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Influence of Volatile Anesthetics on Myocardial Contractility In Vivo: *Desflurane* versus *Isoflurane*

Paul S. Pagel, M.D., John P. Kampine, M.D., Ph.D.,† William T. Schmeling, M.D., Ph.D.,‡ David C. Warltier, M.D., Ph.D.§*

The direct effects of desflurane on myocardial contractility *in vivo* have not been characterized. Therefore, the purpose of this investigation was to systematically examine the effects of desflurane on myocardial contractile function and compare these actions to equianesthetic concentrations of isoflurane in chronically instrumented dogs. Contractility was evaluated using an established index of inotropic state, the preload recruitable stroke work (PRSW) *versus* end-diastolic segment length (EDL) relationship. Since autonomic nervous system tone may influence the hemodynamic effects of the volatile anesthetics *in vivo*, experiments were performed in the presence of pharmacologic blockade of the autonomic nervous system. Two groups of experiments were performed with seven dogs instrumented for measurement of aortic and left ventricular pressure, the maximum rate of increase of left ventricular pressure (dP/dt), subendocardial segment length, coronary blood flow velocity, and cardiac output. After autonomic nervous system blockade, ventricular pressure–segment length loops were generated using preload reduction *via* partial inferior vena caval occlusion. The PRSW *versus* EDL relation was calculated from the pressure–length loops. Dogs were then anesthetized with 1.0 or 1.5 MAC desflurane or isoflurane in a random fashion, and measurements were repeated after 30 min of equilibration at each anesthetic concentration. The PRSW *versus* EDL slope reflected similar changes in contractile state when desflurane or isoflurane was administered (53 ± 4 during control to 26 ± 4 erg · cm^{-2} · 10^{-3} · mm^{-1} at 1.5 MAC desflurane, and 57 ± 5 during control to 31 ± 3 erg · cm^{-2} · 10^{-2} · mm^{-1} at 1.5 MAC isoflurane). In conclusion, desflurane and isoflurane produced equivalent direct decreases in myocardial contractility. (Key words: Anesthetics, volatile: isoflurane; desflurane. Heart: contractility; end-systolic pressure–length relationship; preload recruitable stroke work; inotropic state.)

DESFLURANE is a new volatile anesthetic with several biophysical properties, most notably a very low blood gas partition coefficient[1] and remarkable metabolic stability,[2-4] that make it attractive for clinical use. The effects of this new agent on myocardial contractility have yet to be thoroughly characterized. Studies in healthy volunteers[5] and acutely prepared dogs[6] have suggested that desflurane may preserve cardiovascular stability and reduce mean arterial pressure and cardiac output less than does isoflurane. A preliminary investigation in chronically instrumented dogs in this laboratory[7] supported these findings and implied that such results could be attributed in part to a greater maintenance of myocardial contractility as measured by the rate of increase of left ventricular pressure at 50 mmHg (dP/dt_{50}) when equianesthetic concentrations of desflurane and isoflurane were compared. Conversely, other laboratory[8,9] and clinical[10] studies have shown little difference between the negative inotropic effects of desflurane and isoflurane when cardiac output, stroke volume, and mean arterial pressure are considered indirect indicators of myocardial performance.

The purpose of this investigation was to systematically examine and compare the effects of desflurane and isoflurane on myocardial contractility using heart rate- and load-independent indices of contractile function. Contractility was evaluated using two established methods: the preload recruitable stroke work (PRSW) *versus* end-diastolic length (EDL) relationship (M_W), an easily quantified and relatively afterload-independent index of contractile function in conscious[11] and anesthetized dogs,[12,13] and the end-systolic pressure–length relationship (ESPLR), a measure of contractile state previously shown to be sensitive, linear, and essentially load-independent in both the isolated[14-18] and intact[19-21] heart. Because volatile anesthetics are known to produce indirect effects on systemic hemodynamics mediated through an intact autonomic nervous system[22] and may impart varying degrees of suppression of autonomic reflexes,[23,24] experiments were conducted in the presence of pharmacologic blockade of the autonomic nervous system. Thus, the direct negative inotropic effects of desflurane independent of autonomic reflexes were evaluated and contrasted with those produced by equianesthetic concentrations of isoflurane.

