in Sniper and Simplicity group compared with sham group. However, there is no difference in the BP between Sniper and Symplicity groups. There were no significant changes in serum levels of creatinine and urea. Renal nerves were significantly destroyed in Sniper and Simplicity group. Additionally, there was no significant stenosis of renal artery at 12-week angiographic follow-up.
Conclusions: Catheter-based RDN with the Sniper or Symplicity system lowers BP in hypertensive mini-pigs without a significant renal dysfunction and stenosis of renal artery.

GW25-e4419

Polymer-free dual drug-eluting stents improve endothelialization of stenting coronary artery in a porcine model and the mechanism

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Objectives: To evaluate the endothelialization level of the polymer-free dual drug-eluting stents (DDES) compared to bare metal stents (BMS), polymer-free probucol stents (PES) and polymer-free sirolimus stents (SES) which has been used clinically in a overexpansion porcine coronary model, demonstrating the potential superiority in DDES group with the mechanism of homing more endothelial progenitor cells on local stenting coronary artery.
Methods: Total 160 stents of 4 types-BMS, polymer-free probucol stents (PES), SES and DDES-were randomly assigned and placed in 80 pigs (two stents per pig). At 14 days, 28 days, 90 days and 191 days after implantation, quantitative coronary analysis (QCA), intravascular unltrasound (IVUS), optical coherence tomography (OCT) were repeated on 20 pigs respectively, then stenting coronary arteries were collected after sacrifice the pigs for further study, one part of each artery for scanning electron microscope (SEM), histomorphology and histopathology, the other part for analysising the relative expression quantity of CD31, CD34 and CD133 on mRNA and protein level.
Results: There were not significant differences in lumen loss of QCA, neointima area of IVUS, OCT and HE stain, neointima volume of IVUS, injury scores, inflammation scores and endothelialization scrores of HE stain at the 4 endpoint among the 4 groups. Struts coverage percentage of OCT in PES group (59.37%±22.68%) was higer than SES group (20.11%±9.30%, P=0.001) and DDES group (36.62%± 20.54%, P=0.029) significantly, SEM result demonstrated the same trend. At 28 days after implantation, CD31 mRNA relative expression quantity in PES group (3.61±1.46) was higher than in BMS group (1.39±0.62, P=0.003), SES group (1.99±0.37, P=0.018) and DDES group (1.45±0.47, P=0.004). At 191 days after implantation, CD31 mRNA relative expression quantity in DDES group (11.01±5.90) was higher than in BMS group (2.02±1.10, P=0.009) and PES group (2.82±1.95, P=0.021). CD34 mRNA relative expression quantity in DDES group (4.21±1.27) was higher than in BMS group (0.85±0.36, P=0.009) and PES group (1.12±0.63, P=0.005). CD133 mRNA relative expression quantity in DDES group (3.39±1.35) was higher than in BMS group (0.75±0.51, P=0.003) and PES group (0.84±0.41, P=0.007). Unfortunately, the same variations were not exist on protein level.
Conclusions: Polymer-free dual drug-eluting stents can't further improve endothelialization of stenting coronary artery in the porcine model.

GW25-e4423

Beta-Blockers Should be Prohibited in Type-3 Long QT Syndrome with Marked Sinus Bradycardia

