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Original Article

Sevoflurane washout in obese patients undergoing gastric bypass: low-flow versus decremental delivery

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Abstract: Safe recovery after general anesthesia may be compromised by obesity. In this study, we compared low-flow and decremental sevoflurane delivery to determine which method best facilitates anesthetic recovery in obese patients undergoing laparoscopic gastric bypass procedures. Forty obese patients (body mass index 30 to 50 kg/m^2) presenting for laparoscopic gastric bypass surgery were randomly assigned (1:1 by closed envelope) for either low-flow (group L) or decremental (group D) anesthesia washout. Mean arterial pressure, heart rate, and bispectral index were monitored, and concentrations of sevoflurane at the end of surgery were recorded, along with times from drain placement to end of surgery, eye opening, and extubation. Low-flow delivery was associated with significantly shorter mean times from end of surgery to eye opening and to extubation (7.63 ± 2.10 min and 10.87 ± 2.61 min, respectively, group L vs 12.70 ± 3.25 min and 16.02 ± 3.21 min, group D; $P < 0.05$), significantly lower agitation scores (Riker Sedation Agitation Scale) immediately after extubation (3.95 ± 0.94, group L, vs 4.85 ± 0.93, group D; $P < 0.05$), and a significantly lower incidence of emergence agitation immediately after extubation. There were no significant differences between groups in visual analog scale pain scores at 15 min after extubation (1.60 ± 1.14 vs 1.90 ± 0.97; $P > 0.05$), nor were there differences in $Pa0_2$ (70.98 ± 5.69 mm Hg vs 71.31 ± 7.14 mm Hg) and $PaCO_2$ (41.61 ± 3.65 mm Hg vs 43.51 ± 4.20 mm Hg) (both $P > 0.05$). Low-flow washout of sevoflurane in obese patients undergoing laparoscopic gastric bypass surgery provided higher-quality emergence from anesthesia with less agitation compared to decremental washout.

Keywords: Obesity, sevoflurane, recovery quality, low-flow method, concentration decline method

Introduction

Obesity is characterized by increases in both fat and lean body mass, but the increase in fat is disproportionate, thus impacting and complicating the absorption, distribution, metabolism, and excretion of anesthetic drugs according to their lipid solubility [1-3]. The uptake and clearance of these agents is further altered in obesity by augmented cardiac output (CO) and blood volume [4-6]. Consequently, the kinetics of general anesthetics in obese and nonobese patients diverge even during the recovery phase. Obese patients undergoing general anesthesia are at increased risk of severe complications including acute myocardial infarction, aspiration, acute upper airway obstruction, pulmonary atelectasis, pneumonia, and respiratory failure [7, 8], and an uneventful recovery from anesthesia is important for ensuring stable hemodynamics and appropriate postoperative respiratory function in morbidly obese patients [9].

Obesity is generally associated with slower emergence from anesthesia. Delayed recovery from anesthesia may reflect the effects of inhalation anesthetics that are stored in fat because of return of blood perfusing the fat or because of the transfer of accumulated anesthetic agent from fat to adjacent, highly perfused tissues, such as from the omental/mesenteric fat to the intestine and liver [10].

The volatile anesthetic sevoflurane has a remarkably low (0.63) blood/gas partition coefficient [11] and poor solubility, which allows better intraoperative control of anesthesia and more rapid recovery vs anesthetic agents with higher blood/gas partition coefficients. Sevo-

flurane is widely used in general anesthesia. It is known for its minimal impact on intracranial pressure, respiratory function, and cardiovascular performance [12], and because of its profile of rapid and consistent recovery, it has been promoted as the volatile anesthetic of choice for obese patients [13-15]. Sevoflurane is usually eliminated from the body by alveolar pulmonary arterial flow (ventilated to open air) [16] or merely through diffusion from the wound or skin. Hence, the time required for emergence from sevoflurane anesthesia is primarily affected by solubility and by the blood/gas and tissue/blood partition coefficients and the duration of anesthesia.

