Comparison of the Effects of Sevoflurane, Isoflurane, and Desflurane on Microcirculation in Coronary Artery Bypass Graft Surgery

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Objective: **This investigation was performed to compare the effects of inhalation agents on microcirculation in coronary artery bypass grafting (CABG) using orthogonal polarization spectral imaging.**

Design: **This prospective and randomized study was performed in patients scheduled for CABG surgery from March through September 2010.**

Setting: **Tertiary care university hospital.**

Participants: **Thirty patients undergoing elective CABG.**

Interventions: **Patients were assigned to sevoflurane, desflurane, or isoflurane.**

Measurements and Main Results: **Orthogonal polarization spectral imaging was used to evaluate the sublingual microcirculation. Hemodynamic variables (heart rate, mean arterial pressure, central venous pressure, cardiac output, and pulmonary capillary wedge pressure), laboratory parameters (hematocrit, lactate, and potassium), and microcirculatory variables (total vascular density [TVD] [mm/mm^2], microvascular flow index [MFI] [arbitrary units], perfused vessel density [PVD] [mm/mm^2], and proportion of perfused vessels [PPV] [percentage] were obtained before induction, after induction, during cardiopulmonary bypass, at the end of surgery, and 24 hours after surgery. The greatest alterations in microcirculation parameters were found during cardiopulmonary bypass. In the sevoflurane group, TVD (14.7%), PVD (22%), PPV (5.97%, $p < 0.05$), and MFI (7.69%, $p > 0.05$) were decreased. In the isoflurane group, TVD (14.7%) and PVD (20.3%) were decreased, whereas PPV (1.69%) and MFI (17.99%) were increased ($p < 0.05$). In the desflurane group, there were no changes in TVD and PVD, but MFI (8.99%, $p > 0.05$) and PPV (1.48%, $p < 0.05$) were increased in the small vessels. These changes returned to their initial values 24 hours postoperatively.**

Conclusions: **Sevoflurane had a negative effect on the microcirculation. Isoflurane decreased vascular density and increased flow. Desflurane produced stable effects on the microcirculation. These inhalation agents induced transient alterations in microvascular perfusion.**

KEY WORDS: microcirculation, anesthetic agents, sevoflurane, desflurane, isoflurane, cardiac surgery, cardiopulmonary bypass

ADEQUATE FUNCTION of the microcirculation is essential in providing oxygen to all tissues and organs of the human body, especially in cardiac surgery during cardiopulmonary bypass (CPB). The microcirculation consists of a network of blood vessels <50 μm in diameter (arterioles, capillaries, etc). Adequate blood flow within these microvessels is a prerequisite for normal organ perfusion. The microcirculation functions as a volume reservoir for the blood, so the microcirculation plays an important role in regulating preload and, thus, cardiac output (CO).[1] The pathogenesis of an impaired microcirculation may involve multiple factors, including changes in temperature, hemodynamic parameters, and the coagulation cascade in cardiac surgery with CPB. Moreover, CPB itself affects microcirculation by causing hemodilution.[2]

Until recently, the microcirculation could not be measured directly at the bedside in patients. De Backer et al,[3] in a small study, showed that the proportion of perfused capillaries correlated to organ failure and short-term mortality, and most studies were performed on the easily accessible sublingual microcirculation using orthogonal polarization spectral (OPS) imaging. The effects of blood pressure and perfusion pressure on the microcirculation in septic shock, hypovolemic shock, and heart failure can be analyzed with methods such as OPS imaging.[3-5]

The potent inhalation anesthetics currently used in clinical practice have similar effects in regional tissue perfusion and microcirculation under stable anesthetic conditions, but these effects may be different under pathophysiologic conditions, such as hemorrhage, sepsis, or during CPB. There have been few studies reported on this topic and they have shown contradictory results on the different effects of inhalation agents on organ function. Rörtgen et al[6] reported that the total incidence of postoperative cognitive dysfunction showed no differences between desflurane and sevoflurane groups. However, the Well-Being Scale, Digit Span Test, and Trail Making Test, emergence times, and patients' satisfaction favored desflurane.[6] On the same topic, Kanbak et al[7] found that isoflurane was associated with better neurocognitive function than desflurane or sevoflurane after on-pump coronary artery bypass grafting (CABG). Merin et al[8] found that hepatic arterial blood flows were maintained by desflurane and slightly increased by isoflurane in dogs. Furthermore, isoflurane has been shown to possess more vasodilating effects than cardiac depressant properties.[9] In view of the effects of these inhalation agents, the authors hypothesized that isoflurane would cause more vasodilation compared with sevoflurane and desflurane at the microcirculatory level using OPS imaging.

