Systemic Oxygen Delivery during One-Lung Ventilation: Comparison between Propofol and Sevoflurane Anaesthesia in a Randomised Controlled Trial

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Abstract: Systemic oxygen delivery (DO\textsubscript{2}) is a more comprehensive marker of patient status than arterial oxygen saturation (SaO\textsubscript{2}), and DO\textsubscript{2} in the range of 330–500 mL min\textsuperscript{-1} is reportedly adequate during anaesthesia. We measured DO\textsubscript{2} during one-lung ventilation (OLV) for thoracic surgery—where the risk of pulmonary shunt is significant, and hypoxia occurs frequently—and compared sevoflurane and propofol, the two most commonly used anaesthetics in terms of DO\textsubscript{2}. Sevoflurane impairs hypoxic pulmonary vasoconstriction. Thus, our hypothesis was that propofol-based anaesthesia would show a higher DO\textsubscript{2} value than sevoflurane-based anaesthesia. This was a double-blinded randomised controlled trial conducted at a university hospital from 2017 to 2018. The study population consisted of patients scheduled for lobectomy under OLV (N = 120). Sevoflurane or propofol was titrated to a bispectral index of 40–50. Haemodynamic variables were measured during two-lung ventilation (TLV) and OLV at 15 and 45 min (OLV15 and OLV45, respectively) using oesophageal Doppler monitoring. The mean DO\textsubscript{2} (mL min\textsuperscript{-1}) was not different between the sevoflurane and propofol anaesthesia groups (TLV: 680 vs. 706; OLV15: 685 vs. 703; OLV45: 759 vs. 782, respectively). SaO\textsubscript{2} was not correlated with DO\textsubscript{2} (r = 0.09, p = 0.100). Patients with SaO\textsubscript{2} < 94% showed adequate DO\textsubscript{2} (641 ± 203 mL min\textsuperscript{-1}), and patients with high SaO\textsubscript{2} (> 97%) showed inadequate DO\textsubscript{2} (14% of measurements < 500 mL min\textsuperscript{-1}). In conclusion, DO\textsubscript{2} did not significantly differ between sevoflurane and propofol. SaO\textsubscript{2} was not correlated with DO\textsubscript{2} and was not informative regarding whether the patients were receiving an adequate oxygen supply. DO\textsubscript{2} may provide additional information on patient status, which may be especially important when patients show a low SaO\textsubscript{2}.

Keywords: Delivery of oxygen; one-lung ventilation; propofol; sevoflurane; thoracic anaesthesia

1. Introduction

The concept of systemic delivery of oxygen (DO\textsubscript{2}) is attracting increasing interest in both the context of anaesthesia [1] and the intensive care unit (ICU) [2–4]. DO\textsubscript{2} is calculated as: (haemoglobin × 1.34 × SaO\textsubscript{2} + PaO\textsubscript{2} × 0.003) × cardiac output × 10. It is, thus, a more comprehensive (and important) marker of patient status than arterial oxygen saturation (SaO\textsubscript{2}) [5], being based on haemoglobin, oxygen saturation, and cardiac output.

Normal DO\textsubscript{2} in awake, healthy, subjects is 1000 mL min\textsuperscript{-1} at rest, while O\textsubscript{2} consumption (VO\textsubscript{2}) is 250 mL min\textsuperscript{-1} [5]. A target DO\textsubscript{2} of 330 [6] or 500 mL min\textsuperscript{-1} [7,8] has been suggested for preventing tissue O\textsubscript{2} deprivation under anaesthesia.
There is a significant risk of pulmonary shunt and hypoxia during one-lung ventilation (OLV) in thoracic surgery. Sevoflurane and propofol, the two most common anaesthetics, have been compared in terms of $\text{SaO}_2$, but not in terms of $\text{DO}_2$, during OLV [9].

These anaesthetics may show different associations with $\text{DO}_2$, based on their differential effects on $\text{SaO}_2$ and cardiac output (which are the major determinants of $\text{DO}_2$). Inhalation anaesthetics, including sevoflurane, are thought to reduce hypoxic pulmonary vasoconstriction [10,11], thereby increasing the ‘shunting’ of nonoxygenated blood during OLV and, thus, causing lower $\text{SaO}_2$ [12]. Notably, lower $\text{SaO}_2$ can decrease $\text{DO}_2$. It is not clear whether sevoflurane or propofol yields a higher cardiac output [13–16]. Therefore, in the present study, we measured $\text{DO}_2$ in patients undergoing thoracic surgery with OLV and compared differences therein between sevoflurane- and propofol-based anaesthesia. We hypothesised that sevoflurane-based anaesthesia would be associated with a lower $\text{DO}_2$ than propofol-based anaesthesia. The secondary outcome was the relationship between $\text{SaO}_2$ and $\text{DO}_2$.

