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Comparison of the Systemic and Coronary Hemodynamic Actions of Desflurane, Isoflurane, Halothane, and Enflurane in the Chronically Instrumented Dog

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The systemic and coronary hemodynamic effects of desflurane were compared to those of isoflurane, halothane, and enflurane in chronically instrumented dogs. Since autonomic nervous system function may significantly influence the hemodynamic actions of anesthetics *in vivo*, a series of experiments also was performed in the presence of pharmacologic blockade of the autonomic nervous system. Eight groups comprising a total of 80 experiments were performed on 10 dogs instrumented for measurement of aortic and left ventricular pressure, the peak rate of increase of left ventricular pressure (dP/dt), subendocardial segment length, coronary blood flow velocity, and cardiac output. Systemic and coronary hemodynamics were recorded in the conscious state and after 30 min equilibration at 1.25 and 1.75 MAC desflurane, isoflurane, halothane, and enflurane. Desflurane (+79 ± 12% change from control) produced greater increases in heart rate than did halothane (+44 ± 12% change from control) or enflurane (+44 ± 9% change from control) at 1.75 MAC. Desflurane preserved mean arterial pressure to a greater degree than did equianesthetic concentrations of isoflurane. This result was attributed to a smaller effect on peripheral vascular resistance as compared to isoflurane and greater preservation of myocardial contractility as evaluated by peak positive left ventricular dP/dt and the rate of increase of ventricular pressure at 50 mmHg (dP/dt_{50}) compared to other volatile anesthetics. Increases in diastolic coronary blood flow velocity (+19 ± 6 and +35 ± 12% change from control at 1.75 MAC, respectively) and concomitant decreases in diastolic coronary vascular resistance (−41 ± 12 and −58 ± 6% change from control at 1.75 MAC, respectively) were produced by desflurane and isoflurane. In the presence of autonomic nervous system blockade, the actions of desflurane and isoflurane were nearly identical with the exception of coronary vasodilation. After autonomic nervous system blockade, isoflurane increased coronary blood flow velocity, but desflurane did not. Furthermore, both desflurane and isoflurane continued to produce less depression of myocardial contractility than did halothane and enflurane. In summary, at equianesthetic concentrations, desflurane and isoflurane produced similar hemodynamic effects; however, in the absence of drugs that inhibit autonomic reflexes, desflurane had less negative inotropic activity and produced less decrease in arterial pressure. The coronary vasodilator actions of desflurane and isoflurane within the limitations of this model were not similar. When the increase in heart rate and rate–pressure product produced by desflurane were prevented in dogs with autonomic nervous system blockade, desflurane produced no change in coronary blood flow velocity. (Key words: Anesthetics, volatile: desflurane (I-653); enflurane; halothane; isoflurane. Heart: blood flow; cardiac depression; cardiac output; cardiovascular physiology; contractility; coronary hemodynamics; hemodynamics; myocardial function; ventricular function. Sympathetic nervous system: blockade.)

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THE SYSTEMIC AND CORONARY hemodynamic actions of the new inhalational anesthetic desflurane (I-653) have yet to be completely characterized. An initial study in swine[1] demonstrated that desflurane possesses cardiovascular effects nearly indistinguishable from those of isoflurane. Recent investigations in human volunteers,[2,3] however, suggested that desflurane may preserve cardiovascular stability to a greater degree than does isoflurane. In addition to this potentially beneficial effect, desflurane has several other advantageous characteristics—including a blood gas partition coefficient of 0.42, facilitating rapid induction and emergence[4,5]; stability in soda lime[6]; little or no metabolic breakdown[7,8]; and no demonstrable toxicity[9]—that make this inhalational anesthetic attractive for clinical use.

Since clinical trials of desflurane are now underway, the current investigation was undertaken to examine systematically and to characterize further the systemic and coronary hemodynamic effects of desflurane as compared to equianesthetic concentrations of isoflurane, halothane, and enflurane, in chronically instrumented dogs. Because volatile anesthetics may produce varying degrees of suppression of autonomic reflexes[10,11] and have indirect actions that are mediated through an intact autonomic nervous system, the cardiovascular actions of desflurane were compared to the other agents also after pharmacologic blockade of the autonomic nervous system. Thus, the direct effects of desflurane on systemic and coronary hemodynamics independent of autonomic nervous system reflexes also were evaluated and compared with those produced by isoflurane, halothane, and enflurane.

Materials and Methods

Animal Instrumentation

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

Conditioned mongrel dogs (n = 10) of either sex and weighing 20–30 kg were fasted overnight and then anesthetized with sodium thiamylal (10 mg/kg). After intubation of the trachea, anesthesia was maintained with enflurane (2.5–3.0%) in 100% O_2 *via* positive-pressure ventilation. Under sterile conditions, a thoracotomy was performed in the left fifth intercostal space. Heparin-filled catheters were placed in the descending thoracic aorta for measurement of aortic blood pressure and in the right atrium for fluid or drug administration. An ultrasonic flow probe (Transonics, Ithaca, NY) was positioned around the ascending aorta for measurement of cardiac output. A pair of miniature ultrasonic segment-length transducers (5 MHz) for measurement of changes in regional contractile function (segment shortening) were implanted within the left ventricular subendocardium (10–15 mm apart and 7–9 mm deep) in a circumferential plane in the perfusion territory of the left anterior descending coronary artery. A high-fidelity micromanometer (model P7, Konigsberg Instruments, Pasadena, CA) was implanted in the left ventricle for measurement of left ventricular pressure, the peak rate of increase of left ventricular pressure (dP/dt) and the rate of increase of ventricular pressure at 50 mmHg (dP/dt_{50}). A heparin-filled catheter was placed in the left atrial appendage. 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). A 1.5–2-cm segment of the proximal left anterior descending coronary artery was isolated, and a precalibrated Doppler ultrasonic flow transducer was placed around this vessel for measurement of diastolic coronary blood flow velocity. All instrumentation was secured, tunneled beneath the scapulae, and exteriorized *via* a small incision. The chest wall was closed in layers, and the pneumothorax was evacuated by a chest tube.

After surgery, each dog was treated with procaine penicillin G (25,000 U/kg) and gentamicin (4.5 mg/kg) and 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 end-diastolic segment length (EDL) was determined at the onset of left ventricular isovolumetric contraction. The lengths were normalized according to the method described by Theroux *et al.*[13] Percent segment shortening (%SS) was calculated by use of the equation: $\%SS = (EDL - ESL) \times 100/EDL$. Relative diastolic coronary vascular resistance was calculated as the quotient of diastolic arterial pressure and diastolic coronary blood flow velocity (hertz $\times 10^2$). All hemodynamic data were continuously recorded on a Hewlett Packard polygraph (model 7758A, Hewlett Packard, San Francisco, CA) and digitized on a computer interfaced with an analog-to-digital converter.

Experimental Protocol

Dogs were randomly assigned to receive desflurane, isoflurane, halothane, or enflurane with or without autonomic nervous system blockade on separate days. All dogs were fasted overnight, and fluid deficits were replaced before experimentation with crystalloid (500 ml 0.9% saline). Maintenance fluids were continued at 3 $ml \cdot kg^{-1} \cdot h^{-1}$ (0.9% saline) for the duration of each experiment.

