pagepress

Impact of neurological problems on mechanical ventilation and intensive care unit outcomes in pulmonary intensive care unit patients: a retrospective analysis of a single-center cohort

Zeynep Çınar,[1] Eda Macit Aydın,[1] Nurgul Naurzvai,[2] Ayshan Mammadova,[2] Sümeyye Kodalak,[2] Aygül Abbasova,[2] Gül Gürsel[2]

[1]Division of Critical Care Medicine, Department of Anesthesiology, Gazi University School of Medicine, Ankara; [2]Division of Critical Care Medicine, Department of Pulmonary Medicine, Gazi University School of Medicine, Ankara, Turkey

Correspondence: Zeynep Çınar, Division of Critical Care Medicine, Department of Anesthesiology, Gazi University School of Medicine, Safety District, Mevlana Boulevard No: 29, 06560 Ankara, Turkey.
Tel.: +90 5055578982.
Tel.: +90 (312) 202 40 00.
E-mail: zeynepsahin1980@gmail.com

Key words: intensive care outcomes, neurological problems, mechanical ventilation.

Contributions: concept and design; GG, ZÇ, administrative support; None, collection and assembly of data; ZÇ, EMA, NN, AM, SK, AA, data analysis and interpretation; GG, manuscript writing; GG, ZÇ, final approval of manuscript: GG, ZÇ, EMA, NN, AM, SK, AA

Conflict of interest: no potential conflict of interest was reported by the authors.

Ethics approval and consent to participate: the study was approved by the ethics committee of Gazi University Medical Faculty (ethics committee approval number and date: 868, November 23, 2020).

Informed consent: written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in the future, at the time of data acquisition.

Patient consent for publication: not applicable.

Funding: the authors reported there is no funding associated with the work featured in this article.

Availability of data and materials: the datasets used and/or analyzed during the current study are available from the corresponding author upon acceptable request.

Received: 9 December 2022.
Accepted: 11 April 2023.
Early view: 19 April 2023.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Licensee PAGEPress, Italy
Monaldi Archives for Chest Disease 2024; 94:2506
doi: 10.4081/monaldi.2023.2506

Abstract

Neurological problems (NPs) are frequently connected with different critical illnesses in intensive care unit (ICU) patients, and they may influence ICU outcomes. This study aims to examine the effects of NPs on ICU outcomes, especially in pulmonary ICU patients. This is a retrospective observational study comprising adult pulmonary critical care patients who were hospitalized between 2015 and 2019. The frequency of NPs at admission, their impact on mechanical ventilation (MV), ICU outcomes, the rate of NP development during the ICU stay, and risk factors for them were investigated. A total of 361 patients were included in the study, and 130 of them (36%) had NPs (group 1). The noninvasive ventilation requirement rate in patients with NPs was less than in those without NPs (group 2), and the requirement of MV was significantly more frequent in this group (37% and 19%, p<0.05). The duration of MV (19±27 and 8±6 days, p=0.003) and sepsis rate (31% and 18%, p=0.005) were also higher in group 1. NPs developing after ICU admission increased the MV requirement 3 times as an independent risk factor. Risk factors for ICU-acquired NPs were the existence of sepsis during admission [odds ratio (OR): 2.01, confidence interval (CI) 95%: 1.02-4, p=0.045] and longer MV durations before ICU admission (OR: 1.05, CI 95%: 1.004-41.103, p=0.033). NPs were not independent risk factors for mortality (OR: 0.67, CI 95%: 0.37-1.240, p=0.207). NPs did not increase mortality but more frequently caused MV requirement, more extubation failure, and a longer ICU stay in this study population. Additionally, our data suggest that having sepsis during admission and a longer length of MV prior to admission may increase the neurological complication rate.

Introduction

There are numerous risk factors for neurological destruction in critically ill patients. These factors may be caused by the patient, such as acid-base disorders, sepsis, acute respiratory distress syndrome, hypoglycemia, and electrolyte disorders. It may also be the result of intensive care unit (ICU) treatments such as mechanical ventilation (MV) and the use of uncontrolled sedatives and neuromuscular drugs. Secondary organ dysfunctions that develop as a result of metabolic changes, such as hypoxia and hypotension, cause further disruption of brain dysfunction [1,2]. This situation is described by acute changes in mind ranging from delirium to

coma. Critically ill patients with respiratory failure require longer MV and ICU stays. These conditions are accompanied by increased ICU complications, including infectious and neurological ones [2].

