Original Research Article

Early Light Sedation Increased the Duration of Mechanical Ventilation in Patients With Severe Lung Injury

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Abstract

Introduction: The international guidelines recommend light sedation management for patients receiving mechanical ventilation. One of the benefits of light sedation management during mechanical ventilation is the preservation of spontaneous breathing, which leads to improved gas-exchange and patient outcomes. Conversely, recent experimental animal studies have suggested that strong spontaneous breathing effort may cause worsening of lung injury, especially in severe lung injury cases. The association between depth of sedation and patient outcomes may depend on the severity of lung injury.

Objective: This study aimed to describe the patients' clinical outcomes under deep or light sedation during the first 48 h of mechanical ventilation and investigate the association of light sedation on patient outcomes for each severity of lung injury.

Methods: The researchers performed a retrospective observational study at a university hospital in Japan. Patients aged ≥20 years, who received mechanical ventilation for at least 48 h were enrolled.

Results: A total of 413 patient cases were analyzed. Light sedation was associated with significantly shorter 28-day ventilator-free days compared with deep sedation in patients with severe lung injury (0 [IQR 0–5] days vs. 16 [0–19] days, $P = .038$). In the groups of patients with moderate and mild lung injury, the sedation depth was not associated with ventilator-free days. After adjusting for the positive end-expiratory pressure and APACHE II score, it was found that light sedation decreased the number of ventilator-free days in patients with severe lung injury (−10.8 days, 95% CI −19.2 to −2.5, $P = .012$).

Conclusion: Early light sedation for severe lung injury may be associated with fewer ventilator-free days.

Keywords

acute physiology and chronic health evaluation II score, deep sedation, intensive care unit, tidal volume, ventilator, ventilator-induced lung injury

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Introduction

Sedation is essential for the treatment of patients receiving mechanical ventilation. However, the deleterious effect of deep sedation is known to affect short- and long-term patient outcomes, including increasing the duration of mechanical ventilation, intensive care unit (ICU) length of stay, and mortality rate (Stephens et al., 2018). Therefore, the Pain, Agitation-Sedation, Delirium, Immobility, and Sleep Disruption guidelines recommend maintaining light sedation for patients receiving mechanical ventilation (Devlin et al., 2018).

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One of the benefits of light sedation management is the preservation of spontaneous breathing (Devlin et al., 2018). Mechanical ventilation with spontaneous breathing led to improved gas-exchange throughout increased aeration of dependent lung regions and ventilation-perfusion matching (Mauri et al., 2017; Neumann et al., 2005; Putensen et al., 1999). In addition, spontaneous breathing preserved diaphragmatic activity and prevention of ventilator-induced diaphragm dysfunction (Goligher et al., 2018; Rittayamai et al., 2019). On the other hand, deleterious effects of spontaneous breathing have been reported, including overdistension, increased lung perfusion, and patient–ventilator asynchrony, leading to worsening lung injury (Brochard et al., 2017). The latter phenomenon has been termed "patient self-inflicted lung injury (P-SILI)" (Brochard et al., 2017; Yoshida et al., 2020). Therefore, the currently recommended light sedation strategy may not be feasible for specific patient populations (Brochard et al., 2017; Yoshida et al., 2017).

Review of Literature

Several previous studies have demonstrated that light sedation with spontaneous breathing improves patient outcomes (Mauri et al., 2017; Neumann et al., 2005; Putensen et al., 1999). On the other hand, the mechanism of P-SILI has already been partly demonstrated in experimental animal studies (Yoshida et al., 2012, 2013), and the effects of light sedation may depend on the severity of lung injury.

There are several potential disadvantages of light sedation. In patients with acute respiratory failure, strenuous spontaneous inspiratory efforts lead to large negative swings in intrathoracic pressure and large swings of transpulmonary pressure (Brochard et al., 2017). Furthermore, increased transmural pulmonary vascular pressure in the context of increased vascular permeability greatly increases the risk of pulmonary edema through vascular leakage (Kallet et al., 1999). On the other hand, in patients with severe lung injury, regional forces generated by the respiratory muscles may lead to injurious effects on a regional level (Yoshida et al., 2017). These morphological changes in the alveoli due to excessive transpulmonary pressure and extravascular leakage may be thought to worsen lung injury.

