Current Ventilator and Oxygen Management during General Anesthesia

A Multicenter, Cross-sectional Observational Study

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ABSTRACT

Background: Intraoperative oxygen management is poorly understood. It was hypothesized that potentially preventable hyperoxemia and substantial oxygen exposure would be common during general anesthesia.

Methods: A multicenter, cross-sectional study was conducted to describe current ventilator management, particularly oxygen management, during general anesthesia in Japan. All adult patients (16 yr old or older) who received general anesthesia over 5 consecutive days in 2015 at 43 participating hospitals were identified. Ventilator settings and vital signs were collected 1 h after the induction of general anesthesia. We determined the prevalence of potentially preventable hyperoxemia (oxygen saturation measured by pulse oximetry of more than 98%, despite fractional inspired oxygen tension of more than 0.21) and the risk factors for potentially substantial oxygen exposure (fractional inspired oxygen tension of more than 0.5, despite oxygen saturation measured by pulse oximetry of more than 92%).

Results: A total of 1,786 patients were found eligible, and 1,498 completed the study. Fractional inspired oxygen tension was between 0.31 and 0.6 in 1,385 patients (92%), whereas it was less than or equal to 0.3 in very few patients (1%). Most patients (83%) were exposed to potentially preventable hyperoxemia, and 32% had potentially substantial oxygen exposure. In multivariable analysis, old age, emergency surgery, and one-lung ventilation were independently associated with increased potentially substantial oxygen exposure, whereas use of volume control ventilation and high positive end-expiratory pressure levels were associated with decreased potentially substantial oxygen exposure. One-lung ventilation was particularly a strong risk factor for potentially substantial oxygen exposure (adjusted odds ratio, 13.35; 95% CI, 7.24 to 24.60).

Conclusions: Potentially preventable hyperoxemia and substantial oxygen exposure are common during general anesthesia, especially during one-lung ventilation. Future research should explore the safety and feasibility of a more conservative approach for intraoperative oxygen therapy. **(ANESTHESIOLOGY 2018; 129:67-76)**

POSTOPERATIVE pulmonary complications are common and affect morbidity and mortality in patients undergoing major surgery.[1] Intraoperative ventilation strategies for lung protection include low tidal volume, positive end-expiratory pressure (PEEP), and recruitment maneuvers. These strategies appear to improve clinical outcomes in patients undergoing major abdominal surgery.[2] However, the strategies do not consider supplemental oxygen, which is an essential component of ventilator management.

Supplemental oxygen administration during mechanical ventilation is important for preventing or correcting hypoxemia, both in the intensive care unit and in the operation theater. Several observational studies of intensive care unit patients receiving mechanical ventilation found that conventional oxygen therapy was liberally administered, and this could potentially induce hyperoxemia,[3–6] which

What We Already Know about This Topic

- Despite the potentially harmful effects of oxygen overexposure, supplemental oxygen therapy is commonly prescribed in several clinical conditions. However, little is known about current oxygen administration practices during general anesthesia.

What This Article Tells Us That Is New

- In this multicenter, cross-sectional study of 1,498 patients at 43 hospitals, potentially preventable hyperoxemia and substantial oxygen exposure were common during general anesthesia, especially in patients receiving one-lung ventilation.

is a potentially injurious condition. High oxygen levels can enhance reactive oxygen species formation and oxidative stress, induce peripheral vasoconstriction, and decrease cardiac output.[7,8] Moreover, adverse clinical outcomes

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associated with supplemental oxygen administration and hyperoxemia have been reported in patients with acute exacerbation of chronic obstructive pulmonary disease,[9] ST-segment elevation myocardial infarction,[10] cardiac arrest,[11] or critical illness.[12] Recent clinical trials have applied a more conservative approach to oxygen therapy, and its safety and efficacy have been confirmed in critically ill patients receiving mechanical ventilation.[13–16] Concerns were also raised during the perioperative period, and high fractional inspired oxygen tension (F_{IO_2}) was found to be associated with increased respiratory complications and mortality.[17,18] The latest British Thoracic Society guidelines recommend a target oxygen saturation measured by pulse oximetry (Sp_{O_2}) of 94 to 98% in most surgical patients to avoid potential harm from hypoxemia and hyperoxemia.[19]

Despite these concerns, limited information is available on current oxygen administration practices during general anesthesia. We hypothesized that hyperoxemia would be common in routine ventilatory management during general anesthesia and that surgical adult patients might be exposed to substantial oxygen intraoperatively. Thus, this study examined procedures for ventilator management, especially oxygen management, and assessed the incidence of potentially preventable hyperoxemia (defined as a Sp_{O_2} level of more than 98%, despite a corresponding F_{IO_2} level of more than 0.21) and potentially substantial oxygen exposure (defined as a F_{IO_2} level of more than 0.5, despite a corresponding Sp_{O_2} level of more than 92%) during general anesthesia in a convenience sample of anesthetics drawn from a convenience sample of hospitals in Japan. The study also aimed to determine the predictive factors of potentially substantial oxygen exposure.