METHODS

The institutional ethics committee approved the protocol and informed consent was obtained from each patient. This study was prospective and randomized. Thirty consecutive patients scheduled for

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Table 1. Patient Characteristics and Operative Variables

	Sevoflurane Group (n = 10)	Isoflurane Group (n = 10)	Desflurane Group (n = 10)
Age (y)	67.7 ± 4.6	59.6 ± 11.2	61.0 ± 10.1
Women/men	1/9	2/8	2/8
Height (cm)	169.0 ± 6.7	167.5 ± 9.1	162.9 ± 10.2
Weight (kg)	75.1 ± 14.9	78.5 ± 8.1	77.5 ± 7.7
Ejection fraction (%)	58 ± 10	56 ± 12	63 ± 4
Number of grafts used	3 (2, 3)	2 (2, 4)	2 (1, 3)
Anesthesia period (min)	349.5 ± 92.5	347.0 ± 58.6	318.0 ± 68.8
Surgical period (min)	296.5 ± 94.2	289.5 ± 47.3	272.5 ± 78.4
ACC period (min)	51.3 ± 16.8	76.4 ± 49.1	49.0 ± 24.5
CPB period (min)	93.9 ± 34.0	115.0 ± 58.8	79.6 ± 23.9
Extubation time (h)	7.7 ± 0.9	11.4 ± 9.7	8.9 ± 3.4
Length of ICU stay (h)	63.8 ± 49.4	56.9 ± 29.9	43.1 ± 21
Dopamine requirement (n; dose range in μg/kg/min)	8 (4.5 ± 2.9)	4 (2.0 ± 2.6)	5 (2.8 ± 3.4)

NOTE. Data are presented as mean ± standard deviation or median (25th, 75th percentiles).

Abbreviations: ACC, aortic cross-clamp; CPB, cardiopulmonary bypass; ICU, intensive care unit.

elective CABG with CPB were included in this study. Exclusion criteria were patients with end-stage obstructive/restrictive pulmonary disease, renal failure, liver failure, sepsis, multiorgan failure, previous cardiac surgery, and emergency surgery. All surgeries were performed by the same surgical team.

These patients were assigned randomly to receive sevoflurane (group S, n = 10), desflurane (group D, n = 10), or isoflurane (group I, n = 10) inhalation. The randomization of patients to sevoflurane, desflurane, or isoflurane inhalation was performed with a list of random numbers that was generated by the random function of Excel (Microsoft Corp, Redmond, WA). The list contained the natural numerals 1, 2, and 3. These numbers were allocated as follows: 1, sevoflurane; 2, desflurane; and 3, isoflurane administration. The investigator who analyzed the OPS imagines was blinded to the type of inhalation agent being administered.

The day before surgery, the patients were evaluated before anesthesia administration. All patients continued their cardiovascular medications until the day of surgery. In the operating room, electrocardiogram, pulse oximetry, end-tidal CO_2, and invasive arterial pressure (20-G cannula, right radial artery, BD floSvitch, Swindon, United Kingdom) were monitored. After anesthesia induction; a 9.5F 3-lumen central venous catheter (Multicath, Vygon, Ecouen, France) and a pulmonary artery catheter (Swan-Ganz catheter, 7F, 4 lumens, 110 cm; Edwards Lifesciences, Irvine, CA) were introduced into the right internal jugular vein. A urinary bladder catheter and nasopharyngeal temperature probe were inserted. Arterial blood pressure, central venous pressure, pulmonary arterial pressures, CO, and cardiac index were monitored during surgery.

