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pergin@istanbul.edu.tr - <https://orcid.org/0000-0001-7986-4984>

Yayıncı

Türk Yoğun Bakım Derneği

Yayıncı Adresi

Gümüşsuyu Mah. İnönü Cad. No:53 Kat:4, 34437 Beyoğlu, İstanbul, Türkiye

E-posta: info@yogunbakim.org.tr

Web: www.yogunbakim.org.tr

Yayıncılık Hizmetleri

Akdema Bilişim ve Yayıncılık

Adres: Kızılay Mah. Gazi Mustafa Kemal Bulvarı No: 23/8 06420 Çankaya, Ankara, Türkiye

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pergin@istanbul.edu.tr - <https://orcid.org/0000-0001-7986-4984>

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Selvinaz Yüksel Tanrıverdi¹, Anıl Kuvandık², Çağın Tanrıverdi¹, Hülya Sungurtekin³

¹Department of Anesthesiology and Reanimation, Denizli State Hospital, Denizli, Türkiye

²Department of Anesthesiology and Reanimation, Çiğli Regional Training Hospital, İzmir, Türkiye

³Division of Intensive Care, Department of Anesthesiology and Reanimation, Faculty of Medicine, Pamukkale University, Denizli, Türkiye

ABSTRACT

Objective: The treatment of acute respiratory distress syndrome (ARDS) is highly complex, and its mortality rate remains significant. Positive end-expiratory pressure (PEEP) titration plays a crucial role in mechanical ventilation; however, the optimal approach for PEEP titration has yet to be established. This study evaluated the volume gain at different PEEP levels along the pressure-volume curve, changes in end-expiratory lung volume (EELV) measured via the modified multiple nitrogen wash-out/wash-in technique, and respiratory compliance.

Materials and Methods: Following approval from the ethics committee, 14 patients with ARDS receiving invasive mechanical ventilation in intensive care units were included in the study. According to the Berlin Criteria, there were 2 patients with mild ARDS, 7 with moderate ARDS, and 5 with severe ARDS. The repeated nitrogen wash-out/wash-in technique assessed functional residual capacity (FRC) and EELV at decreasing PEEP levels (± 5 cm H₂O) were determined. Gain and compliance values were calculated based on the dynamic pressure-volume curves generated. Arterial blood gas analysis was conducted to measure oxygenation at each PEEP level.

Results: The highest compliance, gain, and EELV values, as well as the lowest driving pressure and strain values, were observed at a PEEP level of 10 cm H₂O. Conversely, the highest PaO₂ values, representing oxygenation indicators, were recorded at a PEEP level of 15 cm H₂O. Notably, the gain remained largely unaffected by changes in compliance, elastance, driving pressure, and static strain; it was not affected by lung distension.

Conclusions: In PEEP titration, alveolar distension was not detected by EELV or gain parameters. Sufficient evidence could not be obtained solely in clinical practice.

Keywords: functional residual capacity, gain, PEEP, EELV, pulmonary mechanics

ÖZ

Amaç: Akut respiratuvar distres sendromunun (ARDS) tedavi stratejileri oldukça karmaşık, mortalitesi yüksektir. Mekanik ventilasyonda soluk sonu pozitif basınç (PEEP) titrasyonunun önemi büyüktür. Ancak PEEP titrasyonuna optimal yaklaşım net olarak belirlenememiştir. Çalışmamızda basınç-volüm eğrisi üzerinden farklı PEEP seviyelerindeki volüm kazancı (gain), modifiye çoklu azot yıkama tekniği ile ölçülen soluk sonu akciğer hacmi (EELV) değişimi ve kompliyansın, solunum mekanikleri ile değerlendirilmesi amaçlanmıştır.

✉ Selvinaz Yüksel Tanrıverdi • yukselselvinaz@gmail.com

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Gereç ve Yöntem: Etik Kurul onayı alındıktan sonra yoğun bakım ünitelerinde invaziv mekanik ventilasyon uygulanan 14 ARDS hastası çalışmaya alındı. Berlin Kriterlerine göre; 2 hafif, 7 orta, 5 ağır ARDS hastasıydı. Azalan PEEP titrasyon prosedürü (± 5 cm H₂O) ile fonksiyonel rezidüel kapasite (FRK) ve EELV, çoklu azot yıkama tekniği ile ölçüldü. İntratrakeal basınç sensörü ile oluşturulan dinamik basınç-volüm eğrileri üzerinden kazanç ve kompliyans ölçüldü. Her PEEP düzeyinde arteriyel kan gazı ile oksijenasyon değerlendirildi.

Bulgular: En yüksek kompliyans, kazanç, EELV değerine ve en düşük sürücü basınç değerine 10 cm H₂O PEEP düzeyinde ulaşıldı. Oksijenasyon göstergesi olan PaO₂'nin en yüksek değerleri 15 cm H₂O PEEP düzeyinde ölçüldü. Kazancın; kompliyans, elastans, sürücü basıncı, statik strain ile anlamlı olarak değişmediği ve akciğer distansiyonuna duyarlı olmadığı görüldü.

Sonuç: PEEP titrasyonunda alveol distansiyonunun, EELV veya kazanç parametreleri ile belirlemediği görüldü. Klinik pratikte tek başına kullanılabilmesi için yeterli ve güçlü kanıtlar elde edilemedi. Bunun için daha fazla çalışmaya gerek vardır.

Anahtar kelimeler: fonksiyonel rezidüel kapasite, kazanç, PEEP, EELV, pulmoner mekanikler

Introduction

Acute respiratory distress syndrome (ARDS) was first described in the 1960s (1). Clinically, ARDS is characterized as a diffuse, acute inflammatory lung injury marked by rapid-onset hypoxic respiratory failure and alterations in pulmonary mechanics (2). In 2012, the Berlin criteria were established for diagnosing ARDS (3). It is estimated that ARDS affects more than 3 million people worldwide annually, necessitates mechanical ventilation, and carries a mortality rate of 35-46% (2,4). The primary objective of treatment is to improve gas exchange by reducing the respiratory workload (5). In the context of mechanical ventilation, positive end-expiratory pressure (PEEP) may enhance oxygenation and increase end-expiratory lung volume (EELV) (6). However, excessive PEEP may lead to lung overdistension, increased dead space ventilation, and hemodynamic instability due to reduced cardiac output (6-8).

Previous studies have indicated that measuring and monitoring of EELV can be beneficial in cases involving FRC or PEEP adjustments. An optimal PEEP value, defined by the intersection of maximum oxygen transport with the highest static compliance and FRC, has been identified (9). Additionally, it has been demonstrated that the $\Delta\text{EELV}/\Delta\text{PEEP}$ ratio can be utilized alongside maximum respiratory system compliance, as both values typically reach their optimal levels at the same PEEP settings (10). One potential adverse effect of PEEP is lung overdistension, resulting from a PEEP-induced increase in EELV that excessively strains open alveoli. Concepts of lung

stress and strain, derived from EELV measurements, can predict this phenomenon (11).

EELV can be measured using computed tomography (CT) (12). However, CT is unsuitable for routine bedside use. Traditional techniques for EELV measurement rely on tracer gas dilution methods, including sulfur hexafluoride wash-out, closed-circuit helium dilution, or open-circuit multiple nitrogen wash-out (13-15). These techniques, while accurate, require expensive and impractical equipment. A novel method for FRC measurement, based on a modified nitrogen multiple-breath wash-out (NMBW) technique, has been developed. This approach is simplified and integrated into mechanical ventilators, eliminating the need for additional tracer gases or specialized monitoring equipment. The method calculates FRC by analyzing changes in the fraction of inspired oxygen (FiO₂) (16).

Studies have shown that EELV measurements can be used to estimate recruitment volume, which is critical for distinguishing whether PEEP-induced volume increases result from the opening of collapsed alveoli or the overdistension of already open alveoli (17).

The present study aims to evaluate volume gains at different PEEP levels through pressure-volume curve analysis using a protocol of gradually decreasing PEEP values. It also seeks to assess the relationship between EELV and compliance changes measured by the modified nitrogen multiple-breath wash-out technique and respiratory mechanics. Oxygenation was evaluated through arterial blood gas analysis at each PEEP level. Furthermore, the measured volume gains were compared with estimated recruitment volumes calculated using EELV.

Materials and Methods

This study was conducted in the anaesthesiology and reanimation intensive care units of a tertiary hospital with the approval obtained from the 13th board meeting of the Pamukkale University Non-invasive Clinical Trials Ethics Committee (no: 60116787-020/83538, date:13.07.2021). Between August 2021 and August 2022, 14 patients over 18 years of age who met the Berlin criteria (18) and were diagnosed with ARDS were included in the study. These patients were sedated, intubated, and mechanically ventilated. Written informed consent was obtained from their relatives.

The patients were connected to a CARESCAPE R860 (GE Healthcare) mechanical ventilator. Rocuronium bromide was administered intravenously to suppress spontaneous respiratory effort, and opioids were used for sedation. Tidal volume was set at 6 mL/kg based on estimated body weight, respiratory rate was adjusted to ensure normocarbina in blood gas analysis, and FiO₂ was adjusted to maintain PaO₂ levels between 55 and 80 mmHg. The end-inspiratory pause was set at 20%, and the inspiratory/expiratory ratio was adjusted to 1:2.

Gas measurements were conducted using the ECOV-X (GE Healthcare) module, which was attached to the ventilator and allowed to warm up before use. A spirometer kit with heat and moisture retention properties was placed between the Y-piece in the ventilator circuit and the bacterial/viral filter. An intratracheal pressure sensor was inserted to measure pressure levels independent of circuit and tube resistance, and these measurements were analyzed using the SpiroDynamics (GE Healthcare) application. EELV was measured using the ECOV-X module with a modified NMBW technique based on changes in FiO₂. EELV was calculated using oxygen consumption (VO₂) and carbon dioxide production (VCO₂). Once all connections were completed, VO₂ and VCO₂ values were measured. The PEEP titration procedure, Lung InView™ (GE Healthcare), was initiated in

patients whose values stabilized within 30 minutes. Before measurements, a recruitment maneuver was performed for 30-40 seconds at a PEEP level of 20 cm H₂O. Measurements were recorded during a descending PEEP trial conducted at four levels (15, 10, 5, and 0 cm H₂O).

For the same PEEP levels, the shunt fraction decreased when a descending PEEP maneuver was used instead of an ascending maneuver. This observation suggests that the relationship between optimal PEEP and maximum compliance is more accurately determined using descending PEEP trials, which is why the study protocol preferred descending PEEP trials (19).

The measurement time for each PEEP level was set at 10 minutes. At the end of each measurement, static compliance was determined by applying an end-inspiratory pause. Tidal volume, peak pressure, and driving pressure were recorded at each step. Respiratory system elastance was calculated using Henderson et al.'s (20) formula: respiratory system elastance = driving pressure/tidal volume. The static strain was calculated using Protti et al.'s (21) equation, which employs tidal volume at the relevant PEEP value: static strain = tidal volume at PEEP/FRC. The pressure-volume curve generated by the intratracheal pressure sensor at each PEEP level was evaluated using the SpiroDynamics application. Dynamic compliance curves were generated during analysis, and volume changes in these curves were determined for each PEEP level. The difference in EELV between two PEEP levels during a descending PEEP trial (Δ EELV) and the difference between Δ EELV and the volume derived from the pressure-volume curve were calculated as "volume gain" (gain = Δ EELV - volume derived from the curve). The estimated lung volume recovered was calculated using the formula Δ EELV - (Δ PEEP \times Compliance at PEEPlow) and compared with the volume gain (17). The efficiency of the volume gains concept as an indicator of alveolar recruitment volume and its role in personalized PEEP titration was evaluated.

Statistical analysis

The effect size was calculated over the EELV at high and low PEEP levels in the referenced study. The effect size was reported as $d_z=0.974$. Power analysis was conducted, assuming a strong effect size ($F=0.4$) could be achieved. Given that the study involved three distinct PEEP levels, it was determined that a sample size of at least 12 participants would provide 80% power at a 95% confidence level. To account for potential data loss, the study planned to include 14 participants, representing a 20% increase over the minimum required sample size.

Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 25.0; IBM SPSS Statistics, Armonk, NY: IBM Corp.). Continuous variables were expressed as mean \pm standard deviation, while categorical variables were presented as frequencies and percentages. The normality of the data distribution was assessed using the Shapiro-Wilk test. For dependent group comparisons, repeated measures analysis of variance (ANOVA) was applied when parametric test assumptions were met, whereas the Friedman test was used when these assumptions were violated. The Wilcoxon test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. A p -value of <0.05 was considered statistically significant in all analyses.

Results

The mean age of the 14 patients included in our study is 64.50 ± 15.14 years. The mean body weight, height, and body mass index (BMI) were 84.71 ± 10.83 kg, 169.64 ± 7.89 cm, and 29.29 ± 5.59 kg/m², respectively. The cohort consisted of six females and eight males.

Regarding chronic comorbidities, eight patients (57.1%) had hypertension, six (42.9%) had diabetes mellitus, two (14.3%) had coronary artery disease, two (14.3%) had chronic kidney disease, and four (28.6%) had malignancy. Table 1 presents the distribution of diseases leading to ARDS and the severity of ARDS, as classified according to the Berlin Criteria.

Table 1. Risk factors and severity distribution of patients for ARDS

	n	%
ARDS cause		
COVID-19 pneumonia	8	57.1
Femur fracture	1	7.1
Pneumonia	3	21.4
Pulmonary embolism	1	7.1
Fat embolism	1	7.1
ARDS severity distribution		
Mild	2	14.3
Moderate	7	50
Severe	5	35.7

ARDS: Acute respiratory distress syndrome.