Materials and Methods

All experimental procedures and protocols in this investigation were reviewed and approved by the Animal Care Committee of the Medical College of Wisconsin. Furthermore, all conformed to the Guiding Principles in

* Fellow in Anesthesiology.

† Professor and Chairman of Anesthesiology.

‡ Associate Professor of Anesthesiology and Pharmacology.

§ Professor of Anesthesiology, Pharmacology and Medicine, Division of Cardiology, and Vice Chairman for Research, Department of Anesthesiology.

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Address reprint requests to Dr. Warltier: Medical College of Wisconsin, MFRC, Room A1000, 8701 West Watertown Plank Road, Milwaukee, Wisconsin 53226.

the Care and Use of Animals of the American Physiologic Society and were in accordance with the Guide for the Care and Use of Laboratory Animals.¶

Implantation of Instruments

Surgical implantation of instruments is described in detail elsewhere.[12,13] Briefly, conditioned mongrel dogs (n = 7) weighing between 20 and 30 kg were fasted overnight and anesthetized with sodium thiamylal (10 mg/kg). After tracheal intubation, anesthesia was maintained with halothane (1.5–2.0%) in 100% oxygen (1 l/min) *via* positive pressure ventilation. Under sterile conditions, a thoracotomy was performed in the left fifth intercostal space, and heparin-filled catheters were placed in the descending thoracic aorta and the right atrium for measurement of aortic blood pressure and fluid or drug administration, respectively. An ultrasonic flow probe (Transonics, Ithaca, NY) was positioned around the ascending thoracic aorta for measurement of cardiac output.[12] A pair of miniature ultrasonic segment length transducers (5 MHz) for measurement of changes in regional contractile function (segment shortening [%SS]) were implanted within the left ventricular subendocardium. A high-fidelity miniature micromanometer (P7, Konigsberg Instruments, Pasadena, CA) was implanted in the left ventricle for measurement of left ventricular pressure, the maximum rate of increase of left ventricular pressure (dP/dt), and dP/dt_{50}. A heparin-filled catheter was inserted into the left atrial appendage, and the left ventricular micromanometer was cross-calibrated *in vivo* against pressures measured *via* arterial and left atrial catheters (P_{50} pressure transducer, Gould, Oxnard, CA). All instrumentation was secured, tunneled between the scapulae, and exteriorized *via* several small incisions. The pericardium was left widely open, the chest wall closed in layers, and the pneumothorax evacuated by a chest tube. Each dog was fitted with a jacket (Alice King Chatham, Los Angeles, CA) to prevent damage to the instruments and catheters, which were housed in an aluminum box within the jacket pocket.

After surgery, each dog was treated with analgesics (buprenorphine 0.02 mg/kg). Antibiotic prophylaxis consisted of procaine penicillin G (25,000 U/kg) and gentamicin (4.5 mg/kg). Dogs were allowed to recover for a minimum of 7 days prior to experimentation. During the postoperative period, dogs were trained to stand quietly in a sling during hemodynamic monitoring. Segment length and coronary blood flow velocity signals were driven and monitored by ultrasonic amplifiers (Hartley, Houston, TX). End-systolic segment length (ESL) was determined at maximum negative left ventricular dP/dt,[12] and EDL was determined at the onset of left ventricular isovolumetric contraction. The lengths were normalized according to the method described by Theroux *et al.*[25] %SS was calculated by use of the equation: %SS = (EDL − ESL) × 100/EDL. All hemodynamic data were continuously recorded on a Hewlett-Packard 7758A polygraph (Hewlett-Packard, San Francisco, CA) and digitized *via* a computer interfaced with an analog-to-digital converter.

