay.

RESULTS Several crucial findings were reported in this study. First, HIF3A mRNA and protein expression were found downregulated in the whole blood from DCM patients. Second, three CpG-dinucleotides in HIF3A intron 1 (CpG 6, CpG 7 and CpG 11) and the average methylation rate at seven CpG sites (CpG 1, CpG 2, CpG 5, CpG 6, CpG 7, CpG 8 and CpG 11) were highly methylated in DCM patients. Discriminant analysis suggesting the above seven CpG sites exhibited a good sensitivity of 71.2% and specificity of 82.6%, respectively. Third, significant negative correlation was found between HIF3A DNA methylation rates of intron 1 and HIF3A mRNA expression in DCM patients. Furthermore, higher HIF3A methylation levels at CpG 1, CpG 6, CpG 7 and CpG 11 had significant correlation with higher fasting glucose and higher HbA1C levels. Notably, in the case of CpG6, correlations were also significantly positive with NYHA functional class, E/E' ratio and serum collagen biosynthesis biomarkers (PINP, PIIINP and PICP) and significantly negative with E/A ratio, when analyzed by linear regression, with age and sex as covariates. Particularly, we reported higher HIF3A methylation at CpG 6 and CpG 7 were negatively associated with current exercise activity.

CONCLUSIONS This work demonstrated for the first time that higher methylation at HIF3A intron 1 may be involved in the metabolic and myocardial dysfunction of DCM and could be served as a potential marker for DCM patients. Intervention for person with higher methylation at HIF3A intron 1 may prevent progression of DCM.

CARDIOVASCULAR SURGERY

GW30-e0032

The neglected dimension: ascending aortic length enhances risk assessment for aortic adverse events

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OBJECTIVES Little information is available regarding the longitudinal changes of the aneurysmal ascending aorta. We aim to outline the natural history of ascending thoracic aortic aneurysm (ATAA) based on ascending aortic length (AAL) and develop novel predictive tools to better aid risk stratification.

METHODS As part of our ongoing investigations into the natural history of thoracic aortic aneurysm, our database at the Aortic Institute at Yale-New Haven Hospital currently includes a total of 3861 patients with thoracic aortic disease. 522 ATAA patients (with a total of 851 aortic diameter measurements and 645 AAL measurements) form a subset in whom available and suitable radiologic studies have been re-read and re-analyzed in a standardized manner for the purposes of this study. The ascending aortic diameters and lengths, and long-term aortic adverse events (AAE) (rupture, dissection, and aortic death) of 522 ATAA patients were evaluated using comprehensive statistical approaches.

RESULTS An AAL of ≥13 cm was associated with a 4.5-fold higher average yearly rate of AAE compared to an AAL of<9 cm. Two AAL 'hinge points' with a sharp increase in the estimated probability of AAE were detected at 12.5 and 13.5 cm. The mean estimated annual aortic elongation rate was 0.18 cm/year, and aortic elongation was age-dependent. Aortic diameter increased 18% due to dissection while AAL only increased by 2.7%. There was a noticeable improvement in the discrimination of the logistic regression model (AUC=0.8205) due to the introduction of aortic height index (AHI) (AHI=diameter height index (DHI)+length height index (LHI)). AHIs of <9.44, 9.47 to 11.35, 11.43 to 12.90, and ≥12.94 cm/m were associated with a ~3, ~7, ~12, and above 12% average yearly risk of AAE, respectively.

CONCLUSIONS The study supports the following recommendations or conclusions 1. An aortic elongation of 12 cm serves as a potential intervention criterion for ATAA. 2. Aortic length demonstrates a mean growth rate of 0.18 cm annually. 3. Aortic elongation is age-dependent, and relatively immune to dissection. 4. Aortic-Height index (including both length and diameter) (easily discernible via modern imaging modalities) is more powerful than diameter alone in predicting AAE, with a significantly increased area under the ROC curve. The easy-to-use nomogram and 3-D plot provided, incorporating both aortic diameter and length, allows clinical application of this more advanced decision-making tool.

GW30-e0085

Prognostic value of N-terminal pro-B-type natriuretic peptide in tricuspid valve replacement patients

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OBJECTIVES N-terminal pro-brain natriuretic peptide (NT-proBNP) has been documented to have significant predictive values for the risk stratification and prognosis in cardiac surgery. Tricuspid valve replacement (TVR) procedure is an uncommon procedure usually undertaken at a late stage and often carries a significant mortality risk. However, there is no data regarding the prognostic value of NT-proBNP in TVR. We aimed to evaluate the mortality predictive value of NT-proBNP in TVR.

METHODS We analyzed 73 patients (mean age 49.58±13.99 years, 43.8% male) undergoing TVR between May 2011 and December 2017 at our institution, who had NT-proBNP measured before or after operation. The primary endpoint was all-cause death in 6 months after operation. The groups were stratified according to the optimal cut-off value of NT-proBNP levels. The receiver-operating-characteristic curves (ROC) for the three peptides were drawn, and the area under the curves (AUC) calculated.

RESULTS The best cutoff point based on the Youden's index were 450.5 pg/mL, 6385 pg/mL and 3.9189 for NT-pro-BNP levels before operation, NT-proBNP levels after operation, and NT-proBNP changes respectively. Multivariable logistic regression analysis revealed that all the three higher NT-proBNP levels were independently associated with all-cause mortality after adjustment for covariates. Of the three measurement, only the AUC with NT-proBNP before operation added significantly improved the predictive ability, as compared with the traditional model (0.940 vs. 0.880, P=0.032) with net reclassification improvement (NRI) 1.175 (P<0.001) and integrated discrimination improvement (IDI) 0.188 (P=0.001). The inclusion of NT-pro-BNP after operation and NT-proBNP change to traditional model improved the predictive ability, but not reached significance (AUC: 0.911 vs. 0.874; P=0.379 for NT-proBNP after operation; 0.899 vs. 0.875; P=0.324 for NT-proBNP change). Both the inclusion

of NT-proBNP after operation and NT-proBNP change into the traditional model cause significant improvement of NRI (1.003, P=0.0001 for NT-proBNP after operation; 0.842 P=0.003 for NT-proBNP change) and IDI (0.154, P=0.005 for NT-proBNP after operation; 0.083, P=0.005 for NT-proBNP change).

CONCLUSIONS NT-proBNP level before or after operation and NT-proBNP level change are independent significant prognostic factors of all-cause mortality within 6 months.

GW30-e0086

Mid-term outcome after tricuspid valve replacement

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OBJECTIVES Tricuspid valve replacement is an unusual operation. Our study aimed to evaluate the mid-term survival rate after tricuspid valve replacement.

METHODS We retrospectively studied 112 consecutive patients who were undergoing tricuspid valve replacement (TVR) from January 2007 to November 2017. A survival analysis was performed with the Kaplan-Meier method and the log-rank test.

RESULTS The median survival was 63.9 months. The mean age was 47.63±14.35 years. Forty-nine patients (43.8%) were male, and 63 patients (56.3%) were female. A majority of patients (78.5%) were categorized into the New York Heart Association functional class III/IV. Eighty-two patients (73.2%) had only TVR. Fifty-eight patients (51.8%) had previously undergone heart surgery. The Kaplan-Meier survival rates at 1 year, 3 years and 5 years were 58±5%, 51±6% and 47±6%, respectively. A Cox regression analysis demonstrated that the risk factors for mid-term mortality were advanced NYHA class (HR: 3.404, P=0.001) and a need for CRRT treatment (HR: 3.059, P=0.001).

CONCLUSIONS Impaired cardiac function before the operation and a need for CRRT after the operation were significantly associated with higher mid-term mortality in TVR.

GW30-e0237

Relationship between the expression level of PITX2 and KCNQ1 in left atrial appendage tissue and the prognosis in atrial fibrillation patients after modified mini-maze procedure

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OBJECTIVES PITX2 gene in 4q25 locus and KCNQ1 gene in 11p15.5-p15.4 locus which are separately responsible for pulmonary vein formation and potassium voltage-gated channel regulation prove to be associated with atrial fibrillation. This study is designed for analyzing relationship between the expression level of PITX2 and KCNQ1 in left atrial appendage tissue and the prognosis in atrial fibrillation patients after modified mini-maze procedure.

METHODS This study collected left atrial appendage tissue of 59 atrial fibrillation cases who received modified mini-maze procedure and left atrial appendectomy in past years (February 2017-August 2018). The expression level of PITX2 and KCNQ1 were quantitatively analyzed by western blot assay and TMT-based quantitative proteomic analysis further identified proteomics difference between paroxysmal AF and persistent AF in left atrial appendage tissue. The correlation between protein expression and prognosis after surgery were also analyzed based on clinical data.

RESULTS In all 59 atrial fibrillation patients, there are 39 male cases and average age is 61 years±7 years. There are 32 paroxysmal AF cases and 27 persistent AF cases. Three months follow-up after surgery shows that there are 5 atrial flutter cases and three AF cases. There is no perioperative death and cerebral infarction occurred. Cox regression multivariate analysis showed that high expression of PITX2 and KCNQ1 and preoperative enlargement of left atrium are independent risk factors of recurrence after modified mini-maze procedure. Compared with paroxysmal AF, western blot results showed that KCNQ1 expression level was higher (P<0.05) while PITX2 was lower (P<0.05) in persistent AF left atrial appendage tissue. TMT-based quantitative proteomic analysis found 81 differential proteins and results further showed that there are proteomics difference between paroxysmal AF and persistent AF in left atrial appendage tissue.

CONCLUSIONS Proteomics difference exists in left atrial appendage tissue between paroxysmal AF and persistent AF. Compared with paroxysmal AF, the left atrial appendage tissue of persistent AF has higher KCNQ1 expression level and lower PITX2 expression level. KCNQ1 and PITX2 may participate in different biological mechanisms of AF. High expression of PITX2 and KCNQ1 and preoperative enlargement of left atrium are independent risk factors of recurrence after modified mini-maze procedure. Surgical treatment of atrial fibrillation should develop more personalized protocols based on genetic molecules and clinical risk assessment.

GW30-e0467

Correlation between ACTA2 and CYP2A13 gene polymorphisms on the occurrence and prognosis of Debakey type III AD

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OBJECTIVES This study was to investigate the association of TGFβ (transforming growth factor-β) pathway-related genes ACTA2 (α-smooth muscle actin) and CYP2A13 (cytochrome oxidase 2A13) polymorphism with Debakey type III AD (aortic dissection) in Chinese Han population.

METHODS A case-control study was conducted in 157 cases of aortic dissection Debakey III, and 323 cases in the control group without angiography. Real-time PCR was used to identify genotypes of 6 sites of ACTA2 (rs2119685, rs3781211, rs2028493) and CYP2A13 (rs3968432, rs1645694, rs34178072), and the case group was followed up for 2 years to analyze the occurrence and prognosis of type III AD.

RESULTS There were differences in the genotype and allele frequency distribution of ACTA2 (rs2119685) between the case group and the control group (P<0.05). After adjusting for confounding factors, logistic regression analysis showed that the association between ACTA gene polymorphism and type III aortic dissection was associated (OR=0.369, 95% CI: 0.202–0.672, P=0.001). In the 2-year follow-up of the case group, the mortality distribution of the ACTA2 (rs2119685) dominant model (TT vs. TC+CC) in Debakey type III AD patients was statistically significant (P<0.05).

CONCLUSIONS The ACTA2 (rs2119685) gene polymorphism in Chinese Han population is associated with the occurrence and prognosis of Debakey type III AD. The five sites of ACTA2 (rs3781211, rs20284933) and CYP2A13 (rs3968432, rs1645694, rs34178072) are not associated with Debakey type III AD. The results of this study provide reference value for screening and prognosis assessment of Debakey type III AD patients.

GW30-e0517

Differences in clinical presentation, management, and outcomes of aortic dissection in patients with and without end stage renal disease

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OBJECTIVES There are less data on the clinical characteristics, management, and outcomes of patients with end stage renal disease (ESRD) presenting with aortic dissection (AAD).

METHODS ESRD was defined as an estimated glomerular filtration rate <15 mL/min/1.73 m^2. We evaluated the differences of 225 patients with AAD who were diagnosed by Magnetic Resonance Imaging (MRI) or contrast-enhanced computed tomography (CT) in the clinical characteristics, management, and in-hospital outcomes of the cohorts with and without ESRD, and we reviewed patients' medical records and laboratory results to evaluate the clinical characteristics.

RESULTS A history of ESRD was present in 75 of 225 patients. Patients with ESRD were less likely to have triggering factors (5.3 vs. 22.7% P=0.001), and more patients presented with Stanford type B acute aortic dissection (74.7 vs. 58.7%, P=0.018) and had a history of hypertension (80.0 vs. 96.0%, P=0.001), In contrast, ESRD patients were less likely to have presenting typical symptoms (41.3 vs. 16.0%, P<0.001). And more AAD patients with ESRD treated using conservative medical treatment (52 (69.3%) 76 (50.7%), P=0.008). Hyperhomocysteinemia (HCY) level (18.85 vs. 14.85 μmol/L, P=0.012), creatinine (808 μmol/L vs. 83 μmol/L, P<0.0001) and D-dimer (3.98 mg/L vs. 2.63 mg/L, P=0.048) was markedly elevated in patients with aortic dissection with ESRD. No statistically significant differences were observed between open surgery, endovascular aortic repair, and conservative management for hospital mortality, but a trend for increased death was seen in patients with ESRD.

CONCLUSIONS Our study highlights differences in clinical characteristics, management, and outcomes of AAD patients with ESRD. Importantly, patients with ESRD have less triggering factors and typical symptoms, which easily leads to misdiagnosis. Patients with ESRD present Stanford type B acute aortic dissection, which may be associated with hypertension and HCY, and more patients with ESRD using conservative medical treatment.

GW30-e0643

Clinical analysis of acute compartment syndrome after cardiovascular surgery

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OBJECTIVES To analysis the clinical characteristics of acute compartment syndrome after cardiovascular surgery Further understanding of this diseas.

METHODS Retrospective the clinical datas of patients undergoing the acute compartment syndrome after cardiac and aortic surgery from March 2011 to 2017 in our hospital.

RESULTS The symptoms of all the patients are swelling and tense on the affected side with the signs of limbs ischemia like pallor cyanosis Early onset of postoperative symptoms in patients with total aortic arch prosthesis in ascending aorta replacement group Poor prognosis of this patients.

CONCLUSIONS Acute compartment syndrome is an extremely rare complication after cardiovascular surgery with multiply pathogenic factors It is difficult to diagnose Early diagnosis to increase the blood supply on affected limbs and timely operations make great significance to the prognosis and life quality of life.

GW30-e0747

Concomitant surgical left atrial appendage occlusion in patients with atrial fibrillation: a meta-analysis

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OBJECTIVES There is no conclusive evidence regarding the efficiency and safety of concomitant surgical left atrial appendage occlusion (LAAO) in AF patients. Therefore, We conducted a meta-analysis of studies comparing LAAO with non-LAAO in AF patients undergoing cardiac surgery.

METHODS A literature search was performed on PubMed, Embase, and Cochrane Trials databases until 31st April 2018. Studies comparing AF patients who underwent open cardiac surgery with or without LAAO were included. Main outcomes of interest were combined events of cerebrovascular accident (CVA) and thromboembolism (TE) and all-cause mortality. I^2 statistics were used to evaluate heterogeneity, and publication bias was evaluated by Begg's and Egger's tests.

RESULTS We retrieved 8 studies involving a total of 28401 participants (7669 in the LAAO group and 20732 in the non–LAAO group). The surgical LAAO was significantly associated with decreased risk of combined events of CVA and TE (OR=0.66; 95% CI: 0.57–0.75, I^2=0%) when compared with non-LAAO. Stratified analysis showed consistent results in-hospital and long term events strata. The association between LAAO and all-cause mortality was not significant (OR=0.77; 95% CI: 0.34–1.72) and with high heterogeneity across studies (I^2=93%). Sensitivity analysis revealed that differences of concomitant cardiac surgery procedure mainly contributed to heterogeneity.

CONCLUSIONS Our meta-analysis suggests that surgical LAAO may be effective in CVA and TE prevention in AF patients. However, there are insufficient data to support the safety of concomitant LAAO in cardiac surgery, especially in patients undergoing CABG. Further prospective investigations are indicated.

GW30-e0986

Own experience in using the new Bioresorbable Scaffold "meres-100"

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OBJECTIVES To assess the immediate clinical and angiographic success of PCI with the implantation of the new MeRes100TM Scaffold.

METHODS In the conditions of our clinic, a study was started on the use of the Meres scaffold. Currently, we have our own data of 34 patients. The percentage of men was 94%. The average age is 51.7 years.

RESULTS Single-vascular lesions were observed in 70.6% of patients. The average score for SYNTAX was 7.84. The greatest number of lesions was noted in the anterior descending artery (anterior interventricular artery) basin – 70.6%. Immediate clinical success was observed in 94% of cases, the restoration of blood flow in TIMI-3 was 100% of cases. The values of the combined indicator MACE in our study were at the initial stage, i.e. immediately after PCI, zero cases. However, in dynamics, after 3 months of observation, scaffold thrombosis was observed in one patient, due to non-occlusive dissection of the distal edge of the scaffold on the third day of observation. Since the evaluation of the main endpoints, including the combined indicator MACE, is planned in our study at stages 6, 12 and 24 months, the presented three-month results are preliminary.

CONCLUSIONS The use of the "MeRes100TM" device, according to the results of our pilot study, was characterized by a high (94%) clinical and absolute (100%) immediate angiographic success in individuals with 1 or 2 vascular lesions of the coronary vessel, in which the diameter of the damaged vessel was ≥3.0 mm.

GW30-e0988

Characteristics of coronary lesion in female patients with unstable angina

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OBJECTIVES Evaluation of the angiographic characteristics of coronary lesions in unstable angina in women.

METHODS In 2018, 106 patients with unstable angina (UA) were treated at the interventional cardiology department, of which 24 (22.6%) were women. All patients underwent general clinical and laboratory examinations, body mass index (BMI) was calculated and coronary artery angiography was carried out.

RESULTS The average age of women with UA was 62.8±7.2 years. The average values of BMI are 30.2±4.8 kg/m^2. Nosological structure in 100% of cases was represented by angina on exertion. Concomitant hypertension was observed in 91.7% and type 2 diabetes mellitus in 50.0% of patients. Single-vessel disease was present in 62.5%, and lesions of 2 or more coronary vessels in 37.5% of women. Single-vessel disease in 86.7% of cases were observed in the left anterior descending artery (LAD); lesions of 2 or more coronary vessels in 77.8% of cases were located on LAD and right coronary artery (RCA). Totally 32 stents were installed (1.33 stents per patient), of which 5 were bioresorbable scaffolds, the remaining 27 were drug-eluting stents. The average diameter of the stents was 3.3±0.4 mm and the average length was 23.3±6.6 mm.

CONCLUSIONS UA among women is mainly represented by angina on exertion, which in 91.7% of cases is comorbid with hypertension and in 50% with type 2 diabetes mellitus.

CLINICAL DRUG RESEARCH AND DEVICE DEVELOPMENT

GW30-e0160

Efficacy and biosafety of a new bioresorbable vascular scaffold covered with biodegradable film in rabbits: an in vivo study

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OBJECTIVES Coronary artery perforation (CAP) is a fatal complication of percutaneous coronary interventions (PCI). Covered stents are the mainstay of treatment for coronary perforation. However, conventional covered stents have high rate of in-stent thrombosis (IST) and restenosis (ISR) due to stent materials. We firstly developed a new fully bioresorbable vascular scaffold covered with biodegradable poly-L-lactic acid film (BVS-C/Firesorb). Our vitro tests have demonstrated that Firesorb was technically feasible but its biosafety and efficacy warranted to be further validated in vivo. This study aims to evaluate the biosafety and efficacy of Firesorb in rabbits.

METHODS Five Firesorb were deployed at a zone from the abdominal aorta to the right iliac artery in anesthetized New Zealand white rabbits. Angiography was conducted for evaluation of the immediate efficacy and 6-month biosafety and biodegradability of Firesorb. Meanwhile, optical coherence tomography (OCT), histological light microscopy (HLM) and scan electron microscopy (SEM) were performed to evaluate endothelialization, degradation of Firesorb and its covered membrane, and incidence of thrombosis.

RESULTS All Firesorb were successfully implanted without procedure-related complications and all rabbits were accomplished 6-months follow-up. In all treated rabbits, angiography showed that Firesorb had completely sealed the opening of the left iliac artery without blood flow in its branches but with full patency of the right iliac artery immediately post-procedurally while the covered membrane of Firesorb had been degraded and blood flow restored in the left iliac artery and its branches at 6 months. OCT also found that the occluded left iliac artery had been reopened and the stented segment almost fully endothelialized without IST at 6 months with comparable results confirmed by HLM and SEM.

CONCLUSIONS Firesorb is associated with excellent efficacy, biosafety and biodegradability in rabbits, may be promising to replace conventional covered stents for treatment of coronary artery perforation or to be used in other clinical situations.

GW30-e0479

Lower versus standard international normalized ratio targets for thromboembolic prophylaxis in atrial fibrillation: a systematic review and meta-analysis of randomized controlled trials

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OBJECTIVES Warfarin is widely prescribed for thromboembolic prophylaxis in patients with atrial fibrillation (AF). Although Western guidelines recommend an International Normalized Ratio (INR) range of 2.0–3.0 in AF, lower INR ranges such as 1.5–2.0 are frequently used in East-Asia. We performed a systematic review and meta-analysis of randomized controlled trials (RCTs) in AF patients comparing the effect of lower versus standard INR ranges on thromboembolism, major bleeding, and mortality.

METHODS We searched Western databases including Cochrane CENTRAL, Medline, and EMBASE as well as Chinese databases including SinoMed, CNKI, and Wanfang Data. Screening of articles, risk of bias assessment and data extraction were performed independently and in duplicate. We pooled risk ratios (RR) using random-effects model. We grouped INR targets in two ways: 1) INR ranges of approximately 1.5–2.0 versus 2.0–3.0, and 2) study-specific lower versus standard targets. We also evaluated whether study region (East-Asian versus Western) affected the results. We evaluated the overall quality of evidence with the GRADE framework.

RESULTS 74 RCTs (n=12,017) met eligibility criteria, 69 (n=10,411) from East-Asia and 5 (n=1606) from Western countries. All studies were judged to be at high risk of bias due to open-label design or insufficient information regarding methodology. In patients randomized to INR ranges of approximately 1.5–2.0 compared with 2.0–3.0, significantly higher thromboembolic events rates (52 RCTs, n=6738: 6.8 vs. 4.7%, RR 1.36, 95% CI 1.12–1.65, I^2=0%, moderate quality of evidence), significantly lower major bleeding rates (45 RCTs, n=6580: 2.0 vs. 4.4%, RR 0.50, 95% CI [0.38, 0.67], I^2=0%, moderate quality of evidence), and similar mortality rates (20 RCTs: n=3108, 7.5% vs. 6.4% RR 1.07, 95% CI [0.88, 1.30], I^2=0%, low quality of evidence) were observed. Study region was not a significant effect modifier; however, this analysis was underpowered with only 2 Western RCTs, n=322 (Figure). The results were consistent when we pooled the data according to specific target INR ranges or study-specific lower versus standard targets (Table), but study region became a significant effect modifier (Figure). For all outcomes, the quality of evidence was downgraded for risk of bias.

CONCLUSIONS Moderate and low-quality evidence suggests that lower compared with standard INR targets confer significantly lower bleeding risk at the expense of a significant increase in thromboembolic risk. The data are dominated by East-Asian studies, limiting generalizability to Western populations. Until higher quality data demonstrate otherwise, an INR range of 2.0–3.0 should remain the standard for thromboembolic prophylaxis in atrial fibrillation.

GW30-e0680

Optimal duration of vitamin K antagonists anticoagulant therapy after venous thromboembolism or pulmonary embolism: a systematic review and network meta-analysis of randomised controlled trials

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OBJECTIVES The optimal duration of oral anticoagulant therapy after a first episode of venous thromboembolism (VTE) and pulmonary embolism (PE) is still uncertain. It is essential to accurately assess the desired effect of anticoagulant therapy in reducing recurrent VTE against the risk of inducing major bleeding.

METHODS *Data sources:* A systematic literature search was conducted using PUBMED (from inception to August, 2018), Web of Science, Embase, and Cochrane Library of clinical trials database (from 1972 to August, 2018) to identify randomized clinical trials (RCTs) without restrictions on the publication year, or type of publication, along with published evidence-based medicine reviews from inception through August, 2018.

STUDY SELECTION Eligible studies were randomized trials reporting rates of recurrent venous thromboembolism and major bleeding in patients with venous thromboembolism. Of the 1302 studies identified, 11 RCTs representing a total of 3109 patients were included in the analyses. Two reviewers independently extracted trial-level data assessing the number of patients, duration of follow-up, and clinical outcomes. The data were pooled using network meta-analysis.

RESULTS 11 eligible studies with a total of 3109 participants utilizing varied durations of Vitamin K Antagonists (VKA) therapy were included. Longer duration VKA therapy was associated with significantly lower rates of VTE recurrence compared with shorter duration of VKA therapy (OR 0.75, 95% CI 0.57–0.99) both in traditional and frequentist network meta-analysis, with significant difference noted in major bleeding risk (OR 2.31, 95% CI 1.17–4.56) comparing longer versus shorter VKA therapy duration. During anticoagulation duration, patients treated by 6-month VKA regimen had higher risk of major bleeding compared with 3-month VKA regimen (OR 33.45, 95% CI 2.00–559.67). Longer treatments more than 6 months did not show statistical elevation of major bleeding risk.

CONCLUSIONS In conclusion, this meta-analysis shows that VKA treatment strongly reduces the risk of recurrent VTE during anticoagulation therapy. The absolute risk of recurrent VTE declines over time while the risk for major bleeding after 6 months' treatment did not demonstrate a continuous significant increase with extended duration of VKA therapy. Prolonging VKA treatment requires careful assessment of the trade-off between recurrent VTE and bleeding complications.

CARDIOVASCULAR DISEASES IN SPECIAL POPULATIONS (CHILDREN, WOMEN, ETC.)

GW30-e0169

Biventricular myocardial strain correlates with myocardial fibrosis in patients with end-stage dilated cardiomyopathy: a study using three-dimensional speckle tracking echocardiography

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OBJECTIVES Previous results regarding the correlations of the myocardial strain with myocardial fibrosis were discordant. Therefore, the aim of our study was to evaluate the accuracy of biventricular strain by three-dimensional speckle tracking echocardiography (3D-STE) in predicting myocardial fibrosis in patients with end-stage dilated cardiomyopathy (DCM) undergoing heart transplantation.

METHODS We studied 35 patients with end-stage DCM using echocardiography before heart transplantation. Left ventricular (LV) global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS) and right ventricular (RV) free wall longitudinal strain (LS) were measured by 3D-STE. LV and RV ejection fraction (EF) were obtained from cardiac magnetic resonance (CMR) imaging. LV and RV tissue samples were obtained from all patients who underwent heart transplantation. The ratio of the fibrotic to the total sample area (collagen volume fraction, %) determined the extent of fibrosis.

RESULTS LV myocardial fibrosis correlated strongly with GLS (r=0.74, P<0.001), modestly with GRS (r=–0.66, P<0.001), weakly with GCS (r=0.44, P<0.01), but not with CMR-derived LVEF; RV myocardial fibrosis was strongly associated with RV free wall LS (r=0.71; P<0.001), but not with CMR-derived RVEF. Compared with patients with mild myocardial fibrosis, LV GLS, GCS and GRS, and RV LS decreased in patients with severe myocardial fibrosis. LV GLS and RV free wall LS had the highest diagnostic accuracy for detecting severe myocardial fibrosis (LV GLS: AUC=0.86; 95% CI: 0.73 to 0.99; RV LS: AUC=0.85; 95% CI: 0.70 to 0.99). Stepwise multivariate analysis showed that LV GLS (β=0.740, P<0.001) and RV free wall LS (β=0.60, P<0.0001) were independent predictors of LV and RV fibrosis respectively.

CONCLUSIONS Myocardial fibrosis lead to reduced systolic function in the end-stage DCM. LV GLS and RV free wall LS are the most accurate LV and RV global function measurements that correlate with the extent of myocardial fibrosis in patients with end-stage DCM.

GW30-e0296

Effect modification of hypertension status on the association between sleep duration and stroke among middle-aged and elderly Chinese population: a cross-sectional study

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OBJECTIVES We aimed to examine whether hypertension status modified the association between sleep duration and stroke among a middle-aged and elderly population.

METHODS In this cross-sectional study, a total of 10,516 participants aged 45–97 years from the China Hypertension Survey study were analyzed. Self-reported sleep duration, history of stroke were assessed by structured questionnaires. We defined the response categories for sleep duration as short (<6 h), average (6–8 h), and long (>8 h). Multivariate logistic regression analyses were performed to evaluate the association between sleep duration and stroke stratified by hypertension status. Moreover, to further characterize the shape of the associations between sleep duration and stroke in different status of hypertension, a generalized additive model (GAM) and smooth curve fitting (penalized spline method) were conducted. If nonlinearity was detected, we first calculated the turning point using recursive algorithm, and then constructed a two-piecewise binary logistic regression model on both sides of the turning point. 95% confidence interval (CI) for turning point was obtained by bootstrapping.

RESULTS Multiple logistic analyses showed that per 1 hour increment in sleep duration was associated with a 37% higher prevalence of stroke among participants without hypertension odds ratio (OR)=1.37, 95% CI 1.09–1.71; P=0.007. In contrast, each 1 hour increment in sleep duration was associated with a 8% higher prevalence of stroke among subjects with hypertension (OR=1.08, 95% CI 0.95–1.21; P=0.232). There was a significant interaction between hypertension and sleep duration on stroke was statistically significant ($P_{Interaction}$=0.029). Sleep duration was also evaluated for categorical variables. Among participants without hypertension, compared with the reference category of sleep duration (6–8 h), short sleep durtaion (<6 h) was associated with lower prevalence of stroke (OR=0.36, 95% CI 0.09–1.54), but there did not reach statistical significance. Long sleep duration (>8 h) was significantly associated with a 1.21 times higher prevalence of stroke (OR=2.21, 95% CI 1.19–4.14). P for trend in the all models was significant. Compared to hypertensive subjects with average sleep duration, participants with short sleep duration did not have a significantly increased the prevalence of stroke, but there was a significant association between long sleep duration and stroke ($OR_{<6h}$=1.21, 95% CI 0.73–2.01; $OR_{>8h}$=1.59, 95% CI 1.07–2.38; $P_{trend=}$0.309). Analyses using restricted cubic spline presented a linear association between sleep duration and stroke among participants without hypertension, but a threshold, nonlinear association among participants with hypertension. Further, threshold and saturation effect analysis showed that the turning point of sleep duration among hypertensive patients was 8 (95% CI 5–9) h. The ORs (95% CIs) were 0.92 (0.79, 1.06) on the left side of inflection point and 1.60 (1.23, 2.08) on the right side of inflection point, respectively.

CONCLUSIONS Our study indicated that hypertension status modified the association between sleep duration and stroke among a middle-aged and elderly population. The association between sleep duration and stroke was linear in participants without hypertension, but a threshold effect in hypertensive patients. Sleep duration >8 h was positively associated with stroke in hypertensive patients.

GW30-e0397

Identification of subclinical myocardial dysfunction in breast cancer patients with metabolic syndrome after cancer related therapy

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OBJECTIVES Breast cancer patients with metabolic syndrome have an increased risk of cardiovascular disease. These patients are more prone to suffer from cardiotoxicity after cancer therapy. Patients after completion of cancer related therapy, who show normal myocardial function, may already have subclinical myocardial dysfunction. Our objectives were to evaluate the subclinical myocardial dysfunction in breast cancer patients with metabolic syndrome after cancer related therapy.

METHODS In this study, 45 breast cancer patients with metabolic syndrome after completion of cancer related therapy and 45 non-breast cancer patients without metabolic syndrome were enrolled. Left ventricular ejection fraction (LVEF) and global longitudinal (GLS) were measured using echocardiogram.

RESULTS All the patients have normal LVEF. However, nine breast cancer patients (20%) had GLS that lower than –17%, while all the non-cancer patients have normal GLS. Breast cancer patients with metabolic syndrome had a decrease of GLS and LVEF, compared with non-cancer patients with metabolic syndrome. Furthermore, we found that decrease of age was associated with reduction of LVEF, and that use of trastuzumab was a significant factor that associated with reduction of GLS.

CONCLUSIONS Breast cancer patients with metabolic syndrome after completion of cancer related therapy suffered from subclinical myocardial dysfunction. GLS should be routinely performed to early identify subclinical myocardial damage of patients, in order to prevent the cardiotoxicity of cancer related therapy.

GW30-e0411

Postmenopausal female patients with arterial hypertension: non-specific inflammatory response parameters as a predictor of vascular wall stiffness, subclinical atherosclerosis and bone remodeling

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OBJECTIVES To study the role of non-specific inflammatory response parameters as a predictor of vascular wall stiffness, subclinical atherosclerosis and osteoporosis in postmenopausal female patients with arterial hypertension (AH).

METHODS 164 patients (mean age 56.52±6.28 years) were examined and divided into three groups. Gr. 1 included 42 healthy individuals, Gr.2 – 58 female patients with AH and Gr.3 – 64 postmenopausal female patients with AH and osteoporosis (OP). Patients in Gr. 2 and 3 comparable by age. Average history of AH in patients was 12.31±8.91 years. The parameters of 24-hour blood pressure (BP) monitoring; sphygmography (pulse-wave velocity (PWV), osteodensitometry (CA-HA, standard deviation of the peak T –Score); intamamedia thickness (I/MT) of carotid arteries; inflammatory markers (hs-CRP, TNF-alpha, homocysteine, interleukine (IL) 1 β, 6, 8); endothelial dysfunction markers (endothelin-1, nitrites); lipid profile parameters; sex hormones like (estradiol, progesterone and testosterone) and parameters of calcium metabolism (calcium, ionized calcium, vitamin D, calcitonin) were measured.

RESULTS The levels of hs-CRP, homocysteine, IL6 and 8 and endothelin-1, total cholesterol, LDL cholesterol, APO-B have been above the reference value in Gr. 2 and 3. Aditionally, in Gr.3 statistically higher levels of office systolic BP (SBP) and diastolic (DBP), I/MT, lower levels of sex hormones, vitamin D, total calcium, ionized calcium and peak T –Score. Bisides, in Gr.3 there were registered negative correlations between peak T –Score with ade, PWV, office SBP and DBP, duration of menopause, IL6, hs-CRP, homocysteine and between PWV with estradiol; positive correlations between T –Score with progesterone and between PWV with IL6, LDL cholesterol, hs-CRP, TNF-alpha, endothelin-1, mean daytime systolic SBP and mean daytime SBP and DBP variability.

CONCLUSIONS Identifying the features of the markers of a nonspecific inflammatory response in association with the level of sex hormones and calcium parameters may become a personalized direction in managing vascular wall stiffness, subclinical atherosclerosis and osteoporosis in postmenopausal women with arterial hypertension.

GW30-e0504

Superior vena cava syndrome

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OBJECTIVES To determine the best method to treat SVC syndrome due to obstruction by leads.

METHODS To make the diagnosis physical exam is highly suggestive in the proper context, e.g. Distended neck veins, Upper chest varices, facial swelling, Pemberton sign. Symptoms usually occur weeks to months after implanting of the leads and is generally an inflammatory process related to endothelial damage of the Vena Cava. Multiple imaging techniques confirm the diagnosis, e.g. CT angio shows wires in the SVC, venous collaterals in the upper extremity and upper chest and contrast opacification of the quadrate lobe of the liver "hot quadrate sign" Catheter based venogram is the best method to diagnose and treat SVC syndrome.

