

A Comparison of Desflurane and Isoflurane in Patients Undergoing Coronary Artery Surgery

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Animal studies indicate that desflurane and isoflurane have similar hemodynamic effects when administered in equipotent anesthetic concentrations. The authors compared desflurane and isoflurane, used as primary anesthetics for patients undergoing elective coronary artery bypass surgery whose left ventricular ejection fractions were greater than 0.34. After induction of anesthesia with thiopental (dose 180 ± 45 mg [mean \pm standard deviation]) and fentanyl, $10 \mu\text{g} \cdot \text{kg}^{-1}$, either desflurane or isoflurane was administered to maintain systolic blood pressure within 70–120% of, and heart rates less than 120% of, the patients' average preoperative values. If adjusting the end-tidal anesthetic concentration within the range of 0–2.0 MAC could not maintain these predefined hemodynamic limits, additional fentanyl or vasoactive drugs were used. Induction and maintenance of anesthesia was accompanied by a significant decrease in mean arterial pressure in both groups (desflurane 97 ± 12 mmHg at control, decreasing to 71 ± 5 mmHg during skin preparation; isoflurane 95 ± 9 mmHg at control, 74 ± 9 mmHg during skin preparation). One minute after sternotomy, mean arterial pressure in the isoflurane group had returned to control, 97 ± 9 mmHg, which was significantly greater than in the desflurane group, 87 ± 12 mmHg. Systolic arterial pressure was also significantly greater in the isoflurane group 1 min after intubation, during skin preparation, and 1 min after sternotomy. Otherwise, the hemodynamic effects of these volatile agents were similar. There were no differences between groups in the incidence of ECG changes indicative of myocardial ischemia prior to cardiopulmonary bypass, perioperative myocardial infarction, or perioperative mortality. These data confirm animal studies, which indicate that desflurane and isoflurane have similar hemodynamic effects when administered in equipotent anesthetic doses. Desflurane has a very low blood-gas partition coefficient, 0.42, which facilitates rapid adjustment of its end-tidal concentration. These pharmacokinetic differences may account for the lower blood pressures after intubation and sternotomy in the patients given desflurane. (Key words: Anesthesia: cardiovascular. Anesthetics, volatile: desflurane; isoflurane. Heart: coronary artery disease.)

DESFLURANE is a fluorinated ethyl methyl ether, identical in structure to isoflurane except for substitution of the chlorine atom on the α -ethyl carbon with fluorine.¹ Des-

flurane has the lowest blood-gas partition coefficient of any volatile agent studied to date,¹ and, consequently, anesthetic induction and emergence are very rapid. Also, it should be possible with desflurane to adjust anesthetic depth more rapidly, conceivably facilitating hemodynamic control during surgical procedures involving varying levels of noxious stimulation. Animal studies suggest that, at equipotent anesthetic concentrations, the cardiovascular effects of desflurane are similar to those of isoflurane.²⁻⁴ We compared the cardiovascular effects of desflurane and isoflurane in a randomized, open-label, clinical trial in patients with significant coronary artery disease.

Materials and Methods

We studied patients between 35 and 80 yr of age undergoing elective coronary artery surgery whose preoperative left ventricular ejection fraction exceeded 0.34. We excluded patients with unstable angina who required continuous preoperative electrocardiographic monitoring, invasive hemodynamic monitoring, or intravenous (iv) nitroglycerin (NTG). Additional exclusion criteria are listed in table 1. Our Human Studies Committee approved this protocol, and each patient gave written, informed consent. We randomized patients to receive either desflurane or isoflurane as the primary anesthetic for their surgery, using a sequential list prepared with a random-number generator.