Compliance measurements were significantly higher at 5 cm H₂O PEEP compared to 0 cm H₂O, and at 10 cm H₂O compared to both 0 and 15 cm H₂O PEEP. Driving pressure was significantly lower at the 10 cm H₂O PEEP level compared to 0 and 15 cm H₂O levels. Intragroup p values for elastance, EELV, and static strain were not significant (Table 2).

No statistically significant differences were observed in systolic blood pressure, diastolic blood pressure, and heart rate (HR) across different PEEP levels ($p>0.05$). Oxygen saturation (SpO₂) values at PEEP levels of 15 cm H₂O and 10 cm H₂O were significantly higher than those at 0 cmH₂O ($p<0.001$). Similarly, partial arterial oxygen pressure (PaO₂) values were significantly higher at a PEEP of 15 cmH₂O compared to 0 cm H₂O ($p<0.05$). Blood gas saturation (SaO₂) values were also significantly higher at PEEP levels of 15 cm H₂O and 10 cm H₂O compared to 0 cmH₂O ($p<0.05$; Table 3).

When assessing the changes in lung volume during reductions in PEEP by increments of 5 cm H₂O, the highest volume gain was observed when decreasing from a PEEP of 10 cm H₂O to 5 cm H₂O. This change was statistically significant but represented a net volume loss ($p<0.05$). The estimated lung volume and volume gain that were recovered were strongly and positively correlated with the gain observed during high PEEP trials (Table 4).

Table 2. Lung mechanics at different PEEP levels

	15 cm H ₂ O PEEP	10 cm H ₂ O PEEP	5 cm H ₂ O PEEP	0 cm H ₂ O PEEP	in-group p
Static Compliance (mL/cm H ₂ O)	30.86±1.67	43.07±30.68	38.21±13.45	32.36±12.38	0.001*
Elastance (cm H ₂ O/L)	33.93±13.06	33.64±7.52	26.86±8.65	29.07±10.86	0.009
Driving pressure (cm H ₂ O)	15.36±3.00	12.21±3.31	13.07±4.23	15.29±5.44	0.003 α
Static strain (cm H ₂ O)	0.67±0.66	0.64±0.32	0.36±0.23	0	0.257
EELV (mL)	2423.79±1828.44	2535.57±2350.27	1924.71±1442.33	1817.71±1403.36	0.433
Peak pressure (cm H ₂ O)	36.43±3.84	30.71±4.38	26.21±5.58	24.00±7.25	0.0001 β

PEEP: Positive End Expiratory Pressure, EELV: End-Expiratory Lung Volume; *:p=0.002: Static compliance at 15-10 cm H₂O PEEP, p=0.011: Static compliance at 10-0 cm H₂O PEEP, p=0.001: Static compliance at 5-0 cm H₂O PEEP; α :p=0.002: Driving pressure at 15-10 cm H₂O PEEP, p=0.013: Driving pressure at 10-0 cm H₂O PEEP, p=0.007: Driving pressure at 5-0 cm H₂O PEEP; β :p=0.001: Peak pressure at 15-10 cm H₂O PEEP, p=0.001: Peak pressure at 15-5 cm H₂O PEEP, p=0.001: Peak pressure at 10-5 cm H₂O PEEP, p=0.001: Peak pressure at 15-0 cm H₂O PEEP, p=0.001: Peak pressure at 10-0 cm H₂O PEEP, p=0.009: Peak pressure at 5-0 cm H₂O PEEP.

Table 3. SpO₂ (%), PaO₂ (mmHg), PaCO₂ (mmHg), and SaO₂ (%) at different PEEP levels

	15 cm H ₂ O PEEP	10 cm H ₂ O PEEP	5 cm H ₂ O PEEP	0 cm H ₂ O PEEP	p -value
Peripheral SpO ₂ (%)	97.00±2.51	95.5±3.16	93.86±4.1	92.07±5.01	0.001*
pH	7.36±0.12	7.38±0.13	7.35±0.11	7.39±0.12	0.736
PaO ₂ (mmHg)	92.56±42.77	86.84±31.10	77.34±28.71	73.61±34.15	0.008*
PaCO ₂ (mmHg)	52.06±8.03	49.1±10.37	47.98±7.38	50.53±9.29	0.022*
SaO ₂ (%)	92.58±4.28	92.80±4.62	90.84±5.61	86.02±10.15	0.036*

SpO₂: Peripheral oxygen saturation, PaO₂: Partial arterial oxygen pressure, PaCO₂: Partial arterial carbon dioxide pressure, SaO₂: Arterial blood oxygen saturation.

Table 4. Correlation of volume gain and estimated recruitment volume

n=14	RecEstimation	15-10 cm H ₂ O PEEP	10-5 cm H ₂ O PEEP	5-0 cm H ₂ O PEEP
Gain	r	0.930**	0.999**	0.515
	P	0.000	0.000	0.6
Gain (mL)	0.223	-297.79±1418.52	815.07±1421.09	-94±622,95

r: correlation coefficient.

Discussion

The clinical manifestation of acute respiratory failure with bilateral infiltrates on lung imaging, that defies explanation by heart failure and fluid overload is known as ARDS (3). Predisposing risk factors for ARDS include multiple blood product transfusions, sepsis, pneumonia, gastric aspiration, trauma, pancreatitis, severe burns, and exposure to inhaled or systemic toxins (18). The mechanical ventilation strategies for ARDS are primarily based on the "ARMA" study (22). The fundamental recommendations include setting the tidal volume to 6 mL/kg of predicted body weight and maintaining the plateau pressure at or below 30 mmHg (22,23). It is possible to improve oxygenation

with PEEP titration; however, the best strategy must be specified. We know that FRC decreases in patients with ARDS (24). Therefore, using PEEP-induced FRC, i.e., EELV, is of interest. Also, the volume gain, which can be measured simultaneously and shows the recovery of collapsed alveoli, suggests its use in PEEP titration.

TestChest®, a lung stimulator, was employed by Berger-Estilita et al. (25) to evaluate the accuracy of the InView™ system. Their findings demonstrated that the volume differences between measurements obtained using the modified nitrogen flushing technique and the simulator were within an acceptable range and well correlated (25). Based on this evidence, the current study utilized InView™. For EELV measurement (25).

Dellamonica et al. (17) assessed EELV measurement alongside static compliance, PaCO₂, and pH levels at 5 and 15 cmH₂O different PEEP levels in 30 ARDS patients. No statistically significant differences were observed between the groups for these parameters. Similarly, the present study found no significant differences in these parameters. However, Dellamonica et al. (17) reported significant SaO₂, strain, and EELV values at higher PEEP levels. Consistently, the present study demonstrated that both EELV and SaO₂ increased with higher PEEP levels, reaching the highest static strain value at a PEEP of 15 cmH₂O. Dellamonica et al. (17) also estimated the recruitment alveolar volume using EELV, compared it with results from the pressure-volume curve technique, finding a strong correlation between the two methods. In the current study, during calculations of the Rec(estimate) and its correlation with volume gain, a very high correlated value was found when the pressure was moved from 15 to 10 and 10 to 5 cmH₂O PEEP. (Table 4). These findings suggest that volume gain could serve as an indicator of alveolar recruitment at higher PEEP levels. However, this study's absence of correlation at lower PEEP levels and the lack of smaller PEEP transition intervals prevent strong recommendations for routine clinical application.

Chen et al. (26) demonstrated that using a nitrogen-washout approach integrated into the mechanical ventilator could predict recruitment and inflation in 45 patients with moderate to severe ARDS. The study showed significantly higher SpO₂ and EELV values at higher PEEP levels than lower ones. Similarly, in the present study, EELV values were significantly higher at a PEEP level of 10 cm H₂O compared to 0 cm H₂O. The highest compliance value was observed at a PEEP level of 10 cm H₂O, while the lowest was at 0 cm H₂O. This difference may be attributed to the recruitment maneuver performed prior to measurements in the current study and the greater number of PEEP trials conducted. Differences in patient populations, ARDS severity, and the inclusion of COVID-19-related ARDS may contribute to variations in results

Chiew et al. (27) used the patient-specific minimum elastance value as a criterion for PEEP titration in mechanically ventilated ARDS patients. Their study demonstrated that elastance was higher at 0 cm H₂O PEEP and decreased with increasing PEEP. A moderate correlation was identified among elastance, EELV, and work of breathing. The present study consistently observed a strong negative correlation between elastance and increased EELV at 15 and 0 cm H₂O PEEP, aligning with expectations for these extreme levels of PEEP.

Several studies suggest that the PaO₂/FiO₂ ratio is an unreliable marker for evaluating anatomical recruitment in ARDS patients (17,26,28). Instead, monitoring lung volume changes via FRC measurements may be more appropriate for assessing alveolar recruitment or collapse.

The present study achieved optimal EELV, compliance, driving pressure, and volume gain values at a PEEP level of 10 cm H₂O. This finding highlights the potential importance of this PEEP level but does not support its routine clinical use. Personalized PEEP adjustments remain the primary recommendation, as measurements were conducted at only three PEEP levels. The highest PaO₂ and SpO₂ values were observed at 15 cm H₂O PEEP. However, these values may lack clinical relevance regarding target oxygenation thresholds. Consequently, the primary aim of the mechanical ventilation strategy was to achieve a PaO₂ threshold of 60 mmHg while maintaining pulmonary mechanics as part of a balanced approach.

The amount of recruitable lung tissue varies in ARDS, and ARDS severity may be inferred by quantifying recruitable volume (29,30). Grieco et al. (31) used the recruitment-to-inflation (RI) ratio to titrate PEEP in their IPERPEEP trial by monitoring EELV at each step. Similarly, the current study sought to quantify recruited alveoli through EELV, ΔEELV, and volume gain measurements. The findings of the completed IPERPEEP trial will provide additional insights relevant to the context of this study.

The limitations of this study include the inability to thoroughly evaluate dynamic ventilation parameters due to the administration of neuromuscular blockers during measurements. Furthermore, the 10-minute intervals required between PEEP levels during the decremental PEEP trial, aimed at minimizing transmission risks during the COVID-19 pandemic, may have influenced oxygenation parameters in blood gas analyses.

Conclusion

Volume gain at high PEEP levels may guide individualized PEEP as it correlates with the estimated recruited lung volume. However, this correlation was not demonstrated at low PEEP levels. Also, there was no sufficient and robust evidence that volume gain or EELV correlates with compliance, strain, elastance, and driving pressure parameters that predict alveolar overdistension in PEEP titration.

Ethical approval

This study has been approved by the Pamukkale University Non-invasive Clinical Trials Ethics Committee (approval date: July 13, 2021, number: 60116787-020/83538). Written informed consent was obtained from the participants.

Author contribution

Study conception and design: SYT, AK, HS; data collection: SYT, ÇT; analysis and interpretation of results: SYT, ÇT, HS; draft manuscript preparation: SYT, HS. The author(s) reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Associated factors of transfer to intensive care unit among hospitalized patients with COVID-19 disease-related pulmonary thromboembolism

COVID-19 hastalığı ilişkili pulmoner tromboemboli nedeniyle yatan hastalarda yoğun bakım ünitesine nakille ilişkili faktörler

Ümran Özden Sertçelik^{1,2}, Ahmet Sertçelik³, Meltem Fidan Gündüz², Muhammed Furkan Gökteş², Esmehan Akpınar², Ayşegül Karalezli^{1,2}

¹Department of Chest Diseases, Faculty of Medicine, Ankara Yıldırım Beyazıt University, Ankara, Türkiye

²Department of Chest Diseases, Ankara Bilkent City Hospital, Ankara, Türkiye

³Division of Epidemiology, Department of Public Health, Faculty of Medicine, Hacettepe University, Ankara, Türkiye

ABSTRACT

Introduction: The most common thromboembolic condition in coronavirus disease 2019 (COVID-19) is acute pulmonary embolism (APE). Factors associated with transfer to the intensive care unit among cases diagnosed with COVID-19 are separately known for COVID-19 and APE. However, it is important to identify factors associated with transfer to intensive care in patients with COVID-19-related APE. This study aimed to determine these factors in the coexistence of these conditions.

Methods: Adult patients diagnosed with APE by pulmonary computed tomography angiography were included in this cross-sectional study. The patients' demographic and laboratory data, Wells scores, pulmonary embolism severity index (PESI) scores, and imaging findings were recorded. Pairwise comparisons were made between the patients with and without intensive care unit admissions.

Results: Of the 123 patients included in the study, 38 (30.8%) were transferred to the intensive care unit. In pairwise comparisons, age, number of comorbidities, lactate dehydrogenase, neutrophil-to-lymphocyte ratio, C-reactive protein (CRP), CRP-to-albumin ratio, d-dimer values, Wells scores, and PESI scores were higher among patients who transferred to intensive care. A higher Wells score (odds ratio (OR) = 1.70, 95% confidence interval (CI) = 1.13 – 2.56, p=0.011), PESI score (OR = 1.03, 95% CI = 1.00 – 1.07, p=0.048), and CRP (OR = 1.01, 95% CI = 1.00 – 1.02, p=0.049) were associated with admission to the intensive care unit among patients with COVID-19-related APE.

Discussion and Conclusion: High Wells and PESI scores and CRP levels in adult patients hospitalized with a diagnosis of COVID-19-related APE were determined to increase the probability of transfer to the intensive care unit. Therefore, it is recommended to monitor these patients more closely for intensive care needs.

