

# Efficacy of preoxygenation with end-tidal oxygen when using different oxygen concentrations in patients undergoing general surgery: a single-center retrospective observational study

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**Background:** Preoxygenation is a simple but very important procedure for preventing arterial desaturation. A higher fraction of inspired oxygen (FiO<sub>2</sub>) increases atelectasis and 80% oxygen results in significantly less atelectasis than 100% oxygen. We investigated whether there was a difference in the duration of adequate preoxygenation when using 100% and 80% oxygen. The proportion of patients for whom >3 min was required to achieve adequate preoxygenation was also investigated.

**Methods:** The VitalDB database of patients underwent general surgery between February 1, 2021 and November 12, 2021 was reviewed. The time between the start of preoxygenation and the point where a 10% difference between  $FiO_2$  and end-tidal oxygen (EtO<sub>2</sub>) was defined as the preoxygenation time. The patients were classified into 100% and 80% groups according to the oxygen concentration. Propensity score matching (PSM) was performed to control for potential confounding factors.

**Results:** Only 330 of the 1,377 patients had sufficient data for analysis: 179 in the 80% group and 151 in the 100% group. After PSM, 143 patients in each group were analyzed. The median preoxygenation time was 143 s [interquartile range (IQR): 120.5–181.5 s] and 144 s (IQR: 109.75–186.25 s) in the 80% and 100% groups, respectively [P=0.605; median difference =–1 s; 95% confidence interval (CI): –13 to 10]. Of the patients, 27% required >3 min for adequate preoxygenation.

**Conclusions:** No difference in preoxygenation time was found between the 80% and 100% groups. For some patients, breathing for 3 min is not sufficient for adequate preoxygenation.  $EtO_2$  monitoring aids evaluation of whether preoxygenation was adequate.

Keywords: Patient safety; oxygen; resorption atelectasis; general anesthesia; retrospective study

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#### Introduction

Preoxygenation is a simple, but highly important procedure that can increase the body's oxygen reserve, to prevent arterial desaturation during apnea in the anesthesia induction period. To store oxygen efficiently in the body, tidal volume breathing with 100% oxygen for 3 min is considered the standard technique for preoxygenation (1). A high fraction of inspired oxygen (FiO<sub>2</sub>) should be delivered to patients without leakage (2). Given that end-tidal oxygen (EtO<sub>2</sub>) reflects the alveolar fraction of oxygen, EtO<sub>2</sub> can be used as an index of adequate preoxygenation, and as a means of monitoring leakage. Adequate preoxygenation is considered to have been achieved when the difference between the FiO<sub>2</sub> and EtO<sub>2</sub> fractions approaches 10% (2-5).

A higher FiO<sub>2</sub> or EtO<sub>2</sub> will lead to longer duration of apnea without desaturation (DAWD); however, it may also increase resorption atelectasis (2). Since nitrogen in air is not taken up, the alveoli are kept open by nitrogen. When the nitrogen used to splint alveoli washed out, oxygen absorption exceeds carbon dioxide (CO<sub>2</sub>) excretion, potentially accelerating resorption atelectasis; this can reduce the functional residual capacity (6), impair gas exchange, and cause respiratory dysfunction and lung injury (7). This may explain why preoxygenation using 100% oxygen precipitates more atelectasis; this would be consistent with Reber et al., who reported that preoxygenation and hyperoxygenation produced more atelectasis (8). To prevent atelectasis, the use of lower FiO<sub>2</sub> (9-11) or techniques (12) such as the alveolar recruitment maneuver (ARM) and positive end-expiratory pressure (PEEP) have been suggested (6,13).