Neurological problems (NPs) may be associated with preexisting comorbid conditions, critical illnesses, and medications used [3]. They may also occur in critically ill patients other than those in neurology intensive care and have prominent prognostic outcomes [4]. Patients admitted to the pulmonary ICU due to respiratory problems make up a special population as it may require prolonged MV, sedation, steroids, anticoagulants, antiaggregants, and a long hospital stay. The rate of development of NPs and predisposing risk factors after admission to the ICU in this patient group are uncertain. Furthermore, the impact of preexisting NPs on ICU outcomes in this population is unknown.

In this study, we planned to investigate whether NPs have an additional effect on ICU outcomes in pulmonary ICU patients and the risk factors for the development of NPs after admission to the ICU.

Materials and Methods

This is a retrospective observational study comprising adult critical pulmonary patients who were hospitalized in the tertiary ICU of Gazi University Medical Faculty Hospital, Ankara, Turkey, between January 1st, 2015, and December 31st, 2019. The patients included in the study had multiple diagnoses, and all of them had pulmonary problems. Pregnancy, patients under 18 years of age who stayed in the ICU for less than 48 hours, and patients with incomplete data were not included in this study.

All data were obtained from the Nucleus Data System of our hospital by research assistants. The data were first recorded in a case report form and then transferred to the SPSS database for analysis.

Definition of NPs: neurological diseases, including cerebrovascular diseases (CVD), Alzheimer's, Parkinson's, neuromuscular diseases, delirium, and ICU-acquired weakness (ICUAW), can exist before and during admission and develop after ICU admission.

Pulmonary comorbidities were chronic obstructive pulmonary disease (COPD), interstitial lung diseases, and bronchiectasis; cardiac comorbidities were congestive heart failure, hypertension, coronary arterial disease, and atrial fibrillation.

To compare the characteristics of MV and infections in the patients, noninvasive mechanical ventilation (NIMV), invasive mechanical ventilation (IMV), weaning properties, tracheostomy rates, sepsis, and pulmonary and urinary tract infection rates were recorded (Table 1).

Definitions

Patients with NPs were classified as group 1 and those with no NPs as group 2. If NPs develop after admission to the ICU, they are classified as post-ICU NPs.

The presence of delirium in patients was recorded according to the consultation notes that show evaluations based on the confusion assessment method for the ICU criteria [5].

ICUAW in patients who are critically ill commonly appears in three ways: polyneuropathy, myopathy, and/or muscle atrophy. ICUAW was based on patient data from assessments by neurologists and physiotherapists using standardized, validated measurements such as manual muscle strength testing to measure muscle weakness [6,7]. Patients were evaluated according to the weaning consensus of 2007. Simple weaning/difficult weaning/prolonged weaning/extubation failure (EF): reintubation within 48 hours after successful extubation [8]. We defined organ dysfunction according to the sequential organ failure assessment score [9].

In our study, sepsis was evaluated based on the sepsis criteria defined in 2021 [10]. Hospital-acquired pneumonia and ventilator-associated pneumonia (VAP) definitions were based on descriptions made by the American Infectious Diseases Society and the American Thoracic Society in 2016 [11]. Symptomatic urinary tract infection was defined according to the urinary tract infection classification made by the European Urology Association [12].

Table 1. Mechanical ventilation and infectious characteristics of the patients.

	Group 1 n=130 (36%)	Group 2 n=231 (64%)	p value
MV characteristics of the patients			
NIV requirement before ICU admission, n (%)	20%	31%	*0.029
MV requirement before ICU admission, n (%)	20%	11%	*0.020
MV duration before ICU admission, days**	15±23	7±6	*0.046
MV requirement during ICU admission, days**	37%	19%	*0.0001
Total duration of MV, days**	19±27	8±6	*0.003
EF, n (%)	15%	4%	*0.0001
Tracheostomy, n (%)	7%	0%	0.001
Infectious characteristics of the patients			
Sepsis rate at ICU admission, n (%)	31%	18%	*0.005
Sepsis rate after ICU admission, n (%)	16%	8%	*0.022
Sepsis development day after ICU admission**	17±16	8±6	*0.024
Pulmonary infection rate after admission, n (%)	38%	15%	*0.0001
Urinary tract infection rate after admission n (%)	9%	4%	*0.020
ICU outcome of the patients			
Length of ICU stay**	21±25	9±9	*0.0001
Length of ICU stay >10 days, n (%)	59%	26%	*0.0001
ICU mortality, n (%)	33%	18%	*0.001