In four groups of experiments, inhalational induction was accomplished with desflurane, isoflurane, halothane, or enflurane in 100% O_2 after baseline hemodynamics were recorded in the conscious state. After intubation of the trachea, anesthesia was maintained at 1.25 or 1.75 MAC (assigned randomly) in a N_2 (79%)–O_2 (21%) mixture. End-tidal concentrations of volatile anesthetics were determined with a mass spectrometer (Marquette Advantage 2000, St. Louis, MO) for isoflurane, halothane, and enflurane or with an infrared anesthetic gas analyzer (Datex Capnomac, Helsinki, Finland) for desflurane. Canine MAC values for desflurane,[14] isoflurane, halothane, and enflurane used in this study were 7.2, 1.28, 0.86, and 2.2%, respectively. Hemodynamics were recorded after a 30-min period of equilibration at the desired end-tidal concentration. The anesthetic concentration then was changed, and hemodynamics were recorded again after 30 min of equilibration. Arterial blood gases were maintained at conscious levels throughout the experiment.

In four additional sets of experiments, pharmacologic blockade of the autonomic nervous system was achieved with intravenous propranolol (2 mg/kg), atropine methylnitrate (3 mg/kg), and hexamethonium (20 mg/kg) prior to induction of anesthesia. Blockade of the auto-

¶ Department of Health, Education, and Welfare (Division of Health and Human Services): Guide for the Care and Use of Laboratory Animals. DHEW (DHHS) publication no. (NIH) 85-23, revised 1985.

nomic nervous system was used to prevent reflex changes in systemic hemodynamics during anesthetic interventions and to eliminate potential differential effects of various anesthetics on autonomic nervous system tone. A previous investigation in this laboratory[15] demonstrated that the doses of propranolol, atropine methylnitrate, and hexamethonium listed above are adequate to block hemodynamic responses to intravenous acetylcholine and isoproterenol for experiments of longer duration.

After autonomic nervous system blockade was completed and baseline hemodynamics were recorded, inhalational induction was accomplished with desflurane, isoflurane, halothane, or enflurane (assigned randomly), and the trachea was intubated. Anesthesia was maintained at 1.25 or 1.75 MAC (assigned randomly) in a N_2 (79%)–O_2 (21%) mixture for 30 min. Systemic and coronary hemodynamics and end-tidal anesthetic concentrations were recorded at the end of each interval. Arterial blood gases were maintained at conscious levels throughout each experiment.

At the completion of all experiments, anesthesia was discontinued, and emergence was allowed to occur. Prior to subsequent experimentation, each dog was allowed to recover for 1–3 days. Thus, a total of 80 experiments in eight separate sets were completed in the same ten dogs: desflurane, isoflurane, halothane, or enflurane were studied in separate groups with and without pharmacologic blockade of the autonomic nervous system.

Statistical Analysis

Statistical analysis of data within and between groups during the conscious state with and without autonomic nervous system blockade and during anesthetic interventions was performed by analysis of variance (ANOVA) with repeated measures followed by application of Bonferroni's modification of the *t* test. Changes from control within a group or between groups were considered statistically significant when the *P* value was <0.05. All data were expressed as mean ± SEM.

Results

Systemic and Coronary Hemodynamic Effects of Volatile Anesthetics

Results of experiments in which inhalational anesthetics were administered to dogs having intact autonomic nervous system reflexes are outlined in tables 1–4 and figures 1–7. Statistics describing differences between equipotent concentrations of desflurane, isoflurane, halothane, and enflurane in these experiments are summarized in table 5.

No differences in conscious control data among groups were observed. All four anesthetics produced an increase in heart rate. The tachycardia observed was greater with desflurane than with halothane or enflurane (fig. 1; table 5). Increasing concentrations of all anesthetics produced

TABLE 1. Effects of Desflurane on Systemic and Coronary Hemodynamics

	n	Conscious Control	Desflurane	
			1.25 MAC	1.75 MAC
HR (beats per min)	10	74 ± 5	134 ± 5*	128 ± 4*
MAP (mmHg)	10	93 ± 4	76 ± 4*	67 ± 5*†
RPP (beats per min · mmHg · 10^3)	10	9.2 ± 0.7	12.9 ± 0.9*	11.2 ± 0.8
LVSP (mmHg)	10	124 ± 4	97 ± 2*	88 ± 3*
LVEDP (mmHg)	10	10 ± 1	7 ± 1*	8 ± 1
dP/dt (mmHg/s)	10	2458 ± 143	1703 ± 151*	1384 ± 120*†
dP/dt_{50} (mmHg/s)	10	1997 ± 58	1560 ± 116*	1316 ± 118*†
DCBFV (Hz · 10^2)	6	35 ± 4	41 ± 5*	41 ± 4*
DCVR (ru)	6	2.35 ± 0.31	1.70 ± 0.32*	1.41 ± 0.31*
CO (l/min)	9	2.6 ± 0.3	2.4 ± 0.2	2.2 ± 0.2*
SV (ml)	9	36 ± 4	18 ± 2*	17 ± 2*
SVR (dyn · s · cm^{-5})	9	3130 ± 370	2890 ± 400	2790 ± 430
SS (%)	9	17.9 ± 2.0	13.0 ± 1.8*	11.1 ± 1.8*
*p*H	10	7.41 ± 0.01	7.38 ± 0.01	7.38 ± 0.02
P_{CO_2} (mmHg)	10	32 ± 1	34 ± 1	32 ± 1
P_{O_2} (mmHg)	10	85 ± 3	99 ± 7*	105 ± 5*
ET (%)	10	—	9.1 ± 0.1	12.5 ± 0.2†

All data are mean ± SEM.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from 1.25 MAC.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening; ET = end-tidal anesthetic concentration.

TABLE 2. Effects of Isoflurane on Systemic and Coronary Hemodynamics

	n	Conscious Control	Isoflurane 1.25 MAC	Isoflurane 1.75 MAC
HR (beats per min)	10	76 ± 6	125 ± 5*	118 ± 4*
MAP (mmHg)	10	101 ± 5	69 ± 3*	55 ± 5*†
RPP (beats per min · mmHg · 10^{-3})	10	10.1 ± 1.1	10.6 ± 0.6	8.3 ± 0.8
LVSP (mmHg)	10	131 ± 6	87 ± 3*	72 ± 4*†
LVEDP (mmHg)	10	9 ± 1	6 ± 1*	7 ± 1
dP/dt (mmHg/s)	10	2542 ± 167	1451 ± 85*	989 ± 92*†
dP/dt_{50} (mmHg/s)	10	2056 ± 77	1384 ± 80*	919 ± 114*†
DCBFV (Hz · 10^2)	6	33 ± 3	43 ± 4*	44 ± 4*
DCVR (ru)	6	2.64 ± 0.22	1.43 ± 0.09*	1.04 ± 0.06*
CO (l/min)	9	2.3 ± 0.3	2.1 ± 0.2	1.8 ± 0.2*
SV (ml)	9	30 ± 3	17 ± 2*	15 ± 2*
SVR (dyn · s · cm^{-5})	9	3410 ± 340	2560 ± 250*	2520 ± 240*
SS (%)	9	16.7 ± 1.7	13.9 ± 1.9*	10.6 ± 1.7*†
*p*H	10	7.43 ± 0.1	7.41 ± 0.02	7.38 ± 0.2
P_{CO_2} (mmHg)	10	32 ± 1	30 ± 1	32 ± 1
P_{O_2} (mmHg)	10	82 ± 2	100 ± 6*	101 ± 4*
ET (%)	10	—	1.61 ± 0.1	2.32 ± 0.1†

All data are mean ± SEM.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from 1.25 MAC.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening; ET = end-tidal anesthetic concentration.