However, because a high fraction of oxygen is essential to avoid hypoxia, questions have been raised regarding the optimal oxygen concentration (14-16). While  $\leq 80\%$  oxygen could reduce atelectasis (6,9,14), 80% oxygen does not worsen pulmonary gas exchange, or the lung volumes (17). Despite a modest shortening of DAWD (18), we thought that 80% oxygen could be an alternative to 100% oxygen, if it can enhance the efficacy of preoxygenation. Using 80% oxygen may provide many of the benefits of 100% oxygen (17), while atelectasis is much less than 100% oxygen, but comparable to 30% oxygen (9,17).

Many studies have reported on the time required for  $EtO_2$  to reach 90% when using 100% oxygen for preoxygenation (3,19-21); however, few studies have measured the time required for  $EtO_2$  to reach 70% when using 80% oxygen. For this reason, we attempted to determine if there is a difference in preoxygenation time, using  $EtO_2$  as an endpoint, between different oxygen concentrations (100% *vs.* 80%). DAWD is naturally shortened when 80% oxygen is used; thus, the occurrence of desaturation was also investigated. We also wanted to determine the proportion of patients for whom >3 min was required to achieve adequate preoxygenation. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups. com/article/view/10.21037/apm-22-647/rc).

## **Methods**

This was a single-center, retrospective, observational study conducted at a tertiary hospital in Korea. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013), and was approved by Institutional Review Board (IRB) of Soonchunhyang University Bucheon Hospital (No. 2021-11-033). The requirement for informed consent was waived due to the retrospective nature of the study and anonymity of the data. Patient-identifying data were not collected. The reporting of this study conforms to STROBE guidelines.

#### Data selection

All data in this study were obtained from medical records and the VitalDB database at our tertiary hospital. Construction of the database was approved by our IRB (IRB No. 2018-06-012) (22). The VitalDB program collects data from multiple anesthesia devices, including patient monitors, anesthesia machines, ventilators, bispectral index (BIS), and target-controlled infusion (TCI) (23). All data collected using multiple monitors are automatically recorded using the Vital Recorder tool; time-synchronized data are shown (24) in Figure S1.

From the VitalDB database, FiO<sub>2</sub>, EtO<sub>2</sub>, and capnography data were extracted. The start and end times of preoxygenation, start of anesthesia, and start and end times of intubation were also obtained. Data other than VitalDB data were obtained from anesthesia records; demographic data included age, sex, weight, height, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status, smoking status, concomitant pulmonary diseases such as chronic obstructive pulmonary disease (COPD) and asthma, Cormack-Lehane grade (25) during intubation (grade 1, most of the glottis is visible; grade 2, only the posterior extremity of the glottis is visible;



Figure 1 VitalDB database. A continuous exponential increase in end-tidal CO2, and a capnography waveform.

grade 3, no part of the glottis can be seen, but the epiglottis is visible; grade 4, neither the glottis or epiglottis can be seen), and type, site and emergency status of the operation.

Data on patients aged 17-85 years under the care of the Department of General Surgery between February 1, 2021 and November 12, 2021 were reviewed. Bhatia et al. reported that the time taken for EtO<sub>2</sub> to reach 90% when using 100% oxygen in young adults was 157±32 s (19). Assuming that a 5% difference in preoxygenation time is clinically significant, 326 patients were estimated to be needed to achieve 80% power with a two-sided significance level of 0.05 using the two-sample *t*-test. Of the patients who underwent general surgery under general anesthesia, only those with satisfactory EtO<sub>2</sub> and capnography data were included. The patients were classified into 100% and 80% groups according to the oxygen concentration used during preoxygenation. From the start to the end of preoxygenation, if a continuous exponential increase in EtO<sub>2</sub> was identified, and a capnography waveform of the patient's respiration was recorded simultaneously (Figure 1), the data were considered sufficient for analysis. Patients whose data were incomplete were excluded, including those with no or irregular EtO<sub>2</sub> and capnography data; an absent or irregular EtO<sub>2</sub> graph and EtCO<sub>2</sub> waveform before anesthesia induction (Figure S2), or no FiO<sub>2</sub> or EtO<sub>2</sub> data due to technical errors (Figure S3).

