

Postextubation respiratory events in patients admitted to the intensive care unit: a prospective pilot study using overnight respiratory polygraphy

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Background: Before the main trial in which respiratory polygraphy will be used to evaluate postextubation sleep apnea in critically ill patients, we performed a prospective pilot study to ensure that any issues with the conduct of the trial would be identified.

Methods: In the present study, 13 adult patients who had received mechanical ventilation for ≥ 24 hours were prospectively recruited. Among the patients, 10 successfully completed respiratory polygraphy on the first or second night after extubation. Data regarding the types and doses of corticosteroids, analgesics, sedatives, and muscle relaxants as well as the methods of oxygen delivery were recorded.

Results: During the night of respiratory polygraphy, all 10 patients received supplemental oxygen (low-flow oxygen, $n=5$; high-flow oxygen, $n=5$), and seven patients received intravenous corticosteroids. Three of the 10 patients had a respiratory event index (REI) ≥ 5 /hr. All respiratory events were obstructive episodes. None of the patients receiving high-flow oxygen therapy had an REI ≥ 5 /hr. Two of the seven patients who received corticosteroids and one of the other three patients who did not receive this medication had an REI ≥ 5 /hr. Although low- or high-flow oxygen therapy was provided, all patients had episodes of oxygen saturation (SpO₂) $< 90\%$. Two of the three patients with an REI ≥ 5 /hr underwent in-laboratory polysomnography. The patients' Apnea-Hypopnea Index and REI obtained via polysomnography and respiratory polygraphy, respectively, were similar.

Conclusions: In a future trial to evaluate postextubation sleep apnea in critically ill patients, pre-stratification based on the use of corticosteroids and high-flow oxygen therapy should be considered.

Key Words: airway extubation; intensive care unit; pilot projects; sleep apnea

INTRODUCTION

Obstructive sleep apnea (OSA) is prevalent and present in 9%–38% of the general population [1]. OSA is frequently comorbid with cardiovascular, cerebrovascular, and metabolic diseases [2], and is associated with increased health care costs [3] and mortality rates [4]. According to retrospective studies conducted among Caucasian populations, approximately 10% of the patients admitted to the intensive care unit (ICU) had previously been diagnosed with OSA

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[5,6]. In another prospective study, all 16 patients admitted to the ICU for acute hypercapnic respiratory failure had sleep apnea when polysomnography (PSG) was conducted after their ICU discharge [7]. However, until recently, the occurrence of postextubation sleep apnea was not investigated in patients admitted to the ICU. In a recent study in which postextubation sleep apnea was investigated in Caucasian patients admitted to the surgical ICU, 70% of the patients had sleep apnea [8]. In extubated patients, upper airway obstruction may occur due to mechanical tissue injury caused by endotracheal intubation, inflammation in the upper airway [9,10], presence of secretions, and rostral fluid shift [11]. In addition, although the use of opioids during mechanical ventilation improves a patient's tolerance to mechanical ventilation, the risk of respiratory depression is increased [12].

Overnight PSG is the gold standard for the diagnosis of OSA. However, PSG is expensive, time-consuming, and labor-intensive [13]. Furthermore, PSG may not be suitable for critically ill patients because of the potential risks associated with out-of-ICU transportation. Portable respiratory polygraphy is an accepted alternative for OSA diagnosis in uncomplicated patients with an increased risk of moderate to severe OSA. Before the main trial with respiratory polygraphy for the evaluation of postextubation sleep apnea in critically ill patients in South Korea where relevant data are scarce, we performed a prospective pilot study to ensure that any problems with the conduct of the trial would be identified.

MATERIALS AND METHODS

Study Participants and Design

This study was approved by the Institutional Review Board of Seoul National University Hospital (IRB No. H-1802-051-921). All participants provided written informed consent and the study was conducted in accordance with the tenets of the declaration of Helsinki 2013.