2. Experimental Section

This prospective, randomised study was approved by the Institutional Review Board of Samsung Medical Center, Chairperson Prof. Suk-Koo Lee, Seoul, Korea (IRB file number: SMC 2017-06-069-003, IRB approval: 2017-09-05) and registered prior to patient enrolment at the Clinical Research Information Service (KCT0002782; Principal investigator, Tae Soo Hahm; date of first submission, 20 September 2017; date of registration of first patient, 25 September 2017; https://cris.nih.go.kr/cris). Written informed consent was obtained from all participants.

2.1. Study Population

This study was performed between September 2017 and July 2018 at the Samsung Medical Center (Seoul, Korea). During the study period, a total of 144 patients were assessed for eligibility by study staff, and 139 patients were enrolled in the study.

The inclusion criteria were age $\geq 19$ years, American Society of Anaesthesiologists physical status I-III, and elective pulmonary lobectomy under open thoracotomy or video-assisted thoracoscopic surgery (VATS). Cases requiring at least 1 h of OLV were included. The exclusion criteria were forced expiratory volume in 1 s (FEV$_1$) < 40% of predicted value, cardiac ejection fraction < 50%, recent oesophageal surgery or presence of congenital or acquired oesophageal abnormalities (stricture, varices, or fistula), and haemoglobin < 10 g dL$^{-1}$. Patients who did not understand the study objectives or refused to participate were excluded. Dropout criteria included OLV < 1 h, protocol interruption for rescue ventilation (SpO$_2$ < 90%), bleeding > 400 mL, sampling/measurement error, and inotrope or vasopressor administration during measurement.

2.2. Randomisation and Blinding Procedure

Patients were randomised into sevoflurane and propofol groups by computer-generated random numbers with a fixed block size of 4 and a 1:1 ratio, and patient allocations were sealed in an opaque envelope. An attending anaesthesiologist who was not involved in the study opened the sealed envelope just before induction of anaesthesia and provided the designated anaesthetic agents according to the group assignment. Oesophageal Doppler monitoring was performed by a single designated anaesthesiologist who was not involved in the study, while vaporiser, gas monitor, and drug infusion pumps were hidden by an opaque screen. The corresponding author and co-authors collected data by retrieving blinded study logs. Attending anaesthesiologists were not blinded to the patients’ group assignment, but they were not involved in patient allocation or data analysis.

2.3. Intraoperative Management

No premedication was given before induction of anaesthesia. After the patient arrived at the operation room, electrocardiography, a non-invasive blood pressure cuff, pulse oximetry, and bispectral index (BIS) monitor (v. 4.0; Aspect Medical Systems, Natick, MA, USA) were applied.
For induction of anaesthesia, a bolus of 1.5–2.5 mg kg$^{-1}$ propofol with continuous remifentanil infusion (0.05 µg kg$^{-1}$ min$^{-1}$) was used. During surgery, anaesthesia was maintained with sevoflurane or propofol. Propofol was administered using an infusion pump in the range of 80–120 µg kg$^{-1}$ min$^{-1}$. The attending anaesthesiologist titrated sevoflurane or propofol to maintain the BIS index between 40 and 50. Remifentanil (0.05 µg kg$^{-1}$ min$^{-1}$) and rocuronium were continuously infused in both groups. Bolus administration of remifentanil (0.3 µg kg$^{-1}$) was used for intubation and during intensive surgical stimulation.

Intubation was performed using a double-lumen tube after 1.0 mg kg$^{-1}$ rocuronium bolus injection, and the position of the tube was confirmed by fibreoptic bronchoscopy. A radial arterial catheter was placed on the opposite side of surgery. After induction, the oesophageal Doppler probe (CardioQ; Deltex Medical, Irving, TX, USA) was inserted through the oropharynx into the distal oesophagus, approximately 35–50 cm from the incisors. Ringer’s solution was used as the maintenance fluid and was infused at 3–5 mL kg$^{-1}$ h$^{-1}$.

