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Original Article

Relationship of Intraoperative SpO_2 and $ETCO_2$ Values with Postoperative Hypoxemia in Elderly Patients after Non-Cardiac Surgery

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Elderly patients are at higher risk of postoperative hypoxemia due to their decreased respiratory function. The aim of this study was to investigate the relationship of intraoperative oxygen saturation (SpO_2) and end-expiratory carbon dioxide ($ETCO_2$) values with postoperative hypoxemia in elderly patients. The inclusion criteria were: 1) patients aged ≥ 75 years; 2) underwent general anesthesia in non-cardiac surgery; 3) operative time longer than two hours; and 4) admission to the intensive care unit (ICU) following surgery performed between January and December 2019. Intraoperative SpO_2 and $ETCO_2$ values were collected every minute for the first two hours during surgery. The 253 patients were divided into two groups: $SpO_2 \geq 92\%$ and $SpO_2 < 92\%$. The time-weighted averages of intraoperative SpO_2 and $ETCO_2$ were used to compare differences between the two groups. The incidence of postoperative hypoxemia was 22.5%. For similar ventilator settings, patients with postoperative hypoxemia had lower intraoperative SpO_2 and higher $ETCO_2$ values. Sex, ASA classification, and intraoperative SpO_2 were independent risk factors for postoperative hypoxemia. In conclusion, postoperative $SpO_2 < 92\%$ was a frequent occurrence (> 20%) in elderly patients who underwent major non-cardiac surgery. Postoperative hypoxemia was associated with low intraoperative SpO_2 and relatively higher $ETCO_2$.

Key words: oxygen saturation, end-expiratory carbon dioxide, postoperative hypoxemia

The number of elderly patients who undergo major surgery is increasing, despite their higher risk of postoperative complications [1]. Compared with younger patients, elderly people generally have decreased kidney function, greater vascular stiffness, and decreased lung function before surgery. These patients have chest wall stiffening and reduced alveolar surface area that reduces vital capacity, increases residual volume, decreases respiratory flow, and increases ventilatory perfusion heterogeneity, in addition to respiratory muscle weakness, reduced lung reserve, and increased sensitivity to respiratory depressants [2]. These physiological changes can cause postoperative respiratory failure that is related to increased fluid balance, surgical positioning, and metabolic demands [2].

Postoperative pulmonary complications may cause increased postoperative mortality, prolonged hospital stay, and delayed postoperative recovery [2]. The incidence of postoperative pulmonary complications is close to 5%, and one in five patients with postoperative pulmonary complications will die within 30 days of surgery [3]. Postoperative hypoxemia can also be considered a type of postoperative pulmonary complication. Respiratory arrest, which is one of the most serious complications of non-cardiac surgery [4], is usually preceded by a decrease in oxygen saturation (SpO_2), termed hypoxemia [5]. Therefore, postoperative

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hypoxemia is a serious and noteworthy complication.

During general anesthesia, SpO_2 and $ETCO_2$ are normally monitored in every patient to detect respiratory abnormalities. Several studies have suggested an association of lower intraoperative SpO_2 with postoperative pulmonary complications [6]. However, there are few reports of the relationship of intraoperative $ETCO_2$ and postoperative pulmonary complications with postoperative hypoxemia. Respiratory abnormalities should be assessed not only in terms of oxygenation, but also ventilation. Therefore, in this study, the effects of intraoperative SpO_2 and $ETCO_2$ on postoperative pulmonary complications such as postoperative hypoxemia were assessed. We hypothesized that intraoperative SpO_2 and $ETCO_2$ are related to postoperative hypoxemia in elderly patients after non-cardiac surgery.

Materials and Methods

Study design. This retrospective study was conducted at Okayama University Hospital. The aim was to investigate the relationships of intraoperative SpO_2 and $ETCO_2$ values with postoperative hypoxemia in elderly patients. Postoperative hypoxemia was defined as postoperative $SpO_2 \leq 92\%$ for 5 consecutive minutes after extubation in the intensive care unit (ICU).