#### Preoxygenation and induction periods

All preoxygenation and anesthesia methods were performed in accordance with the protocols of our institution. We routinely used 100% oxygen during preoxygenation in the supine position. A head-up or ramped position could be used at the anesthesiologist's discretion. A tight-fitting face mask without leakage, and the use of 100% oxygen, is essential during preoxygenation, but many anesthesiologists in our institution do not perform preoxygenation properly; sometimes there is a gap between the patients' face and the face mask, resulting in leakage. This leakage in turn results in the entrainment of >20% room air, thus lowering the  $FiO_2$  and  $EtO_2$  (26,27). After a journal club session on airway management aimed at reducing atelectasis, we were reminded of the importance of using an appropriately fitting face mask without leakage, using 80% or 100% oxygen at the anesthesiologist's discretion, with a fresh gas flow rate of 6–10 L/min. We also used EtO<sub>2</sub> as an endpoint, rather than the preoxygenation time. This enabled us to collect data using different oxygen concentrations during preoxygenation.

The preoxygenation time was defined as the time between the start and end of preoxygenation. The start of preoxygenation was set as the onset of the capnography waveform (*Figure 2*). The end of preoxygenation was



Figure 2 The preoxygenation time. The preoxygenation time was defined as the time from the start (the presence of a capnography waveform) to the end (a 10% difference between fraction of inspired  $O_2$  and end-tidal  $O_2$ ) of preoxygenation.



Figure 3 The intubation time. The intubation time was defined as the time from the end of the last capnography waveform before intubation to the start of the first capnography waveform after intubation.

defined as the time when a 10% difference between FiO<sub>2</sub> and EtO<sub>2</sub> occurred (EtO<sub>2</sub> =90% and 70% for the 100% and 80% groups, respectively); a 10% difference corresponds to an alveolar nitrogen concentration of approximately 5% (4,28) and alveolar CO<sub>2</sub> proportion of 5% (4). This is considered to reflect adequate preoxygenation (5). Inadequate preoxygenation was defined as failure to achieve a 10% difference between FiO<sub>2</sub> and EtO<sub>2</sub> after a sufficient recording time, which suggests leakage.

The intubation time was defined as that from the end of the last capnography waveform during face mask ventilation to the start of the first capnography waveform after intubation (*Figure 3*). We also checked whether there was a desaturation event, defined as a peripheral oxygen saturation (SpO<sub>2</sub>) lower than 95% or 90% [reflecting "abnormal" and "significant" arterial oxygen desaturation, respectively (29-31)]. The time from the start of propofol administration to the end of intubation was defined as the total induction time.

#### Outcomes

The primary outcome was comparing the preoxygenation time between the 100% and 80% groups to evaluate the efficacy of preoxygenation. Secondary outcomes were the occurrence of a desaturation event during induction period, the ratio of inadequate preoxygenation, and a time more than 3 min to achieve adequate preoxygenation. The Cormack-Lehane grades were also compared between the two groups.

#### Statistical analysis

All continuous variables were assessed for the normality of their distribution using the Shapiro-Wilk test. Normal continuous variables were analyzed using the independent t-test and are expressed as the means  $\pm$  standard deviation (SD). Non-normal continuous variables were analyzed using the Mann-Whitney U test and are expressed as median [interquartile range (IQR)]. Categorical variables were analyzed using the chi-square test or Fisher's exact test as appropriate, and are expressed as numbers (percentages). Propensity score matching (PSM) was performed thorough a logistic regression analysis to reduce selection biasand control of potential confounding factors including age, sex, BMI, ASA physical status, smoking status, COPD, asthma, basal SpO<sub>2</sub>, abdominal surgery, elective surgery, and the Cormack-Lehane grade. After PSM, continuous variables were analyzed using Wilcoxon signed-rank test and categorical variables were analyzed using the McNemar test or McNemar-Bowker test, as appropriate. Binary logistic regression was used to identify risk factors for inadequate preoxygenation, and a difficult airway. The independent variables were age, sex, BMI, and ASA physical status. A P value <0.05 was considered to indicate statistical significance. Statistical analyzes were performed using IBM SPSS Statistics (ver. 26.0; IBM, Armonk, NY, USA).