Materials and Methods

Study Design

We conducted a multicenter, cross-sectional study at 43 hospitals in Japan from September 14 to 18, 2015, or from November 9 to 13, 2015 (participating hospitals selected the study window that was convenient). The ethics committees of the participating institutions approved the study, and informed consent was waived because noninvasive procedures were applied to the study patients only for research purposes. This study was endorsed by the Okayama Research Investigation Organizing Network (ORION) and was prospectively registered in the University Hospital Medical Information Network Clinical Trial Registry (UMIN000018884). Participating centers were recruited from hospitals related to the Okayama Research Investigation Organizing Network and/or hospitals affiliated to Okayama University of Medical Sciences by open invitation through periodic meetings and/or individual contact.

All adult patients (16 yr of age or older) who underwent general anesthesia during the study period were eligible. Patients were excluded if the surgery was completed within 1 h; if they were spontaneously breathing, undergoing cardiopulmonary bypass or extracorporeal membrane oxygenation 1 h after induction of general anesthesia, or if they declined to participate.

Data Collection

Using a case report form, the attending anesthesiologist collected patient, surgical, and anesthesia data. Ventilator settings and vital signs were obtained 1 h after the induction of general anesthesia. Variables included ventilator mode, tidal volume corrected for predicted body weight, peak inspiratory pressure, F_{IO_2}, PEEP, and corresponding Sp_{O_2} and end-tidal carbon dioxide (ET_{CO_2}). Predicted body weight was calculated as $50 + 2.3$ [height (cm)/2.54 − 60] for men and $45.5 + 2.3$ [height (cm)/2.54 − 60] for women.[20]

Outcomes of Interest

The outcomes of interest were the incidences of potentially preventable hyperoxemia and potentially substantial oxygen exposure. Potentially preventable hyperoxemia was defined as Sp_{O_2} greater than 98% with a corresponding F_{IO_2} greater than 0.21 according to British Thoracic Society guidelines[21] and recommendations[22] for a target Sp_{O_2} of 94 to 98% in most acutely ill patients. Potentially substantial oxygen exposure was defined as F_{IO_2} greater than 0.5 with a corresponding Sp_{O_2} greater than 92%, according to an earlier study in critically ill patients.[5]

Statistical Analysis

The estimated sample size was 1,000 according to the mean number of adult surgical patients under general anesthesia per week at each participating hospital. Categorical variables were compared using the chi-square test or Fisher exact test where indicated and were reported as n (%). Continuous, normally distributed variables were compared using the independent t test and were reported as mean (SD). Non-normally distributed data were compared using the Wilcoxon rank-sum test and reported as median (interquartile range). A multivariable logistic regression analysis was performed to estimate the odds ratio of potentially substantial oxygen exposure, controlling for *a priori* selected potential risk factors, including age, sex, weight, American Society of Anesthesiologists (ASA) physical status, emergency surgery, one-lung ventilation, ventilator mode, and PEEP level, using the forced entry method. Age, weight, and PEEP level were assessed in the regression model as continuous variables, whereas ASA physical status was assessed as a five-level categorical variable, and the other variables were quantified as dichotomous variables. Nonlinearity of continuous variables was assessed by introducing nonlinear restricted cubic splines in the regression model, and variables with a P value of less than 0.2 were considered as nonlinear; otherwise the nonlinear effect was refitted as a linear effect in the final regression model. Because patient outcomes in a single center may be similar when compared with outcomes among different

centers, data clusters may exist. To account for center data clustering, we employed Huber–White sandwich estimators for the variance-covariance matrix. A bootstrap internal validation method was used to assess the reproducibility of the regression model, which provides the area under the receiver operating characteristic curve for the assessment of the model fitness. Collinearity was assessed by calculating the variance inflation factor. A two-sided P value of less than 0.05 was considered statistically significant. The data were analyzed using the rms package for R (R Foundation for Statistical Computing, version 2.13.0).

Subgroup Analysis

A *post hoc* subgroup analysis was conducted to assess whether the patterns of association were influenced by the preoperative respiratory function of the patients. We identified patients who had preoperative spirometry data available (forced expiratory volume in 1 s and forced vital capacity) and divided them into the following two subgroups: those with an airway obstructive pattern (ratio of forced expiratory volume in 1 s to forced vital capacity of less than 70%) and those with a normal pattern (ratio of forced expiratory volume in 1 s to forced vital capacity of 70% or higher). All above analyses were repeated in each subgroup.