All patients received the same ventilation protocol, which was tidal volume of 6–8 mL kg$^{-1}$ predicted body weight with 5 cmH$_2$O of positive end-expiratory pressure during two-lung ventilation (TLV) under volume-controlled mode. Tidal volume decreased to 5–6 mL kg$^{-1}$ predicted body weight during OLV. The ventilation rate was adjusted to maintain end-tidal carbon dioxide at 35–40 mmHg. FIO$_2$ was maintained at 100% throughout the study period and was decreased to 50% thereafter. The operation was performed in the lateral decubitus position with the operated side up. OLV was started when the patient was turned to the lateral decubitus position in VATS or when the fascia was incised during open thoracotomy. All patients were extubated upon meeting the extubation criteria and transferred to the ICU after anaesthesia recovery at the post-anaesthetic care unit.

2.4. Measurements

Haemodynamic measurements and arterial blood gas analyses were conducted during TLV in the lateral position immediately before OLV (TLV) and at 15 and 45 min after the initiation of OLV (OLV15 and OLV45, respectively). Stable heart rate and mean arterial pressure were observed for 10 min before haemodynamic measurements without application of vasopressors/inotropes.

Doppler monitoring was performed at TLV, OLV15, and OLV45 by the designated anaesthesiologist. The oesophageal Doppler probe was manipulated with adjustment of depth and rotational position until the characteristic descending thoracic aortic waveform shape was visualised and the distinctive Doppler ‘whip crack’ sound associated with aortic blood flow was heard. The best three waveforms were stored, and the averaged values were used for determination of cardiac output.

The CardioQ and an oesophageal Doppler monitor system continuously monitored stroke volume and cardiac output without external calibration. Stroke volume was calculated as the product of the velocity-time integral, and a calibration factor was derived from a nomogram based on each patient’s age, height, and weight. DO$_2$ was calculated as: (haemoglobin × 1.34 × SaO$_2$ + PaO$_2$ × 0.003) × cardiac output × 10. Alveolar O$_2$ pressure (PAO$_2$) was calculated under the high FIO$_2$ condition as: FIO$_2$ × (P$_b$ – P$_{H2O}$) – PACO$_2$ = FIO$_2$ × (760 – 47) – PACO$_2$.

2.5. Statistical Analysis

The primary endpoint was the difference in DO$_2$ between the two anaesthetic groups. The secondary endpoint was the correlation between SaO$_2$ and DO$_2$. Power analysis showed that a difference in DO$_2$ of 150 mL min$^{-1}$ between the sevoflurane and propofol groups could be regarded as significant. The standard deviation (SD) of each anaesthetic was obtained from previous studies conducted during the induction periods (sevoflurane, 72 mL min$^{-1}$; propofol, 336 mL min$^{-1}$). Assuming a similar reduction and a 20% dropout rate, 120 patients were required for a two-sided alpha of 5% with 80% power (independent t test).

Continuous variables are presented as the mean ± SD or median (interquartile range). Categorical variables are presented as counts (%). The DO$_2$, cardiac output, PaO$_2$/FIO$_2$, alveolar arterial O$_2$, and blood lactate were compared between the two groups using the independent t test or Mann-Whitney
test depending on the data distribution. Comparisons between variables at each time point were performed using repeated-measures ANOVA. The Bonferroni correction was performed for multiple testing. The normality of the distribution of the data was evaluated with the Shapiro-Wilk test. Confidence intervals for non-normally distributed variables were calculated using the Hodges-Lehmann estimator. All $p$-values were two-sided, and $p < 0.05$ was taken to indicate statistical significance. Data were analysed using MedCalc for Windows (ver. 7.3; MedCalc Software, Mariakerke, Belgium) and SPSS software (ver. 25.0; IBM Corp., Chicago, IL, USA).

3. Results

A total of 144 patients were assessed for eligibility. Four patients refused to participate, and one surgery was cancelled; therefore, 139 patients were enrolled in the study. Six patients dropped out because of measurement error or missing data. One patient was converted to open-and-close surgery. OLV did not last 1 h in two patients. Ten patients required intervention for rescue ventilation due to hypoxia ($\text{SpO}_2 < 90\%$). There were no cases with significant intraoperative blood loss (>400 mL). No vasopressors/inotropes were administered during the haemodynamic measurement. Finally, 60 patients in each group (sevoflurane and propofol) were included in the analysis (Figure 1).