Experimental Protocol

Dogs were assigned to receive either desflurane or isoflurane in a random fashion on separate days. All dogs were fasted overnight, and fluid deficits were replaced before experimentation with crystalloid (500 ml lactated Ringer's solution). Maintenance fluids were continued at $3\ ml \cdot kg^{-1} \cdot h^{-1}$ (lactated Ringer's) for the duration of each experiment. After instrumentation was calibrated and baseline hemodynamic data recorded, the autonomic nervous system was pharmacologically blocked with intravenous propranolol (2 mg/kg), atropine methylnitrate (3 mg/kg), and hexamethonium (20 mg/kg). Blockade of the autonomic nervous system was instituted to prevent reflex changes in systemic hemodynamics during alteration of left ventricular preload in the conscious and anesthetized state. Adequacy of autonomic blockade was demonstrated by lack of reflex change in heart rate after abrupt decrease in venous return *via* inflation of the inferior venal caval hydraulic occluder. A previous investigation in this laboratory[26] showed that the doses of propranolol, atropine methylnitrate, and hexamethonium used in the current investigation were adequate to block hemodynamic responses to intravenous acetylcholine and isoproterenol for the duration of the experiment.

Alteration of preload was used to generate left ventricular pressure–segment length loops in both sets of experiments. After control hemodynamics had been recorded and the autonomic nervous system blockade had been completed, ventricular pressure and segment length waveforms were recorded on a digital oscilloscope (Nicolet Model 4094, Madison, WI) in the conscious state. The inferior vena cava was then constricted to reduce left ventricular systolic pressure in 10-mmHg decrements, as described in previous investigations using this technique in this laboratory.[12,13] No changes in heart rate were observed in response to sequential partial occlusion of the inferior vena cava in any experiment. The partial occlusion of the inferior vena cava was released after each reduction of left ventricular systolic pressure. End-expiratory pressure–length loops of six to eight cardiac cycles were obtained at three steady-state decremental levels of left ventricular pressure.

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Inhalation induction of anesthesia was accomplished with desflurane or isoflurane in oxygen. After tracheal intubation, anesthesia was maintained at 1.0 or 1.5 MAC end-tidal desflurane or isoflurane, assigned in a random fashion, in a nitrogen (79%) and oxygen (21%) mixture. End-tidal anesthetic concentrations of desflurane and isoflurane were measured at the tip of the endotracheal tube using an infrared anesthetic gas analyzer (Datex Capnomac, Helsinki, Finland) calibrated by the manufacturer for the detection of desflurane. The gas analyzer was calibrated using known standards prior to and during experimentation. Desflurane was delivered using a modified Ohio DM 5000 (Ohmeda, Madison, WI) anesthesia machine, which incorporated a temperature-controlled vaporizer designed to provide uniform, predictable rates of desflurane vapor administration. Canine MAC values for desflurane[27] and isoflurane used in this study were 7.2 and 1.28%, respectively. After 30 min of anesthetic equilibration, hemodynamics were recorded, and ventricular pressure–segment length loops were obtained in the manner previously described. The anesthetic concentration was changed, and measurements were repeated after similar equilibration. Arterial blood gases were maintained at conscious levels by adjustment of nitrogen and oxygen concentrations throughout the experiment.

A series of four ventricular pressure–segment length loops were obtained during steady-state hemodynamic conditions in the autonomically blocked conscious state and with 1.0 and 1.5 MAC end-tidal desflurane or isoflurane. The pressure–length loops were plotted directly from the digital oscilloscope *via* a digital analog interface. The area of each loop, corresponding to segmental PRSW, was calculated by planimetry. The EDL of each loop was identified on the oscilloscope, digitally amplified to increase precision, and converted to the appropriate units (millimeters) by use of a linear formula generated with voltage–pressure calibration data. The regional PRSW was then plotted against the corresponding EDL for each loop. Linear regression analysis was used to describe the PRSW *versus* EDL slope (M_W) and length intercept (L_W).

Using the oscilloscope, the end-systolic pressure and end-systolic length of each loop also were identified. This point has been shown by Sagawa[16] to correspond to maximum ventricular elastance. These values were digitally amplified and converted to appropriate pressure (mmHg) and length (millimeters) units by use of linear formulas generated from calibration data. End-systolic pressure was plotted against end-systolic length, and linear regression analysis was used to describe the ESPLR slope (E_{MAX}) and length intercept (L_0).