RESULTS Therapy; anticoagulation or thrombolysis, venoplasty, Venoplasty plus stent, Surgery In 2010 Riley reported stented patient and did not remove leads in 72% treated with stenting and 43% treated with surgery with no adverse events in a limited follow-up events My preference for anticoagulation is Warfarin and not a DOAC

CONCLUSIONS Surgery with Removal of Leads, and Bypass of the SVC obstruction with epicardial placement of the leads seem to be the best treatment but venoplasty/stent with or without lead removal seems OK but longer

follow is needed for either therapy. Overall, SVC syndrome remains a rare complication of transvenous cardiac device implantation, and requires an individualized and complex approach to management. Due to its rarity, recognition of the classic presenting signs and symptoms is essential and these may be missed because of the rarity of device occlusion.

GW30-e0781

Aspirin use is associated with a decreased incidence of venous thromboembolism in patients with cancer

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OBJECTIVES Aspirin plays a role in preventing both arterial and venous thromboembolism (VTE). Cancer patients are at higher risk for VTE, but also have a higher risk of bleeding. Our study investigated the role of aspirin use in preventing VTE formation in cancer patients.

METHODS We conducted a retrospective cohort study using the National Inpatient Sample (NIS) 2016. ICD10 codes were utilized to identify/rule out disease, comorbidities, and outcomes. A total of 41,941 cancer patients were identified as the Aspirin group, and 41,941 cancer patients not taking aspirin were included as a propensity-matched cohort (Non-Aspirin group) that best matched with Aspirin group regarding age, gender, race, insurance, patient demographics, and hospital demographics. Primary outcomes were diagnoses of acute pulmonary embolism (PE) or acute deep venous thrombosis (DVT). Secondary outcomes included in-hospital mortality, length of hospital stay (LOS), and total hospitalization cost.

RESULTS Compared with Non-aspirin group, the Aspirin group had a significantly lower incidence of acute PE (unmatched, 2.1 vs. 2.6%, P<0.001; matched, 2.1 vs. 2.7%, P><0.001) and acute DVT (unmatched, 2.3 vs. 3.2%, P><0.001; matched, 2.3 vs. 3.2%, P><0.001), significantly lower in-hospital mortality (unmatched, 3.7 vs. 5.9%, P><0.001; matched, 3.7 vs. 6.4%, P><0.001), shorter LOS (unmatched, 5.31±5.19 vs. 6.29±7.61, P><0.001; matched, 5.31±5.19 vs. 6.27±7.21, P><0.001), and lower total costs (unmatched, 15096±15654$ vs. 17762±25548$, P><0.001; matched, 15096±15654$ vs. 16851±22262$, P><0.001).

CONCLUSIONS Aspirin use in cancer patients is associated with a decreased incidence of VTE and overall in-hospital mortality.

GW30-e1044

The association between grip strength and blood pressure in Chinese children and adolescents

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OBJECTIVES Isometric handgrip resistance exercise, a nonpharmacological lifestyle modification, has been recommended as a first-line treatment for hypertension. However, the association of grip strength with blood pressure (BP) in children has been inconsistent. The purpose of this study is to test the association of grip strength with systolic and diastolic BP in children and adolescents.

METHODS Data were obtained from the cross-sectional survey carried out by the government in 2014 in Liaoning Province, China, which investigated the health status in Chinese school-aged children. The study included 34,303 participants aged 7–18 years old. Grip strength was assessed by using a hydraulic dynamometer and the sum of the maximum grip strength from both hands was used. General linear models were used to examine the associations between grip strength and the outcome variables.

RESULTS After adjusting for age, sex, body mass index, and physical activities, grip strength was significantly and positively associated with systolic and diastolic BP (both P<0.001). There was an increasing trend in systolic BP as grip strength increased from the bottom quartile to the top quartile, with 3.7 mmHg difference between the top and the bottom quartiles (P for trend <0.001). Similar results were obtained for diastolic BP.

CONCLUSIONS We conclude that strong grip strength was positively associated with increased BP in children and adolescents. The implications and underlying mechanisms for these results need further examinations.

GW30-e1061

Relationship between metabolic syndrome components and proinflammatory cytokines in patients with metabolic syndrome

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Relationship between Metabolic Syndrome Components and Proinflammatory Cytokines in Patients with Metabolic Syndrome

OBJECTIVES Prevalence of metabolic syndrome (MS) is high in general population and it is characterized by constellation of several risk factors such as abdominal obesity, hypertension, dyslipidemia, impaired fasting glucose and insulin resistance (IR). Aim of the study was to investigate the relationship of metabolic syndrome components and proinflammatory cytokines in patients with diagnosed metabolic syndrome (MS).

METHODS We have investigated serum concentrations of the proinflammatory cytokines such as, IL-6, IL-12, IL-1β and TNF-α in 92 patients with metabolic syndrome compared to those 60 patients without MS from 2016 September to 2018 June. Blood pressure and anthropometry measurements were taken and venous blood was collected after an overnight fast and was analyzed by ELISA. Metabolic syndrome was defined based on the Harmonized definition of the MS.

RESULTS There was a significant increase of IL-6 (P<0.05), IL-12 (><0.001), IL-1β (P><0.01), and TNF-α (P><0.001) in MS subjects compared to those without MS. Among components of the MS, abdominal obesity (AO; r=0.585, P=0.038), LDL-Cholesterol (r=0.45, P=0.04) and fasting glucose (r=0.415, P=0.042) positively correlated with IL-6 whilst IL-12 is positively associated with AO (r=0.62, P=0.028), hypertension (r=0.450, P=0.045), IR (r=0.320, P=0.03) and fasting glucose (r=0.35, P=0.045). Only AO (r=0.37, P=0.033) and high diastolic blood pressure (r=0.40, P=0.042) positively correlated with IL-1β. TNF-α was not correlated with high blood pressure as IL-12, however there were correlations between TNF-α and AO (r=0.35, P=0.030), fasting glucose (r=0.42, P=0.045) and IR (r=0.25, P=0.05) in MS subjects.

CONCLUSIONS Subjects with MS have high levels of proinflammatory cytokines when compared to those without MS. Among MS components AO following by fasting glucose and IR are the most sensitive components to estimate the patients proinflammatory state.

CARDIOVASCULAR-DISCIPLINARY RESEARCH

PULMONARY VASCULAR DISEASE

GW30-e0058

Contemporary survival of patients with pulmonary arterial hypertension associated with congenital heart disease – a single center experience

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OBJECTIVES To analysis and compare the clinical, functional, and hemodynamic characteristics and current era survival of diagnosed pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD) in a single center cohort in China.

METHODS A total of 507 consecutive patients (age 24.1±13.7 years, median=23.1 years, 68.0% females, 39.1% childeren) with PAH–CHD who were referral to Beijing Anzhen Hospital from at least 27 regions all over China from September 2005 to May 2019 were retrospectively reviewed. Patients were classified into 4 groups: 1) Eisenmenger syndrome (ES), 2) PAH associated with prevalent systemic-to-pulmonary shunts (SP), 3) PAH associated with small defects (SD) and 4) PAH after defect correction (CD).

RESULTS Treatment was per PAH guidelines, including combination therapy, with approved PAH-specific drugs. Over a median follow-up time of 3.60 (0.01–12.19) years, 37 patients (7.3%) died and no one underwent lung/heart-lung transplantation. Patients with Eisenmenger syndrome had far better survival than small defects (HR: 0.20, 95% CI: 0.060–0.692, P=0.011) but no significant statistical advantage compared to postoperative-PAH (HR: 1.04, 95% CI: 0.505–2.136, P=0.918). No patients with SP died during the period of follow-up time. In the overall PAH–CHD population, patients in NYHA functional class III–IV had a more than 22-fold increased risk of death (HR: 22.09, 95% CI: 8.521–57.250, P<0.0001). Amongst patients with Eisenmenger syndrome, patients with pre-tricuspid shunts had a lower increase risk of death (HR: 0.08, 95% CI: 0.018–0.390, P=0.002). Patients with postoperative-PAH had better survival than IPAH (HR 0.3, 95% CI: 0.2–0.5, P<0.001).

CONCLUSIONS PAH–CHD is associated with mid to long-term mortality. Outcome relates closely to functional class, type of PAH–CHD and within the Eisenmenger cohort, with location of the shunt. Patients with small defects show the worst prognosis in the PAH–CHD cohort, while SP was the best, reinforcing the need for lifelong close follow-up of such patients. Patients with Eisenmenger syndromehaveno significant statistical difference in survival rate compared to postoperative-PAH, still need longer term follow-up.

GW30-e0353

Improved hemodynamics and cardiopulmonary function in patients with inoperable chronic thromboembolic pulmonary hypertension after balloon pulmonary angioplasty

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OBJECTIVES Balloon pulmonary angioplasty (BPA) has been demonstrated to improve cardiac function and exercise capacity in patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), but no reports regarding BPA have been reported in China. This study aims to determine the safety and efficacy of balloon pulmonary angioplasty (BPA) and its immediate and lasting effects on cardiopulmonary function in CTEPH patients.

METHODS From May 2018 to January 2019, patients with inoperable CTEPH who underwent BPA sessions were consecutively enrolled. Hemodynamics were measured by right heart catheterization, selective pulmonary angiography and BPA were successively conducted. Hemodynamic variables, WHO functional class (WHO-FC), 6-minute walk distance (6MWD) and serum NT-proBNP were evaluated before and after BPA sessions during hospitalization. Pulmonary function testing and cardiopulmonary exercise testing were performed within 1–3 days pre and post BPA to evaluate the effect of BPA on cardiopulmonary function.

RESULTS Twenty-five patients with inoperable CTEPH who underwent a total of forty BPA sessions were consecutively enrolled. No procedure-related complications occurred. Instant mean pulmonary arterial pressure (47.4±11.9 to 41.5±10.7 mmHg, P<0.001), WHO-FC (2.3±0.5 to 1.9±0.5, P<0.001), 6MWD (350.0±103.4 to 403.6±81.3 m, P<0.001) and NT-proBNP (1161.8 to 671.2 pg/mL, P=0.001) were all significantly improved after single BPA session. Significant improvement in cardiopulmonary function was evident as accessed by pulmonary function testing (forced vital capacity, 3.11±0.83 to 3.21±0.93 l, P=0.037; forced expiratory volume in the first second, 2.26±0.64 to 2.32±0.71 l, P=0.034; maximal voluntary ventilation, 89.4±31.7 to 99.1±34.7 l/min, P<0.001) and CPET (peak work rate, 78.0±40.6 to 86.7±39.8 w, P<0.001; peak VO2, 13.9±3.7 to 15.2±3.3 mL/kg/min, P<0.001; oxygen uptake efficiency slope, 1250.5±508.3 to 1329.1±466.6 mL/min/L/min, P=0.015). Further subgroup analysis among ten CTEPH patients receiving multiple BPA sessions (2–4 sessions) indicated BPA resulted in lasting improvements in hemodynamics and cardiopulmonary function.

CONCLUSIONS BPA, a safe and effective approach, can bring instant and lasting benefits to hemodynamics and cardiopulmonary function for patients with inoperable CTEPH.

GW30-e0354

Targeted therapy in pulmonary veno-occlusive disease: time for a rethink?

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OBJECTIVES Pulmonary veno-occlusive disease (PVOD) is a rare condition with poor prognosis, and lung transplantation is recommended as the only curative therapy. The role of pulmonary arterial hypertension targeted therapy in PVOD remains controversial, and long-term effects of targeted therapy have been rarely reported. This study aims to retrospectively evaluate the role of targeted therapy in PVOD patients and the long-term outcome.

METHODS PVOD patients with good responses to targeted therapies were analyzed, and data pre- and post- targeted therapies were compared. An overview of the effects of targeted therapies on PVOD patients was also conducted.

RESULTS Five genetically or histologically confirmed PVOD patients received targeted therapies and showed good responses. Their mean pulmonary arterial pressure by right heart catheterization was 62.0±11.7 mmHg. Two receiving monotherapy got stabilized, and three receiving sequential combination therapy got improved, cardiac function and exercise capacity significantly improved after treatments. No pulmonary edema occurred. The mean time from the first targeted therapy to the last follow up was 39.3 months, and the longest was 9 years. A systematic review regarding the effects of targeted therapies on PVOD patients indicated majorities of PVOD patients got hemodynamics or 6-minute walk distance improved, and 26.7% patients developed pulmonary edema. The interval from targeted drugs use to death ranged from 71 minutes to over 4 years.

CONCLUSIONS Cautious use of targeted therapy can safely and effectively improve or stabilize hemodynamics and exercise capacity of some patients without any complications. PVOD patients can live longer than expected.

GW30-e0355

Identification of circulating biomarkers for the severity of acute pulmonary embolism: a preliminary proteomic study

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OBJECTIVES Pulmonary embolism (PE) is a common and severe disorder with high morbidity and mortality. Risk stratification of patients with acute PE helps identify patients at high risk of early death who may benefit from more aggressive therapy such as thrombolysis or embolectomy. Protein mass spectrum is a favorable tool to identify biomarkers useful for the risk stratification of patients with acute PE.

METHODS We studied 5 healthy controls (CG), 5 patients presenting with low risk or intermediate-low risk PE (LIG) and 5 patients presenting with intermediate-high risk or high-risk PE (IHG). Two-dimensional difference gel electrophoresis was used to compare their plasma protein abundances. Candidate plasma protein markers were identified by lable-free quantitative mass spectrometry. Gene Ontology (GO) enrichment analysis were used to identify biological processes of altered proteins between three groups.

RESULTS 5159 peptides and 559 protein groups were screened out. GO enrichment analysis indicated these proteins were mainly involved in acute-phase response, platelet aggregation, inflammatory response and response

to hypoxia. Candidate biomarkers such as serum amyloid A-1 protein (IHG: LIG: CG=116.1:6.3:1), neutrophil gelatinase-associated lipocalin (IHG: LIG: CG=22.3:3.7:1), cystatin-C (IHG: LIG: CG=3.9:1.8:1), glutathione peroxidase (IHG: LIG: CG=3.9:2.3:1), haptoglobin (IHG: LIG: CG=1.9:1.45:1), and C-reactive protein (IHG: LIG: CG=87.6: 28.2:1) showed significant differences in plasma abundance and correlated with disease severity among patients with acute PE.

CONCLUSIONS Serum amyloid A-1 protein, neutrophil gelatinase-associated lipocalin, cystatin-C, glutathione peroxidase, haptoglobin, and C-reactive protein were significantly increased in patients with acute PE, and may serve as circulating biomarkers for the severity of acute PE.

GW30-e0445

Electrocardiography analysis of 513 patients with pulmonary thromboembolism

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OBJECTIVES The incidence of pulmonary thromboembolism (PTE) in China has increased by each year. Electrocardiography (ECG) facilitates early diagnosis of pulmonary thromboembolism (PTE) in order to take timely measures to improve the patients' outcomes. This study is designed to investigate the significance of ECG in the diagnosis and risk stratification of PTE.

METHODS The total of 513 consecutive patients with PTE admitted to Beijing Tong Ren Hospital, Capital Medical University from January 2011 to December 2018 were enrolled. The average age was (70.1±12.6) years. They were divided into different groups by gender, age (≥65 years) and risk stratification (hemodynamic status, cardiac biomarkers and right ventricular function). The baseline data and ECG data were collected and analyzed.

RESULTS Among 513 patients diagnosed with PTE, 314 (61.2%) were female patients and 199 (38.8%) were male patients, 356 (69.4%) were elderly patients, 157 (30.6%) were non-elderly patients, 254 (49.5%) patients were at low-risk and 259 (50.5%) patients were at intermedium- and high-risk. The proportion of T wave changes in anterior leads was the highest (308/513, 60.0%), which was followed by S1Q3T3 pattern (157/513, 30.6%). The proportion of T wave changes in V_1~V_4 leads in female PTE patients was significantly higher than that in male patients (P<0.05). The proportion of atrial fibrillation in elderly PTE patients was significantly higher than that in non-elderly patients (P<0.05). V_2~V_6 lead T-wave changes, S1Q3T3 pattern, right axis deviation, atrial fibrillation, sinus tachycardia, median axis and median heart rate in patients with intermedium- and high-risk were significantly higher than those in low-risk patients (P<0.05). Logistic regression analysis indicated that sinus tachycardia (*OR*=4.162, 95% CI: 2.117–8.183, P<0.001), right axis deviation (*OR*=3.731, 95% CI: 1.320–10.548, P=0.013), atrial fibrillation (*OR*=3.589, 95% CI: 1.652–7.796, P=0.001), V_5 lead T wave changes (*OR*=2.184, 95% CI: 1.107–4.309, P=0.024), chest distress/dyspnea (*OR*=1.641, 95% CI: 1.066–2.524, P=0.024), S1Q3T3 pattern (*OR*=1.593, 95% CI: 1.047–2.423, P=0.030) and age ≥70 years old (*OR*=1.583, 95% CI: 1.065–2.354, P=0.023) were independent risk factors for intermedium- and high-risk PTE patients. After risk score assignment and calculating the score fairly predicted intermedium- and high-risk PTE patients with an area under the ROC curve of 0.716 (95% CI: 0.672–0.761, P<0.001) and the cut-off score was 5.

CONCLUSIONS When patients occurred with suspicious symptoms such as chest distress or dyspnea, and ECG indicates simultaneous T wave changes in the right precordial leads (V_1~V_4) and atrial fibrillation, PTE requires great vigilance. Age ≥70 years old, sinus tachycardia, right axis deviation, atrial fibrillation, T wave changes in V_5 and S1Q3T3 pattern were risk factors for intermedium- and high-risk PTE patients.

GW30-e0624

PXDN mediates hypoxia-induced differentiation and migration of PAFs in pulmonary arterial hypertension and its mechanism

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OBJECTIVES Adventitia is recognized as the earliest and most prominent structural change during the Pulmonary artery hypertension (PAH) process. In response to injury and disease, adventitia fibroblasts are activated and undergo proliferation, migration and differentiation, thereby promoting vascular remodeling. Peroxidasin (PXDN), a member of the heme-containing peroxidase family, is highly expressed in the cardiovascular system. In the presence of chloride, PXDN catalyzes the formation of hypochloric acid (HOCl) from H_2O_2 and enhances oxidative stress. Our previous studies demonstrate that changes in the expression and function of peroxidasin (PXDN) have been proposed as a signaling molecule that directly injure endothelial cells, promote vascular smooth muscle cells phenotypic switch and myocardial fibrosis underlying many cardiovascular diseases. We hypothesized that aberrant expression of PXDN regulates this activated pulmonary arterial fibroblasts (PAFs) phenotype and sought to determine the signaling pathways through which PXDN exerts effects.

METHODS Elevated expression of PXDN was detected in hypoxia-induced PAH rat models using immunofluorescence and Western blot. In vitro, knockdown of PXDN with siRNA significantly attenuated hypoxia-induced migration and differentiation of pulmonary adventitia fibroblasts, suppressed the hypoxia-induced expression of α-smooth muscle actin and MMPs in pulmonary adventitial fibroblasts. In addition, knockdown of PXDN with siRNA attenuated hypoxia-inducible factor-1α (HIF-1α) expression in PAFs in hypoxia using Western blot.

RESULTS Same to the methods

CONCLUSIONS These findings indicate that PXDN mediates hypoxia-induced PAFs differentiation and migration by regulating HIF-1α protein expression and contributes to pulmonary vascular remodeling during the development of PAH.

DIABETES, CEREBROVASCULAR DISEASES, KIDNEY DISEASES, CARDIO-ONCOLOGY

GW30-e0066

Protective role of enalapril in chemotherapy-induced cardiotoxicity: grading the evidence through a systematic review and meta-analysis

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OBJECTIVES To assess the protective role of enalapril in preventing and treating anthracycline-induced cardiotoxicity.

METHODS A systematic review and meta-analysis was performed based on electronic databases from inception to January 29, 2019, and included relevant studies that analyzed enalapril as a cardioprotective agent before or during the use of anthracyclines by oncology patients. Homogeneous results from different studies were pooled using Revman 5.3 software.

RESULTS We examined 626 studies, screened them according to specific criteria and finally included 7 that were relevant to the indicated topic. Three studies reported on the incidence of death during 6-month and 12-month follow-up periods. Six studies showed possible positive results regarding a cardioprotective role for enalapril, although only four demonstrated significant differences in the left ventricular ejection fraction after chemotherapy in the groups that used enalapril compared to those in the control groups (WMD=6.60, 95% CI: 5.77–7.43, I^2=95%, P<0.001). Moreover, enalapril was also beneficial in reducing the levels of TnI, CK-MB and NT-proBNP in cancer patients treated with anthracycline.

CONCLUSIONS Although the protective effect of enalapril regarding myocardial toxicity was obtained in terms of LVEF values and the levels of TnI, CK-MB and NT-proBNP, its routine use in the prevention of anthracycline-associated cardiotoxicity requires additional scientific evidence.

GW30-e0069

Protective role of the duration of beta-blockers treatment in anthracycline-induced cardiomyopathy: a systematic review and meta-analysis

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OBJECTIVES Anthracycline-containing chemotherapy is commonly associated with irreversible cardiovascular toxicity. Beta-blockers are currently recommended as first-line drugs for improving cardiac function. However, its effects with respect to cardiac preservation in anthracycline-treated patients and the duration of treatment remain to be unclear.

METHODS We systematically searched PubMed, Embase and Cochrane for randomized controlled trials (published between January, 2000 and January, 2019) to determine the effectiveness of cardiac preservation of beta-blockers in anthracycline-treated patients by accessing pre-chemotherapy and post-chemotherapy left ventricular ejection fraction (LVEF). In addition, we also conducted meta-analysis based on beta-blockers treatment duration and accumulative anthracyclines dose.

RESULTS 11 RCTs were finally included. Beta-blockers were associated with a significant smaller drop in post-chemotherapy LVEF (MD=2.27, 95% CI=0.38 to 4.16, P=0.02) compared to control groups. Besides, in the <6 months and=6 months beta-blockers treatment time, significant difference in LVEF (MD=0.66, 95% CI=−0.23 to 1.54; MD=5.05, 95% CI=1.35 to 8.74; P=0.02) were detected between two groups. The pooled effect sizes according to accumulative anthracyclines dose showed no statistically significant effect on post-chemotherapy LVEF between beta-blockers and control groups.

CONCLUSIONS Prophylactic administration of beta-blockers treatment may be beneficial to the myocardial preservation in anthracycline-treated patients. And long term use of beta-blockers appears to have a positive effect on ameliorating anthracycline-induced cardiomyopathy.

GW30-e0077

Euonymus alatus attenuates diabetic retinopathy

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OBJECTIVES Diabetic retinopathy is a leading cause of blindness. Euonymus alatus shows therapeutic potential in the treatment of diabetes and its chronic complications. But the effect of Euonymus alatus on diabetic retinopathy has not been investigated. The purpose of this study is to evaluate the effect of Euonymus alatus on diabetic retinopathy in vitro and in vivo. Furthermore, the levels of matrix metalloproteinase-9 (MMP9) and nitric oxide (NO) will be examined to clarify its mechanism.

METHODS First, the Euonymus alatus's effect on the retinal vascular endothelial cells was examined. The cells were divided into the normal group (5.5 mmol/L glucose), model group (25 mmol/L glucose) and Euonymus alatus group (25 mmol/L glucose+Euonymus alatus aqueous extractions). After the cells were treated with different media for 72 h, CCK-8 assay was used to determine the toxic doses and effective doses. Then the cells were cultured in different media for 16 h, the Transwell assay was performed to observe the migrated ability. And then the formation assay was carried out to determine the total tube length. Second, the Euonymus alatus's effect was evaluated in vivo. KK-Ay mice were administered Euonymus alatus extract or water for 12 weeks. After ocular blood flow velocities were determined by Doppler ultrasound, the eyes were isolated for electron microscopy and western blot. And levels of nitric oxide in serum were measured by radioimmunoassay.

RESULTS 1. in vitro: Compared with the normal group, the cell viability, the number of migrated cells and the total length of tube formation in the model group was significantly increased. The results of CCK-8 assay showed that compared with the model group, the cell viability were inhibited by Euonymus alatus. The Transwell assay suggested that compared with the model group, the number of migrated cells was decreased by Euonymus alatus. The results of Matrigel assay indicated that compared with the model group, Euonymus alatus extraction could decrease the total tube length. 2. in vivo: Euonymus alatus extract was efficient in improving hemodynamics of central retinal artery and thinning basement membrane of retinal vessel. Euonymus alatus also had a role in inhibiting the expression of Matrix metalloproteinase-9 and decreasing nitric oxide.

CONCLUSIONS Euonymus alatus inhibited the cell viability, the cell migration and the tube formation. Moreover Euonymus alatus has a protective role in diabetic retinopathy, which may be related to downregulation of MMP9 expression and NO level.

GW30-e0130

Serum prealbumin and echocardiography parameters can predict mortality in peritoneal dialysis patients

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OBJECTIVES To evaluate prognostic value of prealbumin and echocardiographic indices in patients with end-stage renal disease (ESRD) treated with maintenance peritoneal dialysis (PD).

METHODS A total of 211PD patients (mean age 49.2±15.4 years, 51.7% male) were prospectively included. Serum prealbumin (PAB) levels and echocardiographic parameters were recorded at baseline. A 4.7-year follow-up was performed based on hospital records, clinics and telephone interviews.

RESULTS Significant difference were observed concerning baseline clinical characteristic (including age, PAB, C-reactive protein) and echocardiographic data between patients who survived or died over 4.7 years of follow-up. In the Cox proportional hazards model, PAB and the following echocardiographic parameters were found to be optimal predictors of all-cause mortality: PAB (P=0.002), aortic root diameter (ARD) (P=0.026), interventricular septum end-diastolic thickness (IVSd) (P=0.036) and left ventricular end-diastolic diameter index (LVEDDI) (P=0.047). And PAB (P=0.048), ARD (P=0.032) and IVSd (P=0.044) were independently predictive of cardiovascular (CV) mortality. The all-cause mortality and CV death rate significantly increased as the number of risk factors increased, namely PAB≤bottom tertile, ARD ≥Top tertile, and IVS ≥Top tertile increased (P<0.001 and P=0.011), reaching as high as 40 and 22% for patients who had all above risk factors.

CONCLUSIONS In PD patients, lower PAB levels and abnormal echocardiographic parameters together were significantly associated with all-cause mortality and CV death, independently of other risk factors. Importantly, combination of PAB and echocardiographic parameters provide additional predictive value for mortality in these patients. In light of these findings, more intensive study into the optimal model, containing PAB and echocardiographic parameters for the prediction of outcomes in ESRD is warranted.

GW30-e0165

Visit-to-visit fasting glucose variability in young adulthood and hippocampal integrity and volume at midlife

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OBJECTIVES To determine whether visit-to-visit fasting glucose (FG) variability in young adulthood is associated with hippocampal integrity and volume at midlife.

METHODS We studied 543 participants from the Coronary Artery Risk Development in Young Adults (CARDIA) Brain MRI sub-study. Visit-to-visit FG variability was defined as by the standard deviation of FG (SD_{FG}), the coefficient of variation of the mean FG (CV_{FG}) and the average real variability (ARV_{FG}) over 25 years of follow-up. Hippocampal integrity evaluated by fractional anisotropy (FA) and tissue volume standardized by intracranial volume (% ICV) were measured by 3T magnetic resonance imaging at the year 25 examination.

RESULTS Of the 543 individuals, the average (SD) of hippocampal FA was 0.32 (0.04) and hippocampus % ICV was 0.57 (0.06). After multivariable adjustment, higher FG variability was associated with lower hippocampal FA: for 1-SD increment of SD_{FG} (unstandardized regression coefficient, −0.015 [95% CI: −0.026, −0.004]), for 1-SD increment of CV_{FG} (−0.009 [95% CI: −0.018, −0.001]) and for 1-SD increment of ARV_{FG} (−0.011 [95% CI: −0.019, −0.002]); higher FG variability was associated with lower hippocampal volume: for 1-SD increment of SD_{FG} (−0.012 [95% CI: −0.023, −0.001]).

CONCLUSIONS Higher visit-to-visit FG variability in young adulthood is associated with hippocampal integrity and volume at midlife. It may have a great use in evaluating the potential risk for damage in hippocampal integrity and volume at midlife.

GW30-e0201

Estimate of ischemic stroke prevalence according to a novel 4-tiered classification of left ventricular hypertrophy: insights from the general Chinese population

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OBJECTIVES Recently, a novel 4-tiered classification of left ventricular hypertrophy (LVH) based on ventricular dilatation (indexed LV end-diastolic volume [EDV]) and concentricity (mass/EDV 0.67) has improved all-cause and cardiovascular mortality risk stratification. However, their possible association with ischemic stroke has not been extensively evaluated in the general population.

METHODS We evaluated a cross-sectional study of 11,037 subjects from the general population of China in whom echocardiographic and ischemic stroke data were available to subdivide patients with LVH into four geometric patterns: indeterminate, dilated, thick and both thick and dilated hypertrophy.

RESULTS Compared with normal LV geometry, indeterminate and thick hypertrophy showed a higher prevalence of ischemic stroke (P<0.05). Ischemic stroke was significantly greater in participants with indeterminate (adjusted odd ratio [OR]: 1.635, 95% confidence interval [CI]: 1.115–2.398) and thick (2.143 [1.329–3.456]) hypertrophy but not significantly in those with dilated (1.251 [0.803–1.950]) and both thick and dilated hypertrophy (0.926 [0.435–1.971]) compared with normal geometry in multivariable analysis.

CONCLUSIONS Indeterminate and thick hypertrophy were significantly associated with the presence of ischemic stroke in the general Chinese population. The new 4-tiered categorization of LVH can permit a better understanding of which subjects are at high enough risk for ischemic stroke to warrant early targeted therapy.

GW30-e0205

Long-term cardiac-specific mortality among 44,292 acute myeloid leukemia patients treated with chemotherapy: a population-based analysis

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OBJECTIVES Acute myeloid leukemia (AML) is a common haematological malignancy treated with regimens containing anthracycline, an agent with cardiotoxicity. However, the cardiac-specific mortality in AML patients receiving chemotherapy remained unknown.

METHODS In this population-based study, patients diagnosed with AML between 1973 and 2015 were identified in the Surveillance, Epidemiology, and End Results database. Cumulative mortality by cause of death was calculated. To quantify the excessive heart death over the general population, standardized mortality ratios (SMRs) were calculated. Multivariate Cox regression analyses were performed to identify risk factors associated with heart death and AML death.

RESULTS A total of 64, 679 AML patients between 1973 and 2015 were identified, with 68.48% of patients (44,292) receiving chemotherapy. Among all possible competing causes of death, AML is associated with the highest cumulative mortality. The AML patients receiving chemotherapy showed excessive cardiac-specific mortality compared with the general population, with an SMR of 6.35 (5.89–6.82). Age, year of diagnosis, sex, and marital status are independently associated with patients' prognosis.

CONCLUSIONS Cardiac-specific mortality in AML patients receiving chemotherapy is higher than that in the general population.

GW30-e0213

Low free triiodothyronine is associated with contrast-induced acute kidney injury and long-term outcome in elderly patients underwent percutaneous coronary intervention

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OBJECTIVES Low free triiodothyronine (fT3) is common in elderly patients with cardiovascular disease. The purpose of this study was to evaluate the relationship between low fT3 and contrast-induced acute kidney injury (CI-AKI), including the long-term outcomes, in elderly patients after a percutaneous coronary intervention (PCI).

METHODS A total of 350 patients aged ≥75 years who underwent PCI between January 2012 and December 2015 were consecutively enrolled. The perioperative thyroid function, including fT3, was measured before PCI. A low fT3 was defined as fT3 <3.1 pmol/L with normal thyrotropin and free thyroxine. CI-AKI was defined as an absolute serum creatinine (SCr) increase ≥0.30 mg/dL or a relative increase in SCr ≥50% from the baseline value within 48 hours after contrast media exposure. A multivariate logistic regression analysis was applied to analyze whether low fT3 was an independent risk factor for CI-AKI. The Cox regression analysis was used to evaluate the relationship between low fT3 and long-term prognosis.

RESULTS A total of 46 (13.1%) patients developed CI-AKI. The incidence of CI-AKI was significantly higher in the low fT3 group than in the normal group (26.5 vs. 9.9%, P<0.01). A multivariable logistic analysis demonstrated that a low fT3 level was significantly related to CI-AKI [odds ratio (OR)=2.41; 95% confidence interval (CI): 1.11–5.27; P=0.027]. The Cox regression analysis showed that a low fT3 was associated with long-term mortality [adjusted hazard ratio (HR)=2.00; 95% CI: 1.04–3.83; P=0.037] during the follow-up of mean 1.67 years.

CONCLUSIONS A low fT3 concentration was independently associated with CI-AKI and poor prognosis in elderly patients who had undergone PCI.

GW30-e0216

Estimate of prevalent diabetes from cardiometabolic index in general Chinese population: a community-based study

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OBJECTIVES Cardiometabolic index (CMI) defines adiposity based on triglycerides (TG) to high-density lipoprotein cholesterol (HDL-C) ratio and waist-to-height ratio (WHtR). This newly proposed metric has been used to detect multiple cardiovascular risk factors, but data relative to diabetes in the general population are lacking. This study aims to validate CMI's utility of discriminating diabetes and compares it with other indexes among general Chinese population.

METHODS Analyses were based on a cross-sectional study of 11,478 participants that underwent assessment of metabolic and anthropometric parameters in rural areas of northeastern China in 2013. CMI was calculated by TG/HDL-C×WHtR. Multivariate logistic regressions were performed to clarify CMI's association with diabetes, ROC analyses were engaged to investigate CMI's discriminating ability for diabetes.

RESULTS The prevalence of diabetes was 9.93% in males while 10.76% in females, and increased with CMI's increment. After full adjustment, each SD increment of CMI had odds ratios (ORs) for diabetes of 1.471 (1.367–1.584) and 1.422 (1.315–1.539) in females and males, respectively. Compared with bottom categories of CMI, the top quartiles had ORs of 3.736 (2.783–5.015) in females and 3.697 (2.757–4.958) in males. The ROC results showed an excellent discriminating power of CMI (AUC: 0.702 for females, 0.664 for males).

CONCLUSIONS An increasing CMI was correlated with higher odds of diabetes, supporting CMI as a useful and economic measure to screen and quantify diabetes in general Chinese population. Monitoring and promoting achievement of dyslipidemia and abdominal obesity based on CMI may improve subclinical and cardiovascular outcomes.

GW30-e0238

Protective effect of erythropoietin derivative HBSP on myocardial injury induced by doxorubicin in rats

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OBJECTIVES This study aimed to investigate the potential mechanisms underlying the protective effects of erythropoietin (EPO) derivative (HBSP) on doxorubicin (DOX)-induced myocardial injury.

METHODS Forty Wistar rats were randomly divided into control (CON), DOX, EPO and HBSP groups. The rats in the model and treatment groups were intraperitoneally injected with doxorubicin. The rats in the treatment group received an intraperitoneal infusion of EPO and HBSP 1 day before DOX administration, 1 day and 3 days after administration for 6 weeks, while those in the control and model groups received infusions of 0.9% NaCl. We measured the levels of cTnI and BNP. Echocardiography parameters were measured using an ultrasonic diagnostic instrument. The expression levels of PI3K and Akt were also detected by semi-quantitative PCR and Western blot.

RESULTS The levels of cTnI and BNP were lower in the treatment group than in the model group (P<0.05). The left ventricular ejection fraction (EF) and fractional shortening (FS) were higher in the rats treated with EPO and HBSP than in the model group (P<0.05), and the left ventricular internal diastolic diameter (LVIDd) were lower in the rats treated with EPO and HBSP than in the model group (P<0.05). The levels of PI3K and Akt in in the myocardium of EPO and HBSP group rats were significantly increased (P<0.05). There was no significant difference between EPO and HBSP groups.

CONCLUSIONS HBSP exerted a protective effect on myocardial injury induced by doxorubicin. The mechanism underlying this effect may be related to the activation of PI3K/Akt signaling pathway.

