Anesthesiology
1996; 85:112–20

Influence of Volatile Anesthetics on Left Ventricular Afterload In Vivo

Differences between Desflurane and Sevoflurane

Dermot Lowe, M.Sc., F.F.A.R.C.S.I., Douglas A. Hettrick, Ph.D.,† Paul S. Pagel, M.D., Ph.D.,† David C. Warltier, M.D., Ph.D.‡*

Background: **This investigation examined the effects of desflurane and sevoflurane on quantitative indices of left ventricular afterload derived from aortic input impedance (Z_{in}) interpreted using a three-element Windkessel model.**

Methods: **After Animal Care Committee approval, dogs (n = 8) were chronically instrumented for measurement of systemic hemodynamics including aortic blood pressure and flow. On separate days, aortic pressure and flow waveforms were recorded under steady-state conditions in the conscious state and after equilibration for 30 min at 1.1, 1.3, 1.5, and 1.7 minimum alveolar concentration of desflurane or sevoflurane. Aortic input impedance spectra were obtained *via* power spectral analysis of aortic pressure and flow waveforms. Characteristic aortic impedance (Z_c) and total arterial resistance were calculated as the mean of the magnitude of Z_{in} between 2 and 15 Hz and the difference between Z_{in} at zero frequency and Z_c, respectively. Total arterial compliance (C) was calculated from aortic pressure and flow waveforms using the Windkessel model.**

Results: **Desflurane and sevoflurane increased heart rate and decreased systolic, diastolic, and mean arterial pressure, left ventricular systolic pressure, left ventricular peak positive rate of increase in left ventricular pressure, percent segment shortening, and stroke volume. Sevoflurane, but not desflurane, decreased cardiac output. Desflurane, but not sevoflurane, decreased systemic vascular resistance. Desflurane decreased R (3,170 ± 188 during control to 2441 ± 220 dynes · second · centimeter^{-5} at 1.7 minimum alveolar concentration) and did not alter C and Z_c. In contrast, sevoflurane increased C (0.57 ± 0.05 during control to 0.79 ± 0.05 ml/mmHg at 1.7 minimum alveolar concentration) and Z_c (139 ± 10 during control to 194 ± 14 dynes · second · centimeter^{-5} at 1.7 minimum alveolar concentration) but did not change R.**

Conclusions: **The results indicate that desflurane and sevoflurane produce substantially different effects on left ventricular afterload in chronically instrumented dogs. Desflurane-induced decreases in systemic vascular resistance occur primarily because of effects on arteriolar resistance vessels. In contrast, sevoflurane increased C and Z_c concomitant with pressure-dependent reductions in aortic diameter, suggesting that this anesthetic may alter left ventricular afterload by affecting the mechanical properties of the aorta. (Key words: Anesthetics, volatile: desflurane; sevoflurane. Heart: left ventricular afterload. Hemodynamics: aortic blood flow; aortic pressure. Signal processing: coherence function; power spectrum analysis.)**

THE two new volatile anesthetics, desflurane and sevoflurane, have been shown to produce cardiovascular effects that share many similarities with older inhalational agents.[1] Like other volatile anesthetics, desflurane and sevoflurane cause dose-related reductions in arterial blood pressure in humans.[2–7] These hypotensive effects have been attributed to depression of myocardial contractility[4,5,8–11] and alterations in ventricular loading conditions.[2–7,9–11] While the vast majority of experimental and clinical evidence suggests that desflurane causes dose-related declines in systemic vascular resistance and end-systolic wall stress similar to isoflurane *in vivo*,[2–5,11] the effects of sevoflurane on these measures of LV afterload are somewhat more controversial.[6,9,10,12,13] Previous investigations from this[9] and other laboratories[12,14–16] have shown that sevoflurane does not alter calculated systemic vascular resistance in experimental animals. In contrast, other studies have implied that sevoflurane reduces systemic vascular resistance concomitant with declines in arterial blood

* Visiting Assistant Professor in Anesthesiology.

† Assistant Professor of Anesthesiology.

‡ Professor of Anesthesiology, Pharmacology, and Medicine (Division of Cardiology); Vice Chairman for Research, Department of Anesthesiology.

Received from the Departments of Anesthesiology, Pharmacology, and Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin, and the Zablocki Department of Veterans Affairs Medical Center, Milwaukee, Wisconsin. Submitted for publication October 16, 1995. Accepted for publication February 23, 1996. Supported by United States Public Health Services grant HL 54280 and Anesthesiology Research Training grant GM 08377.

Address reprint requests to Dr. Warltier: Department of Anesthesiology, MEB, Room 462C, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, Wisconsin 53226.

pressure.[6,10,13] The disparity between these findings may be partially explained because systemic vascular resistance is an inadequate measure of LV afterload that fails to account for the phasic nature of arterial blood pressure and flow. Aortic input impedance (Z_{in}) is an experimental description of LV afterload that incorporates the frequency-dependent, pulsatile characteristics of the arterial system.[17] We demonstrated recently that halothane, isoflurane, and propofol produce differential actions on LV afterload evaluated with Z_{in}.[18,19] The current investigation tested the hypothesis that desflurane and sevoflurane produce differential actions on indexes of LV afterload derived from Z_{in} quantified using the three-element Windkessel model of the arterial circulation in chronically instrumented dogs.