In this prospective study, adult patients who had received mechanical ventilation for ≥ 24 hours and were extubated in the medical ICU at Seoul National University Hospital from August 2018 to May 2019 were recruited. Unconscious patients and those with tracheostomy or immediate need for non-invasive ventilation after extubation were excluded. A type 3 sleep study using respiratory polygraphy (Embla-Embletta; Natus, Pleasanton, CA, USA) was conducted from 10 PM of the first or second night after extubation to 7 AM of the next day. The respiratory polygraphy test included the measurement of airflow, oxygen saturation (SpO_2), and respiratory

KEY MESSAGES

- Our pilot study indicates that pre-stratification based on the use of corticosteroids and high-flow oxygen therapy should be applied in a future trial to evaluate postextubation sleep apnea in critically ill patients.
- In addition, the use of respiratory polygraphy in critically ill patients should be validated against polysomnography.

effort using an oronasal thermal sensor and nasal pressure transducer, pulse oximeter, and dual thoracoabdominal respiratory inductance plethysmography belt, respectively. In the setting of a single-bed room in our medical ICU, a physician connected the respiratory polygraphy device to the patient; however, the overnight recording was unattended.

Measurements

The following data were collected: age, sex, body mass index (BMI), and neck circumference; cardinal symptoms of sleep apnea including excessive daytime sleepiness, nonrestorative sleep, fatigue, insomnia, snoring, and witnessed apnea; snoring, tiredness, observed apnea, high blood pressure, BMI, age, neck circumference, gender (STOP-Bang) score; comorbidities and severity scores obtained from the Acute Physiology and Chronic Health Evaluation II (APACHE II), Simplified Acute Physiology Score (SAPS), and Sequential Organ Failure Assessment (SOFA) upon ICU admission; reason for and duration of mechanical ventilation, type and dose of corticosteroids, analgesics, sedatives, and muscle relaxants administered 48 hours prior to extubation, and methods of oxygen delivery during the night of respiratory polygraphy.

Apnea was defined as $\geq 90\%$ decrease in the peak signal excursion from the pre-event baseline using an oronasal thermal sensor for ≥ 10 seconds. If the signal of the oronasal thermal sensor was not reliable, the nasal pressure sensor was used as an alternative. Hypopnea was defined as $\geq 30\%$ decrease in peak signal excursion from the pre-event baseline using a nasal pressure sensor for ≥ 10 seconds and as $\geq 3\%$ oxygen desaturation from the pre-event baseline [14]. The monitoring time was calculated by subtracting the upright time from the total recording time. The respiratory event index (REI) was calculated as the number of apneas plus hypopneas divided by the monitoring time. A patient with $REI \geq 5/hr$ was diagnosed as having postextubation respiratory events. The oxygen desaturation index (ODI) was defined as episodes of $\geq 3\%$ oxygen desaturations per hour during the monitoring time.

Table 1. Detailed clinical characteristics of each patient

Patient no.	Age (yr)	Sex	BMI (kg/m ²)	Symptom				Neck circumference (cm)	STOP-Bang score	Comorbidity	APACHE II score	Duration of mechanical ventilation (day)	Reason for mechanical ventilation	In-hospital outcome
				EDS	Non-restorative sleep	Fatigue	Insomnia							
1 ^a	77	M	21.7	-	-	-	-	-	HTN, DM, multiple myeloma	35	7	Sepsis	Died 14 days after ICU discharge	
2	56	F	21.7	No	Yes	No	No	37.0	DM, post-lung TPL	21	2	Pneumonia	Survived	
3	58	M	26.2	No	Yes	No	No	39.0	Sarcoma	22	8	Pneumonia	Survived	
4	80	M	27.4	No	No	No	No	42.0	DM, CHF, CVD, AF, lung cancer	13	6	Pneumonia	Survived	
5	67	M	20.8	No	Yes	Yes	No	38.5	CHF, AF, COPD, LC	25	6	CHF	Survived	
6	83	M	14.3	No	No	No	No	38.0	NTM-PD	18	4	Pneumonia	Died 237 days after ICU discharge	
7	70	M	28.7	No	Yes	No	Yes	43.0	Post-lung TPL	15	3	Post-lung TPL	Survived	
8	75	M	25.5	No	No	No	No	45.0	IPF, vasculitis	35	8	Pneumonia	Died 13 days after ICU discharge	
9	69	F	24.9	Yes	Yes	Yes	Yes	40.0	OSA, asthma	20	5	Acute exacerbation of asthma	Survived	
10	74	M	22.5	Yes	Yes	No	No	38.0	Asthma, COPD, CKD, leiomyosarcoma	30	3	Pneumonia	Died 19 days after ICU discharge	

BMI: body mass index; EDS: excessive daytime sleepiness; STOP-Bang: snoring, tiredness, observed apnea, high blood pressure, body mass index, age, neck circumference, and gender; APACHE: Acute Physiology and Chronic Health Evaluation; HTN: hypertension; DM: diabetes mellitus; ICU: intensive care unit; TPL: transplantation; CHF: congestive heart failure; CVD: cardiovascular disease; AF: atrial fibrillation; COPD: chronic obstructive pulmonary disease; LC: liver cirrhosis; NTM-PD: nontuberculous mycobacterial pulmonary disease; IPF: idiopathic pulmonary fibrosis; OSA: obstructive sleep apnea; CKD: chronic kidney disease.