Setting. The institutional review board of our institution waived the need for informed consent (No. 2302-045) with the opportunity to opt-out. Patients admitted to the ICU after surgery performed at Okayama University Hospital between 1 January and 31 December 2019 were studied.

Participants. The inclusion criteria were: 1) patient age ≥ 75 years; 2) duration of surgery longer than two h; 3) underwent general anesthesia in non-cardiac surgery; and 4) admitted to the ICU after surgery. Patients with missing data and those who underwent cardiac surgery were excluded.

Outcomes and variables. The primary outcome was postoperative hypoxemia. Intraoperative SpO_2, $ETCO_2$, fraction of inspired oxygen (F_IO2), and tidal volume (TV) values were all obtained from the electronic anesthesia records, which included the values per minute; the values were collected for two hours, starting at the beginning of surgery. The lowest SpO_2 values in the 48 h after ICU admission were obtained from the electronic recording system in the ICU, which records the patient's SpO_2 values every minute during the ICU stay. SpO_2 values were collected for 48 h only in extubated patients (*i.e.*, after extubation). If patients were already extubated, the lowest SpO_2 value from the first 48 h after ICU admission was used. If patients were extubated after ICU admission, the lowest SpO_2 value in the 48 h after extubation was used. Presurgical patient demographic information obtained from the hospital's electronic information system included age, sex, height, weight, body mass index (BMI), forced vital capacity (FVC), % vital capacity (%VC), forced expiratory volume in 1 min ($FEV_{1.0}$), forced expiratory volume in 1 min/forced vital capacity ($FEV_{1.0}\%$), and American Society of Anesthesiologists (ASA) classification. The duration of anesthesia, duration of surgery, length of ICU stay, and distribution of the surgical departments were also obtained from the electronic medical records.

Grouping. The patients were divided into two groups according to the presence or absence of postoperative hypoxemia. The postoperative hypoxemia group included patients who had postoperative hypoxemia, $SpO_2 < 92\%$, in the 48 hours after extubation during the ICU stay, and the postoperative non-hypoxemia group included those who did not. Postoperative hypoxemia was defined as $SpO_2 < 92\%$ according to the previous reports [7, 8]. The patients were also compared in terms of surgical department (thoracic surgery, gastrointestinal surgery, and hepatobiliary surgery).

Statistical analysis. Patients' demographic data and the intraoperative values are presented as mean ± standard deviation values, and these variables were analyzed using the *t*-test or chi-squared test. Multivariate logistic regression analysis was used to identify independent risk factors for postoperative hypoxemia. A p value less than 0.05 was considered significant. A line chart was used to represent the time course of intraoperative values between the two groups. The time-weighted average (TWA) was calculated as a measure of differences in intraoperative values between the groups.

Results

Patient demographics. Of the 439 eligible patients, 186 were excluded, including 107 with incomplete information, 1 who was not extubated in the ICU, 47 in whom the surgery time was < 2 h, and 31 who underwent cardiac surgery. A final total of 253 patients were included in this study (170 males and 83 females;

age range, 75-93 years) (Fig. 1), of whom 57 (22.5%) had postoperative hypoxemia. Mean patient age was 79.3 ± 3.7 years in those with postoperative hypoxemia and 79.8 ± 4.1 years in those without postoperative hypoxemia. Compared to patients without postoperative hypoxemia, those with postoperative hypoxemia were less likely to be female (12.3% vs 38.8%, $p < 0.0001$), had greater height (160.4 ± 8.1 vs 157.2 ± 9.1 cm, $p =$ 0.0174) and weight (60.0 ± 10.8 vs 55.6 ± 11.1 kg, $p =$ 0.0088), had longer duration of surgery (345.8 ± 151.4 vs 303.6 ± 133.2 min, $p = 0.0428$), duration of anesthesia (439.6 ± 168.5 vs 388.6 ± 144.6 min, $p = 0.0252$), and length of ICU stay (4.0 ± 4.3 vs 2.7 ± 1.7 days, $p = 0.0007$), and higher ASA classification ($p = 0.002$) (Table 1). Table 2 shows the distribution of patients according to surgical department. Of the 253 patients, 100 (35.2%) underwent thoracic surgery, 60 (21.2%) underwent gastrointestinal surgery, and 41 (16.2%) underwent hepatobiliary surgery.

