The effect of sevoflurane, desflurane and propofol on respiratory mechanics and integrated pulmonary index scores in laparoscopic sleeve gastrectomy

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ABSTRACT

Objectives: To compare the effects of sevoflurane, desflurane, and propofol on respiratory mechanics, and integrated pulmonary index (IPI) scores in patients undergoing laparoscopic sleeve gastrectomy.

Methods: A total of 60 patients with a body mass index of ≥40 kg/m², who underwent laparoscopic sleeve gastrectomy between September 2015 and September 2016 at Fatih Sultan Mehmet Health Application and Research Center, Istanbul, Turkey were included in this randomized prospective study. After induction, anesthesia was maintained by sevoflurane in group S, desflurane in group D, and propofol in group P. Peak inspiratory pressure (PIP), plateau pressure (Pplateau), compliance (Cdyn), respiratory resistance (Rrs), and IPI values were recorded. Mann-Whitney U, Kruskal-Wallis, Dunn’s, Friedman, and Fisher-Freeman-Halton tests were performed for statistical analysis. A p value of <0.05 was considered statistically significant.

Results: A significant increase was found in PIP in group S (T1: 25; T2: 27 cmH₂O), and group D (T1: 25; T2: 29.5 cmH₂O) during pneumoperitoneum. Dynamic compliance decreased in all groups during pneumoperitoneum. In group S, the decrease in Cdyn was also statistically significant after pneumoperitoneum (T1: 43.65; T2: 41.25 ml/cmH₂O). Comparison between the groups values of PIP, Pplateau, Cdyn, Rrs, and IPI were similar.

Conclusion: In morbidly obese patients, sevoflurane, desflurane, and propofol are similar in terms of the intraoperative respiratory mechanics, and perioperative respiratory parameters provided with IPI.

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Obesity is accepted as a serious health problem with increasing prevalence all over the world as it causes respiratory, hemodynamic and different systemic disorders. Body mass index (BMI) >35 kg/m² is classified as morbid obesity.¹ Laparoscopic sleeve gastrectomy (LSG) is a primary bariatric surgical method with increasing frequency.² Increased intraabdominal pressure during laparoscopic surgery, under general anesthesia, due to atelectasis and intrapulmonary shunt development leads to aggravation of respiratory dysfunction.³

Obesity has adverse effects on the respiratory mechanics. Patients with obesity are particularly at a high risk for postoperative pulmonary complications, such as hypoxemia, atelectasis, acute respiratory failure, prolonged ventilation, and bronchial infections, particularly after upper abdominal surgery.⁴,⁵

Total intravenous anesthesia with propofol/remifentanil, and inhalation anesthesia with sevoflurane, or desflurane combined with intravenous anesthesia with remifentanil are commonly used in patients with morbid obesity.⁶,⁷ Generally, sevoflurane and propofol can reduce respiratory resistance (Rrs), or peak inspiratory pressure (PIP), and increase dynamic compliance (Cdyn).⁸ Desflurane may cause a temporary increase in bronchial secretions, and airway resistance owing to its known irritant effect on airways, depending on the minimum alveolar concentration (MAC) value.⁹

Integrated pulmonary index (IPI) is a calculated factor based on capnography (end-tidal CO₂, respiratory rate), and pulse oximetry (pulse rate, and peripheral oxygen saturation (SpO₂) parameters. This score, which ranges from 1 (respiratory failure requiring emergency intervention) to 10 (optimal respiratory status), is considered as the sole numerical value for early recognition of respiratory failure.¹⁰ Integrated pulmonary index plays an important role in close monitoring of respiratory status.¹¹

In this study, we aimed to compare the effects of anesthesia induced by sevoflurane, desflurane, and propofol on intraoperative respiratory mechanics parameters, and perioperative IPI scores in patients undergoing LSG owing to morbid obesity.

**Methods.** This study was approved by the ethics committee of the Fatih Sultan Mehmet Training and Research Hospital, Istanbul, Turkey (no: 2015/142), and informed consent was obtained from all participants. This study involved 60 patients with morbid obesity aged between 25, and 55 years, with a BMI of ≥40 kg/m², who were in the American Society of Anesthesiology (ASA) II-III risk class, and who underwent LSG between 29 September 2015 and 20 September 2016 at the Fatih Sultan Mehmet Health Application and Research Center. This double-blind, prospective, randomized study was conducted according to Helsinki Declaration.

