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

Zhang Bin[1], Chen Ming[1], Zheng Bo[1], Wang Xingang[1], Fan Yuanyuan[1], Han Jingyan[2], Huo Yong[1]
[1]Peking University First Hospital, [2]Peking University Health Science Center

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

Zhou Hui[1], Liu Ying[1], Ghani Aliraza[2], Liu Xin[1], Zhang li[2], Hong kui[1]
[1]Cardiovascular Department, the second affiliated hospital of Nanchang University, Jiangxi of China, [2]Center for Clinical Cardiology, Lankenau Institute for Medical Research, Jefferson Medical College, Philadelphia, PA, USA

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

Qiao Weili[1], Wang Cheng[2], Zhang Fan[1], Liu Yaowu[1], Yan Changdong[1], Sun Hong[1], Yin Xiaoxing[1]
[1]Xuzhou Medical College, [2]the Affiliated Hospital of Xuzhou Medical College

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

Mai Jingting, Yangxin Chen, Qiong Qiu, Woliang Yuan, Jingfeng Wang
Department of Cardiology, Sun Yat-sen Memorial Hospital of Sun Yat-sen University

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.