**OBJECTIVES**

Cardiotid artery remodeling, also defined as intima-media thickening, is an important predictive indicator for human cardiovascular disease. Chronic changes in shear stress contribute to vascular remodeling. Orphan nuclear receptor Nur77 is expressed in diseased human vascular tissue, and plays a critical role in vascular physiology and pathology. In this study, we aim to define the exact role of Nur77 in vascular remodeling induced by low shear stress.

**METHODS**

Low shear stress-induced carotid artery remodeling was induced by partial ligation of left common carotid artery in 6- to 8-week-old C57BL/6 mice. After 4 weeks, the left common carotid arteries were harvested. The morphology of remodeling arteries was detected by HE staining, Verhoef-Van Gieson elastic staining, and Picro Sirius-Red staining for collagen. The expression of Nur77 protein in ligated arteries was observed by immunofluorescence staining. Primary rat vascular smooth muscle cells (VSMCs) were cultured and stimulated with platelet-derived growth factor (PDGF) and H2O2 in vitro. The mRNA and protein expression of Nur77 was detected by real-time PCR, Western blotting and immunofluorescence staining. ROS level was assessed by DCFH-DA staining. To investigate the effect of Nur77 on VSMCs proliferation and migration, rat VSMCs were overexpressed Nur77 by adenovirus infection. For further investigation the in vivo role of Nur77 in carotid artery remodeling, wild type (WT) and Nur77-deficient mice were subjected to partial ligation of the left common carotid artery. The morphology of remodeling arteries was detected as mentioned above. In situ matrix metallopeptidase 9 (MMP-9) activities were detected by immunofluorescence staining. The proliferation and apoptosis of VSMCs in remodeling arteries were examined by PCNA and TUNEL staining, respectively.

**RESULTS**

Following vascular remodeling, Nur77 is highly expressed in neointimal VSMCs in ligated carotid arteries. ROS levels were elevated both in remodeling arteries in vivo and after PDGF stimulation in primary rat VSMCs in vitro. Further in vitro experiments indicate that Nur77 is rapidly induced in VSMCs by PDGF and H2O2, while NAC treatment attenuates the increased protein level of Nur77 by H2O2. Moreover, Nur77 overexpression markedly inhibited VSMCs proliferation and migration induced by PDGF. In vivo, Nur77-deficient mice showed increased intima-media area and intima-media thickness in ligated carotid arteries, as well as more severe elastin disruption and collagen deposition compared to WT mice. Immunofluorescence staining indicates an upregulation of VSMC proliferation and MMP-9 production of intima area in Nur77-deficient mice. There was no difference in the number of intimal apoptotic cells between groups.

**CONCLUSIONS**

Taken together, our results indicate that Nur77 may be a sensor of oxidative stress and an inhibitor of vascular remodeling induced by low shear stress. Nur77 as well as its downstream cell signals might be a potential therapeutic target for the suppression of vascular remodeling.

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**GW26-e2456**

Orphan Nuclear Receptor Nur77 deletion exacerbates low shear stress-induced carotid artery remodeling in mice

Yang Yu,1 Zhaohua Cai,1 Mingli Cui,1 Peng Nie,1 Zhe Sun,1 Shiqun Sun,1 Shichun Chu,1 Xiaolei Wang,1 Lianhua Hu,1 Jing Yi,1 Linghong Shen,1 Ben He1

1Department of Cardiology, Renji Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China; 2Department of Cell Biology, Institutes of Medical sciences, School of Medicine, Shanghai Jiaotong University, Shanghai, China

**RESULTS**

Following vascular remodeling, Nur77 is highly expressed in vascular remodeling induced by low shear stress.

**METHODS**

Seven preoperative infants undergoing the low dose cardiac DSCT scanning with prospectively ECG-triggering protocol with acquisition window has optimized low dose CT images for 3D heart model printing. Thus, the objectives of this study were to confirm the feasibility of creating cardiac models from low dose CT data and to assess accuracy by comparing 3D model measurements with intraoperative measurements of cardiac malformations.

**RESULTS**

Seven infants (median 11 months old, range 6-27 months) were found 44 malformations with 10 atrial or ventricular septal defects during surgeries. Seven heart models were printed with all great arterial anomalies, and demonstrated 34 malformations with score A (77.3%, 3), B (8.2%, average), C (2 with score C (15.4%, missed), 0 with score D (0, wrong). Measurements of atrial or ventricular septal defects were obtained. Measurements of cardiac malformations were set as reference standards. Identification and measurements of the cardiac malformations from the 3D model were compared with reference standards, by meticulously double-blind manners.

**CONCLUSIONS**

Three-dimensional heart model printing of complex congenital heart disease based on the low dose cardiac CT images are technically feasible and may accurately reflect cardiac malformation anatomy. Three-dimensional models derived from low dose cardiac CT data represent a new tool in procedural planning for infants with congenital heart disease.

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**GW26-e3978**

Regulatory roles of Angiotensin-Converting Enzyme 2 in NOX4 Expression and Oxidative Stress Levels in Kidneys of Apolipoprotein E-Deficient Mice

Lai-Jiang Chen,1,2 Chen-Zhou Zhang,1,2 Hai-Yan Jin,1,2 Ying-Le Xu,1 Ran Xu,1 Bei Song,1 Ping-Jin Gao,1,3 Gavin Y. Oudit,2 Ji-Chang Zhong1

1State Key Laboratory of Medical Genomics, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine; 2Department of Cardiology, Renji Hospital, School of Medicine; 3State Key Laboratory of Medical Genomics, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai Institute of Hypertension; 4Institute of Health Sciences, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences; 5Department of Mental Health, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine; 6Department of Medicine, University of Alberta, Mazankowski Alberta Heart Institute

**OBJECTIVES**

The renin-angiotensin system (RAS) regulates body fluid balance, renal functions and blood pressure. Angiotensin-converting enzyme 2 (ACE2) is now known as a negative regulator of RAS, and inhibition of the renin-angiotensin system might be a possible alternative target for new drugs, since some protective influences on renal and cardiovascular function have been revealed. We hypothesized that ACE2 would exert beneficial effects on oxidative stress levels and renal injury in apolipoprotein E (ApoE)-knockout (KO) mice.

**METHODS**

In this study, we used 12-week-old wild-type, ApoEKO, and ACE2/ApoE-double knockout (KO) mice, and treated each mouse with recombinant human ACE2 (hrACE2) with the daily dose of 2 mg/kg. We characterized the functional, structural and molecular signaling changes in mice kidneys by quantitative real-time reverse transcription PCR, Western blotting, ROS fluorescent probe dityrosine staining and transmission electron microscope analysis, respectively.

**RESULTS**

Compared with the ApoEKO mice, ACE2 deficiency led to greater increases in renal oxidative stress levels and expression of oxidative stress-inducible proteins NADPH oxidase 4 (NOX4) in the