Title: THE EFFECTS OF ISOFLURANE ON GLOBAL VENTRICULAR MECHANICS

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Introduction. Studies of the hemodynamic effects of isoflurane have reported minimal myocardial depression and significant vasodilatation. These investigations determined the effects of isoflurane on cardiac output or pump function, which are known to be severely affected by both preload and after-load. Such changes obscure the negative inotropic effect of anesthetic agents that are potent vasodilators. The end-systolic pressure-volume relationship superceeds pump function and ejection phase indices as a measure of inotropic state because it is independent of the physiologic parameters of preload and afterload. This study used the pressure-volume relationship to evaluate the inotropic state of the intact dog before, during and after isoflurane anesthesia.

Methods. Five adult dogs were instrumented with an array of piezoelectric ultrasonic dimension transducers that continuously measured myocardial major axis anterior-posterior minor axis and wall thickness. Pneumatic occluders were positioned around the superior and inferior venae cavae. Right ventricular, left ventricular and pleural pressures were measured by high fidelity solid state micromanometers. A pacing electrode was sutured to the right atrium to control heart rate.

Eight to fourteen days following instrumentation, analog measurements from the above transducers were recorded on magnetic tape during repeated caval occlusions in the conscious state, and during anesthesia with isoflurane at 1.25% and 2.0% end-tidal concentration. Subsequent to the experimental procedures, the data were subjected to computer analysis. Analysis of the end-systolic pressure-length ratio assessed the inotropic state in the conscious and anesthetized dog.

Results. Isoflurane at 1.25% end-tidal concentration produced a slight but non significant depression of the slope of the end-systolic pressure-length relationship (IDes). Isoflurane at 2.0% end-tidal concentration produced a profound and highly significant ($p < 0.01$) depression of the slope of IDes. Left ventricular peak pressure and dP/dt were significantly depressed by 1.25% isoflurane and these parameters were further depressed by 2.0% isoflurane.

Discussion. It is difficult, when using the intact animal, to separate the effect of isoflurane on the myocardium from its effect on the peripheral vasculature. This is especially difficult when conventional indices of hemodynamic function are used. The degree of reported depression of inotropy varies with the degree of "contamination" introduced by changes in preload afterload and heart rate. In our study, we used a technique which isolated the effects of these variables from the inotropic state of the heart. This allowed us to precisely describe myocardial function.

In the intact heart, the pressure-volume ratio may be expressed as Pes = IDes (Ves - Vd) where Pes and Ves represent end-systolic pressure and volume respectively. Vd is the volume axis intercept, and IDes represents the slope of the relationship. The constant describing this linear relationship (IDes) is independent of preload and is sensitive to the inotropic state. Inotropic depression shifts the end-systolic pressure-volume ratio to the right and downward so that at any given pressure, end ejection occurs to a larger chamber size. Inotropic stimulation causes the reverse to occur.

Using the quantitative analysis of end-systolic pressure-length relationships, this study more precisely defined the decreased inotropism caused by isoflurane. The lack of a negative inotropic effect of 1.25% isoflurane in the face of a significant decrease in pressure reflects the previously reported vasodilatory properties of isoflurane. This inotropic sparing may be of benefit in the compromised myocardium. The severe depression seen with only a 60% increase in concentration may reflect changes in the diastolic properties of the ventricle rather than inotropic depression and is presently under study.

Table

	Control	1.25%	2%
LVPk Press	116.7 ±5.0	79.3 ±10.1	63.0 ± 7.8
dP/dt	2221 ±451	1247 ±123	831 ±24
-dL/dt	50 ±6	43.82 ±6.4	41.5 ±10.4
Ees	11.91±0.81	9.54 ±0.73	6.24 ±0.43*

mean ± sd $p < .01$