Materials and Methods

All experimental procedures and protocols used in this investigation were reviewed and approved by the Animal Care Committee of the Medical College of Wisconsin. All procedures conformed to the *Guiding Principles in the Care and Use of Animals* of the American Physiological Society and were performed in accordance with the *Guide for the Care and Use of Laboratory Animals*.§

General Preparation

Surgical implantation of instruments has been described previously in detail.[18] Briefly, under general anesthesia and aseptic surgical conditions, dogs (n = 8) underwent a left thoracotomy, and a high-fidelity micromanometer was inserted into the left ventricle for measurement of continuous LV pressure and the maximum rate of increase in LV pressure (dP/dt_{max}). Heparin-filled catheters were placed in the proximal descending thoracic aorta, the right atrium, and the left atrium for measurement of aortic pressure, fluid administration, and calibration of the LV micromanometer, respectively. An ultrasonic transit-time flow probe was positioned around the ascending thoracic aorta for measurement of continuous aortic blood flow. A pair of miniature ultrasonic segment length transducers were implanted in the LV subendocardium for measurement of changes in regional contractile function. All instrumentation was secured, tunneled between the scapulae, and exteriorized *via* several small incisions. The pericardium was left wide open, the chest wall closed in layers, and the pneumothorax evacuated by a chest tube.

All dogs received systemic analgesics (fentanyl) as needed after surgery. Dogs were allowed to recover a minimum of 7 days before experimentation during which time all were treated with intramuscular antibiotics (40 mg/kg cephalothin and 4.5 mg/kg gentamicin) and were trained to stand quietly in an animal sling during recording of hemodynamics. An ultrasonic amplifier was used to monitor segment length signals. End-systolic and end-diastolic segment lengths were measured at 30 ms before maximum negative LV dP/dt and just prior to the onset of LV isovolumic contraction, respectively. Percent segment shortening was calculated using the equation: percent segment shortening = (end-diastolic segment length − end-systolic segment length) · 100 · end-diastolic segment length^{-1}. Hemodynamic data were continuously recorded on a polygraph and digitized by a computer interfaced with an analog to digital converter.[18]

Calculation of Aortic Input Impedance $Z_{in}(\omega)$ Spectra

Aortic input impedance spectra were obtained from digitized, steady-state aortic blood pressure and aortic blood flow waveforms.[20,21] Briefly, data files consisting of 4,096 points were sampled at 100 Hz and divided into five 2,048-point bins with 1,536 point overlap.[18] A Hamming window was applied to each bin to reduce side lobe leakage. The autopower spectrum of the aortic blood pressure [$P_{pp}(\omega)$], aortic blood flow [$P_{ff}(\omega)$] and cross power spectrum between aortic pressure and blood flow wave forms [$P_{pf}(\omega)$] were determined using a Welch periodogram technique.[22,23] Each $Z_{in}(\omega)$ spectrum was calculated as a function of frequency (ω) using the formula: $Z_{in}(\omega) = P_{pp}(\omega) \cdot [P_{pf}(\omega)]^{-1}$ and corrected for the phase response and position of the aortic flow probe and aortic pressure transducer as described previously.[18] Typical $Z_{in}(\omega)$ magnitude and phase spectra in the conscious state and during desflurane and sevoflurane anesthesia are depicted in figures 1 and 2, respectively. Correlation of aortic pressure and flow waveforms at each frequency of $Z_{in}(\omega)$ was determined using the magnitude squared coherence (MSC), where magnitude squared coherence (ω) = $|P_{pf}(\omega)|^2 \cdot [P_{pp}(\omega) \cdot P_{ff}(\omega)]^{-1}$. All $Z_{in}(\omega)$ data with magnitude squared coherence values < 0.8 were discarded.

§ Guide for the Care and Use of Laboratory Animals, Department of Health and Human Services publication NIH 85-23. Washington, DC, Department of Health, Education, and Welfare, 1985.

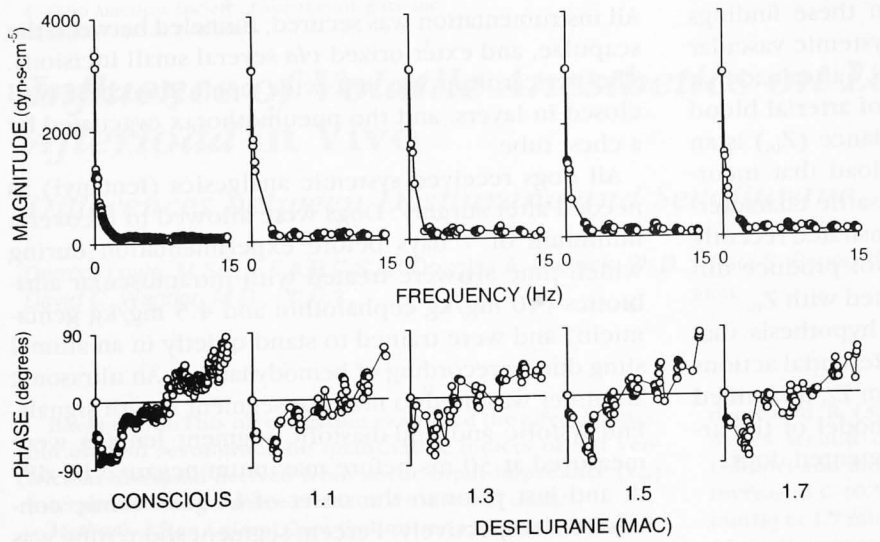

Fig. 1. Aortic input impedance spectrum consisting of magnitude (*top*) and phase components (*bottom*) obtained in the conscious state and during desflurane anesthesia at 1.1, 1.3, 1.5, and 1.7 minimum alveolar concentration in a typical experiment.