Washout of inhalational anesthesia is commonly accomplished by either of two methods. Low-flow delivery involves early discontinuation of the agent, and decremental delivery involves concentration reductions from otherwise standard levels near the end of the operative procedure. Both methods entail high-flow (6 $L \cdot min^{-1}$) agent washout at the end of surgery. However, the preferred method for optimal recovery in obese patients has yet to be established. This study was conducted to compare emergence times and recovery characteristics between low-flow and decremental inhalant washout in obese patients undergoing laparoscopic gastric bypass surgery.

Materials and methods

Patients

The study was approved by the local Ethics Committee, and written informed consent was obtained from all participants. Fifty-one patients with body mass index (BMI) values of 30 to 50 kg/m^2 who were classified as American Society of Anesthesiologists (ASA) physical status II or III and were scheduled to undergo laparoscopic gastric bypass under standard general anesthesia were enrolled in this randomized, double-blind study. The patients were randomly assigned (1:1 by closed envelope) to either low-flow washout (group L) or decremental washout (group D). Exclusion criteria were operative time < 2.5 h or > 3.5 h; patient age < 20 years or > 60 years; and history of coronary artery disease, myocardial infarction, congestive heart failure, chronic obstructive lung disease, drug allergy or drug abuse, neuromuscular diseases, or history of chronic pain. Patients with hepatorenal dysfunction or history of psychosis or neuropathy were likewise excluded because of the possibility of longer required emergence times.

General anesthesia protocols

All patients were fasted for 8 h prior to surgery and did not receive premedication. Peripheral arterial catheters were inserted for intraoperative monitoring of mean arterial pressure (MAP), and neuromuscular monitoring was routinely performed by acceleromyography (TOF-Watch SX; Organon Ltd, Ireland) of the adductor pollicis muscle to assess the response to ulnar train-of-four (TOF) nerve stimulation.

All drug regimens were based on ideal body weight, with the exception of succinylcholine, which was governed by total body weight. Once all standard monitors were connected to the patient, general anesthesia was induced by administration of intravenous (IV) sufentanil (0.5 $\mu g \cdot kg^{-1}$) and propofol (1.5 $mg \cdot kg^{-1}$). Orotracheal intubation was achieved using a cuffed tube, and was facilitated by succinylcholine (1 to 2 $mg \cdot kg^{-1}$). Cisatracurium (0.1 $mg \cdot kg^{-1}$) was administered every 40 to 50 min to provide additional muscle relaxation. Following induction and intubation, ventilation (Drager; Primus, Germany) was performed at tidal volumes of 8 to 10 $mL \cdot kg^{-1}$, based on ideal body weight, with a 1:2 inspiratory-to-expiratory time ratio. Ventilator frequency was initially set at 12 breaths$\cdot min^{-1}$, and was adjusted as needed to maintain an end-tidal carbon dioxide tension ($ETCO_2$), assessed by blood gas analysis, of 35 to 45 mm Hg throughout the procedure.

Sevoflurane (2% to 3%) at 1.3 minimum alveolar concentration (MAC), with a 50% oxygen-mixed flow at 2 $L \cdot min^{-1}$, and remifentanil (0.1-0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$), administered continuously by a syringe pump (Zhejiang University Medical Instrument Co Ltd, Beijing, China), were used for maintenance of general anesthesia. Standard monitoring was used throughout the procedure, and included continuous electrocardiography (ECG; lead II) and heart rate (HR), invasive blood pressure (BP) and MAP, pulse oximetry, $ETCO_2$, and end-tidal concentration of sevoflurane. The bispectral index (BIS) was monitored with BIS Sensor® monitor strips from Aspect Medical Systems Inc, Norwood, MA, USA. According to the manufacturer's recom-

Table 1. Patient characteristics and intraoperative data

	Group L	Group D
Gender (M/F)	6/14	7/13
ASA status (I/II)	8/12	9/11
Age (y)	35.15 ± 8.55	36.55 ± 8.50
Weight (kg)	106.88 ± 15.36	105.75 ± 10.50
BMI (kg/m^2)	38.44 ± 5.33	36.42 ± 3.97
Anesthesia time (min)	196.70 ± 10.16	199.55 ± 7.85

Data are expressed as mean ± SD. Group L: low-flow washout; Group D: decremental washout; BMI: body mass index; ASA: American Society of Anesthesiologists.