GW30-e0293

Cardiometabolic index is an effective discriminator for the risk of diabetes in women: a cross-sectional study of Chinese population

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OBJECTIVES Recent studies have suggested that cardiometabolic index (CMI), a novel marker of visceral adipose tissue because of its integration of dyslipidemia and abdominal obesity, could be used in the evaluation of multiple cardiovascular risk factors. However, the potential utility and clinical significance of CMI in the discrimination diabetes remains uncertain. The purpose of this study was to investigate the usefulness of CMI in detecting diabetes in the general Chinese population.

METHODS This cross-sectional study involved a total of 73,408 participants (mean age: 44.1 years, 59.7% men) who participated in an annual physical examination in the Health Management Center of the Third Xiangya Hospital from January 2016 to December 2016. CMI was calculated by triglyceride to high density lipoprotein cholesterol ratio multiply waist-to-height ratio. Multivariate regressions were performed to determine CMI's association with diabetes, and ROC analyses were employed to investigate CMI's discriminating ability for diabetes.

RESULTS The prevalence of diabetes was 8.2% in men and 3.5% in women. A dose-respond manner was detected for the presence of diabetes, exhibiting a significantly increase from the lowest to the highest quartiles of CMI (5.0–12.8% in men and 0.7–9.0% in women). In fully adjusted multiple logistic regression models, the top quartiles of CMI had ORs of 1.68 (1.41–1.98) in men and 2.19 (1.51–3.19) in women compared with the bottom category. When assessed using ROC curve analyses, CMI exhibited an excellent diagnostic accuracy for identifying diabetes, and the areas under the curves (AUC) in men and women were 0.615 (95% CI: 0.605, 0.625) and 0.765 (95% CI: 0.750, 0.779), respectively.

CONCLUSIONS CMI is significantly associated with the presence of diabetes, and has a high diagnostic accuracy for identifying diabetes in women.

GW30-e0421

The diagnostic value of serum circulating miR-21 for eldly patients with type 2 cardiorenal syndrome

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OBJECTIVES Circulating miRNAs have gained great popularity to act as serum biomarkers in several diseases. In this study, we aimed to evaluate the diagnostic value of circulating miR-21 as novel biomarkers for elderly patients with type 2 cardiorenal syndrome (CRS).

METHODS Based on the inclusion criteria: (i) age over 65 years; (ii) NYHA II-IV; (iii) the occurrence of cardiac insufficiency was earlier than renal insufficiency in CRS group patients and the exclusion criteria: (i) patients with autoimmune diseases, cancer, liver diseases, hematological diseases; (ii) recent surgery or trauma, acute and/or chronic inflammatory state; (iii) CHF induced by primary kidney disease or CKD (i.e., CRS-4). A total of 157 elderly patients with chronic heart failure (CHF) were recruited in the study. According to estimated glomerular filtration rate (eGFR, calculated with the CKD-EPI$_{2009}$ formula) whether lower than 60 mL/min/1.73 m^2, patients were assigned into the CRS group and the CHF group. The expression levels of serum miR-21 and present biomarkers for CRS, such as kidney injury factor-1 (KIM-1), neutrophil gelatinase-related apolipoprotein (NGAL), cystatin C (CycsC), amino-terminal pro-B-type natriuretic peptide (NT-proBNP), N-acetyl-κ-D-glucosaminidase (NAG), heart-type-fatty acid–binding protein (H-FABP) were detected. The differences between the two groups were analyzed with Mann-Whitney U test. The association between biomarkers expression and CRS-2 was analyzed by Spearman rank correlation. Receiver operating characteristic (ROC) curve, sensitivity, specificity and Yoden index were used to estimate the predictive value of the biomarkers. P<0.05 was regarded as statistically significant.

RESULTS The results show that serum miR-21, KIM-1, NGAL, CycsC, NT-proBNP and H-FABP level are significantly higher in the CRS group than the CHF group (P<0.01), while the expression of NAG have no significant difference between the two groups (P>0.05). NT-proBNP (r=0.244, P=0.002), eGFR (r=–0.384, P=0.000), NGAL (r=0.160, P=0.046), H-FABP (r=0.277, P=0.001) and CycsC (r=0.380, P=0.000) are significantly correlated with miR-21 expression, but the correlations with miR-21 are not significant for NAG and KIM-1. Besides, the expression of miR-21 (r=0.427, P=0.000), KIM-1 (r=0.221, P=0.005), NGAL (r=0.330, P=0.000), CycsC (r=0.679, P=0.000), NT-proBNP (r=0.397, P=0.000) and H-FABP (r=0.360, P=0.000) is significantly correlated with CRS. ROC curves demonstrated that the AUC of miR-21 was 0.749, sensitivity 55.95% and specificity 84.93%. Furthermore, miR-21 together with CycsC enhance the AUC to 0.904, sensitivity to 88.1% and specificity to 80.82%.

CONCLUSIONS Our findings suggest that miR-21 combined with CycsC have good diagnose value in eldly patients with type 2 cardiorenal syndrome.

GW30-e0443

Exenatide reduces cardiomyocyte apoptosis by stimulating adiponectin secretion and activating APPL1-AMPK-PPARα axis

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OBJECTIVES To explore the mechanism that exenatide reduces cardiomyocyte apoptosis via the adiponectin pathway in vitro.

METHODS Cardiomyocytes were randomly divided into the control group (group C), diabetic group (group D), diabetic+exenatide treatment group (group DE), diabetic+exenatide treatment+APPL1 overexpression group (group OE), and diabetic+exenatide treatment+APPL1 knock-down group (group KD). After 48 h culture, the apoptosis rate, the adiponectin level in the cell culture fluid, and the expression levels of APPL1, p-AMPK, PPARα and NF-κB were detected by TUNEL, ELISA, and Western blotting, respectively.

RESULTS Compared to group C, the apoptosis rate was markedly increased, the adiponectin level was decreased, the expression of APPL1, p-AMPK and PPARα was down-regulated and that of NF-κB was upregulated in group D (P<0.05); in group DE, the apoptosis rate was significantly decreased, the expression of APPL1, p-AMPK and PPARα was up-regulated and that of NF-κB was down-regulated, as compared with group D (P<0.05). The apoptosis rate in group OE was lower than that in group DE, the expression of APPL1, p-AMPK and PPARα was up-regulated and that of NF-κB was down-regulated (P<0.05). In group KD, the adiponectin level was elevated and the cardiomyocyte apoptosis rate was increased, as compared to group D (P<0.05). Furthermore, the expression of APPL1, p-AMPK and PPARα was down-regulated and that of NF-κB was up-regulated compared with group DE (P<0.05).

CONCLUSIONS Exenatide can activate the "APPL1-AMPK-PPARα" anti-apoptosis signaling axis by promoting adiponectin expression in cardiomyocytes and reducing the apoptosis of diabetic cardiomyocytes, thus protecting cardiomyocytes.

GW30-e0484

BNP as a potential biomarker for cardiac damage of breast cancer after radiotherapy: a meta-analysis

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OBJECTIVES Breast cancer is the most common cancer and the leading cause of cancer death among women worldwide. Chemotherapy and radiotherapy play crucial role in local control and metastasis of breast cancer. However, it has been reported that cardiovascular mortality are observed in breast cancer patients especially for left breast cancer after chemotherapy and/or radiotherapy. Cardiac biomarkers such as brain natriuretic peptide (BNP) and troponin (TnI) may be used to monitor cardiotoxicity and assess early signs of cardiovascular dysfunction. Plasma levels of TnI have been used as a prognostic marker of cardiac disease for high dose chemotherapy, especially for anthracyclines. However, two trials found that in left breast cancer patients, left ventricular ejection fraction (LVEF) did not significantly change after radiotherapy, and was not correlated with TnI levels. Hence, TnI is not considered for biomarker to cardiac damage of breast cancer patients. So, what about BNP? Could it be suitable? There had been already some articles about BNP as biomarker for heart damage in breast cancer patients. We conducted this meta-analysis to evaluate its potential role for biomarker, especially the patients who received radiotherapy and chemotherapy.

METHODS PubMed, Web of Science, ProQuest and Medline were searched using the key words "breast cancer" ("breast tumour", "breast neoplasm", or "breast carcinoma"), "BNP" (or brain natriuretic peptide) and "radiotherapy" (or "radiation therapy"). Studies were considered eligible if they met the following inclusion criteria: (1) The studies involved patients with left breast cancer, without metastasis and recurrence. (2) The patients underwent radical/conserving surgery followed by radiotherapy and/or chemotherapy. (3) The articles were written as full papers in English. Studies were excluded for the following reasons: (1) The publications were review articles, letters, case reports, expert opinions, or meeting records. (2) Non-human research was performed. (3) Patients had recurrent or metastatic disease. (3) Patients were with right breast cancer or cardiac dysfunction. (4) The publications were not written in English. Four articles were selected and analysed using the STATA 12.0 software package. The standard mean difference (SMD) and its standard error for BNP were calculated to assess the relationship between BNP and radiotherapy for breast cancer patients. Forest plots were used to estimate BNP changes after radiotherapy and/or chemotherapy for left breast cancer patients. Funnel plots were generated to assess potential publication bias, and P>0.05 indicated no potential publication bias.

RESULTS According to our previously defined criteria, the initial electronic online search of PubMed databases, Web of Science, ProQest and Medline retrieved 393618 papers. After the selection according to the inclusive criteria, 4 eligible studies were finally included. In total, 172 patients with breast cancer were identified. The pooled SMD was –0.233 (95% CI: –1.113, –0.057). The pooled estimated SMD for all studies showed obvious significant difference (z=3.99, P=0.000). The heterogeneity among studies was not high (I^2=27.9%, P=0.164). There was no publication bias.

CONCLUSIONS This meta-analysis suggested that BNP could be a biomarker of cardiac damage at high heart absorbed doses according to radiotherapy, especially for left breast cancer patients.

GW30-e0512

Association of lipid accumulation product longitudinal trajectories with 5-year incidence of diabetes in Chinese adults

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OBJECTIVES Lipid accumulation product (LAP) is an index used to evaluate over accumulation of lipid. Previous studies stated that LAP is significantly associated with diabetes. However, only baseline LAP with regard to the risk of diabetes has been reported. The effect of long-term LAP trajectories on diabetes risk, which reflect the efficacy of patients' lipid-lowering treatment and lifestyle improvement, have rarely been studied. The aim of this cohort study is to explore the association of lipid accumulation product trajectories with 5-year incidence of diabetes in general Chinese adults.

METHODS This cohort study included 4,508 non-diabetic participants with the mean age of 42 years. Using the group-based trajectory modeling (GBTM), LAP from 2011 to 2016 were determined and identified as three trajectories: low (n=3639), moderate (n=800), and high (n=69). Baseline LAP was divided into three groups percentiles and tertiles respectively to compare with LAP trajectories in predicting new-onset diabetes. The associations between 5-year diabetic incidence and LAP trajectories and baseline LAP were both assessed by generalized linear models.

RESULTS During 2011 to 2016, 169 participants developed diabetes with the 5-year incidence of 3.8%. A significant trend was observed in relative risks (RRs) of 5-year incident diabetes in participants with moderate and high LAP trajectory after full adjustments. However, RRs in neither groups nor tertiles of baseline LAP were found significant trends after full adjustments.

CONCLUSIONS The risk of 5-year diabetic incidence was significantly increased in participants with moderate and high LAP trajectory. The present findings indicate that trajectories of LAP show a stronger association in 5-year diabetic incidence than baseline LAP.

GW30-e0516

Yin Yang 1 ameliorates diabetic nephropathy pathology through transcriptional repression of TGFβ1

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OBJECTIVES Transforming growth factor beta 1 (TGFβ1) has been identified as a major pathogenic factor underlying the development of diabetic nephropathy (DN). However, the current strategy of antagonizing TGFβ1 has failed to demonstrate favorable outcomes in clinical trials. This study aims to identify a novel therapeutic approach and potential natural compounds to prevent DN progression.

METHODS A mass spectrometry-based transcription factor screening method was included to explore potent transcriptional repressors. Detailed mechanism of the regulatory network between Yin Yang 1 (YY1) and TGFβ1 was discovered by western blot assays, RT-PCR assays, luciferase reporter assays, chromatin immunoprecipitation (ChIP) assays, electrophoretic mobility shift assays (EMSA) and site-specific mutagenesis assays. Both type 1 and type 2 diabetic mouse models, as well as cultured renal cells (human mesangial cells, mouse podocytes, rat tubular cells and rat endothelial cells) were involved to detect the expression pattern of YY1. Mice with renal specific overexpression and knockdown of YY1 were constructed to examine the protective effects of YY1 on diabetic kidneys. Renal biopsy slices were collected from DN patients and their clinical parameters were analyzed with the expression of YY1. Specific natural compound was identified to increase YY1 expression and applied to type 2 diabetic mouse models.

RESULTS MS-MS analysis identified YY1 as a potent repressor of *TGFB1*. YY1 bound directly to *TGFB1* promoter regions (−3123/−3115) and repressed its transcription. Notably, YY1 was specifically elevated in mesangial cells during early diabetic renal lesions and decreased in later stages. Knockdown of renal YY1 aggravated glomerulosclerosis, while overexpression of YY1 attenuated it in mouse models. In addition, although with comparable duration of DN, patients with higher YY1 expression developed DN much more slowly compared to those who presented with suppressed YY1 levels. A small molecule, Eudesmin, was identified as a suppressor of TGFβ1 and other pro-fibrotic factors by increasing YY1 expression and consequently attenuating diabetic renal lesions *in vivo* and *in vitro*.

CONCLUSIONS These results suggest that YY1 is a potent transcriptional repressor of *TGFB1* during the development of DN in diabetic mice, and small molecules targeting YY1 may serve as promising therapies for treating DN.

GW30-e0739

VR19 attenuates DOX-induced cardiotoxicity and inhibits MCF-7 breast cancer cells growth through modulation of ROS production, cell apoptosis and proliferation

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OBJECTIVES Anthracyclines, such as doxorubicin (DOX), are extensively used for treatment of solid tumors and hematological malignancies. However, Anthracyclines can cause heart damage in a dose-dependent manner, probably via increasing reactive oxygen species (ROS) production and inducing cardiomyocyte death. VR19 is a 19-amino-acids peptide derived from ribosomal protein 23a (RL23a), which was identified in our former research using mass spectrum and proved to be cardioprotective in ischemic heart disease. Our study aimed to investigate the role of VR19 in attenuating DOX-induced cardiotoxicity and its anti-cancer effects.

METHODS 8–10 weeks old C57BL/6 mice were randomly divided into four groups: Sham group intraperitoneally administrated with saline (4 mL/kg), DOX group with DOX (6 mg/kg) dissolved in saline (4 mL/kg) and DOX+VR19 group with DOX and VR19 dissolved in saline (4 mg/kg) simultaneously, once a week for consecutive four weeks. One week after the final injection, echocardiography was conducted, and mice heart tissue were isolated for HE staining, Masson staining, MDA and SOD concentration detection. H9c2 cells were cultured and seeded in 6-well culture plates, then respectively processed with saline, DOX (1 μM) and DOX (1 μM) plus VR19 (50 μM) for 24 h. Cell apoptosis was analyzed with flow cytometry, western blot and TUNEL staining. Breast cancer cell line MCF-7 underwent VR19 (50 μM) process were used to evaluate the effect of VR19 on tumor proliferation via CCK8 assay, colony formation assay and EdU staining.

RESULTS VR19 improves cardiac function (%EF: Sham 78.4±3.4, DOX 48.3±6.3, DOX+VR19 58.3±5.1, P<0.01; %FS: Sham 39.7±4.2, DOX 23.9±6.9, DOX+VR19 29.3±5.1, P<0.05), and reduce cardiomyocyte atrophy (DOX 19.3±3.2%, DOX+VR19 10.5±4.1%, P<0.05) and fibrosis (DOX 25.1±5.2%, DOX+VR19 17.9±3.9%, P<0.05). Increased SOD (DOX 21.3±3.8 U/mg, DOX+VR19 34.3±4.0 U/mg, P<0.01) and decreased MDA (DOX 623.1±21.4 nmol/ng, DOX±VR19 371.9±18.1 nmol/ng, P<0.01) concentration indicates antioxidant ability of VR19. VR19 attenuates DOX-induced H9c2 cells apoptosis, reflected by decreased Annexin V-FITC stained cells (DOX 62.3±4.9%, DOX+VR19 37.2±5.8%, P<0.01), TUNEL positive cells (DOX 43.8±6.2%, DOX+VR19 25.1±4.1%, P<0.01) and expression of cleaved-caspase 3, cleaved PARP and BAX. MCF-7 cells processed by VR19 shows impaired proliferation compared with control group, with lower growth rate (OD450 nm: Control 1.21±0.13, VR19 0.89±0.09, P<0.01), less colony formation (Control 70.3±10.2, VR19 43.1±8.2, P<0.05) and EdU positive cells (Control 43.1±5.2%, VR19 23.5±3.9%, P<0.01).

CONCLUSIONS Peptide VR19 attenuates DOX-induced cardiotoxicity and exhibits anti-tumor effects through modulation of ROS production, cell apoptosis and proliferation.

GW30-e1007

Association between blood pressure levels and its variability with progression of renal impairment: findings from the Chinese Multi-provincial Cohort Study

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OBJECTIVES To investigate the relationship between blood pressure (BP) levels and its variability with the progression of renal impairment, in order to provide evidence for the etiology and early prevention of renal diseases.

METHODS The participants were recruited from the Chinese Multi-provincial Cohort Study-Beijing project, who participated in the cardiovascular disease risk factors surveys in 2002 and 2007, and were followed up to December 2012. A total of 1 639 subjects were included in the analysis. Renal function was represented by estimated glomerular filtration rate (eGFR) calculated by the MDRD formula for serum creatinine concentration. During follow-up, the eGFR changed from normal level (≥90 mL/min/1.73 m^2) to impaired or further decreased, which was defined as impaired renal function progression. Linear regression model was used to analyze the relationship between BP level in 2007 and renal function impairment from 2007 to 2012. Multivariate Logistic regression model was used to analyze the relationship between long-term variability of BP from 2002 to 2007 and the progression of renal impairment from 2007 to 2012.

RESULTS Of the 1 639 participants, 674 (41.1%) were male, mean (SD) age was 57.1 (7.9) years at baseline. The baseline systolic blood pressure (SBP) was 130.1±18.4 mmHg and diastolic blood pressure (DBP) was 81.7±10.2 mmHg in 2002. The prevalence of impaired renal function was 7.4%, 9.7%, and 16.0% in patients with baseline SBP/DBP <130/80 mmHg, 130–139/80–89 mmHg and

hypertension (≥140/90 mmHg, or oral antihypertensive drugs), respectively (P<0.01). After adjusting for age, gender, body mass index, smoking, fasting plasma glucose, total cholesterol, high-density lipoprotein cholesterol and oral antihypertensive drugs, as SBP and DBP increased by 10 mmHg in 2007, eGFR decreased by 0.632 (95%CI: 0.112–1.152) and 0.942 (95%CI: 0.059–1.825) mL/min/1.73 m^2 in the following 5 years, respectively. Compared with the group whose BP had been maintained at <130/80 mmHg in 5 years, the odds ratio (OR) and 95%CI of progression of renal impairment for participants whose BP increased from 130–139/80–89 mmHg to hypertension, sustained hypertension and decreased from hypertension to 130–139/80–89 mmHg were 2.39(1.10–5.19), 2.40 (1.33–4.31) and 2.59 (1.05–6.36), respectively.

CONCLUSIONS Higher BP was associated with impaired kidney function. People whose BP increased from 130–139/80–89 mmHg to hypertension and decreased from hypertension to 130–139/80–89 mmHg had a higher risk of aggravating renal impairment, and our results highlight the importance of early prevention for people with this BP stratum.

GW30-e1030

HMGB1 regulates endothelium-dependent vasodilation in type 2 diabetes via TLR4/Caveolin-1/eNOS pathway

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OBJECTIVES To explore the relationship between high mobility group box protein B1 (HMGB1) and endothelium-dependent vasodilation in type 2 diabetes.

METHODS The high mobility group box protein B1 (HMGB1) and total nitric oxide (NO) levels in the serum of patients with type 2 diabetes and healthy controls were analyzed. The MyograPh tension dynamic tracing system was used to analyze the diastolic function of the thoracic aorta of type 2 diabetic (db/db) mice and control mice (C57BL/6). The expression levels of HMGB1 and NO in serum and aorta of the two groups were detected. The HMGB1 level in the serum of db/db mice was detected after intraperitoneal injection of glycyrrhizic acid, and the diastolic function of isolated thoracic aorta of db/db mice was evaluated. Recombinant HMGB1 (rHMGB1) was used to isolated thoracic aorta of C57BL/6 mice and TLR4 knockout mice (TLR4-/-), also used to human umbilical vein endothelial cells (HUVEC), then evaluate endothelium-dependent vasodilation and analyzed the NO content in the serum, the expression levels of TLR4, Caveolin-1 and eNOS in blood vessels and cells was analyzed by Western blot and immunofluorescence.

RESULTS Serum HMGB1 levels and total NO levels in patients with type 2 diabetes and healthy controls were (7.89 vs. 4.10 ng/mL, P<0.05) and (307.24 vs. 370.27 umol/L, P<0.05). The endothelium-dependent diastolic function of the thoracic aortas of db/db mice were lower than that in C57BL/6 mice. Serum HMGB1 levels and serum total NO levels of db/db mice, respectively, compared with C57BL/6 mice were (29.0 vs. 9.3 ng/mL, P<0.05) and (82.2 vs. 102.8 umol/L, P<0.05). The expression of HMGB1 in the thoracic aorta of db/db mice were greater than that of C57BL/6 mice, and the levels of eNOS were lower than that of C57BL/6 mice. The endothelium-dependent diastolic function of db/db mice injected with different doses of glycyrrhizic acid were better than that of the uninjected group, the difference was statistically significant. Different concentrations of rHMGB1 interfered the isolated thoracic aortas of C57BL/6 mice and HUVEC, and then the endothelium-dependent relaxation function decreased, lead to up-regulation of TLR4 and Caveolin-1 expression in vascular and HUVEC, and down-regulation of eNOS expression and eNOS/Caveolin-1 ratio in vascular and HUVEC. After the nitric oxide synthase inhibitor was administered, endothelium-dependent relaxation function was restored. After the isolated thoracic aortas of TLR4-/- mice were incubated with rHMGB1, endothelium-dependent vasodilation function and Caveolin-1 and eNOS expression levels were not significantly different from those in the untreated group.

CONCLUSIONS HMGB1 may affect the synthesis of NO in vascular endothelial cells through TLR4/Caveolin-1/eNOS pathway, which may affect endothelial endothelium-dependent relaxation. There is no effective treatment for the reduction of vascular endothelial function in patients with type 2 diabetes, glycyrrhizic acid may be a potential drug to solve the problem.

GW30-e1048

Effect of exercise intervention on LVEF, GLS, BNP and evaluating by thromboelastography in women with breast cancer receiving radiation therapy

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OBJECTIVES Our study was designed to identify the effect of exercise intervention for improving cardiac function in breast cancer patients after radiotherapy according to Left ventricular ejection fraction (LVEF), Global longitudinal strain (GLS), Brain natriuretic peptide (BNP) and to explore the clinical value of TEG.

METHODS Patients of experimental group were accepted exercise therapy. Exercise time generally requires each lasting 50–75 minutes, at least 3 times a week, five to six times a week for people who exercise frequently. Patients should be advised to choose the morning as the optimum exercise time. The optimal exercise intensity is determined and adjusted by the target rate, which is estimated by maximum heart rate reserve using formula of Karvonen et al. [target heart rate=0.6 X (220-age-HR at rest)+HR at rest]. LVEF and GLS were measured by using Doppler echocardiography before, after, 3 months, 6 months and 12 months after radiotherapy in the experimental and control groups. BNP and TEG were examined before, after, 3 months and 6 months after radiotherapy in two groups.

RESULTS 1. Before radiotherapy, there were no significant differences in BNP between two groups (P>0.05). The experimental group showed that BNP significantly decreased at 1 month, 3 months and 6 months after radiotherapy (P<0.01–0.05), while the control group showed that BNP significantly increased at 3 months and 6 months (P<0.01–0.05). The BNP in the experimental group was obviously lower than that in the control group at 1, 3 months and 6 months (P<0.01–0.05). (Fig. 1). 2. There was no significant difference between two groups in LVEF and GLS before radiotherapy (P>0.05). After radiotherapy for 1 month, the LVEF and GLS in the experimental group showed no significant change, while LVEF and GLS in the control group were significantly reduced at 3 months following radiotherapy (P<0.05). Comparing with experimental group, LVEF and GLS in the control group was significantly reduced at 3 months after radiotherapy (P<0.05). 3. There were significant differences in platelet count, neutrophil percentage and lymphocyte percentage before and after radiotherapy in upper limb blood routine of breast cancer patients (P<0.0001). (Fig. 4). 4. TEG parameters R, Angle and MA were abnormal before and after radiotherapy on the affected upper limb of breast cancer, and hypercoagulability after radiotherapy was more serious than that before radiotherapy. (Fig. 5). 5. After nursing intervention, the counts of neutrophils and lymphocytes were much lower than before, and the differences between them were significant. (P<0.00001). (Fig. 6).

CONCLUSIONS 1. The decrease of BNP were significant and delay the occurrence time of radiation-induced heart injury by administration of aerobic exercise. 2. LVEF and GLS in the control group was significantly reduced at 3 months after radiotherapy. Analysis revealed that aerobic exercise improved cardiac function, especially those who received treatment to the left side of breast. 3. The findings in this study are significant because this is the first study of GLS that has shown the beneficial effects of aerobic exercise in improving cardiac function in breast cancer patients. 4. The TEG maybe used as a sensitive method to detect lymphedema in upper limbs. And it could also predict the Upper limb Lymphoedema before and after radiotherapy in patients with Breast Cancer in future.

PERIPHERAL VASCULAR DISEASE

GW30-e0523

Screening and identification of critical biomarkers in atherosclerosis based on bioinformatics analysis

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OBJECTIVES Atherosclerosis, a key underlying mechanism in cardiovascular disease, is characterized by focal thickening of artery walls and the formation of lipid-rich atheromatous lesions. However, previous studies were unable to verify the multiple gene interaction and the development of atherosclerosis accurately. The present study aimed to investigate the genetic signatures of atherosclerosis and identify its potential molecular mechanisms.

METHODS The gene expression profiles of gene series (GSE), downloaded from the Gene Expression Omnibus (GEO) database, contained 385 samples from primary human aortic endothelial cells (HAECs) derived from 96

genetically identical donors of anonymous origin. The GSE included 199 samples treated with 40 ug/mL oxidized 1-palmitoyl-2-arachidonoyl-sn-glycerol–3-phosphatidylcholine (Ox-PAPC) for 4 hours in media 199 containing 1% fetal bovine serum and 186 samples treated by the same media without Ox-PAPC. To further examine the biological functions of the identified differentially expressed genes (DEGs), Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes pathway (KEGG) enrichment analyses were performed, and a protein-protein interaction (PPI) network was mapped using Cytoscape software.

RESULTS In total, 221 DEGs were identified in HAECs treated with or without Ox-PAPC, including 109 up-regulated genes and 112 down-regulated genes. GO and KEGG pathway enrichment analyses indicated that up-regulated genes were significantly enriched in the TNF signaling pathway, MAPK signaling pathway, Cytokine-cytokine receptor interaction, while the down-regulated genes were mainly enriched in Pathways in cancer, Transcriptional misregulation in cancer, Epstein-Barr virus infection ($P<0.05$). From the PPI network, the 10 nodes with the highest degrees were screened as hub genes; these genes were involved in certain pathways, including the TNF signaling pathway and rheumatoid arthritis signaling pathway.

CONCLUSIONS The present study used a bioinformatics analysis of gene profile datasets and identified potential therapeutic targets for atherosclerosis.

PSYCHO-CARDIOLOGY

GW30-e0189

Pinocembrin attenuates autonomic dysfunction and atrial fibrillation susceptibility in a rat model of myocardial infarction

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OBJECTIVES The present study aimed to investigate the effects of pinocembrin on autonomic dysfunction and AF susceptibility in MI rats and the possible mechanism.

METHODS Male rats were randomly divided into three treatment groups: sham-operated+intravenous administration of saline (Sham); MI+intravenous administration of saline (MI) and MI+intravenous administration of pinocembrin (MI+P). MI model in rats were induced by permanent ligation of the left anterior descending (LAD) coronary artery. A week after operation, the heart rate variability (HRV), atrial electrophysiological parameters, norepinephrine (NE), tumor necrosis factor-α (TNF-α), interleukin (IL)-1β and IL-6 levels in the serum and left atrial (LA) were measured. Atrial histology was determined with Masson staining. The proteins levels of connexin (Cx) 43, Cav1.2, IκBα, p-IκBα, p65, and p-p65 were detected by western blot assays.

RESULTS Our results demonstrated that pinocembrin treatment significantly reduced sympathetic activity, augmented parasympathetic activity, improved heart rate variability (HRV), prolonged atrial effective refractory period (ERP) and action potential duration (APD), shortened activation latency (AL), reduced AF inducibility, attenuated atrial fibrosis, and decreased the concentrations of norepinephrine (NE), tumor necrosis factor-α (TNF-α), interleukin (IL)-1β and IL-6 in the serum and the left atrial (LA). Furthermore, pinocembrin treatment significantly increased the expression levels of Cx43 and Cav1.2 and suppressed the phosphorylation of inhibitor-κBα (IκBα) and the activation of nuclear factor-kappa B (NF-κB) subunit p65.

CONCLUSIONS In conclusions, our findings indicate that pinocembrin treatment reduces autonomic remodeling, lowers atrial fibrosis, ameliorates atrial electrical remodeling and suppresses MI-induced inflammatory responses, which suggests a potential novel strategy for atrial arrhythmias.

GW30-e0536

Activated platelets secreted insulin-like growth factor 1 exacerbates anxiety in patients with acute coronary syndrome

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OBJECTIVES Anxiety and coronary artery disease (CAD) are closely correlated. However mechanisms of the association are complicated and still unclear. Platelets play vital roles in both anxiety disorder and CAD. The aim of this study is to investigate the involvement of platelets in anxiety in patients with CAD.

METHODS 191 patients with acute coronary syndrome (ACS), 189 patients with stable CAD (SCAD) and 200 healthy volunteers (HV) were included. Demographic and clinical data were collected. HAM-A was used to evaluate the anxiety. Activation of platelets was assessed by flow cytometry. Platelets and serum were isolated from whole blood samples. Platelets granule secretion was evaluated by immunoblotting of expression of CD62P and insulin-like growth factor 1 (IGF1) and phosphorylation of JNK1 and SNAP23 in isolated platelets. ELISA was used to measure the levels of vWF, soluble tissue factor (sTF) and IGF1 in serum.

RESULTS HAM-A score, platelets activation, serum levels of vWF, sTF and IGF1 were increased in ACS compared with other subjects, which were also higher in SCAD compared with HV. Expression levels of CD62P and phosphorylation levels of JNK1 and SNAP23 were increased in isolated platelets from ACS than other subjects, which were also increased in SCAD when compared with HV. IGF1 expression levels in isolated platelets were reduced in ACS compared with SCAD and HV.

CONCLUSIONS ACS patients exhibit more severe anxiety than SCAD patients and healthy volunteers. Activated platelets were important sources of circulating IGF1 which further exacerbates anxiety in patients with ACS.

CARDIOVASCULAR IMAGING

GW30-e0016

Comparison of unenhanced and contrast-enhanced transthoracic echocardiography for determination of right ventricular size and function

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OBJECTIVES To investigate the incremental value of contrast-enhanced transthoracic echocardiography in improving the accuracy and repeatability for measurements of right ventricular size and function.

METHODS The apical four-chamber views and the three-dimensional full-volume images of the right heart were collected from 12 beagles with unenhanced and contrast-enhanced transthoracic echocardiography. The right ventricular end diastolic longitudinal dimension (RVLD), right ventricular end diastolic area (RVEDA), right ventricular end systolic area (RVESA) and right ventricular fractional area change (RVFAC) were measured respectively with two-dimensional unenhanced and contrast-enhanced echocardiography. Right ventricular three-dimensional full-volume images were processed and analyzed by TomTec software, and right ventricular end diastolic volume (RVEDV), right ventricular end systolic volume (RVESV) and right ventricular ejection fraction (RVEF) were measured respectively with three-dimensional unenhanced and contrast-enhanced echocardiography. The measurements of pathological specimen were taken as the gold standard, the accuracies of measuring RVEDV and RVLD by different methods were evaluated. All indexes were measured again by the same observer and different observers, and the reproducibility of different methods for measuring different indexes was evaluated.

RESULTS 1. The intimal display rate of the right ventricular segment was higher with contrast-enhanced echocardiography than that with unenhanced echocardiography ($P<0.05$). 2. The measurements of RVEDV by three-dimensional contrast-enhanced echocardiography correlated well with the measurements by pathological specimen. And the correlation was higher (0.916 vs. 0.843), the consistency was better than that by unenhanced echocardiography. The measurements of RVLD by two-dimensional contrast-enhanced echocardiography correlated well with the measurements by pathological specimen. And the correlation was higher (0.928 vs. 0.850), the consistency was better than that by unenhanced echocardiography. 3. For inter- and intraobservers, the interclass correlation coefficients of RVLD, RVEDV, RVESV, RVEF, RVEDA, RVESA, RVFAC with contrast-enhanced echocardiography were higher and 95% confidence interval ranges were smaller than those with unenhanced echocardiography.

CONCLUSIONS Contrast-enhanced transthoracic echocardiography can improve the accuracy and repeatability for measurements of right ventricular size and function, providing a new evaluation method for patients with poor image quality of the right ventricle in clinical practice.

GW30-e0024

Interleukin-35 promotes early endothelialization after stent implantation by regulating macrophage activation

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OBJECTIVES Early strut coverage after sirolimus-eluting stent (SES) implantation is associated with the activation of inflammation, but the underlying mechanisms are not completely understood. The present study aimed to identify the relationship between the anti-inflammatory cytokine interleukin (IL) 35 (IL-35) and early strut coverage *in vivo* and *in vitro*.

METHODS We utilized a retrospective study design to measure IL-35 levels in 68 stents from 68 patients with coronary artery disease and recorded serial optical coherence tomography (OCT) images (0 and 3 months) to assess stent endothelialization. The mechanism underlying the regulatory effects of IL-35 on macrophages and human umbilical vein endothelial cells (HUVECs) was also investigated. SESs were surgically implanted into the right common carotid arteries of 200 male New Zealand White rabbits receiving intravenous injections of IL-35 or a placebo.

RESULTS At the 3-month OCT evaluation, complete endothelium coverage was correlated with IL-35 levels. IL-35 induced the activation of an anti-inflammatory M2-like macrophage phenotype by targeting the signal transducer and activators of transcription (STAT)1/4 signalling pathway, and IL-35-treated macrophages induced endothelial proliferation and alleviated endothelial dysfunction. IL-35-treated New Zealand White rabbits with implanted SESs showed lower percentages of cross-sections with an uncovered strut, elevated mean neointimal hyperplasia (NIH) thickness, and inhibited inflammatory responses.

CONCLUSIONS We investigated the effect of IL-35 expression on early stent endothelialization *in vivo* and *in vitro* and identified a crucial role for IL-35 in inducing the activation of an anti-inflammatory M2-like macrophage phenotype. The present study highlights a new therapeutic strategy for early stent endothelialization.

GW30-e0234

Anomalous ductus arteriosus connection and its relationship with right aortic arch

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OBJECTIVES To analyze the sonographic features of anomalous ductus arteriosus (DA) connection in fetus, and to investigate the relationship between anomalous ductal connection and right aortic arch (RAA).

METHODS Detailed fetal echocardiography was performed on 5080 pregnancies referring to our hospital from 2014 to 2018. The three-vessel-trachea (3VT) view, DA transverse and long-axis view were chosen to observe the connection, course, dimension and flow direction of DA. A left/right/double-sided DA or aortic arch was determined by its relative position to trachea. The presence of vascular ring was evaluated in 3VT view. Other associated cardiovascular anomalies were also evaluated during the examination.