However, in clinical practice, there is still an ongoing controversy as to whether fully controlled mechanical ventilation management with deep sedation/neuromuscular blocking agents or spontaneous breathing preservation management with light sedation is more beneficial, especially in the early phase of severe lung injury, such as in patients with acute respiratory distress syndrome (Moss et al., 2019; Papazian et al., 2010; Van Haren et al., 2019).

In this study, the researchers aimed to describe the patients' clinical outcomes under both deep and light sedation during the first 48 h of mechanical ventilation and investigate the association of different depths of sedation on patient outcomes for each severity of lung injury.

Methods

Design

The researchers performed a retrospective, observational, single-center study of patients admitted to the 12-bed ICU of a university hospital in Japan.

Research Question

1. Is there an association between the depth of sedation during the first 48 h of mechanical ventilation and patients' clinical outcomes based on the severity of lung injury?

Sample

Patients aged ≥20 years, admitted to the ICU between April 2013 and March 2018, and who received mechanical ventilation for at least 48 h were identified from ICU electronic patient records and were included in this study.

Exclusion Criteria

Patients who had already received mechanical ventilation for ≥24 h at ICU admission, were treated with extracorporeal membrane oxygenation (ECMO), or had standing "do not attempt resuscitation" (DNAR) instructions were excluded. The researchers excluded cases in which key data on one or more respiration or early sedation variables were missing.

Institutional Review Board Approval

The institutional review board of the university hospital where this work was conducted approved the study protocol and issued a waiver for the requirement for informed consent providing an opt-out option via the Internet and hospital posting because of the retrospective design of the study.

Data Collection

Data were retrospectively collected from the ICU electronic patient records by three registered nurses. Data collection included baseline demographic data (age, sex, comorbidities, Acute Physiology And Chronic Health Evaluation [APACHE] II score, reason for intubation, reason for ICU admission, and diagnosis), setting parameters of mechanical ventilation (tidal volume; V_T, F_IO_2, positive end-expiratory pressure [PEEP], frequency; f, and pressure support; PS), arterial blood gas parameters (pH, PaO_2, and $PaCO_2$), patient's respiratory parameters (respiratory rate; RR, V_T, minute volume; MV, SpO_2, and peak inspiratory pressure; PIP), sedation medication data (depth of sedation within 48 h, Richmond Agitation-Sedation Scale [RASS], types and dose of sedatives, use of neuromuscular blocking agents), and patient outcome data (28-day mortality, 28 ventilator-free days, ICU and hospital length of stay). Data on respiratory

parameters, setting parameters of mechanical ventilation, and sedation medication used were collected at intubation (baseline), 12, 24, 36, and 48 h. The depth of sedation was assessed using the RASS, which was evaluated every 4 h from intubation to 48 h.

Definition

The depth of sedation in the first 48 h was classified into two categories using the sedation index: light and deep sedations (sedation index of 0–2 and 3–5, respectively). The sedation index was calculated as the sum of the negative RASS scores within 48 h after the mechanically ventilated initiation divided by the number of RASS measurements (Shehabi et al., 2018). The RASS is a depth of sedation rating scale used in the intensive care setting to assess the depth of sedation. The depth of sedation is rated on a 10-point scale from "RASS − 5: unarousable" to "RASS + 4: combative" (Sessler et al., 2002).

The severity classification of lung injury was classified based on the Berlin definition of the ARDS diagnostic criteria. The Berlin definition classifies the severity of ARDS as mild (200 mmHg < PaO_2/FiO_2 ≤ 300 mmHg), moderate (100 mmHg < PaO_2/FiO_2 ≤ 200 mmHg), and severe (PaO_2/FiO_2 ≤ 100 mmHg). In this study, the severity of lung injury was also classified according to the above classification (Ranieri et al., 2012). The severity of lung injury was assessed using the initial PaO_2 /FiO_2 (P/F) ratio. Mild lung injury has a P/F ratio equal to or more than 200 (≥200); moderate lung injury has a P/F ratio equal to or more than 100 but less than 200 (≥100 and <200); and for severe lung injury, the P/F ratio is less than 100 (<100). Furthermore, based on the P/F ratio category and sedation index, the researchers classified the patients into six groups as follows: group 1, light sedation in patients with severe lung injury; group 2, deep sedation in patients with severe lung injury; group 3, light sedation in patients with moderate lung injury; group 4, deep sedation in patients with moderate lung injury; group 5, light sedation in patients with mild lung injury; and group 6, deep sedation in patients with mild lung injury.