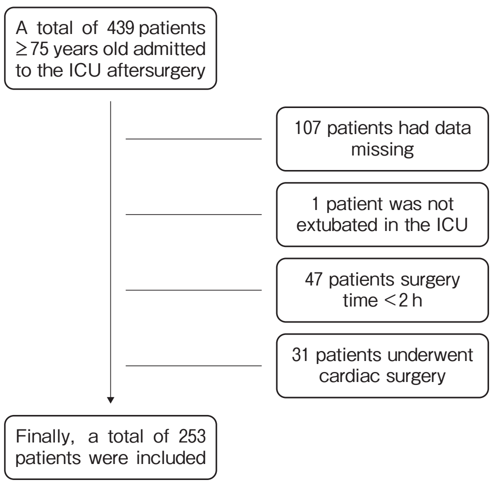

Fig. 1 Flow Chart of patient selection.

Relationship between intraoperative values and postoperative hypoxemia in all patients. Significant differences in intraoperative SpO_2 and $ETCO_2$ were found between the postoperative and non-postoperative hypoxemia groups. Intraoperative SpO_2 was continuously lower (Fig. 2A) and intraoperative $ETCO_2$ was continuously higher (Fig. 2B) in the postoperative hypoxemia group compared with the postoperative non-hypoxemia group. The TWA of SpO_2 in the postoperative hypoxemia group was lower than that in the postoperative non-hypoxemia group (96.9 ± 2.3% vs 98.1 ± 2.2%; $p = 0.0004$). The TWA of $ETCO_2$ was higher in the postoperative hypoxemia group than in the postoperative non-hypoxemia group (39.9 ± 8.7 vs

Table 1 The characteristics of patients

Variables	Postoperative hypoxemia group (N = 57)	Non- postoperative hypoxemia group (N = 196)	*P*-Value
Age	79.28 ± 3.67	79.78 ± 4.12	0.4141
Gender (female%)	7 (12.28%)	76 (38.78%)	< 0.0001
Height (cm)	160.43 ± 8.13	157.23 ± 9.11	0.0174
Weight (kg)	60.03 ± 10.78	55.64 ± 11.13	0.0088
BMI	23.20 ± 3.40	22.34 ± 3.44	0.1001
FVC	2.67 ± 0.60	2.57 ± 0.73	0.3685
%VC	87.53 ± 14.76	91.79 ± 19.20	0.1230
FEV	1.91 ± 0.46	1.92 ± 0.54	0.9398
FEV%	72.47 ± 12.31	75.27 ± 9.92	0.0791
Duration of surgery (min)	345.75 ± 151.38	303.62 ± 133.24	0.0428
Duration of anesthesia (min)	439.56 ± 168.45	388.64 ± 144.64	0.0252
Length of ICU stay	3.96 ± 4.27	2.66 ± 1.71	0.0007
ASA			0.002
1	0 (0%)	14 (7.14%)	
2	30 (52.6%)	112 (57.14%)	
2E	1 (1.8%)	1 (0.51%)	
3	22 (38.6%)	68 (34.7%)	
3E	0 (0%)	1 (0.51%)	
4	4 (7.0%)	0 (0%)	

Data are presented as the mean ± standard deviation or as the number (%). BMI, body mass index; FVC, forced vital capacity; %VC, % vital capacity; $FEV_{1.0}$, forced expiratory volume in 1 min; $FEV_{1.0}$%, forced expiratory volume in 1 min / forced vital capacity; ICU, intensive care unit; ASA, American Society of Anesthesiologists.