Keywords: critical care, pulmonary embolism, pulmonary embolism severity index, SARS-CoV-2 infection, Wells score

ÖZ

Giriş ve Amaç: Koronavirüs hastalığı 2019'da (COVID-19) en sık görülen tromboembolik durum akut pulmoner embolidir (APE). COVID-19 tanısı konulan hastalar arasında yoğun bakım ünitesine nakille ilişkili faktörler COVID-19 ve APE için ayrı ayrı bilinmektedir. Bununla birlikte,

✉ Ümran Özden Sertçelik • umranozdensertcelik@yahoo.com

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COVID-19 ile ilişkili APE'li hastalarda yoğun bakıma nakille ilişkili faktörlerin belirlenmesi önemlidir. Bu çalışma, bu koşulların bir arada görüldüğü durumlarda bu faktörleri belirlemeyi amaçlamıştır.

Yöntem ve Gereçler: Bu kesitsel çalışmaya pulmoner bilgisayarlı tomografi anjiyografi ile APE tanısı konulan erişkin hastalar dahil edildi. Hastaların demografik ve laboratuvar verileri, Wells skorları, pulmoner emboli ciddiyet endeksi (PESI) skorları ve görüntüleme bulguları kaydedildi. Yoğun bakım ünitesine yatışı olan ve olmayan hastalar arasında ikili karşılaştırmalar yapıldı.

Bulgular: Çalışmaya dahil edilen 123 hastanın 38'i (%30,8) yoğun bakım ünitesine nakledildi. İkili karşılaştırmalarda, yaş, komorbidite sayısı, laktat dehidrogenaz, nötrofil/lenfosit oranı, C-reaktif protein (CRP), CRP/albumin oranı, d-dimer değerleri, Wells skorları ve PESI skorları yoğun bakıma nakledilen hastalarda daha yüksekti. Daha yüksek Wells skoru (odds oranı (OR) = 1,70, %95 güven aralığı (GA) = 1,13 – 2,56, p = 0,011), PESI skoru (OR = 1,03, %95 GA = 1,00 – 1,07, p = 0,048) ve CRP (OR = 1,01, %95 GA = 1,00 – 1,02, p = 0,049) COVID-19 ile ilişkili APE'si olan hastalarda yoğun bakım ünitesine nakille ilişkiliydi.

Tartışma ve Sonuç: COVID-19 ile ilişkili APE tanısıyla hastaneye yatırılan erişkin hastalarda yüksek Wells ve PESI skorları ile CRP düzeylerinin yoğun bakım ünitesine nakil olasılığını artırdığı belirlenmiştir. Bu nedenle, bu hastaların yoğun bakım ihtiyacı gelişimi açısından daha yakından izlenmesi önerilmektedir.

Anahtar kelimeler: kritik bakım, pulmoner emboli, pulmoner emboli ciddiyet endeksi, SARS-CoV-2 enfeksiyonu, Wells skoru

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Following its emergence, COVID-19 rapidly spread throughout the world, resulting in a pandemic (1). Thrombotic events may occur in patients with COVID-19 due to endothelial inflammation, complement activation, platelet activation, endothelial dysfunction, and immobilization. In addition to these risk factors, the activation of the coagulation system leads to a predisposition to thrombosis in both the venous and arterial systems. One of the most commonly detected thromboembolic events is acute pulmonary thromboembolism (APE) (2,3), which is among the conditions that result in the need for intensive care in cases of COVID-19.

It is important to determine factors associated with the development of intensive care needs in APE. Thus, patients need to be monitored in intensive care units, which increases the number of intensive care beds required as well as the morbidity and mortality associated with COVID-19 (2). Furthermore, although previous studies have examined factors associated with transfer to the intensive care unit separately in terms of APE and COVID-19, there is only limited research concerning factors associated with transfer to the intensive care unit in patients with COVID-19-related APE.

This study aimed to determine factors associated with transfer to the intensive care unit among hospitalized adult patients diagnosed with COVID-19-related APE.

Materials and Methods

Patients

This cross-sectional study was conducted at a tertiary hospital with approximately 3,100 inpatient beds and 700 intensive care beds in Ankara, Türkiye. The study included patients aged over 18 years who were hospitalized due to COVID-19 and were diagnosed with APE by pulmonary computed tomography (CT) angiography during their hospital stay, from April 1, 2020, through March 17, 2021. No exclusion criteria were applied.

Data and definitions

Data on gender, age, comorbidities, history of cancer, medication use, and length of hospital stay for all patients with COVID-19-related APE were obtained from the hospital's electronic records. Laboratory tests were completed within 24 hours of diagnosis and included the complete blood count, neutrophil-to-lymphocyte ratio (NLR), serum albumin, creatinine, troponin I, brain natriuretic peptide, d-dimer, prothrombin time, activated partial thromboplastin time, lactate dehydrogenase (LDH), C-reactive protein (CRP), procalcitonin, ferritin, and interleukin-6 values.

In addition, echocardiography (ejection fraction and pulmonary artery pressure), lower extremity Doppler ultrasonography, and CT pulmonary angiogram (CTPA) findings were recorded. The CRP-to-albumin ratio was obtained by dividing CRP in mg/dl and serum albumin in g/dl. The NLR was calculated by dividing the neutrophil count by the leukocyte count. The oxygen therapy received by the patients, the treatments applied for COVID-19, and the use of methylprednisolone at a dose of 250 mg/day and

above were also noted. In-hospital mortality was evaluated for all participants. Patients with a COVID-19 diagnosis within 45 days before or 14 days after CTPA were considered to have COVID-19-related APE (4,5). The COVID-19 diagnosis was based on either a positive reverse transcription-polymerase chain reaction (PCR) test for SARS-CoV-2 (i.e., PCR-confirmed diagnosis) or the typical thoracic CT findings of COVID-19 as defined by the British Society of Chest Radiology (i.e., radiological diagnosis) (Figure 1) (6).

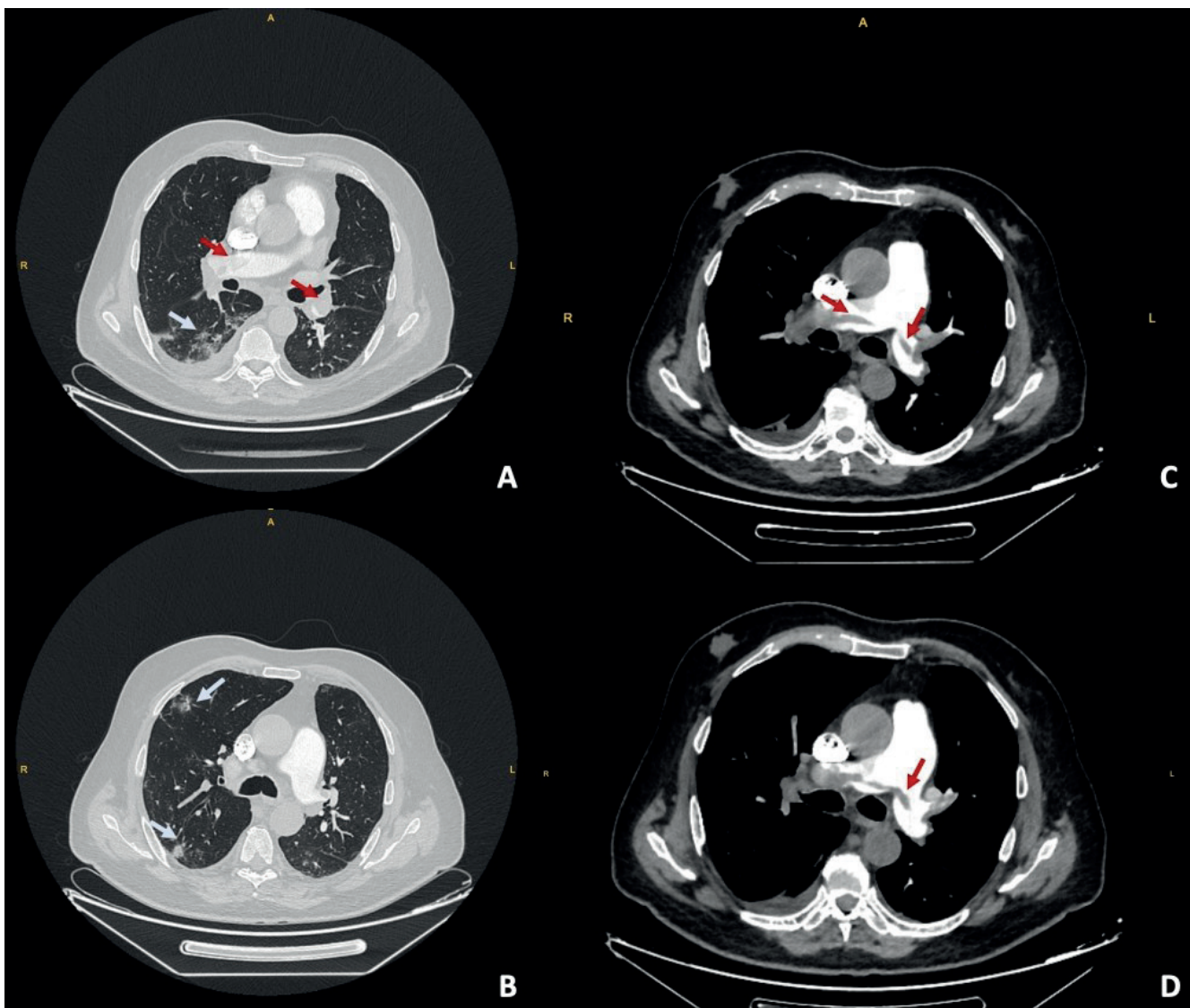


Figure 1. Typical lung parenchymal findings of COVID-19 (peripheral multiple ground glass opacity) (white arrow) and concurrent filling defect in the pulmonary artery (red arrow) (A and B parenchymal window, C and D mediastinal window)

The Wells score and the pulmonary embolism severity index (PESI) were calculated and classified using the 2019 guidelines of the European Society of Cardiology. Accordingly, the patients were classified as having low, intermediate-low, intermediate-high, or high risk (7).

Statistical analysis

Categorical variables were presented as numbers and percentages and compared with the chi-square or Fischer's exact test. Quantitative variables were given as mean \pm standard deviation and median [interquartile range (IQR)] values. Coefficient of variation (<20%), kurtosis/standard error (<1.96), skewness/standard error (<1.96) ratios, visual (histogram and detrended Q-Q plot graphs) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods were utilized to evaluate whether the data were normally distributed. Comparisons between groups were undertaken using the independent-samples t-test (Student-t-test) for variables with a normal distribution, and the Mann-Whitney U test for those that were not normally distributed.

Multivariate logistic regression models were built to determine factors associated with transfer to the intensive care unit. The factors included in the model were age, gender, comorbidity count, presence of malignancy, Wells and PESI scores, localization and side of the embolus/emboli, d-dimer, troponin I, and CRP. The goodness-of-fit of the model was tested with the Hosmer-Lemeshow test. Laboratory tests with high missing data (ferritin, LDH, fibrinogen, procalcitonin, and interleukin-6) and variables that were highly correlated with d-dimer, troponin I, and CRP (lymphocyte count, NLR, and platelet count) were not included in the model even if they were significant in pairwise comparisons. Furthermore, oxygen support needs and related treatments were not included in the regression analysis due to the possibility of missing data before or after transfer to the intensive care unit. Lastly, blood pressure and pulse were excluded from the model since they were already included in the calculation of the PESI score.

The statistical significance level was taken as $p < 0.05$ (two-sided). No imputation was provided for the missing data. Statistical analyses were performed using the the Statistical Products and Service Solutions for the Social Sciences version 23 (IBM SPSS®, Armonk, New York, USA) software package.

Ethical consideration

Ethical approval for the study was obtained from the Clinical Research Ethics Committee of Ankara City Hospital (approval number: E1-21-1628, date: March 17, 2021). The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was not obtained as the data were retrospectively obtained from electronic records without collecting patients' identity information. The results of this study were presented as an oral presentation at the Ankara City Hospital 2021 Annual Congress (online congress) (the Turkish Respiratory Society 2021 Annual Congress (online congress) (October 29 to November 3, 2021) (SS-131).

Results

The study included a total of 123 patients diagnosed with COVID-19-related APE from April 2020 to April 2021, and analyses were performed on the data of all these patients. Eighty-three (66.9%) of the patients were male, and the mean age was 61.89 ± 16.09 years. No patient was diagnosed with APE before hospitalization. They were not previously receiving anticoagulants.

Thirty-eight (30.8%) patients were treated and followed up in the intensive care unit. Age, number of comorbidities, and pulse were found to be statistically higher in patients who were followed up in the intensive care unit ($p = 0.002$, $p = 0.032$, and $p < 0.001$, respectively). COVID-19 was diagnosed by PCR in 69.9% of patients and by typical thorax CT image in the rest. Table 1 presents the demographic and clinical data and distribution of vital signs at the time of admission for patients diagnosed with COVID-

Table 1. Demographic and clinical data and distribution of vital signs at admission in patients with COVID-19-related APE according to the ICU transfer status

	Transferred to ICU, n (%) n = 38	Not transferred to ICU, n (%) n = 85	OR (95% CI)	p-value
Male gender	27 (71.1)	56 (65.9)	1.27 (0.55-2.92)	0.57
Comorbidity	29 (76.3)	51 (60.0)	2.14 (0.90- 5.10)	0.80
Hypertension	16 (42.1)	23 (27.1)	1.96 (0.87-4.37)	0.09
Coronary artery disease	8 (21.1)	9 (10.6)	2.25 (0.79-6.38)	0.12
Diabetes mellitus	6 (15.8)	18 (21.2)	0.69 (0.25-1.92)	0.48
Malignancy	8 (21.1)	7 (8.2)	2.97 (0.99-8.91)	0.04
	Median (IQR)	Median (IQR)	n	p-value
Age (years) (mean ± SD)	68.34 ± 13.87	58.84 ± 16.23	123	0.002*
Number of comorbidities	1.5 (2.0)	1.0 (2.0)	123	0.032
Time from CT scan to COVID-19 diagnosis (days)	0.5 (14.0)	4.0 (15.0)	123	0.27
Body temperature (°C)	36.4 (0.8)	36.4 (0.5)	97	0.40
Pulse (/min)	97.0 (29.0)	87.0 (20.0)	110	<0.001
Systolic blood pressure (mmHg)	113.0 (19.0)	125.0 (11.0)	110	0.002
Diastolic blood pressure (mmHg)	70.0 (20.0)	78.0 (10.0)	110	0.031

APE: Acute pulmonary thromboembolism, ICU: Intensive care unit, OR: Odds ratio, CI: Confidence interval, IQR: Interquartile range, SD: Standard deviation, CT: Computed tomography; *Student's t-test.