Windkessel model parameters were derived from the calculated $Z_{in}(\omega)$ spectra.[18] Characteristic aortic impedance (Z_c) was determined as the mean of the magnitude of $Z_{in}(\omega)$ ($|Z_{in}(\omega)|$) between 2 and 15 Hz.[21,24,25] Total arterial resistance (R) was calculated as the difference between the value of $|Z_{in}(\omega)|$ at zero frequency and Z_c.

The magnitude of $Z_{in}(\omega)$ at zero frequency was equal to systemic vascular resistance determined as the ratio of mean arterial pressure and mean aortic blood flow.[17] Total arterial compliance (C) was calculated using the formula: $C = (A_d \cdot MAQ) \cdot [MAP \cdot (P_{es} - P_{ed})]^{-1}$, where A_d = the area under the diastolic portion of the arterial pressure curve, MAQ = mean aortic blood flow, MAP = mean arterial pressure, and P_{es} and P_{ed} = end-systolic and end-diastolic aortic pressure, respectively.[26] The diastolic period used for the calculation of C was defined as the time between the dichrotic notch and minimal aortic pressure. The value of C was determined from the average of five consecutive beats for each intervention.

Experimental Protocol

Dogs were assigned to receive desflurane or sevoflurane in a random manner on separate experimental days. Fluid deficits were replaced with 0.9% saline (500

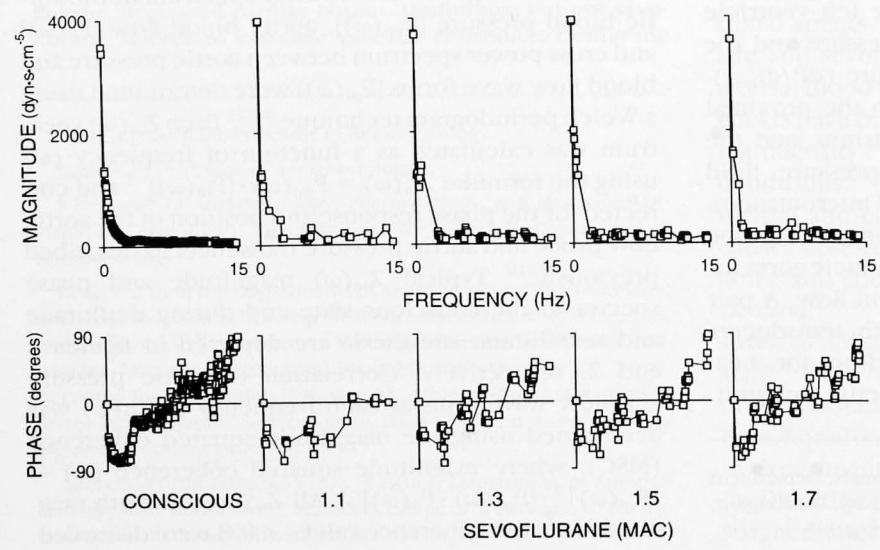

Fig. 2. Aortic input impedance spectrum consisting of magnitude (*top*) and phase components (*bottom*) obtained in the conscious state and during sevoflurane anesthesia at 1.1, 1.3, 1.5, and 1.7 minimum alveolar concentration in a typical experiment.

Table 1. Systemic Hemodynamic Effects of Desflurane

	Control	Desflurane (MAC)			
		1.1	1.3	1.5	1.7
HR (beats/min)	86 ± 2	142 ± 6*	140 ± 6*	140 ± 6*	143 ± 6*
SBP (mmHg)	125 ± 6	102 ± 3*	91 ± 3*	89 ± 3*,†	84 ± 5*,†
DBP (mmHg)	90 ± 5	85 ± 3	76 ± 4*	72 ± 4*	62 ± 5*,†
MBP (mmHg)	100 ± 4	90 ± 3*	83 ± 4*	77 ± 3*,†	68 ± 5*,†
LVSP (mmHg)	126 ± 7	104 ± 4*	95 ± 5*	90 ± 5*,†	84 ± 3*,†
LVEDP (mmHg)	9 ± 1	6 ± 1	6 ± 1	8 ± 1	8 ± 1
dP/dt_{max} ($mmHg \cdot s^{-1}$)	2,457 ± 124	1,880 ± 105*	1,601 ± 108*,†	1,427 ± 94*,†	1,297 ± 102*,†,‡
CO ($L \cdot min^{-1}$)	2.4 ± 0.2	2.3 ± 0.2	2.3 ± 0.1	2.1 ± 0.1	2.1 ± 0.2*
SVR ($dyne \cdot s \cdot cm^{-5}$)	3,424 ± 234	3,152 ± 202	2,884 ± 162	2,995 ± 226	2,763 ± 281*
SV (ml)	28 ± 2	17 ± 1*	17 ± 1*	15 ± 1*	15 ± 2*
SS (%)	22 ± 2	17 ± 2*	16 ± 2*	12 ± 2*,†	12 ± 2*,†

Data are mean ± SEM; n = 8.

HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MBP = mean blood pressure; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; dP/dt_{max} = maximum rate of change of left ventricular pressure; CO = cardiac output; SVR = systemic vascular resistance; SV = stroke volume; SS = segment shortening.

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

† Significantly ($P < 0.05$) different from 1.1 MAC desflurane.