Anesthesia induction was performed using etomidate, 0.4 mg/kg, vecuronium bromide, 0.1 mg/kg, and fentanyl, 1 μg/kg. For the maintenance of anesthesia, all inhalation agents were given at 1 MAC in an oxygen-air mixture. Patients in group S (n = 10) received the volatile anesthetic sevoflurane at 2%-3%[10]; patients in group I (n = 10) received isoflurane at 1%-2%[11]; and patients in group D (n = 10) received desflurane at 4%-6%[12] in a 50%-50% oxygen-air mixture from induction to CPB and from the end of CPB to the end of surgery. During hypothermic CPB, the volatile anesthetics were delivered using a vaporizer that was inserted into the gas supply line of the oxygenator. Isoflurane 1%,[13,14] desflurane 2%,[14] or sevoflurane 1%,[15] in an oxygen-air mixture was added to the oxygenator gas flow line (gas flow, 3 L/min). Remifentanil infusion was administered to all patients before and after CPB at a dose of 0.025-0.05 mg/kg/min. During CPB, remifentanil was infused at 0.025 mg/kg/min.[16] Bispectral index (BIS) monitoring was used, and the anesthesia depth was adjusted to keep the BIS <50.[12] Whenever an inadequate anesthesia depth was observed (heart rate >90 beat/min, systolic arterial pressure >150 mmHg, mean arterial pressure [MAP] >70 mmHg, observation of somatic and autonomic responses: movements, eye opening, deglutition, sweating, tear production, etc), the inhalation concentrations were not changed, but the remifentanil infusion rate was increased in 0.01-mg/kg/min increments until an adequate anesthesia depth was achieved.[16] All patients were ventilated with positive pressure. The ventilation parameters were adjusted to keep the tidal volume, respiratory rate, acid-base balance, and arterial CO_2 levels within physiologic limits.

The CPB circuit consisted of a modified coated system and a fiber membranous oxygenator (COBE Cardiovascular, Inc, CO; Sarns 9000 Perfusion System, 3M Health Care Group, MI, Ltd, Ann Arbor, MI). The priming fluid of the CPB circuit contained Ringer's lactate, 1,500

Table 2. Heart Rate (beats/min) in the Sevoflurane, Isoflurane, and Desflurane Groups

	Sevoflurane Group (n = 10)	Isoflurane Group (n = 10)	Desflurane Group (n = 10)	*p* Value*
Before induction	84 ± 21	75 ± 6	69 ± 11	0.201
After induction	70 ± 17†	76 ± 18	71 ± 12	0.789
At end of surgery	95 ± 18	86 ± 17	83 ± 12	0.227
24 h after surgery	88 ± 17	90 ± 13	91 ± 13*	0.743

NOTE. All data are presented as mean ± standard deviation.

*$p > 0.05$ among the 3 groups.

†$p < 0.05$ compared with basal values (within-group analysis).

Table 3. Mean Arterial Pressure (mmHg) in the Sevoflurane, Isoflurane, and Desflurane Groups

	Sevoflurane Group (n = 10)	Isoflurane Group (n = 10)	Desflurane Group (n = 10)	*p* Value*
Before induction	90 ± 27	102 ± 17	95 ± 11	0.417
After induction	81 ± 25	83 ± 12	89 ± 16	0.239
At end of surgery	72 ± 12	72 ± 13†	75 ± 16	0.239
24 h after surgery	80 ± 9	79 ± 14	78 ± 15*	0.915

NOTE. All data are presented as mean ± standard deviation.

*$p > 0.05$ among the 3 groups.

†$p < 0.05$ compared with basal values (within-group analysis).

Table 4. Cardiac Output (L/min) in the Sevoflurane, Isoflurane, and Desflurane Groups

	Sevoflurane Group (n = 10)	Isoflurane Group (n = 10)	Desflurane Group (n = 10)	*p* Value*
After induction	3.5 ± 0.8	5.0 ± 1.9	4.8 ± 1.5	0.027*
At end of surgery	5.5 ± 2.0†	5.9 ± 1.1	6.7 ± 2.2†	0.343
24 h after surgery	7.4 ± 2.2†	7.6 ± 1.0†	7.6 ± 1.8†	0.983

NOTE. All data are presented as mean ± standard deviation.

*$p < 0.05$ among the 3 groups.

†$p < 0.05$ compared with basal values (within-group analysis).