Figure 1. Flow diagram of patient selection.

In comparisons between the two anaesthesia groups, there were no differences in baseline demographic or operational characteristics (Table 1)
Table 1. Characteristics of patients between sevoflurane and propofol groups.

| Characteristics                  | Sevoflurane Group (n = 60) | Propofol Group (n = 60) |
|----------------------------------|-----------------------------|-------------------------|
| Age (year)                       | 64 (57–71)                  | 62 (55–68)              |
| Male                             | 37 (61.7)                   | 36 (60.0)               |
| Body mass index (kg/m²)          | 24 (22–26)                  | 24 (21–25)              |
| ASA physical status, 1/2/3       | 29/23/8                     | 25/28/7                 |
| Haemoglobin (g/dL)               | 13.5 (12.4–14.4)            | 13.2 (12.5–15.0)        |
| Albumin (g/dL)                   | 4.5 (4.2–4.8)               | 4.5 (4.2–4.7)           |
| History of previous lung surgery| 3 (5)                       | 2 (3)                   |
| Smoking                          | 7 (12)                      | 3 (5)                   |
| Hypertension                     | 18 (30)                     | 16 (27)                 |
| Diabetes mellitus                | 11 (18)                     | 6 (10)                  |
| Pulmonary comorbidities          |                             |                         |
| Recent respiratory infection     | 3 (5)                       | 1 (2)                   |
| History of pulmonary tuberculosis| 1 (2)                       | 2 (3)                   |
| COPD                             | 2 (3)                       | 2 (3)                   |
| Bronchiectasis                   | 0 (0)                       | 3 (5)                   |
| Cardiac disease                  | 3 (5)                       | 4 (7)                   |
| Liver disease                    | 7 (12)                      | 9 (15)                  |
| Renal disease                    | 4 (7)                       | 4 (7)                   |
| Previous chemotherapy and radiotherapy | 5 (8)                   | 4 (7)                   |
| Surgery, Open/VATS               | 12/48                       | 13/47                   |
| Ventilation site, Left/Right     | 40/20                       | 46/14                   |
| Duration of surgery (min)        | 126 (93–157)                | 124 (100–158)           |
| Anaesthesia time (min)           | 176 (142–225)               | 176 (147–202)           |
| Duration of one lung ventilation (min) | 100 (73–146)               | 101 (78–128)            |
| Intraoperative fluid amount (mL) | 900 (650–1150)              | 925 (750–1150)          |
| Intraoperative blood loss (mL)   | 100 (50–187)                | 100 (50–150)            |
| Bispectral index                 | 45 ± 3                      | 44 ± 2                  |

The data are presented as mean ± standard deviation, median (interquartile range), or number (percentage).

History of previous lung surgery included any kind of operation that invaded the pleural space. Smoking was defined as patients who kept smoking or stopped smoking within 1 month before surgery. Recent respiratory infection was defined as pulmonary infection within 1 month from surgery. Cardiac disease included any histories of angina and myocardial infarction. Renal disease was estimated with a glomerular filtration rate of <60 mL/min⁻¹ 1.73 m²⁻¹. COPD, chronic obstructive pulmonary disease; VATS, video-assisted thoracoscopic surgery.

DO₂ was not different between the sevoflurane and propofol groups (TLV: 680 vs. 706 mL/min⁻¹, respectively; OLV15: 685 vs. 703 mL/min⁻¹, respectively; OLV45: 759 vs. 782 mL/min⁻¹, respectively; all, p > 0.05) (Table 2, Figure 2) and increased with time. There was no difference in SaO₂ between the sevoflurane and propofol groups (TLV: 98.8% vs. 98.8%, respectively; OLV15: 97.7% vs. 97.8%, respectively; OLV45: 97.4% vs. 97.8%, respectively; all, p > 0.05) (Table 2).