Group 1, patients with neurological problems; group 2, patients without neurological problems; n, number of the patients; MV, mechanical ventilation; NIV, noninvasive ventilation; ICU, intensive care unit; EF, extubation failure; *according to p values there is a statistically significant difference; **mean values ± standard deviation.

Statistical analysis

The chi-square test and Student's *t*-test were used to compare rates and means, respectively. Receiver operating characteristic curve analysis was used to calculate cut-off points for acute physiology and chronic health evaluation II (APACHE II) level for mortality and length of ICU stay.

Logistic regression analysis was used to assess whether NPs were independent risk factors for mortality, longer ICU stays, the requirement of MV and EF, and to determine risk factors for ICU-acquired NPs.

Results

The study consisted of 361 patients. Their demographics are given in Table 2. The reason for admission to the ICU in 55% of these patients was respiratory failure. 36% of the patients (n=130) had NPs, and 68 of them (19%) developed NPs after ICU admission. Neurologic complications appearing after ICU admission developed an average of 9.6±8.5 [median: 7 (2-27)] days after admission (Table 3).

The diagnosis of patients at admission included respiratory failure in 200 (55%), pneumonia in 124 (34%), acute exacerbation of COPD in 108 (30%), decompensated heart failure in 66 (18%), sepsis in 54 (16%), pulmonary thromboembolism in 36 (10%), acute renal failure in 36 (10%), urinary infection in 25 (7%), trauma in 6 (2%), and others in 15 (4%).

Table 3 shows NPs developed during and before admission to intensive care, as well as after admission to intensive care.

Infections in the patient population

When infectious findings were analyzed, the rate of sepsis before and after admission to the ICU was remarkably higher in group 1 patients. Urinary and pulmonary infections were also significantly higher in these patients ($p<0.05$) (Table 1).

Invasive and noninvasive mechanical ventilation characteristics of the patients

NIMV requirement before and during ICU admission was less in group 1 than in group 2 (Table 1). The need for MV before and after ICU admission was quite higher in group 1 ($p<0.05$). NPs increased the risk of MV requirement after ICU admission more than 3 times as an independent risk factor (p=0001). The duration of MV was seriously longer in group 1 (Table 1). EF was significantly more prevalent in this group, and NPs were independent risk factors for EF, increasing the risk 3 times (Table 4). Tracheostomy rates were also higher in patients with NP [9(7%) d 0(0%) p=0.001] (Table 1).

Table 2. Demographics and intensive care unit characteristics of the patients.

	Group 1 n=130 (36%)	Group 2 n=231 (64%)	p values
Demographics**			
Age	73±14	69±15	*0.013
BMI kg/m^2	27±7	28±7	0.181
APACHE II	23±7	20±8	*0.001
SOFA	5±3	4±3	*0.0001
GCS	11±4	13±3	*0.0001
Comorbidities, n (%)			
Pulmonary	57%	59%	0.649
Cardiac	69%	73%	0.437
DM	35%	28%	0.174
Renal	9%	7%	0.572
Malignancy	24%	19%	0.256

Group 1, patients with neurological problems; group 2, patients without neurological problems; BMI, body mass index; APACHE II, acute physiology and chronic health evaluation II; SOFA, sequential organ failure assessment; GCS, Glasgow coma scale; DM, diabetes mellitus. Because of multiple admission diagnosis and comorbidities total percentages are >100%; *according to p values there is a statistically significant difference; **mean values ± standard deviation.

Table 3. Neurological comorbidity and acute neurological event, post-intensive care unit neurological complications.