At the completion of all experiments, anesthesia was discontinued and emergence allowed to occur. Prior to subsequent experimentation, each dog was allowed to recover for 3 days. Thus, a total of 14 experiments in two (desflurane or isoflurane) separate sets were completed in which the same seven dogs were used.

Statistical Analysis

Statistical analysis of data within and between sets during the conscious state with and without autonomic nervous system blockade and during all anesthetic interventions was performed by analysis of variance (ANOVA) with repeated measures followed by application of Bonferroni's modification of Student's *t* test. Changes from control within and between sets were considered statistically significant when the probability (*P*) value was <0.05. The PRSW *versus* EDL relationship and the ESPLR were described using linear regression analyses. All data were expressed as mean ± SEM.

Results

Autonomic nervous system blockade resulted in a significant ($P < 0.05$) increase in heart rate and decreases in mean arterial pressure, left ventricular systolic pressure, and systemic vascular resistance in both sets of experiments (tables 1 and 2). No changes in rate–pressure product, left ventricular end-diastolic pressure, or cardiac output were observed. The relationship between PRSW and EDL was found to be found to be highly linear ($r^2 \geq 0.97$) in conscious and anesthetized dogs with autonomic nervous system blockade. A linear relationship between end-systolic pressure and ESL ($r^2 \geq 0.96$) also was observed.

Isoflurane anesthesia resulted in significant decreases in heart rate, mean arterial pressure, left ventricular systolic pressure, and cardiac output. No changes in left ventricular end-diastolic pressure or systemic vascular resistance were observed. Isoflurane produced significant decreases in the PRSW *versus* EDL slope (57 ± 5 during control to 31 ± 3 $erg \cdot cm^{-2} \cdot 10^{-3} \cdot mm^{-1}$ at 1.5 MAC), consistent with the negative inotropic effects of this agent (fig. 1). Also observed were similar declines in dP/dt (1,801 ± 79 during control to 893 ± 70 mmHg/s at 1.5 MAC) and in dP/dt_{50} (1,639 ± 49 during control to 831 ± 83 mmHg/s at 1.5 MAC; fig. 2). Segment shortening declined at 1.5 MAC. E_{MAX} and L_0 did not change with the administration of isoflurane (table 3).

Desflurane produced systemic hemodynamic effects in the presence of autonomic nervous system blockade that were similar to those produced by isoflurane. Declines in heart rate, mean arterial pressure, rate–pressure product, and left ventricular systolic pressure were observed. Cardiac output was maintained at 1.0 MAC but decreased at 1.5 MAC. A small but significant increase in left ventric-

TABLE 1. Systemic Hemodynamic Effects of Isoflurane

	Conscious Control	ANS Blockade	Isoflurane (MAC) 1.0	Isoflurane (MAC) 1.5
HR (beats per min)	77 ± 5	112 ± 6*	95 ± 4*†	91 ± 4*†
MAP (mmHg)	90 ± 5	77 ± 4*	59 ± 4*†	47 ± 3*†
RPP (beats per min · mmHg · 10^3)	8.9 ± 0.7	10.3 ± 0.8	7.2 ± 0.6*†	5.7 ± 0.5*†
LVSP (mmHg)	118 ± 3	96 ± 4*	79 ± 4*†	69 ± 2*†
LVEDP (mmHg)	8 ± 1	7 ± 2	9 ± 2	11 ± 3
CO (l/min)	2.7 ± 0.3	2.9 ± 0.3	2.3 ± 0.3†	1.9 ± 0.2*†
SV (ml)	35 ± 3	26 ± 2*	24 ± 2*	21 ± 2*
SVR (dyn · s · cm^{-5})	2810 ± 380	2130 ± 280*	2120 ± 170*	2080 ± 180*
pH (u)		7.39 ± 0.02	7.37 ± 0.02	7.39 ± 0.02
Pa_{CO_2} (mmHg)	—	35 ± 1	31 ± 2	29 ± 2†
Pa_{O_2} (mmHg)	—	83 ± 3	93 ± 3	100 ± 4†
ET (%)	—	—	1.31 ± 0.02	1.95 ± 0.01