^aPatient 1 had missing data regarding symptoms, neck circumference, and STOP-Bang score.

RESULTS

Among the 65 patients who received mechanical ventilation for ≥ 24 hours and were extubated during the study period, 13 were enrolled in the present study. Regarding demographic characteristics, severity scores, reason and duration of mechanical ventilation, and length of ICU stay, differences between enrolled and non-enrolled patients were not observed

(Supplementary Table 1). Among the 13 patients, one was re-intubated due to acute deterioration before applying respiratory polygraphy. The other two patients were excluded from the analysis due to a monitoring time < 4 hours, which was attributed to the detachment of both oronasal thermal and nasal pressure sensors. The clinical characteristics of 10 patients (eight males and two females) are shown in Tables 1 and 2. The median age and BMI of the patients were 72 years and

Table 2. Clinical characteristics based on the presence of postextubation respiratory events

Variable	All patients (n = 10)	Patient with an REI $< 5/hr$ (n = 7)	Patient with an REI $\geq 5/hr$ (n = 3)
Age (yr)	72 (67–77)	74 (67–77)	69 (56–83)
Male sex	8 (80)	7 (100)	1 (33)
BMI (kg/m ²)	23.7 (21.7–26.2)	25.5 (21.7–27.4)	21.7 (14.3–24.9)
Neck circumference (cm) ^a	39 (38–42)	41 (39–43)	38 (37–40)
STOP-Bang score $\geq 3^a$	7 (70)	6 (86)	1 (33)
Charlson comorbidity index	5 (3–8)	6 (5–8)	2 (0–3)
Hypertension	1 (10)	1 (14)	0
Diabetes	3 (30)	2 (29)	1 (33)
Congestive heart failure	2 (20)	2 (29)	0
COPD	2 (20)	2 (29)	0
APACHE II score	22 (18–30)	25 (15–35)	20 (18–21)
SOFA score	6 (5–10)	9 (4–10)	5 (5–7)
SAPS II	48 (32–66)	54 (32–68)	46 (30–50)
Failure during the first intubation attempt	4 (40)	3 (43)	1 (33)
Internal diameter of the endotracheal tubes (mm)	7.5 (7.5–7.5)	7.5 (7.5–7.5)	7.5 (7.0–7.5)
Duration of mechanical ventilation (day)	6 (3–7)	6 (3–8)	4 (2–5)
Reason for mechanical ventilation			
Pneumonia	6 (60)	4 (57)	2 (67)
Acute exacerbation of asthma	1 (10)	0	1 (33)
Heart failure	1 (10)	1 (14)	0
Sepsis	1 (10)	1 (14)	0
Post-lung transplantation	1 (10)	1 (14)	0
Total drug equivalent dose administered 48 hours prior to extubation			
Remifentanyl (mg)	7.4 (4.2–10.6)	9.6 (4.2–22.1)	4.8 (1.8–9.6)
Propofol (mg)	0 (0–1,344)	0 (0–1,728)	0 (0–1,344)
Dexmedetomidine (mg)	1.1 (0.04–3.0)	0.8 (0.04–3.6)	1.5 (0–3.0)
Methylprednisolone (mg)	78 (0–120)	60 (0–160)	100 (0–120)
Method of oxygen delivery during the night of respiratory polygraphy			
Low-flow oxygen therapy via nasal prong	5 (50)	2 (29)	3 (100)
High-flow nasal cannula	5 (50)	5 (71)	0
FiO ₂	0.4 (0.3–0.5)	0.4 (0.4–0.6)	0.3 (0.3–0.4)
Flow (L/min)	23 (2–60)	40 (4–60)	2 (2–6)

Values are presented as median (interquartile range) or number (%).