19-related APE according to their intensive care unit admission.

When the laboratory values of the patients included in the study were examined at the time of the diagnosis of APE, lymphocyte count, platelet count, and albumin levels were found to be lower among those followed up in the intensive care unit. NLR, serum LDH, ferritin, troponin I, d-dimer, CRP, procalcitonin, interleukin-6, and CRP-to-albumin ratio were statistically significantly higher in the intensive care group. The laboratory findings of the groups are shown in Table 2.

The rates of high Wells and PESI scores, PESI class 5, and high risk for early mortality were higher in the intensive care group. Table 3 presents the distribution of the diagnostic and prognostic scores and imaging findings according to transfer to the intensive care unit.

The oxygen need was higher among patients who were transferred to the intensive care unit compared

to those not transferred ($p < 0.001$). It was also determined that the use of methylprednisolone (>250 mg/day) and colchicine were significantly higher in the intensive care group ($p < 0.001$ and $p = 0.005$, respectively). The median length of stay was 16.0 (IQR = 19) in patients who needed intensive care and 9.0 (IQR = 8) days in those without this need ($p < 0.001$). Mortality occurred in 12 (31.5%) patients followed up in the intensive care unit. The distribution of the treatments applied for COVID-19 and the clinical outcomes of the patients in both groups are shown in Table 4.

A multivariate logistic regression analysis was performed to identify factors affecting intensive care unit admission among hospitalized patients diagnosed with COVID-19-related APE. According to both univariate and multivariate analyses, the Wells score, the PESI score, and the CRP level statistically significantly increased the risk of intensive care needs. The detailed results are given in Table 5.

Table 2. Distribution of laboratory data in patients with COVID-19-related APE according to the ICU transfer status

	n	Transferred to ICU	Not transferred to ICU	p-value
Leucocyte (/μL)	119	9,430 (7,215)	8,070 (5,000)	0.24
Neutrophil leukocyte (/μL)	119	7,130 (6,285)	6,230 (4,385)	0.072
Lymphocyte leukocyte (/μL)	119	880 (640)	1,290 (1,090)	0.002
Neutrophil-to-lymphocyte ratio	119	7.90 (5.72)	4.77 (4.76)	<0.001
Hemoglobin (g/dL)	119	13.20 ± 2.04	13.28 ± 2.05	0.83*
Hematocrit (%)	119	40.47 ± 5.85	40.71 ± 5.33	0.82*
Thrombocyte (x1,000/μL)	119	201,000 (141,500)	282,000 (123,500)	0.010
Serum creatinine (mg/dL)	119	0.90 (0.39)	0.87 (0.29)	0.87
eGFR (ml/min)	119	85 (40)	88 (34)	0.19
Serum lactate dehydrogenase (U/l)	106	484.50 (243.5)	293.0 (123.0)	<0.001
Serum albumin (mg/L)	123	35.50 ± 5.00	40.21 ± 4.80	<0.001
Ferritin (μg/L)	100	437.0 (444.0)	202.0 (292.4)	0.018
Troponin I (ng/L)	112	31.78 (79.32)	5.0 (10.50)	<0.001
Brain natriuretic peptide (ng/mL)	112	1,053 (3,360)	115 (381)	0.053
Activated partial thromboplastin time (sec)	98	23.65 (4.5)	24.0 (3.9)	0.88
Prothrombin time (sec)	97	13.35 (2.8)	12.55 (1.7)	0.009
Fibrinogen (mg/dL)	73	4.20 (2.26)	4.22 (2.0)	0.74
D-dimer (ng/mL)	112	12.75 (20.91)	3.55 (6.65)	<0.001
CRP (mg/L)	111	83.0 (95.50)	34.0 (75.0)	0.001
Procalcitonin (ng/mL)	103	0.10 (0.16)	0.04 (0.05)	<0.001
Interleukin-6 (pg/mL)	34	88.15 (121.73)	18.05 (34.15)	<0.001
CRP/Albumin ratio	110	23.71 ± 24.85	9.51 ± 17.02	<0.001
pH	77	7.45 (0.06)	7.44 (0.05)	0.54
pO ₂ (mmHg)	77	55.7 (28.9)	63.4 (24.9)	0.90
pCO ₂ (mmHg)	76	36.5 (12.1)	36.8 (9.0)	0.53
HCO ₃ (mol/L)	77	23.2 (7.8)	23.6 (3.6)	0.77
sO ₂ (%)	72	87.0 (13.8)	91.2 (10.5)	0.76

APE: Acute pulmonary thromboembolism, ICU: Intensive care unit, SD: Standard deviation, eGFR: estimated glomerular filtration rate, CRP: C-reactive protein, pH: power of Hydrogen, pO₂: partial oxygen pressure, pCO₂: partial carbon dioxide pressure, HCO₃: bicarbonate concentration, SO₂: oxygen saturation; * Student's t-test; Data presented as median (interquartile range) or mean ± standard deviation.

Discussion

In this study, it was determined that high CRP levels and Wells and PESI scores in adult hospitalized patients with a diagnosis of COVID-19-related APE were associated with transfer to the intensive care unit. To the best of our knowledge, there is no study in the literature examining factors associated with intensive care needs among patients with a diagnosis of COVID-19-related APE. However, as another negative outcome showing parallelism to the intensive care needs, mortality has been previously investigated in

patients with APE. In the absence of data on COVID-19-related APE, we referred to the available findings in the literature concerning the relationship between APE and adverse clinical outcomes to compare our results.

In a study in which the PESI scale was validated for the prediction of in-hospital mortality in patients diagnosed with COVID-19-related APE, 34.9% of the patients were followed up in the intensive care unit, and 17.6% died (8). In the current study, 30.8% of the patients were transferred to the intensive care unit, and 12.1% died. In this respect, the clinical outcomes

Table 3. Distribution of diagnostic and prognostic scores in patients with COVID-19 related APE according to the ICU transfer status

	Transferred to ICU, n (%) n = 38	Not transferred to ICU, n (%) n = 85	OR (95% CI)	p-value
Deep vein thrombosis	7 (36.8)	16 (27.1)	1.59 (0.53-4.70)	0.42
Median Wells score (IQR)	4.50 (1.5)	3.0 (3.0)	n = 124	0.001
PESI score (mean ± SD)	120.34 ± 39.59	79.06 ± 27.56	n = 123	<0.001*
PESI class				<0.001
Class I (reference)	1 (2.6)	31 (37.3)	1.00	
Class II	5 (13.2)	22 (26.5)	7.05 (0.77-64.58)	
Class III	8 (21.1)	13 (15.7)	19.08 (2.16-168.3)	
Class IV	8 (21.1)	11 (13.3)	22.55 (2.52-201.4)	
Class V	16 (42.1)	6 (7.2)	82.67(9.15-746.9)	
Early mortality risk assessment				<0.001
Low (reference)	8 (21.1)	57 (67.1)	1.00	
Intermediate-low	19 (50)	18 (21.2)	7.52 (2.82-20.07)	
Intermediate-high	6 (15.8)	7 (8.2)	6.11 (1.64-22.81)	
High	5 (13.2)	3 (3.5)	11.88 (2.37-59.48)	
Embolus localization				0.001
Subsegmental artery (reference)	5 (13.5)	13 (15.3)	1.00	
Segmental artery	11 (29.7)	41 (48.2)	0.70 (0.20-2.38)	
Lobar artery	3 (8.1)	18 (21.2)	0.43 (0.09-2.15)	
Main pulmonary artery	18 (48.6)	13 (15.3)	3.50 (1.03-12.67)	
Laterality of embolism				0.011
Unilateral (reference)	6 (15.8)	33 (38.8)	1.00	
Bilateral	32 (84.2)	52 (61.2)	3.38 (1.27-8.97)	
Pulmonary artery pressure (mmHg) (mean ± SD)	39.08 ± 15.08	35.50 ± 12.92	n = 39	0.44*
Median ejection fraction (%) (IQR)	60 (5.0)	60 (5.0)	n = 43	0.15

APE: Acute pulmonary thromboembolism, ICU: Intensive care unit, OR: Odds ratio, CI: Confidence interval, IQR: Interquartile range, PESI: Pulmonary embolism severity index, SD: Standard deviation; *Student's t-test.

obtained from our study are consistent with the literature and even indicate slightly lower intensive care needs and mortality rates.

The Wells score is used to predict the diagnosis of APE (9). In this study, it was determined that each point increase in the Wells score in patients diagnosed with COVID-19-related APE increased their probability of intensive care unit transfer by 1.7 times (OR = 1.70; 95% CI = 1.13 - 2.56; p = 0.011). In addition to the diagnostic use of the Wells score, its association with transfer to the intensive care unit in patients with COVID-19-related APE suggests that this parameter may also have a place in determining the prognosis of these patients. To the best of our knowledge, there

is no study in the literature examining the utility of the Wells score in predicting the prognosis of patients diagnosed with COVID-19-related APE or their intensive care unit needs.

In this study, the mean and standard deviation values of the PESI score were found to be higher in patients diagnosed with COVID-19-related APE followed up in the intensive care unit compared to those without intensive care needs (120.34 ± 39.59 vs. 79.06 ± 27.56) (p < 0.001). Multivariate analysis revealed that each point increase in the PESI score increased the probability of intensive care unit transfer by 1.03 times (95% CI: 1.00–1.07; p = 0.048). In a multicenter retrospective cohort study conducted in Spain and

Table 4. Distribution of treatments applied for COVID-19 and clinical outcomes in patients with COVID-19-related APE according to the ICU transfer status

	Transferred to ICU, n (%) n = 38	Not transferred to ICU, n (%) n = 85	OR (95% CI)	p-value
Oxygen support				<0.001
None (reference)	6 (15.8)	44 (58.7)	1.00	
Nasal cannula	18 (47.4)	29 (38.7)	4.55 (1.61-12.83)	
Mask	1 (2.6)	1 (1.3)	7.33 (0.40-133.30)	
Reservoir mask	6 (15.8)	1 (1.3)	44.00 (4.50-431.10)	
HFNO	2 (5.3)	0 (0)	-	
NIMV	2 (5.3)	0 (0)	-	
IMV	3 (7.9)	0 (0)	-	
Methylprednisolone (≥250 mg)	11 (28.9)	0 (0)	0.24 (0.17-0.33)	<0.001
Colchicine	12 (31.6)	9 (10.8)	3.79 (1.43-10.04)	0.005
Hydroxychloroquine	8 (21.1)	17 (20.2)	1.05 (0.40-2.70)	0.91
Favipiravir				
Median length of stay (days) (IQR) (n = 123)	16.0 (19)	9.0 (8)		<0.001
Mortality	12 (31.6)	3 (3.5)	12.61 (3.30-48.17)	<0.001

APE: Acute pulmonary thromboembolism, ICU: Intensive care unit, OR: Odds ratio, CI: Confidence interval, HFNO: High-flow nasal oxygen, NIMV: Non-invasive mechanical ventilation, IMV: Invasive mechanical ventilation, IQR: Interquartile range.

Table 5. Logistic regression analyses of factors affecting the risk of intensive care unit transfer in hospitalized patients with COVID-19-related APE

	Univariate analysis			Multivariate analysis*		
	OR	95% CI	p-value	Adj OR	95% CI	p-value
Age (years)	1.04	1.01-1.07	0.003	1.01	0.94-1.08	0.801
Male gender	1.27	0.55-2.92	0.57	2.33	0.44-12.22	0.315
Number of comorbidities	1.23	0.95-1.61	0.113	1.07	0.64-1.80	0.785
Malignancy	2.93	0.97-8.80	0.055	0.38	0.04-3.63	0.403
Wells score	1.47	1.16-1.84	0.001	1.70	1.13-2.56	0.011
PESI score	1.04	1.02-1.06	<0.001	1.03	1.00-1.07	0.048
Embolus localization						
Subsegmental (reference)	1.00			1.00		
Segmental	0.70	0.20-2.38	0.565	0.35	0.02-4.48	0.423
Lobar	0.43	0.09-2.15	0.305	0.07	0.003-1.50	0.089
Pulmonary artery	3.60	1.03-12.62	0.045	1.90	0.17-21.47	0.603
Embolism laterality (bilateral vs unilateral)	3.39	1.28-8.98	0.014	4.06	0.73-22.59	0.109
d-dimer	1.08	1.03-1.12	<0.001	1.05	0.98-1.12	0.165
Troponin I	1.0	0.10-1.00	0.86	1.00	0.99-1.00	0.627
C-reactive protein	1.0	1.00-1.01	0.005	1.01	1.00-1.02	0.049

APE: Acute pulmonary thromboembolism, OR: Odds ratio, CI: Confidence interval, adj.: adjusted, PESI: Pulmonary embolism severity index; *This analysis was performed on the data of 98 patients. Nagelkerke R² = 0.63, Hosmer-Lemeshow test p-value = 0.81

France, factors determining in-hospital mortality were examined, and it was reported that a simplified PSI score of 1 or greater in patients with PCR-confirmed COVID-19 who presented with APE increased in-hospital mortality by 2.23 times (95% CI = 1.29 - 3.86) (10). Although the extent of the association may seem different due to the previous authors' use of the simplified version of PESI, the direction, and significance of this association are similar. In another study conducted in Türkiye before COVID-19 to evaluate patients with APE, it was found that a high simplified PESI score increased long-term mortality (30 days and later) by 1.69 times (OR = 1.05; 95% CI = 0.98 - 1.12; $p=0.165$) (11), which supports the findings of the current study.