RESULTS Forty-one fetuses (gestational age 25.4±3.5 weeks) had anomalous DA connection according to detailed fetal echocardiography. A right-sided aortic arch was detected in all 41 cases. Twenty-nine fetuses (29/41) demonstrated a right-sided DA which abnormally connected between pulmonary trunk (PT) or right pulmonary artery (RPA) and descending aorta (DAo). The other twelve cases (12/41) revealed a left-sided DA abnormally connected between left pulmonary artery (LPA) and left subclavian artery (LSA). No vascular ring around the trachea was detected in all 41 cases. Five cases (5/41) were isolated anomalous DA connection with RAA, while the rest 36 cases (36/41) all demonstrated associated cardiac anomalies, including tetralogy of Fallot (14/41), pulmonary atresia (9/41), double outlet right ventricle (6/41), transposition of the great arteries (3/41) and other cardiac anomalies. Reversed flow across DA was observed in thirteen (13/41) cases.

CONCLUSIONS In our study, anomalous DA connection was always associated with RAA, and no vascular ring was detected. The right-sided DA with anomalous connection between PT/RPA and DAo was more frequently seen than the left-sided DA abnormally connecting between LPA and LSA. DA abnormal connection always accompanied with other cardiac anomalies.

GW30-e0235

Multimodal image technologies in diagnose of unilateral absence of the right pulmonary artery: a review of six cases

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OBJECTIVES To highlight the variation in clinical manifestations, imaging and management of six cases of unilateral absence of right pulmonary artery (UARPA).

METHODS Six patients with UARPA were referred to our hospital from 2013 to 2018. They underwent a series of investigations, including chest X-ray, echocardiography, contrast-enhanced computed tomography, pulmonary angiography and aortography.

RESULTS Four patients were children, the remaining two were adults. Four of the six patients were found to have abnormalities by chest X-ray examination, and no abnormalities were found in the other two patients. Five patients were diagnosed as UARPA by echocardiography, and another was misdiagnosed. All patients were eventually diagnosed as UARPA by chest contrast-enhanced computed tomography and pulmonary angiography. All patients had combined with other cardiovascular structural abnormalities which confirmed by echocardiography and chest contrast-enhanced computed tomography. Echocardiography revealed three patients with pulmonary hypertension (PHT), two of which were confirmed by right heart catheterization.

CONCLUSIONS UARPA has a non-specific presentation. Earlier detection of this condition can lead to earlier diagnosis, with multimodal image technologies making an important contribution.

GW30-e0236

The VVI ventricular function assessment in second-third trimester fetus with tricuspid regurgitation

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OBJECTIVES To evaluate the changes of ventricular function in second-third trimester fetus with tricuspid regurgitation by velocity vector imaging (VVI).

METHODS The fetus include in this study diagnosed as tricuspid regurgitation during January 2014 to August 2017 in the Union Hospital of HUST. They were divided in: group A-mild tricuspid regurgitation, group B-severe tricuspid regurgitation. The control group included 36 normal fetuses in the same period. To evaluate the global ventricular motion of the group A, B and the control group by VVI. The following parameters of the left and right ventricular were obtain by manual tracing endocardial at the end of ventricular diastolic in four-chamber view: the global systolic longitudinal velocity (GLVs), the global diastolic longitudinal velocity (GLVd), the global systolic longitudinal strain rate (GLSRs), the global diastolic longitudinal strain rate (GLSRd) and the global longitudinal strain (GLS). The differences of baseline and parameters between groups A, B and the control group were analyzed.

RESULTS (1) Comparison of general data: There were no significant differences among the group A, B and the control group ($P>0.05$). (2) Comparison of right ventricular parameters: There were significant differences among the group A, B and the control group in terms of the right ventricular GLVs, GLVd, GLS, GLSRs and GLSRd ($P<0.01$); there were significant differences between the group B and the control group in terms of the right ventricular GLVs, GLVd, GLS, GLSRs and GLSRd ($P<0.01$). (3) Left ventricle parameter comparison (ANOVA analysis): There were significant differences between group A and B in terms of the left ventricle GLVs, GLVd, GLS, GLSRs and GLSRd ($P<0.01$). There were significant differences between group B and the control group in terms of the GLVs, GLVd, GLS, GLSRs and GLSRd ($P<0.01$).

CONCLUSIONS The ventricular function is significantly different among the fetus diagnosed as mild/severe tricuspid regurgitation and normal, the ventricular systolic and diastolic function is obviously impaired. There were no significant differences between the mild tricuspid regurgitation fetus and control in terms of the ventricular function index, which means mild tricuspid regurgitation did not cause fetal ventricular function damage. The qualitative and quantitative measurements of prenatal fetal tricuspid regurgitation is beneficial to evaluate the effects of cardiac structure, activity and rhythm, which helps to predict the prognosis, guide clinical practices, and give recommendations of good birth and good care.

GW30-e0258

Treatment of acute cardiac transplantation rejection by FK506-loaded microbubbles combined with ultrasound-targeted microbubble destruction (UTMD)

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OBJECTIVES FK506 is an effective immunosuppressant for acute cardiac transplantation rejection. However, its' therapeutic effect is limited by side effects, poor water solubility, and pharmacokinetics variability within different patients. Therefore, to overcome these obstacles and improve the therapeutic effect, we prepared a FK506-loaded microbubble (FK506-MBs) for locally delivery FK506 to damage lesions by Ultrasound-targeted microbubble destruction (UTMD) technique.

METHODS In the present study, FK506-MBs were synthesized by the thin-film hydration method. The size distribution and polydispersity index of FK506-MBs were determined by a dynamic light-scattering system. The concentration was measured by a hemocytometer. The morphology of FK506-MBs were obtained by an optical microscope. Drug-loading and entrapment efficiency

were determined via high performance liquid chromatography (HPLC). We further evaluated immunosuppressive effect on acute cardiac transplantation rejection in rat model by hematoxylin and eosin (H&E) staining.

RESULTS FK506-MBs displayed a uniform size distribution with a single peak. The mean diameter of FK506-MBs was 1.65 μm±0.32 with a low PDI of 0.16±0.09. The mean concentration of FK506-MBs was 4.35±0.18×109 MBs/mL. The drug loading efficiency and encapsulation efficiency was 33.41±2.69% and 77.6±8.0%, respectively. More importantly, we found severe acute graft rejection was happened in PBS group, while after therapy with FK506 or FK506-MBs+UTMD, there was weaker graft rejection. As we expected, the therapeutic effect of same does of FK506 was better in FK506-MBs+UTMD group than in FK506 group.

CONCLUSIONS In summary, we reported a FK506-MBs used for prevention and therapy of acute allograft rejection. Comparing with intravenous drug delivery at the same dosage, FK506-MBs +UTMD can improve the therapeutic effect.

GW30-e0259

Ultrasound molecular imaging detects cardiac acute cellular rejection using lymphocyte-microbubble complexes

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OBJECTIVES Acute cellular rejection (ACR) is one of the main reasons for graft failure after heart transplantation. Lymphocytes are the dominant responsive cells in ACR. To date, invasive endomyocardial biopsy is the gold standard for the diagnosis of ACR. Noninvasive evaluation of ACR at the early stage is still a big challenge for clinicians. Ultrasound molecular imaging with microbubbles has been widely used in monitoring molecular events of diseases. Since lymphocytes were crucial in ACR, we hypothesized that lymphocyte-microbubble complexes (cell-MBs) could function as ultrasound molecular imaging probes to noninvasively monitor cardiac ACR.

METHODS Cell-MBs were fabricated by incubating lymphocytes with anti-CD4 antibody-conjugated microbubbles. Rat heterotopic heart transplantation models were established. In the untreated allogeneic group, 8 Brown Norway (BN) hearts were transplanted into Lewis recipients; in the cyclosporine A (CsA)-treated group, 5 BN hearts were transplanted into Lewis recipients and the recipients were treated with 7.5 mg/kg/d CsA; in the syngeneic group, 4 Lewis hearts were transplanted into Lewis recipients. Ultrasound molecular imaging was performed on grafts of these three groups on post-transplantation day 3. Histology was used to assess graft rejection grades.

RESULTS We detected a significantly stronger ultrasound molecular imaging signal of cell-MBs in the untreated allogeneic group than those in the CsA-treated group and the syngeneic group (13.59±1.58 dB versus 8.00±2.57 dB and 3.48±1.42 dB, respectively, P<0.05). Moreover, the signal in the CsA-treated group was significantly stronger than that in the syngeneic group (8.00±2.57 dB versus 3.48±1.42 dB, P<0.05). Histology confirmed grade 3R ACR in the untreated allogeneic group, grade 2R ACR in the CsA-treated group, and no ACR in the syngeneic group.

CONCLUSIONS We concluded that ultrasound molecular imaging with cell-MBs could detect treatment-needed grade 2R or higher ACR, which may be advisable for timely immunosuppressive adjustment.

GW30-e0260

Left atrial function index predicts cardiovascular mortality in heart transplant recipients

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OBJECTIVES Left atrial (LA) function index (LAFI) combines the adjusted LA volume (LAVi), LA emptying fraction (EF) and stroke volume, and thus reflects both left ventricular (LV) systolic and diastolic function. The association between LAFI and risk for mortality in heart transplant recipients is unclear. The aim of this prospective study was to evaluate LAFI as a predictor of cardiovascular mortality in heart transplant recipients.

METHODS Isolated orthotropic heart transplantation was performed in 395 patients between January 2015 and December 2018 at Wuhan Union Hospital, China. All patients were under routine comprehensive transthoracic 2D, Doppler and 3D echocardiography in our institution. N-terminal pro–B-type, creatinine, C-reactive protein, and invasive hemodynamic parameters were collected on the day of the echocardiographic study. Survival was expressed using Cox regression analysis and Kaplan-Meier analysis.

RESULTS During a median follow-up period of 48±19 months, 63 (16%) died of cardiac causes. LAFI was calculated as LAFI=LAEF′ left ventricular outflow tract-velocity time integral]/[LAVi], and was categorized into 4 quartiles (6.26/12.36/29.22). In a multivariate model, LVEF (hazard ratio, 0.95; 95% CI: 0.80–2.28; P=0.01), and LAFI (hazard ratio, 0.90; 95% CI: 0.97–0.99; P=0.01) were independent predictors of an adverse outcome. Kaplan-Meier event-free survival curves by quartiles of LAFI showed that patients had progressively worse outcomes from quartile 1 to quartile 4 (P<0.01).

CONCLUSIONS Our study results, showing that LAFI might be a noninvasive predictor of mortality and provides increased prognostic value in heart transplant recipients.

GW30-e0261

Characteristics of biventricular myocardial mechanics in pediatric heart transplant patients by three-dimensional speckle tracking echocardiography

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OBJECTIVES Heart transplantation is the only treatment for various end-stage heart diseases. Studies on pediatric HT is not enough, and the understanding is not deep enough, too. In this study, we tried to assess the characteristics of biventricular myocardial mechanics in pediatric HT patients by three-dimensional speckle tracking echocardiography (3D STE), in the hope to better understand the biventricular function of these patients.

METHODS The study enrolled all the pediatric HT patients with stable clinical status who underwent HT after January 1, 2015 in Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, and examined prospectively. Patients underwent comprehensive two-dimensional and three-dimensional echocardiographic examinations.

RESULTS Finally, the study included 30 pediatric HT patients with stable clinical status. We found out that the left atrial (LA), interventricular septum (IVS), post lateral wall (PW), right atrial (RA) length, E peak deceleration time (EDT), mitral and tricuspid E/e all increased and Tricuspid annulus systolic displacement (TAPSE) decreased in pediatric HT patients (P<0.05). Left ventricular (LV) global longitudinal strain (GLS) and global radial strain (GRS), right ventricular (RV) ejection fraction (EF) and RV free wall longitudinal strain (FWLS) decreased in HT pediatric HT patients (P<0.05).

CONCLUSIONS For clinically stable pediatric HT patients with normal conventional echocardiography parameters of ventricular function, their myocardial mechanical function has been impaired.

GW30-e0494

Application of 3D guidance technique in endovascular aortic repair

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OBJECTIVES To evaluate the feasibility and technical advantages of 3D guidance technique in endovascular aortic repair.

METHODS This was a retrospective single center study. From November 2016 to December 2018, 38 patients undergoing thoracic endovascular aortic repair (TEVAR) or endovascular abdominal aortic repair (EVAR) with assistance of 3D guidance technique and intra-operative DynaCT, including 36 males and 2 females with age from 16 to 76 (57.95±13.55). Meanwhile, 40 patients were received standard endovascular aortic repair (control group). Comparative analysis of intra-operative and follow-up data between the two groups was undertaken.

RESULTS The results of this study showed that compared with conventional DSA, 3D guidance technique and intra-operative DynaCT reduced contrast dose (TEVAR 60.31 mL vs. 73.34 mL P=0.032; EVAR 83.43 mL vs. 94.83 mL P=0.013), intra-operative radiation dose (TEVAR 293.04 mGy vs. 385.71 mGy P=0.002; EVAR 431.84 mGy vs. 584.51 P=0.043), number of radiography (TEVAR 2.36 vs. 3.56 P=0.016; EVAR 3.43 vs. 4.01 P=0.029), operation time (TEVAR 64.09 min vs. 71.42 min P=0.001; EVAR 142.14 min vs. 153.39 min P=0.057), meanwhile, reduced the risk of postoperative aorta-related reintervention (2.63 vs. 10% P=0.042), meeting the precise requirements for anatomical positioning and immediate effect determination

during endovascular aortic repair. As for image fusion, the average displacement of the CTA and DynaCT three-dimensional reconstruction images was 2.23±0.69 mm, the TEVAR group was 3.26±2.57 mm, and the EVAR group was 1.93±1.33 mm (P=0.032). After manual correction, all patients completed 3D image fusion and successfully established intraoperative 3D roadmap. The processing time was 15–30 minutes, and the average time was 20.63 min. There was no significant difference between TEVAR group and EVAR group.

CONCLUSIONS 3D guidance technique improves the accuracy during positioning in complex endovascular aortic repair, could reduce aortic-related re-intervention rate, radiation exposure time and contrast dose. Further studies and development are needed to obtain optimal image quality and higher precision.

GW30-e1050

In vitro sights on thrombogenicity of bioresorbable scaffolds with provisional stenting in bifurcations

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OBJECTIVES Provisional single-stenting is considered the gold standard strategy for the treatment of coronary bifurcation lesions. Even though overhanging struts in the side-branch (SB) ostium are thought to act as a focal point for thrombi formation and subsequent possible stent thrombosis (ST), a direct causal effect between jailed struts and thrombogenicity is still yet proven. Herein, we examined the thrombogenicity of bioresorbable vascular scaffold (BVS) at jailed SB ostia using an in-vitro perfusion model.

METHODS In the provisional single-stent bifurcation model, ABSORB BVS (3.0 and 3.5 mm, Abbott Vascular, n=2) were deployed and proximal optimisation with 5.0 mm NC balloons was performed (visually confirmed from OCT pullback). The models were then perfused with porcine blood (with 10% ACD anticoagulant) in a flow loop at a flow rate of 200 mL/min for 4 mins. A longitudinal section of each stent was immunostained with antiplatelet antibodies CD61 and imaged with confocal microscopy. Thrombus was quantitatively evaluated on OCT pullbacks and immunofluorescence images of the stents at 3 segment regions: proximal, distal and SB. Anti-platelets confocal imaging was also performed on a longitudinal section of each stents post perfusion.

RESULTS With the in-vitro perfusion model, we observed in immunofluorescence images that significant higher thrombus occurred at SB, compared with proximal and distal regions (mean intensity: 98.1 vs. 19.2 a.u., P: 0.05 and 98.1 vs. 21.5 a.u., P: 0.06, respectively). A similar trend can be observed in cross-sectional thrombus area in OCT images and mean thrombus area in immunofluorescence (Fig. 1).

CONCLUSIONS Our in-vitro perfusion models demonstrated that BVS struts floating at the SB ostium promote thrombus formation mechanism, which highlights the need of optimal technique for SB dilatation in bifurcation PCI.

GW30-e1059

Evaluation of myocardial deformation during stress echocardiography with adenosine tri-phosphate (ATP) according to the developed methodology on two devices using the speckle tracking method in healthy individuals

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OBJECTIVES The aim of our study was to study the parameters of longitudinal, circumferential and radial strain the left ventricular myocardium based on the speckle tracking technique in healthy individuals and using Vivid E 95 and Aplio 400 devices during stress-echocardiography with stepwise ATP infusion.

METHODS We surveyed volunteers: 1st group 10 people (7 men) (average age 34.2±10) and 2nd group 11 (8 men) 23.4±10 years old) with normal anthropometric indicators (height 177.1±10 and 179.2±9 cm, weight 79.4±15 and 79.8±11 kg), without equivalents of angina pectoris, with normal initial blood pressure data (systolic blood pressure 121±12 and 116±7 mmHg), normal heart rate (68.8±11 and 75.3±10 beats per minute), intact contractile function of the left ventricle (left ventricular ejection fraction 64.8±3 and 65.1±2.8%), normal sizes of heart chambers (end diastolic size of the left ventricle is 46.89±5.2 mm and 45.89±4.7 mm), (left atrium 32.11±4.6 mm and 33.89±3.7 mm), (right atrium 33±3.7 mm and 34.4±3.9 mm). All volunteers were given a pharmacological test with ATP, administered intravenously in a microjet, according to a scheme developed at Rostov State Medical University, with a gradual increase in dose from 140 μg/kg/min to 210 μg/kg/min. obtained by the two methods of 4D-AFI (4D-automated function imaging) and 2D-STE (2D-speckle tracking echocardiography) datas of global and segmental longitudinal strain, global radial and circumferential strain of the LV in the background of the sample when the target blood pressure reduction is reached above 5 mmHg, were subjected to graphic and mathematical processing in order to assess the typical changes in the indicators of deformation of the left ventricular myocardium in healthy volunteers.

RESULTS As a result of the study, hemodynamic and vasodilating effects of ATP were confirmed with stepwise intravenous administration. The data obtained by the two methods were comparable and equivalent according to the graphical and mathematical processing (before the test, the ratio of the average indicators of segmental deformation was 1.01, at the peak of the sample was 0.96 and after the sample was 1.07). As a result of the coronary-dilating effect of ATP indicators of global longitudinal strain to the sample in the 1st group were – 19.7±1.1, in the 2nd group – 20.07±1.6, increased at the peak of the sample 21.9±1.9 and 21.9±1.5, and returned to baseline values after the sample 19.8±1.2 and 20.7±1.4. The global radial strain of the LV changed respectively in the 1st group 34.5±8.6, the 2nd group 30.25±2.79 baseline, 36.125±6.52 and 35.2±1.46 at the peak of injection, 33.125±6.09 and 33.6±2.41 after procedure. The global circumferential strain of the LV changed respectively in the 1st group –19.3±2.83, the 2nd group –20.6±1.85 initially, –19.8±3.12 and –23.5±1.89 at the peak of administration, –19±2.36 and –21.2±1.6 after injection.

CONCLUSIONS The longitudinal, radial and circumferential strain data we obtained confirms the biological plausibility of this stress-echocardiography method and are comparable with ultrasound devices of various manufacturers.

CARDIOVASCULAR NURSING

GW30-e0514

Home-based Tai Chi Program is a promising option in improving cardiovascular health among patients with coronary heart disease: results from a pilot randomized controlled trial

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OBJECTIVES Compared with healthy age-matched person, patients with coronary heart disease (CHD) reported lower physical capacity and more negative affectivity. Tai Chi is accessible, affordable, and acceptable among older adults; yet effectiveness of home-based Tai Chi program are lacking. This study aim to determine the feasibility, acceptability and effects of a 12-week group-plus home-based Tai Chi program on improving cardiovascular health and managing cardiovascular risk factors among patients with CHD.

METHODS A total of 18 adults (mean age=68.2±6.2 years, 16.7% male) with CHD were randomly assigned to either Tai Chi (n=8) or control groups (n=8). The Tai Chi group attended Tai Chi class twice a week for the first two-week, three times a week for the second two-week, and then four times a week for the third two-week. After 6-week group-based Tai Chi section to build or promote the exercise self-efficacy, participants practiced home-based Tai Chi four-times per week for another six weeks. Control participants maintained their usual daily activities and attended non-exercise community activities once a week for six weeks. The primary outcome were feasibility and acceptability of intervention, and physical function (aerobic endurance, leg strength, leg flexibility, stationary and dynamic balance). Secondary outcomes were: fasting blood sugar (FBS), total cholesterol, triglycerides, high and low density lipoprotein, body mass index (BMI), body fat percentage and exercise self-efficacy. Data were collected at baseline, post group-based intervention at 6-week, and post-intervention at 12-week. Analysis of covariance were conducted to compare changes in outcomes.

RESULTS No significant differences between groups at baseline. Study retention rate was 72% (n=13), with 78% (n=7) in the Tai Chi group and 67% (n=6) in the control group. Participants attending the group-based Tai Chi (n=7) attended on average 78% of the scheduled classes. Five of these seven participants attended ≥16 classes (total 18 classes). Participants attending the home-based Tai Chi classes (n=7) attended on average of 4 weeks (4 time/week) of the scheduled sessions. Three of these seven participants insisted for the whole 6-week home-based Tai Chi practice. Tai Chi group showed positive-trend over time on almost all outcomes, except for total cholesterol, triglycerides, low density lipoprotein, FBS and stationary balance. When compared to controls, the Tai Chi group had significantly better dynamic balance at 6-week (P=0.047), and showed largest effect size (0.60) over time.

CONCLUSIONS This group-plus home-based Tai Chi program was feasible and acceptable, and showed positive-trend effects on physical function and cardiovascular risk factors among Chinese patients with CHD. Further investigation with a larger sample size and longer study period is needed to explore potential environmental factors that may have influenced the study results.

GW30-e0650

The white noise can relief the impact on circulatory and respiratory system cause by collecting heel blood in preterm infants

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OBJECTIVES In this study we aimed to evaluate the effect of white noise as a distraction method in relieving procedural pain caused by collecting heel blood for preterm infants.

METHODS This study was performed at NICU in the First Affiliated Hospital of Sun Yat-sen University between July 2018 and March 2019. A total of 254 infants (intervention group=130, control group=124) met the inclusion criteria. We retrospectively reviewed baseline characteristics of infants before the intervention. Preterm infants in the intervention group were exposed to white noise for 1 minute before the collection heel blood. The white noise continued until 1 minute after invasive procedure. The control group were not exposed to white noise. We compared heart rate, respiration rate, and oxygen saturation etc. between two groups during this study.

RESULTS No significant differences were found in sex, gestational age, birth weight, birth length and birth circumference between two groups [56.7 vs. 48.4%, χ^2=1.682; (35.23±1.39) weeks vs. (35.41±1.28) weeks, t=1.793; (2.35±0.25) kg vs. (23.10±0.23) kg, t=1.328; (47.36±2.54) cm vs. (47.62±2.48) cm, t=0.834; (34.83±1.67) cm vs. (34.58±1.92) cm, t=1.112; all P>0.05]. There was no significant difference in heart rate and respiration rate at 15 seconds after the collection of heel blood in two groups [(173.43±21.46) beat vs. (178.37±20.28) beat, t=1.876; (48.58±9.87) beat vs. (49.66±10.34) beat, t=1.734; all P>0.05]. The peak of mean heart rate and respiratory rate at 30 seconds after the collection of heel blood were significant lower in intervention group [(160.58±21.65) beat vs. (169.87±17.91) beat, t=3.713; (43.96±12.78) beat vs. (48.94±11.92) beat, t=3.208; all P<0.05]. The peak of mean heart rate and respiratory rate at 1 minute after collecting heel blood were similar between two groups [(146.32±22.49) beat vs. (143.57±21.52) beat, t=0.994; (35.27±10.53) beat vs. (34.7±9.77) beat, t=0.439; all P>0.05]. There was no significant difference in the oxygen saturation between two groups during this study (All P>0.05).

CONCLUSIONS This study showed that the white noise is an effective nonpharmacologic method to reduce stimulation time of heart and respiratory, control pain, and positively effect vital signs. It is recommended that the use of white noise be practiced on preterm infants that need to receive invasive procedures.

CLINICAL LABORATORY OF CARDIOVASCULAR DISEASE

GW30-e0718

The value of advanced glycation end products in predicting major adverse cardiovascular events: a systematic review and meta-analysis

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OBJECTIVES This Meta-analysis aims to systematically evaluate the prospective association between advanced glycation end products (AGEs) and major adverse cardiovascular events (MACE).

METHODS We searched PubMed, Embase, Cochrane Library form inception up to March 2019 for prospective studies that reported the association of AGEs (measured by skin autofluorescence) with MACE. Multivariable-adjusted hazard ratios (HRs) and their respective 95% confidence intervals reflecting the risk of MACE associated with levels of advanced glycation end products were combined using random-effects meta-analysis.

RESULTS Ten articles with 76,861 participants met the inclusion criteria. A significant association was found between AGEs and the occurrence of MACE (HR: 1.75; 95% CI: 1.46–2.10; I_2=36%), as well as AGEs levels were positively correlated with the risk of MACE in patients with diabetes mellitus (HR: 1.89, 95% CI: 1.44–2.48) and kidney disease (HR: 1.87, 95% CI: 1.36–2.56), regardless of the severity of kidney disease and the type of diabetes. The combined HR values of AGEs predicting MACE were (HR: 1.97, 95% CI: 1.11–3.49) in hemodialysis group, respectively, (HR: 1.72, 95% CI: 1.42–2.08) in non-hemodialysis group. Also, the increase in AGEs in type 1 diabetes (HR: 3.25, 95% CI: 1.40–6.29) or type 2 diabetes (HR: 1.70, 95% CI: 1.25–2.31) is indicative of a greater risk of MACE.

CONCLUSIONS This meta-analysis indicates that higher AGEs measured by skin autofluorescence significantly correlated with a higher pooled risk estimate for major adverse cardiovascular events. AGEs can become a new risk predictor of cardiovascular disease.

TRADITIONAL CHINESE MEDICINE

GW30-e0091

The effect of Xuefu Zhuyu decoction on clopidogrel resistance and its association with the P2Y12 gene polymorphisms and promoter DNA methylation

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OBJECTIVES Some patients experience lesser degrees of platelet inhibition, which is known as clopidogrel resistance (CR). The goal of our study was to investigate the effects of Xuefu Zhuyu Decoction on CR in coronary artery disease patients and whether P2Y12 polymorphisms and its methylation were related to drug response.

METHODS 49 patients diagnosed with CR were randomly divided into control and treatment groups. Platelet functions were measured using Verify Now P2Y12 assay. By restriction fragment length polymorphism polymerase chain reaction, the single nucleotide polymorphisms of rs2046934 and rs6785930 were genotyped. Using bisulphite pyrosequencing assay, we investigated the association of the P2Y12 gene DNA methylation levels and the effects of Xuefu Zhuyu decoction on CR.

RESULTS The results showed that the decoction improved CR (P=0.005), and the patients with the TT genotype in rs2046934 received substantial benefits from Xuefu Zhuyu Decoction, in both P2Y12 reaction units (PRU) and inhibition percentage (P_{PRU}=0.016; $P_{inhibition\ percentage}$=0.028). And patients with lower methylation levels of CpG1 were more likely to be TT carriers in rs2046934 ($CpG1_{TT}$ vs. $CpG1_{TC+CC}$ (%): 39.47±6.20 vs. 45.70±8.47, P=0.044).

CONCLUSIONS In conclusion, our study indicated that Xuefu Zhuyu Decoction might be useful for overcoming CR and the polymorphism of rs2046934 might influence the drug effect.

GW30-e0093

The Xuefu Zhuyu decoction improve the platelet functions as well as blood viscosity in unstable angina patients carried with CYP2C19*2

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OBJECTIVES For the unstable angina patients with CYP2C19*2 genotype, the risk of clopidogrel resistance and cardiovascular events were higher and the clinical effect from modern medicine was different.

METHODS 60 patients diagnosed of unstable angina with CYP2C19*2 genotype were randomly divided into group A and group B. Group A would carry out Xuefu Zhuyu Decoction along with modern medicine for 4 weeks and group B would process only modern medicine. The clinical effect, platelet functions as well as hemorheology would be observed and the risk of cardiovascular events in one month and one year would be collected and analyzed.

RESULTS The clinical effect of group A was better than group B (P=0.030). Meanwhile, in group A, the P2Y12 reaction units (PRU) was decreased significantly (before treatment vs. after treatment: 280.26±31.56 vs. 249.42±27.55; P=0.012) and inhibition percentage was elevated (before treatment vs. after treatment: 0.119±0.055 vs. 0.187±0.097; P=0.023). What was more, the value of plasma viscosity, blood viscosity, and fibrinogen were also lower after treatment by Xuefu Zhuyu Decoction along with modern medicine.

CONCLUSIONS For the unstable angina patients with CYP2C19*2 genotype, Xuefu Zhuyu Decoction might improve the platelet functions as well as blood viscosity, so as to make the clinical effect better.

GW30-e0220

Potential mechanism of Suanzaoren Decoction for treatment of insomnia based on network pharmacology

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OBJECTIVES To study the mechanism of Suanzaoren Decoction (SZR) in the treatment of insomnia by using network pharmacology.

METHODS Chemical components and targets related to the SZR were searched through the traditional Chinese medicine systems pharmacology database and analysis platform (TCMSP), Traditional Chinese Medicines Database @ Taiwan and Traditional Chinese Medicines Integrated Database (TCMID) to construct

the interaction network diagram of the target point of the compounds. The insomnia related targets were screened through GeneCards, MalaCards, NCBI-Gene, OMIM and CTD databases. The interactive target of SZR and insomnia was constructed in PPI database; GO analysis of screened core targets between drug target and disease target was carried out using DAVID database, and the related pathways of core targets were enriched using KEGG database.

RESULTS Using the oral bioavailability (OB) ≥30%, drug likeness (DL) ≥0.18, $CaCO_2$≥0 and 4≤half-life≤8 as screening condition for the compounds, 35 active components and 121 corresponding protein targets of SZR were screened out. A total of 336 enrichment results were obtained, including 301 biological processes, 25 molecular functions, and 10 cell compositions, on the condition of false discovery rate ≤0.0001. The selected targets were enriched by KEGG database and 17 pathways playing an important role in insomnia were screen out.

CONCLUSIONS The synergetic effect of SZR with multi-components and multi-pathway was confirmed by network pharmacology, and the main possible mechanism of SZR in treating insomnia was predicted, which lay a foundation for the identification of effective components, the mechanism of action, and clinical application.

GW30-e0390

Study on the effect of Ruan Jian Qing Mai formula on arteriosclerosis obliterans based on system biology

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OBJECTIVES Arteriosclerosis obliterans (ASO) is a multiple modern disease, which can lead to amputation and even death. The efficacy of Ruan Jian Qing Mai formula (RJQM) is 10% higher than that of the commercially available Tongmai granules, but its effective constituents and action mechanism are unknown. Therefore, this paper comprehensively uses the gene expression profiling, bioinformatics, molecular docking and network pharmacology to explore the possible constituents and mechanism of RJQM, and preliminary verification by in vivo experiments.

METHODS 1. The differential genes (DEGs) between ASO and normal gastrocnemius muscle are screened. WebGestalt software was used to analyze DEGs through GO, KEGG pathway, miRNA, transcription factor, kinase and GSEA analysis; DEGs are input to CMap to obtain ASO-related drug molecules; the 170 active ingredients of RJQM and 42 ASO-related drug molecules are clustering by structural similarities. And 53 drug-related active ingredients were obtained for target prediction and component-target-pathway-disease multivariate network construction. 2. Molecular docking and network model analysis of RJQM are performed to obtain active ingredients, targets and regulatory pathways related to ASO; the toxicity of the active ingredients is predicted by the Protox. 3. We investigate the pharmacological and toxicological effects of RJQM in the treatment of ASO by experimental mice and rabbit ASO model.

RESULTS 1. 524 DEGs (|Fold change|>2, P<0.01, FDR<0.05) were significantly enriched in biological processes including ribonucleotide metabolic process and mitochondrial respiratory chain complex assembly; cell components including oxidoreductase complex and respiratory chain; molecular functions including electron transfer activity and oxidoreductase activity; KEGG pathways including oxidative phosphorylation and TCA cycle; miRNA including MIR-183 and MIR-431; transcription factors including ERR1 and AP4; and kinases including PAK6 and MAPK12. GSEA analysis found signaling pathways such as oxidative phosphorylation and TCA cycle were also enriched. CMap analysis found DEGs are related to mTOR inhibitors, calcium channel blockers, ATPase inhibitors, etc. 53 active ingredients in RJQM have similar structures to the 7 drug molecules in CMap. Then, the 53 components-target-pathway-disease network was constructed, and oxidative phosphorylation and TCA cycle are also significantly enriched. 2. Network topology analysis of multivariate networks yielded 10 active ingredients, 30 targets, and 3 key signaling pathways. Molecular docking results showed the 10 active ingredients could bind to some proteins in the 3 signaling pathways. Computational toxicity estimations showed the median lethal dose (LD50) of the 10 active ingredients was above 1000 mg/kg, and 8 of them did not cause hepatotoxicity, mutagenicity, carcinogenicity, cytotoxicity and immunotoxicity, nor activate 12 toxic pathways. 3. In vivo experiments showed no obvious death and poisoning of mice were observed after RJQM administration, and RJQM can reduce the blood lipid level of rabbit ASO, accelerate lipid metabolism, inhibit inflammation, and thus reduce the effect of atherosclerotic plaque. At the same time, it can promote the formation of collateral circulation in ischemic area and improve blood supply.

CONCLUSIONS RJQM acts on multiple pathways including oxidative phosphorylation, TCA cycle, carbon metabolism to delay and reverse the progression of PAD with good safety and efficacy.

GW30-e0520

Danshen ameliorates TLR4-mediated inflammatory injury in heart failure post-acute myocardial infarction via MyD88/TRIF-NFκB signaling pathway

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OBJECTIVES Salvia miltiorrhiza Burge (Danshen) is a traditional Chinese herb that possesses protective proprieties on heart failure (HF) post-acute myocardial infarction (AMI). Inflammatory injury plays a critical role in HF post-AMI, and Toll-like receptor 4 (TLR4) signaling pathway triggers inflammatory responses that contribute to cardiac pathology. A deluge of studies demonstrated that Danshen exerts anti-inflammatory effects, however, whether it ameliorates inflammation mediated by TLR4 pathway remains unclear to date.

METHODS The efficacy of Danshen on HF was evaluated by using ligation of left anterior descending (LAD)-induced rats and the significant different genes were screened by utilizing RNA-sequence technology. Furthermore, we developed a new quantitative pathway analysis tool to assess the differences of pathways in different groups and to identify the pharmacological contributions of Danshen. Then the related genes in the inflammation-related pathways were verified by real-time polymerase chain reaction (PCR) and Western blot. In vitro, a macrophage-conditioned media (CM)-induced H9C2 cells model was constructed. Cell viability, NO, lactate dehydrogenase (LDH) activity and Prostaglandin E (PGE2) were analyzed by ELISA, levels of cytokines such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), cyclooxygenase-2 (COX-2), and IL-1β were then measured by PCR, the upstreaming proteins of inflammation including TLR4, MyD88, TRIF and nuclear NF-κB p65 protein were assessed by Western blots. TLR4 knock-down by TLR4 siRNA transfection and overexpression by TLR4 DNA transfection were used to further confirm the target of Danshen on inflammatory response.

RESULTS Our results showed that Danshen improved the left ventricular ejection fraction, which confirmed its cardioprotective effect against HF. Differential expression analysis suggested that 106 up-regulated and 257 down-regulated genes were differentially expressed between Danshen-treatment group and Model group. Pathway enrichment analysis indicated that Toll-like receptor signaling pathway related to cardiac inflammation was altered. There are 11 differentially expressed genes in Toll-like receptor pathway between Danshen-treatment and Model group. Experimental validations of the related genes by PCR and Western bolt were consistent with the transcriptome results. In vitro, 600 μg/mL Danshen significantly increased cell viability, decreased the levels of NO, LDH, and PGE2, and attenuated inflammation responses evidenced by reduced secretion of TNF-α, COX-2, IL-6, and IL-1β. Western blot results showed that Danshen blocked TLR4 dimerization, which consequently suppressed recruitment of MyD88 and TRIF, and attenuated the transcriptional activity of NF-κB. TLR4 knock-down/overexpression furtherly confirmed the regulation of Danshen on TLR4 pathway.