TABLE 3. Effects of Halothane on Systemic and Coronary Hemodynamics

	n	Conscious Control	Haloflurane 1.25 MAC	Haloflurane 1.75 MAC
HR (beats per min)	10	80 ± 5	111 ± 4*	111 ± 5*
MAP (mmHg)	10	98 ± 4	70 ± 6*	60 ± 6*
RPP (beats per min · mmHg · 10^3)	10	10.2 ± 0.8	9.5 ± 0.8	8.3 ± 0.8
LVSP (mmHg)	10	127 ± 4	88 ± 6*	75 ± 6*†
LVEDP (mmHg)	10	8 ± 1	7 ± 1	9 ± 1
dP/dt (mmHg/s)	10	2436 ± 164	1148 ± 89*	854 ± 77*
dP/dt_{50} (mmHg/s)	10	2000 ± 99	1084 ± 90*	754 ± 93*†
DCBFV (Hz · 10^2)	6	33 ± 2	29 ± 3	29 ± 4
DCVR (ru)	6	2.61 ± 0.25	2.11 ± 0.31	1.98 ± 0.40
CO (l/min)	9	2.7 ± 0.4	2.0 ± 0.2*	1.7 ± 0.2*
SV (ml)	9	33 ± 4	19 ± 2*	16 ± 2*
SVR (dyn · s · cm^{-5})	9	3270 ± 460	2890 ± 390	3020 ± 410
SS (%)	9	19.5 ± 1.3	12.6 ± 13*	8.6 ± 0.8*†
*p*H	10	7.42 ± 0.01	7.41 ± 0.01	7.42 ± 0.01
P_{CO_2} (mmHg)	10	33 ± 0.7	30 ± 1.3	29 ± 0.9
P_{O_2} (mmHg)	10	81 ± 2	92 ± 4*	101 ± 5*
ET (%)	10	—	1.12 ± 0.01	1.56 ± 0.01†

All data are mean ± SEM.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from 1.25 MAC.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = percent segment shortening; ET = end-tidal anesthetic concentration.

TABLE 4. Effects of Enflurane on Systemic and Coronary Hemodynamics

	n	Conscious Control	Enflurane	
			1.25 MAC	1.75 MAC
HR (beats per min)	10	77 ± 5	111 ± 4*	107 ± 4*
MAP (mmHg)	10	98 ± 4	65 ± 4*	51 ± 4*†
RPP (beats per min · mmHg · 10^3)	10	9.6 ± 0.8	8.9 ± 0.8	6.7 ± 0.6*
LVSP (mmHg)	10	129 ± 5	83 ± 4*	69 ± 4*†
LVEDP (mmHg)	10	10 ± 1	8 ± 1	11 ± 1†
dP/dt (mmHg/s)	10	2453 ± 159	1026 ± 53*	714 ± 38*
dP/dt_{50} (mmHg/s)	10	1933 ± 71	970 ± 48*	590 ± 58*†
DCBFV (Hz · 10^2)	6	34 ± 2	37 ± 2	34 ± 4
DCVR (ru)	6	2.61 ± 0.11	1.66 ± 0.25*	1.57 ± 0.33*
CO (l/min)	9	2.4 ± 0.3	1.9 ± 0.3*	1.5 ± 0.2*†
SV (ml)	9	31 ± 3	16 ± 2*	13 ± 2*
SVR (dyn · s · cm^{-5})	9	3520 ± 270	3080 ± 300	3070 ± 360
SS (%)	9	18.4 ± 1.4	11.0 ± 1.1*	6.6 ± 0.7*†
pH	10	7.39 ± 0.02	7.36 ± 0.02	7.35 ± 0.02
P_{CO_2} (mmHg)	10	34 ± 1	33 ± 2	33 ± 2
P_{O_2} (mmHg)	10	82 ± 3	98 ± 5*	113 ± 7*
ET (%)	10	—	2.74 ± 0.02	3.82 ± 0.02†

All data are mean ± SEM.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from 1.25 MAC.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening; ET = end-tidal anesthetic concentration.

TABLE 5. Differences Between Effects of Anesthetics

	Anesthetic Concentration (MAC)	
	1.25	1.75
HR	D > I > E*> H*	D > I > E* > H*
MAP	D < H < I* < E*	D < H < I* < E*
RPP	D > I* > E* = H*	D > I* > H* > E*
LVSP	D < H < I < E	D < H < I < E
LVEDP	H > E > D > I	E > H > D§ > I§
dP/dt	D < I < H* < E*†	D < I* < H* < E*
dP/dt_{50}	D < I < H*† < E*†	D < I* < H* < E*†
DCBFV	I > D > E > H†	I > D > E† > H†
DCVR	H < D < E < I‡	H < D < E < I‡
CO	I < D < H† < E†	D < I < H < E*
SV	H < I < E < D	H < I < D < E
SVR	D < E < H < I	H < D = E < I
SS	I < D < H < E	I = D < H*† < E*†

No differences in conscious control data between groups were observed. The > or < symbols denote trends in percent changes from control unless specified with notations identifying statistical significance.
* Significantly ($P < 0.05$) different from desflurane.
† Significantly ($P < 0.05$) different from isoflurane.
‡ Significantly ($P < 0.05$) different from halothane.
§ Significantly ($P < 0.05$) different from enflurane.
D = desflurane; I = isoflurane; H = halothane; E = enflurane; HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening.

progressive decreases in mean arterial (fig. 2) and left ventricular systolic pressures. However, the changes produced by desflurane on mean arterial pressure were not as great as those produced by isoflurane or enflurane. Desflurane caused reductions in peak positive left ventricular dP/dt (2,458 ± 143 during control to 1,384 ± 120 mmHg/s at 1.75 MAC) and dP/dt_{50} (1,997 ± 58 during control to 1,316 ± 118 mmHg/s at 1.75 MAC; figure 3). Similarly, depression of regional contractile function as assessed by segment shortening (fig. 4) also was observed with desflurane (17.9 ± 2.0 during control to 11.1 ± 1.8% at 1.75 MAC). Compared to other volatile anesthetics, however, desflurane produced less depression of myocardial contractility than did isoflurane, halothane, or enflurane at 1.75 MAC (table 5).