Table 2 The distribution of patients in every department

Department	Total (N = 253)	Postoperative hypoxemia group (N = 57)	Non- postoperative hypoxemia group (N = 196)
Thoracic Surgery	100 (39.5%)	24 (42.1%)	76 (38.8%)
Gastrointestinal Surgery	60 (23.7%)	19 (33.3%)	41 (21%)
Hepatobiliary Surgery	41 (16.2%)	6 (10.5%)	35 (17.8%)
Neurosurgery	19 (7.5%)	4 (7.1%)	15 (7.7%)
Otorhinolaryngology	13 (5.1%)	2 (3.5%)	11 (5.6%)
Plastic Surgery	8 (3.2%)	0	8 (4%)
Urology	5 (2.0%)	0	5 (2.6%)
Oral Surgery	4 (1.6%)	2 (3.5%)	2 (1.0%)
Breast Endocrine Surgery	1 (0.4%)	0	1 (0.5%)
Orthopedics	2 (0.8%)	0	2 (1.0%)

Data are presented as the number (%).

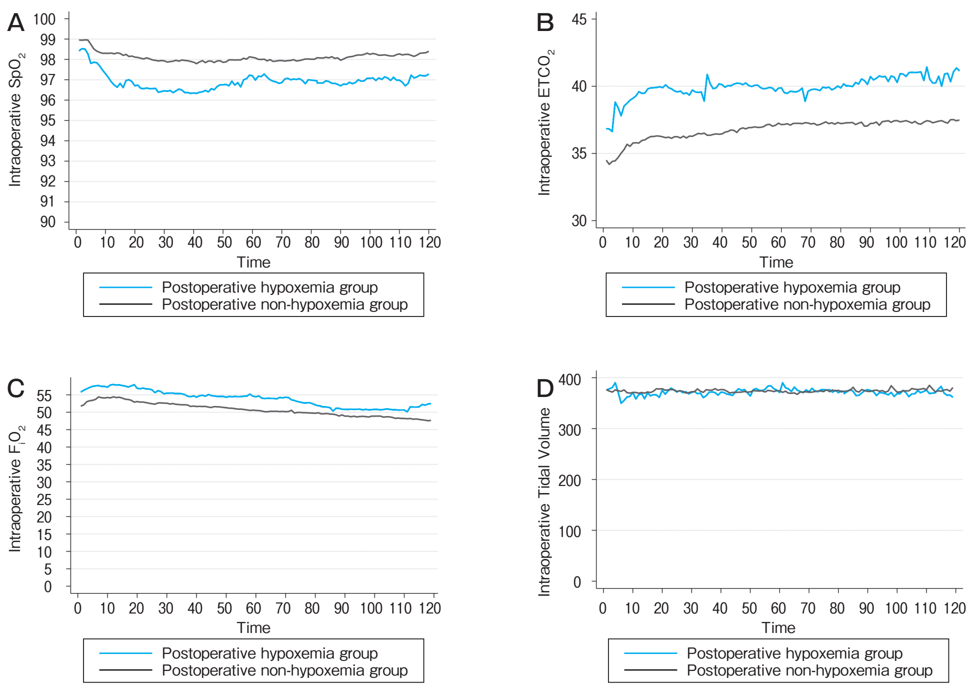

Fig. 2 Intraoperative values in all patients. **A**, Intraoperative SpO_2. *Blue line*: postoperative hypoxemia group (n = 57). *Gray line*: postoperative non-hypoxemia group (n = 156); **B**, Intraoperative $ETCO_2$. *Blue line*: postoperative hypoxemia group (n = 57). *Gray line*: postoperative non-hypoxemia group (n = 156); **C**, Intraoperative F_IO_2. *Blue line*: postoperative hypoxemia group (n = 57). *Gray line*: postoperative non-hypoxemia group (n = 156); **D**, Intraoperative tidal volume. *Blue line*: postoperative hypoxemia group (n = 57). *Gray line*: postoperative non-hypoxemia group (n = 157).

36.8 ± 4.4 mmHg; $p = 0.0003$) (Table 3). There was no difference between the two groups in terms of intraoperative F_IO_2 (Fig. 2C) or intraoperative TV (Fig. 2D). Multivariate logistic regression analysis identified sex, ASA classification, and intraoperative SpO_2 as independent risk factors for postoperative hypoxemia in all patients (Table 4).