‡ Significantly ($P < 0.05$) difference from 1.3 MAC desflurane.

ml), and maintenance fluids (0.9% saline) were continued ($3\ ml \cdot kg^{-1} \cdot h^{-1}$) for the duration of each experiment. After instruments were calibrated, baseline systemic hemodynamics were recorded under steady-state conditions in the conscious state. Continuous aortic blood pressure and aortic blood flow waveforms were recorded for later generation and analysis of $Z_{in}(\omega)$. After inhalational induction and tracheal intubation, anesthesia was maintained during positive pressure ventilation at 1.1, 1.3, 1.5, or 1.7 minimum alveolar concentration (MAC; end-tidal) desflurane or sevoflurane in an air and oxygen (25%) mixture. The order of MAC was assigned randomly. The canine MAC values for desflurane and sevoflurane used in this investigation were 7.20 and 2.36%, respectively. End-tidal concentrations of desflurane and sevoflurane were measured at the tip of the endotracheal tube by an infrared gas analyzer (Datex Capnomac, Helsinki, Finland) that was calibrated with known standards before and during experimentation. Hemodynamics and aortic pressure and blood flow waveforms were recorded after 30 min of equilibration at each anesthetic concentration. Arterial blood gas tensions were maintained at conscious levels by adjustment of air and oxygen concentrations and respiratory rate throughout the experiment. Emergence was allowed to occur at the completion of each experiment. Dogs were allowed to recover at least 2 days before subsequent experimentation. Thus, a total of 16 experiments were performed in 2 groups (desflurane and sevoflurane) using the same 8 dogs.

Statistical Analysis

Statistical analysis of data within and between groups in the conscious state and during anesthetic interventions were performed by multiple analysis of variance with repeated measures followed by application of Student's *t* test with Duncan's correction for multiplicity. The slope of the total arterial compliance-MAP relationship was determined by linear regression for each anesthetic. Parallelism of the linear slopes of the compliance-pressure data also was determined using the method of Tallarida and Murray.[27] Changes within and between groups were considered significant when $P < 0.05$. The data were expressed as mean ± SEM.

Results

Desflurane caused a significant ($P < 0.05$) increase in heart rate (86 ± 2 during control to 143 ± 6 beats/min at 1.7 MAC) and dose-related decreases in systolic, diastolic, and MAP (100 ± 4 during control to 68 ± 5 mmHg at 1.7 MAC), LV systolic pressure, and stroke volume (table 1). No change in LV end-diastolic pressure was observed. Dose-related decreases in dP/dt_{max}

(2457 ± 124 during control to 1297 ± 102 mmHg/s at 1.7 MAC) and percent segment shortening were observed in desflurane-anesthetized dogs, consistent with a negative inotropic effect. Desflurane also caused significant reductions in cardiac output and systemic vascular resistance at 1.7 MAC. A dose-related decrease in R (3,170 ± 188 during control to 2441 ± 220 dynes · second · centimeter^{-5} at 1.7 MAC; fig. 3) occurred. However, no changes in total arterial compliance (C) and characteristic aortic impedance (Z_c) were observed during anesthesia with desflurane (fig. 3).

Sevoflurane produced hemodynamic actions that were somewhat different than those produced by desflurane (table 2). Sevoflurane also caused an increase in heart rate (88 ± 4 during control to 129 ± 4 beats/min at 1.7 MAC). Dose-related decreases in systolic, diastolic, and MAP (99 ± 5 during control to 61 ± 4 mmHg at 1.7 MAC), LV systolic pressure, and stroke volume were observed in dogs anesthetized with sevoflurane. These sevoflurane-induced decreases in systolic, diastolic, and MAPs and LV systolic pressure were greater than those produced by desflurane. No changes in LV end-diastolic pressure occurred. Sevoflurane decreased myocardial contractility as indicated by dose-related declines in dP/dt_{max} (2,343 ± 161 during control to 1,051 ± 80 mmHg/s at 1.7 MAC) and percent segment shortening. These sevoflurane-induced negative inotropic effects were similar to those observed with desflurane. In contrast to the findings with desflurane, sevoflurane produced dose-related decreases in cardiac output (2.4 ± 0.2 during control to 1.5 ± 0.2 l/min at 1.7 MAC). Systemic vascular resistance and R were also unchanged in sevoflurane-anesthetized dogs. Sevoflurane caused dose-related increases in Z_c (139 ± 10 during control to 194 ± 14 dynes · second · centimeter^{-5} at 1.7 MAC) and C (0.57 ± 0.05 during control to 0.79 ± 0.05 ml/mmHg at 1.7 MAC; fig. 3), suggesting that alterations in the mechanical properties of the aorta were primarily responsible for changes in LV afterload during administration of this volatile anesthetic. No difference in the slope of the compliance-pressure relationship was observed between sevoflurane ($-1.87 \cdot 10^{-3}$ ml · mmHg^{-2}) and desflurane ($-1.67 \cdot 10^{-3}$ ml · mmHg^{-2}, t = −0.18, $P >$ 0.05) groups.

