TITLE: ABSOLUTE α-ADRENERGIC REDUCTION IN CORONARY BLOOD FLOW WITH AN INTACT AUTONOMIC NERVOUS SYSTEM

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Introduction: It is somewhat surprising that despite recent clinical interest in the role of neurally-mediated coronary vasoconstriction in the pathogenesis of coronary artery vasospasm, there is little evidence that α-adrenergic vasoconstriction can mediate an absolute reduction in coronary blood flow in the presence of an intact autonomic nervous system. To address this issue, we examined the reflex sensitivity of the coronary circulation to carotid chemoreceptor activation, a stimulus known to result in profound reflex α-adrenergic constriction of peripheral vascular beds.

Methods: Eight conditioned, mongrel dogs were chronically instrumented with a Doppler ultrasonic flow transducer around the right main coronary artery, a solid state pressure transducer in the right ventricle, catheters in the aorta, coronary sinus and carotid artery, and ventricular pacing electrodes. To avoid potentially confounding influences of anesthesia and surgical trauma on neural reflex responsiveness, experiments were conducted three weeks following instrumentation in the intact, conscious dog. Heart rate was held constant by electrical pacing, and respiration was controlled during succinylcholine chloride infusion (0.1 mg/kg/min; iv) in all experiments. Selective carotid chemoreflex activation (CCRA) was achieved by injecting minute quantities of nicotine (0.4μg/kg) into the carotid artery. The response to CCRA was examined first with the autonomic nervous system intact, and then following sequential β-adrenergic blockade (propranolol HCl: 1.0 mg/kg; iv) and α-adrenergic blockade (phentolamine HCl: 2.0 mg/kg; iv). Student's t-test for paired comparisons was utilized to assess the effects of CCRA on the measured variables. Three-way analysis of variance was employed to assess sequential differences in the responses of the measured variables following administration of the pharmacologic antagonists. All values represent mean ±1 SEM.

Results: Selective CCRA elicits a biphasic coronary vascular response in the intact, conscious dog, characterized by an early dilatation and a late constriction. The present study is confined to examination of the late coronary vasoconstrictor response to selective CCRA. As summarized in Table 1, despite significant increases in arterial pressure and right ventricular hemodynamics, selective CCRA elicited a significant, late reduction in right coronary flow, and a concomitant, marked increase in right coronary resistance in conscious dogs with an intact autonomic nervous system. Additionally, whereas arterial O_2 content remained unchanged, selective CCRA induced a significant decrease in coronary sinus O_2 content. β-adrenergic blockade had no significant effect on the magnitude of either the CCRA-induced reduction in right coronary flow (19 ± 5%) or increase in right coronary resistance (54 ± 12%) compared with autonomic activity intact. In contrast, α-adrenergic blockade completely abolished ($p<0.01$) the CCRA-induced decrease in right coronary flow (1 ± 1%) and increase in right coronary resistance (6 ± 4%).

Discussion: Our most important finding was that selective CCRA resulted in a significant, absolute reduction in right coronary flow. These are the first data to document a reflex α-adrenergic reduction in coronary blood flow when the autonomic nervous system is intact. This reflex α-adrenergic coronary vasoconstriction was sufficiently intense to overcome a concomitant increase in coronary perfusion pressure, as well as an increased stimulus for metabolic coronary vasodilatation associated with elevated right ventricular hemodynamics. Finally, the reflex α-adrenergic coronary vasoconstriction was temporally related to a decrease in coronary sinus O_2 content and an increase in myocardial O_2 extraction.

Table 1. Late Response to Selective Carotid Chemoreflex Activation.

	Control	Response (Δ%)
Mean Aortic Pressure (mmHg)	119 ± 3	19 ± 4*
Mean Right Coronary Blood Flow (ml/min)	20.2 ± 1.8	-24 ± 4*
Mean Right Coronary Resistance (mmHg/ml/min)	6.2 ± 0.6	62 ± 13*
Coronary Sinus O_2 Content (vol %)	3.2 ± 0.6	-19 ± 6†
Right Ventricular Systolic Pressure (mmHg)	29 ± 1	12 ± 3*
Right Ventricular End Diastolic Pressure (mmHg)	2.6 ± 0.7	134 ± 65†
Right Ventricular dp/dt max (mmHg/sec)	599 ± 23	12 ± 3*

Significant changes ($p<0.01$; †$p<0.05$) in measured variables from control levels.