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Resveratrol improves mitochondrial energetic pathway and endothelial function in type 2 diabetic female rat heart submitted to ischemia-reperfusion injury

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Introduction: Type 2 diabetic women present high risk of mortality by cardiovascular (CV) disease in comparison to non-diabetic women. Most of anti-diabetic treatments do not decrease patient's CV mortality, therefore new approaches need to be found. Resveratrol (RSV) is a polyphenol found in grapes reported to be beneficial on oxidative stress, endothelial dysfunction and inflammation involved in CV complications of T2D.

Objective: We have investigated the effect of RSV on the tolerance to ischemia-reperfusion (IR) injury of type 2 diabetic female Goto-Kakizaki (GK) rat hearts.

Methods: Four groups were used: a control group, a GK group, a GK group with placebo and a GK group with RSV treatment at the dose of 1 mg/kg/day in drinking water for 8 weeks. After 8 weeks of RSV treatment, tolerance to IR injury was assessed during *ex vivo* experiments, with simultaneous measurement of energy metabolism by ³¹P MRS, myocardial function and coronary flow. At the end of experiments, PCr, creatine, adenine nucleotides contents and citrate synthase activity were assessed in freeze-clamped hearts as well as nitric oxide and sirtuin pathways.

Results: Type 2 diabetic GK rats exhibited cardiac hypertrophy and lower myocardial tolerance to IR injury in comparison to controls. RSV attenuated cardiac hypertrophy and increased myocardial tolerance to IR injury by improving cardiac function, mitochondrial energetic and endothelial pathways. Interestingly, RSV increased ATP, PCr, creatine, total adenine nucleotide heart contents, citrate synthase activity, as well as eNOS, P-Akt and SIRT1 protein expressions in GK rat hearts.

Conclusion: RSV induced cardioprotection against IR injury in type 2 diabetic female rats. Thus, RSV presents high potential for preventing and treating CV complications of type 2 diabetic women.