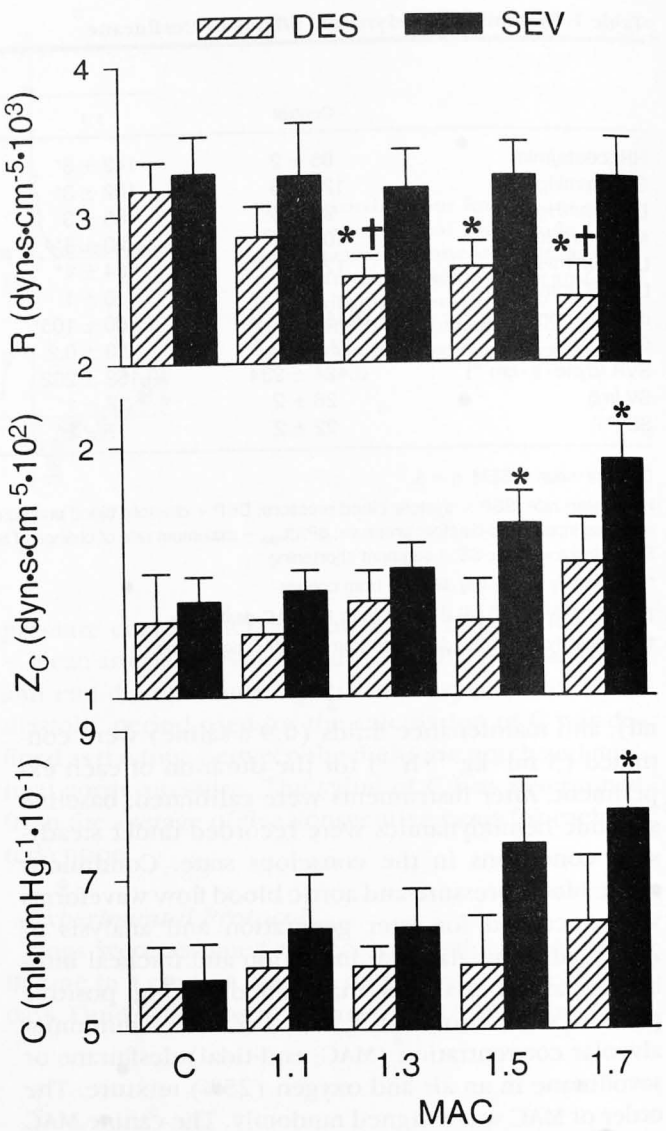

Fig. 3. Histograms depicting the effects of volatile anesthetics on total arterial resistance (R; *top*), characteristic aortic impedance (Z_c; *middle*) and total arterial compliance (C; *bottom*) in the conscious (C) state and at 1.1, 1.3, 1.5, and 1.7 minimum alveolar concentration desflurane (DES) and sevoflurane (SEV). *Significantly ($P < 0.05$) different from conscious; †Significantly ($P < 0.05$) different from sevoflurane.

Discussion

Calculated systemic vascular resistance (the ratio of MAP to mean arterial blood flow) is used commonly to estimate LV afterload *in vivo*. Although this index provides a qualitative description of arterial resistance to LV ejection, systemic vascular resistance cannot be used to strictly quantify alterations in afterload because this index ignores the mechanical properties of the arterial wall, fails to account for the potential effects of arterial wave reflection, and does not consider the dynamic, pulsatile nature of arterial blood pressure and blood

Table 2. Systemic Hemodynamic Effects of Sevoflurane

	Control	Sevoflurane (MAC)			
		1.1	1.3	1.5	1.7
HR (beats/min)	88 ± 4	131 ± 6*	132 ± 6*	128 ± 5*	129 ± 4*
SBP (mmHg)	120 ± 5	92 ± 3*,§	86 ± 3*	81 ± 3*,†	69 ± 2*,†,‡,§
DBP (mmHg)	86 ± 5	74 ± 3*,§	69 ± 2*	63 ± 3*,†	52 ± 5*,†,‡
MBP (mmHg)	99 ± 5	80 ± 3*,§	75 ± 2*	67 ± 3*,†,§	61 ± 4*,†,‡
LVSP (mmHg)	123 ± 7	93 ± 3*,§	87 ± 3*	82 ± 3*,†	70 ± 4*,†,‡,§
LVEDP (mmHg)	9 ± 1	6 ± 1	6 ± 1	8 ± 1	8 ± 1
dP/dt_{max} ($mmHg \cdot s^{-1}$)	2,343 ± 161	1,496 ± 52*,§	1,320 ± 78*	1,116 ± 53*,†	1,051 ± 80*,†,‡
CO ($L \cdot min^{-1}$)	2.4 ± 0.2	2.0 ± 0.2*	1.9 ± 0.2*,§	1.6 ± 0.1*,†,§	1.5 ± 0.2*,†,‡
SVR ($dyne \cdot s \cdot cm^{-5}$)	3,344 ± 224	3,438 ± 377	3,315 ± 218	3,417 ± 214	3,466 ± 266
SV (ml)	28 ± 2	16 ± 2*	14 ± 1*	13 ± 1*	12 ± 1*
SS (%)	23 ± 2	16 ± 2*	15 ± 1*	11 ± 1*,†,‡	11 ± 2*,†,‡

Data are mean ± SEM; n = 8.

HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MBP = mean blood pressure; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure/ dP/dt_{max} = maximum rate of change of left ventricular pressure; CO = cardiac output; SVR = systemic vascular resistance; SV = stroke volume; SS = segment shortening.

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

† Significantly ($P < 0.05$) different from 1.1 MAC sevoflurane.

‡ Significantly ($P < 0.05$) different from 1.3 MAC sevoflurane.