CONCLUSIONS Our findings demonstrated that Danshen inhibits TLR4-mediated NF-κB activation via the MyD88/TRIF signaling pathway and ultimately ameliorates cytokines expressions and inflammatory injury. The current study provides the evidence that TLR4 signaling cascades is an attractive target and Danshen exerts the promising therapeutic effect on HF post-AMI.

GW30-e0645

Tanshinone IIA protects against DOX-induced cardiotoxicity through inhibiting inflammatory response via mTOR-NF-κB signaling pathway

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OBJECTIVES *Background:* Although possessing an impressive anti-neoplastic property for the treatment of cancer, doxorubicin (DOX) is largely limited in clinic due to its detrimental cardiotoxicity with a significant activation of inflammation. Tanshinone IIA (TSA), a major active component extracted from *Salviae miltiorrhizae Bge*, has been widely reported to have an anti-inflammatory effect and potentially protect against DOX-induced cardiotoxicity (DIC). However, its underlying mechanisms on anti-inflammation of DIC need to be further elucidated. This study aimed to investigate whether TSA could protect against DIC from heart injury via inhibiting mammalian target of rapamycin (mTOR) – nuclear factor κB (NF-κB) mediated inflammatory response.

METHODS A DIC model was established *via* tail vein injection with DOX (5 $mg \times kg^{-1}$) weekly for 4 weeks and a DOX-induced H9C2 cell injury model was induced by 1 μmol/L DOX. In vivo, the mice were divided into four groups, control group, model group, TSA-treated and Pravastatin (positive drug) group. Echocardiographic assessment, histological examination and western blot analysis of mTOR-NF-κB-mediated inflammatory signaling pathway proteins were collectively implemented to evaluate the cardioprotective effects of TSA. In vitro, the effects of TSA were evaluated by analyzing cell viability with a microplate reader using cell counting kit-8 (CCK-8). MHY1485, a mTOR agonist, was co-treated with TSA and then western blot was used for detecting the level of mTOR, NF-κB, cyclooxygenase-2 (COX2) and tumor necrosis factor-α (TNF-α), which further verified whether TSA exerted its effect through mTOR-NF-κB-mediated inflammatory response.

RESULTS The result of echocardiography and hematoxylin-eosin (HE) staining displayed that DOX could lead to decline of cardiac function and infiltration of inflammatory cell after 4 weeks. Further western blot analysis indicated that inflammation was notably activated, evidenced by upregulation of mTOR, NF-κB, COX2 and TNF-α in DIC model group. Impressively, the structures and the functional alterations of heart could be restored by TSA treatment, meanwhile, the expression of mTOR, NF-κB, COX2 and TNF-α were also inhibited by TSA treatment, which suggested that TSA may play an anti-inflammatory effect via mTOR-NF-κB pathway. Where after, we further verified this molecular mechanism on H9C2 cell. Consistently with in vivo result, the CCK8 and western blot results showed that TSA (1 μmol/L) had protective effect and inhibited the expression of mTOR-NF-κB pathway proteins in DOX-induced H9C2 cell injury model. Interestingly, the effect of TSA on mTOR-NF-κB pathway were abolished by MHY1485 in vitro, which demonstrated that TSA could inhibit inflammatory response via inhibiting mTOR-NF-κB pathway.

CONCLUSIONS Our study suggested that TSA protects against DIC via inhibiting mTOR-NF-κB-mediated inflammatory response. This study will provide a potential combination therapy for the treatment of clinical myocardial toxicity of DOX.

GW30-e1042

The experimental research on Bushen Kangshuai Tablet interfering pulmonary inflammatory reaction in a mouse model of atherosclerosis

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OBJECTIVES In order to provide experimental basis for clinical application of Bushen Kangshuai Tablet, we designed this research to explore the role of Bushen Kangshuai Tablet in the process of pulmonary inflammatory reaction induced by atherosclerosis, and discussed the possible mechanism.

METHODS In this study, we used ApoE-/- mice fed with high-fat diet as a model of lung injury induced by atherosclerosis. C57BL/6J wild type mice as control group were fed normal diet. ApoE-/- mice were randomly divided into: model group, Bushen Kangshuai group, simvastatin group, 4-PBA group. After 4, 8, 12 weeks respectively, 8 mice of each group were selected randomly to sacrificed for dynamic observation of the indexes. A series of assays were used to detect the effect and mechanism of Bushen Kangshuai Tablet on level of total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), angiotensin II (Ang II) and homocysteine (Hcy) in serum, morphology of aortic sinus and lung tissue, expression of IRE1α, TXNIP, NLRP3 and IL-1β in lung tissue.

RESULTS In the process of atherosclerosis, the pathological changes accompanied obvious lung tissue injury, and the lesions were further aggravated with the extension of time, indicating time dependence. Compared with model group, Bushen Kangshuai Tablet had effect on improving the lesions of aortic sinus and lung tissue at 4, 8 and 12 weeks. After 12 weeks, Bushen Kangshuai Tablet increased the level of HDL-C, while reduced the level of Ang II and Hcy, at the same time decreased the expression of endoplasmic reticulum stress (ERS) related protein IRE1α and oxidative stress related protein TXNIP in lung tissue. To a certain extent, the drug also reduced the expression of inflammasome related proteins NLRP3 and IL-1β in lung tissue.

CONCLUSIONS Bushen Kangshuai Tablet can inhibit atherosclerosis and related lung tissue injury. Its mechanism may be related to improve lipid metabolism, reduce Ang II and Hcy level in serum and decrease the risk of pulmonary inflammatory reaction caused by excessive ERS.

CARDIOVASCULAR PREVENTION & REHABILITATION

EPIDEMIOLOGY AND EVIDENCE-BASED MEDICINE

GW30-e0155

Developmental trajectories of body mass index during 19 years of follow-up and hypertension risk among Chinese adults

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OBJECTIVES We aimed to identify the BMI change pattern over the recent fast-changing time period of China, and explore their association with risk of incident hypertension.

METHODS Data were obtained from the China Health and Nutrition Survey 1997–2015. Group-based modeling approach was used to identify distinct trajectories of BMI change among adults over 19 years. A Cox proportional hazards model was performed to estimate the association between BMI trajectory groups and risk of incident hypertension, with stratification for age.

RESULTS Nineteen thousand three hundred and three individuals were included in this study. Four distinct BMI trajectory groups were identified: normal-stable (N=4465, 23.13%), normal-increase (N=8817, 45.68%), overweight-increase (N=4874, 25.25%) and obese-increase group (N=1147, 5.94%), which shared similar increase patterns. Results of Cox regression analysis showed that groups stared with elevated BMI level at baseline surveys and had increasing trends were significant associated with higher risk of hypertension. Compared with individuals of normal-stable group, hazards ratios of hypertension associated with BMI trajectory groups of normal-increase, overweight-increase and obese-increase were 1.65, 3.53 and 5.51. The magnitude of BMI trajectory groups on developing hypertension was attenuated with age.

CONCLUSIONS Our findings have depicted a long picture of trajectories of BMI in the Chinese context. Besides, this study has highlighted the importance of higher initial BMI and weight gain in increasing the risk of hypertension.

GW30-e0179

Critical appraisal of guidelines for coronary artery disease on dual antiplatelet therapy: more consensus than controversies

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OBJECTIVES Dual antiplatelet therapy (DAPT) in the form of aspirin plus a P_2Y_{12} inhibitor, when indicated, is one of the key treatments in coronary artery disease (CAD). Many recommendations on DAPT in patients with CAD based on current guidelines are largely inconsistent. In our current study, we aimed at systematically reviewing DAPT-relevant clinical practice guidelines, and highlighting their commonalities and differences for better informed decision-making.

METHODS Contemporary guidelines in English were searched in MEDLINE, Embase and websites of guideline organizations and professional societies. Guidelines with recommendations on DAPT for CAD patients were included. Guideline quality was appraised with the 6-domain Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument. The reporting of conflicts of interest (COI) was assessed individually with supplementary items from the RIGHT (Reporting Item for Practice Guidelines in Healthcare) checklist. Meanwhile, extraction of recommendations was performed.

RESULTS A total of 17 guidelines fulfilled our inclusion criteria. Most of them were graded with relatively good scores averaging from 42 to 74%. Domains for lower scores were in "stakeholder involvement" and "application". The reporting of COI was satisfactory. For the recommendations on DAPT, most guidelines with high AGREE II scores included consistent recommendations on the timing and P_2Y_{12} inhibitor selection. Nonetheless, conflicts still exist on the duration of DAPT.

CONCLUSIONS Quality of guidelines for DAPT in CAD was relatively high, though defects existed in "Applicability" and "Stakeholder Involvement". As these guidelines developed, DAPT recommendations gradually converged on a consensus. Clinical decision should be made on an individual basis.

GW30-e0195

Potential usefulness and clinical relevance of a novel 4-tiered classification of left ventricular hypertrophy in the detection of reduced glomerular filtration rate: insights from general Chinese population

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OBJECTIVES A new 4-tiered classification of left ventricular hypertrophy (LVH) that accounted for LV dilatation (high LV end-diastolic volume [EDV] index) in addition to concentricity$^{0.67}$ (mass/end-diastolic volume$^{0.67}$ [M/EDV$^{0.67}$]) has recently been developed to isolate high-risk phenotypic patterns and assess their prognostic significance. The utility of this novel 4-group LVH classification to predict reduced estimated glomerular filtration rate (eGFR) in a general Chinese population has not been evaluated.

METHODS A total of 11,037 participants aged ≥35 years in rural China underwent an epidemiological investigation where clinical characteristics and echocardiographic parameters were determined. Patients with LVH were divided into 4 groups where eccentric LVH is subdivided into "indeterminate hypertrophy" and "dilated hypertrophy" and concentric LVH into "thick hypertrophy" and "both thick and dilated hypertrophy," based on the presence of increased LVEDV. Reduced GFR was considered if meeting estimated GFR <60 mL/min/1.73 m^2.

RESULTS The prevalence of reduced eGFR was 1.2% with no LVH, 3.5% with indeterminate, 4.0% with dilated, 8.0% with thick, and 9.9% with both thick and dilated hypertrophy (P for trend<0.001). Further, reduced eGFR was significantly greater in participants with dilated hypertrophy (adjusted odd ratio [OR]:1.551, 95% CI: 1.044–2.303), thick hypertrophy (2.875 [1.522–5.421]) and both thick and dilated hypertrophy (2.908 [1.534–5.513]) but not significantly in those with indeterminate hypertrophy (1.401 [0.941–2.085]) compared with normal geometry in multivariable logistic regression analyses adjusted age, sex, race, family income, education level, physical activity, smoking, drinking, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, total cholesterol, high-density lipoprotein-cholesterol, body mass index, and LV mass/height$^{2.7}$.

CONCLUSIONS Patients with relatively mild left ventricular hypertrophy (LVH) without either increased LV volume or concentricity (i.e., indeterminate hypertrophy) have similar risk of reduced eGFR with individuals normal LV mass. Specifically, this novel 4-tiered classification of LVH enables reclassification of eccentric LVH patients who were labeled as indeterminate by conventional two-group classification with improved prediction of reduced kidney function. Our results suggest that a more refined subclassification of LVH patterns provide insight into the unfavorable cardiovascular outcomes associated with concentric than eccentric LVH in most but not all studies, and its incorporation into clinical practice may help eliminate indeterminate results and improve future adverse events prediction.

GW30-e0197

Ideal cardiovascular health score and Fuster-BEWAT score as predictors of left ventricular hypertrophy classification

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OBJECTIVES The AHA recommends focusing on ideal cardiovascular health score (ICHS) for primary prevention of CVD. Simpler tools not requiring laboratory tests, such as the Fuster-BEWAT (blood pressure [B], exercise [E], weight [W], alimentation [A], and tobacco [T]) score (FBS), are also available. We hypothesized that it is likely that the protective effects of the ICHS and FBS on cardiovascular events may be mediated by its favorable effects on subclinical CVD, as assessed by the new 4-group left ventricular hypertrophy (LVH) model.

METHODS The sample consisted of 11,261 participants aged ≥35 years (mean age, 54 years; 54% women) of general Chinese population who were enrolled in Northeast China Rural Cardiovascular Health Study. Patients with LVH were divided into 4 groups: neither increased concentricity nor increased LV end-diastolic volume (EDV) ("indeterminate hypertrophy," n=1536); increased concentricity without increased LVEDV ("thick hypertrophy," n=1024); increased LVEDV without increased concentricity ("dilated hypertrophy," n=232); and increased concentricity with increased LVEDV ("both thick and dilated hypertrophy," n=185). Individuals were classified as having poor, intermediate, or ideal cardiovascular health based on the number of favorable ICHS or FBS.

RESULTS When the ICHS and FBS were modeled as a categorical variable, those with ideal ICHS and FBS profiles had 88 and 74% lower odds, respectively, of having both thick and dilated hypertrophy compared with adults with poor profiles (odds ratio [OR]: 0.12; 95% confidence interval [CI]: 0.03–0.47 vs. OR:

0.26 [0.10–0.72]). A similar pattern was evident in those with thick hypertrophy for both the favorable ICHS (OR: 0.12 [0.04–0.38]) and FBS groups (OR: 0.19 [0.07–0.52]). Further, with poor ICHS and FBS as references, those with optimum ICHS and FBS presented substantially lower adjusted odds of having indeterminate hypertrophy (OR: 0.26 [0.20–0.34] vs. OR: 0.28 [0.20–0.38]) and dilated hypertrophy (OR: 0.73 [0.57–0.94] vs. OR: 0.57 [0.43–0.76]). For the total ICHS and FBS on a continuous scale from 0 (all 7 poor) to 7 (all 7 ideal), risk reductions of the four distinct LVH patterns were of comparable magnitude for each 1-point increment of ICHS and FBS. The discrimination accuracy of the FBS (C-statistics: 0.698, 95% CI: 0.663–0.733) was identical to that of the ICHS with respect to concentric dilated LVH (C-statistics: 0.711 [0.678–0.744]) as well as for identifying thick hypertrophy (C-statistics: 0.650 [0.615–0.684] vs. C-statistics: 0.658 [0.624–0.692]). The AUC analysis showed equivalent predictive performance levels for both models in estimating dilated hypertrophy: ICHS C-statistic of 0.684; FBS C-statistic of 0.686; and very similar values in discriminating indeterminate hypertrophy, with ICHS C-statistic of 0.737 and FBS C-statistic of 0.731.

CONCLUSIONS Better profiles of CV health behaviors and risk factors, reflected by higher ICHS and FBS metrics, are strongly associated with a lower prevalence and a lower extent of new 4-tiered categorization of LVH in general Chinese population. Our findings complement previous study by demonstrating that FBS appears capable of performing just as well as ICHS in predicting the novel 4-group classification of LV geometric abnormalities and is a simpler and more feasible option with which to offer fresh insight into alleviating LVH burden as part of primordial prevention of CVD.

GW30-e0203

Relationship of arterial stiffness with 10-year atherosclerotic cardiovascular disease (ASCVD) risk in general middle and aged population

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OBJECTIVES To identify independent risk factors for antherosclerotic cardiovascular disease (ASCVD) and to assess the association between brachial-ankle pulse wave velocity (baPWV) and 10-year ASCVD risk.

METHODS We conducted a community-based, cross-sectional study in a general middle and aged population to assess various potential risk factors of predicting ASCVD. A total of 1768 subjects was recruited to examine the relevant factors of ASCVD in Lujiazui Community, Shanghai. The baseline characteristics were obtained via the use of a questionnaire. Measurement of baPWV, laboratory tests, and echocardiography were conducted in the morning after a 12 h overnight fast. According to Pooled Cohorts Equations model made by ACC/AHA, the 10-year ASCVD risk was defined as: high risk of ASCVD (10-year risk ≥7.5%), low risk of ASCVD (10-year risk <7.5%). Multiple correspondence analyses and logistic regression analyses were subsequently performed following data collection.

RESULTS Among the 1768 subjects, there were a total of 776 subjects with high risk of ASCVD and 992 subjects with low risk. Mean age of subjects was 59.43±8.57 years, 32.7% of which were male. The level of baPWV was markedly higher in the group with high risk of ASCVD [13.96 (12.71, 15.42) vs. 17.07 (15.02, 19.55), P=0.00]. After adjustment for gender, history of Diabetes, smoking, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and medical treatment of hypertension, logistic-regression analysis demonstrated that ankle brachial index (ABI) [OR 5.279, 95% CI 1.204–12.229] and baPWV [OR 3.250, 95% CI 1.470–7.185] were independently correlated with 10-year ASCVD risk. The area under ROC curve for baPWV to predict 10-year ASCVD risk was 0.799 (95% CI: 0.778–0.820, P<0.001).

CONCLUSIONS Increased arterial stiffness is correlated with 10-year ASCVD risk in general middle and aged populations. ABI and baPWV are independent markers for 10-year ASCVD risk. Subjects with baPWV above 16 m/s are more likely to encounter a higher 10-year ASCVD risk.

GW30-e0294

Risk prediction of placenta growth factor level for adverse outcomes in patients with coronary artery disease: a meta-analysis

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OBJECTIVES Coronary artery disease (CAD) is the most common type of cardiovascular disease and still is the major cause of death in developed countries. Further risk evaluation for CAD is mandatory to avoid needless hospitalizations and to prevent deaths caused by complications of CAD. In recent study, placental growth factor thought to reflect the pathophysiological constituents of coronary artery disease and have also proved to be independent predictors of future cardiovascular events. However, its prognostic value for CAD is still controversial.

METHODS In the meta-analysis, risk of all-cause death or secondary cardiovascular disease predictor relevance of circulating PLGF level after onset of CAD was investigated in 10,282 participants with Acute Coronary Syndrome (ACS) or Stable Angina Pectoris (SAP) in total from 8 studies through searching PubMed, Embase, Web of Science and Cochrane Library.

RESULTS Higher circulating PLGF level was significantly associated with higher all-cause mortality or secondary CV events in ACS patients (HR=1.77. 95% CI=(1.44, 2.02), P<0.001). And no changes in direction or significance in overall effect was observed in long-term risk prediction (random-effect model: HR=1.58. 95% CI=(1.06, 2.27), P=0.02, I^2=89%) or short-term risk prediction (fixed-effect model: HR=1.93. 95% CI=(1.33, 1.93), P=0.0005, I^2=21%). No statistically significant association between circulating PLGF level and all-cause mortality in SAP patients were observed (HR=1.00, 95% CI: (0.57, 1.76), P=0.99).

CONCLUSIONS In the present meta-analysis, PIGF prove a useful addition to the armamentarium of predictors for prognosis especially for short-term prognosis of Acute Coronary Syndrome but not for Stable Angina Pectoris.

GW30-e0331

The main ECG characteristic differences between urban and rural in normal Chinese adults: results from China national survey of ECG parameters

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OBJECTIVES Today, patients with cardiovascular diseases in China are about 290 million. In recent years, the mortality rate of cardiovascular diseases in rural areas has been higher than that in urban areas. Conventional 12-lead resting electrocardiogram is a common tool for clinical examination of cardiovascular diseases because it is a simple, noninvasive and inexpensive method. Many studies have found that ECG parameters are affected by age, gender, race and other factors. However, it is not clear whether there are differences in main ECG characteristics between urban and rural areas. We aimed to compare the main parameters of resting 12-lead ECG in Chinese healthy adults between urban and rural areas, including heart rate, PR interval, QRS duration, QT interval, QT interval corrected by heart rate and R wave voltage in lead V5.

METHODS The China National Survey of ECG Parameters, a cross-sectional study was designed and conducted in China during 2012–2013. A multi-stage, stratified cluster sampling method was applied to select the representative Chinese adults aged 18–85 years old, and about half of the individuals were from urban and half from rural. To satisfy our study purpose, the subjects had to have normal blood pressure and body mass index, and have no history of any disease that may affect the ECG parameters. Resting 12-lead ECG was performed by using GE MAC-5500 with a sampling rate of 1000 Hz and analyzed automatically by utilizing Marquette 12SL algorithm in MUSE Cardiology Information System (GE Healthcare, USA). Generalized linear model adjusted for age, gender and population distribution, was used to compare the main ECG parameters between urban and rural. SAS 9.4 software was used to statistical analysis.

RESULTS Of the 10,732 respondents, 4341 Chinese normal adults were included and analyzed. Among them, 2365 (54%) were from urban and 1976 (46%) were from rural. The results showed that there were no significant differences in heart rate (71.7±0.2 vs. 71.3±0.2 beats per minute, P>0.05), QRS duration (87.2± 0.2 vs. 87.0±0.2 ms, P>0.05) and QT interval (386.3±0.5 vs. 385.2±0.6 ms, P>0.05) between urban and rural population. The PR interval of urban population was longer than that of rural population (149.2±0.4 vs. 146.9±0.5 ms, P<0.01). The results of QTc of heart rate corrected by Bazzet formula and Fridericia formula also showed that urban people were slightly longer than rural people (419.1±0.5 vs. 416.3±0.5 ms, 407.7±0.4 vs. 405.6±0.4,

P<0.01). We also presented that R amplitude in lead V5 in rural areas was higher than that in urban areas (1581.6±11.2 vs. 1532.1±10.3 mV, P<0.01). These results suggest that the main ECG parameters of normal adults in China are different between urban and rural areas.

CONCLUSIONS The main ECG parameters of normal adults in China are different between urban and rural areas. Further study is warranted to explore the causes of ECG differences between urban and rural.

GW30-e0363

Plasma homocysteine levels associated with a corrected QT interval

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OBJECTIVES Little is known about the relationship between homocysteine (Hcy) levels and the QT interval. We examined the association of different Hcy levels with corrected QT (QTc) intervals in a general population.

METHODS Plasma levels of Hcy were assessed in a population-based study of 7002 participants 35 years of age and older from 2012 to 2013. Twelve-lead ECGs were performed on all participants and analyzed automatically.

RESULTS The distribution of Hcy levels was determined for an entire population after the data were grouped into quartiles (Q1: ≤11.1 μmol/L; Q2: 11.1–13.8 μmol/L; Q3: 13.8–18.2 μmol/L; Q4>18.2 μmol/L). The mean value of the QTc interval in each quartile was 433.2±23.8 ms, 430.0±24.6 ms, 429.2±24.5 ms and 430.6±25.7 ms. Multiple logistic regression analyses showed that, compared with the second quartile, and after fully adjusting for potential confounding factors, the odds for QTc >440 ms in the first and fourth quartile increased (P<0.05), (OR: 1.23, 95% CI: 1.05–1.43 for Q1; OR: 1.40, 95% CI: 1.19–1.65 for Q4).

CONCLUSIONS QTc interval was associated with the Hcy level in this general population.

GW30-e0364

Diagnosed but not undiagnosed diabetes is associated with depression in rural areas

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OBJECTIVES There is a lack of study on the relation between undiagnosed diabetes and depression in the general population.

METHODS A total of 11,531 adults were examined using a multistage cluster sampling method to select a representative sample of individuals who were at least 35 years old. Subjects were classified into three groups: no diabetes (ND), diagnosed diabetes (DD), and undiagnosed diabetes (UD). The participants were surveyed with the Patient Health Questionnaire-9 (PHQ-9).

RESULTS Of all the 11,531 participants, the prevalence of depression was higher in the DD group than in the other two groups. Multi variable logistic regression analyses show that the DD group had significantly higher odds for depression compared with the ND group (P<0.01), while the UD group showed no significant differences compared to the ND group. Subgroup analyses show that diagnosed diabetes in subjects with a lower educational level, compared with subjects with an educational level of high school or above, had higher odds for a PHQ-9 score ≥5 (P<0.01).

CONCLUSIONS In this general population, diagnosed but not undiagnosed diabetes was significantly associated with depression. Much higher odds for depression were found among diagnosed diabetic individuals with a lower level of education.

GW30-e0365

Metabolism rather than obesity is associated with ischemic stroke: a cross-sectional study in rural northeastern China

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OBJECTIVES Little is known about stroke with different obesity phenotype as determined using the Adult Treatment Panel-III criteria with metabolic health or not. This study aimed to investigate the effects of metabolically healthy and unhealthy obesity on ischemic stroke in a general population.

METHODS A total of 11,150 adults were examined using a multi-stage cluster sampling method to select a representative sample of individuals 35 years or older. Ischemic stroke was defined as history of a cerebrovascular event, as documented by doctors via either cranial CT or MR scan within the past 2 years. All subjects were categorized as having metabolically healthy non-obesity (MHNO), metabolically unhealthy non-obesity (MUNO), metabolically healthy obesity (MHO) or metabolically unhealthy obesity (MUO) using the Adult Treatment Panel-III criteria. Stratified analysis were done based on different body mass index group.

RESULTS For the total population, multiple regression analyses revealed that individuals with MUNO and MUO were more likely to experience ischemic stroke compared with those with MHNO (OR 2.136, 95% CI 1.677–2.720; OR 2.712, 95% CI 1.798–4.092; all P<0.001). The OR for ischemic stroke did not significantly differ between MHO and MHNO.

CONCLUSIONS Stratification based on different BMI group showed that, compared with people who were normal weight without Mes, participants who were in Mes with overweight or obesity had significantly higher OR for ischemic stroke (both P<0.05); participants who were not in Mes with overweight or obesity did not showed OR significantly higher. Ischemic stroke is likely associated with poor metabolic health rather than with obesity itself.

GW30-e0367

Relation of heavy alcohol consumption to QTc interval prolongation

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OBJECTIVES Until now, few studies have examined QT intervals in subjects who consume alcohol. We performed this study to evaluate the associations between alcohol consumption and the QTc interval based on a general population.

METHODS A total of 11,269 adults were examined using a multistage cluster sampling method to select a representative sample of subjects aged ≥35 years. Participants were asked to provide information about their alcohol consumption, and all participants received electrocardiograms and echocardiograms. A prolonged QTc interval was defined according to the national guidelines, which specify thresholds of ≥460 ms in women and ≥450 ms in men. Patients were divided into 3 categories, based on the amount of alcohol they consumed: heavy drinkers (>15 g/day for women and >30 g/day for men), moderate drinkers (≤15 g/day for women and ≤30 g/day for men), and non-drinkers (0 g/day).

RESULTS The results showed that the heavy drinkers had longer QTc intervals than did the nondrinkers. Multivariate logistic regression analyses revealed that men who were heavy drinkers had approximately 1.4-fold higher odds of having a prolonged QTc interval (odds ratio 1.431, 95% confidence interval [CI] 1.033–1.982, P=0.031) than nondrinkers; in women, heavy drinkers had ~2.3-fold higher odds of having a prolonged QTc interval (odds ratio 2.344, 95% CI 1.202–4.571, P=0.012) than nondrinkers. Neither men nor women who were moderate drinkers exhibited a significant increase in risk for prolonged QTc interval.

CONCLUSIONS In conclusion, heavy alcohol consumption was found to be a risk factor for a prolonged QTc interval.

GW30-e0368

The relation of moderate alcohol consumption to hyperuricemia in a rural general population

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OBJECTIVES Although alcohol abuse is known to increase serum uric acid, the relation between moderate drinking and uric acid have remained poorly understood. We performed this study to evaluate whether different alcohol consumption level has different effects on the risk of hyperuricemia based on a rural general population.

METHODS Multi-stage cluster sampling method was used to select a representative sample of individuals aged 35 years or older. Participants were asked to provide information about their alcohol consumption. Data regarding the demographic and lifestyle characteristics and the blood biochemical indexes of these participants were collected by well-trained personnel.

RESULTS In total, 11,039 participants aged 35 years or older were included (4997 men and 6042 women). The prevalence of hyperuricemia in the different male alcohol consumption groups was 11.9% in non-drinkers, 12.6% in

moderate drinkers, and 16.3% in heavy drinkers (P<0.001). In females, the rates were 6.3% in non-drinkers, 8.1% in moderate drinkers, and 6.6% for heavy drinkers (P=0.818). In males, multivariate logistic regression analyses shows heavy drinkers had an approximately 1.7-fold higher risk of hyperuricemia (OR: 1.657, 95% CI: 1.368–2.007, P<0.001) than non-drinkers; moderate drinkers did not experience a significant increase in risk (OR: 1.232, 95% CI: 0.951–1.596, P=0.114). Multivariate logistic regression analyses of females showed that, compared with non-drinkers, neither moderate nor heavy drinkers had a significantly increased risk of hyperuricemia (OR: 1.565, 95% CI: 0.521–4.695, P=0.425 for heavy drinkers; OR: 0.897, 95% CI: 0.117–6.855, P=0.916 for moderate drinkers).

CONCLUSIONS Heavy alcohol consumption increased the risk of hyperuricemia for males but not for females. Among both males and females, moderate alcohol consumption did not increase the risk of hyperuricemia.

GW30-e0369

The association between alcohol consumption and left ventricular ejection fraction

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OBJECTIVES The results of previous studies on the relation between alcohol consumption and heart failure (HF) have been inconsistent. This study aimed to evaluate the association between alcohol consumption and left ventricular ejection fraction (LVEF) in a general population.

METHODS A total of 10,824 adults were examined using a multistage cluster sampling method to select a representative sample of individuals who were at least 35-years old. The participants were asked to provide information about their alcohol consumption. Echocardiograms were obtained, and LVEF was calculated using modified Simpson's rule.

RESULTS Of the 10,824 participants included in the present study, 46.1% were males, and the mean participant age was 54 years; age ranged from 35 to 93 years. The overall prevalence of LVEF<0.50 and LVEF<0.40 in the studied population was 11.6 and 2.9%, respectively. The prevalence of LVEF <0.5 and LVEF <0.04 was higher in both the moderate and heavy drinker groups than in the nondrinker group (P<0.05). Multivariate logistic regression analyses corrected according to the different levels of alcohol consumption showed that moderate and heavy drinkers had an – 1.3-fold and 1.2-fold higher risk of LVEF <0.5, respectively, than nondrinkers (OR: 1.381, 95% CI: 1.115–1.711, P=0.003 for moderate drinkers; OR: 1.246, 95% CI: 1.064– 0.460, P=0.006 for heavy drinkers). Heavy drinkers had an ~1.5-fold higher risk of decreased LVEF <0.4 than nondrinkers (OR: 1.482, 95% CI: 1.117–1.965, P=0.006). Moderate drinkers did not show a risk of decreased LVEF <0.4 that was significantly higher than that of nondrinkers (OR: 1.183, 95% CI: 0.774–1.808, P=0.437).

CONCLUSIONS According to these results, we concluded that increased alcohol consumption was associated with decreased LVEF compared with no alcohol consumption in this general population.

GW30-e0370

Alcohol consumption and cardiovascular diseases in rural China

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OBJECTIVES This study aimed to update the current information on alcohol consumption and evaluate the associations between drinking status and cardiovascular diseases in a general population from rural China.

METHODS The study examined a total of 11,269 adults using a multi-stage cluster sampling method to select a representative sample of individuals 35 years or older. Related medical histories were obtained using a standard questionnaire, and blood biochemical indexes were collected by well-trained personnel. Participants were asked for information about whether they regularly consumed alcohol, their average alcohol consumption per day, and the number of days per month that they consumed alcohol.

RESULTS This population consisted of 75.8% non-drinkers, 7.5% moderate drinkers, and 16.7% heavy drinkers. And the mean alcohol consumption per day for the total population was 15.29±0.35 g/d (women:1.0±0.11 g/d and men 32.5±0.69 g/d, P<0.001). Multivariate logistic regression analysis showed that heavy drinkers had an approximately 1.3-fold and 1.7-fold greater risk for coronary heart disease and hypertension, respectively (OR: 1.252, 95% CI: 1.012–1.549; OR: 1.741, 95% CI: 1.519–1.994, respectively) compared with that of the non-drinking group. After fully adjusting the data for all variables, the data showed no significant association between moderate alcohol consumption and CHD, HT or ischemic stroke.

CONCLUSIONS Alcohol consumption in rural populations is high, particularly in men. Heavy drinking is a risk factor for coronary heart disease and hypertension, but not for ischemic stroke. There was no significant association between moderate alcohol consumption and CHD, HT or ischemic stroke.

GW30-e0371

Grim status of hypertension in rural China: results from Northeast China rural cardiovascular health study 2013

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OBJECTIVES The last study that reported the prevalence of hypertension in rural Northeast China was conducted approximately 10 years ago. We aimed to update the data on the prevalence and epidemiologic features of hypertension in rural Northeast China.

METHODS This study examined a total of 11,576 adults using a multi–stage cluster sampling method to select a representative sample of individuals 35 years or older. Sitting blood pressure was measured three times for each participant by trained observers using a standardized electric sphygmomanometer after resting for 5 minutes. Related medical histories were obtained using a standard questionnaire, and blood biochemical indexes were collected by well–trained personnel.

RESULTS Prevalence of hypertension was 51.1%; 53.9% for men and 48.7% for women. Among subjects with hypertension, 43.5% were aware of the diagnosis, and 31.2% were taking antihypertensive medications, but only 6% had their blood pressure controlled. Besides traditional risk factors, multiple logistic regression analysis indicated that obesity, diabetes, dyslipidemia, and hyperuricemia were becoming risk factors for hypertension in this rural area.

CONCLUSIONS The status of hypertension is grim currently in rural Northeast China. The prevalence of hypertension remains seriously high, while the control rate is still frustratingly low. Obesity, diabetes, dyslipidemia, and hyperuricemia were more likely to be associated with hypertension in this rural area.

GW30-e0372

Prehypertension in rural northeastern China: results from the northeast China rural cardiovascular health study

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OBJECTIVES This study aimed to determine the present status of prehypertension in rural China.

METHODS It was conducted between January and August 2013, using a multistage clustering method to select a representative sample of individuals (≥35 years old), resulting in a study population of 11,576 adults. Prehypertension was defined as a systolic blood pressure (BP) in the range of 120 mmHg to 139 mmHg and/or a diastolic BP between 80 mmHg and 89 mmHg according to the Seventh Report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).

RESULTS The results showed that the mean±standard deviation systolic and diastolic BP values for the entire population were 141.8±23.5 mmHg and 82.1±11.8 mmHg, respectively. Among the whole population, 35.1% of men and 32.5% of women were prehypertensive. Multiple logistic regression analysis showed that high body mass index, advanced age, alcohol consumption, diabetes, high triglyceride and low-density lipoprotein cholesterol levels, and elevated diet score were risk factors for prehypertension.

CONCLUSIONS This study indicates that there is a high prevalence of prehypertension in rural China and confirms the importance of healthy lifestyles – including the control of obesity, diabetes, and dyslipidemia – to decrease the incidence of prehypertension.

GW30-e0385

Metabolic syndrome and depressive symptoms among rural northeast general population in China

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OBJECTIVES Previous researches aiming to estimate the association between metabolic syndrome and depressive symptoms come out with inconsistent

results. Besides, most of them are conducted in the developed areas. There is lack of the data from rural China. The aim of this study is to confirm whether gender difference exists among the relationship between MetS, metabolic components and depressive symptoms in the rural Chinese population.

METHODS A cross-sectional analysis enrolled 11430 subjects' aged ≥35 from rural Northeast China. Metabolic and anthropometric indicators were measured according to standard methods. Depressive symptoms were defined using the Patient Health Questionnaire-9 (PHQ-9).

RESULTS The prevalence of depressive symptoms was 6% among rural Northeast general population and the prevalence of MetS and its components were 39.0% for MetS, 42.9% for abdominal obesity, 67.1% for elevated blood pressure, 47.1% for hyperglycemia, 32.1% for hypertriglyceridemia, 29.5% for low HDL-C. Depressive symptoms were associated with triglyceride component (OR=1.24, 95% CI: 1.05–1.46, P=0.01) but not MetS (OR=1.11, 95% CI: 0.94–1.30, P=0.23). Moreover, depressive symptoms were associated with triglyceride component (OR=1.21, 95% CI=1.00–1.47, P=0.05) in women only. But once adjusted for menopause status, depressive symptoms were no longer statically associated with triglyceride component (OR=1.20, 95% CI=0.99–1.46, P=0.07).