All data are means ± SEM; n = 7.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; ET = end-tidal anesthetic concentration.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from ANS blockade.

ular end-diastolic pressure was observed after administration of desflurane but not after isoflurane. Small increases in arterial oxygen tension (Pa_{O_2}) were noted in anesthetized dogs but no changes in pH or arterial carbon dioxide tension (Pa_{CO_2}) were observed (table 2).

Like isoflurane, desflurane resulted in a dose-dependent decrease in the PRSW *versus* EDL slope (53 ± 4 during control to 26 ± 4 erg · cm^{-2} · 10^{-3} · mm^{-1} at 1.5 MAC), indicating a direct negative inotropic effect (fig. 1). This finding was reflected in similar dose-dependent changes in dP/dt (1,750 ± 78 during control to 931 ± 86 mmHg/s at 1.5 MAC) and dP/dt_{50} (1,662 ± 63 during control to 901 ± 94 mmHg/s at 1.5 MAC; fig. 2). As was observed in the experiments using isoflurane, E_{max} and L_0 did not change when increasing doses of desflurane were administered (table 4).

Direct comparison of the effects of desflurane and isoflurane on contractility demonstrated no significant differences in left ventricular dP/dt, dP/dt_{50}, and ESPLR slope (E_{MAX}) and length intercept (L_0). Both anesthetics produced equivalent decreases in contractile function (55 ± 4% of control for isoflurane compared to 47 ± 5% of control for desflurane at end-tidal 1.5 MAC) as evaluated by M_W.

Discussion

The effects of the new inhalational anesthetic desflurane on myocardial contractility have yet to be completely

TABLE 2. Systemic Hemodynamic Effects of Desflurane

	Conscious Control	ANS Blockade	Desflurane (MAC) 1.0	Desflurane (MAC) 1.5
HR (beats per min)	76 ± 5	106 ± 6*	91 ± 5*†	87 ± 5†
MAP (mmHg)	91 ± 3	68 ± 6*	59 ± 4*	50 ± 4*†
RPP (beats per min · mmHg · 10^3)	8.8 ± 0.6	9.6 ± 1.0	7.1 ± 0.6†	5.8 ± 0.5*†
LVSP (mmHg)	119 ± 3	94 ± 6*	85 ± 3*	76 ± 3*†
LVEDP (mmHg)	7 ± 1	8 ± 1	12 ± 1*†	14 ± 1*†
CO (l/min)	2.8 ± 0.4	3.0 ± 0.3	2.5 ± 0.2	2.1 ± 0.2*†
SV (ml)	37 ± 5	29 ± 2	27 ± 2*	24 ± 3*
SVR (dyn · s · cm^{-5})	2840 ± 320	1890 ± 220*	2000 ± 160*	1980 ± 220*
pH (u)	—	7.38 ± 0.01	7.38 ± 0.03	7.36 ± 0.02
Pa_{CO_2} (mmHg)	—	32 ± 1	30 ± 2	31 ± 1
Pa_{O_2} (mmHg)	—	83 ± 2	93 ± 9	103 ± 5†
ET (%)	—	—	7.3 ± 0.03	10.6 ± 0.02

All data are mean ± SEM; n = 7.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; ET = end-tidal anesthetic concentration.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from ANS blockade.