We found that the rate of embolism in the main pulmonary artery was significantly higher in patients who were transferred to the intensive care unit compared to those without an intensive care need. In the presence of variables such as oxygen support and respiratory rate in the PESI score, localization seems to lose its statistical significance in multivariate analysis. Similar to the findings of our study, a multicenter study conducted in Spain and France did not detect a statistically significant relationship between embolism localization and in-hospital mortality (10).

Arterial blood gas results of almost all patients who were transferred to the intensive care unit were available from the electronic recording system, whereas the results of about half of the patients who were not transferred to the intensive care unit were available. It is considered that the statistical significant difference between these groups could not be shown because most of the available arterial blood gas results were taken under oxygen therapy, the group in which arterial blood gas results were taken in the group that was not transferred to the intensive care unit probably had a more severe clinic, and the number of the group with arterial blood gas results was relatively low (type 2 error).

In a study that investigated the prognostic value of the serum albumin level in 269 patients with APE,

it was shown that a low serum albumin level also increased long-term mortality (11). Consistently, in the current study, the serum albumin value was found to be lower in patients with COVID-19-related APE who were transferred to the intensive care unit compared to those who were not transferred to intensive care ($p < 0.001$).

In this study, the CRP level was higher in patients followed up in the intensive care unit compared to the remaining patients ($p = 0.001$). In a meta-analysis examining laboratory parameters with early prognostic value in COVID-19, elevated white blood cell count, CRP, lactate dehydrogenase, and d-dimer levels and a low lymphocyte count were found to increase mortality (12).

In our sample, the median d-dimer value was found to be 12.75 (IQR: 20.91) mg/L in patients followed up in the intensive care unit and 3.55 (6.65) mg/L in those who did not need intensive care, and the difference between the two groups was statistically significant ($p < 0.001$). When factors affecting intensive care needs were examined in a binary regression analysis, d-dimer was determined to be statistically significant in univariate analysis, while this significance was lost in multivariate analysis (OR: 1.05; 95% CI: 0.98-1.12; $p = 0.165$). Since d-dimer is a fibrin degradation product, it is associated with thrombus burden and prognosis (13,14). It also probably increases due to the inflammatory response and hypoxia-inducible transcription factor-dependent signaling pathway induced by SARS-CoV-2 infection (15). Therefore, we consider that d-dimer may have lost its significance in the presence of the PESI score and CRP, which represent the inflammatory response in our logistic regression model.

We determined that the NLR was higher in patients who were transferred to the intensive care unit compared to the other patient group. In a previous study, a high NLR was found to increase both 30-day and one-year mortality in patients with APE who were followed up in a center in Israel between 2007 and 2021 (16). Covering a period beginning before

COVID-19 and spanning a portion of the pandemic, the study indicated that the NLR, which stands out as a factor in the prognosis of COVID-19 patients, is also essential in the prognostic assessment of APE.

When the CRP-to-albumin ratio was examined, the mean value was determined to be 23.71 ± 24.85 in patients followed up in the intensive care unit and 9.51 ± 17.02 in those who did not need intensive care. There was a statistically significant difference between the two groups ($p < 0.001$). In a previous study investigating the prognostic value of the CRP-to-albumin ratio in 186 patients diagnosed with APE in Türkiye, 54 patients were determined to be at moderate risk, 34 at high risk, and 98 at very high risk according to the PESI score. The PESI score had a moderate, positive correlation with the CRP-to-albumin ratio ($r = 0.584$, $p < 0.0001$) and troponin ($r = 0.521$, $p < 0.0001$, respectively) (17). Our findings are in agreement with the literature.

This study has certain limitations. First, data were collected retrospectively through the hospital's computer system. Therefore, there were missing data due to some examinations not having been carried out within a pre-determined protocol. Nevertheless, the necessary data were obtained for many variables in most patients. Second, the single-center design of the study limits its external validity. Third, the small sample size limits the evaluation of rarer clinical outcomes, especially mortality. However, to the best of our knowledge, previous studies have only included a subgroup analysis of a very small number of patients for a special patient population, such as those with COVID-19-related APE. A strong aspect of the current study is that this special group exclusively constituted the sample, and the number of patients was higher than in previous subgroup analyses. Furthermore, we included patients diagnosed with APE by CTPA, which is considered the gold standard for the diagnosis of this condition. This minimized the possibility of a doubtful APE diagnosis. However, it is

possible that some patients developed APE but did not undergo CTPA. Nevertheless, since the patients in this group are likely to have a milder clinical course, the association is biased toward the null.

In conclusion, this study showed that high Wells and PESI scores and serum CRP in hospitalized patients with COVID-19-related APE increased their probability of transfer to the intensive care unit. Therefore, it is recommended to monitor these patients more closely in terms of the development of intensive care needs.

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Ethical approval

This study has been approved by the Ankara City Hospital No. 1 Clinical Research Ethics Committee (approval date: March 17, 2021, number: E1-21-1628). Written informed consent was obtained from the participants.

Author contribution

Study conception and design: UOS, AS, AK; data collection: UOS, MeFiGü, MuFuGö, EA, AK; data analysis and interpretation of results: UOS, AS, MeFiGü, MuFuGö, EA, AK; draft manuscript preparation: UOS, AS. The authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Glycemic variability and mortality in critically ill patients: higher risk in non-diabetic patients

Kritik hastalarda glisemik değişkenlik ve mortalite: diyabetik olmayan hastalarda daha yüksek risk

Pervin Hancı¹, Mehmet Serdar Cengizhan², Çağla Yıldız³, Volkan İnal⁴

¹Division of Intensive Care Medicine, Department of Pulmonology, Faculty of Medicine, Trakya University, Edirne, Türkiye

²Department of Intensive Care, Tarsus State Hospital, Ministry of Health, Mersin, Türkiye

³Department of Internal Medicine, Besni State Hospital, Ministry of Health, Adıyaman, Türkiye

⁴Division of Intensive Care Medicine, Department of Internal Medicine, Faculty of Medicine, Trakya University, Edirne, Türkiye

ABSTRACT

Objective: Glycemic variability (GV) is associated with increased morbidity and mortality in critically ill patients. This study aimed to contribute to the knowledge on the subject and to investigate the situation in our intensive care patient population.

Method: Patients who were admitted to the Intensive Care Unit (ICU) between January 2015 and August 2020 were screened using the hospital's database. The following data were collected: demographic characteristics of the patients, comorbidities, APACHE II scores, SOFA scores, mean amplitude of glycemic excursions (MAGE) based on daily blood glucose measurements from the first day of ICU admission until discharge up to the 28th day of their stay, length of stay (LOS), and 28-day mortality status.

Results: In this study, 136 patients were enrolled and divided into high (n=70) and low GV (n=66). No differences were found between the two groups in terms of age, gender, comorbidity, APACHE II, mean SOFA scores, treatments, ICU LOS, and mortality. MAGE was higher in nonsurvivors (78.8 ±32.2) compared to survivors (65.4 ±22.5) (t=-2.78, p= 0.005). Regarding the mortality, the AUC value for GV was 0.611 (p=0.02) for MAGE >61 mg/dl, with a sensitivity of 68.5% and specificity of 50%. Patients were grouped according to GV (MAGE>65) and the presence of diabetes mellitus (DM). Mortality was highest in patients with high GV and without DM (53.3%).

Conclusion: In this study, MAGE levels were higher in non-survivors than survivors, and glycemic variability was moderately associated with mortality. Patients with high GV and without DM had a higher mortality rate compared to those with DM.

Keywords: glycemic variability, critically ill, mortality

ÖZ

Amaç: Glisemik değişkenlik (GD), yoğun bakım hastaları için mortalite ve morbidite artışı dahil olmak üzere önemli klinik etkilere sahip olabilir. Bu çalışma, konuyla ilgili bilgi birikimine katkıda bulunmak ve yoğun bakım hasta popülasyonumuzdaki durumu ortaya koymak amacıyla yapılmıştır.

✉ Pervin Hancı • pervinhanci@trakya.edu.tr

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Telif hakkı © 2025 Yazar(lar). Türk Yoğun Bakım Derneği tarafından yayımlanmıştır. Açık erişimli bu makale, orijinal çalışmaya uygun şekilde atıfta bulunulması koşuluyla, herhangi bir ortamda veya formatta sınırsız kullanım, dağıtım ve çoğaltmaya izin veren [Creative Commons Atıf Lisansı \(CC BY\)](#) ile dağıtılmıştır.

Yöntem: Ocak 2015 ve Ağustos 2020 tarihleri arasında Yoğun Bakım Ünitesine kabul edilen hastalar hastanenin veri tabanı kullanılarak taranmıştır. Hastaların demografik özellikleri, komorbiditeleri, APACHE II skorları, SOFA skorları, yoğun bakım ünitesine kabul edildikleri ilk günden taburculuğa veya yoğun bakım ünitesinde kaldıkları 28. güne kadar günlük kan şekeri ölçüm değerlerinden ortalama glisemik ekssürsion amplitüdü (MAGE), yatış süresi ve 28 günlük mortalite durumu kaydedilmiştir.

Bulgular: Bu çalışmaya 136 hasta dahil edilmiş; yüksek (n=70) ve düşük GD (n=66) olarak iki gruba ayrılmıştır. Gruplar arasında yaş, cinsiyet, komorbidite, APACHE II, ortalama SOFA skorları, tedaviler, yoğun bakımda kalış süresi ve mortalite açısından fark saptanmamıştır. MAGE'nin hayatta kalmayanlarda (78,8 ±32,2) hayatta kalanlara (65,4 ±22,5) kıyasla daha yüksek olduğu görülmüştür (t=-2,78, p= 0,005). GD'nin mortaliteyi tahmin gücünü belirlemek için ROC analizi yapılmıştır. Eğri altında kalan alan 0.611 (p=0.02) saptanmıştır. MAGE >61 mg/dl eşik değeri alındığında duyarlılık %68,5 ve özgüllük %50 bulunmuştur. Hastalar GD'nin yüksek veya düşük olması (MAGE>65 mg/dl) ve diyabetes mellitus (DM) varlığına göre gruplandırılarak mortalite açısından karşılaştırılmıştır. Mortalite, yüksek GD'li ve DM'si olmayan hastalarda en yüksekti (%53,3).

Sonuç: Bu çalışmada MAGE düzeylerinin hayatta kalmayanlarda hayatta kalanlara kıyasla daha yüksek olduğu bulunmuştur. GD mortaliteyi orta derecede öngörmüştür. GD yüksek olan ve DM olmayan hastalarda mortalite oranı diyabeti olan hastalara göre daha yüksekti.

Anahtar kelimeler: glisemik değişkenlik, kritik hastalık, mortalite

Introduction

Numerous metabolic abnormalities that critically ill patients experience can have a major effect on their clinical fate. Maintaining glycemic control, which has been demonstrated to lower morbidity and mortality, is an essential part of their care (1). Intensive Care Unit (ICU) patients frequently have hyperglycemia, which is associated with an increased risk of infection, longer hospital stays, and higher mortality (2,3). Hypoglycemia has been shown to have adverse effects on these patients too (4,5). Attentive glycemic control is advised to avoid the negative consequences of both hypoglycemia and hyperglycemia. The American Diabetes Association (ADA) recommends targeting blood glucose levels between 140 and 180 mg/dL in critically ill patients (6), while the Society of Critical Care Medicine (SCCM) recommends maintaining blood glucose levels between 110 and 150 mg/dL (7).

Blood glucose variations that deviate from the desired range are known as glycemic variability (GV). The stress reaction to severe illness is one of the main causes of GV (8). Studies have shown that higher GV is associated with increased morbidity and mortality, longer hospital stays, and a higher risk of infections (9-11). GV can occur due to several causes. These include the type and timing of nutritional support, the presence of comorbidities, the severity of the illness, and the use of drugs such as vasopressors and corticosteroids (4). In order to reduce GV in ICU

patients, it is imperative to recognize and control these factors.

This study was conducted to understand GV status in our patient population. The primary objective was to investigate the relationship between glycemic variability (GV) and mortality in patients admitted to the ICU. Additionally, the effects of potential risk factors on GV were analysed.

Method

The hospital database was used to do a retrospective screening of patients hospitalized to the Internal Medicine Intensive Care Unit between January 2015 and August 2020.

Patient's demographics, comorbid conditions, Acute Physiology and Chronic Health Evaluation II (APACHE II) scores (12) and their corresponding predicted mortality rates (APACHE II-PMR); Sequential Organ Failure Assessment (SOFA) scores (13) at ICU admission; and information on the use of insulin, corticosteroids, vasopressors, and beta-blockers were documented, as were the ICU length of stay (LOS) and 28-day mortality status. As an institutional protocol, blood glucose had been measured at least 4-6 times daily using a bedside glucose analyser. Samples were taken from capillary blood. Following international guidelines, the target blood glucose range in the intensive care unit was 140-180 mg/dL (6).

Insulin administration was managed protocol-based on these targets. All patients received nutritional support to meet their daily caloric needs of 25-30 kcal/kg.