## Results

The study reviewed 1,377 patients under the care of the Department of General Surgery between February 1, 2021 and November 12, 2021. After excluding 1,047 patients due to insufficient data (891 patients, no or an irregular  $EtO_2$  graph and capnography waveform; 156 patients, missing data due to technical errors), data from 330 patients were extracted to analyze the efficacy of preoxygenation (*Figure 4*). Of these, 179 patients were classified into the

80% group and 151 into the 100% group, according to the oxygen concentration. After PSM, 143 patients in each group (total of 286 patients) were matched.

Demographic data before and after PSM are presented in *Table 1*. Before PSM, there were no significant differences in age, sex, weight, height, BMI, the proportion of smokers, COPD, asthma, abdominal surgery and emergency surgery, or basal SpO<sub>2</sub> between the two groups. However, there was a significant difference in ASA physical status (P<0.05). After PSM, none of the demographic characteristics differed between the two groups.

After PSM, the preoxygenation time also did not differ significantly between the two groups [median difference =-1; 95% confidence interval (CI): -13 to 10; P=0.605]. There were also no differences in the overall rate of inadequate preoxygenation (12% vs. 6%, P=0.143) or the proportion of patients for whom >3 min was required for adequate preoxygenation (26% vs. 28%, P=0.118) (*Table 2*). No demographic characteristics were associated with inadequate preoxygenation.

There was only one case of significant arterial oxygen desaturation (SpO<sub>2</sub> <90%), of a 39-year-old woman (height, 155 cm; weight, 110 kg; BMI, 45.8 kg/m<sup>2</sup>; basal SpO<sub>2</sub>, 95%; current smoker, 10 pack-years) scheduled for a laparoscopic cholecystectomy. She breathed 100% oxygen until the EtO<sub>2</sub> reached >90% (preoxygenation time: 64 s). However, her SpO<sub>2</sub> fell gradually to 88% after the propofol infusion. Despite facemask ventilation, the SpO<sub>2</sub> remained at 90%. Her Cormack-Lehane grade was 4 and tracheal intubation was attempted at least twice, judging from the capnography waveform (Figure S4). The SpO<sub>2</sub> fell to 78% during the second intubation attempt, but recovered to 97% after intubation.

Despite the significant group difference in laryngeal grade (P=0.004 after PSM), the intubation time did not differ significantly between the two groups (P=0.772 after PSM). Assuming that Cormack-Lehane grades 1 and 2 represent easy intubation, and grades 3 and 4 difficult intubation (32), the rate of difficult airway was 9.1% (26 of 285 patients) after PSM. BMI [odds ratio (OR) =1.14; 95% CI: 1.04 to 1.24; P=0.004 after PSM] was identified as a risk factor for difficult airway by logistic regression.

#### **Discussion**

We found that the preoxygenation time, defined as the time taken to achieve a 10% difference between  $FIO_2$  and  $EtO_2$ , did not differ significantly between the 100% and



Figure 4 Study flow chart. Study flow chart according to the STROBE statement. STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