REI: respiratory event index; BMI: body mass index; STOP-Bang: snoring, tiredness, observed apnea, high blood pressure, body mass index, age, neck circumference, and gender; COPD: chronic obstructive pulmonary disease; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; SAPS: Simplified Acute Physiology Score; FiO₂: fraction of inspired oxygen.

^aPatient 1 had missing data regarding neck circumference and STOP-Bang score.

23.7 kg/m², respectively. The median neck circumference was 39 cm, and seven of nine patients had a STOP-Bang score ≥ 3. All patients presented with at least one chronic disease and the median APACHE II score was 22. The median duration of mechanical ventilation was 6 days. Muscle relaxants or midazolam were not administered 48 hours prior to extubation. Propofol and dexmedetomidine were administered 48 hours prior to extubation to three and eight patients, respectively. Remifentanyl was used as an analgesic in all patients. Seven patients received systemic corticosteroids. The drug dose for each participant is listed in Table 3. During the night of respiratory polygraphy, all patients received supplemental oxygen. Specifically, five patients received high-flow nasal cannula (HFNC) therapy.

Table 3 shows the findings of respiratory polygraphy for each patient. All respiratory events were obstructive episodes. Three patients had REI ≥ 5/hr. None of the patients receiving HFNC therapy had REI ≥ 5/hr (Figure 1A). Furthermore, two (29%) of the seven patients who received corticosteroids and one (33%) of the other three who did not receive the drug had REI ≥ 5/hr (Figure 1B). All patients had episodes of SpO₂ < 90% although low- or high-flow oxygen therapy was provided, and one patient (patient 10) receiving HFNC therapy with a flow rate of 40 L/min and fraction of inspired oxygen (FiO₂) of 0.6 had SpO₂ < 90% during 20% of the monitoring time (Table 3). The median lowest SpO₂ was 86% (82%–87%) and the ODI varied from 0.1–14.7/hr.

Two of the three patients with REI ≥ 5/hr underwent type 1 attended in-laboratory PSG. At the time of PSG, the patients were medically stable after ICU discharge and did not require oxygen supplementation. Patient 2 was a 56-year-old female with diabetes mellitus who had received a lung transplantation due to connective tissue disease-associated interstitial lung disease (Sjogren’s syndrome) approximately 1 year ago. She was admitted to our medical ICU due to aspiration pneumonia with type 1 respiratory failure. Respiratory polygraphy was performed on the second night after extubation. She was treated with intravenous corticosteroids and oxygen supplementation via nasal prong during the type 3 sleep study. Her REI was 7.5/hr and the lowest SpO₂ was 74%. Furthermore, during the 537-minute monitoring period, the time spent with SpO₂ < 90% was 5 minutes and the ODI was 8.1/hr. Twelve days after ICU discharge, the patient underwent PSG and her Apnea-Hypopnea Index (AHI) was 7.6/hr. Patient 9 was 69 years old and had asthma and a history of pulmonary tuberculosis. She had used the continuous positive airway pressure machine after the diagnosis of OSA 8 years previously, howev-

Table 3. Drug doses, methods of oxygen delivery, and results of respiratory polygraphy

Patient no.	Total drug equivalent dose administered 48 hours prior to extubation			Method of oxygen delivery during the night of respiratory polygraphy				REI (/hr)	Mean SpO ₂ (%)	Lowest SpO ₂ (%)	Time spent (%) with SpO ₂ < 90%	ODI (/hr)
	Remifentanyl (mg)	Propofol (mg)	Dexmedetomidine (mg)	Methylprednisolone (mg) ^a	Device	Flow rate (L/min)	FiO ₂ of HFNC					
1	5.3	0	2.9	0	Low-flow via nasal prong	4	-	1.1	92	83	5.9	3.5
2	1.8	0	3.0	100	Low-flow via nasal prong	6	-	7.5	97	74	1.0	8.1
3	10.6	0	0.7	160	HFNC	60	0.6	2.1	93	85	1.5	2.0
4	9.6	0	2.0	60	HFNC	60	0.4	0.3	93	86	4.4	0.3
5	2.0	0	0.04	0	Low-flow via nasal prong	2	-	0.8	98	86	0.2	1.8
6	4.8	0	1.5	0	Low-flow via nasal prong	2	-	8.8	97	87	0.3	5.0
7	22.1	4,722	0.8	250	HFNC	40	0.4	0.1	93	87	1.8	0.1
8	26.4	0	3.6	96	HFNC	60	0.5	0.1	94	88	0.2	0.3
9	9.6	1,344	0	120	Low-flow via nasal prong	2	-	7.7	92	75	13.3	14.7
10	4.2	1,728	0	40	HFNC	40	0.6	0.4	90.8	82	19.4	1.5

FiO₂: fraction of inspired oxygen; HFNC: high-flow nasal cannula; REI: respiratory event index; SpO₂: oxygen saturation; ODI: oxygen desaturation index.