CONCLUSIONS Depressive symptoms were associated with triglyceride component but not MetS in rural Chinese population. Routine lipid screening should be recommended among rural depressed residents especially among female.

GW30-e0389

Self-reported snoring is associated with dyslipidemia, high total cholesterol, and high low-density lipoprotein cholesterol in obesity: a cross-sectional study from a rural area of China

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OBJECTIVES Studies to explore the relationship between self-reported snoring and dyslipidemia, especially high total cholesterol (TC) and high low-density lipoprotein cholesterol (LDL-C), in the general population are still lacking.

METHODS Our study was designed to examine whether self-reported snoring is significantly associated with dyslipidemia and ascertain the effects of different snoring intensities on dyslipidemia.

RESULTS There were 10,139 participants in our study. After adjustment for all confounding factors, self-reported snoring (OR=1.207; P=0.003), moderate (OR=1.229; P=0.015), strong (OR=1.222; P=0.033), and very strong (OR=1.467; P=0.012) snoring intensity, but not low (OR=1.110; P=0.224) snoring intensity, were significantly associated with dyslipidemia among adults with BMI (body mass index) ≥ 25 kg/m2. In addition, self-reported snoring was significantly associated with high TC (OR=1.167; P=0.048) and high LDL-C (OR=1.228; P=0.044), rather than low HDL-C (OR=1.171; P=0.057) and high triglyceride (TG) (OR=1.110; P=0.141).

CONCLUSIONS In conclusion, adults with BMI ≥ 25 kg/m2 and who experience snoring, especially moderate, strong, and very strong intensity levels of snoring, should be on the alert regarding the possibility of dyslipidemia, especially high LDL-C and high TC.

GW30-e0394

Antihypertensive medication and blood pressure control rate among Mizo population from north east India

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OBJECTIVES Earlier study conducted among the Mizos from Mizoram, North East India revealed 15.9% prevalence of hypertension with significant urban–rural (18.9% versus 13.2%, P<0.001) differences. The present study assessed the use of antihypertensive treatment by the hypertensive subjects from this population and achievement of treatment target goal.

METHODS It was a population-based cross-sectional study which included a total of 12,313 subjects (male: 5707, female: 6606) from urban (n=5853) and rural (n=6460) localities. Of these, 1957 (15.9%) hypertensive subjects were the study population for the present communication. Achievement of treatment target goal and blood pressure control were defined as per JNC VIII criteria.

RESULTS It was found that of all hypertensive subjects, 1041(53.2%) were male and 916 (46.8%) were females. Eight hundred fifty (43.4%) were from rural location and 1107 (56.6%) were from urban location. Antihypertensive treatment was taken by 549 (28.1%) hypertensive subjects and only 259 (13.2%) out of total hypertensive subjects (1957) achieved BP treatment target goal. Older age, urban location and obesity were found to be significant independent predictors for poor blood pressure control in hypertensive subjects.

CONCLUSIONS We conclude that proportion of hypertensive subjects taking medication and subjects achieving treatment target goal are low among Mizo hypertensive subjects. Intervention measures to create awareness and intensify antihypertensive treatment for strict blood pressure control should be initiated to reduce cardiovascular morbidity and mortality.

GW30-e0406

Stress in family in open urban population: gender differences

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OBJECTIVES To study stress parameters in family in dependence on age in males and females aged 25–64 years of open population from middle-urbanized Siberian city.

METHODS The study was conducted within cardiological screening in males aged 25–64 years among workable Tyumen population in the times of the world social and economic crises (2008–2009). Representative sample was formed out of the voting lists of one of the administrative regions of Tyumen in amount of 1000 males, 250 people from each of four life decades (25–34, 35–44, 45–54, 55–64 years). Respond was 85.0% – 850 participants. Parameters of stress in family and at work were revealed according to the World Health Organization program «MONICA-psychosocial» (the questionnaire «Knowledge and attitude to health»). Tests coding was performed through the construction of index component and scores calculation according to the suggested algorithm of the program MOPSY (MONICA-psychosocial). Statistical analysis was conducted using the package of programs SPSS, version 7.

RESULTS The question «Has your marital status changed within the last year?» received an answer «One change» from males of young age 25–34 years more often than in comparison with females of the same age category (21.0–8.2%, P<0.01). Males aged 45–54 and 55–64 years did not have any changes in marital status more often than females of the same age categories 45–54 years (86.1–76.3%, P><0.01) and 55–64 years (91.6–78.0%, P><0.001). Females aged 55–64 years had more changes in marital status answering «one change» (6.1–14.0%, P><0.01) and «several changes» (2.3–7.9%, P><0.01).

CONCLUSIONS Our study shows that young males aged 25–34 years have more changes in marital status than females of the same age category. The situation is different in the elder age category (55–64 years): females have more changes in marital status than males. The results of the study of non-organized Tyumen population can be used as scientific foundation for planning complex socially oriented programs in other middle urbanized Siberian cities as well, having priority for the social risk groups (young males, elder females).

GW30-e0407

Tobacco smoking in males of open population with and without coronary artery disease

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OBJECTIVES To state prevalence of smoking and associations with prevalence of coronary artery disease (CAD) in Tyumen males aged 25–64 years of open population.

METHODS A cross-sectional epidemiological study was conducted based on representative sample formed of the voting lists of 1000 males (250 people from each four life decades) from one of the administrative regions of Tyumen, the respond was 85.0%. Separation of various CAD forms was performed based on the standard methods (WHO questionnaire on effort angina, resting ECG and Minnesota coding) used in epidemiology researches. "Certain" CAD (CCAD) and "possible" CAD (PCAD) were selected. The questionnaire of WHO – MONICA "Knowledge and attitude to health" including 33 questions about attitude to health and diseases prevention was used to analyze attitude to smoking.

RESULTS CAD morbidity as per the expanded epidemiological criteria in open population of Tyumen males aged 25–64 years was 12.4%. CCAD was revealed in 6.6% as per exact criteria and PCAD was revealed in 5.7% as per inexact criteria. Analyses revealed that 27.1% of males never smoked, 24.0% of males gave up smoking, 10.8% of males were smoking less, and 14.3% of males stated that they stopped smoking for a while. The share of people unsuccessfully trying to give up smoking was 15.8% and the share of people who never tried to give up smoking was 7.9%. In general, 65.0% of Tyumen males were trying to change something in their smoking habit. Answering the question "Have you ever tried to change something in your smoking habit?" people with PCAD and CAD as per the expanded epidemiological criteria in comparison with the control group (people without CAD) had positive change in tobacco smoking. Thus, an answer "I used to smoke" was detected among males with PCAD and with CAD as per the expanded epidemiological criteria more often than in the control group (35.6–23.5%, P<0.05; 33.1–23.5%, P><0.05, respectively).

CONCLUSIONS The received data showed the need of preventive measures aimed at decrease of the behavioral risk factors impact and the need to strengthen the "high risk" prevention strategy.

GW30-e0408

Physical activity and dysregulation disorders of autonomic nervous system in boys aged 12–17 years

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OBJECTIVES To estimate epidemiological situation of the main risk factors of coronary artery disease in Tyumen pupils to design the main fields of preventive measures.

METHODS A cross-sectional epidemiological study of randomly selected 750 boys aged 12–17 years from one of Tyumen administrative regions was conducted; the respond was 87.7%. Cardiological screening was performed with the standard methods and included complains questionnaire; anthropometry with Quetelet index (QI), heart rate (HR) (beats per minute – BPM); standard measurement of blood pressure (BP) applying criteria of the elevated systolic BP (SBP) /diastolic BP (DBP) for pupils: 10–12 years old – >120/75 mmHg; 13–14 years old– >130/80 mmHg; 15–17 years old – >135/85 mmHg. Ethical standards were followed. Mathematical treatment of the results was conducted with the program «Statistika 6.0» with correlation analysis, and the differences in case of p.

RESULTS It was revealed that 67.5% of boys aged 12–17 years were doing sports regularly, not less than once a week, and it took an average 7.8+5.7 hours per week. 13.1% of boys spent less than 4 hours per week going in for sports, 8.2% of teenagers played sports more than 14 hours per week. Pupils going in for sports more than 14 hours per week did morning exercises 1.5 times more often. Incidence of elevated BP was lower in the group of pupils doing sports not less than 14 hours per week than in the group doing sports less than 4 hours per week (11.3 vs. 13.4% respectively, P<0.05). The same tendency was noticed regarding HR (80.3 BPM vs. 86.0 BPM). Compared to the groups of pupils doing sports more than 14 hours per week, pupils doing sports less than 4 hours per week had more complains about headache (51.0 vs. 48.4%), heartbeat (22.4 vs. 11.3%, P><0.05), increased fatigability (26.5 vs. 24.2%), irritation (36.7 vs. 32.3%, P><0.05), sweating (26.5 vs. 22.6%, P><0.05), poor sleep (14.3 vs. 11.3%, P><0.05), syncopal conditions (11.2 vs. 6.5%, P><0.05). A reliable correlation between physical activity and SBP, DBP and complains was revealed (r=0.14–0.22, P><0.05).

CONCLUSIONS Thus, our study showed that pupils aged 12–17 years had high morbidity of elevated low physical activity. Besides, group of pupils with low physical activity had higher prevalence of elevated BP, higher frequency of complains about vegetative dysfunction; significant associative relation between all the factors mentioned above was revealed; and it should be considered in planning of preventive actions since one's childhood.

GW30-e0412

Gender differences in the diet and medical activity at cardiovascular diseases in open population of Tyumen

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OBJECTIVES To establish gender differences as per the attitude to the diet in correlation with medical activity in case of cardiovascular diseases in open Tyumen population.

METHODS The study was carried out on representative selection formed out of 1000 males aged 25–64 years and 1000 females from the voting lists of one of the administrative districts of Tyumen. Respond to the cardiological screening was 85.0 and 70.4%, respectively. The attitudes to the diet and medical activity were studied by a standard questionnaire WHO "MONICA – Psychosocial" in a framework of cardiological screening. A method of the population survey was used by self-filling of the questionnaire. Questions were followed by the list of the fixed answers. Statistical analysis was conducted by a package of programs SPSS, version 21.0.

RESULTS A significantly fewer number of males from the category "I did not need to keep dieting" would apply to a doctor in case of any ache or cardiac discomfort in comparison with females (25.3 and 33.6% respectively, P<0.05). Seven percent of males would not apply to a doctor in case of any ache or cardiac discomfort in relation to a significantly fewer number of females – 3.3% (P><0.01). Correlation between males and females was revealed in the category of persons who had changed the diet for their health with low regularity of applying to a doctor (39.6 and 22.4% respectively, P><0.001). A much more significant number of males, who changed the diet for their health, would apply to a doctor in case of any ache or cardiac discomfort in relation to females (31.3 and 22.4%, respectively, P><0.05); but a much larger number of males, who had a severe ache or cardiac discomfort would not apply to a doctor (2.1%, P><0.01), however, such persons were not revealed in females.

CONCLUSIONS Thus, the low medical activity was noted in Tyumen population who did not find necessity of getting on a diet, but a significantly lower indicator was in males in case of not only any, but also severe ache or cardiac discomfort. Low medical activity was revealed in persons, who had changed the diet for their health in case of any ache or cardiac discomfort, but significantly lower indicator was noticed in females.

GW30-e0418

Is social support a gender specific factor for myocardial infarction incidence in general population? WHO epidemiological program MONICA-psychosocial study

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OBJECTIVES To determine the gender differences in the effect of social support on risk of myocardial infarction (MI) in an open population 25–64 years in Russia/Siberia.

METHODS Under the third screening of WHO program MONICA-Psychosocial a random representative sample of both gender aged 25-64 years in Novosibirsk was examined in 1994 (n=1346, males 48.8%, mean age 44.9±0.4 years). Indices of close contacts (ICC) and social relations (SNI) were evaluated at the baseline by Berkman-Syme test. New-onset MI incidences were identified over 16-years (1994–2010 yy) of follow-up in the cohort.

RESULTS The prevalence of low ICC levels was higher in men compared to women (63.9 and 57.1%, respectively); the prevalence of low SNI levels was higher in women compared to men (77.7 and 43%, respectively). The risk of MI over 16 years of follow-up was 5.2-fold higher in men (95% CI 1.947–19.383; P<0.05) and4.9-fold higher in women (1.108–21.762; P><0.05) with low ICC. Low SNI increases risk of MI in 3.1 times in men (1.138–9.247; P><0.05) and in 2.9 times in women (95% CI 1.040–8.208; P><0.05). After adjustment for social variables multivariate model showed significant results in higher risk of MI in those males who are living alone with manual occupational status and in women with low educational degree.

CONCLUSIONS Social support is a protective factor for MI incidence both in men and women. Better social gradient improves this influence. Family status and occupation are stronger to be attributable to risk in males while level of degree in females with low social support.

GW30-e0419

22-year trends in prevalence of nontraditional risk factors of cardiovascular diseases in young and middle-aged adults in the Russia/Siberia. WHO program Monica-psychosocial

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OBJECTIVES To determine 22-year trends of non-traditional cardiovascular risk factors as vital exhaustion, hostility, social support in young and middle-aged people 25–44 years in the Russia.

METHODS Representative samples of urban population were examined in consequent screening surveys. From 1994 to 1995 under the WHO program MONICA-psychosocial (MOPSY) 618 inhabitants were examined (53.4% of males, mean age – 34.8±0.4 years, response rate – 77.3%). From 2013 to 2016 within the framework of the screening studies covered by state task a random representative sample at the same city district was examined (n=975, 43.7% of males, mean age – 34.5±0.4 years, response rate – 71.5%). Vital exhaustion and hostility were evaluated with using test MOPSY (vital exhaustion and hostility subscales); social support – scale Berkman-Syme.

RESULTS Rates of vital exhaustion were higher in women than in men during the entire study period. In 1994–1995 there was a high prevalence of the low index of close contacts and social networks both in men and women. No gender differences were found. In 2013–2016 the negative levels of vital exhaustion and social support decreased significantly. In the same period (1994–1995) adverse level of hostility was higher in women than men; in 2013–2016 this indicator for women decreased, while for men it remained at the same level.

CONCLUSIONS A significantly positive decline in high values of non-traditional risk factors for cardiovascular diseases and an increase in high levels of social support in both genders in young and middle-aged adult have been established.

GW30-e0529

Prevalence and comorbidities of isolated left vertebral artery in Chinese population

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OBJECTIVES The reported frequency of isolated left vertebral artery (ILVA) was 0.8–6.0% in western population. The ILVA complicated with aortic dissection or aortic aneurysm is not rare. However, only limited studies have assessed the prevalence of aortic arch patterns in Chinese people. Our study sought to investigate the prevalence and comorbidities of ILVA in Chinese population through an aortic computed tomography angiography (CTA) database.

METHODS This study retrospectively analyzed the database including outpatients and hospitalized patients who underwent aortic CTA examinations at our institution from August 2015 to October 2018. Aortic CTA was most commonly performed in the following clinical scenarios: suspected aortic etiology based on symptoms, signs, or other testing; evaluation and follow-up of subjects with aortic disease; or evaluation of the complications about procedures. For patients who had more than one report during this period, the first examination record was analyzed. All the aortic CTA reports were reviewed by experienced radiologists and cardiologists (Figure 1).

RESULTS A total of 185 reports of ILVA were identified from 8948 aortic CTA records of 5540 patients. The incidence of ILVA was 3.34% (185/5540) in the entire cohort, 3.26% (138/4238) in men and 3.61% (47/1302) in women. The mean age in the ILVA group was lower than those in the control group (54.7±15.2 years vs. 58.4±14.9 years, P=0.022). The percentage of aortic dissection was higher in the ILVA group than those in the control group (48.1 vs. 30.5%, P<0.001; respectively). While the percentage of aortic aneurysm was lower in the ILVA group than those in the control group (18.4 vs. 22.5%, P=0.182) (Table 1).

CONCLUSIONS The incidence and comorbidities of ILVA in Chinese were similar to that in the western population. As the presence of a vertebral artery is related to the strategies of the method of cerebral protection during the procedure of reconstruction of the aortic arch, more attention should be given to the ILVA, especially those complicated with aortic dissection.

GW30-e0540

Features of arterial hypertension in patients with type 2 diabetes mellitus in the Azerbaijani population, depending on the functional state of the kidneys

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OBJECTIVES Study of the characteristics of hypertension, depending on the functional state of the kidneys in patients with type 2 diabetes mellitus (DM2).

METHODS The study included 528 patients aged 30–69 years (mean age 54.1±0.3 years). Information was obtained about the features of hypertension and the tactics of antihypertensive therapy through the questionnaire "ARİC". The level of blood pressure (BP) was measured twice, in the sitting position with a 5-minute break and with an accuracy of 2 mmHg, and took the average values of 2-fold measurement. Diagnosis of hypertensive angiopathy was carried out by an oculist based on changes in visual acuity and ophthalmoscopy. The glomerular filtration rate (GFR) was calculated by the Cockroft-Gault method, the level of microalbuminuria (MAU) was determined using test strips. Statistical analysis was carried out using the methods of variation, dispersion and discriminant.

RESULTS MAU and decrease in GFR detected in 4/5 patients with hypertension. In patients with MAU, compared with those without albuminuria, the frequency of hypertension was 4–8 times higher, and in individuals with GFR≥90 mL/min, this figure was lower than in those with GFR0.05). A decrease in GFR and MAU was more common in persons with grade 1 hypertension (1/3 patients), while in grade 2 and 3 hypertension, MAU severity increased (P>0.05). With an increase in MAU, compared with individuals without albuminuria, the mean values of systolic BP and diastolic BP increased (P=0.016 and P=0.670, respectively). With a decrease in GFR, the levels of systolic BP and diastolic BP increased (P<0.01). In individuals who did not receive antihypertensive treatment, 30 mg/dL of MAU (21.4%) and grade 1 chronic kidney disease (CKD) (24.1%) prevailed, the highest rates of MAU and a decrease in GFR (50.0%) were observed in patients who received the combined therapy. The treatment with beta-blockers showed the highest MAU 300 indices, and against the background of monotherapy with calcium channel blockers – 100 mg/dL (respectively 7.1 and 12.5%), monotherapy with angiotensin-converting enzyme inhibitors reduced the incidence of MAU progression and decreased GFR (P>0.05). Compared with patients receiving antihypertensive drugs only with increased BP and in the form of a course of treatment, the highest incidence of MAU was 300 mg/dL and CKD grade 2 (respectively, 76.9 and 56.7%; P>0.05). In patients with hypertensive angiopathy, the frequency of MAU 100 mg/dL (25.9%) and grade 2 CKD (25.9%) was the highest (respectively, P=0.001 and P=0.048).

CONCLUSIONS In order to prevent CKD, it is necessary to strengthen measures to increase adherence to treatment and adequate control of hypertension in patients with DM2.

GW30-e0646

Effect of obstructive sleep apnea on perioperative outcomes of patients undergoing aortic valve replacement

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OBJECTIVES Obstructive sleep apnea (OSA) is a significant public health problem with increasing prevalence in adult. The potential effect of OSA on perioperative outcomes in patients undergoing aortic valve replacement (AVR) is unclear. Also, no current studies had looked into whether transcatheter AVR (TAVR) or surgical AVR (SAVR) would be a better choice for OSA patients.

METHODS We conducted this study using datasets from the National Inpatient Sample database (NIS, 2011 to 2014). Adult patients (≥18 years of age) undergoing TAVR or SAVR were included. Multivariate logistic regression analysis was applied to explore the association between OSA and AVR outcomes, and the difference of outcomes between TAVR and SAVR in OSA patients.

RESULTS A total of 68,333 patients were included, 6578 (9.63%) patients carry the diagnosis of OSA. In the SAVR group, patients with OSA had a lower risk of in-hospital mortality (Odds Ratio (OR): 0.77, 95% Confidence Interval (CI): 0.64–0.93, P=0.0054), major adverse cardiovascular events (OR: 0.75, 95% CI: 0.68–0.84, P<0.0001), acute myocardial infarction (OR: 0.71, 95% CI: 0.62–0.82, P<0.0001), sepsis (OR: 0.68, 95% CI: 0.56–0.83, P<0.0001), blood transfusion (OR: 0.86, 95% CI: 0.81–0.92, P<0.0001) and increased the demand of noninvasive mechanical ventilation (NIMV) (OR: 3.56, 95% CI: 3.12–4.07, P<0.0001) compare with no-OSA patients. In TAVR group, patients with OSA were less likely to be sepsis and more likely to be NIMV. In-hospital mortality was similar between OSA-SAVR and OSA-TAVR group (OR: 1.17, 95% CI: 0.68–2.03, P=0.5628), while OSA-TAVR patients had a lower risk of preoperative complications and higher risk of permanent pacemaker placement.

CONCLUSIONS In the SAVR group, OSA patients had significantly lower mortality and complications compared with patients without this comorbidity. For OSA patients, TAVR may be a better choice than SAVR.

GW30-e0870

Evidence-based shared decision-making in clinical management of stable angina: preliminary results from a randomized clinical trial

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OBJECTIVES To investigate the process quality and outcome of evidence-based shared decision-making (EBSDM) in clinical practice compared to traditional physician-led decision-making.

METHODS The EBSMD model involves three key elements: (1) providing patients with a self-designed paper-based Decision Aid with synthesized clinical evidence from systematic reviews and meta-analysis (i.e. regarding the possible benefits and risks of different medication options for stable angina pectoris) supported by the narrative personal stories of target patients from in-depth interviews; (2) one nurse-patient decision-support consultation meeting; and (3) one physician-patient shared decision-making meeting. Both the physicians and the nurse receive systematic and uniform training in shared-decision making, communication techniques and the use of relevant scales. The physicians receive person-to-person comments on their own consultation video and are trained to behave in the SDM way of conducting consultations. According to sample calculation based on the assumed score difference in the primary outcome,

100 patients are currently being recruited and randomized at an 1:1 ratio to receive EBSDM (the SDM group) or traditional decision-making consultation (the TDM group). Written consent is required from each patient. Consultation meetings are video-taped to allow assessment of the decision-making process from multifocal perspectives (i.e., nurse/patient/physician/observer) using the MAPPIN'SMD tools, and outcome measurements including decisional conflict, decision-specific knowledge, decision preference, patient satisfaction and compliance are measured. This study was approved by the Ethics Review Committee of the Second Affiliated Hospital of Tianjin University of Traditional Chinese Medicine (Approval No. 2018-030-01). This study is funded by the National Natural Science Foundation of China (Grant No.81603495) and the National Science and Technology Major Project (Grant No. 2018ZX09734002).

RESULTS Seventy-six patients with stable angina pectoris were involved in this study, including 37 patients in the SMD group and 39 in the TDM group. Recruiting and following-up is going on. Drop-out rate in the SMD group is greater than in the control group. The reasons for drop-outs include discontinuing treatment due to symptom relief and lost to follow-up. Preliminary statistical analysis shows patients in the SMD group have higher decision-specific knowledge levels and less decisional conflicts after the nurse-patient decision-support consultation meeting.

CONCLUSIONS By investigating the difference between SDM and TDM, the findings from this research may help inform health policy-makers of the promise of practicing SDM in the integrated medical practice context – i.e. in terms of improving health decision-making quality, and patient compliance and satisfaction.

GW30-e0976

Gender-specific difference in cholestery ester transfer protein activity and its association with known cardiovascular risk factors

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OBJECTIVES This study was designed to explore the gender-specific difference in cholestery ester transfer protein (CETP) activity and its association with known cardiovascular risk factors.

METHODS Participants in this study were recruited from the Beijing project in the Chinese Multi-provincial Cohort Study (CMCS). A total of 1353 participants with complete data were finally included, with 627 males and 726 females. CETP activity was determined by the BioVision's CETP Activity Fluorometric Assay Kit, which uses a self-quenched fluorescent neutral lipid that can be measured when transferred to an acceptor molecule. Analysis was done on the difference in CETP activity between genders and its association with known cardiovascular risk factors.

RESULTS (1) The CETP activity in the total participants was 83.22 (66.30–103.75) pmol/uL/h, and it was higher in males than in females [86.61 (69.56–106.82) pmol/uL/h vs. 79.91 (62.78–100.29) pmol/uL/h, P<0.01]. (2) Age, waist circumference, systolic blood pressure, diastolic blood pressure, smoking rate, and the prevalence of hypertension were significantly higher in males than in females (P<0.01), while total cholesterol, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) were significantly lower (P<0.05). (3) Spearman correlation analysis showed that CETP activity was positively correlated with waist circumference, and triglyceride, and negatively correlated with HDL-C and APOE-containing HDL-C in both genders (P<0.01). The CETP activity in females was positively correlated with body mass index, yet unrelated (P>0.05) in males. (4) After adjustment for age, body mass index, systolic blood pressure, LDL-C, HDL-C, triglycerides, blood glucose, high-sensitivity C-reactive protein, smoking, and lipid-lowering drugs in a multiple logistic regression model, CETP activity was still significantly higher in females than in males (OR=0.539, 95% CI: 0.394–0.735, P<0.01].

CONCLUSIONS CETP activity and its association with known cardiovascular risk factors differed between genders. This gender-specific difference in CETP activity still presents after adjustment for known cardiovascular risk factors in this cohort.

PREVENTION RESEARCH

GW30-e0063

Fibroblast growth factor-21 prevents diabetic cardiomyopathy via AMPK-mediated anti-oxidation and lipid-lowering effects in the heart

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OBJECTIVES Our previous studies showed that both exogenous and endogenous FGF21 inhibited cardiac apoptosis at the early-stage of type 1 diabetes. Whether FGF21 induces preventive effect on type 2 diabetes-induced cardiomyopathy was investigated in the present study.

METHODS High-fat-diet/streptozotocin-induced type 2 diabetes was established in both wild-type (WT) and FGF21-knockout (FGF21-KO) mice followed by treating with FGF21 for 4 months. Cardiac function, morphological changes, cardiac hypertrophy, fibrosis as well as apoptosis, oxidative stress and inflammation were diagnosed.

RESULTS Diabetic cardiomyopathy (DCM) was diagnosed by significant cardiac dysfunction, remodeling and cardiac lipid accumulation associated with increased apoptosis, inflammation and oxidative stress, which was aggravated in FGF21-KO mice. However, the cardiac damage above was prevented by administration of FGF21. Further studies demonstrated that the metabolic regulating effect of FGF21 is not enough contributing to FGF21-induced significant cardiac protection under diabetic condition. Therefore, other protective mechanisms must exist. The in vivo cardiac damage was mimicked in primary neonatal or adult mouse cardiomyocytes treated by HG/Pal, which was inhibited by FGF21 treatment. Knockdown of AMPKα1/2, AKT2 or NRF2 with their siRNAs revealed that FGF21 protected cardiomyocytes from HG/Pal partially via up-regulating AMPK -AKT2-NRF2-mediated anti-oxidative pathway. Additionally, knockdown of AMPK suppressed fatty acid β-oxidation via inhibition of ACC-CPT-1 pathway. And, inhibition of fatty acid β-oxidation partially blocked FGF21-induced protection in cardiomyocytes. Further in vitro and in vivo studies indicated that FGF21-induced cardiac protection against type 2 diabetes was mainly attributed to lipotoxicity rather than glucose toxicity.

CONCLUSIONS FGF21 functions physiologically and pharmacologically to prevents type 2 diabetic lipotoxicity-induced cardiomyopathy through activation of both AMPK -AKT2-NRF2-mediated anti-oxidative pathway and AMPK-ACC-CPT-1-mediated lipid-lowering effect in the heart.

GW30-e0193

Fuster-BEWAT score versus ideal cardiovascular health score to predict arterial stiffness: implications in rural communities

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OBJECTIVES The Fuster-BEWAT Score (FBS) has been recently developed for use in lifestyle-based cardiovascular disease (CVD) prevention, presenting similar accuracy in predicting the subclinical atherosclerosis and left ventricular hypertrophy with ideal cardiovascular health score (ICHS), but it is unclear whether both scores exhibit comparable predictive values for detection of arterial stiffness. We evaluated the effectiveness of ICHS and FBS in assessing the presence of arterial stiffness among the general population of rural China.

METHODS The study population consisted of 11,163 community-based adults (mean age 53.9 years; 54% female) who were recruited in the NCRCHS (Northeast China Rural Cardiovascular Health Study) between January 2012 and August 2013. Subjects were grouped into three categories according to the number of favorable ICHS or FBS: ideal (5–7 ICHS or 4–5 FBS metrics), intermediate (3–4 ICHS or 2–3 FBS metrics), and poor (0–2 ICHS or 0–1 FBS metrics). Arterial stiffness was assessed by the pulse pressure/stroke volume indexed to height$^{2.04}$ (PP/SVi). Participants with the highest tertile of PP/SVi were considered "high arterial stiffness". Linear and logistic regression models were constructed to estimate associations of the ICHS and FBS with the presence of arterial stiffness defined as having PP/SVi in the third tertile.

RESULTS For every unit increase in overall ICHS and FBS (indicating better cardiovascular health category), PP/SVi decreased by 0.080 and 0.132 mmHg/mL (both P<0.001), respectively, after adjusting for age, sex, race, education level, family annual income, and alcohol consumption, marital status, and family history of cardiovascular diseases. With poor ICHS and FBS as references, those with optimum ICHS and FBS showed substantially lower adjusted odds of having increased arterial stiffness (ICHS odds ratio [OR]: 0.46; 95% confidence interval [CI]: 0.39 to 0.55 vs. FBS OR: 0.38; 95% CI: 0.31 to 0.47). Taken together, the odds for high arterial stiffness decreased in a graded manner in adults with intermediate and ideal ICHS and FBS compared with subjects with poor ICHS and FBS (P for trend <0.001). In addition, similar OR estimates were seen for 1-point higher of ICHS and FBS for 2-element Windkessel model of arterial stiffness (OR: 0.86; 95% CI: 0.83 to 0.89 vs. OR: 0.80; 95% CI: 0.77 to 0.84). Furthermore, the AUC analysis indicated identical levels of discriminating accuracy of ICHS (C-statistic: 0.663; 95% CI: 0.653 to 0.674) and FBS (C-statistic: 0.664; 95% CI: 0.653 to 0.674) in identifying the presence of increased arterial stiffness.

CONCLUSIONS Our study provides the first demonstration that ICHS and FBS perform similarly for 2-element Windkessel model of arterial stiffness prediction in a large community-based Chinese sample, underscoring the value of the FBS as a simpler and more feasible option for evaluating the risk of arterial stiffness, as well as supporting the relevance of targeting this metric as part of primordial prevention. Given the ability to assess risk in health care

resource scare settings without the requirement of expensive laboratory blood tests, FBS may have benefits for prevention of vascular end-organ damage and resulting CVD at the population level, perhaps in part by favorable influence on arterial stiffness.

GW30-e0248

Impact of bariatric surgery on body composition and aerobic exercise capacity

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OBJECTIVES Weight loss reduced by bariatric surgery (BS) directly and indirectly affecting obesity subject's aerobic exercise capacity. The purpose of this study is to explore how does the heart, lungs and muscles contribute to limit the physical condition after BS 6 months later.

METHODS Thirteen obese subjects (BMI: 40±3 kg/m²) without major complications underwent BS, and 13 health control subjects (BMI: 23±2 kg/m²) matched with gender, age and height. All subjects performed body composition determined by dual-energy X-ray absorptiometry, respiratory and limbs muscle strength measurements, pulmonary function testing, global physical activity questionnaire and cyclo-ergometer incremental cardiopulmonary exercise test. Obesity subjects were tested before and 6 months after BS.

RESULTS Visceral adipose tissue (VAT), fat mass (FM) and lean mass (LM) were decreased, but still higher than control group. The peak VO_2 relative was increased with downtrend in peak VO_2 absolute and decrease in VO_2 absolute at first ventilatory threshold (VT1), both of which were lower than the control group. Heart rate reserve and resting blood pressure were decreased, and O_2 pulse was unchanged. Force vital capacity was increased with uptrend in others spirometer and lung diffusion capacity parameters. Uptrend in respiratory muscles strength and increase in relative quadriceps strength, which was lower than the control group. The changes in VO_2/LM was positively correlated with the decrease in LM, and negatively correlated with the decreased VAT. The changes in heart rate at rest was positively correlated with the changes in VO_2/LM and VT% VO_2 peak. The changes in O_2 pulse was positively correlated with the changes in peak VO_2, VO_2/LM at VT1, VT1% VO_2 peak and workload at VT1. The decrease in FM trunk and VAT were negatively correlated with the changes in spirometer parameters and maximal inspiratory pressure (MIP). The changes in VE maximum was positively correlated with the decrease in LM gynoid, peak VO_2 and workload at VT1. The decreased VT1%VO_2 peak was positively associated with the changes in resting pulmonary function parameters and VE at VT1. The increased relative quadriceps strength was negatively associated with the increased FM/LM ratio.

CONCLUSIONS Six months after bariatric surgery fat mass loss is concomitant to visceral fat and lean mass loss without affecting maximal aerobic exercise capacity but with a reduction of the ventilatory threshold. The autonomic nervous system balance and resting lung function were improved. The decrease in aerobic capacity was related to muscular deconditioning aggravated by loss of lean mass, although the static muscular strength did not decreased.

GW30-e0405

Estimation of attitude to the preventive measures among the population of middle-urbanized Siberian city in the gender aspect

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OBJECTIVES To study attitude to the preventive measures among males and females aged 25–64 years of open urban population.

METHODS Under the cardiological screening, a cross-sectional epidemiological study was conducted based on two representative samples among 2000 males and females aged 25–64 years. Respond to cardiological screening was 85.0% in males and 70.3% in females. A standard questionnaire MONICA-psychosocial of the World Health Organization was used in the study. Statistical analysis was conducted using SPSS, version 11.5.

RESULTS The question «Can a healthy person of your age avoid some serious diseases in case of taking preventive measures?» received a definite answer «Yes, he absolutely can» in 64.3% of males and 67.0% of females of open population. Besides, statistically significant gender differences of this question were noticed in junior and senior age groups (25–34 years: 58.2–71.2%, P<0.05; 55–64 years: 70.7–57.0%, P><0.01). The answer «It is probably so» was given by 34.8% of males and 32.2% of females; statistically significant differences were defined in the same age categories, however, more often in males than in females (25–34 years: 41.8–28.2%, P><0.05; 55–64 years: 28.8–42.1%, P><0.01). A small amount of males and females with no dependence on age (0.9–0.8%) gave an answer «It is impossible». And to the question «Do you think that a healthy person of your age can get a serious illness within the nearest 5–10 years?» the majority of population responded «It is possible» (62.8% of males and 64.9% of females); 36.2% of males and 32.6% of females gave an answer «It is likely to happen». In both cases, statistically significant gender differences in population and age groups were not stated according to these parameters. The answer «It is impossible» was given by the minimum amount of males and females (0.9–2.5%, P><0.05), statistically significant gender differences were received in the entire population and in the age category 55–64 years (0.9–2.5%, P><0.05).

CONCLUSIONS Thus, the most favorable conditions for the forming of complex prevention program in the middle-urbanized Siberian city are noticed among young females and males of the elder age category.

GW30-e0662

A follow-up study on women with high levels of troponin T and NT-proBNP for the prevention of cardiovascular disease caused by hypotension

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OBJECTIVES The Troponin T and NT-proBNP levels are known to be higher in CAH patients than the normal subjects. It is known that the negligence of hypotension in women results in an increased probability of severe cardiovascular diseases. Especially, when patients with ischemic heart disease are compared, the patients with hypotension have a 2.57-fold increase in mortality compared to patients with normal blood pressure. The mortality and recurrence rates were similar in CAH patients when they were treated with drug or treated by stent surgery, this indicates that the drug treatment had the same therapeutic effect as stenting. Upon drug treatment for women with hypotension, the levels of Troponin T and NT-proBNP are expected to decrease. Therefore, for the prevention and effective treatment of hypotension in women, it is crucial to quantify the levels of Troponin T and NT-proBNP levels. Herein, we present the BMT 9G testTM ultra-Troponin T /NT-proBNP products that aid in the monitoring of the treatment in hypotensive women (30 s–60 s) indicated by changes in Troponin T and NT-proBNP levels before and after treatment.