80% groups (median difference =-1; 95% CI: -13 to 10 after PSM). To our knowledge, no studies have compared the time taken for adequate preoxygenation using 100% and 80% oxygen, although this result may be a result of the physiological law of exponential wash-in (33). In addition, our endpoint was the time required for a 10% difference between FiO<sub>2</sub> and EtO<sub>2</sub>, not 3 min; other studies have tended to report the EtO<sub>2</sub> at 3 min after preoxygenation (4,19,34). Studies have reported the time required for EtO<sub>2</sub> to reach 90% when using 100% oxygen (3,35), but we uniquely also measured the time required for EtO<sub>2</sub> to reach 70% when using 80% oxygen. Tidal volume breathing for 3 min, considered a standard technique for preoxygenation, did not achieve adequate preoxygenation in 27% of our patients after PSM. Using 90% EtO<sub>2</sub> as the endpoint when applying 100% oxygen during preoxygenation, Machlin et al. reported that it took 154 (range, 43-364) s to achieve adequate preoxygenation (3), while Bhatia et al. reported that it took 157 (range, 54-180) s in young adults and 164

(range, 110–180) s in elderly patients (19). These values are similar to those in our study, of 152 (range, 77–356) s and 151 (range, 60–288) s after PSM for the 80% and 100% groups, respectively; however, the data were not normally distributed. In our study, the preoxygenation time was in accordance with the  $EtO_2$ , which is an objective indicator, rather than the 3 min used is routine in actual clinical practice.

Guidelines for anticipated and unanticipated difficult intubation recommend that all patients should be preoxygenated before airway manipulation (5,36-38). However, few anesthesiologists routinely perform preoxygenation (39); in fact, it is frequently neglected (40). Although the  $EtO_2$  is a ventilator parameter used in clinical practice, it is not monitored routinely (41). The importance of  $EtO_2$  has been emphasized in emergency departments, wherein rapid sequence intubation is commonly performed (42,43);  $EtO_2$  monitoring improved the quality of preoxygenation, resulting in a reduction in hypoxemic