^aSix of the seven patients who were treated with corticosteroids received methylprednisolone intravenously. Patient 10 received 50 mg hydrocortisone intravenously four times for 48 hours prior to extubation. Five of the seven patients who received corticosteroids were treated with long-term corticosteroid therapy. The remaining two patients, patients 4 and 10, were treated with corticosteroids for 15 days and 2 days, respectively.

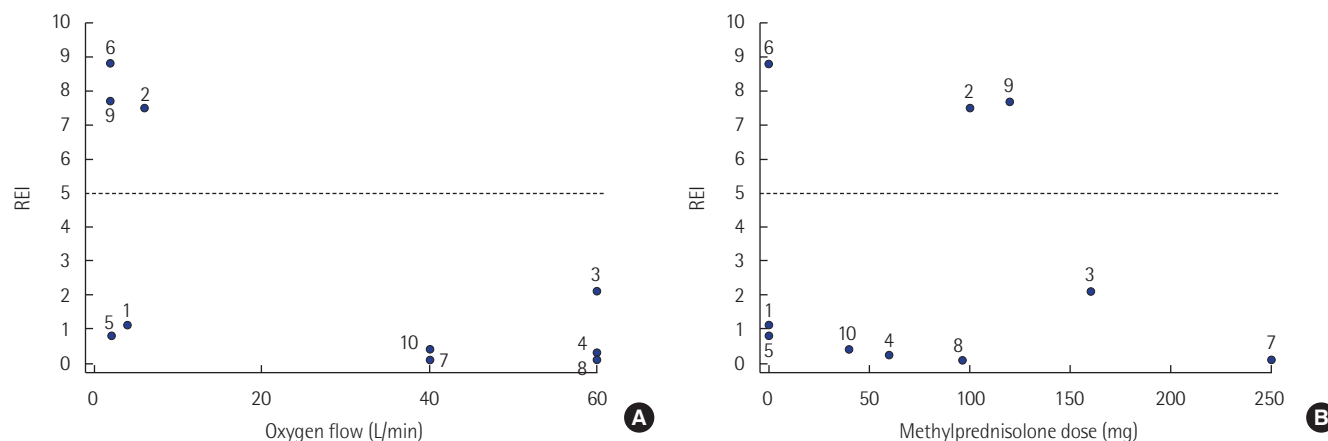


Figure 1. Scatter plots of the postextubation respiratory event index (REI) and (A) the flow rate of oxygen during the night of respiratory polygraphy, and (B) the equivalent dose of methylprednisolone administered 48 hours prior to extubation.

er, the use of the device was discontinued due to intolerance. The patient was then admitted to our medical ICU and treated with mechanical ventilation due to type 2 respiratory failure caused by an acute exacerbation of asthma. Respiratory polygraphy was conducted on the first night after extubation. She was treated with intravenous steroid and oxygen supplementation *via* nasal prong during the study. Her REI was 7.7/hr and the lowest SpO₂ was 75%. During the 536-minute monitoring period, the time spent with SpO₂ <90% was 54.8 minutes and the ODI was 14.7/hr. When the patient underwent PSG 9 days after ICU discharge, her AHI was 10.7/hr.

DISCUSSION

In this prospective pilot study, three of 10 patients admitted to the medical ICU had postextubation respiratory events on the first or second night after extubation from mechanical ventilation. Furthermore, the patients experienced frequent oxygen desaturation during those nights. In previous studies conducted in the ICU, the prevalence of postextubation sleep apnea in Caucasians was reportedly approximately 70% [8,15,16]. The low rate of postextubation respiratory events in the current study could be explained in several ways. First, different types of the sleep study (type 3 vs. type 1) and study populations (medical vs. surgical ICU patients, Asians vs. Caucasians) could produce different results. Respiratory polygraphy may result in an underestimation of the severity of sleep apnea because the estimation of REI using this device is based on the monitoring time rather than total sleep time. Furthermore, PSG allows for the scoring of hypopnea based on SpO₂ as well as arousal [17,18].