The primary and secondary outcomes were the 28-day all-cause mortality and 28-day ventilator-free days, respectively.

Statistical Analysis

The researchers performed an analysis of the six groups, divided by lung injury and depth of sedation, to test differences among the groups with regard to baseline characteristics, clinical outcomes, respiratory parameters, and administered sedation medication. The categorical data were compared using Fisher's exact test and expressed proportion (%). The continuous variables were compared using one-way analysis of variance (ANOVA) or the Kruskal–Wallis test and expressed as means ± standard deviation or median (interquartile range [IQR]). Moreover, the Bonferroni or median tests were performed as post hoc tests.

A generalized linear mixed model was used to clarify the interaction of depth of sedation and the P/F ratio on the 28-day ventilator-free days. Baseline covariates analyzed in the generalized linear mixed model were the APACHE II score, PEEP, depth of sedation, P/F ratio severity, and the interaction between the P/F ratio and depth of sedation. The results are shown as the beta coefficient with a 95% confidence interval (CI) and are shown as the estimated mean values. Using a generalized linear model to account for the repeated measurements in each group, the researchers evaluated the association between the sequential transition of the P/F ratio from baseline to 48 h of each group and the patient outcomes. The level of significance was set at $P < .05$. All analyses were performed using SPSS version 25 (SPSS Inc., Chicago, IL).

Results

Sample Characteristics

Among the 459 patients included in the study, 46 were excluded, and finally, the data of 413 patients (age, 64 ± 15 years; APACHE II score, 22.5 ± 7.5) were analyzed (Figure 1). The demographic characteristics were similar among the groups. The main reason for intubation was heart disease. There were no differences in the reasons for intubation among the groups. Light sedation in the severe lung injury group (group 1) was the only respiratory disease. Patients' characteristics in each group stratified according to lung injury severity and the depth of sedation are shown in Table 1.

There were no significant differences in respiratory parameters among the six groups. In the sedation data (Table 2), post hoc analysis after one-way ANOVA showed that only in the mild lung injury group, the administration of propofol was higher in the deep sedation than in the light sedation group (group 5 vs. group 6). No differences were found in the other sedation data among the six groups (Table 2). In group 1, the patients ($n = 5$) were controlled to have a V_T of 4–10 ml/kg of predicted body weight at 24 h after intubation. The PIP and the PEEP were maintained between 15 and 30 cmH_2O and between 5 and 12 cmH_2O, respectively. The ventilation and physiologic variables for each group stratified according to lung injury severity and depth of sedation are shown in Table 2.

Research Question Results

In the univariate analysis, group 1 had significantly shorter ventilator-free days than group 2 (0 [IQR 0–5] days vs. 16 [0–19] days, $P = .038$). In the moderate and mild lung injury groups, the depth of sedation was not associated with 28-day ventilator-free days (Table 3). After adjustment for APACHE II and PEEP in the generalized linear model, the sequential transition of the P/F ratio from baseline to 48 h was compared between the light and deep sedation groups (group 1 vs. group 2, group 3 vs. group 4, group 5 vs. group 6). The sequential transition of the P/F ratio was