Diseases, n (%)	Neurological problems exist before ICU admission n=62 (17%)	Neurological problems developed after ICU admission n=68 (19%)
CVD	28 (45)	7 (10)
Seizure	7 (11)	-
Alzheimer/Dementia	16 (26)	-
Parkinson	6 (1)	-
ICU acquired weakness	-	39 (57)
Delirium	-	22 (32)
Neuromuscular diseases	5 (8)	-

n, number of the patients in each group; CVD, cerebrovascular diseases; ICU, intensive care unit.

Risk factors for intensive care unit-acquired neurological problems

The presence of sepsis, the need for IMV, and high APACHE II scores during admission to the ICU were identified as risk factors for the development of NPs in the ICU (p<0.05) (Table 4).

Intensive care unit outcomes

NPs were not independent risk factors for mortality [odds ratio (OR): 0.67, confidence interval (CI) 95%: 0.37-1.240, p=0.207). The presence of NPs prolonged the duration of stay in the ICU significantly and increased the risk of stay in the ICU for more than 10 days by 3 times (OR: 3.48, CI 95%: 2.168-5.617, p=0.0001) (Table 4).

Discussion

The results of this study showed that NPs that patients had during ICU admission or developed during ICU had an important impact on ICU morbidity but not mortality. In this study, we particularly investigated the effects of NPs on MV and weaning in our study population and compared them with the literature. 130 (36%) patients had NPs in this study population. 62 of them (17%) had developed before ICU admission, and 68 (19%) had developed after ICU admission. We corrected it in Table 3 as well.

In a study by Park *et al*., in which they investigated the effects of neurological diseases on ICU outcomes, in 52 ICU patients infected with COVID-19, the rate of patients with pre-existing neurological disease was (n=19) 36.5%, and the rate of newly developed neurological damage in ICU follow-up was (n=23) 44.5% [13]. The high rate of newly developing NPs in ICU follow-up in this study may be due to two reasons. Firstly, the number of patients in the ICU was lower than the one in our study. Secondly, it may be that coagulopathy due to COVID-19 disease predisposes to NPs. Patients with NPs required MV more frequently than patients without NPs. In the same study, while the need for NIMV did not differ significantly between the group with neurological disease (group 1) and the group without neurological disease (group 2) (28% and 25%, p=1), it was significantly higher in group 1 in need of IMV compared to group 2 (52.6% and 39.4%, p=0.015). Since the Glasgow coma scale (GCS) was lower in group 1 than in group 2, it may be thought that NIMV cannot be tolerated by the patients. On the other hand, patients with NPs may not be able to control their airways, and they may face the risk of aspiration more frequently. Therefore, the rate of IMV may have been significantly higher in group 1 than in group 2. This supports our results [13].

According to the study conducted by Harder *et al.*, 35% of the 1349 patients admitted to the ICU needed MV. The MV requirement due to NPs was reported as 22%, which was lower than the result we obtained (37%) because the number of patients with chronic pulmonary problems or respiratory failure was higher in our study population [14]. The requirements and complications of MV were very high in patients with NPs, and NPs were independent risk factors for EF. Respiratory work is a phenomenon that involves the respiratory center, lungs, and respiratory muscles. A disorder in any of these steps makes breathing difficult. Many critically ill ventilated patients have weakness of the respiratory muscle, prolonged weaning from the ventilator, and an increased length of ICU and hospital stay [15]. Respiratory muscle weakness, bronchospasm, and an overdose of narcotics can cause weaning failure [16]. It was found that the EF rate was as high as 38% in a series that included only patients with brain damage [17]. In our study, the rate of unsuccessful extubation was found to be 15% in patients with NPs and 4% in patients without NPs (p<0.05). In a prospective study of 123 general ICU patients by Kifle *et al*., the EF rate was found to be 34.15% [18]. The EF rate in this study was also found to be higher than our results. This may be due to the fact that the patients participating in the study had different severity of critical illness, advanced age, and different treatment protocols that could directly affect weaning, for example, liberal or conservative use of fluid therapy or long-term infusion of neuromuscular agents.

It was reported in a review by Salluh *et al*. that patients with delirium as NPs had a mean duration of MV 1.79 days longer than those without delirium (OR: 1.79, CI 95%: 0.31-3.27, p<0.001) [19]. In our study, the mean total duration of MV was 19 days in group 1 and 8 days in group 2 (p=0.003). Although our results support the literature, the total duration of MV was found to be longer than the literature. This may be related to the high rate of detection of more severe NPs, such as ICUAW and CVD, other than delirium, in our study population. On the other hand, in our study population, the GCS of the patients in group 1 was lower than in group 2. This may explain the longer total MV duration in group 1.