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Objectives: Encoding Nav1.5 sodium ion channels, mutations of SCN5A are responsible for type-3 long QT syndrome (LQT3) and sudden infant death syndrome (SIDS). This study aimed to determine the cause of sudden death (SD) in a Chinese teenager with markedly prolonged QT interval and a strong family history of SIDS.
Methods: Genotype-phenotype investigation was conducted in a Chinese family, in which the proband, a 12-year-old Chinese girl, was clinically diagnosed with LQTS and treated with beta-blockers as the baseline therapy. ECG screening and the candidate gene search of LQT1-3 were performed in the proband and her blood relatives. The acquired pcDNA-SCN5AWT/Mut was transfected into HEK-293 cells.Patch-clamp recording was performed to study the electrophysiological changes of the mutant ion channel after site-directed mutagenesis and transfection.
Results: The ECG of the proband showed a very slow heart rate for age (48 bpm, female at age 12), markedly prolonged QTc (660 ms) with late onset biphasic T waves that is typical to LQT3. On the 3rd day of metoprolol intake (50 mg/d), the proband died suddenly at rest. There were four SIDS cases in her family including her twin sister, her mother's sister and her manternal grandmother's sister. SCN5AMut (P.V411M), a point mutation, was identified in the proband and her mother (QTc 424ms). The functional effect of P.V411M was examined by patch-clamp analyses on HEK-293 cells. The peak current-voltage (I-V) relationship curves demonstrated that P.V411M produced a gain of function in the Nav1.5 channel The peak current density ws increased by 1.28 times compared to WT. The enhanced activation with a negative shift in the peak I-V relationship was significantly higher by -50mV voltage than WT (85.00%±7.43% VS 41.50 %±2.60%, P<0.01), while its voltage-dependent Na channel availability (SSI) curves were nearly unchanged, ranging from -140mV to 70mV voltage range.
Conclusions: SCN5A-P.V411M produced a gain of function in the Nav1.5 channel. P.V411M causes LQT3 and is high likely responsible for SIDS in this Chinese family. Beta-blockers are unsuitable to LQT3 with marked bradycardia, and perhaps should be prohibited.

GW25-e4430

Ibuprofen Attenuates Cardiac Fibrosis via Restoring the Imbalance of ACE and ACE2 in Diabetic Rat

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Objectives: Cardiac fibrosis is an important pathological change in the diabetic heart, and its induction and progression involves chronic inflammation. However, whether ibuprofen, a typical non-steroidal anti-inflammatory drug, has anti-fibrotic effect in the diabetic heart remains incompletely clear. This current study was to investigate the effects of ibuprofen on cardiac fibrosis in a rat model of type 1 diabetes.
Methods: Rats were grouped into: normal, diabetic, diabetic+ibuprofen and Rats were grouped into: normal, diabetic, diabetic+ibuprofen and diabetic+pioglitazone. The diabetic model was established by injecting streptozotocin (60 mg/kg, ip) into the rats. Then, ibuprofen (40 mg/kg/day) or pioglitazone (25 mg/kg/day) was given though a gavage for eight weeks. The amounts of collagen, laminin, α-smooth muscle actin (α-SMA) and fibroblast-specific protein 1 (FSP-1) were measured by histopathological and immunohistochemical analyses for assessing cardiac fibrosis. The major components of renin-angiotensin system, angiotensin converting enzyme (ACE), angiotensin II (AngII), angiotensin II type 1 receptor (AT1-R), ACE2, Ang (1-7) and Mas receptor (Mas-R) were detected by immunohistochemical and western blot analysis or ELISA assay. Transforming growth factor β_1 (TGF-β_1) and the mammalian target of rapamycin (mTOR) were evaluated by immunohistochemical and western blot analyses diabetic+pioglitazone. The diabetic model was established by injecting streptozotocin (60 mg/kg, ip) into the rats. Then, ibuprofen (40 mg/kg/day) or pioglitazone (25 mg/kg/day) was given though a gavage for eight weeks. The amounts of collagen, laminin, α-smooth muscle actin (α-SMA) and fibroblast-specific protein 1 (FSP-1) were measured by histopathological and immunohistochemical analyses for assessing cardiac fibrosis. The major components of renin-angiotensin system, angiotensin converting enzyme (ACE), angiotensin II (AngII), angiotensin II type 1 receptor (AT1-R), ACE2, Ang (1-7) and Mas receptor (Mas-R) were detected by immunohistochemical and western blot analysis or ELISA assay. Transforming growth factor β_1 (TGF-β_1) and the mammalian target of rapamycin (mTOR) were evaluated by immunohistochemical and western blot analyses.
Results: The serum glucose levels were increased and the body weight was decreased in the diabetic group compared with those in the normal group. Chronic treatment with ibuprofen decreased the levels of serum glucose, but had no effect on body weight. Excessive deposition of collagen, and increases in laminin, α-SMA and FSP-1 in the cardiac tissue were detected in the diabetic group. However, they were alleviated by ibuprofen treatment. The protein expression of ACE and AT1-R and the amount of AngIIwere higher, and the protein expression of ACE2 and Mas-R and the amount of Ang (1-7) were lower in the diabetic group. The ratio of ACE to ACE2 was raised in the diabetic group. All these changes were ameliorated by ibuprofen administration. In addition, the protein expression of TGF-β_1 and mTOR were raised in the hearts of the diabetic group and were attenuated by ibuprofen treatment. There was no significant difference between the ibuprofen and the pioglitazone groups.
Conclusions: The results suggested that treatment with ibuprofen could ameliorate the cardiac fibrosis in diabetic rats. The anti-fibrotic effects of ibuprofen were realized by reduction of ACE/AngII/AT1-R axis and enhancement of ACE2/Ang (1-7) /Mas-R axis, leading to the decrease of TGF-β_1 and mTOR expression.