| Table 1 Patient der                 | nographics                                 |                                     |  |                                    |                                     |   |                                |                     |
|-------------------------------------|--|-------------------------------------|--|------------------------------------|-------------------------------------|---|--------------------------------|---------------------|
|                                     |  | Before PSM                          |  |                                    |                                     | After PSM                                     |                                |                     |
| variaures                           | Total (n=330)                              | 80% group (n=179)                   | 100% group (n=151)   | P value                            | Total (n=286)                       | 80% group (n=143)                             | 100% group (n=143)             | P value             |
| Sex (male:female)                   | 143:187 (43%:57%)                          | 78:101 (44%:56%)                    | 65:86 (43%:57%)  | 0.923 <sup>†</sup>                 | 122:164 (43%:57%)                   | 62:81 (43%:57%)                               | 60:83 (42%:58%)                | 0.8991              |
| Age (years)                         | 58.5 [48, 66]                              | 59 [51, 69]                         | 58.5 [47, 65]  | 0.174 <sup>‡</sup>                 | 58 [48, 67.5]                       | 57.5 [48.8, 68]                               | 58.5 [44.5, 65]                | 0.6261              |
| Weight (kg)                         | 63.0 [56.1, 72.1]                          | 63.0 [54.7, 70.8]                   | 63.4 [57.3, 72.9]  | 0.105 <sup>‡</sup>                 | 62.7 [55.9, 71.7]                   | 62.3 [54.7, 70.1]                             | 64.0 [57.3, 73.6]              | 0.084               |
| Height (cm)                         | 160.5 [154.5, 167.0]                       | 160.0 [153.9, 165.4]                | 160.6 [155.4, 168.6]   | 0.138 <sup>‡</sup>                 | 160.4 [154.5, 166.9]                | 160.1 [153.2, 165.5]                          | 160.6 [155.4, 168.4]           | 0.175 <sup>††</sup> |
| BMI (kg/m²)                         | 24.7 [22.1, 26.7]                          | 24.9 [22.1, 26.9]                   | 24.4 [22.4, 26.6]  | 0.879 <sup>‡</sup>                 | 24.5 [21.8, 26.7]                   | 24.7 [21.6, 26.6]                             | 24.7 [22.4, 26.9]              | 0.459 <sup>††</sup> |
| ASA classification<br>(I:II:III:IV) | 97:161:71:1<br>(29%:49%:22%:0%)            | 41:95:42:1<br>(23%:53%:23%:1%)      | 56:66:29:0<br>(37%:44%:19%:0%)                                   | 0.035 <sup>§</sup>                 | 91:136:59:0<br>(32%:48%:21%:0%)     | 39:73:31:0<br>(27%:51%:22%:0%)                | 52:63:28:0<br>(36%:44%:20%:0%) | 0.122 <sup>#‡</sup> |
| Smoking<br>(none:current:ex)        | 277:35:18<br>(84%:11%:5%)                  | 153:18:8<br>(85%:10%:4%)            | 124:17:10<br>(82%:11%:7%)  | 0.632 <sup>†</sup>                 | 240:30:16<br>(84%:10%:6%)           | 121:14:8<br>(85%:10%:6%)                      | 119:16:8<br>(83%:11%:6%)       | 0.860#              |
| СОРD                                | 8 (2%)                                     | 3 (2%)                              | 5 (3%)   | 0.477 <sup>§</sup>                 | 6 (2%)                              | 3 (2%)  | 3 (2%)                         | 1.000 <sup>¶</sup>  |
| Asthma                              | 17 (5%)                                    | 12 (7%)                             | 5 (3%)   | $0.165^{\dagger}$                  | 11 (4%)                             | 6 (4%)  | 5 (3%)                         | 1.000               |
| Basal SpO $_2$                      | 97 [97, 98]                                | 97 [96, 98]                         | 97 [97, 98]  | $0.240^{\ddagger}$                 | 97 [97, 98]                         | 97.5 [99, 98]                                 | 97 [97, 98]                    | 0.396 <sup>††</sup> |
| Abdominal surgery                   | 278 (84%)                                  | 151 (84%)                           | 127 (84%)  | $0.950^{\dagger}$                  | 240 (84%)                           | 120 (84%)                                     | 120 (84%)                      | 1.0001              |
| Emergency<br>surgery                | 5 (2%)                                     | 2 (1%)                              | 3 (2%)   | 0.664 <sup>‡</sup>                 | 4 (1%)                              | 2 (1%)  | 2 (1%)                         | 1.000 <sup>¶</sup>  |
| The values are me                   | edian [1Q, 3Q] or nur<br>test DSM property | hber (%). <sup>†</sup> , Chi-square | ) test; <sup>‡</sup> , Mann-Whitne)<br>body mass indev: <u>A</u> | y U test; <sup>§</sup><br>≳∆ Ameri | <sup>8</sup> , Fisher's exact test; | 1, McNemar test; <sup>++</sup> , <sup>1</sup> | Wilcoxon signed-rank           | test; #,            |

obstructive pulmonary chronic ב 200 esiologists; ō society nerican Ā McNemar-Bowker test. PSM, propensity score matching; BMI, body mass index; ASA, disease; SpO<sub>2</sub>, peripheral oxygen saturation.