Blood glucose values were recorded from the first day of admission to the intensive care unit until discharge, up to a maximum of 28th days of their intensive care unit stay. The mean amplitude of glycemic excursion (MAGE) index was used to determine glycemic variability. The MAGE index is calculated by measuring the difference between the peak and trough glycemic excursion over 24 hours. The MAGE index was calculated using the formula: $MAGE = 1/n * \sum |G[i] - G[j]|$, where $G[i]$ and $G[j]$ represent the glucose values at two consecutive peaks or nadirs, and n is the total number of peaks and nadirs that meet the threshold criteria. Then, the average of daily MAGE indices was calculated (Sum of daily MAGE/ICU stay). Referring to a previous study (14), high GV was defined as a MAGE >65 mg/dL.

This study received approval from the Trakya University Clinical Research Ethics Committee (TÜTF-BAEK 2020/438, 07.12.2020). Written informed consent was obtained from the participants' legal guardians or next of kin. According to the study clinic's regulatory procedures, patients or their legally authorized relatives provided written consent for 'processing and publishing patients' medical records (with names disclosed) for scientific purposes.'

Statistical analyses

IBM SPSS version 26.0 (IBM Corporation, Armonk, NY) was used for statistical analyses. Descriptive statistics were presented as counts (percentages) for categorical variables and medians [25th-75th percentiles] for numerical variables. Baseline characteristics, scores, and outcomes were compared between low and high GV groups using Chi-square tests and Fisher's exact tests for categorical variables, and the Mann-Whitney U test for numerical variables where appropriate. The receiver operating characteristic (ROC) curve was

employed to assess the predictive prognostic value of the MAGE index. A 5% type-I error rate was applied to determine statistical significance.

Results

Medical records of 612 patients admitted to the ICU between January 2015 and August 2020 were reviewed. In total, 136 patients whose medical records were fully accessible were included in the study. Demographic characteristics (age, gender), comorbidities, SOFA, APACHE II and APACHEII-PMR at the ICU admission; use of insulin, corticosteroid, vasopressor, and beta-blocker therapy, length of stay, and 28-day mortality status of the patients are shown in Table 1. The median age was 71 [63-77] years. Men were in the majority (57.4%). One hundred six (77.1) patients had diabetes mellitus (DM), which was the leading comorbidity. The median APACHE-II score was 22 [16-29]. The median MAGE index was 66.7 [50.0-87.5]. ICU length of stay was 9.5 [6.0-27.5] days. In-hospital mortality was 39.7%. According to the APACHE-II predicted mortality, the standardised mortality ratio was 0.93 (95% CI: 0.68-1.17).

Patients were categorised into low or high GV groups according to the MAGE index and compared (Table 1). Groups were not different in terms of age, gender, comorbidities, or scores. Insulin therapy was used more frequently in patients with high GV (74.3%) than in patients with low GV (36.4%) ($p < 0.001$).

The length of stay in the ICU and hospital mortality did not differ between the low and high GV groups. However, MAGE was higher in nonsurvivors (78.8 ± 32.2) compared to survivors (65.4 ± 22.5) ($t = -2.78$, $p = 0.005$). In the ROC analysis for predicting mortality based on GV, the AUC was 0.611 ($p = 0.02$) (MAGE > 61 mg/dl, Sensitivity 68.5%, Specificity 50%) (Figure 1). Mortality was compared by grouping patients according to GV (MAGE > 65) and the presence of DM. (Figure 2) Mortality was highest in patients with high GV and without DM (53.3%).

Table 1. Characteristics of the patients categorized by glycaemic variability

	All (n=136)	Low GV (MAGE \leq 65) (n=66)	High GV (MAGE >65) (n=70)	p
Age. years *	71 [63-77]	69 [62-76]	73.5 [63.7-78.0]	0.23
Gender. Male (n, %)	78 (57.4)	36 (54.5)	42 (60.0)	0.52
Comorbidities, (n, %)				
DM	106 (77.9)	51 (77.3)	55 (79.6)	0.26
Type-1	2 (1.5)	0 (0)	2 (2.9)	
Type-2	104 (76.5)	51 (77.3)	53 (75.7)	
Chronic Pulmonary Disease	35 (25.7)	16 (24.2)	19 (27.1)	0.69
Cerebrovascular Disease	47 (34.6)	21 (31.8)	26 (37.1)	0.51
Malignity	31 (22.8)	16 (24.2)	15 (21.4)	0.69
Chronic Renal Disease	65 (47.7)	35 (53)	30 (42.9)	0.23
Chronic Liver Failure	4 (2.9)	1 (1.5)	3 (4.3)	0.62
Cardiovascular System	37 (27.2)	20 (30.3)	17 (24.3)	0.43
Hypothyroidism	9 (6.6)	5 (7.6)	5 (7.1)	0.41
SOFA score	6.9 [4.6-9.6]	7.1 [5.2-9.6]	6.6 [4.0-9.9]	0.34
APACHE II*	22 [16-29]	22.5 [16.7-31.0]	21.5 [16.0-27.2]	0.28
APACHE-PMR *	0.39 [0.17-0.64]	0.45 [0.17-0.67]	0.38 [0.15-0.62]	0.33
Average MAGE*	66.7 [50.0-87.5]	49.9 [43.7-56.0]	86.3 [73.4-100.5]	<0.001
Therapies				
Corticosteroid	82 (60.3)	35 (53.0)	47 (67.1)	0.09
Insulin	76 (55.9)	24 (36.4)	52 (74.3)	<0.001
Vasopressor	102 (75)	49 (74.2)	53 (75.7)	0.84
Beta-blocker	74 (54.4)	38 (57.6)	36 (51.4)	0.47
ICU Length of Stay *	9.5 [6.0-27.5]	9.0 [6.7-28.0]	11 [5.0-26.2]	0.72
Mortality (n. %)	54 (39.7)	23 (34.8)	31 (44.3)	0.29

Definition of abbreviations: GV: Glycaemic variability, MAGE: mean amplitude of glycaemic excursions, DM: Diabetes mellitus, SOFA: Sequential organ failure assessment, APACHE II: Acute Physiology and Chronic Health Evaluation, PMR: Predicted Mortality Ratio. Data was expressed as n (%) and *: median [25-75th percentiles].

Discussion

This study showed that MAGE was higher in non-survivors than survivors, and glycemic variability moderately predicted mortality. Patients with high glycemic variability and without DM had higher mortality than patients with DM. Glycemic variability was associated with insulin therapy.

The management of glycaemia in critically ill patients has been the subject of extensive research and controversy over the years. Although it's well known that hyperglycemia is a compensatory mechanism to provide sufficient substrate to vital organs as a stress response (8), its association with increased morbidity and mortality has been documented (2,3). However,

adverse outcomes and increased mortality have been reported in randomised trials evaluating the efficacy of tight glycemic control. (15) Several factors, such as optimal glycemic targets, risk of hypoglycemia, glycemic variability, appropriate target populations, and insulin infusion protocol, have complicated this issue. Recent studies have also highlighted the importance of each patient's pre-existing glycemic milieu, further complicating the determination of appropriate glycemic thresholds (16,17).

Studies have shown that there is a correlation between GV and mortality in critically ill patients. (10,18-20) GV was also found to be more strongly associated with mortality than hyperglycemia and hypoglycemia

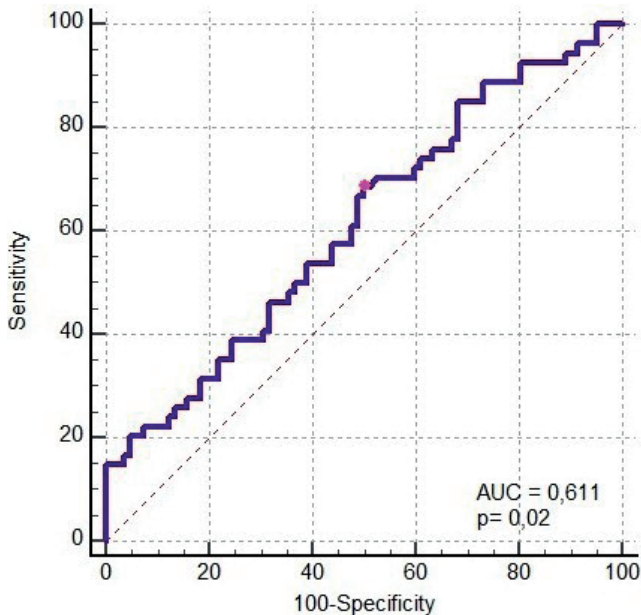


Figure 1. Receiver operating characteristics curve for ability of the MAGE to identify mortality

Definition of abbreviations: MAGE: mean amplitude of glycaemic excursions

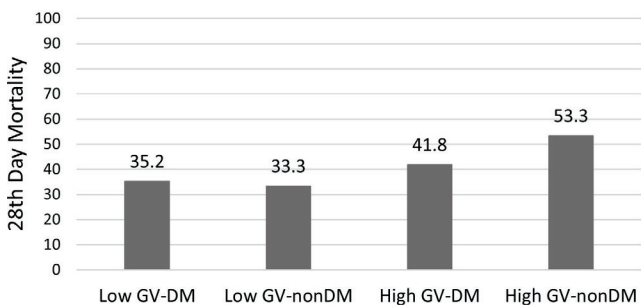


Figure 2. 28th-day mortality of the patients according to the glycemic variability and diabetes mellitus status

Definition of abbreviations: GV: Glycaemic variability, DM: Diabetes mellitus

in the paediatric population (21). This association of glycaemic variability with mortality is initiated by increased oxidative stress, neuronal damage, mitochondrial damage, and coagulation activity, as in hyperglycemia (19,22,23).

Many indices are used in evaluating glycaemic variability, such as MAGE, glucose variability index (GVI), glycemic lability index (GLI), coefficient of

variation (CV), continuous overlap-ping net glycaemic action (CONGA), and mean of daily differences (MODD) (24). In this study, we used the MAGE index with a cut-off value of 65 to group patients as high and low GV, referring to a study by Service et al. (14) Similar to our study, Chao et al. also used this cut-off value (10). In their study, they calculated MAGE on the first day of ICU admission in patients with sepsis and examined its relationship with mortality in this patient group. The results showed a higher mortality rate of 36.7% in patients with high GV than in patients with low GV, who had a mortality rate of 26.6%. They also found a correlation between GV and 30-day mortality using Kaplan-Meier analysis (log-rank test, $p=0.018$). Our study differs from Chao et al.'s in that we did not focus on a specific group of patients. We also utilized the mean of daily MAGE indices measured daily during the ICU stay to group the patients. This may explain our finding that glycemic variability predicted mortality moderately.

Our findings align with a recent systematic review and meta-analysis by Hyrciw et al., which included 41 studies investigating the association between GV and short-term mortality in intensive care patients (25). This meta-analysis found a consistent association between increased measures of glycemic variability and higher short-term mortality. In studies where MAGE was used, MAGE was 0.24 mmol/L higher (95% CI: -0.23 to 0.70) in patients who died compared to survivors. Additionally, for every 1 mmol/L increase in MAGE, the adjusted odds of mortality increased by 4% (aOR: 1.04; 95% CI: 1.01–1.08), while patients in the highest quartile of MAGE had a 61% higher risk of mortality than those in the lowest quartile (aOR: 1.61; 95% CI: 1.01–2.56). These findings emphasize that higher glycemic variability, as measured by MAGE, is associated with an increased risk of mortality in critically ill patients. Although the certainty of the evidence is low and should be interpreted cautiously, this reinforces the importance of monitoring and minimizing glycemic variability as a potential strategy to improve patient outcomes.

In our study, non-diabetic patients with high glycaemic variability had higher mortality than diabetic patients. Krinsley et al. conducted a crucial study that compared the impact of glycaemic variability on mortality in critically ill patients who were grouped based on their DM status (26). In this study, mean capillary blood glucose level (MGL) and coefficient variation (% standard deviation/MGL) measured during ICU stay were used to assess GV. Supporting the results of our study, GV was found to have a strong and independent relationship with mortality in patients without DM, whereas this relationship was not found in patients with DM. The mechanism of high glycemic variability may have a worse effect on the survival of non-diabetic patients than those with DM during critical illness is not well known. Patients with DM may have developed a tolerance to the cellular and microvascular complications caused by high blood sugar levels. On the other hand, sudden changes in glucose levels may trigger a cytokine storm in patients without DM. Additionally, non-diabetic patients may require a higher release of cytokines or hormones than diabetic patients in response to the same level of glucose change, which could be linked to the severity of the disease and the risk of mortality. Our study found no difference between APACHE-II in high and low GV groups. Although this supports the hypothesis of tolerance to glycaemic complications, we cannot make a clear statement since we did not perform multivariable logistic regression analysis.

The study has limitations that need to be considered while interpreting the results. First, the retrospective nature of the study inherently limits control over data quality and the capacity to account for all potential confounders. Second, the relatively small sample size may restrict the generalizability of the results. Furthermore, although nutritional support was provided to meet daily caloric requirements (25–30 kcal/kg/day), patients could not be consistently categorized according to the route of nutrition (enteral or parenteral) due to practical constraints in adhering to a single method throughout the ICU

stay. This variability in nutritional strategies may have impacted glycemic variability and mortality outcomes. Additionally, the number and timing of blood glucose measurements were not standardized. Measurements were conducted four to six times daily, based on clinical requirements, with adjustments made according to the patient's condition. On the other hand, irregular timing may affect the precision of variability evaluations, and fewer measurements may result in an underestimation of glycemic variability. Because of variations in metabolic reactions and dietary factors, acute and chronic stages of illness may show different patterns of glycemic fluctuation. These limitations will be addressed in future prospective studies that examine feeding patterns and routine blood glucose testing schedules. Lastly, the study did not account for possible confounding variables that can impact glycemic control, such as the severity of the condition and the use of other drugs. In conclusion, this study highlights the importance of GV as a determinant of mortality in critically ill patients; a higher GV is associated with an increased risk of death, which is particularly evident in non-diabetic patients. These findings contribute to the ongoing debate about glycemic management in critical care. Future research should focus on developing strategies to reduce GV in critically ill patients.