Table 2. Major haemodynamic variables.

| Variables                | TLV   | OLV 15 | OLV 45 |
|--------------------------|-------|--------|--------|
| DO₂ (mL/min)             |       |        |        |
| Sevoflurane              | 680 ± 173 | 685 ± 209 | 759 ± 201 |
| Propofol                 | 706 ± 191 | 703 ± 208 | 782 ± 222 |
| SaO₂ (%)                 |       |        |        |
| Sevoflurane              | 98.8 ± 0.5 | 97.7 ± 2.0 | 97.4 ± 2.0 |
| Propofol                 | 98.8 ± 0.4 | 97.8 ± 1.8 | 97.8 ± 1.7 |
| Stroke volume (mL)       |       |        |        |
| Sevoflurane              | 54 ± 15 * | 61 ± 23  | 62 ± 22  |
| Propofol                 | 60 ± 14  | 63 ± 20  | 70 ± 24  |
Table 2. Cont.

| Variables                          | TLV      | OLV 15   | OLV 45   |
|------------------------------------|----------|----------|----------|
| Heart rate (per min)               |          |          |          |
| Sevoflurane                        | 70 ± 11  | 71 ± 11  | 75 ± 11  |
| Propofol                           | 68 ± 12  | 69 ± 12  | 71 ± 13  |
| Mean arterial pressure (mmHg)      |          |          |          |
| Sevoflurane                        | 85 ± 14  | 85 ± 14  | 81 ± 11  |
| Propofol                           | 87 ± 14  | 87 ± 14  | 80 ± 11  |
| Cardiac output (L/min)             |          |          |          |
| Sevoflurane                        | 3.8 ± 1.0| 4.0 ± 1.2| 4.4 ± 1.1|
| Propofol                           | 3.9 ± 1.0| 4.0 ± 1.0| 4.5 ± 1.1|
| Haemoglobin (g/dL)                 |          |          |          |
| Sevoflurane                        | 12.6 ± 1.2| 12.6 ± 1.1| 12.6 ± 1.2|
| Propofol                           | 12.7 ± 1.3| 12.7 ± 1.5| 12.6 ± 1.3|
| Alveolar-arterial O₂ difference (mmHg) |          |          |          |
| Sevoflurane                        | 181 ± 92 | 426 ± 107| 366 ± 146|
| Propofol                           | 190 ± 101| 418 ± 105| 367 ± 121|
| PaO₂/FIO₂                           |          |          |          |
| Sevoflurane                        | 483 ± 88 | 235 ± 110| 244 ± 133|
| Propofol                           | 479 ± 105| 249 ± 108| 257 ± 121|
| Plasma lactate (mmol/L)            |          |          |          |
| Sevoflurane                        | 1.39 ± 0.49| 1.40 ± 0.53 | 1.42 ± 0.48† |
| Propofol                           | 1.23 ± 0.39| 1.23 ± 0.37 | 1.21 ± 0.36 |
| Anion gap (mmol/L)                 |          |          |          |
| Sevoflurane                        | 11.4 ± 1.8| 11.1 ± 2.0| 11.1 ± 2.5|
| Propofol                           | 11.1 ± 2.0| 10.9 ± 1.9| 10.3 ± 2.8|

The data are presented as mean ± SD. *p = 0.037 and †p = 0.006, compared to the propofol group. Bonferroni correction.

**Figure 2.** DO₂ between sevoflurane and propofol in each time point. There was no difference in DO₂ between the propofol and sevoflurane groups. DO₂ increased with time. p = 0.0001 between TLV and OLV45, p = 0.0001 between OLV15 and OLV45, Bonferroni correction. TLV, two-lung ventilation; OLV15, 15 min after initiation of one-lung ventilation; OLV45, 45 min after initiation of one-lung ventilation.

Stroke volume was higher in the propofol group (TLV: 54 vs. 60 mL, p = 0.037; OLV15: 61 vs. 63 mL, p = 0.507; OLV45: 62 vs. 70 mL, p = 0.072, for sevoflurane vs. propofol, respectively, Bonferroni correction). Heart rate and cardiac output (TLV: 3.8 vs. 3.9 L min⁻¹; OLV15: 4.0 vs. 4.0 L min⁻¹; OLV45: 4.4 vs. 4.5 L min⁻¹, for sevoflurane vs. propofol, respectively) were not different between the two groups (Table 2).
The alveolar-arterial O\(_2\) difference, which reflects pulmonary shunt, was not different between the two groups (TLV: 170 vs. 179 mmHg; OLV15: 413 vs. 405 mmHg; OLV45: 390 vs. 387 mmHg, for sevoflurane vs. propofol, respectively). PaO\(_2\)/FiO\(_2\) was not different between the two groups (TLV: 483 vs. 479 mmHg; OLV15: 235 vs. 249 mmHg; OLV45: 244 vs. 257 mmHg, for sevoflurane vs. propofol, respectively).

