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**Loss of Angiotensin-Converting Enzyme 2 Exacerbates Renal Inflammation and Injury in the Apolipoprotein E-Deficient Mice**

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**OBJECTIVES** Clinical trial evidence indicates that atherosclerosis is considered one of the major risk factors for the chronic kidney disease (CKD) and the blockade of renin-angiotensin system (RAS) has been shown to delay the progression of CKD to end-stage renal diseases and reduce renal events in patients. Angiotensin-converting enzyme 2 (ACE2) is known as a negative regulator of the RAS, but its role in atherosclerotic renal injury is poorly understood. We hypothesized that ACE2 would exert beneficial effects on renal injury in apolipoprotein E (ApoE)-knockout (KO) mice.

**METHODS** The 3-month-old wild-type (WT), ApoEKO, ACE2KO, and ACE2/ApoE double-KO mice were used in this study. Systolic blood pressure (SBP) level of mouse was measured non-invasively using the tail-cuff method. We examined changes in pro-inflammatory cytokines/chemokines and adhesion molecules, renal tubule and glomerulus ultra-structure and pathological signaling assessed by real-time PCR, Western blotting, and transmission electron microscope analyses, respectively.

**RESULTS** Compared to WT control mice, plasma total cholesterol (CHO) and triacylglycerol (TG) concentrations were elevated in both the ACE2KO and ACE2/ApoE double-KO mice (P < 0.05, respectively). ACE2 deficiency was linked with increased circulating Ang II levels and a modest elevation in SBP levels in both the ACE2KO and ACE2/ApoE double-KO mice. Compared with the ApoEKO kidneys, the level of pro-inflammatory cytokines/chemokines and adhesion molecules were increased in the ACE2/ApoE double-KO kidneys, including intereylanin-1 (IL-1), chemokine ligand 2 (CCL2), TNFRSF5/1A, RANTES, and intercellular adhesion molecule 1. Renal dysfunction and ultrastructure injury were aggravated in the ApoE/ACE2 double-KO mice associated with increases of plasma creatinine and blood urea nitrogen levels (P < 0.01, respectively). However, ACE2 deficiency had no effect on renal TNFRSF1B expression and circulating lipid levels in the ACE2/ApoE double-KO mice (P > 0.05, respectively).

**CONCLUSIONS** Loss of ACE2 exacerbates kidney inflammation and adverse renal injury in the ApoE-deficient mice via activation of the TNF-alpha/TNFRSF1A signaling pathway. These observations indicate detrimental effect of ACE2 deficiency on inflammation and renal dysfunction and point to ACE2 as a novel target for kidney-protective therapies. Strategies aimed at enhancing ACE2 action may have important therapeutic potential for atherosclerotic renal injury and CKD. This work was supported by Training Program of the National Major Research Plan (90139018), the National Basic Research Program of China (2014CB542300), and the National Natural Science Foundation of China (81370362 & 81170246).

GW26-e2293

**Renal Sympathetic Nerve Modulates Ventricular Electrophysiological Characteristics**

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**OBJECTIVES** Recently, renal sympathetic nerve (RSN) has become a hot target for therapeutic intervention in several cardiovascular diseases, including ventricular arrhythmias. However, the role of RSN in the modulation of ventricular electrophysiological characteristics is still poorly understood. The present study aimed to evaluate the effect of RSN activation (RSN-A) or denervation (RSN-D) on ventricular electrophysiology.

**METHODS** Twenty-one dogs were randomly assigned into RSN-A group (n=8), RSN-D group (n=8) and control group (n=5). Animals in RSN-A group received 3 hours of high frequency stimulation (20 Hz, 2 ms duration) at the voltage required to increase the systolic blood pressure by 10% to simulate a hyperactive state of RSN. RSN-D was achieved by ablatiing bilateral renal nerves. High frequency stimulation (20 Hz, 2 ms duration, 15 mA, 60s) was applied before and after each ablation to confirm the adequacy of denervation. Ventricular electrophysiological characteristics were measured at baseline and after intervention in each group.

**RESULTS** Both RSN-A and RSN-D significantly prolonged ventricular effective refractory period (ERP) (RSN-A group: 174 ± 12 vs 192 ± 15 ms; RSN-D group: 176 ± 10 vs 190 ± 11 ms, P < 0.05 for both), and QT interval (RSN-A group: 226 ± 7 vs 249 ± 9 ms; RSN-D group: 227 ± 8 vs 246 ± 8 ms, P < 0.05 for both) was achieved by ablating bilateral renal nerves. High frequency stimulation (20 Hz, 2 ms duration, 15 mA, 60s) was applied before and after each ablation to confirm the adequacy of denervation. Ventricular electrophysiological characteristics were measured at baseline and after intervention in each group.

**CONCLUSIONS** Loss of ACE2 exacerbates kidney inflammation and adverse renal injury in the ApoE-deficient mice via activation of the TNF-alpha/TNFRSF1A signaling pathway. These observations indicate detrimental effect of ACE2 deficiency on inflammation and renal dysfunction and point to ACE2 as a novel target for kidney-protective therapies. Strategies aimed at enhancing ACE2 action may have important therapeutic potential for atherosclerotic renal injury and CKD. This work was supported by Training Program of the National Major Research Plan (90139018), the National Basic Research Program of China (2014CB542300), and the National Natural Science Foundation of China (81370362 & 81170246).

GW26-e2161

**Optimal Cutoff of the Triglyceride to High-Density-Lipoprotein Cholesterol Ratio to Detect Cardiovascular Risk Factors Among Han Adults in Xinjiang**

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**OBJECTIVES** To determine whether triglyceride/high-density lipoprotein cholesterol ratio (TG/HDL-C), which has been shown to be an indicator of the metabolic syndrome (MetS) and insulin resistance (IR), can predict cardiovascular risk factors in the Chinese Han population in Xinjiang.