Ethical approval

This study has been approved by the Trakya University Faculty of Medicine Scientific Research Ethics Committee (approval date: December 7, 2020, number: 20/03). Written informed consent was obtained from the participants.

Author contribution

Study conception and design: MSC; data collection: MSC, ÇY; analysis and interpretation of results: PH; draft manuscript preparation: PH, Vİ. The author(s) reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Research on attitudes of senior anesthesia assistants and intensive care physicians towards compliance with the “pain, agitation/sedation, immobility, and sleep disruption” guidelines and symptom management in the intensive care units in Türkiye

Türkiye’deki yoğun bakım ünitelerinde kıdemli anestezi asistanı ve yoğun bakım hekimlerinin “ağrı, ajitasyon/sedasyon, hareketsizlik ve uyku bozulması” kılavuzuna uyum ve semptom yönetimine ilişkin tutumları üzerine bir araştırma

Melih Seyda Doğan¹, Mehmet Selim Çömez¹, Onur Koyuncu¹, Sedat Hakimoğlu¹, Senem Urfalı¹, Serhat Hakkoymaz¹

¹Department of Anesthesiology and Reanimation, Tayfur Ata Sökmen Faculty of Medicine, Hatay Mustafa Kemal University, Antakya, Hatay, Türkiye

ABSTRACT

Introduction: It was aimed to investigate the attitudes of senior anesthesia assistants and intensive care physicians in Türkiye towards compliance with the “Pain, Agitation/Sedation, Immobility and Sleep Disruption” (PADIS) Guidelines and symptom management in the intensive care unit (ICU).

Methods: The survey, consisting of 40 questions was sent to the participants electronically. The answers to the questions were evaluated according to the recommendations in the PADIS 2018 guidelines.

Results: While anesthesiology and reanimation specialists gave less compatible answers (58.9%) with the guideline in “identifying risk factors affecting pain”; responses were more consistent with the guideline (100%, 69.5%, and 85.3%, respectively) in “use of medication in addition to opioids”, “use of medication to prevent delirium”, and “pharmacological interventions to improve sleep”

Discussion and Conclusion: This study demonstrates that intensive care physicians, including anesthesiology and reanimation assistants in Türkiye, generally exhibit a compatible attitude with the PADIS 2018 guideline in the management of “pain, agitation/sedation, delirium, immobility and sleep disruption” symptoms in critically ill adults in the ICU. Additionally, as the medicine career progresses, more guideline-compliant responses in the management of some symptoms have demonstrated the importance of clinical experience in critically ill adults management.

Keywords: PADIS, pain, agitation, sedation, delirium, immobility, sleep disruption, survey

✉ Mehmet Selim Çömez • drmcomez313@gmail.com

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Telif hakkı © 2025 Yazar(lar). Türk Yoğun Bakım Derneği tarafından yayımlanmıştır. Açık erişimli bu makale, orijinal çalışmaya uygun şekilde atıfta bulunulması koşuluyla, herhangi bir ortamda veya formatta sınırsız kullanım, dağıtım ve çoğaltmaya izin veren [Creative Commons Atıf Lisansı \(CC BY\)](#) ile dağıtılmıştır.

ÖZ

Amaç: Türkiye'de kıdemli anestezi asistanları ve yoğun bakım hekimlerinin yoğun bakım ünitesinde (YBÜ) "Ağrı, Ajitasyon/Sedasyon, İmmobilite ve Uyku Bozukluğu" (PADIS) Kılavuzuna uyum ve semptom yönetimine yönelik tutumlarının araştırılması amaçlandı.

Yöntem: 40 sorudan oluşan anket katılımcılara elektronik ortamda gönderildi. Sorulara verilen cevaplar PADIS 2018 kılavuzundaki önerilere göre değerlendirildi.

Bulgular: Anesteziyoloji ve reanimasyon uzmanları "ağrıyı etkileyen risk faktörlerinin belirlenmesi" konusunda kılavuza daha az (%58,9) uyumlu yanıtlar verirken; "opioidlere ek olarak ilaç kullanımı", "deliryumu önlemek için ilaç kullanımı" ve "uykuyu iyileştirmeye yönelik farmakolojik müdahaleler" konularında kılavuzla daha tutarlı yanıtlar verdi (sırasıyla %100, %69,5 ve %85,3).

Tartışma ve Sonuç: Bu çalışma, Türkiye'de anesteziyoloji ve reanimasyon asistanları da dahil olmak üzere yoğun bakım hekimlerinin, yoğun bakımdaki yetişkin kritik hastalarda "ağrı, ajitasyon/sedasyon, deliryum, hareketsizlik ve uyku bozukluğu" semptomlarının yönetiminde PADIS 2018 kılavuzuna genel olarak uyumlu bir tutum sergilediğini göstermektedir. Ek olarak, tıp kariyeri ilerledikçe, bazı semptomların tedavisinde kılavuzlarla daha uyumlu yanıtların alınması, kritik hastalığı olan yetişkinlerin yönetiminde klinik deneyimin önemini ortaya koymuştur.

Anahtar kelimeler: PADIS, ağrı, ajitasyon, sedasyon, deliryum, immobilite, uyku bozulması, anket

Introduction

Given the characteristics of critically ill adults, such as mental status changes, use of invasive procedures and devices, sleep disturbances, and immobility, the approach to pain assessment and management is crucial (1). Pain in the intensive care unit (ICU) occurs during routine procedures that are not adequately considered, such as patient positioning, endotracheal tube suctioning, chest tube removal, arterial or venous line placement, or wound care (2). Structured pain management in the ICU may be important for the patient and the provider institution (3).

Critically ill adults who receive mechanical ventilation for a long time are exposed to negative experiences such as fear, anxiety, pain, insomnia, helplessness, weight loss and loneliness (4). Sedative agents are frequently administered to critically ill adults to relieve anxiety, reduce the stress of mechanical ventilation, and prevent harm due to agitation (5). Analgesia and sedation are effective in critically ill patients, yet excessive sedation is associated with prolonged mechanical ventilation and ICU stay. Analgesia and sedation are associated with a high rate of delirium, increased mortality, longer hospital stay, higher hospital costs, and long-term adverse outcomes in poorly managed critically ill adults (6,7).

Delirium is common in critically ill adults and is associated with prolonged ICU stay and long-

term cognitive impairment. Although delirium has previously been often overlooked, physicians are becoming increasingly aware of the vital role that acute brain dysfunction plays in the course and subsequent outcomes of critical illness. Combined pain, agitation, and delirium protocols appear to improve outcomes in critically ill adults and may reduce the incidence of delirium (8).

Survivors of critical illness often live with many long-term sequelae, such as ICU-induced muscle weakness (ICU-AW). ICU-AW may be found in 25-50% of critically ill adults (9). Additionally, there are important relationships between analgesia and sedation practices and pain and sedation status regarding patients' participation in rehabilitation/mobilization in the ICU. Early mobilization of critically ill adults through selected rehabilitation strategies has been demonstrated in many studies to shorten hospital stay, reduce the incidence of delirium, increase the number of ventilator-free days, and improve physical condition (10,11).

Poor quality sleep is a common source of distress for critically ill patients (4). Sleep disturbance is hypothesized to contribute to delirium in the ICU (12), prolonged mechanical ventilation (13), immunosuppression (14), and neurocognitive impairment (3). The PADIS 2018 Clinical Practice Guidelines provide a roadmap for the development of patient-centered and evidence-based protocols (3).

Building on the Pain, Agitation, and Delirium (PAD) Guideline published by the Society of Critical Care Medicine (SCCM) in 2013, the PADIS 2018 guideline includes a number of methodological innovations, including input from critical illness survivors. In addition to the PAD guideline, it also addresses challenges and offers recommendations regarding immobility and sleep disorder management (15). This study aimed to investigate the attitudes of senior anesthesia assistants and intensive care physicians in Türkiye towards compliance with the PADIS guideline and symptom management in the ICU.

Materials and Methods

This study was carried out between 15 October 2023 and 15 January 2024, after receiving the approval of Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (approval date: October 12, 2023, number: 19). A preliminary study was carried out by applying the created survey questions to 15 people who were not included in the study, in order to ensure the understandability of the survey. Survey data collection was achieved through an electronic data form. The survey was sent electronically to 1200 senior anesthesia assistants (AR-A), anesthesiology and reanimation specialists (AR-S), intensive care specialists (IC-S) and intensive care assistants (IC-A) whose e-mail addresses were known. It was also directly communicated to the participants at the 57th Turkish Anesthesiology and Reanimation Congress (TARK2023), which was held in November 2-5, 2023.

The survey consisted of three parts and 40 questions. The first part consisted of participants' demographic information, the second part included the participants' institutional information, and the third part consisted of questions that evaluated the suitability of the participants' attitudes towards the PADIS symptoms in intensive care patients according to the recommendations of the PADIS 2018 guidelines. The survey was prepared in the form of a Google Form

(Annex-1) and presented to the participants in a virtual environment, and their consent to participate in the survey was obtained with the help of the survey. "Senior anesthesia assistant" was defined as anesthesiology and reanimation specialist student who completed their 3rd year. Sample size in the study: Since an online response was expected from all individuals of the population (physicians working in ICU), the highest rate (50%) was taken into account in the response distribution, and by estimating a tolerable error of 7%, it was concluded that the sample size should be 190 intensive care physicians with 95% confidence.

Responses to the survey questions were evaluated according to the PADIS 2018 guideline recommendations (3):

Pain management

1. "Do you have a protocol-based (analgesedation) pain assessment and management program in the care of critically ill adults?" The answer "Yes" to the question was considered as compatible with the guideline.
2. "Are the risk factors (anxiety, depression, young age, comorbidity, pain intensity before the procedure, underlying diagnoses, etc.) that affect pain both at rest and during the procedure (thoracic tube insertion, etc.) in critically ill adults determined?" The answer "Yes" to the question was considered as compatible with the guideline.
3. "What is the pain scale you use in communicative critically ill adults?" The answers "Numeric Rating Scale, Visual Analog Scale, Verbal Descriptor Scale" to the question were considered as compatible with the guideline.
4. "What is the pain scale you use in critically ill adults who cannot communicate?" The answers "Behavioral Pain Scale, Critical-Care Pain Observation Tool" to the question were considered as compatible with the guideline.

5. "When appropriate and the patient cannot self-report, are family and loved ones included in the pain assessment process?" The answer "Yes" to the question was considered as compatible with the guideline.

6. "Are vital signs used in pain evaluation?" The answer "It is used as a clue to initiate the evaluation using valid pain assessment methods" to the question was considered as compatible with the guideline.

7. "Can you specify any medications you use in addition to opioids for pain management (to reduce pain intensity and opioid consumption) in critically ill adults?" The answers "Acetaminophen, Ketamine, and Gabapentin, Carbamazepine or Pregabalin for the treatment of neuropathic pain" to the question were considered as compatible with the guideline.

8. "What pharmacological agents do you use for pain management during bedside interventional procedures in critically ill adults?" The answers "The lowest effective dose of opioid and NSAID (IV, oral or rectal)" to the question were considered as compatible with the guideline.

9. "Which of the non-pharmacological methods do you use for pain management in critically ill adults?" The answers "Massage (in suitable patients), Music therapy (for pain due to intervention or not), Cold Application, Relaxation techniques (such as breathing exercises)" to the question were considered as compatible with the guideline.

Agitation/sedation management

10. "What is your preferred type of sedation in mechanically ventilated critically ill adults?" The answer "Light sedation" to the question was considered as compatible with the guideline.

11. "Which sedative agent do you use for sedation in adults receiving mechanical ventilation after cardiac

surgery?" The answer "Propofol" to the question was considered as compatible with the guideline.

12. "Which is your primary preferred sedative agent for sedation in critically ill adults (non-cardiac surgery)?" The answers "Propofol and Dexmedetomidine" to the question were considered as compatible with the guideline.

Delirium management

13. "Is there routine evaluation for delirium risk factors in critically ill adults after admission to the ICU?" The answers other than "Not evaluated" to the question were considered as compatible with the guideline.

14. "What scale do you use to monitor delirium in critically ill adults?" The answers other than "Routine delirium monitoring is not performed" to the question were considered as compatible with the guideline.

15. "Do you use pharmacological agents (haloperidol, atypical antipsychotic, dexmedetomidine, statin, ketamine, etc.) to prevent delirium in critically ill adults?" The answer "No" to the question was considered as compatible with the guideline.

16. "Do you use a pharmacological agent (haloperidol, atypical antipsychotic, etc.) to treat Subsyndromal delirium (ICDSC 1-3) in critically ill adults?" The answer "No" to the question was considered as compatible with the guideline.

17. "Do you use pharmacological agents (haloperidol, atypical antipsychotic, dexmedetomidine, statin, ketamine, etc.) to treat delirium in critically ill adults?" The answer "Not routinely used" to the question was considered as compatible with the guideline.

18. "Do you use dexmedetomidine in critically ill adults with delirium when agitation prevents weaning from mechanical ventilation?" The answer "Yes" to the question was considered as compatible with the guideline.

19. "Do you use non-pharmacological methods to reduce delirium?" The answer "Multi-component (Improving sleep, reducing sedation, mobilization, improving hearing or vision)" to the question was considered as compatible with the guideline.

Immobility management

20. "Do you implement a mobilization or rehabilitation program for critically ill adults?" The answer "Yes" to the question was considered as compatible with the guideline.