MONITORING

Prior to induction of anesthesia, we connected an ambulatory electrocardiographic (ECG) monitor (Marquette Series 8500) for 24-h recordings of ECG leads II and CS₅. Systemic oxygen saturation was monitored continuously. We inserted iv, radial arterial, and pulmonary arterial catheters under local anesthesia. Bilateral frontomastoid leads were placed for monitoring the electroencephalograph (EEG) processed by aperiodic analysis.⁵ Oscilloscopic and digital displays of ECG leads II and V₅, systemic arterial pressure, pulmonary artery pressure (PAP), and central venous pressure (CVP) were continuously monitored. During anesthesia, we continuously monitored the inspired concentration of oxygen and end-tidal concentrations of carbon dioxide and volatile anesthetic, using an infrared analyzer (Datex) and sampling from the Y-connector of the circle system. We measured cardiac out-

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TABLE 1. Exclusion Criteria

- Body weight > 110 kg
- Hematocrit <25%
- Oral temperature $\leq 35^{\circ}\text{C}$ or $\geq 38^{\circ}\text{C}$
- Clinically significant disease of the central nervous system
- Chronic exposure to or abuse of alcohol or drugs affecting the central nervous system
- General anesthesia within 7 days before the study
- Adverse reaction to anesthetics or opioids
- Personal or familial history of malignant hyperthermia
- Respiratory disease sufficient to alter inhaled anesthetic uptake
- Recent use of any experimental drug or device

put intermittently in triplicate by the thermodilution technique, using 10 ml of room-temperature injectate.

ANESTHETIC TECHNIQUE

Patients received morphine $0.1\text{ mg}\cdot\text{kg}^{-1}$ and scopolamine $6\text{ }\mu\text{g}\cdot\text{kg}^{-1}$ intramuscularly 1 h preoperatively, and nasal oxygen $3\text{ l}\cdot\text{min}^{-1}$ until induction of anesthesia. For 5 min prior to induction we administered 100% oxygen via a circle absorber system. After administration of $5\text{--}7\text{ ml}\cdot\text{kg}^{-1}$ Ringer's lactate solution iv, anesthesia was induced with thiopental $2\text{ mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ iv until loss of the lash reflex, followed by fentanyl $10\text{ }\mu\text{g}\cdot\text{kg}^{-1}$ and pancuronium $0.1\text{ mg}\cdot\text{kg}^{-1}$ iv over 5 min. We concomitantly administered either desflurane or isoflurane in oxygen, adjusting the concentration to reduce systolic arterial pressure (SAP) to 70–80% of the average ward value or until we achieved an end-tidal agent concentration equal to 1.0 times the minimum alveolar concentration (MAC) for the agent in use. The trachea was then intubated. Thereafter, anesthesia was maintained with either volatile agent, using end-tidal concentrations up to 2.0 MAC and attempting to maintain SAP between 70 and 80% of the average preoperative value. Desflurane was administered via a specially modified DM-5000 anesthetic machine (Ohmeda). Isoflurane was administered via a Modulus II-Plus anesthetic machine (Ohmeda). We assumed a MAC value of 1.15% for isoflurane⁶ and 6.00% for desflurane.⁷

No volatile anesthetic was administered during cardiopulmonary bypass. Midazolam, $0.25\text{ mg}\cdot\text{kg}^{-1}$ was added to the priming solution of the bypass apparatus. During cardiopulmonary bypass, if the EEG indicated less cerebral depression than was present prior to initiation of cardiopulmonary bypass, fentanyl was administered.

After separation from cardiopulmonary bypass, either volatile agent was used as required to maintain SAP within predefined limits. If the patient's cardiovascular status precluded administration of the volatile agent, and if the EEG demonstrated increased cortical activity, fentanyl was administered.

HEMODYNAMIC CONTROL

Heart rate and SAP were maintained within strict limits throughout anesthetic induction and the period prior to

cardiopulmonary bypass. The last five preoperative determinations of heart rate and SAP, or all preoperative values if fewer than five were recorded, were averaged and used as a baseline. Tachycardia (heart rate > 120% of ward average) was initially treated by increasing the end-tidal anesthetic concentration to up to 2.0 MAC. If this was ineffective, or associated with hypotension (SAP < 70% of ward average), or increased pulmonary artery wedge pressure (PAWP), fentanyl $2\text{ }\mu\text{g}\cdot\text{kg}^{-1}$ iv (up to $6\text{ }\mu\text{g}\cdot\text{kg}^{-1}$ over 30 min) or iv propranolol were administered. Hypertension (SAP > 120% of ward average) was treated primarily by progressively increasing the end-tidal anesthetic concentration up to 2.0 MAC. If this was ineffective or poorly tolerated, additional iv fentanyl (as above) or NTG was given. Hypotension (SAP < 70% of ward average) was managed by decreasing the end-tidal anesthetic concentration and giving iv crystalloid. Failing this, phenylephrine was administered iv. ST-segment depression of $\geq 0.1\text{ mV}$ was treated with iv NTG or propranolol. The protocol specified neither a lower limit for heart rate nor an upper limit for PAWP, and these were treated at the discretion of the attending anesthesiologist with iv atropine or NTG, respectively.