GW25-e5210

Endothelial-mesenchymal transition contributes to cardiac fibrosis induced by dyssynchronous heart failure through heterogeneity of mechanical stretch in a canine model

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Objectives: To explore the role and potential mechanism of endothelial-mesenchymal transition (EndMT) in dyssynchronous heart failure-induced cardiac fibrosis.
Methods: Twelve dogs received 3-week rapid right ventricular pacing to develop dyssynchronous heart failure and then were randomly divided into right ventricular pacing (RVP) group (n=6; kept RVP for another 3-week) and biventricular pacing (BiVP) group (n=6; changed to BiVP for 3-week), and another 6 dogs were selected as control group (sham operation). EndMT were respectively assayed by confocal microscope (Z-stack) in heart samples and western blot in cardiac endothelial cells from fresh heart fragments.
Results: BiVP slightly improved contractile function compared with RVP (P<0.05), but two groups still remained significant heart failure and similar ventricular dilatation. RVP induced significant cardiac fibrosis, elevated collagen 1A2 expression and depressed bone morphogenetic protein 7 expression in left ventricular lateral wall (late-contracting and high-stress) compared with anterior wall, which could be alleviated by BiVP. EndMT, transforming growth factor-beta (TGF-β) /snail signaling, collagen 1A2 and integrin β_1 expresson were significantly elevated in the endothelial cells from RVP lateral wall but reversed by BiVP. In vitro study, cyclic stretch could independently induce EndMT and enhance the pro-EndMT effect of TGF-β in HUVECs, which could be partly blocked by integrin β_1 siRNA.

Conclusions: RVP-induced dyssynchronous heart failure could aggravate fibrosis due to regional heterogeneity of mechanical stress, and it could be partly attenuated by BiVP, in which mechanical stress-induced EndMT might play pivotal role through integrin β_1 pathway.

GW25-e5212

Lipoxin A4 inhibits lipid uptake and oxLDL-induced apoptosis in macrophages with suppressed biosynthesis in atherosclerotic arteries

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Objectives: To test whether anti-inflammatory lipid mediator Lipoxin A_4 (LXA_4) can inhibit foam cell formation and macrophages apoptosis, and determine the circulating and local LXA_4 biosynthesis status in atherosclerosis.
Methods: Macrophages apoptosis was evaluated by TUNEL and Annexin V. Mitochondrial membrane potential was assayed by JC-1 Assay Kit. Serum and tissue levels of LXA_4 were assayed by ELISA kits.
Results: LXA_4 significantly suppressed cholesterol uptake genes CD36 and SR-A expression in a dose-dependent manner in THP-1 macrophages and human monocyte derived macrophages (from coronary artery disease patients), which could be abolished by LXA_4 receptor antagonist BOC-2. Furthermore, LXA_4 could inhibit oxLDL-induced CD36 upregulation. The uptake of Dil-oxLDL and Dil-acLDL as well as foam cell formation were inhibited under LXA_4 stimulation. It was observed that LXA_4 could reduce oxLDL-induced apoptosis in macrophages through inhibiting caspase-3 activation and restoring mitochondrial membrane potential. Moreover, cotreatment with LXA_4 significantly inhibited JNK pathway activated by ox-LDL. Circulating levels in stable coronary artery disease patients were much higher than that in nonobstructive patients. Local LXA_4 levels were lower but IFN-γ levels were higher in rabbit atherosclerotic vessel walls. In addition, in vitro experiment found that IFN-γ could suppress LXA_4 production in activated macrophages and foam cells.
Conclusions: LXA_4 could inhibit foam cell formation and oxLDL-induced apoptosis in macrophages. Increase of circulating LXA_4 and decrease of local LXA_4 were observed in atherosclerosis, which indicated that locally but not systematically inadequate production of resolution mediators might be the key reason in maintaining nonresolving inflammation in atherosclerosis.