The plasma lactate level was higher in the sevoflurane group than the propofol group (TLV: 1.39 vs. 1.23 mmol L\(^{-1}\), \(p = 0.063\); OLV15: 1.40 vs. 1.23 mmol L\(^{-1}\), \(p = 0.051\); OLV45: 1.42 vs. 1.21 mmol L\(^{-1}\), \(p = 0.006\); for sevoflurane vs. propofol, respectively, Bonferroni correction) (Table 2). DO\(_2\) was not correlated with SaO\(_2\) (\(r = 0.09, p = 0.100\), Figure 3; sevoflurane group, \(r = 0.02\); propofol group, \(r = 0.16\)).

The DO\(_2\) cut-off for the lowest 10th percentile was 478 mL min\(^{-1}\) (36 of 360 measurements), while the mean SaO\(_2\) was 97.5% for those measurements. The lowest DO\(_2\) was 255 mL min\(^{-1}\), and the SaO\(_2\) was 98.7% at that point. DO\(_2\) was well-maintained at 641 mL min\(^{-1}\) in patients with SaO\(_2\) < 94% (21 of 360 measurements) (Table 3).

### Table 3. Relationship between DO\(_2\) and SaO\(_2\).

| Categories                  | Mean DO\(_2\) (mL min\(^{-1}\)) | Mean SaO\(_2\) (%) |
|-----------------------------|---------------------------------|--------------------|
| DO\(_2\), at <lower 10th percentile | 412 ± 52                      | 97.5 ± 2.3         |
| DO\(_2\), at <500 mL min\(^{-1}\) cut-off | 435 ± 56                      | 97.6 ± 2.2         |
| DO\(_2\), at the lowest        | 255                            | 98.7               |
| DO\(_2\), at SaO\(_2\) < 94%   | 641 ± 203                      | 92.4 ± 1.1         |

The data are presented as mean ± standard deviation.

**Figure 3.** DO\(_2\) was not correlated with SaO\(_2\) (\(r = 0.09, p = 0.100\)). Lines are a regression line with 95% confidence intervals. A dot is each measurement (n = 360). TLV, two lung ventilation; OLV15, 15 min after initiation of one-lung ventilation; OLV45, 45 min after initiation of one-lung ventilation.

### 4. Discussion

In this study, we found no difference in DO\(_2\) between sevoflurane- and propofol-based anaesthesia. Furthermore, SaO\(_2\) was not correlated with, and did not reflect the level of, DO\(_2\).

Sevoflurane and propofol, the two most commonly used anaesthetics, have previously been compared in terms of SaO\(_2\), but not in terms of DO\(_2\), during OLV [9]. DO\(_2\) reflects the circulation and oxygenation status, and it is increasingly being used in critical care [4]. Our study is the first to measure DO\(_2\) during OLV and to investigate whether DO\(_2\) differs according to the anaesthetic used.
Previously, inhalation anaesthetics, including sevoflurane, were thought to reduce hypoxic pulmonary vasoconstriction [10,11], thereby increasing the ‘shunting’ of nonoxygenated blood during OLV and, thus, causing lower SaO₂ [12]. In the current study, there was no difference between the two anaesthetic groups in the alveolar-arterial O₂, which reflects pulmonary shunting. Therefore, our results are consistent with the findings of previous reports, which suggested that sevoflurane and propofol had similar effects on shunt fraction [17] and SaO₂ [9] during OLV.

Cardiac output was not different between the two groups in this study. Previous studies reported inconsistent results regarding cardiac output in association with sevoflurane and propofol [14–16,18]. One study showed that when the anaesthetic was titrated to ~1 minimum alveolar concentration (MAC) to maintain the BIS between 40 and 60, the cardiac-suppressive effect was negligible [16]. Cardiac output subsequently increased during OLV in both groups in our study. Therefore, the increase in DO₂ with time seems to be due to the increase in cardiac output over time.

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The lack of difference in DO₂ between our groups may be explained by the lack of difference in shunt amount and cardiac output between the two anaesthetics at 1 MAC and BIS 40–60.