**METHODS** The Cardiovascular Risk Survey (CRS) was conducted from October 2007 to March 2010. A total of 14618 representative participants were selected using a four-stage stratified sampling method. A total of 5727 Han participants were included in the study. The present statistical analysis was restricted to the 5595 Han subjects who had complete anthropometric data. The sensitivity, specificity, and distance on the receiver operating characteristic (ROC) curve in each TG/HDL level were calculated. The shortest distance in the ROC curves was used to determine the optimal cutoff of the TG/HDL-C ratio for detecting cardiovascular risk factors.

**RESULTS** The prevalence of hypertension, hypercholesterolemia and hypertriglyceridemia were higher with higher TG/HDL-C ratio for both men and women. The TG/HDL-C ratio was positively associated with systolic blood pressure, diastolic blood pressure and serum concentrations of total cholesterol. The optimal TG/HDL-C ratio cutoffs for predicting hypertension, dyslipidemia, diabetes and ≥ two of these risk factors for Han adults in Xinjiang were 1.3, 1.3, 1.4, 1.4 in men and 0.9, 1.0, 1.0, 1.1 in women, respectively.

**CONCLUSIONS** The evaluation of TG/HDL-C ratio should be considered for one of cardiovascular risk factor predictors among Han adults in Xinjiang.
tissue engineering as biologic scaffold in recent years. Before achieving the ultimate goal of engineering a functional heart, however, some challenges regarding the scaffold preparation and the sources of seeding cells still need to be addressed. The purpose of this study was to establish and optimized the methodology of decellularized heart scaffold. It’s also expected to establish a platform for the decellularized heart tissue-based scaffold evaluation in vitro.

**METHODS**

The decellularized heart scaffold was prepared by coronary perfusion. Histological staining, DNA content assay and scanning electron microscopy (SEM) were performed to evaluate the decellularized heart scaffold. Neonatal rat cardiac cells and rat bone marrow multipotent stromal cells (rBMSCs), which have the potential to transdifferentiate into cardiomyocytes, were adopted to serve as seed cells respectively to construct a tissue-engineered 3D cardiac model. To improve the viability of cells on 3D scaffold, rotary cell culture system (RCCS) was also applied to enhance the mass transport during the cultivation in vitro. The tissue-engineered 3D model was evaluated by histological staining, SEM as well as quantitative real-time RT-PCR analysis.

**RESULTS**

Both histological staining and SEM detection revealed that decellularized heart scaffold preserves the ultrastructural conformation of the heart with few nuclei. The DNA content of the scaffold was 1.64±0.03 ng/mg, which is significantly lower than that of the control group (native heart tissue). Histological staining and SEM images showed their good viability during the 3D culture. Majority of the seeded neonatal rat cardiac cells or rBMSCs grew on the surface of the scaffold under the static culture condition. By contrast, a number of cells distributing within the scaffolds were observed in the dynamic cultures, indicating its good mass transport and microenvironment for cell growth. Quantitative real-time RT-PCR analysis revealed that expression level of transcript factor Gata 4 in the induced rBMSCs was improved significantly when compared to the negative control. Similarly, the gene expression of Gata 4 in the rBMSCs inoculated into the decellularized heart scaffold is much higher than that of the negative control and the induced group (5-azacytidine-treated).

**CONCLUSIONS**

The decellularized heart scaffolds prepared in the present study were decellularized completely and preserved the full extracellular matrix. It possesses not only good biocompatibility but also naturally occurring three-dimensional structure. Moreover, our research indicates that the decellularized heart scaffold might potentially induce the differentiation of rBMSCs into cardiomyocytes. Combined with the RCCS cultivation, the tissue-engineered 3D cardiac model based on decellularized heart scaffold can better simulate the microenvironment in vivo and might potentially be utilized for cardiac tissue engineering.

**GW26-e2370**

Red Cell Distribution Width and Risk of Long-Term All-Cause Mortality and Cardiovascular Events Among Patients With Acute Coronary Syndrome: A Meta-Analysis of Observational Studies

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**OBJECTIVES**

Red cell distribution width (RDW) might be a novel biomarker that reflects multiple physiological impairments related to atherosclerosis and acute coronary syndrome (ACS). We conducted this systematic review and meta-analysis to evaluate the association of RDW between risk of major adverse cardiovascular Events (MACEs), all-cause and cardiovascular mortality in ACS patients.

**METHODS**

Relevant studies were searched and identified in the Cochrane Library, PubMed and Embase databases. English-language studies that reported risk estimates for RDW and MACEs and cardiovascular outcomes were included. Data were extracted regarding the characteristics and clinical outcomes, and a quality assessment was conducted. Results were extracted for the average RDW level, and meta-analyses were carried out using random effects models.

**RESULTS**

We collected 14 articles. 9 investigated the association between RDW and all-cause mortality, 3 evaluated the association between RDW and risk of cardiovascular mortality, and 7 reported the association between RDW and risk of MACEs. We found that RDW was associated with a significantly increased risk of all-cause mortality (HR: 3.372; 95% CI: 2.104 - 5.645; P < 0.001), cardiovascular mortality (HR: 2.342; 95% CI: 1.760 - 3.100; P < 0.001) and MACEs (HR: 2.120; 95% CI: 1.515 - 2.965; P < 0.001).

**CONCLUSIONS**

The meta-analysis indicates that RDW significantly increased the risk of MACEs, all-cause and cardiovascular mortality in ACS patients.