Relationship between intraoperative values and postoperative hypoxemia in three surgical subgroups. Subgroup analysis according to surgical department (thoracic, hepatobiliary, and gastrointestinal surgery) showed no significant difference in intraoperative F_IO_2 or TV among the subgroups. In the thoracic surgery subgroup, intraoperative $ETCO_2$ was higher in patients with

Table 3 The Time Weighted Average of intraoperative values

	Postoperative hypoxemia group (N=57)	Non- postoperative hypoxemia group (N=196)	*P*-value
Intraoperative SpO_2			
All patients	96.92±2.28	98.12±2.22	0.0004
Thoracic surgery	95.70±2.40	96.85±2.67	0.0622
Gastrointestinal surgery	97.60±1.63	98.23±2.23	0.2859
Hepatobiliary surgery	98.16±1.51	99.50±0.60	0.0004
Intraoperative $ETCO_2$			
All patients	39.92±8.65	36.76±4.44	0.0003
Thoracic surgery	41.75±12.24	36.24±4.10	0.0011
Gastrointestinal surgery	39.67±4.57	40.58±6.06	0.5659
Hepatobiliary surgery	37.52±3.45	35.44±2.26	0.0609
Intraoperative F_iO_2			
All patients	53.90±20.42	50.80±17.50	0.2574
Thoracic surgery	66.03±19.67	64.91±14.62	0.7663
Gastrointestinal surgery	49.25±19.47	47.24±16.53	0.6803
Hepatobiliary surgery	36.68±7.77	35.56±2.86	0.5149
Intraoperative TV			
All patients	371.41±74.90	374.02±68.38	0.8501
Thoracic surgery	344.05±72.37	344.05±72.37	0.3795
Gastrointestinal surgery	391±67.58	380.59±67.93	0.5851
Hepatobiliary surgery	428.68±60.27	409.58±54.87	0.4426

Data are presented as the mean±standard deviation. SpO_2, oxygen saturation; $ETCO_2$, end-expiratory carbon dioxide; F_iO_2, fraction of inspiration oxygen; TV, tidal volume.

Table 4 Multivariate Logistic Regression Analyses for postoperative hypoxemia patients

Variables	OR	95%CI	*P*-value
Gender (female)	0.654	0.476–0.898	0.009
Duration of surgery	1.000	0.999–1.000	0.219
ASA	1.126	1.009–1.255	0.033
Intraoperative SpO_2	0.999	0.998–1.000	0.010
Intraoperative $ETCO_2$	1.000	0.999–1.002	0.058

ASA, American Society of Anesthesiologists; SpO_2, oxygen saturation; $ETCO_2$, end-expiratory carbon dioxide; OR, odds radio; CI, confidence interval.

postoperative hypoxemia than in those without postoperative hypoxemia (Fig. 3A). In the hepatobiliary surgery subgroup, intraoperative SpO_2 was lower in patients with postoperative hypoxemia than in those without postoperative hypoxemia (Fig. 4C). In the gastrointestinal surgery subgroup, there was no difference in intraoperative SpO_2 or $ETCO_2$ according to the presence or absence of postoperative hypoxemia (Figs. 3B, 4B).

Discussion

In this retrospective study that assessed the relationship of intraoperative SpO_2 and $ETCO_2$ values with postoperative hypoxemia in patients aged ≥75 years, the incidence of postoperative hypoxemia was 22.5% (57/253 patients). Male sex, greater height and weight, longer duration of surgery, and higher ASA classification were identified as risk factors for postoperative hypoxemia. Although the ventilator settings were similar between the groups, patients with postoperative hypoxemia had lower intraoperative SpO_2 and higher $ETCO_2$ values than patients who did not have postoperative hypoxemia. In the subgroup analysis, intraoperative $ETCO_2$ values were higher in the respiratory surgery subgroup, and intraoperative SpO_2 values were lower in the hepatobiliary surgery subgroup in patients who had postoperative hypoxemia. The present results suggest that lower intraoperative SpO_2 and relatively higher $ETCO_2$ levels can cause postoperative hypoxemia, and that postoperative hypoxemia is affected by patients' demographic, clinical, and surgical characteristics.

