The effect of sRAGE improvement on cardiac systolic dysfunction and inhibition on myocardial apoptosis induced by ischemia/reperfusion

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OBJECTIVES Ischemia/reperfusion (I/R) is a pathological process that results in extensive cell death. However, ischemic tissue of the myocardium is susceptible to be further injured deriving from reperfusion. Although the mechanism of I/R injury involves multiple cellular processes, apoptosis is an important pathogenesis of myocardial I/R injury. soluble receptor for advanced glycation end products (sRAGE), the N-terminal extracellular domain of the receptor for advanced glycation end products (RAGE), can be derived either from enzymatic cleavage of full-length cell-surface receptor or endogenous secretion of splice variants of RAGE. RAGE, expressed in many tissues, is a transmembrane protein member of the immunoglobulin superfamily. Activation of RAGE induces a number of cell processes, including inflammation, apoptosis, proliferation and auto-phagy. sRAGE may counteract RAGE-mediated pathogenesis by acting as a decoy. Previous studies have shown that sRAGE has a protective effect on coronary artery disease. However, the therapeutic effects of sRAGE in heart injury after I/R remain unclear. We hypothesized that sRAGE inhibits apoptosis induced by I/R in cardiomyocytes in vivo.

METHODS C57BL/6J mice exposure to left anterior descending coronary artery ligation were used as in vivo models. At the end of reperfusion, cardiac function was evaluated with echocardiography, the myocardial infarct size was determined by the Evans blue/2, 3, 5-triphenyltetrazolium chloride (TTC) double staining, myocardial apoptosis was detected by TUNEL staining and caspase-3 activity.

RESULTS Compared to sham group, I/R decreased the cardiac systolic function in mice: lowered the Left ventricular anterior wall (LVAW) [0.80±0.07]mm vs [1.80±0.07]mm (P<0.05), and Left ventricular posterior wall (LVPW) [0.80±0.02]mm vs [1.80±0.01]mm (P<0.05), increased Left ventricular inside diameter (LVID) [3.17±0.15]mm vs [2.13±0.18]mm (P<0.05), and Left ventricular volume (LV vol) [(40.33±1.67)μl vs (15.52±3.47)μl, P<0.05], decreased left ventricular ejection fractions (EF) [30.9±3.2]% vs [72.4±2.1]% (P<0.05), and left ventricular fractional shortening (FS) [(15.1±2.0)% vs (40.7±1.6)%), P<0.05] decreased the myocardial infarct area (I/R,36.3% ±2.5% of AAR vs. sham, 0% of AAR, P<0.05), TUNEL-positive myocytes [20.0±1.6]% vs [1.0±0.2]%, P<0.05, and caspase-3 activity [2.64±0.4]% vs [1.00±0.2]%, P<0.05]. Compared to I/R group, sRAGE pre treatment significantly improved EF [66.5±2.0]% vs [39.9±1.9]%, P<0.05], FS [(22.0±1.1)% vs (15.1±2.0)%, P<0.05], lowered the myocardial infarct area (18.0%±1.1% of AAR vs 36.3% ±2.3% of AAR), diminished TUNEL-positive myocytes [9.2±1.0]% vs [20.0±1.6]%, P<0.05, and caspase-3 activity [0.94±0.1]% vs [2.64±0.4]%, P<0.05]. There were rare TUNEL-positive nuclei both in sham and sham-sRAGE group (P>0.05). There were no differences in LVAW, LVPW, LVID and LV vol between I/R and I/R+sRAGE groups.

CONCLUSIONS These results suggest that sRAGE protects against I/R-induced myocardial injury via inhibiting apoptosis.

Relation of Birth Weight to Infant Growth on Body Fat Composition in Childhood

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OBJECTIVES To investigate the relation of birth weight to infancy growth on body fat composition in childhood.

METHODS This cross-sectional study included 382 children aged 5 to 7 years old in Guangzhou. Birth weight and length was obtained from medical records as recorded in the delivery room. Weight and length during infancy (birth to 2 years old) were available from routinely collected from the individual health book. Physical examination included body weight, body height and body fat composition indexes (body mass index (BMI), percentage of body fat (PBF), waist circumference (WC) to height ratio (WHR), BFP were assessed by bioelectric impedance analysis (BIA)). PBF of 120 children 5 ~ 6 years old were assessed by multi-frequency bioelectric impedance (Tanita, model BC-751). PBF of 262 children 6 ~ 7 years old were assessed by multi-frequency bioelectrical impedance (Bio-space, InBody 3.0). According to birth weight tertile from low to high the children were divided into three groups: BW-I, BW-II, BW-III group. Then according to change in weight SDS between birth and 2 years the children were divided into three groups: changers up (CU), non-changers (NC), changers down (CD) group. Relation of birth weight to infancy growth on body fat composition was analyzed. Statistical analysis was performed by using analysis of variance, q test and χ2 test. P values less than 0.05 were considered statistically significant.

RESULTS Change in weight SDS between birth and 2 years was higher in BW-I group than in the BW-II group and BW-III group (P<0.05). Birth weight of the CU group was lower than that of the NC group and the CD group (P<0.05). Among the BW-I group, the proportion of subjects in the BW-I-CU group (61.76%) was higher than that in the non-BW-I-CU group (38.24%) (P<0.05). The body fat composition indexes (BMI, PBF and WHR) were higher in the BW-II group than in the BW-I group and BW-II group (P<0.05). The body fat composition indexes were higher in the CU group than in the NC group and the CD group (P<0.05). In the CU group, the body fat composition indexes were higher in the BW-III-CU group than in the BW-I-CU group and BW-II-CU group (P<0.05).

CONCLUSIONS Both lower birth weight individuals with more weight change-up growth in infancy and higher birth weight individuals had greater body fat composition in childhood. They were high-risk people of obesity. There is a need to develop public health policies that adopt preventive measures to prevent different birth weight individuals from the same accumulation of metabolic syndrome during pregnancy and infancy is necessary to prevent from fat mass accumulation and further to prevent adult metabolic syndrome.