Prior to surgery, the study protocol was explained to the participating patients. The patients were randomly assigned to one of the 3 groups by a sealed envelope method: group S (n=20); patients receiving sevoflurane during the maintenance of anesthesia, group D (n=20); patients receiving desflurane during the maintenance of anesthesia, and group P (n=20); patients receiving total intravenous anesthesia with propofol. Randomization was conducted by an anesthesiologist not involved in data collection, and patients were not informed regarding the group they were involved.

Electrocardiography, non-invasive blood pressure values, SpO₂ values, end-tidal carbon dioxide (EtCO₂) values (Drager Infinity Delta XL* monitor-Germany), Bispectral Index for monitoring the depth of anesthesia (BIS) (Covidien*-Singapore), and IPI (Oridion Capnostream,* Needham, USA) were used for monitoring, and evaluation of changes in the respiratory status in all patients taken into the operating room. Preoperative low-molecular-weight heparin, and proton pump inhibitors were routinely administered to all patients. Sedation was achieved with midazolam in the operating room.

Anesthesia induction was performed as per our standard protocol, which involved propofol 2-2.5 mg/kg, fentanyl 1-2 µg/kg, and rocuronium 0.6 mg/kg. After adequate muscle relaxation, and a BIS value of <60 were achieved, the patients underwent orotracheal intubation with 8.0 mm endotracheal tube in men, and 7.5 mm in women. For maintenance of anesthesia, sevoflurane (Sevorane* AbbVie, Istanbul, Turkey) 2%-2.5% was used in group S, desflurane (Suprane* Baxter, Istanbul, Turkey) 5%-6% was used in group D, and propofol (Propofol 2%* Fresenius Kabi, Istanbul, Turkey) 4-12 mg/kg/hour was used in group P. In addition, remifentanil 0.05-0.5 µg/kg/min (Ultiva Glaxo Smith Kline, Istanbul, Turkey) was administered.

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to all patients. The concentrations of anesthetic agents were titrated to maintain BIS values between 40 and 60, and avoid a decrease in the mean arterial pressure to >20% from baseline.

Mechanical ventilation was achieved with a tidal volume of 8 ml/kg, positive end expiratory pressure (PEEP) of 5 cmH₂O, inspiration: expiration ratio of 1:2, administering a mixture of 50% O₂ in air with a flow rate of 3 lt/min. The respiratory rate was maintained between 12 to 14 breaths/min to achieve end-tidal carbon dioxide (EtCO2) of 35±5 mmHg. Pneumoperitoneum pressure values were recorded during surgery.

Mean arterial pressure (MAP), heart rate (HR), SpO₂, EtCO₂, and IPI score of patients were recorded before induction (T₀), after intubation (T₁), 5 minutes after pneumoperitoneum (T₂), 15 min after pneumoperitoneum (30° head-up position) (T₃), 30 min after pneumoperitoneum (30° head-up position) (T₄), 5 min after desufflation (T₅), 5 minutes after extubation (T₆), at postoperative one hour (T₇), and at postoperative 24 hours (T₈). In addition, PIP, inspiratory plateau pressure (Pplat), dynamic lung compliance (Cdyn), and airway resistance (Rrs) were recorded at T₁, T₃, T₅, T₇, and T₈ time points, and then compared among the groups. The parameters of respiratory mechanics were obtained by the Drager (Perseus A500, Lübeck, Germany) anesthesia device in all patients. During IPI monitoring, 2 lt/min nasal O₂ was given to patients during spontaneous respiration with nasal cannula of IPI monitor. During mechanical ventilation, IPI monitorization was achieved by an IPI line that is integrated into the anesthesia circuit. At the end of the surgery, to antagonize muscle relaxant, neostigmine 0.03-0.05 mg/kg, and atropine 0.01-0.02 mg/kg were administered intravenously. When the extubation criteria were fully met, patients were extubated, and taken to the post-anesthesia care unit (PACU). The duration of anesthesia was recorded. Patients were followed-up in PACU during the first postoperative hour, and patients in whom adequate analgesia (visual analogue pain scale <3), and an adequate level of consciousness (modified Aldrete score = 9) were achieved were transferred to the surgical ward. Intraoperative and postoperative data were collected by anesthesiologists that were blind to patients’ groups.