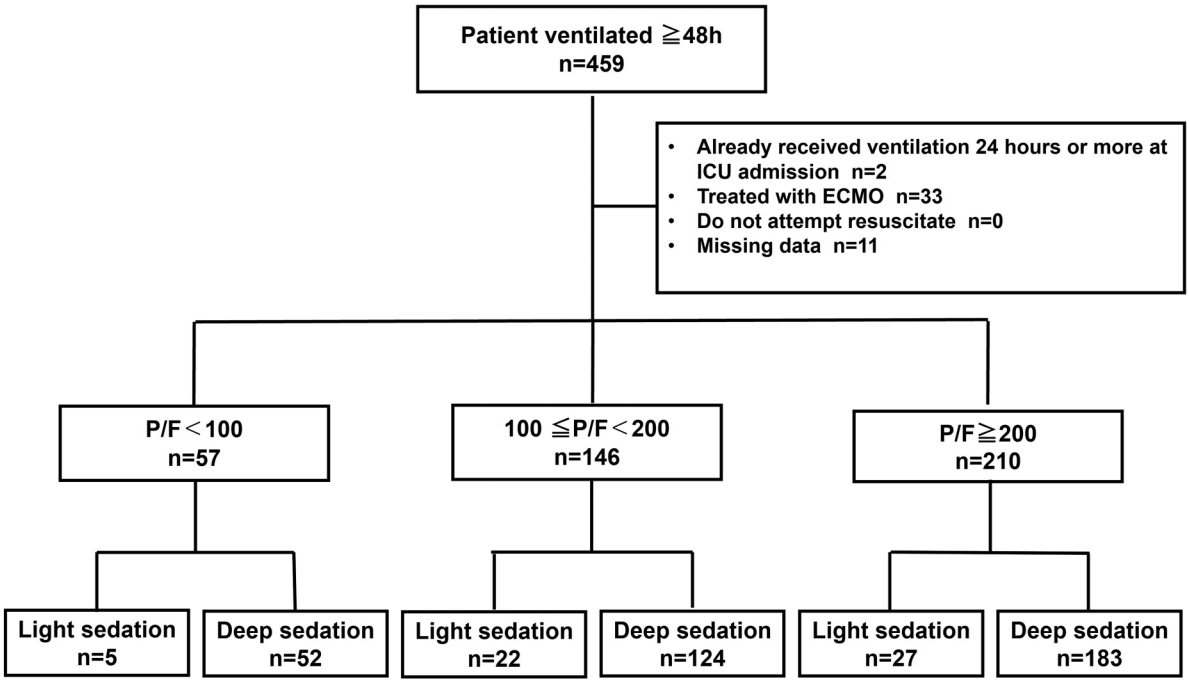

Figure 1. Study flow diagram. The depth of sedation in the first 48 h was classified into two categories using the sedation index. The sedation index is calculated as the sum of the negative Richmond Agitation-Sedation Scale scores within 48 h after mechanically ventilated initiation divided by the number of measurements. The severity of lung injury was classified into three categories using the initial PaO_2/FiO_2 ratio. Mild lung injury has a P/F ratio equal to or more than 200 (≥200); moderate lung injury has a P/F ratio equal to or more than 100 but less than 200 (≥100 and <200); and for severe lung injury, the P/F ratio is less than 100 (<100). Light sedation, sedation index of 0–2; Deep sedation, sedation index of 3–5; ECMO, extracorporeal membrane oxygenation.

Table 1. Comparison of Baseline Characteristics for the Six Groups by One-Way ANOVA.

	Severe lung injury P/F < 100 mmHg		Moderate lung injury 100 ≤ P/F < 200 mmHg		Mild lung injury P/F ≥ 200 mmHg	
Sedation level	light ($n = 5$)	deep ($n = 52$)	light ($n = 22$)	deep ($n = 124$)	light ($n = 27$)	deep ($n = 183$)
Age, mean ± SD	52 ± 15	62 ± 16	64 ± 17	67 ± 13	68 ± 11	63 ± 17
Woman, *n* (%)	4 (80)	12 (23)*	12 (55)	48 (39)	11 (41)	66 (36)
APACHE II, Mean ± SD	21 ± 8	25 ± 9	20 ± 6	23 ± 7	17 ± 4	22 ± 7*
Cause, *n* (%)						
Heart	0 (0)	16 (31)	6 (27)	67 (54)	6 (22)	66 (36)
Respiratory	5 (100)	25 (48)	10 (46)	36 (29)	5 (19)	18 (10)
Gastrointestinal	0 (0)	3 (6)	3 (14)	6 (5)	5 (19)	28 (15)
Head	0 (0)	0 (0)	0 (0)	3 (2)	1 (4)	32 (18)
Sepsis	0 (0)	5 (10)	1 (5)	7 (6)	2 (7)	11 (6)
Other	0 (0)	3 (6)	2 (9)	5 (4)	8 (30)	28 (15)