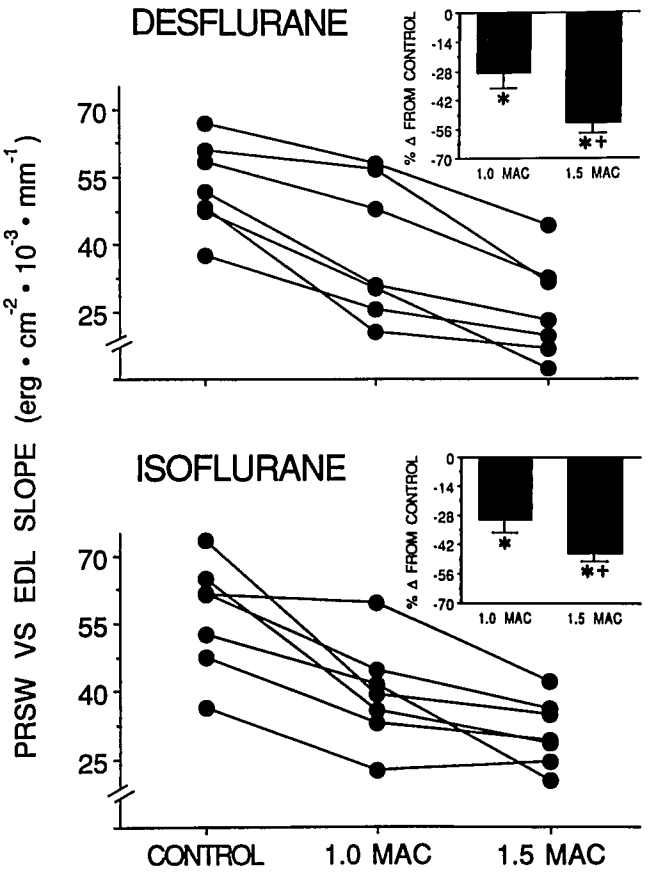

FIG. 1. Preload recruitable stroke work (PRSW) *versus* end-diastolic length (EDL) slope for each dog during control and at 1.0 and 1.5 end-tidal MAC of desflurane (*top*) and isoflurane (*bottom*). Figure insets depict percent changes from control. *Significantly ($P < 0.05$) different from control. †Significantly ($P < 0.05$) different from 1.0 MAC.

characterized. Weiskopf *et al.*[8] and more recently Merin *et al.*[9] examined the cardiovascular effects of desflurane in chronically instrumented swine and dogs, respectively, and showed that desflurane possessed myocardial depressant properties as evaluated by cardiac index, stroke volume, and mean aortic blood pressure, which were nearly indistinguishable from those produced by equianesthetic concentrations of isoflurane. Similar conclusions were drawn Cahalan *et al.*[10] in a study of the cardiovascular actions of desflurane and nitrous oxide in humans, although some of their evidence suggested that desflurane produces more myocardial depression than does isoflurane. In contrast, an investigation from the same laboratory[5] in healthy volunteers showed that desflurane, even at high concentrations, maintained cardiac output at near conscious levels, which indicates indirectly that this agent may produce less myocardial depression than does isoflurane.

Cardiac index also was maintained with increasing concentrations of desflurane in a recent investigation[6] of cerebral, metabolic and hemodynamic effects of desflurane in acutely prepared barbiturate-anesthetized dogs; progressive reductions in arterial pressure also were observed, consistent with declines in systemic vascular resistance. Also, in a preliminary investigation from this laboratory,[7] desflurane produced less depression of myocardial contractility as indicated by left ventricular dP/dt_{50} than did isoflurane; however, differences in the decreases in mean arterial pressure produced by isoflurane and desflurane may partially account for these observed differences in dP/dt_{50}. Conversely, maintenance of contractile function may explain the preservation of cardiovascular stability during desflurane anesthesia as compared to isoflurane anesthesia, as suggested by several of these studies.[5–7]

Although a possible qualitative difference between the effects of desflurane and isoflurane on myocardial contractility may be inferred from previous investigations,[5–7] the indices of contractility used in these studies were either indirect indicators of global left ventricular function (cardiac output and stroke volume) or are sig-