Statistical analysis. The data were examined by the Shapiro-Wilk test regardless of normal, or non-normal distribution. Non-normally distributed data were presented as medians with interquartile range, and were compared using the Mann-Whitney U, and Kruskal-Wallis tests. For measurement of IPI at different time points repeated measures ANOVA was performed. For measurements of PIP, Pplat, Cydn and Rs at different time points, percentage changes (percent change = [post value-baseline value]/baseline value) and differences were calculated according to the baseline measurement. These percentage changes and differences were compared among the groups using a Kruskal-Wallis test. Post hoc analyses were performed using the Dunn’s test. The Friedman test was used for comparing dependent variables within each group. Categorical variables were compared using Fisher-Freeman-Halton test. A p value of <0.05 was considered statistically significant. Statistical analyses were performed using Statistics Package for Social Sciences for Windows, version 23.0 (IBM Corp, Armonk, NY, USA). Sealed Envelope Ltd, 2012. Power calculator for continuous outcome non-inferiority trial (https://www.sealedenvelope.com/power/continuous-noninferior/) was used for power analysis. According to power analysis for non-inferiority trials, based on the pilot study conducted using a pooled standard deviation of PIP (4.98) and non-inferiority limit as 4, indicated that a total sample size of 60 individuals would be needed with a power of 80%, and an alpha value of 0.05 on a 2-sided test.

Results. Data of 60 patients, 20 patients in each group, were analyzed. There was no significant difference among the groups in terms of age, gender distribution, BMI, ASA, intraabdominal pressure, and duration of anesthesia (p>0.05) (Table 1).

The values of HR, MAP, SpO₂, and EtCO₂ were within normal limits, and remained stable in all groups. In group S and group D, there was a significant increase in PIP at T₃, T₅, and T₇ time points compared with that at T₀; conversely, there was a significant decrease in PIP at T₂ in group P (p<0.05). There was a significant increase in Pplat in all groups at T₃, T₅, and T₇ time points compared with that at T₀. There was no statistically significant difference among the groups in terms of PIP, and Pplat measurements at different time points (p>0.05) (Table 2).

There was a significant decrease in all groups in Cydn at T₃, T₅, and T₇ time points compared with that at T₀ (p<0.05). In group S, the decrease in Cydn at T₅ was also statistically significant. Compared with T₀, Rrs was significantly lower in all groups at T₃. There was no statistically significant difference among the groups in terms of time-dependent measurements of Cydn and Rrs (p>0.05) (Table 3).

Results for IPI scores indicated a significant main effect of time, F(5.24, 298.45)=4.275, p=0.001, but
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Table 1 - Patients' characteristics and duration of anesthesia (N=60).

| Characteristics       | Group S (n = 20) | Group D (n = 20) | Group P (n = 20) | P-value |
|-----------------------|-----------------|-----------------|-----------------|---------|
| Age                   | 39.5 (9.5)      | 45 (8.0)        | 40.5 (19.75)    | 0.458   |
| Gender (female) (%)   | 16 (80.0)       | 17 (85.0)       | 19 (95.0)       | 0.505   |
| BMI, kg/m²            | 46.5 (11.2)     | 47.95 (7.85)    | 45 (7.9)        | 0.588   |
| ASA (%)               |                 |                 |                 |         |
| II                    | 16 (80.0)       | 16 (80.0)       | 15 (75.0)       | 1.000   |
| III                   | 4 (20.0)        | 4 (20.0)        | 5 (25.0)        | 1.000   |
| IAP (mmHg)            | 14 (0.75)       | 14 (0.0)        | 14 (0.0)        | 0.998   |
| Duration of anesthesia (min) | 120 (38.75) | 125 (45.0)    | 132.5 (52.5)    | 0.639   |

Continuous variables are expressed as median (interquartile range). ASA - American Society of Anesthesiologists' classification of physical health, BMI - body mass index, IAP - intraabdominal pressure.

Table 2 - Inter- and intra-group comparison of peak inspiratory airway and inspiratory plateau pressure.