Another study showed that patients with unsuccessful weaning

Table 4. Risk factor analysis for intensive care unit outcomes.

Risk factors for mortality	OR (CI 95%)	p value
Neurological problems	0.678 (0.370-1.240)	0.207
Sepsis during ICU admission	4.177 (2.222-7.854)	*0.0001
IMV necessity during admission	5.292 (2.862-9.786)	*0.0001
APACHE II >13	11.732 (1.524-90.33)	*0.018
Risk factors for post-ICU MV necessity		
Neurological problems	3.426 (2.022-5.804)	*0.0001
APACHE II >13	19.32 (2.61-142.79)	*0.004
Sepsis during ICU admission	1.344 (0.745-2.424)	0.326
Risk factors for extubation failure		
Neurological problems	3.104 (1.327-7.256)	*0.009
Sepsis during ICU admission	3.481 (1.542-7.858)	*0.003
Risk factors for ICU stay longer than 10 days		
Neurological problems	3.489 (2.168-5.617)	*0.0001

OR, odds ratio; CI, confidence interval; ICU, intensive care unit; MV, mechanical ventilation; IMV, invasive mechanical ventilation; APACHE II, acute physiology and chronic health evaluation II; *according to p values there is a statistically significant difference.

had a seven-fold increased risk of death, 31 times more economic losses, hospitalizations lasting longer than 14 days, and 6 times more need for palliative care [20]. In our study, longer ICU stay time (21±25, p=0.003), higher EF rates (15%, p=0.0001), higher tracheostomy application rates (7%, p=0.0001), and higher mortality rates (33%, p=0.001) were found in group 1. Our results are consistent with the literature. Long hospital stays and long-term MV applications will bring high costs.

Not surprisingly, infectious complications, particularly pulmonary and urinary infections, were significantly higher in group 1 (38% and 15%, p=0.0001). Pulmonary infections develop more frequently in immobilized patients who cannot cough adequately and are one of the leading causes of death [21]. Pneumonia increases hospital stays and mortality, and it mainly develops due to aspiration. The VAP rate studied by Harde *et al.* in critically ill neurological patients was found in 18 (18%) of the 102 patients who were intubated for neurological reasons [14]. In our study, 48 patients in group 1 developed MV needs during ICU hospitalization, and 37% of them developed a pulmonary infection. The pulmonary infection rate that we found in our study was high compared to the literature, probably due to the higher frequency of chronic pulmonary disease in our study population.

One of the most common complications after stroke is urinary tract infections. Various studies have reported that it is seen in 15-60% of patients after stroke [22]. In our study, urinary tract infection was observed at a rate of 9% in patients with NPs after admission to the ICU, and 4% in patients without NPs (p=0.020) Although this rate is not close to the literature due to the differences in patient population, the fact that the frequency of urinary infections in group 1 was higher than in group 2 supports the literature.

Bleck *et al*. reported that 12.3% of 1758 medical ICU patients admitted during a 2-year study period developed neurological complications, and these complications were most commonly associated with sepsis (38.8%) [4]. In previous studies, more than 30% of patients with sepsis were reported to have epileptiform movements or slow activity on electroencephalography [23]. The combination of sepsis with multiple organ failure may contribute to unconsciousness [24]. In our study, the rate of sepsis in patients with NPs (31%) was more frequent than in those without NPs (18%), and it was statistically significant (p=0.005). However, we found that sepsis increased the need for MV (p=0.003) and mortality as an independent risk factor in patients with NPs (p=0.0001).

Previous studies have shown that between 4.4% and 15% of all strokes are detected during follow-up and treatment in hospitals [4,25]. This may be due to various conditions, such as discontinuation of antithrombotic drugs, heart diseases, vascular invasive procedures, immobilization, or fever [26]. In our study, CVD was detected in 28 (45%) patients during hospitalization in the ICU. CVD developed in 7 (10%) patients during ICU follow-up. While more patients had a stroke during admission and were admitted because of stroke complications, 10% of patients developed a stroke during their ICU stay. Some of them were probably related to anticoagulant complications. Renal and hepatic failure and drug interactions frequently influence anticoagulant levels in ICU patients. On the other hand, critical patients may have a tendency to both bleeding and thrombosis due to sepsis, uremia, bone marrow suppression, and many other reasons. Our results suggest that maximum effort should be made for this purpose.