Data Validation Analysis

Because data were collected at one point, we performed a *post hoc* data validation analysis to determine the certainty of our results. We retrospectively reviewed electronic anesthesia records at one of the participating hospitals where a total of 98 patients were enrolled and investigated current oxygen management during general anesthesia using all available information on F_{IO_2} and Sp_{O_2} (measured electronically and recorded at 1-min intervals throughout the operative period).

Results

Study Population

During the study period, we screened 2,075 patients who underwent surgery under general anesthesia, and 1,786 patients were found to be eligible. Of these patients, 1,610 were enrolled, and 1,498 completed the study (fig. 1). Details of the participating hospitals are shown in Supplemental Digital Content 1 (http://links.lww.com/ALN/B673). Approximately half of the eligible patients were female (49%), with a median age of 65 yr (interquartile range, 48 to 74; table 1). Most patients (85%) had an ASA physical status of I or II. Most received inhalation anesthesia (79%), and tracheal intubation was the most frequent method of airway management (90%). Physiologic parameters and ventilator settings 1 h after the induction of general anesthesia are presented in table 2. The patients had a median Sp_{O_2} of 100% (interquartile range, 99 to 100) and ET_{CO_2} of 35 mmHg (interquartile range, 32 to 37) 1 h
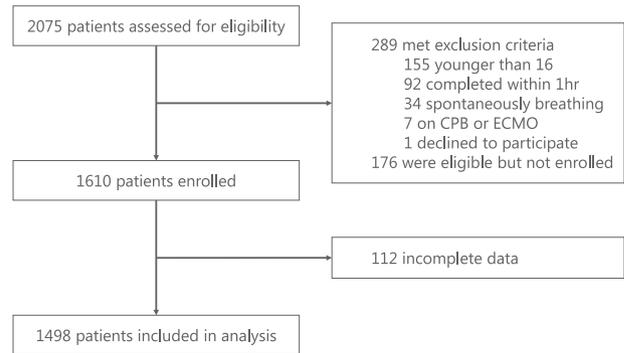

Fig. 1. Patient recruitment flow chart. CPB = cardiopulmonary bypass; ECMO = extracorporeal membrane oxygenation.

after induction of general anesthesia. Volume control mode (52%) and pressure control mode (48%) were nearly equally applied. The median F_{IO_2} was 0.47 (interquartile range, 0.4 to 0.6). F_{IO_2} of between 0.31 and 0.6 was noted in 1,385 patients (92%), whereas F_{IO_2} of 0.3 or less was noted in very few patients (1%). The median tidal volume was 8.2 ml/kg predicted body weight (interquartile range, 7.3 to 9.2). PEEP was applied in 956 patients (64%) at a median level of 4 cm H_2O (interquartile range, 4 to 5). PEEP of at least 5 cm H_2O was applied in 28% of patients. The distribution of these variables is presented in figure 2 and Supplemental Digital Content 2 (http://links.lww.com/ALN/B674).

Oxygen Management and Potentially Substantial Oxygen Exposure

Potentially preventable hyperoxemia occurred in 1,236 patients (83%; 95% CI, 81 to 84). Most received F_{IO_2} of 0.31 to 0.6 (fig. 3). A total of 483 patients (32%; 95% CI, 30 to 35) were exposed to potentially substantial oxygen during general anesthesia. On comparing patients who were exposed to potentially substantial oxygen and those who did not receive potentially substantial oxygen, it was found that patients who were exposed to potentially substantial oxygen were older (67 yr [55 to 76] *vs.* 64 yr [48 to 74], $P = 0.001$), had more severe comorbidities (ASA physical status of III or higher: 18% *vs.* 14%, $P = 0.031$), and were more likely to undergo emergency surgery (10% *vs.* 5%, $P < 0.001$; table 1). One hour after the induction of general anesthesia, one-lung ventilation was more frequently performed in patients exposed to potentially substantial oxygen (17% *vs.* 2%, $P < 0.001$).

