GW26-e0480
The predictive value and correlation analysis on structural heart disease in patients with ventricular arrhythmias by studying of heart rate variability
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OBJECTIVES To investigate the predictive value and correlation analysis on structural heart disease in patients with ventricular arrhythmias by studying of heart rate variability (SDNN in the time-domain analysis and sympathetic/vagal ratio in the frequency domain analysis) via ambulatory electrocardiogram monitoring.

METHODS 24 hours ambulatory electrocardiogram monitoring was administered during March 2012 and October 2013, and SDNN in the time-domain analysis and sympathetic/vagal ratio in the frequency domain analysis were collected and retrospectively analyzed in 300 patients.

RESULTS Structural heart disease with SDNN <100ms group have significantly higher incidence rate of ventricular arrhythmias than control group (39.5% vs 4.1%; P < 0.01). The sympathetic / vagal ratio of structural heart disease with ventricular arrhythmia group was significantly higher than control group (19.9 ±2.3 vs 10.1 ±1.7; P < 0.01). Incidence of ventricular arrhythmias increased significantly along with the rise of sympathetic/vagal ratio (P < 0.05). Time domain (SDNN) and frequency domain (sympathetic / vagal ratio) were negatively correlated (r = 0.819, P < 0.01).

CONCLUSIONS SDNN <100ms and increase of sympathetic/vagal ratio can be considered as ventricular arrhythmias predictors in patients with structural heart disease from two perspectives.

GW26-e0482
MicroRNA-350 Induces Cardiomyocyte Hypertrophy by inhibiting MAPK14 and JNK
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OBJECTIVES To explore the mechanisms of miR-350 inducing cardiomyocyte hypertrophy by regulating MAPK14 and JNK expression.

METHODS miR-350 over-expression and MAPK14 shRNA vector were constructed and transfected into H9c2 cells. Then cells were observed in cell morphology and the area of the individual H9c2 cell was measured. Immunocytochemistry technique was used to observe nuclear translocation of NFATc. Western blotting was performed to assay the protein expression of MAPK14 and JNK, and RT-PCR was applied to detect the mRNA expression of MAPK14 and JNK.

RESULTS Three days after transfection, the area of the individual H9c2 cell significantly increased in AngII, miR-350 or sh-MAPK14 vector treated cells. Both miR-350 and sh-MAPK14 vector induced significant increase of NFATc nuclear translocation. However, only miR-350 suppressed MAPK14 and JNK protein expression, but without affecting mRNA levels.

CONCLUSIONS miR-350 may lead to cardiomyocyte hypertrophy by repression both MAPK14 and JNK protein expression and affecting NFATc nuclear translocation.

GW26-e0673
ALDH2 Improves Left Ventricular Function in C57 Mouse Model of Metabolic Syndrome
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OBJECTIVES The objectives of the present study was to observe the enhanced myocardial damage in MS, to verify ALDH2’s ability to improve cardiac function and to elucidate the potential molecular mechanisms in MS mice.

METHODS A mouse model of MS was established by high-fat diet. 42 MS mice were further divided into three groups: MS group (n=14), GFP group (n=14), ALDH2 group (n=14). The same-aged C57 BL/6j mice rats were selected as the normal control group (n=15). The myocardial lesions were identified by echocardiogram, transmission electron microscope. TUNEL technique were used to detect cardiomyocyte apoptosis. Immunohistochemistry and Western blot were performed to analysis the proteins in signal transduction pathway, including 4-HNE, p-JNK, AP-1, p-IRS-1(Ser 307), IRS-1.

RESULTS In the MS group, ALDH2 activity in heart mitochondria was markedly decreased (P < 0.01). 4-HNE expression were significantly higher (P < 0.01). We found decreased EF and FS (P < 0.01). The swelling mitochondrial increased and accumulated. The number of TUNEL positive cells was significantly increased (P < 0.01). Compared with MS and GFP group, 4-HNE expression decreased significantly (P < 0.01). EF and FS increased significantly (P < 0.05). The swelling mitochondrial were obviously improved. The number of TUNEL positive cells decreased significantly (P < 0.01). The protein of p-JRS-1(Ser 307), IRS-1 significantly decreased in the ALDH2 group, accompanied by decrease of p-JNK and AP-1 protein (P < 0.05).

CONCLUSIONS ALDH2 plays a better cardioprotective role in MS mouse by reducing 4-HNE and improving insulin resistance. After transfection with ALDH2 lentiviral vector, cardiac function was improved through JNK/AP-1 pathway.

GW26-e0804
Human cardiosphere-derived cells from advanced heart failure patients improve ventricular function in myocardial infarction
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OBJECTIVES This study sought to compare the regenerative potency of cardiosphere-derived cells (CDCs) from healthy and diseased human hearts.

