Introduction: Recent studies have demonstrated that glucose fluctuations have a more harmful effect on the cardiovascular system than persistent high blood glucose, and may be related with coronary diseases. The aim of this study was to investigate the molecular mechanisms of glucose fluctuations on BK channel dysfunction.

Methods: The rat model with diabetes mellitus (DM) was established through injection of streptozotocin. Diabetic rats with glucose fluctuations were induced by fasting and additional insulin injections. Rat coronary arteries were isolated and coronary vascular tension was tested after three weeks. Rat coronary artery smooth muscle cells were isolated and whole-cell BK channel currents were recorded using patch clamp technique. Human coronary artery smooth muscle cells in vitro were used to explore the underlying mechanisms.

Result: Compared with the controlled DM (C-DM) group, coronary constriction and BK channel dysfunction were aggravated in the uncontrolled DM (U-DM) group and more pronounced in the glucose fluctuation (GF-DM) group. The levels of muscle ring finger protein 1 (MuRF1), nuclear factor (NF)-κB and protein kinase C (PKC)α were significantly increased in the GF-DM group. Activation of PKCα and NF-κB induced by glucose fluctuations promoted BK channel dysfunction, while inhibition of reactive oxygen species, PKCα, NF-κB and MuRF1 reversed this effect.

Conclusion: Glucose fluctuations aggravate BK channel dysfunction via the PKCα/NF-κB/MuRF1 signaling pathway.