DATA COLLECTION

End-tidal anesthetic concentration was recorded every 1 min during induction and every 15 min thereafter. A 6-channel polygraph (Siemens) was used to record the ECG and hemodynamic variables, at $2\text{ mm}\cdot\text{s}^{-1}$, throughout the study. ECG leads II and V_5 , systemic arterial pressure, PAP, and CVP, at $25\text{ mm}\cdot\text{s}^{-1}$, were recorded every 1 min during induction and every 15 min after intubation. Complete hemodynamic profiles, including PAWP and cardiac output, were recorded at the following times: 1) prior to induction (control), 2) after induction, 3) 1 min after intubation, 4) during skin preparation, 5) 1 min after skin incision, 6) 1 min after sternotomy, and 7) just prior to cannulation of the heart. Arterial pH, arterial oxygen tension, and carbon dioxide tension, were also measured at each of these times.

Postoperatively, we obtained 12-lead ECGs and creatine kinase MB (CK-MB)-fraction concentrations for 3 days. All patients were interviewed postoperatively and questioned specifically about intraoperative awareness, and their clinical status was followed until discharge.

DATA ANALYSIS

The 24-h ECG recordings were analyzed with a microcomputer-based system (Altair, Diagnostic Medical Instruments). This full-disclosure system stores 24 h of digitized two-channel ECG data on a hard disk. High-quality ECG tracings from any time interval can be generated using a laser printer. It also provides a 24-h ST-segment histogram. The program identifies all user-de-

finned ischemic episodes and notes their duration. Ischemia was defined as ST-depression equal to or greater than 0.1 mV or ST-elevation equal to or greater than 0.2 mV, persisting for 1 min or longer, in either lead CS₅ or lead II. All recordings were reviewed by an experienced observer (I.R.T.) who was blinded to anesthetic management, who verified all computer-identified ischemic episodes. ST-segment displacement was measured with respect to the PR interval, 80 ms after the S-wave nadir. The observer also reviewed ECG tracings corresponding to all suspicious areas of the ST-segment histogram. Finally, the entire recording was reviewed at high speed in the superimposition mode, looking for possible episodes of ST-segment displacement. In this mode, three consecutive ECG complexes are superimposed on the display terminal. As each new complex is added, the oldest is removed. Transient ST-segment changes are usually readily apparent.

Preoperative and postoperative ECG tracings were reviewed by an investigator (M.A.F.) who was not aware of the anesthetic agent used. Possible myocardial infarction was defined as the development of new Q waves greater than 0.04 s in duration on the postoperative ECG or a CK-MB concentration of more than 54 IU · l⁻¹ in a sample drawn approximately 16 h postoperatively.⁸ Definite myocardial infarction was diagnosed if both ECG and CK-MB criteria were fulfilled.

STATISTICAL ANALYSES

Demographic data were analyzed by Student's *t* test, χ^2 analysis, Fisher's exact test, or Wilcoxon's rank-sums test. Hemodynamics, blood gases, and anesthetic agent concentrations were compared by analysis of variance (ANOVA) for repeated measures. When ANOVA indicated a statistically significant group-time interaction (*P* less than 0.05), we rejected the null hypothesis that the choice of volatile anesthetic agent did not influence the variable in question. When ANOVA indicated either a

TABLE 2. Demographics

	Desflurane (n = 21)	Isoflurane (n = 20)
Age (yr)	60 ± 8	62 ± 6
Weight (kg)	84 ± 13	82 ± 11
Sex (F/M)	3/18	3/17
Preoperative β -adrenergic blocking agents	11	9
Preoperative Ca ²⁺ -entry blocking agents	19	16
Preoperative nitrates	19	19
Ejection fraction	0.57 ± 0.13	0.54 ± 0.10
Heart rate (beats per min)*	64 ± 8	66 ± 8
Systolic arterial pressure (mmHg)*	122 ± 11	123 ± 6
Diastolic arterial pressure (mmHg)*	74 ± 8	72 ± 5
Number of grafts	3.3 ± 0.9	3.9 ± 1.0

Values are means ± SD.