Note. ANOVA, analysis of variance; SD, standard deviation; APACHE II, Acute Physiology and Chronic Health Evaluation II; P/F, PaO_2/FiO_2 ratio. *$P < .05$ vs. light sedation.

not significantly different between the light and deep sedation groups (Figure 2). There was no significant difference in the 28-day all-cause mortality between the light and deep sedation groups for each severity of lung injury.

Adjusting for the APACHE II scores and PEEP using the generalized linear mixed model to identify the effect of 28-day ventilator-free days on the interaction term between the sedation depth and P/F ratio, the researchers found decreased ventilator-free days in group 1 (−10.8 days, 95% CI, −19.2 to −2.5, $P = .012$) (Figure 3).

Discussion

The researchers performed a retrospective observational study to determine whether early light sedation for severe lung injury was associated with the clinical outcomes after

Table 2. Comparison of Respiratory Parameters and Administered Sedation Medication for the Six Groups.

	Severe lung injury P/F < 100 mmHg		Moderate lung injury 100 ≤ P/F < 200 mmHg		Mild lung injury P/F ≥ 200 mmHg	
Sedation level	light ($n = 5$)	deep ($n = 52$)	light ($n = 22$)	deep ($n = 124$)	light ($n = 27$)	deep ($n = 183$)
Respiratory data (after 24 h) (Mean ± SD)						
TV (ml/kg of PBW)	8.4 ± 3.8	9.3 ± 2.7	8.1 ± 1.6	9.1 ± 2.6	8.0 ± 1.7	8.8 ± 2.2
MV (L/min)	6.6 ± 3.7	7.5 ± 1.8	6.8 ± 1.6	7.0 ± 1.9	5.9 ± 1.7	6.6 ± 2.2
PIP (cm of water)	22 ± 8	23 ± 4	21 ± 5	21 ± 4	18 ± 5	18 ± 4
PEEP (cm of water)	8.0 ± 5.9	7.9 ± 4.1	8.0 ± 2.0	7.3 ± 2.6	6.5 ± 2.1	5.8 ± 1.6
RR (breaths/min)	16.6 ± 5.6	16.3 ± 5.1	17.6 ± 4.0	15.8 ± 4.7	14.8 ± 3.9	15.2 ± 5.1
Sedation data (during 48 h) (Mean ± SD)						
Fentanyl (μg/kg/h)	1.42 ± 0.91	1.21 ± 0.94	1.12 ± 0.55	1.09 ± 0.69	1.20 ± 0.92	1.08 ± 0.82
Propofol (mg/kg/h)	0.56 ± 0.68	1.07 ± 0.97	0.60 ± 0.74	1.18 ± 1.18	0.39 ± 0.54	1.27 ± 1.31*
Dexmedetomidine (μg/kg/h)	0.25 ± 0.28	0.28 ± 0.34	0.18 ± 0.21	0.28 ± 0.32	0.35 ± 0.33	0.21 ± 0.26
Midazolam (mg/kg/h)	0.00 ± 0.00	0.04 ± 0.08	0.002 ± 0.008	0.18 ± 1.73	0.002 ± 0.01	0.02 ± 0.07
Neuromuscular blockade n (%)	0 (0)	4 (7.7)	0 (0)	7 (5.6)	0 (0)	14 (7.7)

Note. SD, standard deviation; TV, Tidal volume; MV, Minute volume; PIP, Peak inspiratory pressure; PEEP, Positive end-expiratory pressure; RR, Respiratory rate; P/F, PaO_2/FiO_2 ratio. *$P < 0.05$ vs. light sedation.

mechanical ventilation. The analysis was divided into six groups based on the depth of sedation and severity of lung injury. The researchers found no significant difference in the 28-day all-cause mortality between the light sedation and deep sedation groups at each level of severity of lung injury. In contrast, the 28-day ventilator-free days significantly decreased only in the light sedation groups with severe lung injury. After adjusting for PEEP and APACHE II in the multivariate analysis, in the severe lung injury groups, the estimated mean value of the 28-day ventilator-free days tended to be shorter by 10.8 days in the light than in the deep sedation group.

