Title: FUNCTIONAL EFFECTS OF ISOFLURANE-INDUCED CORONARY STEAL DEPEND ON CHANGES IN SUBENDOCARDIAL PERFUSION

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INTRODUCTION: Isoflurane can produce a maldistribution of myocardial blood flow (MBF) distal to a critical coronary stenosis. Subendocardial (ENDO) MBF decreases but subepicardial MBF remains the same or increases, a change attributed to transmural coronary steal (1). The functional consequences of isoflurane-induced transmural steal, however, are disputed (1,2). In these studies, isoflurane produced different degrees of change in blood pressure and heart rate, two of the major factors controlling ENDO perfusion distal to a critical stenosis. Because regional myocardial function is largely determined by the adequacy of ENDO perfusion (3), we hypothesized that the discrepancies between earlier studies could be explained by different effects on ENDO perfusion. To test this hypothesis, we determined the effect of changes in ENDO MBF (produced by different concentrations of inspired isoflurane) on regional function distal to critical stenosis.

METHODS: Critical stenosis of the left circumflex artery (CX) was produced by adjusting a screw-clamp occluder until the reactive hyperemic response to temporary complete occlusion was eliminated in 8 mongrel dogs anesthetized with a baseline anesthetic of chloralose plus fentanyl (used to produce a slow baseline heart rate). CX pressure was measured with a 22 g catheter distal to the critical stenosis. Regional myocardial blood flow was measured with radionuclide-labelled microspheres injected into the left atrium utilizing the reference withdrawal method. Regional myocardial function was measured using two pairs of sonomicrometers aligned to measure transmural wall thickness. One pair was placed in the area supplied by the left anterior descending (LAD) artery and one pair was in the CX area. Epicardial venous catheters inserted into the regions supplied by the LAD and CX arteries allowed calculation of oxygen extraction and consumption. Left atrial, pulmonary, arterial and left ventricular pressures were continuously recorded. Control measurements were made under chloralose/fentanyl anesthesia. Isoflurane was then administered at end tidal concentrations of 0.7, 1.4 and 2.1%, allowing 20 min at each concentration. Finally, baseline levels of mean arterial pressure were restored using phenylephrine with isoflurane at 2.1%. Statistical analysis of the data was by analysis of variance (ANOVA). Comparison of LAD vs CX using two factor repeated measures ANOVA revealed direct and interactive effects, so both factors were analyzed separately.

RESULTS: Hemodynamic, wall thickening and blood flow data are summarized in Table 1. Production of critical stenosis reduced BP distal to the stenosis to 69% of the mean systemic BP, but did not change regional MBF or function. Systemic and distal CX pressures progressively decreased as the inspired isoflurane was increased; a constant gradient was maintained between the CX and systemic pressures. Global ventricular function (dP/dt) was decreased by the higher doses of isoflurane, but was improved when the mean arterial pressure was restored with phenylephrine. MBF in the LAD area increased with isoflurane. Wall thickening (dWT) in the LAD area was not affected by increasing concentrations of isoflurane. Wall thickening in the CX area, however, decreased when isoflurane was used. No change in mean MBF in the CX area occurred, but there was a marked redistribution of blood away from the ENDO layers resulting in a decreased endo-epi ratio (Table 1). Regression analysis on the pooled flow-function data are shown in Figure 1 to demonstrate the strong dependence of transmural function on changes in ENDO myocardial perfusion. A quadratic equation best described the relationship between changes in wall thickening and ENDO MBF.

DISCUSSION: Isoflurane reduced perfusion pressure distal to a critical stenosis in the CX artery. Consequently, ENDO perfusion was reduced and regional wall thickening deteriorated in proportion to the decrease in ENDO MBF. This study explains the apparently conflicting results of previous studies (1,2) by supporting the hypothesis that regional myocardial dysfunction only occurs when ENDO blood flow is reduced. The effect of isoflurane on regional function distal to a critical stenosis depends on the magnitude of change produced in perfusion pressure and heart rate. This in turn determines the degree of change in subendocardial MBF. Different effects on regional function will be obtained depending on the degree of change produced in subendocardial perfusion.

References:

(1) Tatekawa S, Traber KB, Hantler CB et al: Anesth Analg 66: 1073-1082, 1987.

(2) Priebe HJ, Foex P: Anesthesiology 66: 293-300, 1987.

(3) Gallagher KP, Matsuzaki M, Kotziol JA et al: Am J Physiol 247: H727-H738, 1984.

		CONTROL	ISOFLURANE 0.7%	1.4%	2.1%	2.1%+Phe
M.A.P.(systemic)		104±6	85±7 *	67±4 *	57±5 *	105±5
M.A.P.(CX)		72±6	47±6 *	33±4 *	27±5 *	48±7 *
H.R. b/min		87±7	108±7 *	119±8 *	123±6 *	105±6 *
% dP/dt		100	94±8	71±5 *	56±4 *	83±12
% Δ dWT	LAD	100	97±4	100±7	89±6	78±7 *
	CX	100	91±9	65±12 *†	51±9 *†	61±9 *
Mean myocardial blood flow mls/gr/min	LAD	0.8±0.1	1.1±0.2	1.6±0.2 *†	1.5±0.3 *†	2.4±0.4 *†
	CX	1.0±0.2	1.1±0.2	0.8±0.2	0.8±0.2	1.5±0.3 *
Endo/ Epi	LAD	1.3±0.1	1.3±0.1	1.3±0.1	1.2±0.1	1.2±0.2
	CX	1.1±0.1	0.9±0.1 †	0.6±0.1*†	0.5±0.1 *†	0.6±0.1 *†

All values are mean ± S.E.M.
* p<0.05 vs Control (rm ANOVA)
† p<0.05 LAD vs CX (one factor ANOVA)

Fig 1;CHANGE IN REGIONAL MYOCARDIAL FUNCTION WITH ENDOCARDIAL BLOOD FLOW IN AREA OF CRITICAL STENOSIS