| Pressure    | Group S (n = 20) | Group D (n = 20) | Group P (n = 20) | P-value† |
|-------------|-----------------|-----------------|-----------------|---------|
| PIP (cmH₂O) |                 |                 |                 |         |
| T₁         | 25 (5.8)        | 25 (4.75)       | 26 (6.0)        | 0.511   |
| T₂         | 27 (5.8)*       | 29.5 (4.5)*     | 27.5 (4.5)      | 0.067   |
| T₃         | 28 (4.0)*       | 28.5 (5.0)*     | 27 (5.25)       | 0.075   |
| T₄         | 27 (4.8)*       | 28.0 (5.0)*     | 27.5 (2.8)      | 0.130   |
| T₅         | 26 (5.8)        | 25.5 (5.0)      | 24.5 (4.0)*     | 0.051   |
| P-value*   | <0.001          | <0.001          | <0.001          |         |
| P_plateau (cmH₂O) |                |                 |                 |         |
| T₁         | 22 (5.0)        | 21.5 (5.0)      | 21.5 (4.0)      | 0.662   |
| T₂         | 24 (5.8)*       | 25 (3.0)*       | 24.5 (3.8)*     | 0.345   |
| T₃         | 25 (3.0)*       | 25 (3.0)*       | 24 (5.0)*       | 0.167   |
| T₄         | 24 (3.8)*       | 25 (3.0)*       | 25 (2.8)*       | 0.751   |
| T₅         | 22 (4.0)        | 22 (4.5)        | 21.5 (4.8)      | 0.212   |
| P-value*   | <0.001          | <0.001          | <0.001          |         |

Variables are expressed as median (interquartile range). *Statistically significant (p<0.05) compared with T₁ value in each group. †The comparison of the groups was made on the percent change values. PIP - peak inspiratory airway pressure, P_plateau - inspiratory plateau pressure, T₁ - after intubation, T₂ - 5 minutes (min) after pneumoperitoneum (supine), T₃ - 15 min after pneumoperitoneum (30° head-up position), T₄ - 30 min after pneumoperitoneum (30° head-up position), T₅ - 5 min after desufflation.

Discussion. Based on the results of our study, we observed that inhalation anesthesia with sevoflurane, and desflurane, and intravenous anesthesia with propofol had similar effects on the Cdyn, Rrs, PIP, and P_plateau parameters measured during mechanical ventilation in patients undergoing LSG owing to morbid obesity. After pneumoperitoneum, increases in the PIP, and P_plateau values, and decreases in the Cdyn values were observed in all patients, whereas the increase in PIP values was lower in patients treated with propofol than in those treated with volatile anesthetics. In the early pneumoperitoneum period, PIP values increased significantly due to sevoflurane; however, there was a slight increase in Rrs while the patients were under desflurane, and propofol-induced anesthesia. However, no statistically significant difference was found among the groups. Based on the IPI scores obtained from all patients, we observed that the respiratory functions were within normal limits during the intraoperative, and postoperative periods with all 3 anesthetic agents, and no pathological condition requiring respiratory support (hypoxia, or hypercapnia) was encountered.

Functional residual capacity and lung compliance decreases due to anesthesia administration and supine position during general anesthesia in obese patients. Pulmonary compliance decreases due to increased intraabdominal pressure during laparoscopic surgery while peak inspiratory and plateau pressures increase. Salihoglu et al showed that PIP, and Rrs increased with
pneumoperitoneum, and a decrease was observed in Cdyn that was more prominent in patients with super-
morbid obesity. Adverse changes in respiratory mechanics become more prominent when intraabdominal pressure
exceeds 15 mm Hg. In our study, the intraabdominal pressure median values during pneumoperitoneum were
14 mm Hg in all patients, and there was no difference between intraabdominal pressures among the groups
that may have affected pulmonary functions.

In our study, we observed a decrease in Cdyn in the supine position with an increase in the intraabdominal
pressure in all patients. The decrease in Cdyn was 15% with sevoflurane, 17% with desflurane, and 14%
with propofol. Statistically, there was no significant
difference among the anesthetic agents, but we observed that the compliance values remained below
the baseline in patients treated with sevoflurane after desufflation. Anesthetic agents have different effects
on respiratory mechanics. Although PIP, and airway
resistance are expected to increase due to anesthesia,
and increased intraabdominal pressure, not much
change is observed due to bronchodilation caused by
volatile anesthetics. Volatile anesthetics, especially
sevoflurane, act directly on smooth muscles, suppress
smooth muscle contractility, indirectly inhibit the vagal
reflex circuit in the airways, and show a bronchodilator
effect. Desflurane, as is known, shows a concentration-
dependent irritating effect on airways. Airway irritation

Table 3 - Inter- and intra-group comparison of Cdyn and Rs.