GW25-e5275

Association between PPARγ Gene Polymorphism Haplotypes and Metabolic Syndrome in Chinese Population, Case-control and Family-based Study

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Objectives: We thought to evaluate the possible association between several polymorphisms in PPARγ gene and metabolic syndrome (MS), using two approaches, a case-control study and a family-based study.
Methods: Subjects and Measurements Subjects of 605 participated in the study. Case patients (of MS) of 94 and 131 control subjects participated in a case-control study. Family-based study included 149 probands and 231 siblings (from 90 families). BMI, fasting blood sugar (FBS), TC, TG, and HDL-c levels were measured. Genotyping We detected 7 polymorphisms of PPARγ gene, including two prevalence polymorphisms Pro12Ala (rs1801282) and C161T (rs3856806) and other five single-nucleotide polymorphisms (SNP): -553T/C (from the beginning of exon A2), -267T/A (from the beginning of exon A2), -628G/A (from the beginning of exon 1), rs7650213G/T, and rs13306747C/G, using a method of RFLP-PCR. Statistical Analysis Differences of quantitative traits were compared with one way ANOVA. SPSS software 13.0 was used. Pairwise linkage disequilibrium (LD) expressed in terms of D' and r^2 parameters and haplotype frequencies were estimated using the THESIAS program. A P value$<$0.05 was considered significant. The transmission of alleles to affected subjects with MS or unaffected subjects was analyzed using the transmission disequilibrium test (TDT) by TRANSMIT software. The proportion T of "overtransmitted" or "high-risk" alleles from informative parents was estimated by counting informative transmissions.
Results: Case-Control Study: No significant differences could be observed between the cases and controls of seven polymorphisms (P$>$0.05). Six common haplotypes were analyzed. The corresponding ORs of the MS for carriers of the rare allele versus homozygotes for the common allele of the seven polymorphisms varied from 0.26 to 0.74 (all P$>$0.05). A lower risk of the MS was observed of haplotype TTCGGCT versus common homozygote haplotype TTCGGCC. The TTCGGCT haplotype was lower frequent in MS patients than in control subjects. But it was not significant (P=0.086) .In pairwise linkage disequilibrium analysis, the polymorphism rs1801282 (all D'$>$0.5) and rs7650213 (all D'$>$0.7) were in linkage disequilibrium with other six polymorphisms.

Family-based Study: In TDT analysis of the pedigree of MS probands of seven polymorphisms, the patients were more likely to inherit the homozygotes of two polymorphisms, C allele (Pro) of rs1801282 and the C allele of rs3856806 (P$<$0.05). Similar results were not found in other five polymorphisms. There was a significant lower transmission of the haplotypes CTGGTCC (P$<$0.05) in haplotypes analysis of seven polymorphisms. Other haplotypes were not found overtransmitted or lower transmitted.
Conclusions: In case-control study, seven polymorphisms and their haplotypes of PPARγ are not associated with MS. While in family-based study, two polymorphisms of PPARγ gene, rs1801282 (Pro12Ala) and the rs3856806 (C161T) decrease the risk of the MS. And the haplotype CTGGTCC of seven polymorphisms can decrease the risk of MS in MS families. Therefore, PPARγ polymorphisms are associated with MS especially in families.