| Variables   |                                |                              | After PSM                      |                    |                   |              |
|---|--------------------------------|------------------------------|--------------------------------|--------------------|-------------------|--------------|
|   | Total (n=286)                  | 80% group (n=143)            | 100% group (n=143)             | P value            | Median difference | 95% CI       |
| Preoxygenation time (s)                             | -                              | 143 [120.5, 181.5]           | 144 [109.75, 186.25]           | $0.605^{\dagger}$  | -1                | -13 to 10    |
| Preoxygenation success/failure                      | 260:26 (91%:9%)                | 126:17 (88%:12%)             | 134:9 (94%:6%)                 | 0.143 <sup>‡</sup> | -                 | -            |
| Time for adequate preoxygenation<br>(≤3 min:>3 min) | 190:70 (73%:27%)               | 93:33 (74%:26%)              | 97:37 (72%:28%)                | 0.118 <sup>‡</sup> | -                 | -            |
| SpO <sub>2</sub> <95%                               | 3 (1%)                         | 1 (0.7%)                     | 2 (1.4%)                       | 1.000 <sup>‡</sup> | -                 | -            |
| SpO <sub>2</sub> <90%                               | 1 (0.3%)                       | 0 (0%)                       | 1 (0.7%)                       | 0.143 <sup>‡</sup> | -                 | -            |
| Minimal SpO <sub>2</sub>                            | 100 [99, 100]                  | 100 [99, 100]                | 100 [99, 100]                  | $0.136^{\dagger}$  | 0                 | –5 to 0      |
| Intubation time (s)                                 | 41 [35, 49]                    | 41 [35, 49]                  | 40 [35, 48]                    | $0.772^{\dagger}$  | 0                 | –3 to 2      |
| Cormack-Lehane grade (1:2:3:4)                      | 168:91:22:4<br>(59%:32%:8%:1%) | 96:38:8:1<br>(67%:27%:6%:1%) | 72:53:14:3<br>(50%:37%:10%:2%) | 0.004 <sup>§</sup> | -                 | -            |
| Total induction time (s)                            | 354 [323, 407]                 | 348 [325, 417]               | 365 [321, 418]                 | 0.071 <sup>†</sup> | -14.5             | –30.5 to 1.5 |

 Table 2 Induction period data

The data are the median [IQR] or number (%). <sup>†</sup>, Wilcoxon signed-rank test; <sup>‡</sup>, McNemar test; <sup>§</sup>, McNemar-Bowker test. PSM, propensity score matching; CI, confidence interval; SpO<sub>2</sub>, peripheral oxygen saturation; IQR, interquartile range.

events during intubation (44). Adequate preoxygenation confirmed by  $EtO_2$  monitoring will improve patient safety by checking for the presence of a leak and optimizing oxygen wash-in, which makes the induction of anesthesia more comfortable and relaxed.

The frequency of inadequate preoxygenation was reported to be 11.5% (23 out of 200 patients) by Machlin *et al.* (3). In our study, 9% of the patients (26 of 286) had inadequate preoxygenation after PSM. Leakage is suspected when there is either no capnography waveform or the  $EtO_2$  is lower than expected. Perhaps the rate was lower in our study because we checked only for "a failure to reach a 10% difference between FiO<sub>2</sub> and  $EtO_2$ " among patients in whom complete capnography was acquired.

Machlin *et al.* reported that, for 26% (46 of 177) of their patients, >3 min was required for adequate preoxygenation (3), while Berry *et al.* reported that this applied to 22.5% (9 of 40) of patients (4). For 27% (70 out of 260) of our patients it took >180 s after PSM to achieve adequate preoxygenation. Thus, 3-min preoxygenation is not sufficient for some patients. EtO<sub>2</sub> can be a useful indicator of whether adequate preoxygenation has been attained or whether leakage is present (41,43).

As the technique has improved, more comfortable and reliable equipment has been commercialized to improve patient safety, including a videolaryngoscope. We routinely used a videolaryngoscope during intubation, which improves intubation time in difficult airways compared with direct laryngoscopy (45-47). This may explain why there was no significant group difference in intubation time in our study, despite a significant difference in Cormack-Lehane grade. However, since the risk of difficult mask ventilation and intubation is unpredictable and we never know when we will encounter such situations, it is important to administer oxygen accurately, monitor how much oxygen is delivered, and begin the induction of anesthesia.  $EtO_2$  monitoring might be an essential element of preoxygenation and is of sufficient value for continuous monitoring and evaluation.