| Pressure | Group S (n=20) | Group D (n=20) | Group P (n=20) | P-value1 |
|----------|----------------|----------------|----------------|----------|
| Cdyn (ml/cmH2O) |                 |                 |                |          |
| T1       | 43.65 (12.93)   | 39.75 (13.08)   | 40.55 (12.78)  | 0.542    |
| T2       | 38.3 (9.83)*    | 34.25 (5.48)*   | 33.4 (9.30)*   | 0.334    |
| T3       | 35.5 (7.15)*    | 34.65 (7.80)*   | 34 (9.43)*     | 0.875    |
| T4       | 35.15 (6.78)*   | 34.8 (5.73)*    | 33.5 (10.80)*  | 0.541    |
| T5       | 41.25 (9.58)*   | 39.45 (13.18)   | 40.7 (9.80)    | 0.087    |
| Rs (ml/cmH2O) |                |                 |                |          |
| T1       | 14 (3.75)       | 15 (8.25)       | 14.5 (6.75)    | 0.582    |
| T2       | 13.5 (3)        | 16.5 (6.75)     | 16 (7.75)      | 0.311    |
| T3       | 14 (2)          | 14 (7.00)       | 14 (5.75)      | 0.389    |
| T4       | 13 (2)          | 14 (7.57)       | 13.5 (4.00)*   | 0.300    |
| T5       | 12 (3.5)*       | 12 (3.00)*      | 12 (3.00)*     | 0.076    |

Variables are expressed as median (interquartile range). *Statistically significant (p<0.05) compared with T1 value
in each group. P>0.05. The comparison of the groups was made on the percent change values. Cdyn - dynamic lung
compliance, Rs - airway resistance, T1 - after intubation, T2 - 5 min after pneumoperitoneum (supine),
T3 - 15 min after pneumoperitoneum (30° head-up position), T4 - 30 min after pneumoperitoneum (30° head-up
position), T5 - 5 min after desufflation.

Table 4 - Descriptive statistics of integrated pulmonary index.

| IPI          | Group S (n = 20) | Group D (n = 20) | Group P (n = 20) |
|--------------|-----------------|-----------------|-----------------|
| T0           | 9.75 (0.55)     | 9.85 (0.49)     | 9.7 (0.57)      |
| T1           | 9.5 (0.61)      | 9.75 (0.44)     | 9.65 (0.59)     |
| T2           | 9.8 (0.41)      | 9.9 (0.45)      | 9.85 (0.37)     |
| T3           | 9.9 (0.31)      | 9.85 (0.49)     | 9.9 (0.31)      |
| T4           | 9.95 (0.22)     | 9.85 (0.37)     | 9.85 (0.37)     |
| T5           | 9.95 (0.22)     | 9.95 (0.22)     | 9.95 (0.22)     |
| T6           | 9.7 (0.66)      | 9.75 (0.44)     | 9.9 (0.31)      |
| T7           | 9.85 (0.37)     | 9.95 (0.22)     | 9.95 (0.22)     |
| T8           | 9.9 (0.31)      | 9.85 (0.37)     | 10 (0)          |

Descriptive statistics are presented as mean (standard deviation). IPI - integrated pulmonary index.
T0 - before induction, T1 - after intubation, T2 - 5 minutes (min) after pneumoperitoneum (supine),
T3 - 15 min after pneumoperitoneum (30° head-up position), T4 - 30 min after pneumoperitoneum
(30° head-up position), T5 - 5 min after desufflation, T6 - 5 min after extubation,
T7 - postoperative hour 1, T8 - postoperative 24 hours.
Our study differs from similar studies in terms of comparing the effects of 3 anesthetic agents on respiratory mechanics and IPI scores during the anesthesia in sleeve gastrectomy. There are certain limitations of our study. Propofol infusion was performed with traditional infusion pumps owing to our capabilities at the time of the study. We could have adjusted the propofol dose more accurately if we had used a target-controlled infusion system. Another limitation was that only the early postoperative period was examined in our study, and thus, the patients were not evaluated in terms of mobilization, and time of discharge. Another limitation of our study is the lack of evaluation of postoperative pulmonary functions of the patients with spirometric measurements. Furthermore, 60 patients were included in the study, a larger sample size might have showed a difference between the groups.

In conclusion, in morbidly obese patients who underwent laparoscopic sleeve gastrectomy, sevoflurane, desflurane and propofol had similar effects on intraoperative respiratory mechanics and it was concluded that they maintained perioperative respiratory parameters when evaluated with IPI. We believe that all 3 anesthetic agents can be safely used depending on the personal experiences of the users.

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