* Average of up to five preoperative determinations.

None of the differences is significant (*P* < 0.05).

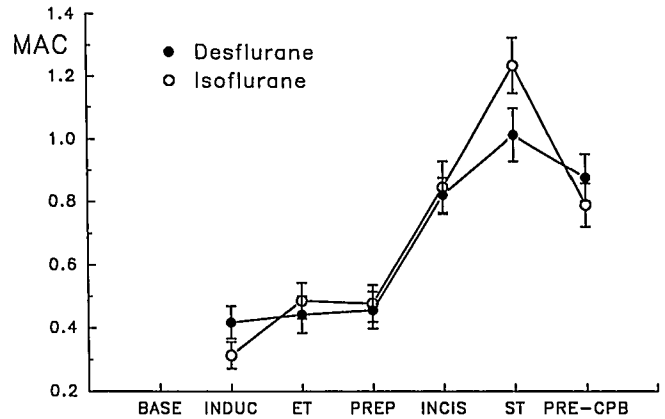


FIG. 1. End-tidal anesthetic concentrations (mean ± SEM) before cardiopulmonary bypass. BASE = control measurements before induction; INDUC = after induction; ET = 1 min after intubation; PREP = during skin preparation; INCIS = 1 min after skin incision; ST = 1 min after sternotomy; PRE-CPB = during cannulation of the heart.

significant group-time interaction, intergroup difference, or time effect, appropriate multiple comparisons were performed using the least squares means test. We applied Bonferroni's correction to compensate for the effect of multiple comparisons by the least squares means test. Therefore, we rejected null hypotheses when *P* was less than 0.0083 for multiple intragroup comparisons with control, and when *P* was less than 0.0071 for multiple intergroup comparisons. Variability is reported using the sample standard deviation.

Results

Forty-one patients participated in this study. Twenty-one received desflurane and 20 isoflurane. The two groups did not differ significantly with respect to age, sex, weight, ejection fraction, preoperative hemodynamics, antianginal therapy, or the number of distal coronary artery anastomoses performed (table 2). All patients were well oxygenated throughout the study period. ANOVA demonstrated no significant differences in pH, arterial carbon dioxide tension, or arterial oxygen tension within or between groups during the period prior to cardiopulmonary bypass.

The mean dose of thiopental used for induction of anesthesia was 183 ± 43 mg in the desflurane group and 177 ± 46 mg in the isoflurane group. Prior to cardiopulmonary bypass, the total dose of fentanyl was 985 ± 292 μ g and 900 ± 212 μ g in the desflurane and isoflurane groups, respectively (*P* not significant).

The end-tidal desflurane concentration varied from 2.5 ± 1.4% at end-induction, to a peak of 6.1 ± 2.3% at sternotomy. The respective end-tidal isoflurane concentrations were 0.4 ± 0.2 and 1.4 ± 0.5%. When end-tidal agent concentrations were expressed as multiples of MAC, there were no significant intergroup differences in the

anesthetic doses administered prior to cardiopulmonary bypass (fig. 1).

Hemodynamic data for the period prior to cardiopulmonary bypass are displayed in table 3. There were no significant group-time interactions for heart rate, PAP, CVP, PAWP, or systemic vascular resistance index (SVRI). Heart rate increased in both groups following intubation and sternotomy. PAP, CVP, PAWP, and systemic vascular resistance index all decreased significantly following induction. PAP and CVP returned to control levels at the time of sternotomy. In the isoflurane group, the systemic vascular resistance index increased significantly at sternotomy. ANOVA revealed statistically significant group-time interactions for SAP and mean arterial pressure (MAP). SAP in both groups decreased with induction of anesthesia and remained less than control values until initiation of cardiopulmonary bypass. However, SAP was higher in the isoflurane group after intubation, during skin preparation, and after sternotomy (table 3). MAP declined significantly following induction in both groups and returned to the control level in the isoflurane group at the time of sternotomy. The MAP was significantly higher with isoflurane, compared to desflurane, at the time of sternotomy (97 ± 9 vs. 87 ± 12 mmHg). Although a significant group-time interaction was noted for cardiac index, least-squares means analyses could not pinpoint a significant intergroup difference at any specific measurement interval.