METHODS Subjects, ethics and study designAbout 400 women participants were enrolled in this study. The 200 samples were collected from women with normal blood pressure and without cardiac diseases. The other 200 samples were collected from the women with hypotension. AssayscTnT and NT-proBNP measurements were performed in Ethylenediaminetetraacetic acid (EDTA) plasma using BMT 9G test TM ultra-Troponin T and BMT 9G test™ ultra NT-proBNP (Biometrix Technology Inc., Chuncheon, South Korea). The 9G test™ ultra-Troponin T quantifies plasma cTnT levels in the analytical detection range of 1–120 pg/mL at room temperature in 30 min. The reported limit of blank (LoB) and limit of detection (LoD) are 0.2 pg/mL and 0.87 pg/mL, respectively. The coefficient of variation (CV) was reported to be less than 10% in the entire detection range. The 9G test™ ultra-NT-proBNP allows measurement of plasma NT-proBNP in 30 min at 25°C in the linear detection range of 7.0–600 pg/mL. The LoB, LoD, and limit of quantification were reported to be 2.0 pg/mL, 3.7 pg/mL, and 7 pg/mL, respectively. The CV was reported to be less than 10% in the whole detection range.

RESULTS The Troponin T and NT-proBNP levels were compared in a healthy population, a hypotensive patient group with drug treatment and a hypotensive group without drug treatment during the study period. The women without hypotension did not show any changes in their Troponin T and NT-proBNP levels during the study period. Similarly, the hypotensive patient group, which did not receive drug treatment, also did not show significant changes in their Troponin T and NT-proBNP levels. However, the hypotensive patient group, which received drug treatment during the study period showed a decrease in the levels of Troponin T and NT-proBNP.

CONCLUSIONS The results of this study indicate that the Troponin T and NT-proBNP levels can be used for the monitoring of the treatment in the women suffering from hypotension. The BMT 9G test TM ultra-Troponin T /NT-proBNP products can accurately quantify the changes in Troponin T and NT-proBNP levels before and after treatment. The monitoring of the therapy in hypotensive women (30 s–60 s) can help in treating this health condition and may allow improving the life expectancy.

GW30-e0740

Association between beverage consumption and body mass index in university students

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OBJECTIVES With the flourishing of economy and the continuous improvement of standard of living in university students, the growth of drinking consumption among university students and the diversification of consumption patterns, beverage had gradually become a part of university students' daily diet. The relationship between intake of beverages and health in university students is not clear. Obesity was not only a chronic disease that did harm to health, but also a risk factor for cardiovascular disease. Knowing the relationship between the consumption habits and the prevalence rate of overweight (including obesity) in university students can help university students to establish a healthy lifestyle, control weight and lead a reasonable beverage consumption. Thus the association between the beverage consumption habit of university students and the prevalence of overweight were investigated.

METHODS A questionnaire survey was conducted in university students (115 females and 130 males) of one university. It was a self-filling questionnaire which includes the consumption of beverages, the frequency and the variety of beverage per week. The students were divided into beverage group and non-beverage group. Weight, height, hip circumference and waist circumference of all subjects were determined, the BMI and waist-hip ratio were calculated. Alpha reliability coefficient, non-parametric test, chi-square test, kruskal-wallis H test, non-conditional Logistic regression analysis of dichotomies and Logistic multivariate analysis were used for statistical analysis.

RESULTS (1) The intake of different kinds of beverage in university students was as follows: the sugared beverage (carbonic acid and juice) was up to 55.5%, the functional beverages was 25%, the dairy products was 19.5%, and the tea beverage (no sugar or low sugar) was 12.5%. (2) Female students drunk fruit juice more than male students ($P<0.01$), and the consumption of carbonic acid beverage in male students was significantly higher than in female students ($P<0.01$). (3) The overweight and central obesity rate of female and male students were roughly equivalent ($P>0.05$). Overweight and obese (BMI≥24) students consumed more sugary beverages than normal weight students ($P<0.05$). (4) Multifactor's logistic regression analysis illustrated that the risk factors associated with overweight and obesity were sugary beverages and purchase times; the risk factors associated with central obesity included sex and the frequency of beverage purchased.

CONCLUSIONS The consumption sugary beverages in overweight and obese university students were higher than in normal weight students. Female university students liked juice and milk beverages more than male students, while male university students liked carbonated and tea beverages more than female students. Sugary beverage is a risk factor to obesity. Female students are more likely to be central obese than male students. The intake of sugar beverages was closely correlated to overweight and central obesity. It's important for university students to reduce the intake of sugary beverages appropriately and establish a right and healthy consumption concept of beverage in order to prevent cardiovascular disease.

GW30-e0916

Association between cumulative blood pressure and the risk of cardiovascular disease: a 25-year follow-up of the Chinese multi-provincial cohort study

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OBJECTIVES To investigate the association of cumulative blood pressure (BP) levels with the long-term risk of cardiovascular disease (CVD).

METHODS Data from the Chinese Multi-provincial Cohort Study (CMCS) were analyzed. The 15-year cumulative BP was calculated by summing the product of the average BP for each pair of consecutive examinations in 1992, 2002, and 2007 and the time interval between these two consecutive examinations in years among 2401 participants with BP recorded in at least 1992 and 2007 and free of CVD in 2007. Cardiovascular events (including coronary heart disease and stroke) occurred during 2007 and 2017 were registered. Multivariate Cox proportional hazards regression was used to obtain hazard ratios (HRs) of CVD incidence associated with quartiles of cumulative BP, adjusting for age, sex, smoking status, diabetes, and levels of total cholesterol and high-density lipoprotein cholesterol in 1992.

RESULTS Of the 2401 participants, 42.6% were men, mean (SD) age at baseline was 46.5 (8.0) years. During up to 10 years (mean, 7.8 years) of follow-up (18,882 person-years), 105 CVD events were recorded. The CVD incidence rates were 180.1, 349.4, 532.6 and 1248.3 per 100,000 person-years for participants with the 1st–4th quartile of cumulative systolic BP, respectively, and the counterpart rates were 220.2, 454.6, 599.3 and 1005.7 per 100,000 person-years for cumulative diastolic BP, respectively. Participants with higher levels of cumulative systolic or diastolic BP exhibited significantly higher incidence risk of CVD during follow-up ($P<0.001$). Compared with the lowest quartile of cumulative systolic BP, the HR (95% CI) of CVD was 1.73 (0.77–3.91), 2.46 (1.14–5.31), and 5.54 (2.69–11.41) for the 2nd–4th quartile of cumulative systolic BP, and 1.87 (0.91–3.86), 2.38 (1.18–4.80), and 3.74 (1.90–7.34) for the 2nd–4th quartile of cumulative diastolic BP, respectively. Participants with 15-year cumulative BP levels higher than the median, i.e. 1971/1240 mmHg×year for cumulative systolic/diastolic BP, which was equivalent to maintaining a systolic/diastolic BP level higher than 131/83 mmHg in 15 years, had significantly higher risk of CVD in the next 10 years.

CONCLUSIONS Elevated cumulative systolic or diastolic BP was associated with increased CVD risk in the Chinese population. Cumulative exposure to moderate elevation of BP at the prehypertension level should not be ignored.

GW30-e0946

Determination of risk factors for cardiovascular diseases

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OBJECTIVES To study was to evaluate the role of determining the total cardiovascular risk on the SCORE scale in primary care in the prevention of Cardiovascular Diseases (CVD).

METHODS The sampling was carried out by random sampling of 793 people from the population. 475 (59.89%) were women and 318 (40.1%) men aged 40–60 years. Cardiovascular risk factors for cardiovascular diseases such as smoking, hypercholesterolemia (HCh), abdominal obesity (AO), low of physical activity (FA), frequency of arterial hypertension (AH) were assessed.

RESULTS At the same time, the occurrence of significant differences between men and women was not. 233 (29.4%) of the surveyed had AO, while obesity was more common in women – 156 (32.8%). Smoking as a risk factor was found in 192 (24.2%) patients, while every other 174 (54.7%) man belongs to the category of smokers, while for women this indicator was 18 (3.8%). The results of the study of the total cardiovascular risk on the SCORE scale in 414 patients examined revealed: low cardiovascular risk was detected in 82% of cases, the average – in 9.0%. Moderate risk in 4%, high in 4% and very high risk in 1% of patients. We also analyzed other risk factors of CVD: heredity – burdened by CVD was recorded in 274 (68.5%) of the surveyed. All participants were interviewed about the risk factors for cardiovascular diseases and their prevention.

CONCLUSIONS The activity of preventive measures should be the greater, the higher the initial cardiovascular risk in a person.

GW30-e1049

Correlation analysis between body composition and exercise capacity in obesity subjects

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OBJECTIVES Obese individuals may have excessive subcutaneous, visceral tissue mass (VAT) which can impair cardiorespiratory fitness and muscle quality, although obesity subjects have more total muscles mass than normal weight subjects. However, there are less report on the association of body composition with others indicators related to exercise capacity.

METHODS This is a observational study included 26 health obese subjects and 26 control subjects matched with gender, age and height (men/women: 9/17; age: 47±13 & 48±13 years; height: 169±9 cm & 171±10, body composition index (BMI): 39±4 & 23±2 kg/m^2). Body composition determined by dual-energy X-ray absorptiometry, respiratory and limbs muscle strength, pulmonary function, global physical activity questionnaire and aerobic exercise capacity determined by cyclo-ergometer incremental cardiopulmonary exercise test were performed.

RESULTS VAT was negatively correlated with VO2/LM at peak and VT1, both in obesity and control groups; VAT positively correlated with VE/VO2 slope and weekly sedentary activities time only in control group. Total and regional (gynoid and legs) fat mass/lean mass ratio (FM/LM ratio) were negatively correlated with maximal expiratory pressure (MEP) and quadriceps strength, both in obesity and control groups; the maximal inspiratory pressure (MIP) was negatively correlated with trunk FM/LM ratio in obesity group and with

total FM/LM ratio in control group. The negatively correlation between total FM/LM ratio and resting lung function, VA and sniff nasal inspiratory pressure (SNIP) were only in control group; but total and regional FM/LM ratio were negatively correlated with relative quadriceps strength, physical and mental score, only in obesity group; android FM/LM ratio was negatively correlated with weekly moderate activities time, only in obesity group. Total and regional FM/LM ratio were negatively correlated with absolute and relative peak VO2 normalized by body weight, and workload maximal, only in obesity group; negatively correlated with minute ventilation maximal (VE max) and heart rate reserve (HRR), only in control group.

CONCLUSIONS Higher VAT lead to lower VO2/LM at peak and at VT, and higher FM/LM ratio caused by excessive FM lead to lower relative quadriceps strength, both in obesity and control subjects. The VAT, trunk and android FM/LM ratio, especially negatively associated with maximal aerobic exercise capacity (absolute peak VO2 and workload maximal) in obesity subjects. Increase of VAT associated with more weekly sedentary time in control subjects, increase of FM/LM ratio impaired physical and mental score in obesity subjects.

CARDIAC REHABILITATION

GW30-e0166

Evolution of early postoperative cardiac rehabilitation in patients with acute type-A aortic dissection

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OBJECTIVES Routine physical exercise performed at a safe level is important for all individuals, including the patient after aortic dissection. However, surgically treated type-A aortic dissection patients are often restricted from physical exercise due to a lack of knowledge about the blood pressure increase. Physical training at moderate intensity seems feasible and beneficial in post-surgical type I aortic dissection patients. But cardiac rehabilitation (CR) in patient with aortic dissection still understudied in recent years. The aim of this study is to describe the evolution of early postoperative CR for patients with acute type-A aortic dissection.

METHODS Thirty-six patients with acute type-A aortic dissection underwent surgical treatment and referred to CR department from 1 May 2015 to 1 July 2018 were included. An incremental symptom-limited exercise stress test (EST) on a cyclo-ergometer has been performed before and after CR. CR program including bicycle continuous training (30 minutes) at 60–80% of heart rate reserve combined with gymnastics (30 minutes), 5 sessions/week. Two patients who cannot perform bicycle training were excluded. Systolic and diastolic blood pressure (sBP and dBP) monitoring took before and after exercise training sessions.

RESULTS Thirty-four patients (25 men, 73.5%; age 60.6±9.7 years; Hypertension=55.9%; Smoking=61.8%; Sedentary=35.3%; BMI 24.6±4.4; LVEF 60.6±8.8%; baseline sBP/dBP 126.1±15.7/71.9±10.1 mmHg; Serum creatinine 94.3±57.8 μmol/L; C-reactive protein 57.8±48.2 mg/L) started CR 25.4±12.3 days after surgery. During 3.9±1.8 weeks, they underwent 12.8±3.6 sessions of bicycle training and 11.9±4.3 sessions of gymnastics. The intensity of exercise training improved significantly from 27.7±14.7 to 47.2±20.2 watts, which is equivalent an increase from 2 to 3 METs (P<0.05). Maximum sBP/dBP during exercise training were 142.4±14.8/81.4±14.8 mmHg. At the end of CR, the maximum workload of EST was higher than baseline (88.2±32.8 vs. 61.9±22.8 watts; 4.3±1 vs. 5.6±1 METs, P><0.05). Maximum sBP/dBP during EST were also higher compared with the first EST (169.8±39.0/95.7±30.2 vs. 155.5±25.7/80.2±21.4 mmHg, P><0.001).

CONCLUSIONS The study shows that early postoperative CR is feasible and safe in patients with acute type-A aortic dissection. The CR effect is remarkable, but it requires a BP monitoring during training.

GW30-e0307

Time-dependent changes of blood pressure and its clinical significance in female patients with hypertension during cardiopulmonary exercise test

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OBJECTIVES To investigate the time-dependent changes of blood pressure and its clinical significance in female patients with hypertension during cardiopulmonary exercise test.

METHODS Sixty-four women (hypertension group) who did not take beta blockers and non-dihydropyridine calcium antagonists were selected from women with grade 1 or 2 hypertension who were expected for myocardial ischemia by cardiopulmonary exercise test. Eighty-six age matching healthy women (non-hypertension group) who were excepted for myocardial ischemia by cardiopulmonary exercise test at the same time. The all subjects were selected for retrospective analysis. The time-dependent changes of blood pressure with increasing exercise intensity were compared between the two groups.

RESULTS Compared with the non-hypertensive group, the systolic blood pressure in the hypertensive group was significantly higher at rest for 3 minutes than that in the non-hypertensive group (the systolic blood pressure in the hypertensive group was 127.5±17.3 mmHg, the systolic blood pressure in the non-hypertensive group was 113.8±17.1 mmHg, P<0.001; the diastolic blood pressure in the hypertensive group was 80.4±10.2 mmHg, and that in the non-hypertensive group was 74.8±7.9 mmHg, P<0.001). The blood pressure at anaerobic threshold in hypertension group was significantly higher than that in non-hypertension group (systolic blood pressure was 156.6±21.5 mmHg in hypertension group, 137.6±24.2 mmHg in non-hypertension group, P<0.001; diastolic blood pressure was 82.9±10.9 mmHg in hypertension group, 77.2±9.8 mmHg in non-hypertension group, P<0.01). The peak systolic blood pressure in hypertension group was significantly higher than that in non-hypertension group (the peak systolic blood pressure in hypertension group was 182.9±18.2 mmHg; the peak systolic blood pressure in non-hypertension group was 163.9±24.1 mmHg, P<0.001; the peak diastolic blood pressure in hypertension group was 90.7±13.2 mmHg; the peak diastolic blood pressure in non-hypertension group was 81.9±11.9 mmHg, P<0.001). However, there was no significant difference in peak oxygen uptake ($VO_{2\ peak}$) between the two groups.

CONCLUSIONS (1) The blood pressure at rest for 3 minutes, at anaerobic threshold and at peak in exercise test of patients with grade 1 or 2 hypertension were significantly higher than that of non-hypertension group, but there was no significant difference in exercise endurance. (2) Because the blood pressure of the patients with grade 1 or 2 hypertension is more susceptible to exercise and easy to increase excessively, it suggests that the patients with hypertension should pay more attention to the changes of blood pressure in daily sports training and sports rehabilitation, so as to avoid the injury caused by the excessive increase of blood pressure.

GW30-e0334

Home-based cardiac rehabilitation versus conventional care for patients with atrial fibrillation treated with catheter ablation: a randomized controlled trial

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OBJECTIVES Radiofrequency ablation (RFA) is often undertaken in symptomatic patients and has been achieved a very high success rate. However, the symptoms like palpitations, dyspnea and fatigue are common and the exercise capacity decreases. This study was aimed to assess the effects of comprehensive home-based cardiac rehabilitation compared with usual care on cardiac function and mental health for patients treated with catheter ablation for atrial fibrillation.

METHODS Patients with atrial fibrillation treated by catheter ablation were randomized to cardiac rehabilitation consisting 8-week home-based physical exercise and smartphone-based follow-up versus usual care. The exercise proposal required the patients to exercise at the target heart rate for at least 150 minutes per week and report completion via a smartphone-based follow-up system. The primary endpoint was the value of V_{O_2} peak. The secondary outcomes included performance in 6-minute walk, self-rated mental health measured by the Short Form-36 questionnaire and Zung's Self-Rating Anxiety Scale, sleep quality assessed by Pittsburgh sleep quality index scale.

RESULTS Fifty-six patients (mean age: 55.2±9.2, 78.6% male, 27 subjects in control and 29 in cardiac rehabilitation group) completed the follow-up. Baseline characteristics were comparable between the two groups. Compared with usual care, the cardiac rehabilitation group showed a significant improvement in cardiac function assessed by V_{O_2} peak (baseline vs. 8-week follow-up, 18.8±5.6 vs. 28.9±7.5 mL/kg×min; P<0.001) and 6-minute walk (baseline vs. 8-week follow-up, 456,408, 496 vs. 495[480, 543] m; P<0.001). Meanwhile, there was significant improvement in self-rated mental health in cardiac rehabilitation group, but not in usual care group. In addition, multivariate logistic regression analysis showed that rehabilitation was the only factor associated with improvement in exercise performance measured by V_{O_2} peak after adjustment (OR [95% CI], 16.3 [2.9-92.4]; P=0.002).

CONCLUSIONS Comprehensive home-based cardiac rehabilitation had a positive effect on physical capacity compared with usual care in atrial fibrillation patients treated with catheter ablation in a short period, as well as on mental health.

GW30-e0528

Mindfulness meditation ameliorates symptoms associated with chest pain in patients with coronary heart disease after percutaneous coronary intervention

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OBJECTIVES Not many studies have examined the efficacy of a Mindfulness-Based Stress Reduction (MBSR) intervention on psychological and physiological functioning in patients with CHD after PCI until yet. This trial aims to assess the efficacy of the addition of MBSR program to usual optimal medications for patients with coronary heart disease (CHD) after percutaneous coronary intervention (PCI).

METHODS A total of 95 patients with CHD after PCI were randomized into either a treatment group (n=52) receiving the 8-week the MBSR program plus usual optimal medications, or a control group (n=41) receiving only usual optimal medications. The MBSR intervention followed the format of the traditional program, meeting for weekly 2.5-hour sessions for 8 weeks. Both formal and informal mindfulness practices were introduced including instruction/discussion, an attention-focusing technique, sitting meditation, and a series of simple yoga positions taught as a means of encouraging relaxed and focused movement. The primary outcomes are change in perceived stress, sleep disturbance, pain, physical functioning, and symptom severity, with gains maintained at follow-up. The Perceived Stress Scale was used to assess perceptions of stress over the past month. Sleep quality was assessed using the summary score from the Stanford Sleep Questionnaire, which assesses problems getting to sleep, getting up at night, getting up in the morning and daytime sleepiness. Fatigue was measured using the summary score of the Fatigue Symptom Inventory. Physical functioning and symptom severity were measured using the Pain Impact Questionnaire. The secondary outcomes are major adverse cardiac events defined as all-cause and cardiovascular death, atrial and ventricular arrhythmias, unstable angina, and other events leading to hospital admission or clinical evaluation. Assessments were carried out first at baseline, second at post-program (2 months), and third at follow-up (4 months after baseline, 2 months after the post-program assessment).

RESULTS Both groups did not differ in baseline characteristics including age, sex, coronary artey stents, medical, or outcome variables. The MBSR program significantly reduced perceived stress, sleep problems, fatigue, and symptom severity at the post-program assessment (all $P<0.05$). Post-program effects on pain, and physical functioning did not reach significance. Dose-response effects of MBSR were significant for home mindfulness practice but not session attendance. Specifically, slopes analyses revealed that mindfulness practice (times per week at two-month follow-up; M=5.0) predicted persistent reductions in pain (Visual Analog Scale; $R2=0.66$; $P<0.01$, partial $r=-0.45$) and symptom severity (Pain Impact Questionnaire; $R2=0.29$, $P<0.05$, partial $r=-0.43$). In contrast, significant dose-response effects were not observed on perceived stress, sleep, fatigue, or physical functioning (all $P>0.238$). Serious adverse events were not statistically different during supervised intervention (at post-program) or at follow-up at 4 months after baseline, 2 months after the post-program assessment (the treatment group, 15%; the control group, 13%; $P=0.25$).

CONCLUSIONS MBSR alleviated some of the major symptoms of associated with chest pain in patients with CHD after PCI and reduced subjective illness burden. Further exploration of MBSR effects on physiological stress responses is warranted. These results support use of MBSR as a junctive treatment for patients with CHD after PCI.

GW30-e0653

Mechanisms of aerobic exercise combined with statins on regulating metabolism of blood lipids and PCSK9

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OBJECTIVES This study was designed to test aerobic exercise could further reduce LDL-C and inhibit the increase of plasma PCSK9 concentration in patients with CHD taking statins with an aim of illustrating its mechanism.

METHODS (1) Compare the plasma lipid profiles and PCSK9 levels in CHD patients in the statin group and statin combined with aerobic exercise group, so as to make clear that the plasma PCSK9 concentration was decreased by aerobic exercise in patients with CHD taking statin. (2) Using sEHi to maintain TPPU concentration and its activity in vitro and in vivo. (2.1) AML-12 hepatocytes were cultured and incubated with different concentrations of TPPU and/or different statins for 24 hours. (2.2) Different concentrations of EETs antagonist (14,15-EEZE) were added in AML-12 hepatocytes in the presence of 2.1. Western blot and RT-qPCR were used to detect the change of PCSK9 expression and LDLR, SREBP2, HMGCR, FoxO3a, Sirt6. (3) Cultured AML-12 hepatocytes and transfected with $siRNA_{FoxO3a}$ and $siRNA_{Sirt6}$ in advance. Incubation with different concentrations of TPPU and/or atorvastatin, Western blot and RT-qPCR were used to detect the expression of HMG-CoA reductase, PCSK9, LDLR.

RESULTS (1) Compared with the control group, TC, LDL-C, and non-HDL-C were significantly decreased in the exercise group. (2) In the control group, the plasma PCSK9 concentration increased by 28.23% after treatment, while in the exercise group, the plasma PCSK9 concentration increased by 5.58% after treatment. (3) In the cell experiment, on the basis of atorvastatin intervention and adding different concentrations of TPPU, he expression of PCSK9 was significantly decreased compared with the atorvastatin group. Meanwhile, the expression of LDLR was higher than that of the atorvastatin group after TPPU+atorvastatin group. (4) After the addition of 14, 15-EEZE, the regulatory effects of TPPU above was re weakened. (6) The expression of pFoxO3a and Sirt6 was up-regulated in the TPPU+atorvastatin group compared with the atorvastatin group. There was no significant difference in the expression of PCSK9 between the two groups after blocking the FoxO3a-Sirt6 axis with siRNAFoxO3a and siRNA Sirt6.

CONCLUSIONS (1) Aerobic exercise can further reduce TC, LDL-C, and non-HDL-C levels in patients with CHD based on statin therapy. (2) Statin treatment alone could significantly increase plasma PCSK9 concentration in patients with CHD. Aerobic exercise combined with statin treatment could antagonize the increase of PCSK9 concentration accompanying statin treatment to some extent. (3) Within a certain range of appropriate concentrations, TPPU could inhibit the expression of PCSK9 in mouse AML-12 hepatocytes with concentration-dependent. (4) TPPU could inhibit the increase of PCSK9 in mouse AML-12 hepatocytes during statin treatment, and could further increase LDLR. (5) The decreasing effects of TPPU in PCSK9 during statin ther.

GW30-e0955

Effect of prehabilitation on functional capacity and postoperative complications in esophageal cancer surgery: a randomized clinical trial

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OBJECTIVES Esophagectomy remains the cornerstone management of esophageal cancer, however, it is commonly associated with challenging postoperative morbidity and mortality, including decreased functional capacity, complications as well as impaired quality of life. Prehabilitation, which refers to a preoperative conditioning intervention to optimize physical status and cardiopulmonary endurance, has appealed surgeons' attention recently. However, the efficacy of prehabilitation on preserving functional capacity and preventing postoperative complications in patients undergoing esophagectomy cancer has been well validated hitherto, especially among the Chinese population. Therefore, this study aimed to examine the efficacy of a prehabilitation (PR) program on improving functional status and reducing postoperative complications in patients undergoing esophagogastric cancer resection.

METHODS It was a prospective randomized controlled trial. Eligible participants diagnosed as esophageal cancer (stage I–III) were recruited in The Sixth Affiliated Hospital of Sun Yat-sen University. Participants enrolled were then randomly assigned to either PR group or normal control group using randomized numbers generated by the statistical software. Totally 16 subjects were recruited, with 8 individuals in each group. The PR group received standardized preoperative rehabilitation for 7 days and followed by a systemic postoperative rehabilitation, while the normal group only received post-operative care without any prehabilitation. The functional capacity of each participant was measured using the 6-minute walk distance (6MWD). The postoperative complications were evaluated using the Utrecht Pneumonia Scoring System (UPSS) and the Clavien-Dindo classification (CDC). The cancer-related quality of life was assessed by Functional Assessment of Cancer Therapy-Esophagus (FACT-E). The length of hospital stay, mortality rate and adverse events were also recorded. The outcome parameters were evaluated at baseline (To), pre-op (after prehabilitation) (T1), 1-week post-op (T2) and 12-week after surgery (T3).

RESULTS The average age of the esophageal cancer participants was 63±6.1 years and most of the participants were male. There were no significant differences between the two groups in terms of complications ratings as CDC grade, UPSS scores as well as FACT-E scale. Statistical differences were discovered between groups in the changes of 6MWD from T3 to T1 and T1 to To ($P<0.05$) and in 6MWD change ratio of that in T1/To ($P<0.05$). No adverse events were reported in both groups.

CONCLUSIONS Prehabilitation can improve the functional capacity in esophageal cancer patients before surgery and meanwhile facilitate post-operative functional recovery. As it is a safe and feasible intervention in the clinical practice, further evidence is warranted to prove its positive effectiveness in preventing complications and promoting quality of life for esophageal cancer survivors in the long run.

GW30-e0966

Rehabilitation programs in patients with chronic heart failure

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OBJECTIVES Assess the impact of a set of physical training on the indicators of tolerance to exercise, quality of life and cardiac hemodynamics of patients with chronic heart failure (CHF).

METHODS The 137 patients with I, II and III functional class (FC) CHF were examined. The course of physical rehabilitation included a set of physical exercises: morning exercises, aerobic training in the form of dosed walking.

RESULTS After 6 months of treatment with the inclusion of a set of exercises, a significant increase in exercise tolerance was noted with an increase in the 6-minute walk test distance in patients with FC I, II and III by 14.0, 14.9 and 12% ($P<0.001$). An increase in tolerance to physical activity of patients was accompanied by an improvement in the quality of life indicators, which was reflected in a decrease in the total index by 32.4% ($P><0.01$), 23.0% ($P><0.001$) and 9.5% ($P><0, 05$) with I, II and III FC CHF, Improving the clinical course of the disease, which was accompanied by a decrease in FC CHF. A significant inverse correlation was noted between the quality of life parameters and the results of the 6-minute walk test with a correlation coefficient $r=-0.809$, respectively.

CONCLUSIONS The inclusion of a course of physical rehabilitation in the complex treatment of patients with CHF increases tolerance to physical exertion and improve the quality of life of patients.

OTHERS

OTHERS

GW30-e0003

Short-term efficacy and safety of atorvastatin for the treatment of non-alcoholic steatohepatitis with hypercholesteremia

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OBJECTIVES Nonalcoholic steatohepatitis (NASH) has become a growing public health concern. Currently, there is no established therapy for NASH. The aim of our study was to evaluate the efficacy and safety of atorvastatin in the treatment of NASH associated with hypercholesteremia in short term.

METHODS We conducted an observational study of 181 Chinese patients with biopsy-proven NASH with serum low-density lipoprotein cholesterol (LDL-c) >160 mg/dL, who were treated with atorvastatin 20 mg daily. Serum lipids, creatine phosphokinase (CPK), bilirubin, and hepatic enzymes were prospectively measured 4, 12, and 24 weeks after atorvastatin initiation.

RESULTS Over the 24-week period following atorvastatin initiation, serum levels of total cholesterol (TC) and LDL-c and the ratio TC/high-density lipoprotein cholesterol (HDL-c) decreased steadily (P<0.001). Average absolute reductions of these three parameters were –47.7 mg/dL, –44.6 mg/dL, and –0.8, respectively. No significant changes from baseline were observed in serum levels of triglycerides, HDL-c and bilirubin. The drug was suspended due to liver toxicity in 8 (4.4%) patients and due to muscle toxicity in 4 (2.2%) patients. All adverse reactions resolved rapidly after atorvastatin withdrawal.

CONCLUSIONS Atorvastatin (20 mg/day) administered to the subjects with NASH and hypercholesteremia significantly lowered LDL-C, TC, and TC/HDL-c and was safe and well tolerated in short term.

GW30-e0004

Short-term efficacy and safety of atorvastatin for the treatment of non-alcoholic steatohepatitis with chronic hepatitis B and hypercholesteremia

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OBJECTIVES To evaluate the efficacy and safety of atorvastatin in the treatment of NASH associated with chronic hepatitis B and hypercholesteremia in short term.

METHODS We conducted an observational study of 51 biopsy-proven NASH accompanied by chronic hepatitis B with serum low-density lipoprotein cholesterol (LDL-c) >160 mg/dL, who were treated with atorvastatin 20 mg daily. Serum lipids, hepatic enzymes, bilirubin, creatine phosphokinase (CPK) and hepatitis B virus DNA (HBV DNA) were prospectively measured 4, 12, and 24 weeks after the initiation of the drug.

RESULTS Over the 24-week period following atorvastatin initiation, serum levels of total cholesterol (TC) and LDL-c and the ratio TC/high-density lipoprotein cholesterol (HDL-c) decreased steadily (P<0.001). Average absolute reductions of these three parameters were –47.7 mg/dL, –44.6 mg/dL, and –0.8, respectively. No significant changes from baseline were observed in serum levels of triglycerides, HDL-c, bilirubin, or HBV DNA. The drug was suspended due to liver toxicity in 3 (5.9%) patients and due to muscle toxicity in 1 (2.0%) patient. All adverse reactions resolved rapidly after atorvastatin withdrawal.

CONCLUSIONS Our study supports atorvastatin (20 mg/day) as a reasonable therapy for NASH with chronic hepatitis B and hypercholesterolemia. This treatment was safe and well tolerated in short term. However, controlled trials are needed to further investigate and resolve this.

GW30-e0057

Neural stem cell-derived exosomes inhibit apoptosis of neurons induced by hypoxia neural cells

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OBJECTIVES To investigate whether neural stem cell-derived exosomes promote the viability and inhibit the apoptosis of neurons under cobalt chloride ($COCl_2$)-induced hypoxia in vitro.

METHODS The exosomes were isolated based on ultracentrifugation. The exosomal markers, ALG-2-interacting protein X (Alix) and tumor susceptibility gene 101 (TSG101) were identified by Western blot. The shape of exosomes was observed under transmission electron microscope (TEM). The size distributions of exosomes were analyzed by nanoparticle analysis (qNano). The neurons were exposed in $COCl_2$ at different doses (200–600 μmol/L) for 24 h. The exosomes were co-cultured with the neurons pre-treated with $COCl_2$. The viability and apoptosis of the neurons were measured by CCK-8 assay and TUNEL method.

RESULTS The exosomes released from the neural stem cells expressed exosomal markers Alix and TSG101. They also displayed a cupshaped appearance observed under TEM and their sizes were (95.0±23.5) nm (n=370). The neuronal viability was significantly inhibited by $COCl_2$ in a dose-dependent manner (P<0.05). After treatment with exosomes, the viability of the neuron pre-treated with $COCl_2$ was increased and the apoptotic rate was decreased (P<0.05).

CONCLUSIONS Neural stem cell-derived exosomes promote the viability and inhibit the apoptosis of rat neurons under hypoxia.

GW30-e0059

Fibroblast growth factor 21 attenuates diabetes-induced renal fibrosis by negatively regulating TGF-β-p53-Smad2/3-mediated EMT via activation of AKT

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OBJECTIVES Epithelial-to-mesenchymal transition (EMT) is required for renal fibrosis, which is a characteristic of diabetic nephropathy (DN). Our previous study demonstrated that fibroblast growth factor 21 (FGF21) prevented DN associated with the suppressing renal connective tissue growth factor expression, a key marker of renal fibrosis. Therefore, the effects of FGF21 on renal fibrosis in a DN mouse model and the underlying mechanisms were investigated in this study.

METHODS Type 1 diabetes was induced in C57BL/6J mice by intraperitoneal injections of multiple low doses of streptozotocin. Then, diabetic and non-diabetic mice were treated with or without FGF21 in the presence of pifithrin-α (p53 inhibitor) or 10-DEBC hydrochloride (Akt inhibitor) for 4 months.

RESULTS DN was diagnosed by renal dysfunction, hypertrophy, tubulointerstitial lesions, and glomerulosclerosis associated with severe fibrosis, all of which were prevented by FGF21. FGF21 also suppressed the diabetes-induced renal EMT in DN mice by negatively regulating transforming growth factor beta (TGF-β)-induced nuclear translocation of Smad2/3, which is required for the transcription of multiple fibrotic genes. The mechanistic studies showed that FGF21 attenuated nuclear translocation of Smad2/3 by inhibiting renal activity of its conjugated protein p53, which carries Smad2/3 into the nucleus. Moreover pifithrin-α inhibited the FGF21-induced preventive effects on the renal EMT and subsequent renal fibrosis in DN mice. In addition, 10-DEBC also blocked FGF21-induced inhibition of renal p53 activity by phosphorylation of mouse double minute-2 homolog (MDM2).

CONCLUSIONS FGF21 prevents renal fibrosis via negative regulation of the TGF-β/Smad2/3-mediated EMT process by activation of the Akt/MDM2/p53 signaling pathway.

GW30-e0103

Anxiety and depression in patients with newly diagnosed hematologic malignancy

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OBJECTIVES The aimed of the study is to evaluate the risks of anxiety and depression in patients with newly diagnosed hematologic malignancy and provide necessary professional support.

METHODS Patients with newly diagnosed hematologic malignancy were enrolled in the study. Demographic characteristics were noted and Hospital Anxiety and Depression Scale (HADs) was used to assess anxiety and depression. HADs is an assessment scale developed by Zigmond and Snaith to determine the risks and assess the severity of anxiety and depression. The questionnaire has a total of 14 items; seven of which measure anxiety and the remaining seven measure depression. Each item is scored from 0 to 3 points.