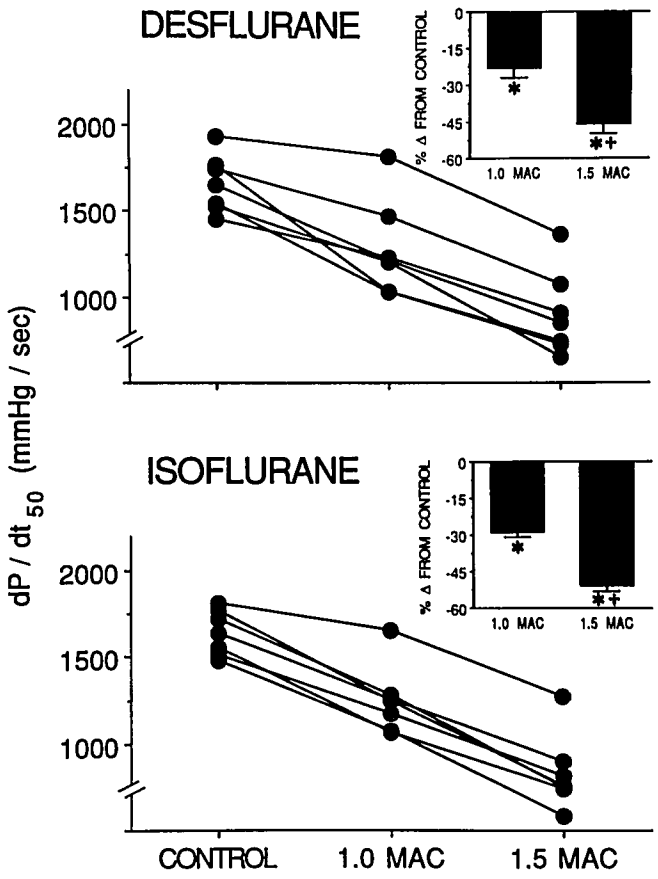

FIG. 2. dP/dt_{50} for each dog during control and at 1.0 and 1.5 end-tidal MAC desflurane (*top*) and isoflurane (*bottom*). Figure insets depict percent changes from control. *Significantly ($P < 0.05$) different from control. †Significantly ($P < 0.05$) different from 1.0 MAC.

TABLE 3. Effects of Isoflurane on Contractile Function

	ANS Blockade	Isoflurane (MAC) 1.0	Isoflurane (MAC) 1.5
dP/dt (mmHg/s)	1801 ± 79	1274 ± 83*	893 ± 70*†
dP/dt_{50} (mmHg/s)	1639 ± 49	1249 ± 75*	831 ± 83*†
SS (%)	22.6 ± 1.9	20.4 ± 1.3	15.0 ± 1.5*†
PRSW *versus* EDL slope (M_W) ($erg \cdot cm^{-2} \cdot 10^{-3} \cdot mm^{-1}$)	57 ± 5	39 ± 4*	31 ± 3*†
PRSW *versus* EDL intercept (L_W) (mm)	14.1 ± 1.0	13.7 ± 1.2	14.9 ± 1.5
ESPLR slope (E_{MAX}) (mmHg)	17 ± 2	16 ± 2	14 ± 2
ESPLR intercept (L_O) (mm)	10.2 ± 1.2	10.3 ± 1.4	11.1 ± 1.5

All data are mean ± SEM; n = 7.
ANS = autonomic nervous system; SS= segment shortening; EDL = end-diastolic length; PRSW = preload recruitable stroke work; ESPLR = end-systolic pressure–length relationship.
* Significantly ($P < 0.05$) different from ANS blockade.
† Significantly ($P < 0.05$) different from 1.0 MAC.

nificantly dependent on heart rate and ventricular loading conditions (maximum left ventricular dP/dt). Furthermore, these studies may have been substantially influenced by the direct effects of the volatile anesthetics on the systemic circulation[22] and by differential actions of the anesthetics on reflexes mediated through an intact autonomic nervous system.[23,24] The current investigation was undertaken to systematically examine the effects of desflurane on myocardial contractility and to compare these actions to those produced with equianesthetic concentrations of isoflurane using indices of myocardial performance that have been shown to be less dependent on heart rate and loading conditions. In addition, pharmacologic blockade of the autonomic nervous system was used to prevent reflex changes in systemic hemodynamics produced by anesthetics before or during the alterations in preload necessary to generate ventricular pressure–segment length loops in the conscious and anesthetized states. Thus, the direct myocardial depressant effects of desflurane and isoflurane were evaluated independent of autonomic nervous system tone.