Table 2. Depth of anesthesia and BIS

	Group L	Group D
Time from drain placement to end of surgery	23.88 ± 3.56	24.13 ± 2.73
BIS at point of drain placement	43.95 ± 2.52	44.50 ± 2.50
BIS at end of surgery	63.65 ± 4.80	65.40 ± 3.07
End-tidal MAC at point of drain placement	1.14 ± 0.09	1.12 ± 0.11
End-tidal MAC at end of surgery	0.49 ± 0.07	0.50 ± 0.08
Remifentanil dose (mg)	0.86 ± 0.12*	0.65 ± 0.09

Data expressed as means ± SD. *P < 0.05 vs Group D. Group L: low-flow washout; Group D: decremental washout; BIS: Bispectral Index; MAC: minimum alveolar concentration.

Table 3. Emergence and extubation times

	Group L	Group D
Emergence time	7.63 ± 2.10*	12.70 ± 3.25
Extubation time	10.87 ± 2.61*	16.02 ± 3.21

Data are expressed as means ± SD. *P < 0.05 vs Group D. Group L: low-flow washout; Group D: decremental washout.

mendations, BIS values of 45 to 55 were established to ensure adequate depths of anesthesia during maintenance of general anesthesia. Parecoxib sodium (40 mg IV) was given to all patients 30 min before the end of surgery as prophylaxis against postoperative pain, along with ramosetron hydrochloride (0.3 mg IV) to curb postoperative nausea and vomiting. A single IV bolus of sufentanil (0.15 μg·kg^{-1}) was given at the time of drain placement along with neostigmine (1 mg IV) and atropine (0.5 mg IV) to antagonize residual muscle relaxation indicated by ulnar TOF stimulation > 90%.

Anesthesia washout

Anesthesia washout at the close of surgery began at the time of drain placement. According to our preliminary experimental results, for the low-flow washout method sevoflurane was discontinued and fresh gas flow was set at 0.5 L·min^{-1}, while for the decremental washout method, a gradual titration of end-expiratory sevoflurane concentration, to 0.5 MAC, with fresh gas flow maintained at 2 L·min^{-1} was performed by decreasing the vaporization every 3 to 5 min to achieve decrements of 0.5%. The remifentanil dose was adjusted for all patients in both groups to maintain BIS values of up to 65 during the washout period. After the last skin suture, remifentanil and sevoflurane (group D), were discontinued, and fresh gas flows were boosted to 6 L·min^{-1} for all patients.

Data collection

An anesthesiologist who was blinded to the surgery recorded the measured intraoperative variables, including MAP, HR, and BIS, at the following time (T) intervals: T1 (baseline), T2 (drain placement), T3 (suturing of skin), T4 (end of skin suturing), T5 (eye opening), and T6 (extubation). Concentrations of sevoflurane and doses of remifentanil at the end of surgery were recorded. The times from drain placement to end of surgery, eye opening on verbal command (emergence time), and extubation (extubation time) were also recorded.

Extubation was performed when the TOF exceeded 90% and the patient was sufficiently awake (making purposeful movements), capable of sustained spontaneous ventilation, and generating tidal volumes of > 5 mL/kg with adequate oxygenation, defined as oxygen saturation [SpO2] > 90% when spontaneously breathing room air via the endotracheal tube for 1 min.

After extubation, patients were transferred to the postanesthesia care unit (PACU), where a nurse (also blinded to the operative details) used the Riker Sedation-Agitation Scale (SAS;

Table 4. Incidence of emergence agitation by group

	Group L	Group D
Agitated	2 (10.0%)	4 (20.0%)
Very agitated	2 (10.0%)	5 (25.0%)
Dangerous agitation	0 (0.0%)	2 (10.0%)
Total	4 (20.0%)*	11 (55.0%)

Values are *n* (%). *$P < 0.05$ vs Group D. Group L: low-flow washout; Group D: decremental washout.