Results One hundred and five patients were included in the study. 42 (40.0%) of these patients were diagnosed with acute myeloid leukemia (AML), 28 (26.7%) with acute lymphoblastic leukemia (ALL), 10 (9.5%) with chronic myeloid leukemia (CML), 17 (16.1%) with non-Hodgkin's lymphoma (NHL), 8 (7.6%) with multiple myeloma (MM). Median age of the patients was 39 (range: 17–65). Forty one patients (39.0 %) were female and 64 (60.9%) were male. Anxiety evaluation revealed that 48.5% of all patients in the study experienced anxiety. 52.2% of the female and 46.5% of male patients had anxiety, the difference was not statistically significant (P>0.05). Depression evaluation revealed that 73.1% of all patients in the study. 81.2% of the female patients had depression and it was 65.6% in male patients (P>0.05). Correlation analysis revealed a positive correlation between anxiety and depression (r=0.855; P<0.01).

CONCLUSIONS Percent of anxiety and depression in newly diagnosed hematologic malignancy patients is quite high. Assessing anxiety and depression in these patients is necessary during the course of treatment. A professional psychological support in the medical team is important for the treatment of these patients.

GW30-e0118

Postoperative complication of incidence of heart failure and cardiac mortality after surgical operation of intertrochanteric femoral fractures using two different internal fixators

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OBJECTIVES Patients of surgical operation of intertrochanteric femoral fractures are undergoing at risk for heart failure and cardiac mortality. The two internal fixators were more common used in recently years, which were Proximal Femoral Nail Antirotation (PFNA) and Proximal femoral locking plates. The objective of our work is to identify the postoperative complication of incidence of heart failure and cardiac mortality in surgical patients of intertrochanteric femoral fractures using the two different internal fixators.

METHODS During the same hospital stay, from October 2011 to October 2016, 62 patients of intertrochanteric femoral fractures (more than 70 years) were treated with PFNA (Group A), including 10 males and 18 females. Another 34 patients were treated with Proximal femoral locking plates (Group B) including 15 males and 19 females. The average follow-up period was 20 months, ranging from 13 months to 36 months. Follow-up assessment included the operation time, amount of bleeding, the incision length, postoperative complication. Independent samples t-test, grade data used rank sum test were used to compare the two groups.

RESULTS Twenty five cases and 24 cases were successfully followed up in Group A and Group B respectively. In Group A, the operation time was (81.3±5.3) min, the amount of bleeding was (128.5±12.6) mL, the length of incision was (7.2±2.3) cm, three cases reported for heart failure, need to send to the internal ward for more treatment. One case died of cardiac cause more than 6 months. One case for short femoral neck. One case for coxa vara. In Group B, the operation time was (93.5±4.7) min, the amount of bleeding was (228.3±14.6) mL, the length of incision was (17.2±1.8) cm, five cases reported for heart failure within 3 months, three cases died of cardiac cause within 6 months, one case for incision infection, three cases for coxa vara. Group A was superior to Group B in amount of bleeding and length of incision. The difference of postoperative complication between the two groups was statistically significant.

CONCLUSIONS Patients of intertrochanteric femoral fractures who undergo surgery had high cardiac mortality rate, no matter how the internal fixator is PFNA or Proximal femoral locking plates. Compare to the patients who take the operation with Proximal femoral locking plates, the patients who had the operation with PFNA had less amount bleeding, less incision length, less risk of the incidence of heart failure and cardiac mortality.

GW30-e0138

Patient characteristics and clinical determinants associated with cardiomyopathy and the effect of therapeutic compliance on quality of life

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OBJECTIVES To determine the prevalence of CM and its subtype, patient characteristics, clinical determinants associated with cardiomyopathy and the effect of therapeutic compliance on QoL.

METHODS We conducted the study in two phases. Phase I was a retrospective set-up that involved obtaining online medical records of cardiomyopathy patients, both ischemic and non-ischemic cases from a tertiary hospital in Malaysia. After the enrolment process was completed the study moved towards phase II that comprises of an intervention involving therapeutic compliance over a follow-up period of 6 months.

RESULTS The mean age of our study population was 52.25±14.28 years (range 17–84 years) with 52.3% of patients aged over 50 years. The proportion of male patients was slightly higher in existence (61.5%) in comparison to females, while ethnic distribution focused vastly on Malay population (56.5%) followed by Chinese (26.2%) and Indian (18.5%). Majority of the patients were non-smokers (60%) while 23.1% active smokers. There was a slight difference in ischemic and non-ischemic cases and 84.6% of the cases were reported to be DCM.

CONCLUSIONS Despite having several studies and advancements in developed countries, cardiomyopathy still holds insufficient knowledge and awareness in the context of Malaysian healthcare system; thereby it's essential to further identify the associated factors and carry out preventive measures through utilisation of therapeutic compliance as well as monitor the quality of life among cardiomyopathy patients.

GW30-e0308

The study of cardiac safety and the effectiveness of long-term therapy with sildenafil in men with erectile dysfunction and coronary heart disease

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OBJECTIVES Study of the efficacy and safety of course therapy with low doses of sildenafil in men with coronary heart disease (CHD) in the group of low and medium risk according to the Priston consensus and erectile dysfunction (ED).

METHODS An open, randomized, and comparative clinical study included 120 men aged 40–69 years with stable angina (CHD), low and medium risk according to the Priston consensus, and ED. Men with CHD and ED by randomization are divided into two groups comparable by main indicators. The main group (n=63), along with the previous basic therapy of CHD, received sildenafil in a dose of 25 mg 3 times a week. After 1 month, the dose of the drug was increased to 50 mg. The control group (n=57) received only the previous basic therapy of CHD. The duration of therapy and observation was 6 months. Before and after the study, the dynamics of ED, urination symptoms, severity of chronic stress, hemodynamic, anthropometric parameters and ECG parameters were evaluated.

RESULTS At the end of the course therapy with sildenafil, the ED (according to the ICEF questionnaire) improved by 50%, which turned out to be statistically significant both in comparison with the baseline and with the control group (P<0.01). Against the background of the treatment with sildenafil, there is a decrease in urination symptoms, assessed using the IPSS scale by an average of 30% (P><0.05), whereas in the control group the dynamics of the total indicator on the above questionnaire are not monitored. According to the survey in the main group, there is a decrease in the level of chronic stress by 34% (P><0.05). In the control group, the dynamics of the severity of stress was not reliable. An analysis of the ECG at rest against the background of therapy with sildenafil at a dosage of 50 mg per day did not reveal negative dynamics in the frequency of rhythm disturbances, conduction and myocardial blood supply indices. In both groups, the concentration of total cholesterol, fasting glucose, fibrinogen in the blood, as well as blood pressure and waist circumference did not change during the course of therapy.

CONCLUSIONS PDE type 5 inhibitors in small doses as a course of therapy can be considered for the treatment of ED in patients with CHD, low and medium risk according to the Priston consensus as part of complex therapy.

GW30-e0333

Same day discharge following percutaneous coronary intervention: our patient and family experiences

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OBJECTIVES The aim of this study was to explore patient and family experiences during the introduction of same day discharge (SDD) following percutaneous coronary intervention (PCI).

METHODS This was an interpretative study undertaken in the cardiac service of an Australian tertiary hospital. Semi-structured phone interviews with 31 patients and 23 family members were conducted. Binary responses were coded and quantified in numbers (percentages). Content analysis was used to analyse the qualitative data.

RESULTS Thirty-one patients who were initially eligible for SDD before the PCI procedure participated in the study, of whom, 17 went home the same day. Approximately 50% patients and family members were informed of the possibility of SDD. Two-thirds of patients received discharge instructions while

most family members did not. Content analysis revealed that most patients and family members considered SDD as a preferred option because of feeling more comfortable at home and more logistically convenient. Several SDD patients and family members expressed uncertainty towards SDD as feeling nervous, overwhelmed and apprehensive. Only those patients who were initially eligible for SDD but subsequently required overnight admission following PCI and their family members related negative experiences of SDD due to either feeling scared of potential complications or fearing of being blamed due to perceived lack of ability to look after their loved ones at home following SDD from the family perspective.

CONCLUSIONS Most patients and family members perceived SDD as a good option. The identified experiences provide guidance for healthcare providers in developing strategies to promote positive hospital experiences of SDD for patients and family members.

GW30-e0495

Effect of PPARγ agonist on cholesterol content in vascular smooth muscle cell derived foam cells

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OBJECTIVES To determine the effect of PPARγ agonist, Pioglitazone (PG) on cholesterol content in smooth muscle cell foam.

METHODS 1. Primary VSMC were extracted from the aorta of C57BL/6J mice using tissue affixing method and identified; 2. ox-LDL induced VSMC to form foam cell and identified foam cell by oil red O staining; 3. At 24 h after using different concentrations of Pioglitazone (0, 5, 10, 20 μmol/L) on the vascular smooth muscle cell derived-foam cells, The levels of cholesteryl esters (CE) were determined by a cholesterol content assay kit; Western blot and qRT-PCR was used to detect cholesterol efflux end regulator ATP binding cassette transporter A1 (ABCA1); 4. The degree of foaming of smooth muscle cells in each group was detected by oil red o staining and oil red extraction experiments.

RESULTS 1. PPARγ agonist, PG could significantly reduce the content of cholesteryl esters (CE) in the vascular smooth muscle cell derived-foam cells, and increase the mRNA and protein expression of ABCA1; 2. Oil red O staining showed that ox-LDL could promote lipid accumulation in vascular smooth muscle cell derived-foam cells, but PPARγ agonist, PG could inhibit its effect.

CONCLUSIONS PPARγ agonist, PG may decrease the content of cholesterol ester in vascular smooth muscle cell derived-foam cells by upregulating the mRNA and protein expression of ABCA1.

GW30-e0527

Prolonged versus intermittent infusions of antibiotics for the treatment of acute infections

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OBJECTIVES Acute and severe infections are an absolute indication for the use of intravenous broad-spectrum antibiotics. However, previous studies have found inconsistent clinical advantages of prolonged (extended (≥3-hour per infusions)/continuous (24-hour fixed-rate infusions)) over intermittent (6, or 8, or 12 interval hours infusion) infusion. The clinical superiority between prolonged and intermittent infusion in treating acute and severe infections thus continues to be elusive. We conducted a meta-analysis to summarize all published randomized controlled trials (RCT), prospective and retrospective observational studies to determine whether prolonged infusion, as opposed to intermittent infusion, correlate with a decrease in mortality and better outcome in clinical treatment.

METHODS We performed a literature search using MEDLINE (source PubMed, January 1, 1966–August 31, 2018) and EMBASE (January 1, 1980–August 31, 2018) with no restrictions to collect RCTs and observational studies comparing prolonged infusion with intermittent infusion of the same antibiotics administered intravenously in hospitalized adult patients. A total of 43 studies with 3610 patients were identified that were eligible for inclusion in the meta-analysis, comprising 30 RCTs, 5 prospective comparative studies and 8 retrospective observational studies published between 1977 and August 2018.

RESULTS In comparison with intermittent infusion, prolonged infusion of antibiotics was associated with a reduction in all-cause mortality (pooled relative risk [RR]=0.77, 95% confidence interval [CI]=0.66–0.89) and improvement in clinical cure (RR=1.11, 95% CI=1.04–1.19), which was also observed in subgroup analyses such as non-RCTs (mortality, RR=0.63, 95% CI=0.48–0.81; clinical cure RR=1.33, 95% CI=1.13–1.57) or studies with patients and APACHE II scores ≥15 (mortality, RR=0.74, 95% CI 0.63–0.89; clinical cure RR=1.19, 95% CI=1.071–0.32). Moreover, in RCTs, mortality (RR=0.86, 95% CI 0.72–1.03) between the two dosing strategies was not remarkably changed but clinical cure (RR=1.07, 95% CI=1.01–1.13) showed a significant advantage for prolonged infusion over intermittent infusion. Additionally, no significant differences in mortality between the two dosing strategies was found (RR=0.87, 95% CI=0.70–1.09) but a distinct improvement in clinical cure was observed (RR=1.14, 95% CI=1.02–1.28) in the prolonged infusion group for septic patients. In the two infusion modes, statistically significant severe adverse events were not reported (RR=0.83, 95% CI=0.62–1.13).

CONCLUSIONS Better outcomes in hospitalized patients, especially in those who were critical ill, were reported in prolonged infusion of intravenous antibiotics compared with traditional intermittent infusion.

GW30-e0537

Using deep learning method to assess the severity of coronary artery stenosis in young adults

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OBJECTIVES To explore the early coronary stenosis warning effect of deep learning (DL) model based on routine physical examination such as blood routine and urine routine.

METHODS Two hundred and twenty patients aged less than 45 years who underwent coronary angiography for chest pain from July 1, 2017 to December 30, 2018 were enrolled in this study. There were 191 males and 29 females. The body height, weight, blood pressure, blood sugar, total cholesterol (TC), uric acid (UA) and homocysteine (Hcy) were measured. Several machine learning models of these indexes, such as multiple linear classification, support vector machine and deep learning model, were established. Machine learning and classification were carried out according to the results of coronary angiography. The classification results were compared with Gensini score of coronary angiography.

RESULTS By comparing the models, it is found that the accuracy of the left-one cross-validation of DeepFM model is 99%, which is better than other models such as multivariate linear model and support vector machine model. After the establishment of the model, this paper explores the possible causes of coronary heart disease in young and middle-aged people through the sensitivity analysis of various indicators and the influence of the combination of independent variables on the model.

CONCLUSIONS The model established by DeepFM algorithm can accurately predict the possibility of coronary artery disease in patients through routine physical examination indicators, which is similar to the Gensini score of coronary angiography. The model has high correlation, accuracy and availability, and strong generalization. Through the analysis of the model, we found that homocysteine (Hcy) and other indicators may be related to the occurrence of coronary heart disease in young and middle-aged people.

GW30-e0615

Is sleep disturbance really separate from acute mountain sickness? Results from large cohort of Chinese young men

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OBJECTIVES The 1993 Lake Louise Score Questionnaire (LLSQ) has been widely used to be diagnostic criteria of acute mountain sickness. This questionnaire mainly evaluated 5 symptoms (Headache, Dizziness/Lightheadedness, Gastrointestinal symptoms, Sleep disturbance, Fatigue and/or weakness) in high altitude. LLSQ has been reported to be one factor structure with all five items, and sleep disturbance was weakly associated with the other 4 items of LLSQ. The revised 2018 Lake Louise AMS score removed the sleep disturbance item from the 5 symptoms. However, the external validity of this conclusion has not been explored in Chinese population. Given that male soldiers are mainly acute high-altitude exposure population, we aimed to explore the factor structure and internal insistency of LLSQ in Chinese young male soldiers.

METHODS Chinese male soldiers living at lower altitudes were recruited for altitude-training mission. Three independent cohorts were observed in this study. Group A, 1026 soldiers traveled from 500 m to 3700 m by airplane within 2.5 hours, observation were performed after arriving 3700 m on the next day (n=1026), the 3rd day (n=567), the 5th day (n=530) and the 7th day (n=490). Group B, 308 participants traveled from 400 m to 3450 m by bus in 4 days, observation were performed after exposure to high altitude on the next day. Group C, 349 participants adapted 33 days at an intermediate high altitude of 3650 m and then ascended to 4400 m in 3 hours by car, observation were also performed on the next day after exposure to high altitude. Exploratory factor analysis (EFA)

and confirmatory factor analysis (CFA) were performed to explore the factor structure of LSSQ. Ordinal alpha coefficient was calculated to determine the internal consistency.

RESULTS One thousand nine hundred and sixty six individuals were enrolled in this survey, the mean age was 22.6 years, and 86.8% of them were Han. Only one factor with eigenvalue greater than 1.0 was recognized in each situation (group A, B, and C, and each day in group A). Thus the one-factor structure with 5 items was further introduced into CFA, and all of the CFA models had acceptable fit. The standardized factor loadings of the 5 items were similar in all situations. There were moderate or weak polychoric correlations between the items. The ordinal alpha coefficient for LLSQ did not show notable difference in each situation. Deleting the item of sleep disturbance from LLSQ generated lower alpha coefficients.

CONCLUSIONS Our results did not support deletion sleep quality item from the 5 items at least in Chinese young men. More research in different populations should be performed in the future.

GW30-e0633

The relationship between bronchopulmonary dysplasia and nutritional intake in very low birth weight infants with postnatal growth failure

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OBJECTIVES The study aimed to explore the relationship between bronchopulmonary dysplasia (BPD) and nutritional intake in very low birth weight infants (VLBWIs) with postnatal growth failure (PGF) during hospital stay.

METHODS We retrospectively collected the data of VLBWs (birth weight of <1500 g, gestational age of <37 weeks, and hospitalized within 24 h of birth) admitted in the First Affiliated Hospital of Sun Yat-sen University from June 1, 2010 to March 30, 2019. All eligible VLBWIs were divided into 2 groups according to the change of Z-score (Δweight SDS) between birth and correct gestational age at discharge for body weight. We retrospectively reviewed baseline characteristics, nutrition management, incidence of BPD between not postnatal growth failure (notPGF) group (Δweight SDS ≥1.0) and postnatal growth failure (PGF) group (Δweight SDS <1.0) in VLBWIs during hospital stays.

RESULTS A total of 248 infants (notPGF group=118, PGF group=130) met the inclusion criteria. No significant differences were found in baseline characteristics between the two groups (All P>0.05). The notPGF group had lower incidence of BPD (34.7 vs. 51.5%, respectively; χ^2=7.10, P<0.01). The notPGF group received higher parenteral lipids from day 5 to day 7 [(d5: (2.05±0.79) vs. (1.62±0.93) g/kg/d, *t*=3.103; d6: (2.24±0.67) vs. (1.79±0.83) g/kg/d, *t*=3.521; d7: (2.44±0.88) vs. (2.09±0.92) g/kg d, *t*=2.917, P<0.01) and higher enteral feeding volume from day 5 to week 5 than the PGF group [d5: (22.11±18.21) vs. (14.91±13.94) mL/kg/d, *t*=2.103; d6: (25.93±13.42) vs. (17.89±15.72) mL/kg/d, *t*=2.984; d7: (31.50±11.73) vs. (20.77±19.08) mL/kg/d, *t*=2.896; w2: (64.10±31.30) vs. (39.78±25.80) mL/kg/d, *t*=3.572; w3: (85.98±37.28) vs. (56.69±27.60) mL/kg/d, *t*=3.397; w4: (108.90±42.59) vs. (79.49±37.66) mL/kg/d, *t*=3.154; w5: (120.70±44.72) vs. (90.34±40.68) mL/kg/d, *t*=2.911; w6: (123.79±38.44) vs. (102.68±41.31) mL/kg/d, *t*=1.956; P<0.05 or P<0.01].

CONCLUSIONS This study showed that BPD was closely related to greater nutritional intakes. Adequate parenteral lipid and energy at the first week of life and earlier enhanced enteral feeding volume might significantly improve the VLBWIs' weight Z-scores and reduce the incidence of BPD.

GW30-e0637

Artificial movement in rats induced by different temperatures cross Experimental study of the pattern of muscle syndrome dissolution

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OBJECTIVES Rhabdomyolysis syndrome is a medical emergency, with a complex etiology, sudden onset, complex diagnostic procedures that can lead to clinical features of multiple complications. In recent years, its presence is gradually coming into view, appeared in a variety of medical events in the news. Corresponding rock climbing, mountaineering, skiing, surfing and extreme sports related to the outside temperature, leading to rhabdomyolysis cases is also increasing.

METHODS This study selected 40 SD rats after feeding in their natural environment adaptability week, the rats were randomly divided into four groups: normal control group, the low exercise group swimming, swimming group at room temperature, heat swimming group. In addition to the experimental group started the other three groups adaptive swimming training once a day, the time increments from 5 minutes to 30 minutes, then began a formal swimming.50 cm×50 cm×50 cm training conducted sink, static depth 40 cm, once started swimming every morning. The experiment was conducted 3 months, during which rats were measured immediately after every experiment rectal temperature, body weight was measured once every 3 days, after 3 months for the three groups of rats sacrificed immediately after exhaustive exercise, peritoneal venous blood of kidney and indicators gastrocnemius organizations rat blood creatine kinase levels, serum creatinine level, myoglobin levels, muscle fine organizations.

RESULTS When the core temperature of hot and cold environment movement in rats with changes in the external environment changes, the ambient temperature affect the body's core temperature by increasing the degree of rhabdomyolysis syndrome. Hot and cold environment than the normal temperature environment, the more impact CK and MB level, in other words, high-intensity exercise in a cold environment for a long time, for more serious damage to muscle tissue. Of course, large temperature environments intensity exercise the same muscle tissue damage. Serum creatinine level indicates the degree of kidney damage, extreme environments significantly elevated serum creatinine movement, the environmental movement, said the cold damage the kidneys, may cause acute renal failure. Through the analysis of various physiological and biochemical indicators of operating in extreme environments will cause serious damage to the body. Performance in terms of damage to the core temperature changes, organ tissue. All test indicators, data were processed by statistical methods.

CONCLUSIONS Low-temperature environment during exercise in rats core temperature will drop, blood ck, serum creatinine, myoglobin levels higher than the normal temperature group, indicating that the movement of the body temperature environment in muscle tissue damage and renal function.

A sharp rise in high-temperature environments ck, serum creatinine, myoglobin indicators compared with other groups of rats blood, indicating that the thermal environment in the body from exercise-induced rhabdomyolysis syndrome highest probability.

Groups of rats at room temperature in high-intensity exercise in blood ck, serum creatinine, myoglobin levels higher than the control group, indicating that at room temperature, high-intensity exercise will also cause damage, but a lesser degree of injury.

Induced rhabdomyolysis syndrome produce large intensity exercise dominant, but in extreme environments Exacerbate rhabdomyolysis syndrome generation.

GW30-e0668

Adipose-derived stem cells restore fertility of mice with premature ovarian failure

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OBJECTIVES To investigate if the role of Adipose-Derived Stem Cells (ADSCs) in soluble collagen scaffolds can restore fertility of mice with Premature Ovarian Failure (POF).

METHODS Four groups of mice were involved in our experiment: A. cyclophosphamide induced POF mice treated with ADSCs only, B. POF mice treated with ADSCs in soluble collagen scaffolds, C. wild type C57BL/6J mice and D cyclophosphamide induced POF mice injected with saline. Estrous cycle were closely observed. The estradiol level in serum and the expression of Fox protein family 3 (Foxp3), Interleukin-10 (IL-10), B-cell lymphoma-2 (Bcl-2), Tumor suppressor P53 (P53) – all four factors are related to apoptosis-in ovary were detected.

RESULTS Mice group A, B and D showed estrous cycle disorder. The level of estradiol in group D is lower than group C. Group A showed remarkable higher level of estradiol than group D, even higher than group C. Group B exhibited an increase trend of estradiol, but didn't restore to control level. Comparing to group C, mice in group D showed significantly decreased level of Foxp3, IL-10, Bcl-2 and increased of P53. Except the expression of IL-10 didn't restored by ADSCs, other three factors showed similar level between A and C, which means ADSCs help to improve the damage caused by cyclophosphamide in mice. ADSCs in soluble collagen scaffolds increased the level of Foxp3, IL-10 significantly.

CONCLUSIONS ADSCs might inhibit apoptosis in mice with POF. The function of ADSCs in soluble collagen scaffolds is not determined because we failed to set a soluble collagen scaffolds control group.

GW30-e0741

Questioning the role of cardiac magnetic resonance imaging as the gold standard for echocardiographic left ventricular 2D and 3D volume measurements

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OBJECTIVES Cardiac magnetic resonance imaging (CMRI) is thought to be the most accurate imaging method to measure left ventricular (LV) diastolic

(EDV) and systolic (ESV) volumes due to its 3D approach independent of LV geometry, and superior imaging quality. A number of studies have shown variable underestimation (compared to CMRI) of LV volumes by 2D echocardiography (Echo) – less with 3D measurements – explained by the geometrical assumptions inherent in the 2D methods. New generation Echo systems have greatly enhanced 2D imaging quality and 3D image resolution. To compare CMRI with Echo measurements of EDV and ESV obtained using standard 2D (Simpson) and 3D (mesh) formulas, and a multislice 3D method simulating CMRI measures.

METHODS In 10 normal subjects and 30 patients with coronary artery disease and dilated, hypertrophic and amyloidotic cardiomyopathy (age 21–81 y., HR 47–103 bpm), undergoing CMRI followed (48 h) by 2D (Vivid 9 GE) and 3D (6-beats full volume acquisition) Echo, we measured EDV and ESV using: (1) 2D biplane disk summation formula (Echo2D); 3D mesh method (Echo3D); 3D "Multislice" method (Echo3Dm) by manually tracing 9 LV short-axis endocardial borders, and measuring LV long axis. Bland-Altman's bias and 95% CI of the CMR-Echo2D, CMR-Echo3D, and CMR-Echo3Dm differences were obtained, and we analysed the influence on the differences of: M-mode LV mass; 2D LV sphericity index; LV contractility (Tei index); LV longitudinal systolic function (mitral annulus tissue Doppler); LV filling pressures (EACVI algorithm); maximum left atrial volume; pulmonary systolic pressure (tricuspid regurgitation); TAPSE.

RESULTS Mean EDV, ESV and EF were respectively: CMRI=206±78 mL, 124±83, 44±16%; Echo2D=130±59 mL, 73±55, 49±16%; Echo3D=129±50 mL, 74±47, 46±15%; Echo3Dm=131±51 mL, 78±48, 43±16%. Echo2D, Echo3D and Echo3Dm correlated highly with CMRI (EDV, r=0.91–0.93, P<0.001; ESV, r=0.97–0.98, P<0.001; EF, r=0.8–0.9, P<0.001), but bias (95% CI) was high for EDV, ESV and EF, respectively: Echo2D=–85 mL (–21, –149), –51 mL (14, –117), 4.5% (16, –7); Echo3D=–86 mL (–13, –159), –54 mL (29, –137), 3% (26, –20); Echo3Dm=–80 mL (–8, –151), –45 mL (29, –120), 1% (–17, –19). Bland–Altman's graphs showed that volume bias increased in parallel with LV dilatation. The CMRI-Echo2D difference correlated positively with LV mass index (r=0.54, P=0.15), sphericity index (r=0.75, P<0.001) and Tei index (r=0.67, P=0.001): thus increase in bias increased with LV dilatation, sphericity, and reduced contractility.

CONCLUSIONS Echo 2D and 3D volumes are similar, but there is a marked difference between CMR and Echo volumes, including a 3D CMR-mimicking formula, which is proportional to LV dilatation. Our data question the notion that ultrasound volumes are underestimated secondary to geometrical assumptions in calculations, and advocate caution in the use of CMR as a "gold standard" technique when accurate evaluation of both 2D and 3D LV volumes is required.

GW30-e0748

Estimation of pulmonary wedge pressure by an algorithm based on noninvasively measured pulmonary diastolic pressure in cardiac patients independent of left ventricular ejection fraction

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OBJECTIVES Pulmonary artery diastolic pressure (PADP) correlates closely with pulmonary wedge pressure (PAWP), therefore we sought to evaluate whether an algorithm based on PADP estimation by the Doppler pulmonary regurgitation (PR) end-diastolic gradient (PRG) may aid in assessing PAWP in cardiac patients with reduced or preserved left ventricular (LV) ejection fraction (EF).

METHODS Right heart catheterization, with estimation of PAWP, right atrial pressure (RAP), and PADP, and Doppler echocardiography were carried out in 183 consecutive patients with coronary artery disease (n=63), dilated cardiomyopathy (n=52) and aortic stenosis (n=68). One-hundred and seventeen patients had LVEF<50%. From tricuspid regurgitation velocity (TRV) and PR velocity, the pressure gradients across the tricuspid and pulmonary valves were measured. Doppler-estimated PADP (e-PADP) was obtained by adding the estimated RAP to PRG. An algorithm based on e-PADP to predict PAWP, that included TRV, left atrial volume index and mitral E/A, was developed and validated in derivation (n=90) and validation (n=93) subgroups.

RESULTS Both invasive PADP (r=0.92, P<0.001) and e-PADP (r=0.72, P><0.001) closely correlated with PAWP, and e-PADP predicted PAWP (AUC: 0.85, CI: 0.79–0.91) with a 94% positive predictive value (PPV) and a 55% negative predictive value (NPV), after exclusion of 5 patients with pre-capillary pulmonary hypertension. The e-PADP-based algorithm predicted PAWP with higher accuracy (PPV=94%; NPV=67%; accuracy=85%; kappa: 0.65, P><0.001) than the ASE-EACVI 2016 Recommendations (PPV=97%; NPV=47%; accuracy=68% undetermined=18.9%; kappa: 0.15, P><0.001).

CONCLUSIONS An algorithm based on noninvasively e-PADP can accurately predict PAWP in patients with cardiac disease and reduced or preserved LVEF.

GW30-e0749

Ischemic stroke in patient with atrial septal defect and Eisenmenger syndrome: a case-report

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OBJECTIVES An atrial septal defect (ASD) is a congenital heart disorder that is the second most commonly found after ventricular septal defect. In general, ASD rarely cause any significant symptoms, hence most cases of ASD are diagnosed for the first time during adulthood. ASD can now be managed either by surgery or closure with catheterization and with high success rate. However, ASD in adulthood still poses a challenge for clinicians because of other comorbidities and complications caused by ASD itself. In adulthood, certain complications can occur due to these comorbidities, one of which is ischemic stroke. Ischemic stroke in ASD can occur due to arrhythmias, residual shunts, hyperviscosity that can be found in ASD patients with Eisenmenger syndrome, and other cardiac abnormalities. According to a study by Mandalenakis et al. the risk of these patients having an ischemic stroke/hazard ratio is 10.8% (95% CIM, 8.5–13.6). Ischemic stroke incidence was reported as 0.5% in pediatric patients and young adults with ASD in Sweden. This is a factor that worsens the prognosis of patients with ASD. Therefore in this article we discuss the clinical presentation, treatment, and prognosis of atrial septal defect with new onset of ischemic stroke in adult patients and give insight to clinicians how to manage patients with ASD and ischemic stroke.

METHODS Case Report.

RESULTS A 25-year old man, came to the emergency room at the Jakarta Heart Center accompanied by his parents complaining of bluish skin and shortness of breath a week before going to the emergency room. From the results of the physical examination, the patient presented with cyanosis, BP: 138/82 pulse: 92×/minute, RR: 25×/minute SpO2: 54% room air. On the physical examination of the lungs, the rales are presented both of the lung fields although minimal, while the examination of the heart showed no abnormalities. In all four extremities showed clubbing. Echocardiography showed the presence of secundum atrial septal defect, balance shunt, severe tricuspid regurgitation, high probability of PH, and mild PR. The electrocardiogram shows RVH and biatrial enlargement. Blood gas analysis results showed a respiratory acidosis. During the fifth day there was a decrease in consciousness accompanied by right hemiparesis. The head CT scan shows the presence of an ischemic stroke in the area of the left hemisphere.

CONCLUSIONS Adult patients with ASD are at a risk for ischemic stroke. It had hazard ratio 10.8% (95% CIM, 8.5–13.6) Therefore, risk stratification is needed to prevent the emergence of these complications which can worsen the patient's prognosis.

GW30-e0810

Does menopause have an impact on plasma HDL-C levels? a systematic review and meta-analysis

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OBJECTIVES Whether HDL-C levels declined in postmenopausal women is still unclear, with some studies showing decreased HDL-C levels in postmenopausal women while other studies suggesting no reduction compared with premenopausal women. We performed this present systematic review and meta-analysis trying to clarify this controversy. Design: Systematic review and meta-analysis.

METHODS Searches were performed in PubMed, EMBASE, Cochrane Library and Web of Science for articles published between 2008 and 2018. Studies reporting HDL-C, LDL-C, TC and TG levels of both postmenopausal and premenopausal population were included. The standard mean difference with a 95% confidence interval was estimated in a random effects model.

RESULTS Eleven cross-sectional studies and two cohort studies met the inclusion criteria, which included 4601 postmenopausal women and 6901 premenopausal women. There is no significant difference in HDL-C levels between postmenopausal and premenopausal women (SMD=0.012, 95% CI: –0.243 to 0.259, P=0.925), which is not affected by districts, TC, TG and LDL-C levels in meta-regression analysis. However, HDL-C levels were significantly decreased in a larger sample (SMD=–0.212, 95% CI: –0.413 to –0.011, P=0.039) and a publication year before 2012 in the subgroup analysis in postmenopausal women.

CONCLUSIONS No difference was found in this first meta-analysis researching on HDL-C levels between pre- and postmenopausal women, whereas, in large population studies, postmenopausal women have lower HDL-C levels

compared to premenopausal women. Prospective studies with large population on HDL-C levels as well as HDL functions in menopause status are imperative in the future.

GW30-e0857

Medical staff's attitude to shared decision-making and the use of decision aids: a nation-wide cross-sectional survey

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OBJECTIVES (1) To investigate medical staff's opinion on shared decision-making (SMD) and evidence-based Decision Aids (DAs); (2) To analyze factors influencing their attitudes.

METHODS This is part of a cross-sectional survey conducted in 52 secondary and tertiary hospitals from 32 cities of 11 provinces and 3 municipalities across mainland China. Stratified multi-stage sampling is used. Hospitals are selected based on regions of different economic development (i.e., the East, the Middle, the West and the Northeast). A self-designed paper questionnaire is drafted based on comprehensive literature review and an expert consensus meeting. This part of the survey includes 4 questions regarding medical staff's opinion on having patients acquire decision-specific evidence, on the use of DAs, on the value of disseminating evidence-based DAs, and on their understanding of all stakeholders necessary to be involved in a clinical decision-making. Statistics are described using frequencies and percentages. Preliminary exploration of possible variables influencing attitudes is performed by Spearman rank correlation analysis. Analyses are conducted using the SPSS 14.0 software. This study is funded by the National Natural Science Foundation of China (Grant No.81603495) and the National Science and Technology Major Project (Grant No. 2018ZX09734002).

RESULTS One thousand nine hundred and eighty-four questionnaires are distributed from July 2018 to January 2019. One thousand seven hundred and thirty two participants respond (response rate is 87.3%) and 1415 complete questionnaires (effective rate is 81.7%). 46.6% participants believe patients should acquire evidence regarding the decision in any circumstance. Only 1.7% regard it as unnecessary. 90.6% participants support the use of DAs among patients. Over half of the respondents believe the use of DAs could have positive outcomes, including promoting guideline uptake, easing patient-physician tensions, and enhance work efficiency.

CONCLUSIONS We learn from correlation analysis that doctors with higher education, higher professional titles and longer working years are more likely to share decision-specific clinical evidence with the patient. Also they are more likely to think positively on the use of evidence-based DAs. The current understanding of all stakeholders of a clinical decision-making needs to be broadened.

GW30-e0911

CB1 receptor improve the outcome of Win55, 212-2 pharmacological hypothermia after cardiopulmonary resuscitation through ERK in rats

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OBJECTIVES To investigate whether CB1 receptor improve the outcome of Win55, 212-2 pharmacological hypothermia after cardiopulmonary resuscitation through extracellular signal-regulated kinase (ERK) pathway.

METHODS Cardiac Arrest (CA) was induced by transoesophageal ventricular pacing in Sprague-Dawley rats. Five minutes after onset of CA, cardiopulmonary resuscitation (CPR) was started. At 5 min post-resuscitation, 40 animals were randomized into 3 groups (n=10 in each group): (1) Win55, 212-2 group (W group); (2) Control group (C group); (3) Win55, 212-2 + CB1 antagonist SR141716A group (W+S1 group). Animals received SR141716A (5 mg/kg) or placebo. After 30 min of ROSC, animals in drug groups were received continuous intravenous infusion of Win55, 212-2 (1 mg/kg/h) for 4 h while which in control group were received 5% DMSO. Brains were harvested for detecting p-ERK 1/2 level at 24 h after ROSC respectively.

RESULTS Temperatures of rats in Win55, 212-2 group decreased from 37°C to 34°C in 4 hours, which could be blocked by CB1 antagonist SR141716A. p-ERK1/2 in the W+S1 group decreased significantly than that in W group.

CONCLUSIONS CB1 receptor improved the outcome of Win55, 212-2 pharmacological hypothermia after cardiopulmonary resuscitation through ERK pathway.

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