§ Significantly ($P < 0.05$) different from same MAC desflurane (table 1).

flow.[28] In contrast, $Z_{in}(\omega)$ has been shown to be a quantitative measure of LV afterload that incorporates arterial viscoelasticity, frequency-dependence, and wave reflection.[17] Vasoactive drugs, including volatile and intravenous anesthetics, have been shown to alter $Z_{in}(\omega)$ by affecting the mechanical properties of the arterial vascular tree.[18,19,24,29] However, changes in $Z_{in}(\omega)$ produced by pharmacologic agents are difficult to quantify in a physiologically relevant way because analysis of $Z_{in}(\omega)$ is conducted in the frequency domain. As a result, $Z_{in}(\omega)$ often is interpreted using a simplified electrical model of the arterial system known as the three-element Windkessel.[21] The Windkessel model displays most of the frequency-dependent features of $Z_{in}(\omega)$.[30] Windkessel-derived variables can be used to estimate $Z_{in}(\omega)$ as a function of frequency: $Z_{in}(\omega) = Z_c + R \cdot (1 + j \cdot \omega \cdot C \cdot R)^{-1}$, where Z_c = characteristic aortic impedance, R = total arterial resistance, C = total arterial compliance, and $j = (-1)^{1/2}$.[31] Z_c is determined by the Poiseullian resistance of the aorta and the compliance of this vessel. Characteristic aortic impedance is represented as a resistor in the model for simplicity and because its value does not vary significantly with frequency.[29,32] R represents the combined Poiseullian resistances of the entire arterial vascular tree. The sum of R and Z_c is mathematically equivalent to systemic vascular resistance calculated as the ratio of MAP to mean aortic blood flow. The magnitude of Z_c is small in relation to R owing to the relative contributions to systemic vascular resistance of the aorta and the remaining arterial circulation, respectively. Total arterial compliance is the energy storage component of the Windkessel. These elements of the arterial system interact with the mechanical properties of the left ventricle to determine overall cardiovascular performance.

In the current investigation, Windkessel variables were used to quantify $Z_{in}(\omega)$ spectra in the conscious state and during desflurane and sevoflurane anesthesia. The results indicate that desflurane caused a dose-related reduction in R concomitant with decreases in calculated systemic vascular resistance. These findings confirm and extend the results of previous studies demonstrating that desflurane-induced decreases in systemic vascular resistance contribute to declines in MAP.[2–5] Decreases in total arterial and systemic vascular resistance caused by desflurane were similar to those observed with isoflurane and propofol (table 3) in previous investigations from our laboratory.[18,19] In contrast to the findings with isoflurane and propofol, however, desflurane did not alter C and Z_c. These results indicate that desflurane reduces LV afterload by affecting resistance arterioles and not the mechanical properties of the aorta. Total arterial compliance is primarily deter-

Table 3. Relative Effects of Anesthetics and Sodium Nitroprusside on Indices of Left Ventricular Afterload

	Halothane	Isoflurane	Desflurane	Sevoflurane	Propofol	Nitroprusside
R	↔	↓	↓	↔	↓	↓
Z_c	↑	↑	↔	↑	↑	↔
C	↑	↑	↔	↑	↑	↑

R = total arterial resistance; Z_c = characteristic aortic impedance; C = total arterial compliance; ↑ = increase; ↓ = decrease; ↔ = no change.

mined by the compliance of the aorta itself[33,34] and is inversely related to intraluminal pressure and radius.[35,36] Changes in characteristic aortic impedance also are determined by the inherent viscoelastic properties of the aorta and are inversely related to the fourth power of its radius.[29] A pressure-induced decrease in aortic diameter may result in increases in both C and Z_c. When compared to the results of our previous study,[18] desflurane maintained mean aortic pressure to a relatively greater degree than isoflurane at approximate end-tidal concentrations of 1.3, 1.5, and 1.7 MAC. Thus, the failure of desflurane to increase C or Z_c at higher anesthetic concentrations in the current study is probably related to the less pronounced reductions in mean aortic pressure and, presumably aortic diameter, produced by this agent when compared to its structural analog.

In contrast to the findings with desflurane, no changes in R and systemic vascular resistance occurred during administration of sevoflurane. These findings are similar to those observed previously with halothane[18] and indicate that sevoflurane does not affect LV afterload by altering peripheral arteriolar tone in dogs. Unlike desflurane, sevoflurane also increased C and Z_c, suggesting that this inhalational agent affects aortic compliance and impedance. However, sevoflurane caused relatively greater declines in mean aortic pressure than desflurane in dogs. These findings suggest that sevoflurane-induced increases in C and Z_c were determined primarily by pressure-dependent reductions in aortic diameter and not by alterations in the fundamental mechanical properties of this great vessel. The slopes of the compliance-pressure relationship for sevoflurane and desflurane observed in the current investigation were not different than those of isoflurane ($-1.41 \cdot 10^{-3}$ ml · mmHg^{-2}; t = 1.02 *vs.* desflurane, $P > 0.05$; t = 1.13 *vs.* sevoflurane, $P > 0.05$) and halothane ($-1.43 \cdot 10^{-3}$ ml · mmHg^{-2}; t = 0.68 *vs.* desflurane, $P > 0.05$; t = 0.79 *vs.* sevoflurane, $P > 0.05$) as found in our previous study.[18] These results indicate that volatile anesthetics produce similar compliance-pressure relationships that remain relatively flat between MAPs of 50 and 100 mmHg. In contrast, propofol and sodium nitroprusside cause significant increases in the slope of the compliance-pressure relation over this range of MAPs,[18,19] indicating that these arterial vasodilators probably exert direct actions on the mechanical properties of the aorta.

Total arterial compliance represents an important component of afterload that has recently been shown to directly influence LV wall stress and myocardial oxygen consumption independent of alterations in systemic vascular resistance.[37] Thus, although desflurane, isoflurane,[18] and propofol[19] cause dose-related reductions in R, propofol may have the most beneficial effects on LV afterload because of simultaneous and more profound increases in C (table 3). Such an increase in C may improve the rectifying characteristics of the aorta, a feature that could theoretically reduce LV energy expenditure during ejection, maintain diastolic arterial pressure, and enhance coronary perfusion under these conditions. The sevoflurane-induced increases in Z_c that occurred at 1.5 and 1.7 MAC may indicate a greater resistance to LV ejection at these concentrations. These increases in Z_c result in wasted LV energy transfer and less efficient coupling between the left ventricle and arterial circulation.[29] These effects of changes in Z_c should be observed relative to the changes in the magnitude of R and C. The impact of changes in Z_c is small in comparison to changes in R and C.