In this study, light sedation management tended to decrease the 28-day ventilator-free days in patients with severe lung injury. Possible explanations for this outcome include that light sedation in patients with severe lung injury may cause dyspnea, patient–ventilator asynchrony, and strong spontaneous breathing effort, thus resulting in P-SILI. The beneficial effect of light sedation management is the preservation of spontaneous breathing, which leads to improvement in gas-exchange and in patient outcomes (Mauri et al., 2017; Neumann et al., 2005; Putensen et al., 1999). However, patients under light sedation experience discomfort symptoms, such as pain, thirst, and dyspnea more frequently than those under deep sedation (Puntillo et al., 2014). In particular, dyspnea is reported in half of mechanically ventilated patients (Puntillo et al., 2014). Patients who present with dyspnea often also experience tachypnea, patient–ventilator asynchrony, and strong spontaneous breathing effort. Strong spontaneous breathing effort is suggested to worsen lung injury in patients receiving mechanical ventilation and has recently been recognized as a concept of P-SILI (Brochard et al., 2017; Yoshida et al., 2020). The main mechanism of P-SILI is overdistension, increased pulmonary perfusion, and patient–ventilator asynchrony due to spontaneous breathing effort (Brochard et al., 2017). Yoshida et al. demonstrated that strong spontaneous breathing during moderate V_T causes high intrapleural pressure combined with increased V_T and RR, which can cause lung injury (Yoshida et al., 2012). In addition, high transpulmonary pressure (P_L) and RR may worsen lung injury due to repeated overstretch and the collapse of the dependent lung regions (Yoshida et al., 2013). These phenomena may have caused the 28-day ventilator-free days to decrease in the present data as well.

On the other hand, the evidence of P-SILI or detrimental effects of spontaneous breathing have not been clarified by clinical studies. Papazian et al. demonstrated that administration of neuromuscular blocking agents improved the 90-day survival rate and increased the number of ventilator-free days (Papazian et al., 2010). Although this result may indirectly support the detrimental effects of P-SILI, a recent randomized controlled trial showed conflicting results (Moss et al., 2019). In addition, a recent large international observational study reported that spontaneous breathing was observed in 46% of patients with severe acute respiratory distress syndrome, with a significantly increased number of ventilator-free days and lower ICU and hospital mortality in the spontaneous breathing group (Van Haren et al., 2019). Several factors may explain why the findings of this study differed from those of other studies (Moss et al., 2019; Papazian et al., 2010; Van Haren et al., 2019). First, the researchers used a relatively lower PEEP compared to a previous study, even in patients with severe lung injury (Moss et al., 2019). High PEEP has been reported to prevent exacerbation of lung injury (Morais et al., 2018). It is possible that the relatively low PEEP strategy followed at the institution where this study was conducted may

Table 3. Comparison of Clinical Outcomes for the Six Groups.

	Severe lung injury P/F < 100 mmHg		Moderate lung injury 100 ≤ P/F < 200 mmHg		Mild lung injury P/F ≥ 200 mmHg	
Sedation level	light ($n = 5$)	deep ($n = 52$)	light ($n = 22$)	deep ($n = 124$)	light ($n = 27$)	deep ($n = 183$)
28-day all-cause mortality n (%)	0 (0)	8 (15.4)	4 (18)	16 (13)	2 (7)	18 (10)
28-day ventilator-free days median (IQR)	0 (0–5)	16 (0–19)*	17 (0–23)	19 (0–23)	22 (15–24)	20 (6–23)

Note. IQR, interquartile range; P/F, PaO_2/FiO_2 ratio. *$P < 0.05$ vs. light sedation.