METHODS In a mouse model of acute myocardial infarction (MI), we compared the regenerative potential and functional benefits of CDCs derived from 3 groups: 1) non-failing (NF) donor: healthy donor hearts; 2) MI patients who had an MI 9 to 35 days before biopsy; and 3) heart failure (HF): advanced cardiomyopathy tissue explanted at cardiac transplantation.

RESULTS Cell growth and phenotype were identical in all 3 groups. Injection of HF CDCs led to the greatest therapeutic benefit in mice, with the highest left ventricular ejection fraction, thickest infarct wall, most viable tissue, and least scar 3 weeks after treatment. In vitro assays revealed that HF CDCs secreted higher levels of stromal cell-derived factor (SDF)-1, which may contribute to the cells’ augmented resistance to oxidative stress, enhanced angiogenesis, and improved myocardial survival. Histological analysis indicated that HF CDCs engrafed better, recruited more endogenous stem cells, and induced greater angiogenesis and cardiomyocyte cell-cycle re-entry. CDC-secreted SDF-1 levels correlated with decreases in scar mass over time in both CADUCEUS patients with acute MI and HF patients with advanced HF.

CONCLUSIONS CDCs from advanced HF patients could improve ventricular function post-MI, possibly through SDF-1-mediated mechanisms.

GW26-e1061
MiR-590-5p Targets Lectin-type Oxidized LDL receptor 1 in the Formation of angiogenesis
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OBJECTIVES MicroRNAs are small non-coding single stranded RNAs, which regulate almost all the physiological and pathological processes in mammals. We aim to find the effect of miR-590-5p on angiogenesis through regulating lectin-type oxidized LDL receptor 1 (LOX-1), a pivotal regulator for angiogenesis.

METHODS HUVECs treated with ox-LDL were transfected with different concentration of miR-590-5p mimics and inhibitors. Capillary tube formation and VEGF were measured by matrigel assay and western blotting. To prove LOX-1 is a direct target of miR-590-5p, pmir-LOX-1-3’UTR and pmir-LOX-1-1 mutant 3’UTR were co-transfected with miR-590-5p mimic into HUVECs. To confirm the function of miR-590-5p on the redox-sensitive pathway, NADPH oxidases subunits such as p22phox, p47phox and reactive oxygen species (ROS), and pro-inflammatory signals p38 MAPK, ERK1/2 and NF-κB were measured.
RESULTS We observed sustained increases in capillary tube formation and LOX-1 expression when HUVECs were treated with different concentration of ox-LDL. Enhancement of miR-590-5p expression by miR-590-5p mimic transfection inhibited this effect in HUVECs, while the inhibitory of miR-590-5p by miR-590-5p inhibitors showed opposite effects on that. Luciferase assay showed a decrease in LOX-1 activity in miR-590-5p-mimic-LOX-1 3′UTR co-transfected HUVECs, while that remained unchanged in the mutant-LOX-1-transfected cells. The similar patterns were seen in the expression of NADPH oxidases subunits, ROS generation, and the activity of proinflammatory signals.

CONCLUSIONS miR-590-5p inhibits angiogenesis through targeting LOX-1 and simultaneously suppressing redox sensitive pathways in HUVECs.

GW26-e1348 Exendin-4 protects adipose-derived mesenchymal stem cells (ADMSCs) from apoptosis induced by Hydrogen Peroxide through PI3K/Akt-Sfrp2 pathways
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OBJECTIVES Evidences from many researches have accumulated for the roles of ADMSCs’ grafts in the treatment of myocardial infarction. However, the reported functional improvements are generally modest partly due to the low cellular survival rate triggered by oxidative injury in vivo. Therefore, understanding its mechanisms by which oxidative injury cause donor cell death and protection of these cells from apoptosis, would have a vital influence on promoting the use of ADMSCs-based therapy. Exendin-4, an antidiabetes drug, exerts cell-protective influences on several kinds of cells. This study mainly explored the mechanisms by which oxidative stress injury caused ADMSCs apoptosis, and investigated the detailed survival signals regarding the anti-apoptotic actions of Exendin-4 on ADMSCs.

METHODS ADMSCs were acquired from inguinal adipose tissue of SD rats, and characterized by flow cytometry analysis and multilineage differentiation. The change of cell proliferative capacity and GPL-1 receptor expression under different doses of Exendin-4 were investigated. ADMSCs apoptosis induced by H2O2 in vitro. And the role of caspase9-related mitochondrial death pathways in ADMSCs apoptosis were detected. Besides, Exendin-4 was applied to protect the ADMSCs against apoptosis. Furthermore, the association between the PI3K/Akt-Sfrp2 pathways and anti-apoptotic effect of Exendin-4 was explored.