Previous studies have reported postoperative pulmonary complications in 0.3-5% of younger patients after non-cardiac surgery [3, 9]. However, it has been reported that, even in patients with a median (IQR) age of 50 (43, 63) years, the incidence of postoperative

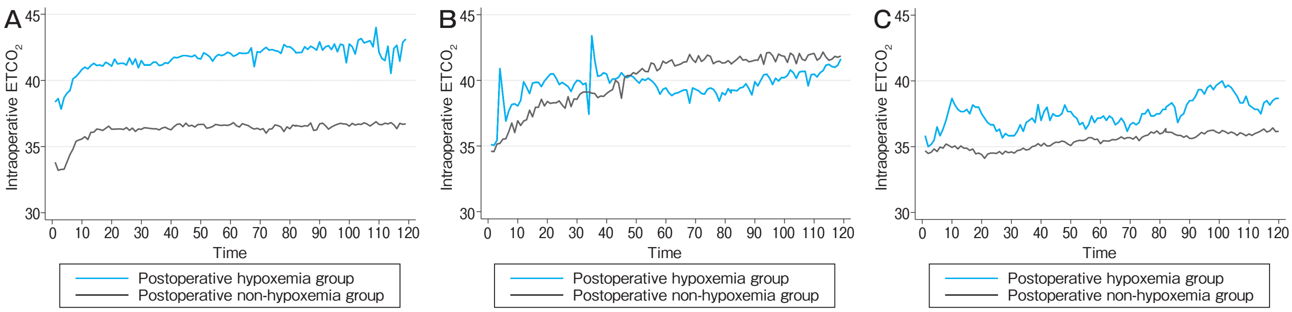

Fig. 3 Intraoperative $ETCO_2$ in the three subgroups. A, Respiratory surgery group. *Blue line*: postoperative hypoxemia group (n=24). *Gray line*: postoperative non-hypoxemia group (n=76); B, Digestive surgery group. *Blue line*: postoperative hypoxemia group (n=19). *Gray line*: postoperative non-hypoxemia group (n=41); C, Hepatobiliary surgery group. *Blue line*: postoperative hypoxemia group (n=6). *Gray line*: postoperative non-hypoxemia group (n=35).

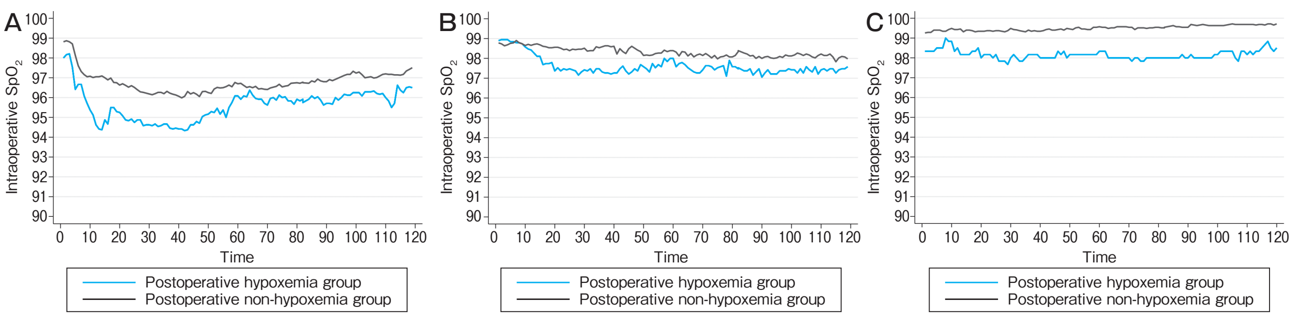

Fig. 4 Intraoperative SpO_2 in the three subgroups. A, Respiratory surgery group. *Blue line*: postoperative hypoxemia group (n=24). *Gray line*: postoperative non-hypoxemia group (n=76); B, Digestive surgery group. *Blue line*: postoperative hypoxemia group (n=19). *Gray line*: postoperative non-hypoxemia group (n=41); C, Hepatobiliary surgery group. *Blue line*: postoperative hypoxemia group (n=6). *Gray line*: postoperative non-hypoxemia group (n=35).

hypoxemia was around 20%. [10]. Another study reported that the incidence of postoperative hypoxemia was 30.2% in elderly patients with femoral neck fractures (age range, 65-104 years; average age, 79 years) [1]. Of 399 extreme elderly patients (mean age, 84.9 years) who underwent spinal anesthesia for femoral fracture surgery, 50 (12.5%) had postoperative desaturation [11]. The results of these studies suggest that the incidence of postoperative hypoxemia in the present elderly patients was similar to that in younger populations and in previous reports of elderly patients.

