Title: EFFECTS OF PRELOAD AND AFTERLOAD ON THE CONTRACTION OF POST-ISCHEMIC MYOCARDIUM

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Repeated episodes of short-term, regional myocardial ischemia characteristic of "supply-side" or "non-hemodynamic" events result in dysfunctional zones of viable myocardium. How these stunned areas respond to changes in preload and afterload is unknown. We tested the hypotheses that post-ischemic myocardium resembles the failing heart and is less sensitive than normal myocardium to increases in preload and more sensitive to increases in afterload.

Eight dogs underwent thoracotomy with morphine and chloralose anesthesia for insertion of piezoelectric crystals to measure wall thickness in both a test zone and in a remote area of the left ventricle. Heart rate was controlled by ventricular pacing at 100 b/min following creation of a permanent A-V heart block. Wall thickness was measured while left atrial pressure was controlled at 3, 6, and 9 cmH_2O by blood infusion or withdrawl at each of 3 mean arterial pressures (70, 90, and 110 mmHg; adjusted with sodium nitroprusside or angiotension). Baseline measurements of wall thickening during systole (SWT) were compared by Anova to values obtained with identical loading conditions after 10 min of total ischemia of the test zone and 1 h reperfusion (I&R).

SWT was reduced about 40% by I&R ($p<0.001$). SWT was inversely related to mean arterial pressure both before ($p=0.008$) and after I&R ($p=0.014$); however, the positive correlation of SWT with left atrial pressure ($p=0.003$) before I&R became non-significant after stunning. When contraction in the test zone was compared to that in a remote area, increased afterload produced picture of regional dysfunction.

These data indicate: 1. SWT in post-ischemic myocardium is not improved by increases in preload over a physiologic range; 2. SWT is sensitive to increased afterload following stunning; 3. Apparent regional wall motion abnormalities may occur as a result of increased afterload when a zone of myocardium is post-ischemic.

Systolic Thickening (mm)

			Mean Art Pres (mmHg) 70	90	110
L A P r e s s u r e	3	B	3.0	2.8	2.7
		S	2.0	2.1	1.6
	6	B	3.6	2.9	2.7
		S	2.3	1.9	1.5
	9	B	3.9	3.6	3.2
		S	2.6	2.1	1.6

Means only; n=8
B=Baseline S=Stunned

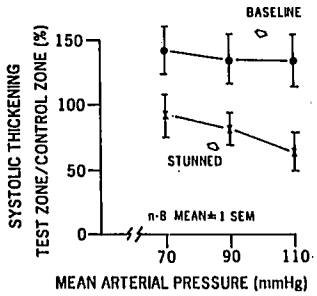

Figure shows response of test zone (relative to a remote control zone) to increases in afterload before and following I&R. The interaction of these zones creates an impression of regional dysfunction.

TITLE: ATTENUATION OF BAROREFLEX RESPONSE TO ACUTE HYPOTENSION BY NITROPRUSSIDE DURING INTRACORONARY INFUSION OF ATP

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Chemical and mechanical stimulation to left ventricular baroreceptors associated with vagal afferent fibers have been implicated in attenuating sympathetic activity and arterial baroreflex responses.[1] It was previously reported that ATP attenuates reflex renal sympathetic nerve activity (RSNA) by a vagal mechanism.[2] The goal of this study was to determine whether ATP attenuates the arterial baroreflex control of RSNA by stimulating ventricular baroreceptors.

Fourteen mongrel dogs were anesthetized with alpha-chloralose, intubated and mechanically ventilated with oxygen. Thoracotomy was performed and a 27 ga hypodermic needle was inserted into the left circumflex coronary artery. The left renal sympathetic nerves were isolated and placed on a bipolar silver electrode for measurement of RSNA. During intracoronary infusion of saline (SAL-IC) or ATP (ATP-IC: 50-100 µg/kg/min) for 5 min with infusing rate of 0.5 ml/min, a baroreflex depressor test was performed using nitroprusside (5-10 µg/kg IV). The dose of ATP was adjusted in a way that mean arterial pressure (MAP) did not fall significantly. Increments of RSNA (ΔRSNA) were plotted with respect to every 10mmHg decrease in MAP, and a slope was derived from each linear regression curve for a statistical analysis with ANOVA followed by Newman-keuls' method.

The baroreflex responses fit to linear regression curves are shown in Fig 1. The average baroreflex slope was significantly depressed during ATP-IC (-0.77 ± 0.11 %Δ/mmHg) compared with SAL-IC (-1.58 ± 0.08 %Δ/mmHg) ($p<0.01$) (Fig 2). Attenuation of baroreflex response to nitroprusside caused by ATP-IC was completely abolished by vagotomy (Fig 3,4).

This study demonstrated that infusion of ATP into the circumflex coronary artery attenuated the baroreflex response by cardiac vagal afferent mechanisms during hypotension. It has been speculated that endogenous ATP and adenosine may play a role in limiting the sympathetic overstimulation by endogenous cathecholamines released due to hypotension.[3] Results may indicate that ATP regulates the baroreflex control of sympathetic outflow by stimulating ventricular baroreceptors associated with a vagal afferent pathway.

References: 1. Circulatory Physiology. pp153-176. 1984
2. ANESTHESIOLOGY 71: A58 1989
3. Circ Res 46: I175-I182 1980