GW25-e0242

Urine may be a preferred source to generate induced pluripotent stem cell-derived cardiomyocytes for cardiac regenerative medicine

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Objectives: To test proof-of-principle if human iPSCs can be established by the transduction of transcription factors (Oc-t4, Sox-2, Klf-4, and c-Myc) into human adult urine cells and observe whether these iPSCs can be differentiated into cardiomyocytes.
Methods: We used directed differentiation protocols to derive cardiomyocytes using serum-free, chemically-defined media supplemented with BMP4, Activin A, bFGF, VEGF and DKK-1 in stage specific manner as previously described.
Results: In our study, positive results were obtained from the immunofluorescence staining of Oct-4, SSEA-4, Nanog, TRA-1-60 and alkaline phosphatase staining of our putative human iPS cells, which indicated that the reprogrammed human urine cells were expressing these typical embryonic stem cell (ESC) markers. The putative iPSCs were ESC-like and showed excellent differentiation potential into lineages derived from the primary three embryonic germ layers both in vitro and in vivo. Importantly, after cardiac differentiation from the above iPSCs, spontaneously beating outgrowths appeared approximately 14 to 21 days in embryoid bodies. Stable action potential (AP) recorded from spontaneously beating clusters and expression of the cardiac specific markers (troponin-T, α- actinin, MLC-2v, MLC-2a and HCN4) clearly confirmed the differentiation of iPSCs into cardiomyocyte in our study.
Conclusions: With these findings, we hypothesize that urine may be a preferred source in a totally noninvasive manner for generating iPS cell-derived cardiomyocytes for cardiac regenerative medicine.

GW25-e0271

The progress of cardiac stem cell study

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Objectives: At present the treatment of heart disease have much difficulty. The main causes are due to that drug therapy and percutanenus coronary intervention (PCI) or coronary artery bypass grafting (CABG) could not increase the number of cardiomyocytes, so the cardiac function does not enhanced much better. According to this, the numbers of cardiomyocytes is the key. In a single day the heart failure happens, both drug therapy and PCI can also not increase the number of cardiomyocytes and the heart function. With the development about stem cell researches, many studies have testified that transplanting of cardiac stem cells can enhanced the ejection fraction (HF) and cardiac function. The stem cell treatment outstandingly prolongs life-span and improves the prognosis of the patient suffering from heart failure
Methods: The paper summarized the recent results and clarified the kinds of cardiac stem cells. The paper overviews the method inducing stem cells into cardiomyocytes. It also shows the clinic works having been made about cardiac stem cells.
Results: All clinic studies have a significative conclusion increasing ejection fraction of heart. Through that it discusses the modifying technology regulating stem cells.
Conclusions: At last the article reveals the biological organ future of clinic transplantation.

GW25-e0423

MicroRNA-19b Acts as Potential Anti-thrombotic Protector in Coronary Artery Disease by Targeting Tissue Factor

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Objectives: Thrombosis plays a critical role in the pathogenesis of acute coronary events. Microparticles (MPs) are the major carrier of miRNAs in circulation. Tissue factor (TF), the initiator of extrinsic coagulation cascade, may be regulated by microRNAs (miRNAs). The aim of this study was to determine the potential role of miRNAs in regulating gene experession involved in thrombosis in coronary artery disease (CAD) .
Methods: MiRNA expression profiles in the plasma of patients with typical unstable angina (UA) and angiographically documented CAD compared with individuals with clinical suspicion of CAD but negative angiography were analyzed using Taqman low-density miRNA array. Levels of selected five miRNAs in plasma and plasma MPs were validated by real-time PCR. The characteristic of endothelial microparticles (EMPs) from plasma were analyzed by flow cytometry. In endothelial cells (ECs, EA.hy926 cells) and MPs releasd by ECs incubated with TNF-α, the levels of miR-19b were examined by real-time PCR. The target gene of miR-19b associated with thrombosis were pridicted by TargetScan and miRanda. Luciferase reporter assays were performed to confirm the binding of miR-19b to TF mRNA. TF expression induced by TNF-α in ECs was tested by real-time PCR. ECs were transfected with miR-19b mimic and the expression of TF were analyzed by real-time PCR and western blotting. Procoagulant activity of TF was analysed in miR-19b overexpressed ECs.
Results: Amomg 36 differential expressed miRNAs, miR-19b was the most obviously upregulated one. In UA patients, miR-19b level was upregulated in plasma