The average heart rate, MAP, and end-tidal MAC values for the entire period prior to cardiopulmonary bypass were calculated using the trapezoidal method. ANOVA did not demonstrate any significant differences between groups. Variability in hemodynamics and the dose of volatile anesthetic prior to, and following separation from, cardiopulmonary bypass was assessed by calculating the range (the difference between the lowest and highest measured values) of each of these variables for each patient and comparing the ranges by Student's *t* test (table 4).

Sixty percent of patients required iv administration of either propranolol, NTG, supplemental fentanyl, or a combination of these, to achieve satisfactory hemodynamic control prior to cardiopulmonary bypass (table 5). However, the incidence of these interventions did not differ significantly between groups. After separation from cardiopulmonary bypass 18 of the 21 patients in the desflurane group required the volatile agent (mean 0.63 ± 0.18 MAC) to maintain satisfactory hemodynamics. Nineteen of the 21 patients in the isoflurane group received 0.59 ± 0.14 MAC after bypass. None of these differences is significant ($P > 0.05$). Postoperatively, no patients had any recollection of intraoperative events.

ECG changes indicative of myocardial ischemia prior to induction of anesthesia were found in two patients in

TABLE 3. Hemodynamics Prior to Cardiopulmonary Bypass

	Group	Control	After Induction	1 min after Intubation	During Skin Preparation	1 min after Incision	1 min after Sternotomy	Before Cannulation	Probability of Group-Time Interaction by ANOVA (P)
Heart rate (beats per min)	Desflurane	53 ± 10	58 ± 7	63 ± 9*	56 ± 8	56 ± 6	62 ± 9*	61 ± 9	NS
	Isoflurane	59 ± 12	61 ± 12	72 ± 16*	60 ± 9	59 ± 8	67 ± 9*	64 ± 11	
Systolic arterial pressure (mmHg)	Desflurane	149 ± 19	107 ± 13*	109 ± 10*	100 ± 7*	112 ± 16*	119 ± 14*	110 ± 15*	0.019
	Isoflurane	154 ± 18	114 ± 19*	123 ± 17**†	110 ± 13**†	117 ± 13*	138 ± 14**†	114 ± 16*	
Mean arterial pressure (mmHg)	Desflurane	97 ± 12	72 ± 9*	77 ± 9*	71 ± 5*	81 ± 10*	87 ± 12*	77 ± 11*	0.026
	Isoflurane	95 ± 9	73 ± 12*	81 ± 10*	74 ± 9*	81 ± 9*	97 ± 9†	78 ± 11*	
Pulmonary arterial pressure (mmHg)	Desflurane	26 ± 7	20 ± 5*	20 ± 4*	19 ± 4*	21 ± 5*	23 ± 6	22 ± 6*	NS
	Isoflurane	23 ± 6	19 ± 4*	21 ± 6	18 ± 4*	20 ± 5*	23 ± 6	19 ± 6*	NS
Central venous pressure (mmHg)	Desflurane	13 ± 4	10 ± 3*	9 ± 3*	10 ± 3*	11 ± 3	12 ± 3	9 ± 2*	NS
	Isoflurane	11 ± 3	10 ± 3	9 ± 2*	9 ± 2*	10 ± 2	11 ± 3	8 ± 2*	NS
Pulmonary arterial wedge pressure (mmHg)	Desflurane	22 ± 7	14 ± 4*	13 ± 4*	13 ± 4*	16 ± 5*	17 ± 5*	15 ± 5*	NS
	Isoflurane	19 ± 5	13 ± 3*	13 ± 4*	12 ± 4*	15 ± 5*	17 ± 6*	12 ± 4*	0.016
Cardiac index (l · min ⁻¹ · m ⁻²)	Desflurane	2.5 ± 0.5	2.2 ± 0.4	2.3 ± 0.3	2.2 ± 0.5	2.1 ± 0.3*	2.3 ± 0.6	2.6 ± 0.8	
	Isoflurane	2.6 ± 0.6	2.4 ± 0.5	2.5 ± 0.5	2.2 ± 0.3*	2.3 ± 0.4*	2.3 ± 0.4*	2.4 ± 0.5	
Systemic vascular resistance index (dyne · s · cm ⁻⁵ · m ²)	Desflurane	2822 ± 711	2277 ± 380*	2349 ± 412*	2333 ± 483*	2691 ± 544	2796 ± 701	2239 ± 695*	NS
	Isoflurane	2631 ± 536	2178 ± 449*	2298 ± 400	2421 ± 462	2548 ± 435	3041 ± 543*	2452 ± 590	

* $P < 0.0083$ versus control value for that group (LSM test).