The current results must be interpreted within the constraints of several possible limitations. The calculation of Z_{in} (ω) was performed with arterial pressure waveforms measured using a chronically implanted, fluid-filled catheter. Despite the use of appropriate corrections for the magnitude and phase of Z_{in} (ω),[17] an improved frequency response may have been obtained with a high-fidelity micromanometer placed at the aortic root. Z_{in} (ω) magnitude spectra obtained in anesthetized dogs were somewhat less continuous than those obtained in the conscious state because more frequencies between the fundamental and corresponding harmonics were excluded on the basis of mean squared

coherence criteria. Generation of multiple heart rates by random cardiac pacing during anesthesia would have provided a greater number of fundamental and harmonic frequencies, resulting in more continuous Z_{in} (ω) magnitude spectra in the presence of desflurane or sevoflurane. However, the observed spectral discontinuity resembles spectra generated with standard Fourier series analysis, an established method for evaluating aortic input impedance under a variety of physiologic conditions.[17,29]

In summary, desflurane and sevoflurane produce differential effects on LV afterload determined with Z_{in} (ω) and interpreted using a three-element Windkessel model. Desflurane, but not sevoflurane, caused dose-related reductions in R and systemic vascular resistance, indicating that this new volatile anesthetic decreases LV afterload by affecting peripheral arteriolar tone. In contrast, sevoflurane, but not desflurane, increased C and Z_c at higher anesthetic concentrations concomitant with greater reductions in MAP. The results indicate that desflurane and sevoflurane cause changes in Z_{in} (ω) that are similar to those described previously with isoflurane and halothane, respectively, in chronically instrumented dogs.[18]

The authors thank Dave Schwabe and John Tessmer, for technical assistance, and Angela Barnes, for preparation of the manuscript.

References

1. Eger II EI: New inhaled anesthetics. ANESTHESIOLOGY 1994; 80: 906–22

2. Jones R, Cashman J, Mant T: Clinical impressions and cardiovascular effects of a new fluorinated inhalational anaesthetic, desflurane (I-653),in volunteers. Br J Anaesth 1990; 64:11–5

3. Cahalan MK, Weiskopf RB, Eger II EI, Yasuda N, Ionescu P, Rampil IJ, Lockhart SH, Freire B, Peterson NH: Hemodynamic effects of desflurane/nitrous oxide anesthesia in volunteers. Anesth Analg 1991; 73:157–64

4. Weiskopf RB, Cahalan MK, Eger II EI, Yasuda N, Rampil IJ, Ionescu P, Lockhart SH, Johnson BH, Freire B, Kelley S: Cardiovascular actions of desflurane in normocarbic volunteers. Anesth Analg 1991; 73:143–56

5. Weiskopf R, Cahalan M, Ionescu P, Eger II EI, Yasuda N, Lockhart S, Johnson B, Friere B, Peterson N: Cardiovascular actions of desflurane with and without nitrous oxide during spontaneous ventilation in humans. Anesth Analg 1991; 73:165–74

6. Shigematsu T, Kobayashi M, Miyazawa N, Yorozu T, Toyuda Y, Ueda E, Yoshikama T, Tachikawa S: Effects of sevoflurane on hemodynamics during the induction of anesthesia compared with those of isoflurane, enflurane and halothane. J Anesth 1993; 42:1748–53

7. Kikura M, Ikeda K: Comparison of effects of sevoflurane-nitrous oxide and enflurane-nitrous oxide on myocardial contractility in humans. Load-independent and noninvasive assessment with transesophageal echocardiography. ANESTHESIOLOGY 1993; 79:235–43

8. Pagel PS, Kampine JP, Schmeling WT, Warltier DC: Evaluation of myocardial contractility in the chronically instrumented dog with intact autonomic nervous system function: Effects of desflurane and isoflurane. Acta Anaesthesiol Scand 1993; 37:203–10

9. Harkin CP, Pagel PS, Kersten JR, Hettrick DA, Warltier DC: Direct negative inotropic and lusitropic effects of sevoflurane. ANESTHESIOLOGY 1994; 81:156–67

10. Bernard JM, Walters PF, Doursart MF, Florence B, Chelly JE, Merin RY: Effects of sevoflurane and isoflurane on cardiac and coronary dynamics in chronically instrumented dogs. ANESTHESIOLOGY 1990; 72:659–62

11. Merin RG, Bernard J-M, Doursout M-F, Cohen M, Chelly J: Comparison of the effects of isoflurane and desflurane on cardiodynamics and regional blood flow in the chronically instrumented dog. ANESTHESIOLOGY 1991; 74:568–74

12. Manohar M, Parks CM: Porcine systemic and regional organ blood flow during 1.0 and 1.5 minimum alveolar concentrations of sevoflurane anesthesia without and with 50% nitrous oxide. J Pharmacol Exp Ther 1984; 231:640–8

13. Kazama T, Ikeda K: The comparative cardiovascular effects of sevoflurane with halothane and isoflurane. J Anesth 1988; 2: 63–8

14. Crawford MW, Lerman J, Saldivia V, Carmichael FJ: Hemodynamic and organ blood flow responses to halothane and sevoflurane anesthesia during spontaneous ventilation. Anesth Analg 1992; 75: 1000–6