Desflurane and isoflurane caused small changes in cardiac output only at high concentrations (tables 1 and 2, respectively). Halothane (table 3) and enflurane (table 4) produced progressive dose-related decreases in this variable (fig. 5). Isoflurane caused a significant decrease in systemic vascular resistance (3,410 ± 340 during control to 2,520 ± 240 dyn · s · cm^{-5} at 1.75 MAC), whereas desflurane, halothane, and enflurane did not (fig. 6). One dog was excluded from measurement of cardiac output and derived parameters in all experiments because of technical problems with instrumentation. No changes in arterial pH or arterial CO_2 tension (Pa_{CO_2}) were observed

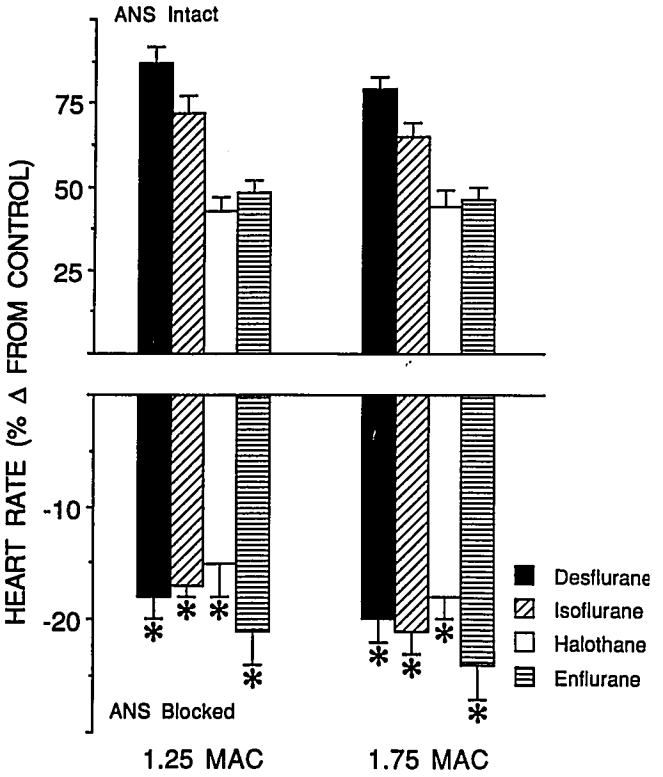

FIG. 1. Effects of anesthetics (1.25 and 1.75 MAC) on heart rate in autonomically (ANS) intact and blocked dogs. All values are significantly ($P < 0.05$) different from the baseline conscious control. *Significantly ($P < 0.05$) different from the same concentration in the autonomically intact dog.

in any group. Small increases in arterial O_2 tension (Pa_{O_2}) occurred in all anesthetized animals during positive-pressure ventilation.

Desflurane caused significant increases in diastolic coronary blood flow velocity (35 ± 4 during control to 41 ± 4 Hz × 10^2 at 1.75 MAC; fig. 7) and concomitant decreases in diastolic coronary vascular resistance (table 1). Similar changes in coronary flow were observed with isoflurane (table 2; fig. 7). In contrast, enflurane produced no changes in diastolic coronary blood flow velocity but did produce significant decreases in diastolic coronary vascular resistance (table 4). No change in either variable was observed with halothane (fig. 7). Four dogs were excluded from measurement of diastolic coronary blood flow velocity in all experiments because of technical problems with coronary instrumentation.

Systemic and Coronary Hemodynamic Effects of Volatile Anesthetics in Autonomically Blocked Dogs

No differences in conscious control data among groups were observed. In all groups, autonomic nervous system blockade produced increases in heart rate and decreases in mean arterial pressure, left ventricular systolic, and end-diastolic pressures, left ventricular dP/dt and dP/dt_{50}, diastolic coronary vascular resistance, stroke volume, and systemic vascular resistance. No changes in coronary blood flow velocity, cardiac output and segment shortening were observed. The results of these experiments are summarized in tables 6–9 and figures 1–7. Statistics describing differences between equipotent concentrations of desflurane, isoflurane, halothane, and enflurane are shown in table 10.

In the presence of autonomic nervous system blockade, all volatile anesthetics decreased heart rate (fig. 1), mean arterial pressure (fig. 2), rate–pressure product, and left ventricular systolic pressure, and increased left ventricular end-diastolic pressure. No differences among anesthetic agents were observed.

Desflurane and isoflurane caused similar decreases in left ventricular dP/dt and dP/dt_{50} (fig. 3), segment shortening (fig. 4), and cardiac output (fig. 5). Depression of these indices of contractility by desflurane and isoflurane was less than that observed for halothane and enflurane (table 10). No change in systemic vascular resis-

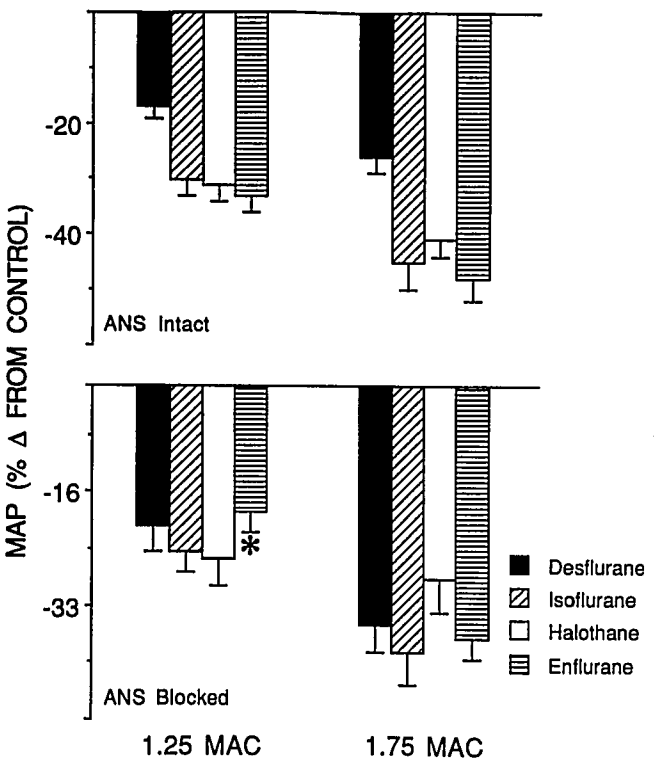

FIG. 2. Effects of anesthetics (1.25 and 1.75 MAC) on mean arterial pressure (MAP) in autonomically (ANS) intact and blocked dogs. All values are significantly ($P < 0.05$) different from the baseline conscious control. *Significantly ($P < 0.05$) different from the same anesthetic at the same concentration in the autonomically intact dog.

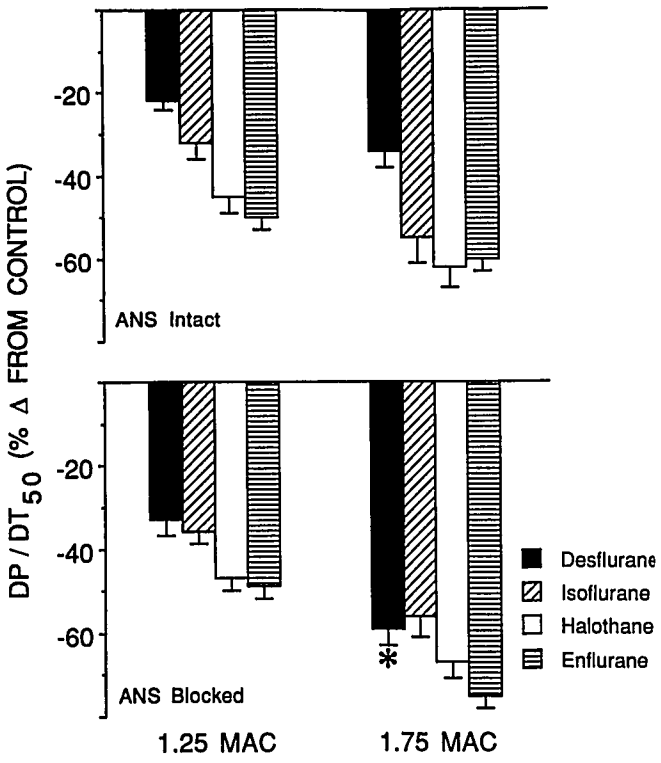

FIG. 3. Effects of anesthetics (1.25 and 1.75 MAC) on left ventricular dP/dt_{50} in autonomically (ANS) intact and blocked dogs. All values are significantly ($P < 0.05$) different from the baseline conscious control. *Significantly ($P < 0.05$) different from the same anesthetic at the same concentration in the autonomically intact dog.

tance (fig. 6) was observed with increasing concentrations of anesthetic with the exception of enflurane at 1.75 MAC. No changes in arterial blood *p*H or Pa_{CO_2} were observed in any group. Pa_{O_2} was slightly elevated in all anesthetized animals.