In a normal 75 kg adult partaking in low-intensity daily activities, the amount of O₂ consumption (VO₂) is approximately 250 mL min⁻¹ [5]. During anaesthesia, VO₂ was reported to be 175 mL min⁻¹ in one study [19]. However, VO₂ varies considerably among patients, as well as over time, during anaesthesia [7,8]. In a recent meta-analysis, VO₂ was shown to decrease (by ~65 mL min⁻¹) from baseline following the induction of anaesthesia. Moreover, it increased after surgical incision and during the postoperative period [20]. Shibutani et al. [6] suggested that a DO₂ of at least 330 mL min⁻¹ is required under anaesthesia to prevent tissue O₂ deprivation. Skykes et al. [7,8] suggested that anaesthetists using low flows should aim for a DO₂ closer to 500 mL min⁻¹, which should also be the target in emergency situations. In high-risk patients undergoing major noncardiac surgery, the critical threshold for DO₂ was reported as 390 mL min⁻¹ m²⁻¹ during anaesthesia [21]. We found that DO₂ was generally maintained above 500 mL min⁻¹ during OLV (693, 694, and 770 mL min⁻¹ at TLV, OLV15, and OLV45, respectively).

There was no correlation between SaO₂ and DO₂ (r = 0.09, p = 0.100, Figure 3). DO₂ was maintained at 641 mL min⁻¹ in patients with SaO₂ < 94%. Importantly, a high SaO₂ does not guarantee that a patient is receiving adequate DO₂; 14% of our DO₂ measurements were below 500 mL min⁻¹, which was regarded as the safety cut-off in previous studies [7,8]. The mean SaO₂ was 97.6% for those measurements. The mean SaO₂ was 97.5% in the lowest 10th percentile of DO₂ (cut-off: 412 mL min⁻¹). Based on the maximum oxygen extraction ratio (70%), patients in the lowest 10th percentile of DO₂ are in the “danger zone” [5]. In our study, the SaO₂ was 98.7% at the lowest DO₂ (255 mL min⁻¹).

If accompanied by high DO₂, low SaO₂ usually arises from increased cardiac output and subsequently increased pulmonary shunt during thoracic surgery. Therefore, a low SaO₂ does not result in inadequate oxygen delivery if the cardiac output and DO₂ are well maintained [5]. Our results support the necessity of measurement of DO₂ during OLV.

In this study, the plasma lactate level was higher with sevoflurane than with propofol. The aetiology of this difference is unclear, but it may have been related to the tendency towards a lower stroke volume in the sevoflurane group than in the propofol group. Lactate is a metabolite associated with inadequate DO₂ to tissues and is, therefore, widely used as a surrogate for tissue hypoxia. DO₂ reflects haemodynamics and real-time systemic oxygen delivery. Therefore, DO₂ and lactate can be used to complement each other.

This study had several limitations. Firstly, we used oesophageal Doppler monitoring to measure cardiac output instead of the thermodilution technique. However, a pulmonary artery catheter is rarely used for thoracic surgery, while oesophageal Doppler monitoring has high validity for determining changes and trends in cardiac output and is closely correlated with pulmonary artery catheter and echocardiography data [22–24]. However, DO₂ is calculated based on cardiac output values on oesophageal Doppler monitoring, and uncertainties in the cardiac output measurements may have influenced the results. Secondly, DO₂ represents global oxygen delivery, and not tissue
oxygen delivery specifically. However, if patients do not have microcirculation or cellular oxygen uptake abnormalities, which are typically observed in severe vascular disease or sepsis, DO₂ closely reflects tissue oxygen delivery. Thirdly, we excluded patients with severe pulmonary or cardiovascular dysfunction. Haemodynamic suppression may be more severe, and pulmonary shunt may show a greater increase by anaesthesia in these patients; the effect may be different between sevoflurane and propofol. This study is the first to measure DO₂ change during OLV in relatively healthy patients. Based on our results, future studies with more seriously ill patients should be possible.

5. Conclusions

In this study, the type of anaesthetic (propofol or sevoflurane) did not have a significant impact on DO₂. Furthermore, we found no correlation between SaO₂ and DO₂. DO₂ data may provide useful additional information on patient status, especially in those with a low SaO₂ level.

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