Table 5. Arterial blood gas determinations

	Group L	Group D
pH	7.35 ± 0.47	7.37 ± 0.31
PaO_2 (mm Hg)	70.98 ± 5.69	71.31 ± 7.14
$PaCO_2$ (mm Hg)	41.61 ± 3.65	43.51 ± 4.20

Data are expressed as mean ± SD. Group L: low-flow washout; Group D: decremental washout.

Table 6. Awareness and postoperative nausea and vomiting

	Group L	Group D
Awareness	0	0
Nausea and vomiting	2 (10.0%)	3 (15.0%)

Values are *n* (%). Group L: low-flow washout; Group D: decremental washout.

Table 7) to assess each patient's consciousness and level of agitation immediately upon arrival and 15 min later. Pain intensity at 15 min after extubation was assessed by the visual analog scale (VAS), with 0 corresponding to no pain and 10 to maximum pain. Arterial blood gas values were obtained 15 min after extubation. In addition, awareness and postoperative nausea and vomiting (PONV) were assessed within 24 h after surgery by a postoperative postanesthesia interview.

Statistical analysis

Descriptive statistics are reported as frequencies and proportions for categorical variables and as means with standard deviation (SD) for continuous variables. Age, weight, BMI, anesthesia time, BIS at the time of drain placement and at the end of surgery, remifentanil dose, emergence time, extubation time, pH, PaO2, $PaCO_2$, SAS, and VAS were compared by independent samples t-test, and gender, ASA status, incidence of emergence agitation, and postoperative nausea and vomiting were analyzed using either chi-squared or Fisher's exact test, as appropriate. All statistical analyses were performed with standard software (SPSS v19.0; SPSS Inc, Chicago, IL, USA) and statistical significance was set at $P < 0.05$.

Results

Among the total 51 patients who were enrolled during the study period, 4 declined to participate and 2 were excluded by 1 or more of the exclusion criteria. In addition, 3 patients in group L and 2 in group D were excluded from the final analysis because the time from drain placement to the end of surgery was longer than expected and the end-tidal MAC at the end of surgery was < 0.5.

Patient characteristics and intraoperative data were similar in the two groups (**Table 1**). Depth of anesthesia and BIS values were also similar in the two groups (**Table 2**). BIS and end-tidal MAC values were similar in the two groups at drain placement, at the end of surgery, and during the period from drain placement to the end of surgery, with a significantly higher remifentanil dose in group L than in group D (**Table 2**). There were no significant differences in hemodynamic parameters at any of the designated time intervals (**Figures 1**, **2**).

The times from the end of surgery to eye opening (emergence time) and from the end of surgery to extubation (extubation time) were significantly shorter in group L than in group D (**Table 3**). Furthermore, the SAS scores immediately after extubation were significantly lower in group L (3.95 ± 0.94) than in group D (4.85 ± 0.93; $P < 0.05$), while the differences between groups in SAS and VAS scores at 15 min after extubation were not significant (**Table 8**).

The incidence of emergence agitation was significantly lower in group L than in group D ($P < 0.05$) (**Table 4**), but no significant between-group differences were noted with respect to pH, PaO_2, or $PaCO_2$ at 15 min after extubation (**Table 5**). According to the postanesthesia interviews, there were no significant differences between groups in occurrences of awareness or PONV (**Table 6**).

Discussion

In general, body tissues can be grouped, according to blood supply and capacity to retain an anesthetic agent, as vessel-rich organs,

Table 7. Riker sedation-agitation scale

Score	Term	Description
7	Dangerous agitation	Pulling at endotracheal tube, trying to remove catheters, climbing over bed rail, striking at staff, thrashing side to side
6	Very agitated	Does not calm, despite frequent verbal reminding of limits; requires physical restraints, biting endotracheal tube
5	Agitated	Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions
4	Calm and cooperative	Calm, awakens easily, follows commands
3	Sedated	Difficult to arouse; awakens to verbal stimuli or gentle shaking, but drifts off again; follows simple commands
2	Very sedated	Arouses to physical stimuli, but does not communicate or follow commands, may move spontaneously
1	Unable to rouse	Minimal or no response to noxious stimuli, does not communicate or follow commands

