TITLE: DEPRESSED REFLEX CORONARY VASOCONSTRICTION IN CONSCIOUS DOGS WITH RIGHT VENTRICULAR HYPERTROPHY

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Introduction: The development of chronic, pressure-overload right ventricular hypertrophy (RVH) alone or in combination with right heart failure is characterized by a markedly depressed α-adrenergic mediated reflex increase in right coronary vascular resistance in response to carotid sinus hypotension.[1] The exact locus of dysfunction responsible for this abnormal reflex response, and the extent to which this abnormality reflects a generalized depression in overall reflex cardiovascular control with RVH is unknown. The goal of the present study was to assess the effects of severe RVH on reflex chronotropic, coronary and peripheral vascular responses to carotid chemoreflex activation (CCRA), a potent reflex stimulus that activates both the parasympathetic and sympathetic nervous systems. In this study, CCRA is utilized as a powerful experimental tool to identify mechanisms responsible for abnormal reflex control of the circulation, which may be important during the anesthetic induction of patients with RVH.

Methods: Seventeen conditioned, mongrel dogs were chronically instrumented with right main coronary (Doppler) and iliac artery (electromagnetic) flow transducers, a solid state transducer in the right ventricle, catheters in the aorta and carotid artery, ventricular pacing electrodes, and a hydraulic occluder around the main pulmonary artery. RVH was induced by gradually inflating the pulmonary artery occluder over a 9-12 month period. CCRA was achieved by injecting minute quantities of nicotine (0.4 μg/kg) into the carotid artery. All experiments utilized conscious dogs with controlled respiration during succinylcholine chloride infusion (0.1 mg/kg/ min; iv). Student's t-test for paired comparisons was utilized to assess the effects of CCRA on the measured variables. Student's t-test for grouped comparisons was employed to assess differences in the responses of the measured variables to CCRA between 9 dogs subjected to chronic pulmonary artery stenosis and 8 normal dogs. Values presented are mean ± 1 SEM.

Results: Chronic pulmonary artery stenosis increased ($p<0.01$) RV weight to body weight ratio from 1.36 ± 0.05 g/kg to 2.74 ± 0.18 g/kg. As summarized in Table 1, RVH was characterized by a marked attenuation in the magnitude of the right coronary vasoconstrictor response to CCRA (heart rate constant). The attenuated CCRA-induced increase in right coronary resistance was not enhanced following β-adrenergic blockade (27 ± 5%), but was abolished ($p<0.01$) following α-adrenergic blockade (5 ± 4%). In contrast to this abnormal coronary response, CCRA-induced constriction of the iliac artery bed was normal, and the CCRA-induced increase in cardiac cycle length was slightly enhanced in dogs with RVH.

Discussion: These are the first data to describe the effects of severe RVH on reflex cardiovascular responses to CCRA. The most striking finding of this study was that the magnitude of the CCRA-induced coronary vasoconstriction was markedly attenuated following the development of RVH. It appears unlikely that this attenuated right coronary vasoconstriction reflects a generalized abnormality in reflex responsiveness to CCRA, because the parasympathetic CCRA-induced increase in cardiac cycle length was slightly enhanced in dogs with RVH. Moreover, the attenuated right coronary constriction is apparently not the result of an overall depression in reflex sympathetic α-adrenergic vascular responsiveness to CCRA, because α-adrenergic constriction of the iliac artery vascular bed was entirely normal. Thus, these results imply a somewhat selective abnormality in sympathetic α-adrenergic control of the coronary circulation supplying the hypertrophied right ventricle.

Table 1. Late Response to Selective Carotid Chemoreflex Activation

		Control	Response (Δ%)
Mean Arterial Pressure (mmHg)	Normal	119 ± 3	19 ± 4*
	RVH	126 ± 2	14 ± 3*
		NS	NS
Right Coronary Flow (ml/min)	Normal	20 ± 2	-24 ± 4*
	RVH	36 ± 3	-13 ± 3*
		p<0.01	p<0.01
Right Coronary Resistance (mmHg/ml/min)	Normal	6.2 ± 0.6	62 ± 13*
	RVH	3.6 ± 0.5	33 ± 7*
		p<0.01	p<0.05
Iliac Artery Flow (ml/min)	Normal	143 ± 9	-68 ± 4*
	RVH	117 ± 8	-72 ± 7*
		p<0.01	NS
Cardiac Cycle Length (msec)	Normal	629 ± 25	348 ± 27*
	RVH	602 ± 51	452 ± 47*
		NS	p<0.06

*Significant ($p<0.01$) effect of CCRA on measured variables. p values represent comparisons between normal dogs and dogs with RVH. NS is not significant.

References:

1. Murray PA, Vatner SF: Carotid sinus baroreceptor control of right coronary circulation in normal, hypertrophied and failing right ventricles of conscious dogs. Circ Res 49:1339-1349 (1981)