In dogs given autonomic nervous system blockade, diastolic coronary blood flow velocity remained constant during desflurane, halothane, and enflurane anesthesia but increased with isoflurane at 1.75 MAC (fig. 7). Comparison among all four anesthetics revealed similar decreases in diastolic coronary blood flow velocity vascular resistance, however (table 10).

Discussion

Desflurane (I-653) is a new inhalational anesthetic possessing several physical characteristics, most notably a very low blood gas partition coefficient[4] and remarkable metabolic stability,[6–9] which make it attractive for clinical use. The systemic and coronary hemodynamic effects of desflurane have yet to be firmly established. Weiskopf *et al.*[1] studied the hemodynamic effects of desflurane in swine and found that desflurane was less potent than isoflurane but possessed cardiovascular depressant properties nearly indistinguishable from equianesthetic concentrations of isoflurane. In contrast, other investigations from the same laboratory[2,3] in healthy volunteers identified several significant differences between desflurane and isoflurane. Desflurane produced a smaller decrease in mean arterial pressure and systemic vascular resistance than did isoflurane. Desflurane also appeared to reduce cardiac output less than did isoflurane, especially at higher concentrations. The authors concluded that desflurane maintained cardiovascular stability to a greater degree than did isoflurane. A recent investigation of cerebral, metabolic and hemodynamic effects of desflurane in acutely prepared, barbiturate-anesthetized dogs by Lutz *et al.*[16] showed that desflurane caused progressive decreases in arterial blood pressure and systemic vascular resistance. Cardiac index and heart rate, however, were maintained at near-control levels except at concentrations greater than 1.5 MAC.

None of the aforementioned studies examined the effects of desflurane on the coronary circulation or on myocardial contractility. Thus, the current investigation was undertaken to further define the cardiovascular actions of desflurane, including effects of this agent on contractile function and coronary blood flow. Direct comparison of

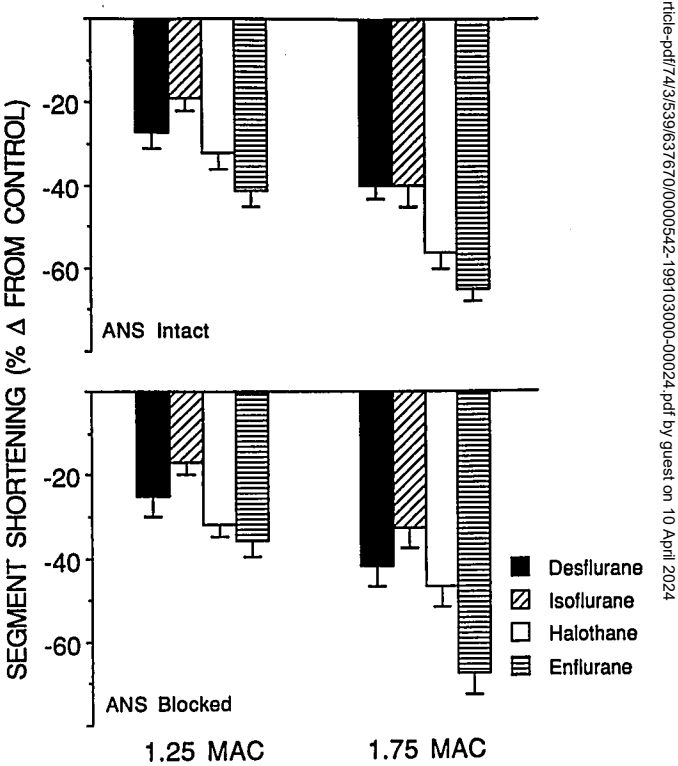

FIG. 4. Effects of anesthetics (1.25 and 1.75 MAC) on segment shortening in autonomically (ANS) intact and blocked dogs. All values are significantly ($P < 0.05$) different from the baseline conscious control. *Significantly ($P < 0.05$) different from the same anesthetic at the same concentration in the autonomically intact dog.

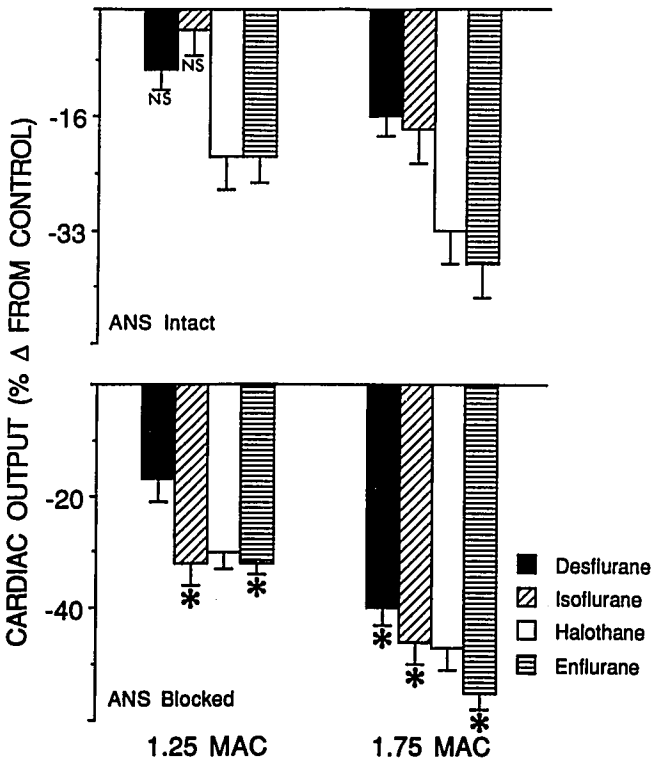

FIG. 5. Effects of anesthetics (1.25 and 1.75 MAC) on cardiac output in autonomically (ANS) intact and blocked dogs. Values are significantly ($P < 0.05$) different from the baseline conscious control except when indicated by NS (not significant). *Significantly ($P < 0.05$) different from the same anesthetic at the same concentration in the autonomically intact dog.

desflurane with equianesthetic concentrations of isoflurane, halothane, and enflurane were made in the same chronically instrumented dog on different days to reduce experimental variability and so permit comparisons within the same animal.

Hemodynamic effects of isoflurane, halothane, and enflurane observed in this investigation in chronically instrumented dogs were consistent with previous findings from this[17,18] and other laboratories.[19–22] Although desflurane and isoflurane produced similar cardiovascular actions, several differences between these two agents were noted. Like isoflurane, desflurane of increasing concentrations caused a significant tachycardia that was greater than that produced by halothane or enflurane. The increases in heart rate observed with desflurane at 1.25 MAC were similar to increases in heart rate observed by Weiskopf *et al.* in chronically instrumented swine.[1] In contrast, little change in heart rate was observed at lower concentrations in humans, although tachycardia resulted at 1.5 MAC.[3]

The reasons for the variation between results in experimental animals and humans are unclear. Desflurane reduced arterial blood pressure to a smaller extent than did isoflurane, halothane, or enflurane. Both halothane and enflurane produced progressive declines in cardiac output, whereas desflurane and isoflurane had only minimal effects. Isoflurane significantly decreased systemic vascular resistance, whereas desflurane, halothane, and enflurane did not. Hence, although desflurane was found to possess cardiovascular depressant properties, this new agent maintained arterial blood pressure to a greater degree than did isoflurane, halothane, or enflurane.