In multivariable analysis (table 3), emergency surgery (odds ratio, 1.98; 95% CI, 1.17 to 3.36; $P = 0.012$) and one-lung ventilation (odds ratio, 13.35; 95% CI, 7.24 to 24.60; $P < 0.001$) predicted potentially substantial oxygen exposure. Patient age appeared to have a nonlinear effect, with a reduction in the odds of potentially substantial oxygen exposure from young age to around 50 yr. On the other hand, a trend of increasing odds of potentially substantial oxygen exposure was observed in patients aged more than 50 yr (P for overall effect = 0.028; P for nonlinear effect = 0.025;

Table 1. Characteristics of Study Patients and Potentially Substantial Oxygen Exposure

Variable	Total (N = 1,498)	Exposure (n = 1,015)	No Exposure (n = 483)
Age, yr	65 [48–74]	64 [48–74]	67 [55–76]
Sex, female	766 (49%)	550 (54%)	216 (45%)
Height, cm	160 [153–167]	159 [153–166]	160 [154–167]
Weight, kg	57.0 [50.0–66.9]	57 [50–66]	58.8 [51–67.5]
Predicted body weight, kg	53.9 [46.8–62.4]	53.3 [46.3 –62.4]	55.6 [47.0–63.1]
Body mass index, kg/m^2	22.7 [20.2–25.2]	22.5 [20.1–25.1]	22.9 [20.4–25.4]
ASA physical status			
I	391 (26%)	288 (28%)	103 (21%)
II	881 (59%)	588 (58%)	293 (61%)
III	215 (14%)	135 (13%)	80 (17%)
IV	11 (1%)	4 (0.4%)	7 (1%)
Emergency surgery	95 (6%)	48 (5%)	47 (10%)
Type of surgery			
Thoracic	109 (7%)	27 (3%)	82 (17%)
Cardiovascular	71 (5%)	41 (4%)	30 (6%)
Abdominal (open)	290 (19%)	224 (22%)	66 (14%)
Abdominal (laparoscopic)	250 (17%)	182 (18%)	68 (14%)
Head and neck	195 (13%)	146 (14%)	49 (10%)
Neurologic	47 (3%)	31 (3%)	16 (3%)
Orthopedic	220 (15%)	132 (13%)	88 (18%)
Spine	126 (8%)	86 (9%)	40 (8%)
Other	190 (13%)	146 (14%)	44 (9%)
Type of anesthesia			
Inhalation anesthesia	1,188 (79%)	796 (78%)	392 (81%)
Total intravenous anesthesia	310 (21%)	219 (22%)	91 (19%)
Epidural anesthesia	346 (23%)	237 (23%)	109 (23%)
Airway management			
Endotracheal intubation	1,355 (90%)	909 (90%)	446 (92%)
Supraglottic airway devices	126 (8%)	92 (9%)	34 (7%)
Tracheostomy	17 (1%)	14 (1.4%)	3 (1%)
One-lung ventilation	95 (6%)	15 (1.5%)	80 (17%)
Laparoscopic pneumoperitoneum	201 (13%)	146 (14%)	55 (11%)
Body position			
Supine	986 (66%)	705 (70%)	281 (58%)
Prone	125 (8%)	83 (8%)	42 (9%)
Lateral	205 (14%)	90 (9%)	115 (24%)
Other	182 (12%)	137 (13%)	45 (9%)

The data are presented as median [interquartile range] and number (percentage).
ASA = American Society of Anesthesiologists.

table 3; fig. 4). Patients who received volume-controlled ventilation and high levels of PEEP were significantly less likely to be exposed to potentially substantial oxygen. In subgroup analysis, we identified 1,088 patients who had preoperative spirometry data available. Similar results were found without clinically meaningful differences in patients with an airway obstructive pattern and normal pattern (Supplemental Digital Content 3, http://links.lww.com/ALN/B675).

Data Validation Analysis

A total of 98 patients from one of the participating hospitals were included in a data validation analysis. Using all available intraoperative data, measured electronically and recorded at 1-min intervals, we determined that F_{IO_2} was unchanged throughout the intraoperative period in 83% of patients. Notably, in 51 of 53 patients with a minimum SpO_2

of more than 98% during surgery, F_{IO_2} was never adjusted despite F_{IO_2} being more than 0.21.

Discussion

Key Findings

This multicenter, cross-sectional study assessed current ventilator management, especially oxygen management, during general anesthesia in 43 hospitals in Japan. Strategies for intraoperative lung protection, including the use of low tidal volumes and adequate levels of PEEP, were not widely implemented. Regarding oxygen therapy, potentially hyperoxemia and substantial oxygen exposure were common. Old age, emergency surgery, and one-lung ventilation were independently associated with increased potentially substantial oxygen exposure, whereas use of volume control ventilation

Table 2. Physiologic Parameters and Ventilator Settings 1 h after the Induction of General Anesthesia and Potentially Substantial Oxygen Exposure