RESULTS 1. ADMSCs expressed CD31-,CD34-,CD45-,CD29-,CD90-. 2. A concentration-dependent inhibition of cell viability and endothelial expression of Txnip in ADMSCs apoptosis were detected. 3. Exendin-4 increased the number of AMDCs in a concentration-dependent manner. 4. H2O2-improved the ratio of apoptotic cells and the ROS and MDA concentrations, but reduced GSH and SOD contents. Besides, H2O2 led to lower mitochondrial potential that caused the cyt-c release into the cytoplasm. And more apoptotic proteins (Bax, caspase9 and caspase3) and less anti-apoptotic proteins (Bcl-2, c-IAP1 and c-IAP2) appeared in ADMSCs. 5. Exendin-4 could reduce the number of apoptotic cells, maintain the mitochondrial potential and inhibit the leakage of cyt-c. Moreover, Exendin-4 increased GSH and SOD but reduced ROS and MDA. Furthermore, higher anti-apoptotic proteins and lower apoptotic proteins expression emerged with Exendin-4 treatment. 6. Exendin-4 was able to activate the Sfrp2 via the PI3K/Akt pathway. However, blockade of PI3K/Akt pathways or knockdown of Sfrp2 with siRNA obviously abolished the protective effects of Exendin-4 on mitochondrial function and anti-apoptotic proteins, reversing the beneficial actions of Exendin-4 on ADMSCs apoptosis under oxidative stress injury.

CONCLUSIONS 1. Exendin-4 could increase the ADMSCs proliferation in a dose-dependent manner in vitro. 2. H2O2 induced ADMSCs apoptosis through caspase-9-dependent mitochondrial death pathways. 3. Exendin-4 could enhance antioxidant defense systems to indirectly reduce ROS, and inhibit mitochondrial death pathways through recruitment of anti-apoptotic proteins by activation of the PI3K/Akt-Sfrp2 pathways, leading to the ADMSCs survival under oxidative stress injury.

GW26-e1490 MiR-101 is involved in atrial electrical remodeling in human persistent atrial fibrillation
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OBJECTIVES MicroRNAs have been investigated to involve in electrical remodeling in atrial fibrillation (AF). MicroRNA-101 (miR-101) has a high expression level in heart, but the role of miR-101 in AF remains elusive. The goal of this study is to evaluate the changes of miR-101 in patients with persistent AF and to find its target gene.

METHODS The right atrial appendage tissue were obtained during cardiac surgery from patients (16 sinus rhythm and 14 persistent AF). The expression level of miR-101 was assayed by real time PCR. The effects of miR-101 on target gene expression were evaluated in myocardial cells isolated from mice which injected mice.

RESULTS The expression level of miR-101 was significantly decreased in persistent AF patients compared with SR patients. Transfection of miR-101 mimics to mice myocardial cells resulted in the decrease of SK3 expression level.

CONCLUSIONS Atrial miR-101 is significantly decreased in AF, leading to SK3 downregulation and possibly contributing to the electrical remodeling in AF.

GW26-e1584 The anti-inflammation related Txnip-Wnt pathway aberration in cardiac endothelium contributes to the myocardial infarction intolerance
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OBJECTIVES The mechanism how angiogenesis is impaired in diabetic heart is evasive and strategies to restore angiogenesis are limited under the myocardial infarction context.

METHODS Expression of Tnxip and Wnt activity in control and diabetic mouse heart were compared by immunohistochemistry, qPCR and Western Blot.

RESULTS Increased Txnip was found in diabetic mice heart, especially in the endothelium, which correlated well with higher ROS level, lower nuclear β-catenin expression, insufficiency of angiogenesis and the poor survival upon myocardial infarction. High glucose treatment on HUVEC cells mimicked the effects of diabetic myocardial cells isolated from mice which injected with HUVEC cells. Knockdown of Txnip in endothelial cells restored the Wnt activity and cell proliferation and migration. Cardiac topically injection of lentivirus expressing VE-Cadherin driven shTxnip reduced Txnip expression in vivo and significantly rescued the Wnt activity in endothelial cells together with increased the angiogenesis, cardiac function and survival rate. Similarly, one dose of LiCl injection also increased the angiogenesis and cardiac function.

CONCLUSIONS Significantly increased expression of Txnip in diabetic heart endothelial cells results excessive ROS and reduces Wnt activity, which in turn impairs the angiogenesis in response to ischemia. Either knockdown of Txnip in endothelial cells or LiCl treatment rescues the angiogenesis capacity and improves the prognosis, suggesting a potential implication in diabetic myocardial infarction.

GW26-e2465 Low frequency electromagnetic fields in noninvasive left stellate ganglia stimulation prevents ventricular arrhythmia in myocardial infarction canine model
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OBJECTIVES To investigate if low frequency electromagnetic fields (LF-EMF) can suppress left stellate ganglia (LSG) neural activity and...