In critically ill patients, new-onset seizures occur in 0.8% to 4% of patients and are widely focal. It is often associated with metabolic disorders, sepsis, organ failure, and drugs [13,27]. In our study, the rate of epileptic seizures developing during admission to the ICU and follow-up in the ICU was 11%. Post-arrest admission, drugs, and severe hypoxemia persistent to MV treatment were the most frequent reasons causing seizures in our study population.

ICUAW in the combination of sepsis and multi-organ dysfunction syndrome was found to be 46% (CI 95%: 43-49%) [27]. In a systematic review of 31 studies, it was reported that the median prevalence of ICUAW was 43% [28]. In our study, 57% (n=39) of the 68 patients who developed NPs after admission to our ICU developed ICUAW.

Salluh *et al*. identified 42 studies involving a total of 16,595 patients [19]. Delirium was detected in about one-third of ICU patients. It developed in 32% of our study population; this finding is consistent with the literature. In a review investigating the incidence and prevalence of delirium in adult ICUs in 2018, it was found that delirium was higher in the population with higher disease severity [21]. In our study, the patients with NPs were also older and had more severe diseases at presentation (Table 2).

In 28 published studies, patients with delirium had longer ICU hospitalizations than those without delirium [7]. In one study, it was found that patients with neurological complications had 2.5 times longer stay in the ICU and 2 times longer stay in the hospital than patients without neurological complications [26]. In our study, NPs appear to be an independent risk factor that prolongs the length of stay in the ICU. This may be due to MV requirements, infections, delirium, and ICUAW. In addition, obtaining family consent for a tracheostomy and performing the procedure afterward may extend the length of stay in the hospital.

In the study of Bleck *et al.,* 12.3% of 1758 patients developed neurological complications, and neurological complications were associated with increased disability, longer hospital stays, and increased mortality [4].

Despite many studies [13,19] reporting NPs as an independent risk factor for ICU mortality, we did not reach the same result. In our study, mortality was 33% in the patient group with NPs, while it was 18% in the group without NPs (p=0.001). On the other hand, NPs were not independent risk factors affecting mortality (p=0.207). The most likely explanation for this result may be the existence of higher ICU infection and sepsis rates and more frequent MV requirements in this group. In multivariate analysis, we found sepsis and MV to be independent risk factors for mortality. The second possible explanation is that if the patient does not have problems such as sepsis and other organ failures that will cause high mortality, these patients can be referred from ICU to home or private care centers with home MV treatment, and this may lead to a decrease in ICU mortality. Lastly, in recent years, advances in the follow-up and treatment of critically ill patients, especially early sepsis diagnosis and treatment efforts, strategies to prevent diaphragm damage associated with ventilation, and the sensitivity of clinicians in enteral nutrition have increased. For these reasons, the presence of NPs may not be an independent risk factor for mortality.

Limitations

Since our study is retrospective, we have a high probability of missing some neurological patients. In addition, we could not find any data to classify encephalopathies as hepatic, hypoxic, uremic, or hypercapnic encephalopathies.

Conclusions

Our results suggest that NPs may increase the necessity of MV, which may cause an increase in EF and a longer ICU stay but not mortality. Improved ICU and post-ICU care and technological

development may cause this result. More detailed prospective studies are needed to evaluate the effects of NPs on MV and ICU outcomes and to determine exactly which factors predispose to the development of NPs during ICU follow-up.