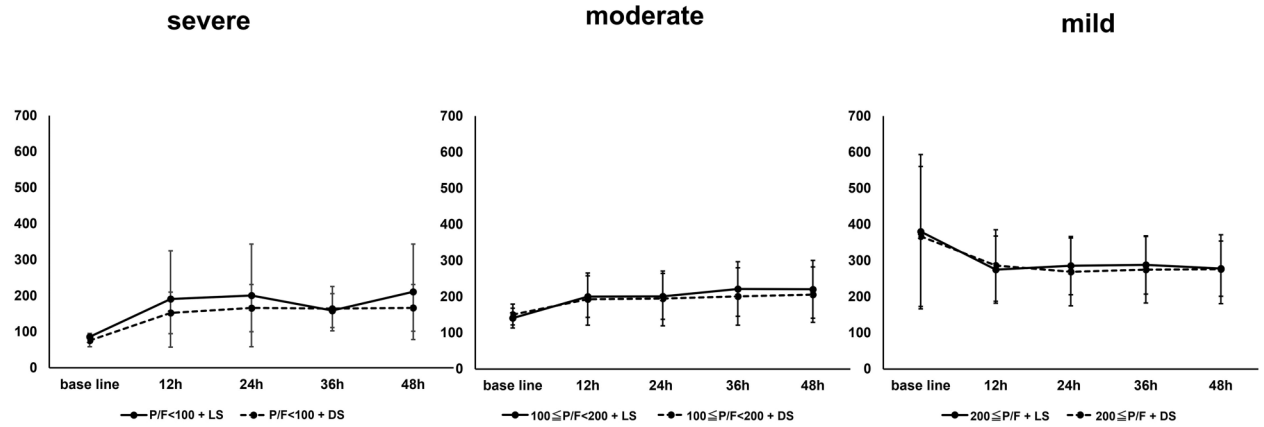

Figure 2. Time course of the PaO_2/FiO_2 ratio in each group. The severity of lung injury is classified into three categories using the initial PaO_2/FiO_2 ratio (mild: $PaO_2/FiO_2 \geq 200$, moderate: $100 \leq PaO_2/FiO_2 < 200$, severe: $PaO_2/FiO_2 < 100$). P/F, PaO_2/FiO_2 ratio; LS, light sedation; DS, deep sedation.

have contributed to the harm of spontaneous breathing. Second, this study had different stratification of patients from a previous observational study (Van Haren et al., 2019). Although the previous study stratified patients by a P/F ratio of 150, this study stratified patients into three groups to focus on severe lung injury. In addition, the researchers stratified the patients by the sedation index rather than by the presence or absence of spontaneous breathing. The purpose of sedation is to relieve symptoms. Therefore, stratification by sedation depth may better reflect dyspnea, patient–ventilator asynchrony, and spontaneous breathing effort with increased P_L than stratification by spontaneous breathing. For these reasons, the 28-day ventilator-free days may have decreased, although mortality was not affected. However, the researchers did not directly measure the dyspnea, patient–ventilator asynchrony, and spontaneous breathing effort and strength. Therefore, it is not clear how light sedation management in the early phase of severe lung injury will affect patient outcomes at this time, and further research focusing on this point is needed.

Although several previous studies have demonstrated that light sedation with spontaneous breathing improves patient outcomes (Mauri et al., 2017; Neumann et al., 2005; Putensen et al., 1999), this study's results suggest that light sedation management may provide different results depending on the severity of lung injury. Thus, sedation and mechanical ventilation management may be required after considering the patient's physical status, such as severe lung injury. In addition, discomfort symptom management, such as dyspnea, should be performed to ensure patient comfort (Puntillo et al., 2014). Especially for patients with severe lung injury, it may be more important to control their spontaneous breathing effort in addition to lung protection strategy and perform their sedation management accordingly.