15. Crawford MW, Lerman J, Saldivia V, Orrego H, Carmichael FJ: The effect of adenosine-induced hypotension on systemic and splanchnic hemodynamics during halothane or sevoflurane in the rat. ANESTHESIOLOGY 1994; 80:159–67

16. Yamada T, Takeda J, Koyama K, Sekiguchi H, Fukushima K, Kawazoe T: Effects of sevoflurane, isoflurane, enflurane, and halothane on left ventricular diastolic performance in dogs. J Cardiothorac Vasc Anesth 1994; 8:618–24

17. Milnor WR: Hemodynamics. Baltimore, Williams & Wilkins, 1989

18. Hettrick DA, Pagel PS, Warltier DC: Differential effects of isoflurane and halothane on aortic input impedance quantified using a three element Windkessel model. ANESTHESIOLOGY 1995; 83:361–73

19. Lowe D, Hettrick DA, Pagel PS, Warltier DC: Propofol alters determinants of left ventricular afterload. ANESTHESIOLOGY 1996; 84: 368–76

20. Taylor MG: Use of random excitation and spectral analysis in the study of parameters of the cardiovascular system. Circ Res 1966; 18:585–95

21. Burkhoff D, Alexander Jr J, Schipke J: Assessment of Windkessel as a model of aortic input impedance. Am J Physiol 1988; 255:H742–H53

22. Challis RE, Kitney RI: Biomedical signal processing (in four parts). Part 3. The power spectrum and coherence function. Med Biol Eng Comput 1991; 29:225–41

23. Marple Jr SL: Digital spectral analysis with applications. Englewood Cliffs, Prentice-Hall, 1987

24. Pepine CJ, Nichols WW, Curry Jr RC, Conti CR: Aortic input impedance during nitroprusside infusion: A reconsideration of afterload reduction and beneficial action. J Clin Invest 1979; 64:643–54

25. Murgo JP, Westerhof N, Giolma JP, Altobelli SA: Aortic input

impedance in normal man: Relationship to pressure wave forms. Circulation 1980; 62:105–16

26. Liu Z, Brin KP, Yin FCP: Estimation of total arterial compliance: An improved method and evaluation of current methods. Am J Physiol 1986; 251:H588–600

27. Tallarida RJ, Murray RB: Manual of Pharmacologic Calculations with Computer Programs. New York, Springer, 1987

28. Fung YC: Biomechanics: Mechanical Properties of Living Tissues. 2nd edition. New York, Springer, 1993

29. Nichols WW, O'Rourke MF: McDonald's Blood Flow in Arteries: Theoretic, Experimental and Clinical Principles. Philadelphia, Lea & Febiger, 1990

30. Elzinga G, Westerhof N: Pressure and flow generated by the left ventricle against different impedances. Circ Res 1973; 32:178–86

31. Sagawa K, Maughan L, Suga H, Sunagawa K: Cardiac contraction and the pressure-volume relationship. New York, Oxford University Press, 1988, p 251

32. O'Rourke MF: Vascular impedance in studies of arterial and cardiac function. Physiol Rev 1982; 62:570–623

33. Westerhof N, Bosman F, De Vries CJ, Noordergraaf A: Analog studies of the human systemic arterial tree. J Biomech 1969; 2:121–43

34. Ferguson III JJ, Miller MJ, Sahagian P, Aroesty JM, McKay RG: Assessment of aortic pressure-volume relationships with an impedance catheter. Cathet Cardiovasc Diagn 1988; 15:27–36

35. Alexander Jr J, Burkhoff D, Schipke J, Sagawa K: Influence of mean pressure on aortic impedance and reflections in the systemic arterial system. Am J Physiol 1989; 257:H969–78

36. Van Den Bos GC, Westerhof N, Elzinga G, Sipkema P: Reflection in the systemic arterial system: Effects of aortic and carotid occlusion. Cardiovasc Res 1976; 10:565–73

37. Saeki A, Recchia F, Kass DA: Systolic flow augmentation in hearts ejecting into a model of stiff aging vasculature. Influence on myocardial perfusion-demand balance. Circ Res 1995; 76:132–41

Anesthesiology
1996; 85:121–8

Effect of Propo Place Conditio

L. Pain, M.D.,* P. Oberling, M.D

Background: Whether propofo state remains unclear from cl study, the effect on affective s esthetic doses of propofol was with rats in a place condition compared with methohexital.

Methods: In the place condit duced effect was repeatedly p guishable compartments of the induced effect was repeatedly partment. During a subsequen for the drug-paired compart compartment would be indica by the drug. For all experim lasted 8 days and consisted of one compartment and four pa of vehicle with the other co four groups of rats were desig propofol that they received in mg/kg. In experiment 1B, the subanesthetic doses of ketrape or 30 mg/kg. In experiment 2, the recovery period from s group, anesthesia was indu whereas for the other group equivalent anesthetic dose of

* Consultant Anesthetist, Serv rurgicale.

† Assistant Professor of Physio et de la Recherche Médicale.

‡ Professor of Physiology, l'In Recherche Médicale.

§ Behavioral Neurobiologist.

Received from Service d'Anes JC Otteni), Hopitaux Universit Neurophysiologie et Biologie de Laboratoire de Psychopathologi (U405 INSERM), Strasbourg, Fra 2, 1994. Accepted for publica was supported by grants from l (DRET 92170) and by l'Institut N Médicale (INSERM 911012).

Address reprint requests to D mation Chirurgicale, CHU Hau Strasbourg, France.