Since nitrogen in air is not taken up, the alveoli are kept open by nitrogen. This may explain why preoxygenation using 100% oxygen precipitates more atelectasis; this would be consistent with Reber et al., who reported that preoxygenation and hyperoxygenation produced more atelectasis (8). However, because a high fraction of oxygen is essential to avoid hypoxia, questions have been raised regarding the optimal oxygen concentration (14-16). While  $\leq 80\%$  oxygen could reduce atelectasis (6,9,14), 80% oxygen does not worsen pulmonary gas exchange, or the lung volumes (17). Despite a modest shortening of DAWD (18), we thought that 80% oxygen could be an alternative to 100% oxygen, if it can enhance the efficacy of preoxygenation. However, there was no difference in the adequate preoxygenation rate between 80% and 100% oxygen, which may be a result of the physiological law of exponential wash-in.

Although there was only one desaturation case in our

series, our sample was small, and difficult mask ventilation or intubation cannot be predicted. Many studies reduced atelectasis using 100% oxygen by applying continuous positive airway pressure (CPAP), the ARM, or PEEP (12,48-51). In addition, the median total induction time was 353.5 s (IQR: 322.75–406.5 s) after PSM. Edmark *et al.* reported DAWD values of 414±84 and 303±59 s using 100% and 80% oxygen, respectively (9). Based on those values, only 75% and <50% of the patients would be able to endure in the event of "cannot intubate, cannot oxygenate" when using 100%, and 80% oxygen, respectively. Therefore, 100% oxygen should be used during preoxygenation with CPAP, ARM and PEEP to reduce atelectasis, until a large study proves that 80% oxygen differs in safety from 100% oxygen during the induction period.

There are several limitations to our study. First, our study was retrospective, and the method of preoxygenation was not protocolized, and was adjusted at the anesthesiologist's discretion. And the period of data collection differed, so selection bias is inevitable. The choice of which oxygen concentration to be used could also affect. For those reasons, we performed PSM to reduce selection bias, but many patients were already excluded because we analyzed only those with objective data, and there was still a significant difference in Cormak-Lehane grade between the two groups. Second, there may also have been technical problems in performing preoxygenation, although they might have been insignificant because we selected only patients with sufficient data for analysis. The preoxygenation time was influenced by several factors, such as position (supine, head-up or ramped) or respiratory pattern (minute ventilation). Some patients breathed shallowly and rapidly, while others breathed deeply and slowly; hyperventilation can achieve adequate preoxygenation in a short period of time (52). Precise tidal volume breathing, through education or guidance of patients, would improve preoxygenation times. Further protocolized and randomized studies were needed to confirm our results. Third, we could not measure DAWD due to the retrospective nature of the study; DAWD measurements are not performed routinely in actual clinical practice. However, the efficiency of preoxygenation is also important when evaluating the effectiveness of preoxygenation. We are currently conducting a prospective study to evaluate the effectiveness of preoxygenation. Finally, the independent variables in the logistic regression analysis were written demographic characteristics. Baillard et al. reported that the main predictors (OR >9) of inadequate preoxygenation are the  $FiO_2$ , an ASA score of 4, and facial hair (53). In our study, these risk factors may not have been present due to the small sample size and limited number of variables. More attention should be paid to patients with these factors, as they may overlap with the risk factors for difficult mask ventilation (44,53).

## Conclusions

In conclusion, we found no difference in preoxygenation time between 100% and 80% oxygen, using  $EtO_2$  as an endpoint. Currently, preoxygenation for 3 min is considered the standard, but many patients required more than 3 min for adequate preoxygenation. Therefore, it is helpful to use  $EtO_2$  to confirm adequate preoxygenation.  $EtO_2$  monitoring would complement evaluations of preoxygenation adequacy.

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#### Footnote

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*Conflicts of Interest*: All authors have completed the ICMJE uniform disclosure form (available at https://apm. amegroups.com/article/view/10.21037/apm-22-647/coif). The authors have no conflicts of interest to declare.

*Ethical Statement*: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by IRB of Soonchunhyang University Buchoen Hospital (IRB No. 2021-11-033) and individual consent for this retrospective analysis was waived due to the retrospective nature of the

study and anonymity of the data.

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