Strengths and Limitations

This study had a few limitations. First, the researchers conducted a single-center retrospective, observational study, and the sample size, especially that of severe lung injury patients, was small. The small sample size between groups may be a false positive, although it is suggested that it may have decreased the 28-day ventilator-free days. Nevertheless, the 28-day ventilator-free days were significantly shorter in the light than in the deep sedation group within the severe lung injury group. A larger prospective study should be conducted in the future to examine the results. Second, during the 5-year period in which data were collected, there might have been changes in healthcare in guidelines, medications, and treatments. Third, the researchers targeted the depth of sedation for analysis, and the researchers did not measure parameters, such as spontaneous breathing effort, patient–ventilator asynchrony, P_L, and driving pressures.

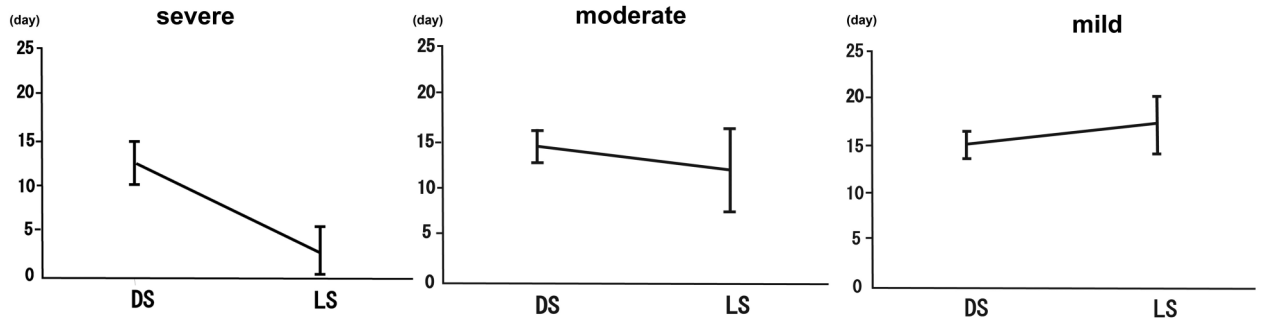

Figure 3. Multivariable analysis predicting 28-day ventilator-free days. The severity of lung injury is classified into three categories using the initial PaO_2/FiO_2 ratio (mild: $PaO_2/FiO_2 \geq 200$, moderate: $100 \leq PaO_2/FiO_2 < 200$, severe: $PaO_2/FiO_2 < 100$). The figure shows the estimated mean value of ventilator-free days after adjustment in the generalized linear mixed model using the APACHE II score and PEEP. LS, light sedation; DS, deep sedation.

Therefore, the researchers do not know the exact mechanism of the decrease in 28-day ventilator-free days, and further research focusing on this point is needed.

Implications for Practice

This study suggests that light sedation management may provide different results depending on the severity of lung injury. Thus, sedation and mechanical ventilation management may be required considering the patient's physical condition and comfort level. Especially in patients with severe lung injury, control of spontaneous breathing effort, in addition to lung protection strategies, is more important. Clinical indicators of spontaneous breathing effort include P_L, V_T, RR, and patient–respiratory asynchrony. In current clinical practice, P_L measurement is common, but this measurement requires special procedures. Therefore, early detection of spontaneous breathing effort using more easily measured clinical indicators, for example, airway obstruction pressure (P0.1), is considered more useful in current clinical practice (Telias et al., 2020).

Conclusions

This study describes differences in patient's clinical outcomes according to each severity of lung injury and the different depths of sedation. Although there were no differences in patient characteristic and mortality, the 28-day ventilator-free days differed by each severity of lung injury and the different depths of sedation. Early light sedation for severe lung injury may be associated with fewer ventilator-free days. Further studies are needed to determine the association between lung injury and depth of sedation.

Author Contributions

CH: conceptualization, methodology, investigation, formal analysis, and writing—original draft. HS: conceptualization, methodology, formal analysis, and writing—original draft. AO: formal analysis, and writing—review & editing. NS: writing—review & editing. YI: supervision and project administration. This work was performed at the University of Tsukuba Hospital in Japan.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics Approval and Informed Consent

The Institutional Review Board approved this study of the University of Tsukuba Hospital (approval number: H30-129), and the informed consent requirement was waived owing to the retrospective design of the study.

Clinical Trial Registration Number

UMIN Clinical Trials Registry: 000040400.

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