References

1. Gu M, Mei XL, Zhao YN. Sepsis and cerebral dysfunction: BBB damage, neuroinflammation, oxidative stress, apoptosis and autophagy as key mediators and the potential therapeutic approaches. Neurotox Res 2021;39:489-503.
2. Smith M, Meyfroidt G. Critical illness: the brain is always in the line of fire. Intensive Care Med 2017;43:870-3.
3. Barlas I, Oropello JM, Benjamin E. Neurologic complications in intensive care. Curr Opin Crit Care 2001;7:68-73.
4. Bleck TP, Smith MC, Pierre-Louis SJ, et al. Neurologic complications of critical medical illnesses. Crit Care Med 1993;21:98-103.
5. Khan BA, Perkins AJ, Gao S, et al. The confusion assessment method for the ICU-7 delirium severity scale: a novel delirium severity instrument for use in the ICU. Crit Care Med 2017; 45:851-7.
6. Jolley SE, Bunnell AE, Hough CL. ICU-acquired weakness. Chest 2016;150:1129-40.
7. Symeonidou Z, Theodoraki K, Chalkias Athanasios A, et al. Critical illness polyneuropathy (CIP): a multicenter study on functional outcome. G Ital Med Lav Ergon 2019;41:58-64.
8. Boles JM, Bion J, Connors A, et al. Weaning from mechanical ventilation. Eur Respir J 2007;29:1033-56.
9. Jones AE, Trzeciak S, Kline JA. The sequential organ failure assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. Crit Care Med 2009;37:1649-54.
10. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021;47:1181-247.
11. Kalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;9:63:e61-111.
12. Johansen TE, Botto H, Cek M, et al. Critical review of current definitions of urinary tract infections and proposal of an EAU/ESIU classification system. Int J Antimicrob Agents 2011;38:64-70.
13. Park J, Kwon YS, Kim HA, et al. Clinical implications of neurological comorbidities and complications in ICU patients with COVID-19. J Clin Med 2021;10:2281.
14. Harde Y, Manimala Rao S, Sahoo J, et al. Detection of ventilator associated pneumonia, using clinical pulmonary infection score (CPIS) in critically ill neurological patients. J Anesthesiol Clin Sci 2013;2:20.
15. Jonkman AH, Jansen D, Heunks LM. Novel insights in ICU-acquired respiratory muscle dysfunction: implications for clinical care. Crit Care 2017;21:64.
16. Jung B, Vaschetto R, Jaber S. Ten tips to optimize weaning and extubation success in the critically ill. Intensive Care Med 2020;46:2461-3.
17. Asehnoune K, Seguin P, Lasocki S, et al. Extubation success prediction in a multicentric cohort of patients with severe brain injury. Anesthesiology 2017;127:338-46.
18. Kifle N, Zewdu D, Abebe B, et al. Incidence of extubation failure and its predictors among adult patients in intensive care unit of low-resource setting: a prospective observational study. PLoS One 2022;17:e0277915.
19. Salluh JI, Wang H, Schneider EB, et al. Outcome of delirium in critically ill patients: systematic review and meta-analysis. BMJ 2015;350:h2538.
20. Epstein SK, Ciubotaru RL. Independent effects of etiology of failure and time to reintubation on outcome for patients failing extubation. Am J Respir Crit Care Med 1998;158:489-93.
21. Krewulak KD, Stelfox HT, Leigh JP, et al. Incidence and prevalence of delirium subtypes in an adult ICU: a systematic review and meta-analysis. Crit Care Med 2018;46:2029-35.
22. Ayşe G, Nilda T, Suat T, et al. Stroke complications management in intensive care unit. Turk J Cerebrovasc Dis 2015;3:153-60.
23. Oddo M, Carrera E, Claassen J, et al. Continuous electroencephalography in the medical intensive care unit. Crit Care Med 2009;37:2051-6.
24. Warrior L, Bleck PT. Neurological emergencies in the intensive care unit. Clin Pulm Medi 2019;26:53-60.
25. Kelley RE, Kovacks AG. Mechanism of in-hospital cerebral ischemia. Stroke 1986;17:430-3.
26. Nadav L, Gur AY, Korczyn AD, Bornstein NM. Stroke in hospitalized patients: are there special risk factors? Cerebrovasc Dis 2002;13:127-31.
27. Stevens RD, Dowdy DW, Michaels RK, et al. Neuromuscular dysfunction acquired in critical illness: a systematic review. Intensive Care Med 2007;33:1876-91.
28. Ortega-Gutierrez S, Wolfe T, Pandya DJ, et al. Neurologic complications in non-neurological intensive care units. Neurologist 2009;15:254-67.