Obesity decreases the contribution of K_v channels to hypoxic coronary vasodilation

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Background and Hypothesis: Our group previously demonstrated that reductions in the functional expression of voltage-dependent K^+ (K_v) channels contribute to impaired metabolic control of coronary blood flow in the setting of obesity. This study tested the hypothesis that obesity diminishes the contribution of K_v channels to coronary vasodilation in response to hypoxemia.

Experimental Design or Project Methods: Control lean (*n* = 7) and obese (*n* = 5) swine were anesthetized and the heart exposed via left lateral thoracotomy. Coronary blood flow was measured in response to hypoxemia, before and after inhibition of K_v channels by 4-aminopyridine (4-AP; 0.3 mg/kg, iv), by a flow probe placed about the left anterior descending coronary artery. Hypoxemia was induced by progressive increases in the amount of nitrogen introduced into the ventilator. Arterial blood samples were obtained at each reduction in arterial oxygenation via a catheter placed in the femoral artery.

Results: Blood pressure decreased from ~88 ± 5 mmHg to ~68 ± 6 mmHg (*P* = 0.01) as arterial PO_2 was reduced below 50 mmHg in both lean and obese swine (*P* = 0.51). In lean swine, coronary flow progressively increased from ~0.6 to >3.0 ml/min/g as arterial PO_2 was reduced. This response was decreased by ~40% in obese swine and by ~30% in lean swine treated with 4-AP. Administration of 4-AP had no effect on coronary flow in obese swine.

Conclusion and Potential Impact: These data support that K_v channels contribute to increases in coronary flow in response to hypoxemia in lean swine and that reductions in K_v channel function contribute to impaired hypoxic coronary vasodilation in obese swine. We propose that therapeutic targeting of obesity associated pathways (angiotensin-aldosterone system) known to influence K^+ channel expression could improve coronary microvascular function and cardiovascular outcomes in subjects with obesity. Supported by R01 HL136386; T35 HL 110854.