Variable	Total (N = 1,498)	Exposure (n = 1,015)	No Exposure (n = 483)
Physiologic parameters			
Heart rate, beats/min	63 [56–73]	62 [56–72]	65 [58 –75]
Mean arterial pressure, mmHg	71 [64–80]	71 [64–80]	72 [64–81]
SpO_2, %	100 [99–100]	100 [99–100]	100 [99–100]
$ETCO_2$, mmHg	35 [32–37]	35 [32–37]	35 [32–38]
Ventilator settings			
Ventilator mode			
Volume-controlled ventilation	778 (52%)	592 (58%)	186 (39%)
Pressure-controlled ventilation	720 (48%)	423 (42%)	297 (62%)
Carrier gas composition			
Oxygen	39 (3%)	6 (0.6%)	33 (7%)
Oxygen + air	1,444 (96%)	995 (98%)	449 (93%)
Oxygen + nitrous oxide	15 (1%)	14 (1.4%)	1 (0.2%)
FIO_2	0.47 [0.4–0.6]	0.47 [0.40–0.47]	0.60 [0.60–0.60]
Tidal volume, ml	440 [389–500]	440 [400–500]	440 [370–500]
Tidal volume, ml/kg PBW	8.2 [7.3–9.2]	8.2 [7.3–9.2]	8.1 [7.0–9.2]
PEEP, cm H_2O	4 [0–5]	4 [0–5]	4 [0–5]
Peak inspiratory pressure, cm H_2O	16 [14–18]	16 [14–18]	16 [14–20]
Respiratory rate, beats/min	10 [10–12]	10 [10–12]	10 [10–12]

The data are presented as median [interquartile range] and number (percentage).

$ETCO_2$ = end-tidal carbon dioxide; FIO_2 = inspiratory fraction of oxygen; PBW = predicted body weight; PEEP = positive end-expiratory pressure; SpO_2 = pulse oximeter oxygen saturation.

and PEEP were associated with decreased oxygen exposure. Particularly, one-lung ventilation was a strong independent predictor of potentially substantial oxygen exposure.

Relationship to Previous Findings

We found that liberal oxygen therapy is a standard practice. This finding is consistent with other studies from various clinical settings. In a single-center observational study at a U.S. hospital, Rachmale *et al.*[5] found that 74% of mechanically ventilated patients in intensive care units were exposed to excessive oxygen for a median duration of 17 h. A Dutch retrospective observational study reported frequent hyperoxemia in mechanically ventilated intensive care unit patients. In most cases, ventilator settings were not adjusted if FIO_2 was less than 0.41.[6] Two observational studies from Australia revealed infrequent FIO_2 adjustments in hyperoxemic patients.[3,4] To the best of our knowledge, this is the first study describing oxygen management during general anesthesia.

Previous studies have described mechanical ventilation practices during general anesthesia. In a large retrospective observational study with 29,343 U.S. patients, the median tidal volume was 8.6 ml/kg predicted body weight (interquartile range, 7.7 to 9.6), with a minimal PEEP of 4.0 cm H_2O (interquartile range, 2.2 to 5.0).[23] Another study from Australia reported that the median tidal volume corrected for predicted body weight was 9.5 ml/kg (interquartile range, 8.5 to 10.4). In this study, PEEP was used in 54% of patients, with a median value of 5.0 cm H_2O (interquartile range, 4.0 to 5.0).[24] The findings are consistent with

our observations and suggest that protective lung ventilation strategies, including low tidal volume with PEEP, are uncommon in current clinical practice settings during general anesthesia.

In a recent French multicenter, randomized trial, Futier *et al.*[2] reported that intraoperative lung protective ventilation with a tidal volume of 6 to 8 ml/kg predicted body weight, a PEEP of 6 to 8 cm H_2O, and recruitment maneuvers repeated every 30 min improved clinical outcomes as compared with nonprotective ventilation with a tidal volume of 10 to 12 ml/kg predicted body weight, no PEEP, and no recruitment maneuvers. In another recent multicenter study of patients undergoing abdominal surgery throughout Europe and North and South America, the incidence of postoperative pulmonary complications in the first 5 days after surgery was comparable between patients who received a high PEEP (12 cm H_2O) and recruitment maneuvers and those who received a low PEEP (less than or equal to 2 cm H_2O) and no recruitment maneuvers. Thus, optimal PEEP levels and the role of recruitment maneuvers during general anesthesia are uncertain.[25] These observations were reflected in our results where PEEP was applied in almost half of the patients at different levels, although we did not investigate the use of recruitment maneuvers.

