Glucose Fluctuations Promoted Aortic Fibrosis through ROS/p38 MAPK/Runx2 Signaling Pathway

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**Introduction**: Glucose fluctuations may be responsible for the onset of arterial hypertension. However, the mechanisms still remain unclear. The purpose of this study was to investigate the mechanisms of aortic fibrosis and aortic stiffening induced by glucose fluctuations.

**Methods**: Sprague Dawley (SD) rats with injection of streptozotocin (STZ) were randomly divided into three groups: controlled STZ-induced diabetes (C-STZ); uncontrolled STZ-induced diabetes (U-STZ); STZ-induced diabetes with glucose fluctuations (STZ-GF). Fluctuated blood glucose was induced by repeated fasting along with additional insulin injections. After three weeks, rat blood pressure was tested and aortic fibrosis was detected by Masson trichrome staining. The levels of p38 mitogen activated protein kinase (p38 MAPK), runt-related transcription factor 2 (Runx2), collagen type 1 (collagen I) and NADPH oxidases (NOXs) were determined by western blot. The rat vascular smooth muscle cells (VSMCs) in vitro were used to explore the underlying mechanisms.

**Result**: Compared with C-STZ group, aortic fibrosis and aortic stiffening were aggravated in U-STZ group, which were more pronounced in STZ-GF group. The levels of p38 MAPK, Runx2, collagen I were significantly increased in STZ-GF group. In vitro, applications of inhibitors of reactive oxygen species (ROS) and p38 MAPK reversed glucose fluctuations-induced aortic fibrosis.

**Conclusion**: Blood glucose fluctuations aggravate aortic fibrosis via ROS/p38 MAPK/Runx2 signaling pathway.