Preservation of arterial blood pressure by desflurane in this investigation appeared to be due to two factors. First, desflurane produced less peripheral vasodilation and less subsequent decrease in arterial pressure than did isoflurane. Second, desflurane had a smaller effect on left ventricular function as assessed by dP/dt and dP/dt_{50} than did the other three volatile anesthetics, although no differences between desflurane and isoflurane were observed when regional contractility (SS) or indirect indicators of contractile state (cardiac output and stroke volume) were considered.

The results of this investigation clearly support the findings of Cahalan *et al.*[2] and Weiskopf *et al.*[3] in human

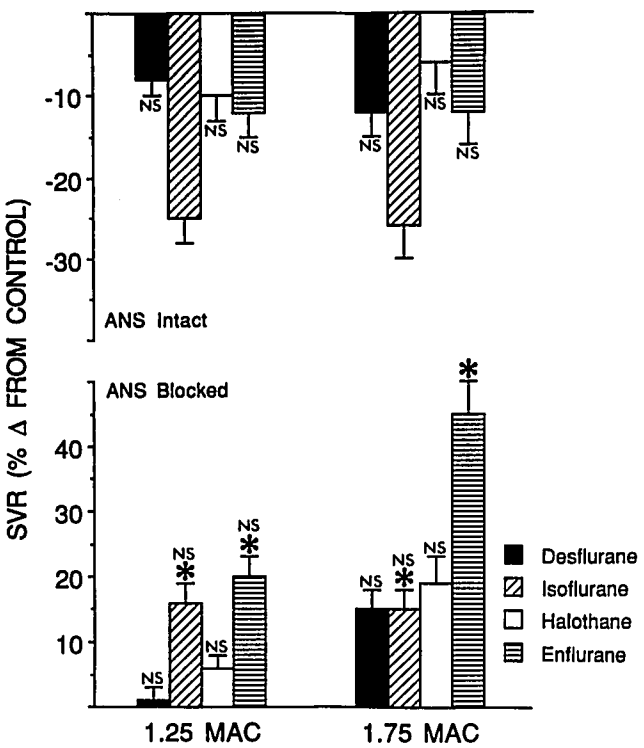

FIG. 6. Effects of anesthetics (1.25 and 1.75 MAC) on systemic vascular resistance (SVR) in autonomically (ANS) intact and blocked dogs. Values are significantly ($P < 0.05$) different from the baseline conscious control except when indicated by NS (not significant). *Significantly ($P < 0.05$) different from the same anesthetic at the same concentration in the autonomically intact dog.

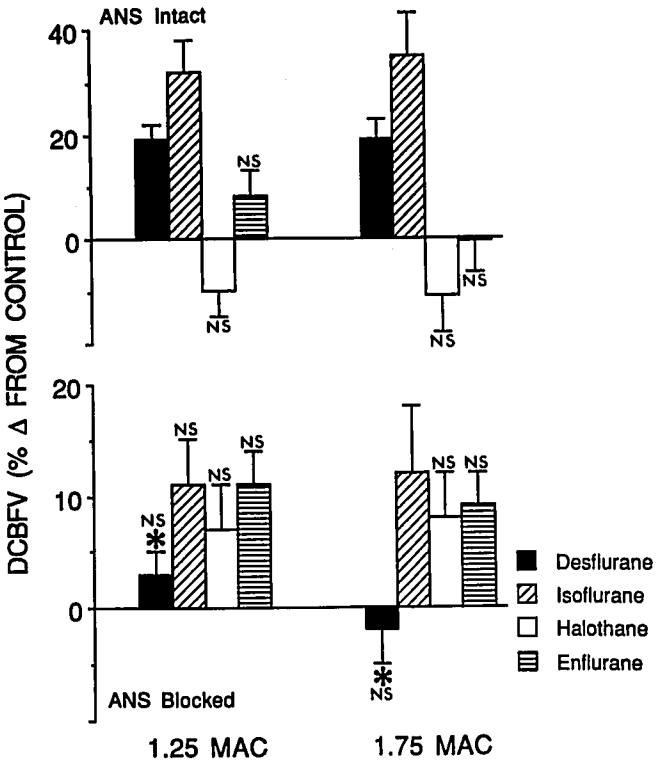

FIG. 7. Effects of anesthetics (1.25 and 1.75 MAC) on diastolic coronary blood flow velocity (DCBFV) in autonomically (ANS) intact and blocked dogs. Values are significantly ($P < 0.05$) different from the baseline conscious control except when indicated by NS (not significant). *Significantly ($P < 0.05$) different from the same anesthetic at the same concentration in the autonomically intact dog.

volunteers. The results only partially support those findings of Lutz *et al.*[16] in an acute canine preparation, although the presence of a high baseline heart rate, neuromuscular blockade with pancuronium, and extensive neurosurgical manipulation in the latter study makes direct comparison to the current work difficult. In contrast to the findings of the current investigation, a study of the effects of desflurane and isoflurane in chronically instrumented swine revealed that both anesthetics resulted in equivalent dose-dependent decreases in mean arterial pressure, systemic vascular resistance, and cardiac output.[1] It is unclear why hemodynamic effects similar to those observed in the current study were not present when desflurane was studied in chronically instrumented swine, although species variation may partially account for discrepancies between the results.

Because volatile anesthetics may produce differential suppression of autonomic reflexes and have indirect actions on systemic hemodynamics mediated through an intact autonomic nervous system,[10,11] the cardiovascular actions of desflurane also were compared to those of other volatile anesthetics after pharmacologic blockade of the autonomic nervous system. This allowed examination of the direct effects of these agents on intrinsic cardiovascular function, independent of autonomic reflexes. In the presence of autonomic blockade, all anesthetics, including desflurane, caused similar decreases in heart rate, consistent with depression of phase-4 sinoatrial node depolarization described for isoflurane, halothane, and enflurane *in vitro* by Bosnjak and Kampine.[23] Autonomic nervous system blockade also eliminated the differences in dP/dt and dP/dt_{50} between desflurane and isoflurane.

Left ventricular dP/dt and dP/dt_{50} have been shown[12,24] to quantitatively reflect the inotropic state only in the presence of relatively constant heart rate, preload, and afterload. It is possible that in the current investigation, differences in the effects of desflurane and isoflurane on dP/dt and dP/dt_{50} in dogs with a functional autonomic nervous system are attributable to differences in heart rate and loading conditions observed between groups. An equally likely explanation, however, is that desflurane produced less depression of sympathetic tone and autonomic reflexes than did isoflurane, and thereby resulted in greater contractility at any given level of anesthetic depth. This smaller depression also may explain why desflurane produced a less significant effect on arterial pressure but greater increases in heart rate. Both desflurane and isoflurane produced less depression of dP/dt and dP/dt_{50} than did equianesthetic concentrations of halothane and enflurane in the autonomically blocked dog.