Clinical Implications

Potentially substantial oxygen exposure during general anesthesia is concerning. Perioperative supplemental oxygen decreases the incidence of surgical site infection. A
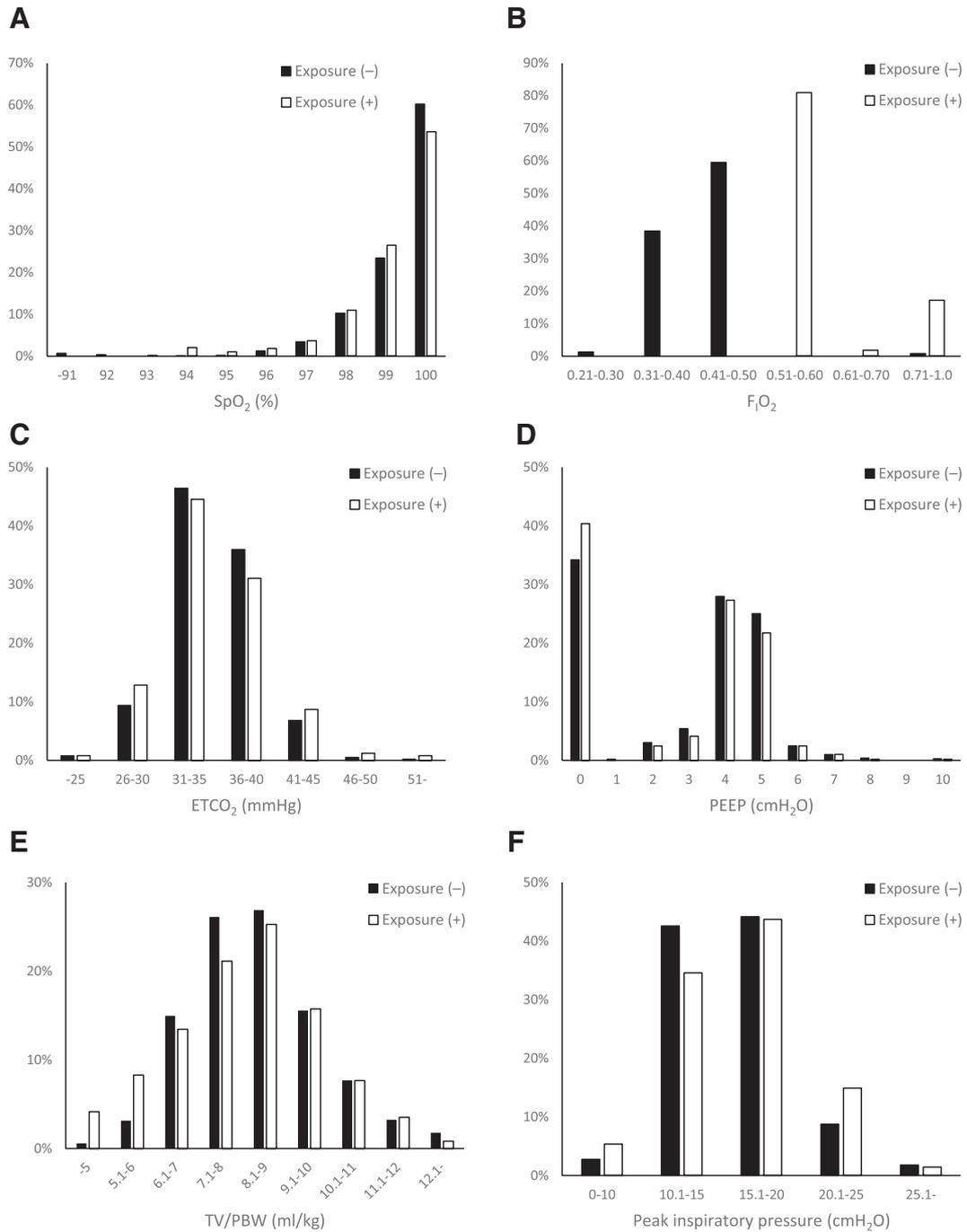
Fig. 2. Distribution of oxygen saturation measured by pulse oximetry (SpO_2; *A*), fractional inspired oxygen tension (F_{IO_2}; *B*), end-tidal carbon dioxide ($ETCO_2$; *C*), positive end-expiratory pressure (PEEP; *D*), tidal volume corrected for predicted body weight (*E*), peak inspiratory pressure (*F*), and potentially substantial oxygen exposure. PBW = predicted body weight; TV = tidal volume.

meta-analysis of nine randomized clinical trials reported marginal beneficial effects of high intraoperative F_{IO_2} on surgical site infection.[26] Another meta-analysis identified no reduction of surgical site infections with the use of intraoperative supplemental oxygen therapy.[27] Thus, the benefits of intraoperative supplemental oxygen therapy remain uncertain.