Second, the seven patients (70%) in the present study received systemic corticosteroids, which were administered

throughout the ICU stay including the pre-extubation and postextubation periods. The use of corticosteroids can reduce upper airway edema caused by mucosal injury and can prevent airway obstruction after extubation [19,20]. Although the seven patients received corticosteroids for reasons other than laryngospasm or laryngeal edema (e.g., immune modulator), the use of corticosteroids before extubation might have an effect on upper airway edema in the present study.

Third, the relatively low rate of postextubation respiratory events could be explained by the extensive use of HFNC. In the present study, half of the patients received HFNC therapy, and all patients receiving HFNC had REI <5/hr. In several studies, HFNC reduced arousals and AHI, and improved oxygenation in both children and adults [21-25]. The mechanism of action is apparently an increase in end-expiratory pharyngeal pressure which reduced upper airway obstruction [22,26].

In the present study, the patients with REI <5/hr had a high STOP-Bang score and were more likely to be male and older and have higher BMI and neck circumference than patients with REI ≥5/hr. Furthermore, the patients with REI <5/hr appeared to be more severely ill and have more comorbidities and longer duration of mechanical ventilation. The frequent use of HFNC in more severely ill patients might lead to a low rate of postextubation respiratory events.

The present study had several limitations. First, the pilot study was limited by a small sample size. Second, although a cuff leak test before extubation was routinely performed, an evaluation of the upper airway after extubation was not consistently implemented. Third, prolonged wake after sleep onset, as a reflection of sleep fragmentation, is commonly observed in patients admitted to the ICU [27]. Because sleep architecture was not evaluated, and total sleep time could not

be accurately assessed, the occurrence of postextubation sleep apnea may have been underestimated [17,18]. Based on this limitation, the lights were turned off and noise and patient-care activities (e.g., nursing rounds and blood tests) reduced in the setting of a single-bed room to promote sleep at night. Finally, as a diagnostic tool in critically ill patients, respiratory polygraphy has not been validated but is not inferior to PSG in diagnosing uncomplicated OSA in the general population [17, 28]. Nonetheless, the REI and AHI obtained using respiratory polygraphy and PSG, respectively, were similar in the two patients in our study.

To evaluate postextubation sleep apnea with respiratory polygraphy in critically ill patients, a future main trial with adequate power should be conducted. The present pilot study results indicate pre-stratification based on the use of corticosteroids and HFNC should be applied. In addition, the use of respiratory polygraphy in critically ill patients should be validated against PSG.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Conceptualization: JL, JC. Data curation: YJL. Formal analysis: YJL. Methodology: YJL, SML, JL. Project administration: SML, JL. Visualization: YJL. Writing—original draft: YJL. Writing—review and editing: JC, SML, JL.

SUPPLEMENTARY MATERIALS

Supplementary materials can be found at <https://doi.org/10.4266/acc.2020.00479>.

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Supplementary Table 1. Clinical characteristics of patients enrolled and not enrolled during the study period

Variable	Unenrolled patient (n=52)	Enrolled patient (n=13)	P-value
Age (yr)	66 (57–77)	70 (60–75)	0.35
Male sex	28 (54)	10 (77)	0.13
Body mass index (kg/m ²)	23.2 (19.8–25.4)	24.9 (21.7–25.7)	0.23
APACHE II score	23 (17–30)	25 (20–35)	0.37
SOFA score	9 (5–13)	9 (5–12)	0.99
SAPS II	50 (34–70)	54 (39–66)	0.79
Reason for mechanical ventilation			0.26
Respiratory	37 (71)	9 (69)	
Cardiovascular	13 (25)	2 (15)	
Sepsis or septic shock	2 (4)	2 (15)	
Duration of mechanical ventilation (day)	3 (2–6)	5 (3–7)	0.17
Length of ICU stay (day)	6 (3–10)	8 (6–10)	0.27

Values are presented as median (interquartile range) or number (%).

APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; SAPS: Simplified Acute Physiology Score; ICU: intensive care unit.