These results suggest that desflurane, like isoflurane, may have less intrinsic negative inotropic properties than halothane and enflurane. Further studies with more sensitive and specific indices of contractility[12] that are less dependent on heart rate and loading conditions are warranted to confirm and quantify these results. The differences between isoflurane and halothane observed in this experiment are consistent with previous investigations from this[12] and other[19,21,22] laboratories.

Desflurane, like isoflurane, increased diastolic coronary blood flow velocity and decreased diastolic coronary vascular resistance in dogs with a functional autonomic nervous system. This may be due to direct coronary vasodilator actions. However, coronary blood flow is autoregulated to myocardial O_2 demand, and in the current investigation, desflurane may have increased O_2 demand, as indicated by an increase in the rate–pressure double product at 1.25 MAC. The increase in coronary blood flow velocity and rate–pressure product were eliminated with autonomic nervous system blockade. The relative lack of coronary vasodilation with desflurane after autonomic blockade indicates that this agent has only minimal direct vasodilator properties *in vivo*. However, these results must be qualified, since no specific measurements of myo-

TABLE 6. Effects of Desflurane on Systemic and Coronary Hemodynamics during Autonomic Nervous System Blockade

	n	Conscious Control	ANS Blockade	Desflurane 1.25 MAC	Desflurane 1.75 MAC
HR (beats per min)	10	73 ± 4	108 ± 5*	89 ± 3*†	86 ± 3*†
MAP (mmHg)	10	95 ± 2	73 ± 3*	58 ± 4*†	47 ± 4*†‡
RPP (beats per min · mmHg · 10^3)	10	9.2 ± 0.4	10.5 ± 0.5	7.2 ± 0.7*†	5.7 ± 0.6*†
LVSP (mmHg)	10	124 ± 3	94 ± 3*	80 ± 4*†	68 ± 4*†‡
LVEDP (mmHg)	10	12 ± 1	7 ± 1*	10 ± 1†	12 ± 1†
dP/dt (mmHg/s)	10	2,310 ± 171	1,715 ± 134*	1,145 ± 102*†	768 ± 75*†‡
dP/dt_{50} (mmHg/s)	10	1,885 ± 112	1,618 ± 118*	1,097 ± 105*†	688 ± 89*†‡
DCBFV (Hz · 10^2)	6	30 ± 3	34 ± 5	35 ± 5	34 ± 6
DCVR (ru)	6	2.98 ± 0.33	2.17 ± 0.35*	1.76 ± 0.31*	1.54 ± 0.28*†
CO (l/min)	9	2.3 ± 0.2	2.5 ± 0.3	2 ± 0.2†	1.5 ± 0.2*†‡
SV (ml)	9	31 ± 3	23 ± 2*	22 ± 2*	17 ± 2*†‡
SVR (dyn · s · cm^{-5})	9	3,530 ± 250	2,580 ± 280*	2,410 ± 190*	2,700 ± 190*
SS (%)	9	18.3 ± 2.1	18.4 ± 1.9	13.9 ± 1.8*†	10.6 ± 1.3*†
*p*H	10	—	7.41 ± 0.01	7.37 ± 0.02	7.37 ± 0.02
P_{CO_2} (mmHg)	10	—	33 ± 1	31 ± 1	31 ± 2
P_{O_2} (mmHg)	10	—	81 ± 4	100 ± 6†	106 ± 5†
ET (%)	10	—	—	9.0 ± 0.02	12.4 ± 0.16‡

All data are mean ± SEM.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from ANS blockade.
‡ Significantly ($P < 0.05$) different from 1.25 MAC.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening; ET = end-tidal anesthetic concentration.

TABLE 7. Effects of Isoflurane on Systemic and Coronary Hemodynamics during Autonomic Nervous System Blockade

	n	Conscious Control	ANS Blockade	Isoflurane 1.25 MAC	Isoflurane 1.75 MAC
HR (beats per min)	10	73 ± 5	109 ± 4*	90 ± 4*†	86 ± 4*†
MAP (mmHg)	10	98 ± 2	75 ± 3*	56 ± 5*†	46 ± 7*†
RPP (beats per min · mmHg · 10^3)	10	9.3 ± 0.7	10.5 ± 0.7	6.8 ± 0.7*†	5.3 ± 0.7*†
LVSP (mmHg)	10	130 ± 3	98 ± 3*	78 ± 5*†	66 ± 6*†
LVEDP (mmHg)	10	10 ± 1	7 ± 1*	10 ± 1	11 ± 1†
dP/dt (mmHg/s)	10	2,384 ± 137	1,724 ± 94*	1,121 ± 113*†	797 ± 110*†‡
dP/dt_{50} (mmHg/s)	10	1,917 ± 83	1,583 ± 64*	1,024 ± 113*†	703 ± 102*†‡
DCBFV (Hz · 10^2)	6	35 ± 6	36 ± 6	42 ± 7	46 ± 6†
DCVR (ru)	6	2.89 ± 0.42	2.08 ± 0.35*	1.33 ± 0.17*†	1.03 ± 0.18*†
CO (l/min)	9	2.28 ± 0.2	2.6 ± 0.2*	1.8 ± 0.2†	1.4 ± 0.2*†
SV (ml)	9	31 ± 3	24 ± 2*	20 ± 2*	16 ± 2*†
SVR (dyn · s · cm^{-5})	9	3,840 ± 330	2,400 ± 200*	2,740 ± 300*	2,880 ± 260*
SS (%)	9	19.6 ± 2.0	20.0 ± 1.9	16.6 ± 1.6†	13.0 ± 1.1*†‡
*p*H	10	—	7.41 ± 0.02	7.39 ± 0.02	7.39 ± 0.01
P_{CO_2} (mmHg)	10	—	33 ± 1	31 ± 1	31 ± 1
P_{O_2} (mmHg)	10	—	78 ± 2	95 ± 6†	99 ± 7†
ET (%)	10	—	—	1.61 ± 0.13	2.35 ± 0.14‡

All data are mean ± SEM.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from ANS blockade.
‡ Significantly ($P < 0.05$) different from 1.25 MAC.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening; ET = end-tidal anesthetic concentration.

TABLE 8. Effects of Halothane on Systemic and Coronary Hemodynamics during Autonomic Nervous System Blockade

	n	Conscious Control	ANS Blockade	Halothane 1.25 MAC	Halothane 1.75 MAC
HR (beats per min)	10	81 ± 4	107 ± 5*	91 ± 3*†	87 ± 3†
MAP (mmHg)	10	99 ± 3	75 ± 4*	55 ± 4*†	45 ± 5*†
RPP (beats per min · mmHg · 10^3)	10	10.4 ± 0.5	10.5 ± 0.8	6.5 ± 0.5*†	5.1 ± 0.6*†
LVSP (mmHg)	10	128 ± 3	96 ± 4*	75 ± 3*†	65 ± 4*†
LVEDP (mmHg)	10	9 ± 1	6 ± 1*	9 ± 1	11 ± 1†
dP/dt (mmHg/s)	10	2,520 ± 135	1,753 ± 83*	924 ± 49*†	653 ± 46*†‡
dP/dt_{50} (mmHg/s)	10	2,009 ± 43	1,628 ± 65*	865 ± 64*†	526 ± 61*†‡
DCBFV (Hz · 10^2)	6	36 ± 3	37 ± 4	41 ± 6	42 ± 7
DCVR (ru)	6	2.53 ± 0.20	1.92 ± 0.29*	1.30 ± 0.23*†	1.05 ± 0.20*†
CO (l/min)	9	2.3 ± 0.2	2.2 ± 0.2	1.6 ± 0.2*†	1.2 ± 0.2*†
SV (ml)	9	30 ± 3	22 ± 2*	18 ± 2*	14 ± 2*†
SVR (dyn · s · cm^{-5})	9	3,720 ± 330	2,750 ± 210*	2,870 ± 310	3,260 ± 510
SS (%)	9	19.0 ± 1.76	18.1 ± 1.5	11.8 ± 1.1*†	8.1 ± 0.9*†
*p*H	10	—	7.40 ± 0.01	7.39 ± 0.01	7.39 ± 0.01
P_{CO_2} (mmHg)	10	—	33 ± 1	31 ± 1	31 ± 1
P_{O_2} (mmHg)	10	—	84 ± 2	105 ± 5†	98 ± 5†
ET (%)	10	—	—	1.10 ± 0.01	1.53 ± 0.02‡