In contrast, the adverse effects of hyperoxemia have been reported in different clinical settings, including patients

with acute exacerbations of chronic obstructive pulmonary disease,[9] cardiac arrest,[11] and critical illness.[12] A few studies have also reported the adverse influence of hyperoxemia during the intraoperative period. A follow-up study of a randomized controlled trial showed that patients undergoing cancer surgery randomized to receive 80% perioperative oxygen had an increased long-term mortality risk, compared with those who received 30% oxygen.[17] A recent large-cohort observational study reported that high intraoperative
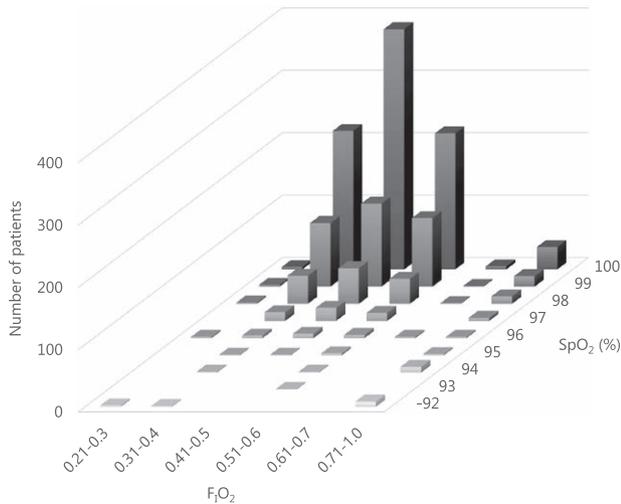
Fig. 3. Distribution of patients according to fractional inspired oxygen tension (F$_{IO_2}$) and the corresponding oxygen saturation measured by pulse oximetry (SpO$_2$).

Table 3. Multivariable Regression Analysis for Excessive Oxygen Exposure

Variable	Adjusted OR [95% CI]	P Value
Age, yr	1.27 [1.00–1.61]	0.028
Sex, female	1.03 [0.77–1.39]	0.825
Weight, kg	1.24 [0.99–1.54]	0.061
ASA physical status		
I	Reference	
II	1.20 [0.73–1.97]	0.465
III	1.37 [0.86–2.18]	0.190
IV	3.46 [0.89–13.44]	0.073
Emergency surgery	1.98 [1.17–3.36]	0.012
One-lung ventilation	13.35 [7.24–24.60]	< 0.001
Volume-controlled ventilation	0.46 [0.23–0.93]	0.029
PEEP	0.54 [0.24–1.22]	0.136

For all continuous variables, OR reflects changes in odds for the comparison between the 25th percentile and the 75th percentile in each variable. For example, in a comparison of patients 48.2 and 74 yr old, odds of having an excess oxygen exposure increases by 1.27-fold with all other variables held constant. For weight, OR of 1.24 reflects the change in odds between those who with weight of 50 and 66.9 kg. For PEEP, OR of 0.54 reflects the change in odds between those with PEEP of 0.0 to 5.0. The area under the receiver operating characteristic curve of the model predictability was 0.7 after bootstrap correction. The bootstrap optimism estimate was 0.9. The maximum variance inflation factor was 3.4.

ASA = American Society of Anesthesiologists; OR = odds ratio; PEEP = positive end-expiratory pressure.

F$_{IO_2}$ was associated in a dose-dependent manner with major respiratory complications and with 30-day mortality.[18] The British Thoracic Society guidelines for oxygen use have recommended a target SpO$_2$ of 94 to 98% for most acutely ill patients,[21] and the indication was expanded to include perioperative care in the latest version.[19] Thus, a more conservative approach to oxygen therapy should be considered to avoid hyperoxemia during operations under general anesthesia. Importantly, our observation that most episodes of
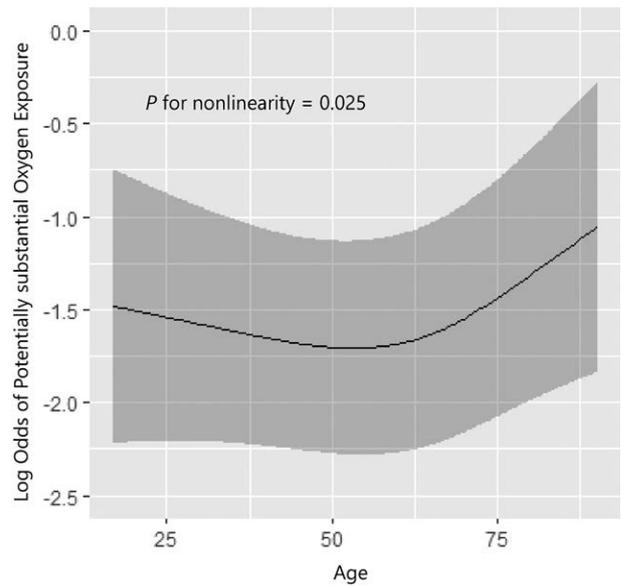

Fig. 4. Age and the incidence of potentially substantial oxygen exposure. Old age was independently associated with the incidence of potentially substantial oxygen exposure with a *P* value for overall effect of 0.028 and a *P* value for nonlinear effect of 0.025. Point estimates and the 95% CI for these relationships are shown by the *black line* and the *gray band*, respectively. Log odds of potentially substantial oxygen exposure decreases as age increases to around 50 yr, and it increases for age being older than 50.

hyperoxemia occurred at a relatively low F$_{IO_2}$ indicates that a further decrease in F$_{IO_2}$ is likely easy and safe.