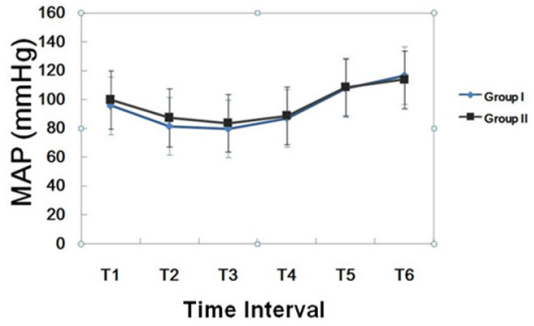

Figure 1. Comparison of mean arterial pressures over time. All data are presented as means, with error bars depicting 1 SD. Time intervals: T1= baseline; T2 = drain placement; T3 = start of skin suturing; T4 = end of skin suturing; T5 = eye opening; T6 = extubation.

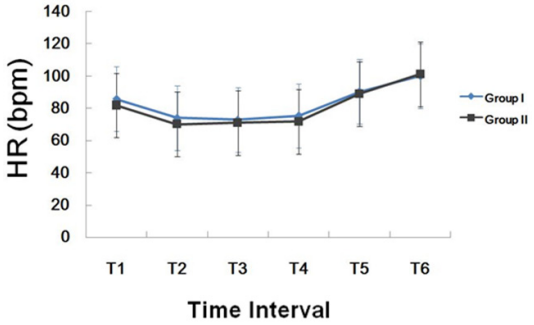

Figure 2. Comparison of heart rates over time. All data are presented as means, with error bars depicting 1 SD. Time intervals: T1 = baseline; T2 = drain placement; T3 = start of skin suturing; T4 = end of skin suturing; T5 = eye opening; T6 = extubation.

muscle, and fat [11-16]. The vessel-rich group (VRG), consisting of brain, heart, liver/intestine, and kidney, receives the largest fraction of cardiac output (CO), and thus initially takes up the highest proportion of anesthetic. Comparatively less anesthetics is initially taken up by the muscle group (MG), which is commensurate with its CO fraction, and because the fat group (FG) in a healthy lean adult receives the smallest CO fraction, it initially takes up the least amount of anesthetic.

Accordingly, in surgeries of short duration, inhalational drugs are first delivered to the VRG (i.e., brain and pulmonary alveoli), thus conferring the anesthetic effect, while proportionally less of the agent, based on CO, is taken up by the FG. In this scenario, patient recovery from anesthesia will be rapid. However, as the duration of anesthesia is increased, some portion of the inhalational drugs within the VRG will pass into the adjacent tissues, particularly the fat, via intertissue diffusion. Intertissue diffusion can account for up to 30% of anesthetic uptake [17-21], and prolonged anesthesia culminating in greater deposition of the anesthetic agent in the muscle and fat groups tends to delay recovery [22, 23]. By this mechanism, upon cessation of anesthetic inhalation, the anesthetic agent, particularly if it is a more soluble agent, and including that portion of the agent acquired by intertissue diffusion, returns to the circulation, leading to an increased effect on other tissue compartments and delayed recovery [24], with increased risk of emergence agitation in patients.

The depth of anesthesia is typically reduced before the end of surgery, either by using low-flow delivery or through a gradual decrease in the concentration of the inhalant (decremental delivery). Decremental delivery is suitable for all types of volatile anesthetics, and Manuel et al. have reported respective emergence and extubation times of 5.6 and 9.4 min when the inhalational agent is decreased to 0.5 MAC at the start of wound closure and then stopped, followed by the delivery of 100% oxygen at 6 $L \cdot min^{-1}$, at the end of surgery [25].

With the low-flow technique for reducing the depth of anesthesia, the low-flow inhalation is usually initiated less than 30 min before the

Table 8. The riker sedation-agitation scale and visual analog scale

	Group L	Group D
Ex SAS	3.95 ± 0.94*	4.85 ± 0.93
Ex15 SAS	3.90 ± 0.85	3.95 ± 0.76
Ex15 VAS	1.60 ± 1.14	1.90 ± 0.97

Data expressed as means ± SD. *$P < 0.05$ vs Group D. Ex = score at extubation; Ex15 = score at 15 min after extubation. Group L: low-flow washout; Group D: decremental washout; SAS: Sedation Agitation Scale; VAS; Visual Analog Scale.

end of surgery, although some studies have even suggested that an earlier cut off of an agent supplied in closed-circuit anesthesia may lead to reduced consumption of anesthetic and shorter emergence times [26, 27].

