

Cardiovascular Effects of Sodium Glucose Cotransporter-2 (SGLT-2) Inhibition in the Setting of Ischemia/Reperfusion Injury

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Background and Hypothesis: Recent evidence indicates that sodium glucose cotransporter-2 inhibitors (SGLT2i) significantly reduce the incidence of major adverse cardiovascular events in high risk patients. However, the specific effects of SGLT2i on the cardiovascular system remain poorly defined. This study was designed to test the hypothesis that SGLT2i improves cardiac function and mitigates myocardial infarct size following regional myocardial ischemia and reperfusion injury.

Experimental Design: Lean domestic swine received placebo (n=6) or canagliflozin (n=6; 300 mg PO) 24 hours prior to and the morning of an experiment. Hemodynamics, left ventricular pressure and volume were measured in open chest, swine at baseline, during a 60 min coronary occlusion, and during a 2-hour reperfusion period. The degree of myocardial infarction was assessed by staining with 1% tetrazolium.

Results: At the onset of ischemia, SGLT2i produced a significant parallel increase in both left ventricular end diastolic (85 ± 9 mL to 129 ± 10 mL; $P < 0.05$) and end systolic volumes (29 ± 8 mL to 78 ± 9 mL; $P < 0.01$). This increase in ventricular filling was associated with significant increases in stroke volume ($P < 0.05$) and stroke work ($P < 0.05$) relative to untreated controls swine during ischemia. SGLT2i decreased infarct size from $9.4 \pm 2.1\%$ in control swine to $3.1 \pm 0.98\%$ in SGLT2i treated swine.

Conclusion: SGLT2 inhibitors significantly improve cardiac contractile function and mitigate myocardial infarct size following regional myocardial ischemia and reperfusion injury in domestic swine.