All data are mean ± SEM.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from ANS blockade.
‡ Significantly ($P < 0.05$) different from 1.25 MAC.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening; ET = end-tidal anesthetic concentration.

TABLE 9. Effects of Enflurane on Systemic and Coronary Hemodynamics during Autonomic Nervous System Blockade

	n	Conscious Control	ANS Blockade	Enflurane 1.25 MAC	Enflurane 1.75 MAC
HR (beats per min)	10	76 ± 4	104 ± 5*	81 ± 5†	79 ± 5†
MAP (mmHg)	10	99 ± 3	67 ± 3*	54 ± 2*†	41 ± 2*†‡
RPP (beats per min · mmHg · 10^3)	10	9.7 ± 0.5	9.4 ± 0.6	5.8 ± 0.5*†	4.4 ± 0.3*†‡
LVSP (mmHg)	10	127 ± 4	90 ± 3*	75 ± 3*†	59 ± 3*†‡
LVEDP (mmHg)	10	8 ± 1	5 ± 1*	8 ± 1	10 ± 1†
dP/dt (mmHg/s)	10	2,352 ± 127	1,666 ± 82*	898 ± 55*†	560 ± 51*†‡
dP/dt_{50} (mmHg/s)	10	1,960 ± 81	1,596 ± 72*	826 ± 71*†	396 ± 46*†‡
DCBFV (Hz · 10^2)	6	32 ± 4	29 ± 4	32 ± 5	32 ± 5
DCVR (ru)	6	3.08 ± 0.46	2.15 ± 0.34*	1.69 ± 0.31*	1.25 ± 0.18*
CO (l/min)	9	2.1 ± 0.2	2.2 ± 0.1	1.5 ± 0.1*†	1.0 ± 0.1*†
SV (ml)	9	28 ± 2	22 ± 1*	19 ± 1*	13 ± 1*†‡
SVR (dyn · s · cm^{-5})	9	4,040 ± 320	2,470 ± 175*	2,920 ± 172*	3,570 ± 390†
SS (%)	9	18.6 ± 1.5	18.2 ± 1.1	11.6 ± 1.0*†	5.8 ± 1.0*†
*p*H	10	—	7.39 ± 0.02	7.37 ± 0.02	7.38 ± 0.02
P_{CO_2} (mmHg)	10	—	33 ± 2	33 ± 2	31 ± 1
P_{O_2} (mmHg)	10	—	81 ± 2	102 ± 7†	101 ± 7†
ET (%)	10	—	—	2.75 ± 0.02	3.84 ± 0.03‡

All data are mean ± SEM.
* Significantly ($P < 0.05$) different from conscious control.
† Significantly ($P < 0.05$) different from ANS blockade.
‡ Significantly ($P < 0.05$) different from 1.25 MAC.
HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening; ET = end-tidal anesthetic concentration.

TABLE 10. Differences Between Effects of Anesthetics during Autonomic Nervous System Blockade

	Anesthetic Concentration (MAC)	
	1.25	1.75
HR	H < I < D < E	H < D < I < E
MAP	E < D < I < H	D < E < H < I
RPP	D < I < H < E	I < D < H < E
LVSP	D < E < I < H	D < I = H < E
LVEDP	D > E > H > I	D > E > H > I
dP/dt	D< I < E*,† < H*,†	D = I < H < E*,†
dP/dt_{50}	D < I < H* < E*	I < D < H < E*,†
DCBFV	I = E > H > D	I > E > H > D
DCVR	D < E < I < H	D < I < E < H
CO	D < H* < I* = E*	D < I < H*,† < E*,†
SV	D < E < I < H	D < I < H < E
SVR	E < I < H < D	E > H > D = I
SS	I < D < H† < E†	I < D < H† < E*,†

No difference in data during autonomic nervous system blockade between groups were observed. The > or < symbols denote trends in percent changes from control unless specified with notations identifying statistical significance.

* Significantly ($P < 0.05$) different from desflurane.

† Significantly ($P < 0.05$) different from isoflurane.

D = desflurane; I = isoflurane; H = halothane; E = enflurane; HR = heart rate; MAP = mean arterial pressure; RPP = rate–pressure product; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; DCBFV = diastolic coronary blood flow velocity; DCVR = diastolic coronary vascular resistance; CO = cardiac output; SV = stroke volume; SVR = systemic vascular resistance; SS = segment shortening.

cardial O_2 extraction or coronary sinus O_2 tension were made, and since interpretation of coronary blood flow velocity measurements may be difficult due of simultaneous changes in O_2 demand and coronary perfusion pressure.

The above results contrast those obtained with isoflurane, a known coronary vasodilator. This agent increased diastolic coronary flow velocity in the presence of autonomic blockade. These data support the contention that increases in coronary blood flow velocity and decreases in coronary vascular resistance observed during desflurane anesthesia in the dog with normal autonomic reflexes may be attributed to metabolic autoregulation rather than to intrinsic coronary vasodilating actions. Nonetheless, although desflurane may have few direct effects on the coronary vasculature, desflurane does have indirect effects similar to those produced by isoflurane. Therefore, the potential for desflurane to cause "coronary steal" cannot be completely excluded on the basis of the results of this investigation.

In summary, the current investigation confirms and extends the results of Cahalan *et al.*[2] and Weiskopf *et al.*[3] The effects of desflurane on systemic and coronary hemodynamics were similar to but not identical with those produced by isoflurane in the autonomically intact, chronically instrumented dog. Specifically, desflurane had less effect on mean arterial pressure and left ventricular dP/dt and dP/dt_{50} than did equianesthetic concentrations of isoflurane. Desflurane produced little if any direct coronary vasodilation within the limitations of the current model. The changes observed in diastolic coronary blood flow velocity with desflurane were due probably to autoregulation in response to increases in myocardial O_2 demand secondary to increases in heart rate.

Comparison of desflurane with isoflurane, halothane, and enflurane in the autonomically blocked dog revealed that desflurane and isoflurane were nearly identical in action, with the exception of actions on the coronary circulation. In the presence of autonomic blockade, both desflurane and isoflurane caused equal depression of myocardial contractility as assessed by dP/dt, dP/dt_{50}, and segment shortening, and this depression was less than that produced by halothane and enflurane. These results may indicate that desflurane has less depressant effects on autonomic activity than do other volatile anesthetics, and therefore that during desflurane anesthesia, hemodynamics are maintained closer to those during consciousness.

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