In the current investigation, myocardial contractility was assessed using two linear models: the PRSW *versus* EDL relationship and the ESPLR. The PRSW *versus* EDL slope has been shown to be effective in characterizing changes in myocardial contractility in conscious[11] and anesthetized[12,13] dogs, providing an easily quantified, relatively afterload-independent index of contractile function. End-systolic pressure–length and pressure–volume relationships have also been shown to be sensitive and essentially heart rate- and load-independent measures of contractile state in both isolated[14–18] and intact[19–21] heart preparations, although some recent evidence[12,28–31] has questioned the utility of end-systolic pressure–dimension relationships as indices of depressed contractility *in vivo*.

The results of this investigation indicate that equianesthetic concentrations of desflurane and isoflurane produced progressive decreases in the PRSW *versus* EDL

TABLE 4. Effects of Desflurane on Contractile Function

	ANS Blockade	Desflurane (MAC) 1.0	Desflurane (MAC) 1.5
dP/dt (mmHg/s)	1750 ± 78	1303 ± 111*	931 ± 86*†
dP/dt_{50} (mmHg/s)	1662 ± 63	1286 ± 105*	901 ± 94*†
SS (%)	21.8 ± 1.6	17.8 ± 2.0	13.3 ± 2.4*†
PRSW *versus* EDL slope (M_W) ($erg \cdot cm^{-2} \cdot 10^{-3} \cdot mm^{-}-1$)	53 ± 4	39 ± 6*	26 ± 4*†
PRSW *versus* EDL intercept (L_W) (mm)	12.8 ± 1.9	14.6 ± 1.4	14.4 ± 1.9
ESPLR slope (E_{MAX}) (mmHg)	14 ± 2	15 ± 1	14 ± 2
ESPLR intercept (L_O) (mm)	11.1 ± 1.2	11.7 ± 1.2	12.4 ± 1.6

All data are mean ± SEM; n = 7.
ANS = autonomic nervous system; SS= segment shortening; EDL = end-diastolic length; PRSW = preload recruitable stroke work; ESPLR = end-systolic pressure–length relationship.
* Significantly ($P < 0.05$) different from ANS blockade.
† Significantly ($P < 0.05$) different from 1.0 MAC.

slope that were nearly identical, consistent with equivalent decreases in contractile function. These findings were supported by reductions in inotropic state demonstrated by left ventricular maximum positive dP/dt and dP/dt_{50}. These findings should be qualified, however, because the observation that desflurane produced a significant increase in left ventricular end-diastolic pressure suggests that desflurane produces a more direct effect on contractility than does isoflurane. The isovolumetric indices of global contractile function have been shown in previous studies[12,32] to closely reflect alterations in contractile state when preload and afterload are relatively constant, as was observed in the current experimental preparation. The changes in the PRSW *versus* EDL slope (M_W) observed for isoflurane were similar to but more pronounced than those described in a previous investigation,[12] possibly reflecting measurement of end-tidal rather than inspired anesthetic concentrations. In contrast to the PRSW *versus* EDL slope findings, neither ESPLR slope (E_{MAX}) nor length intercept (L_0) were statistically different from the conscious, autonomically blocked state when increasing concentrations of either isoflurane or desflurane were administered. These observations support evidence from this[12] and other laboratories[28-31] that changes in E_{max} and L_0 may be inadequate to describe depressed contractile function in the intact heart.

In summary, in the current investigation using PRSW *versus* EDL slope as index of contractility, desflurane has been shown to cause similar degrees of myocardial depression as those produced by equianesthetic concentrations of isoflurane. ESPLR slope (E_{MAX}) and length intercept (L_0) did not demonstrate decreases in contractile function with either anesthetic, supporting previous findings from this[12] and other laboratories[28-31] that question the use of these measures as indices of reduced contractility *in vivo*.

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