† $P < 0.0071$ between groups at the indicated times (LSM test).

Values are means ± SD.
NS = not significant.

TABLE 4. Range of Heart Rate, Mean Arterial Pressure, and End-Tidal MAC

	Group	Range of Heart Rate (beats per min)	Range of Mean Arterial Pressure (mmHg)	Range of MAC
Pre-CPB	Desflurane	25 ± 13	30 ± 12	1.1 ± 0.3
	Isoflurane	26 ± 17	33 ± 10	1.2 ± 0.3
Post-CPB	Desflurane	10 ± 7	18 ± 9	0.6 ± 0.3
	Isoflurane	11 ± 7	19 ± 9	0.6 ± 0.3

Values are means ± SD.

Pre-CPB = before cardiopulmonary bypass; post-CPB = after separation from cardiopulmonary bypass.

the desflurane group and three patients in the isoflurane group. These changes resolved with induction of anesthesia in one of the patients given desflurane and worsened in the other. Myocardial ischemia evident prior to induction in two patients in the isoflurane group persisted after induction and worsened in the third patient in this group.

Five patients developed new or worsened ST-depression of 0.1 mV or more lasting more than 1 min during the period prior to cardiopulmonary bypass. Two of these received isoflurane and three desflurane (*P* not significant). One patient given isoflurane had an increased CK-MB concentration 16 h postoperatively. None of the other 4 patients had any evidence suggesting myocardial infarction.

The mean CK-MB concentrations in blood samples drawn approximately 16 h after the end of surgery were 36.4 ± 40.3 IU · l⁻¹ in the desflurane group and 38.0 ± 36.1 IU · l⁻¹ in the isoflurane group. Five patients in each group had greater than 54 IU · l⁻¹ CK-MB at that time. One of these in the desflurane group also had new Q waves on the postoperative 12-lead ECG. Therefore, possible intraoperative myocardial infarction, defined as either CK-MB greater than 54 IU · l⁻¹ 16 h postoperatively, or new Q waves, occurred in four patients in the desflurane group and in five patients given isoflurane. A definite myocardial infarction (both enzymatic and ECG criteria present) occurred in 1 patient in the desflurane group, who subsequently died. There were no definite myocardial infarctions in the isoflurane group. None of the differences in any of the indicators of perioperative myocardial infarction is statistically significant.

Three patients died prior to discharge. Two had received desflurane, and one, isoflurane. The two patients who died after desflurane anesthesia had similar courses. Both tolerated desflurane well in the prebypass period. Neither patient had any myocardial ischemia prior to cardiopulmonary bypass, and neither required any pharmacologic intervention prior to bypass. Neither patient received desflurane after cardiopulmonary bypass. Anal-

ysis of the 24-h ECG recordings demonstrated that both patients had significant myocardial ischemia postoperatively. Although only one of these patients had documented ECG and CK-MB changes suggesting infarction postoperatively, at autopsy both had evidence of recent myocardial infarction. The patient who died after isoflurane anesthesia had an intraoperative cerebral infarction, which was probably embolic in etiology. He subsequently suffered a perforation of the cecum and died of sepsis.

Discussion

Our results suggest that desflurane is very similar to isoflurane when used as the primary anesthetic agent for patients undergoing elective coronary artery surgery. The hemodynamic response to anesthesia and surgery was comparable in both groups. However, the majority of patients in both groups required either additional fentanyl, propranolol, or NTG, to maintain hemodynamics within the desired limits during surgery. In part, the similar hemodynamic effects reflect the use of these interventions. However, requirements for these interventions did not differ, suggesting that the underlying hemodynamic effects of desflurane and isoflurane are similar. Good hemodynamic control may have contributed to the relatively low overall incidence of myocardial ischemia (12.2%) detected prior to cardiopulmonary bypass.