We found that patients receiving one-lung ventilation were more likely to receive potentially substantial oxygen. One-lung ventilation could damage lung tissue secondary to hyperperfusion and hyperinflation of the ventilated lung, coupled with surgical manipulation, atelectrauma, and re-expansion/reperfusion injury of the operated lung.[28–30] Therefore, patients receiving one-lung ventilation are more vulnerable to perioperative hyperoxia/hyperoxemia.[31,32] Consequently, these are the patients for whom optimized oxygen therapy procedures are likely to have a significant impact.

Strengths and Limitations

This was a prospective, multicenter study that included several large teaching/academic hospitals. This approach enhanced the clinical utility of our findings. We investigated not only F$_{IO_2}$ but also the corresponding SpO$_2$ during general anesthesia, which makes the current study more informative. We included more than the expected number of participants, which increases the precision of analysis. The number of independent variables in the logistic regression model did not exceed the allowable number.[33] Additionally, optimism was estimated as 0.9 by bootstrapping internal validation procedure, which did not indicate a problem of overfitting and suggested an excellent degree of reproducibility. The bootstrapped area under the receiver operating

characteristic curve was 0.7, which indicates a fair level of model fit. We also carefully presented our study findings with a focus on clinical effects instead of just presenting *P* values not to consider a meaningless and small association as statistically significant. Thus, our results provide detailed descriptions of current oxygen management strategies during surgery and useful information for future study design. Nevertheless, our study had several limitations. First, our findings might not reflect oxygen management during all general anesthesia procedures because we collected data at one point. However, a data validation analysis revealed that, in most cases, F_{IO_2} was never adjusted throughout general anesthesia, which makes our findings robust. Second, potentially substantial oxygen exposure was defined according to a previous study,[5] which found such exposure was likely associated with worsening lung function in mechanically ventilated, critically ill patients and not in patients exclusively undergoing general anesthesia. We also defined potentially preventable hyperoxemia according to the British Thoracic Society guidelines[21] and recommendations,[22] although they have not been validated. However, there is no evidence or consensus on best practices for the intraoperative use of oxygen therapy. Recently, conservative oxygen therapy (target Sp_{O_2} of 88 to 92% using the lowest F_{IO_2}) has been implemented to avoid both hyperoxemia and hypoxemia and shown to be feasible and safe in several clinical settings.[14,34] Thus, potentially substantial oxygen exposure might be unnecessary, and the current study shows the need for further research. Third, the results cannot be fully applied to other countries, because this study was conducted in a single country, and our study population might be unique to Japan. For example, the distribution of ASA physical status was comparable to that reported in Europe,[35] but not to that reported in the United States[23] or Australia.[24] The proportion of patients intubated instead of managed with a supraglottic device was comparable to that reported in the United States,[23] but not to that reported in Europe[35] or Australia.[24] Thus, our findings need to be confirmed or refuted in different countries. Fourth, we had no information on the number of anesthesiologists included in this study. However, we screened all patients undergoing surgery under general anesthesia at the participating hospitals during the study period, and most of the eligible patients were included in this study. Thus, our results could reflect the real-world practice in hospitals in Japan. Fifth, the quality and accuracy of the data collection might not have been standardized across all the participating hospitals because we did not have dedicated research coordinators. Sixth, owing to the prospective, observational design of this study, the attending anesthesiologists were not blinded to the purpose of this study, and the Hawthorne effect might have occurred. However, considering the very high incidence of potentially preventable hyperoxemia observed, it is unlikely that this was an important issue. Finally, because this was not an outcome study, we were not able to assess the relationship between ventilator management during general anesthesia

and patient-centered outcomes. However, considering that supplemental oxygen is both commonly used and not without risk, our findings underscore the need for a prospective safety and feasibility study of conservative approaches for oxygen use during general anesthesia. They also could be used to determine the characteristics and oxygen-related parameters of a possible control group for future study.

Conclusions

Potential hyperoxemia and substantial oxygen exposure were common during general anesthesia, especially in patients receiving one-lung ventilation in this multicenter, observational study. Our findings support the need for future clinical trials to evaluate the safety and feasibility of conservative approaches for oxygen use during general anesthesia, especially in patients receiving one-lung ventilation.

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Competing Interests

The authors declare no competing interests.

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Appendix

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