The present patients with postoperative hypoxemia had lower intraoperative SpO_2 and higher $ETCO_2$ values compared to those without postoperative hypoxemia. To the best of our knowledge, no study has reported similar results; however, several previous studies have suggested that pre-operative and intra-operative hypoxemia might be risk factors for postoperative hypoxemia and/or pulmonary complications [3,10,12,13]. Interestingly, no studies have examined the relationship between intraoperative $ETCO_2$ and postoperative hypoxemia and/or pulmonary complications. The present results suggest associations of intraoperative lower SpO_2 and relatively higher $ETCO_2$ with postoperative hypoxemia.

A previous study showed that the surgical site has an impact on postoperative pulmonary complications, and that upper abdominal surgery and intrathoracic surgery are independent risk factors for postoperative pulmonary complications [14]. In the present study, 100 patients (39.5%) underwent thoracic surgery, 60 patients (23.7%) underwent gastrointestinal surgery, and 41 patients (16.2%) underwent hepatobiliary surgery, and the incidence of postoperative hypoxemia in each subgroup was 24% (24/100), 31.7% (19/60), and 14.6% (6/41), respectively. It is important to note that the type of intraoperative ventilation required varies according to operation type. All thoracic surgeries required one-lung ventilation during surgery, and 18 of the 60 gastrointestinal surgery patients underwent esophagectomy and also required one-lung ventilation. If we compare the one-lung ventilation patients with non-one-lung ventilation patients, the incidence of postoperative hypoxemia was 26.3% vs 21.6%, respectively ($p = 0.0307$). We believe that not only the type of surgery, but also the type of ventilation during surgery has an impact on the incidence of postoperative hypoxemia.

Limitations. The present study has several limitations. First, since the present study was retrospective in design, only the relationship of intraoperative SpO_2 and $ETCO_2$ values with postoperative hypoxemia can be discussed. Further studies will be required to investigate causality. Second, only patients who were admitted to the ICU after surgery were included. Therefore, the generalizability of the present findings is limited to this population. Third, all types of surgery except cardiac surgery were included, and due to the variation in types, it was difficult to control for several confounding factors, including ventilator settings. Fourth, the relationships of intraoperative SpO_2 and $ETCO_2$ values with postoperative hypoxemia were explored, but postoperative pulmonary complications were not explored. Because of the retrospective nature of the present study, it was not easy to define the postoperative pulmonary complications of patients. Fifth, $ETCO_2$, not $PaCO_2$, was analyzed. $ETCO_2$ is often discrepant with $PaCO_2$, especially in the low respiratory function setting, including elderly patients. Thus, the abnormal $PaCO_2$ patients were missed. However, $ETCO_2$ is continuous and easy to measure in almost all patients. This advantage would be useful to manage ventilator setting, especially during surgery. Sixth, detailed information on the timing of intubation was not available. This could have affected the results, but only the lowest SpO_2 values in the 48 hours after postoperative extubation could be collected. Seventh, SpO_2 was used instead of PaO2 or the P/F ratio, which would be better parameters of oxygenation. However, it is difficult to obtain continuous values of PaO2, and especially in the postoperative period, it is also difficult to determine the exact F_IO_2 in extubated patients. In our view, SpO_2 can be a surrogate, continuous marker of hypoxemia in this situation. Finally, patients' long-term survival was not explored. Further studies will be required to examine this topic.

In conclusion, in patients aged over 75 years, the incidence of postoperative hypoxemia was 22.5% (57/253). Lower intraoperative SpO_2 and relatively higher $ETCO_2$ values were associated with postoperative hypoxemia in the ICU. Postoperative hypoxemia is affected by respiratory management during surgery, as well as the type of surgery.

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