Decremental and low-flow methods have both proven to be viable options for the washout of general anesthetics in patients of normal weight. However, during prolonged anesthesia, sevoflurane accumulation in the bulky fat depots of obese patients causes it to have washout kinetics that is comparable to those of highly soluble agents. Decremental delivery has been associated with a slightly slower recovery in this setting, but few studies have addressed the low-flow method in the same scenario.

In our study, the mean extubation time was significantly shorter after low-flow delivery (10.87 ± 2.61 min) compared with decremental delivery (16.02 ± 3.21 min; $P < 0.05$). The difference might be related to the voluminous fat depots available for storage of anesthetic in obese patients, as follows. In the group L patients, the sevoflurane release into the arterial circulation stopped after the vaporizer was removed and fresh gas flow was set at 0.5 $L \cdot min^{-1}$. Sevoflurane stored in the fat returned to the arterial circulation by step-down concentration gradients (fat-to-blood and blood-to-lung) and was continuously cleared by ventilation. Because sevoflurane was synchronously eliminated from the central nervous system, its contribution in the breathing circuit, in conjunction with release of sevoflurane stored in fat, maintained the depth of anesthesia while prolonging the washout from fat to circulation.

By contrast, in group D, the end-tidal concentration of sevoflurane was gradually reduced by normal fresh gas flow. At the same time, the sevoflurane from the vaporizer might have contributed to ongoing accumulation of sevoflurane in the fat, which affects every compartment and leads to delayed washout from fat. The actual times of sevoflurane washout from fat were not the same between groups. However, the end-tidal MAC values at the time of drain placement and at the end of surgery, as well as the length of time between drain placement and the end of surgery, were similar. During the elimination phase, patients in group D had higher concentrations of sevoflurane in the brain because of tangible physiologic impediments, i.e., alveolar-pulmonary capillary and blood-brain barriers [16]. The amount of sevoflurane stored in fat could not be measured, and the similar BIS values in both groups at the end of surgery only demonstrated similar depths of anesthesia. The higher dose of remifentanil that was necessary to maintain an adequate depth of anesthesia during the washout period in group L was indicative of the lower brain concentration of sevoflurane in those patients, and this may have contributed to the more rapid and smooth emergence from anesthesia in group L. Furthermore, the lower concentration of sevoflurane in the central nervous system after low-flow delivery aided in preventing imbalance in the clearance of sevoflurane and further contributed to the rapid and high-quality emergence in the patients in Group L.

Given the proper depth of anesthesia and steady washout of sevoflurane in group L patients, their SAS scores immediately after extubation were significantly lower (3.95 ± 0.94) than those in group D (4.85 ± 0.93; $P < 0.05$) (**Table 8**), and the incidence of agitation was also significantly lower. Anesthetic imbalances in various parts of the central nervous system can sensitize the central focus to more readily produce emergence agitation [28, 29]. When the sevoflurane was washed out by high-flow fresh gas at 6 $L \cdot min^{-1}$ over a short period of time, residual sevoflurane in the patients in group D may have contributed to inconsistent recovery times. Thus, immediately after extubation, the activity of the cerebral cortex remained inhibited, whereas the subcortical center was overexcited, and stimuli such as pain, hypoxia, or irritation caused by the urethral catheter would have much more easily led to agitation. By 15 min after extubation, the sevoflurane

was completely washed out of the brain in both groups. Therefore, the differences in SAS and VAS scores between groups at that time were not significant (**Table 8**).

The limitations of this study include not comparing the changes in end-tidal concentration of sevoflurane during the washout process, and not recording the amounts of sevoflurane consumed in both groups of patients.

In conclusion, this randomized study found that low-flow sevoflurane, with earlier cessation, led to an improved quality of anesthesia emergence and a decreased rate of emergence agitation compared to decremental delivery in obese patients undergoing laparoscopic gastric bypass surgery.

Disclosure of conflict of interest

None.

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