The only striking intergroup differences in hemodynamics were the significantly lower MAP in the desflurane group at the time of sternotomy, and lower SAP after intubation and sternotomy. Why this should have occurred is unclear, since patients in both groups were receiving equipotent doses of anesthetic during the entire period before cardiopulmonary bypass. It is possible that because of its relatively low blood-gas partition coefficient, an effective end-tidal anesthetic concentration was achieved sooner with desflurane than with isoflurane. Desflurane's slightly lower brain-blood partition coefficient, 1.29 *versus* 1.57 for isoflurane,⁹ might also have accelerated the deepening of anesthesia after intubation and sternotomy. Alternatively, the assumed MAC of either isoflurane or desflurane may have been incorrect. We did not adjust MAC for age, and the mean age of our patients was higher than the mean age of the patients in the studies determining MAC.^{6,7} Also, it is possible that desflurane and isoflurane interact differently with the

TABLE 5. Number of Patients Given Pharmacologic Interventions Prior to Cardiopulmonary Bypass

	β-blocker	Nitroglycerin	Fentanyl	Any Intervention
Desflurane	6	8	9	13
Isoflurane	6	6	5	11

None of the differences is significant (*P* < 0.05).

combination of thiopental and fentanyl. However, we have no data to substantiate any of these explanations.

Other explanations of the intergroup difference in MAP at sternotomy must be considered. Since this was an open-label trial, investigator bias may have influenced the way in which the agents were used. The majority of patients required intervention with fentanyl, propranolol, or NTG prior to cardiopulmonary bypass. Nonrandom application of these interventions might also explain our findings. However, there was no difference between groups in the incidence of these interventions (table 5). Airway gases were sampled between the endotracheal tube and the Y-connector of a circle system. It is possible that end-tidal specimens were slightly contaminated with inspired gas. The mean end-tidal anesthetic concentrations progressively increased until the time of sternotomy (fig. 1). Therefore, because of its greater blood-gas partition coefficient, the inspired to end-tidal concentration ratio of isoflurane was probably greater than that of desflurane for much of the period prior to cardiopulmonary bypass. Thus, contamination of the sample with inspiratory gases would cause a relatively greater overestimation of the end-tidal anesthetic concentration of isoflurane.

One final explanation must be considered. MAC describes one point on a concentration-response curve. There is no assurance that the concentration-response curves for desflurane and isoflurane are parallel. If the desflurane concentration-response curve is steeper than that of isoflurane, then, for example, 1.5×1 MAC would be a relatively more potent concentration of desflurane.

The 7.3% mortality in this study was unexpected. For comparative purposes, we reviewed perioperative mortality for the 273 patients undergoing elective, primary coronary artery surgery at our hospital during the calendar year (1989) immediately preceding this study. Ten patients operated upon in 1989 died, for a mortality rate of 3.66%. Assuming that the population mortality rate is, in fact, 3.66%, the Poisson statistic¹⁰ indicates that the probability of observing 3 deaths in 41 subjects is 0.126. Therefore, the mortality rate for the patients in this study was not significantly different than that of comparable patients at our hospital. During the prebypass period the volatile agents were well tolerated by patients who died postoperatively. None of the patients who died received desflurane in the postbypass period. The possibility that these mortalities were related to the use of volatile anesthetic agents seems remote.

We studied a relatively small number of patients, and, because a special anesthetic machine was required to administer desflurane, we could not conduct a blinded study. Taking these limitations into consideration, we conclude that desflurane and isoflurane are remarkably similar when used as the primary anesthetic agent for patients

undergoing coronary artery surgery. There is the possibility that desflurane provides superior blood pressure control during sternotomy and during other periods of intense noxious stimulation. This may be due to its low solubility, although confirmation of this observation is required. Desflurane may be a reasonable alternative to isoflurane in patients with coronary artery disease, and it deserves further investigation. Our study was not large enough to determine whether or not the choice of volatile agent influenced outcome. Definitive demonstration of the safety of desflurane in patients with severe coronary artery disease will require determination of the outcomes of a larger number of patients.

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