Sleep management

21. "Do you provide non-pharmacological interventions to improve sleep in critically ill adults?" The answers "Assisted Controlled Ventilation mode selection at night, NIV use at night in patients requiring NIV, Noise and light reduction" to the question were considered as compatible with the guideline.

22. "Do you use pharmacological interventions to improve sleep in critically ill adults?" The answer "No" to the question was considered as compatible with the guideline.

23. "Do you use a sleep-promoting protocol (earplugs, eye shields, relaxing music, etc.) in critically ill adults?" The answer "Yes" to the question was considered as compatible with the guideline.

In this study, the data were evaluated with the SPSS-27 (Statistical Package For The Social Sciences, IBM, USA) program. According to the answers given to the survey, frequency and percentage from descriptive statistics were used. Since all the answers examined were categorical variables, means and standard deviations were not used. The relationship between categorical variations was examined with the chi-square test. For all calculations, the significance limit was accepted as $p < 0.05$. The adjusted p value was accepted as $0.05/8 = 0.00625$ in the post-hoc calculation of the chi-square test. The p value of the

hypothesis was obtained by calculating the chi-square distribution $X^2 = \sum (O_i - E_i)^2 / E_i$ for 1 degree of freedom and the Adjusted Residual calculated by SPSS.

Results

Demographic characteristics of the participants and hospital characteristics were listed in Table 1.

PADIS 2018 guideline compliance assessments

1. Pain management

It was found that physicians' response rates compatible with the guideline were respectively 68.9% in "protocol-based pain management", 68.4% in "evaluation of pain risk factors", 88.9% in "use of pain assessment scale in patients with whom communication can be established", 69.5%, in "use of pain assessment scale in patients with whom communication can not be established". 33.7% in "participation in pain assessment of family and loved ones", 28.4% in "use of vital signs in pain assessment", 94.7% in "use of drugs in addition to opioids", 77.4% in "use of pharmacological agents in interventional procedures", and 31.7% in "non-pharmacological agent use in pain management" (Table 2).

When examining how the answers given were affected by the medicine career, in "identifying the risk factors affecting pain", AR-A gave 75.2%, IC-A 100% and IC-S 100% compatible answers, while AR-S gave 58.9% less consistent answers with the guideline (adjusted $p < 0.00625$). While IC-S gave 100%, AR-A 89.4% and IC-A 80% responses compatible with the guideline regarding "use of drugs in addition to opioid", AR-S gave 100% answers that were significantly more compatible with the guideline (adjusted $p < 0.00625$). These results were statistically significant ($p < 0.05$; Table 2). Other answers regarding pain management did not change according to medicine career ($p > 0.05$; Table 2).

Table 1. Demographic data, hospital and intensive care characteristics

Variables	What is your medical career?				
	AR-A n (%)	AR-S n (%)	IC-A n (%)	IC-S n (%)	Total n (%)
Age (year)					
20-30	52 (61,2)	2 (2,1)	2 (40)	0 (0)	56 (29,5)
31-40	33 (38,8)	54 (56,8)	3 (60)	1 (20)	91 (47,9)
41-50	0 (0)	34 (35,8)	0 (0)	2 (40)	36 (18,9)
51-60	0 (0)	5 (5,3)	0 (0)	1 (20)	6 (3,2)
60+	0 (0)	0 (0)	0 (0)	1 (20)	1 (0,5)
Gender					
Male	52 (61,2)	49 (51,6)	5 (100)	5 (100)	111 (59,4)
Female	33 (38,8)	46 (48,4)	0 (0)	0 (0)	79 (41,6)
Branch					
Anesthesiology and Reanimation	85 (100)	95 (100)	0 (0)	4 (80)	184 (96,8)
Internal Medicine	0 (0)	0 (0)	5 (100)	1 (20)	6 (3,1)
Intensive care experience (year)					
0-2	67 (78,8)	2 (2,1)	3 (60)	0 (0)	72 (37,9)
3-5	16 (18,8)	40 (42,1)	1 (20)	0 (0)	57 (30,0)
6-10	2 (2,4)	39 (41,1)	1 (20)	3 (60)	45 (23,7)
11-20	0 (0)	13 (13,7)	0 (0)	0 (0)	13 (6,8)
20+	0 (0)	1 (1,1)	0 (0)	2 (40)	3 (1,6)
Type of hospital					
University	52 (61,2)	9 (9,5)	5 (100)	3 (60)	69 (36,3)
State	3 (3,5)	62 (65,3)	0 (0)	1 (20)	66 (34,7)
Training and Research	30 (35,3)	22 (23,2)	0 (0)	1 (20)	53 (27,8)
Private	0 (0)	2 (2,1)	0 (0)	0 (0)	2 (1,1)
ICU type					
Anesthesiology and Reanimation	84 (98,8)	52 (54,7)	0 (0)	4 (80)	140 (73,6)
Mixed	0 (0)	44 (46,3)	0 (0)	0 (0)	44 (23,2)
Internal Medicine	1 (1,2)	0 (0)	5 (100)	1 (20)	6 (3,2)
ICU level					
Level 1	1 (1,2)	0 (0)	0 (0)	0 (0)	1 (0,5)
Level 2	3 (3,5)	39 (41,1)	0 (0)	1 (20)	43 (22,6)
Level 3	81 (95,3)	56 (58,9)	5 (100)	4 (80)	146 (76,8)
Number of ICU beds					
0-10	22 (25,9)	25 (26,3)	2 (40)	1 (20)	50 (26,3)
10-20	50 (58,8)	55 (57,9)	3 (60)	1 (20)	109 (57,4)
20-30	13 (15,3)	10 (10,5)	0 (0)	3 (60)	26 (13,7)
30-40	0 (0)	3 (3,2)	0 (0)	0 (0)	3 (1,6)
40+	0 (0)	2 (2,1)	0 (0)	0 (0)	2 (1,1)
Number of patients per nurse in a shift					
1	2 (2,4)	1 (1,1)	0 (0)	0 (0)	3 (1,6)
2	45 (52,9)	52 (54,7)	3 (60)	4 (80)	104 (54,7)
3	36 (42,3)	39 (41,1)	2 (40)	1 (20)	78 (41,1)
4	2 (2,4)	2 (2,1)	0 (0)	0 (0)	4 (2,1)
5	0 (0)	1 (1,1)	0 (0)	0 (0)	1 (0,5)
Medical career	85 (44,7)	95 (50)	5 (2,6)	5 (2,6)	190

Abbreviations; AR-A= Anesthesiology and Reanimation Assistant, AR-S= Anesthesiology and Reanimation Specialist, IC-A= Intensive Care Assistant, IC-S= Intensive Care Specialist. Categorical variables are expressed as n and %.

Table 2. Evaluation of pain management according to medical career**

Medical career		AR-A	AR-S	IC-A	IC-S	Total	P
		n (%)	n (%)	n (%)	n (%)	n (%)	
Protocol based management	GR	56 (65,9)	66 (69,5)	4 (80)	5 (100)	131 (68,9)	0,404
	nonGR	29 (34,1)	29 (30,5)	1 (20)	0 (0)	59 (31,1)	
Identifying risk factors	GR	64 (75,3)	56 (58,9)	5 (100)	5 (100)	130 (68,4)	0,015* / ^{b1}
	nonGR	21 (24,7)	39 (41,1)	0 (0)	0 (0)	60 (31,6)	
Use of scales in patients who can communicate	GR	71 (83,5)	89 (93,7)	4 (80)	5 (100)	169 (88,9)	0,125
	nonGR	14 (16,5)	6 (6,3)	1 (20)	0 (0)	21 (11,1)	
Use of scales in patients who cannot communicate	GR	59 (69,4)	65 (68,4)	4 (80)	4 (80)	132 (69,5)	0,903
	nonGR	26 (30,6)	30 (31,6)	1 (20)	1 (20)	58 (30,5)	
Family involvement in the pain assessment process	GR	29 (34,1)	29 (30,5)	3 (60)	3 (60)	64 (33,7)	0,317
	nonGR	56 (65,9)	66 (69,5)	2 (40)	2 (40)	126 (66,3)	
Use of vital signs as a clue in pain assessment	GR	24 (28,2)	26 (27,4)	1 (20)	3 (60)	54 (28,4)	0,444
	nonGR	61 (71,8)	69 (72,6)	4 (80)	2 (40)	136 (71,6)	
Use of analgesics in addition to opioids	GR	76 (89,4)	95 (100)	4 (80)	5 (100)	180 (94,7)	0,006* / ^{b2}
	nonGR	9 (10,6)	0 (0)	1 (20)	0 (0)	10 (5,3)	
Pharmacological agents used in interventional procedures	GR	72 (84,7)	68 (71,6)	3 (60)	4 (80)	147 (77,4)	0,150
	nonGR	13 (15,3)	27 (28,4)	2 (40)	1 (20)	43 (22,6)	
Non-pharmacological method used	GR	27 (32,1)	29 (31,5)	2 (40)	1 (20)	59 (31,7)	0,922
	nonGR	57 (67,9)	63 (68,5)	3 (60)	4 (80)	127 (68,3)	

Abbreviations; AR-A= Anesthesiology and Reanimation Assistant, AR-S= Anesthesiology and Reanimation Specialist, IC-A= Intensive Care Assistant, IC-S= Intensive Care Specialist. Categorical variables are expressed as n and %. GR=Guideline-compliant response, nonGR=non-guideline response. Categorical variables are expressed as n and %. *p<0.05 was considered statistically significant. **Chi-square test. b1: Bonferroni correction, adjusted p<0.00625, AR-S group creating the statistical difference. b2: AR-A and AR-S groups that make up the statistical difference.

2. Agitation/sedation management

It was found that physicians' response rates compatible with the guideline were respectively %64,2 in "sedation depth preference", 22.2% in "sedative agent selection after cardiac surgery" and 83.2% in "sedative agent selection in non-cardiac surgery patients". When the relationship between agitation/sedation management compliance with the guideline and medicine career was evaluated, no statistically significant difference was found (p>0.05; Table 3).

1. Delirium management

It was found that physicians' response rates compatible with the guideline were respectively 33.2% in "assessment of delirium risk factors", 41.6% in "delirium monitoring", 60.5% in "use of pharmacologic agent to prevent delirium", 66.3% in "pharmacologic agent use in subsyndromal delirium", 55.8% in

"routine use of pharmacologic agent for the treatment of delirium", 89.4% in "use of dexmedetomidine when agitation caused by delirium prevents weaning from mechanical ventilation", and 71.6% in "use of non-pharmacological methods to reduce delirium" (Table 4).

When examining how the answers given were affected by the medical career, it was found that in "use of medication to prevent delirium" AR-S of 69.4%, IC-S of 80%, AR-A of 50.5%, and IC-A of 40% responded in accordance with the guideline. These results were statistically significant (p<0.05; Table 4). No significant results were found in the post-hoc analysis. It can be said that this situation arised from the answers given by the AR-A and AR-S groups, which gave results closest to significance and had equal p values. No significant change was observed in the answers to other questions according to medicine career (p>0.05; Table 4).

Table 3. Evaluation of agitation/sedation management according to medical career*

Medical career		AR-A	AR-S	IC-A	IC-S	Total	P
		n (%)	n (%)	n (%)	n (%)	n (%)	
Sedation depth preference	GR	53 (62,4)	59 (62,1)	5 (100)	5 (100)	122 (64,2)	0,117
	nonGR	32 (37,6)	36 (37,9)	0 (0)	0 (0)	68 (35,8)	
Sedative agent preference after cardiac surgery	GR	23 (27,4)	16 (16,8)	2 (40)	1 (20)	42 (22,2)	0,282
	nonGR	61 (72,6)	79 (85,2)	3 (60)	4 (80)	147 (77,8)	
Sedative agent preference for non-cardiac surgery	GR	71 (83,5)	80 (84,2)	3 (60)	4 (80)	158 (83,2)	0,565
	nonGR	14 (16,5)	15 (15,8)	2 (40)	1 (20)	32 (16,8)	

Abbreviations; AR-A= Anesthesiology and Reanimation Assistant, AR-S= Anesthesiology and Reanimation Specialist, IC-A= Intensive Care Assistant, IC-S= Intensive Care Specialist. Categorical variables are expressed as n and %. GR=Guideline-compliant response, nonGR=non-guideline response. Categorical variables are expressed as n and %. *Chi-square test. $p < 0.05$ was considered statistically significant.

Table 4. Evaluation of delirium management according to medical career**

Medical career		AR-A	AR-S	IC-A	IC-S	Total	P
		n (%)	n (%)	n (%)	n (%)	n (%)	
Risk factors assessment	GR	26 (30,6)	31 (32,6)	3 (60)	3 (60)	63 (33,2)	0,319
	nonGR	59 (70,9)	64 (67,4)	2 (40)	2 (40)	127 (66,8)	
Delirium monitoring	GR	35 (41,2)	37 (38,9)	3 (60)	4 (80)	79 (41,6)	0,260
	nonGR	50 (58,8)	58 (61,1)	2 (40)	1 (20)	111 (58,4)	
Use of pharmacological agents to prevent delirium	GR	43 (50,6)	66 (69,5)	2 (40)	4 (80)	115 (60,5)	0,039*
	nonGR	42 (49,4)	29 (30,5)	3 (60)	1 (20)	75 (39,5)	
Use of pharmacological agents for subsyndromal delirium	GR	58 (68,2)	63 (66,3)	2 (40)	3 (60)	126 (66,3)	0,619
	nonGR	27 (31,8)	32 (33,7)	3 (60)	2 (40)	64 (33,7)	
Use of pharmacological agents to treat delirium	GR	48 (56,5)	53 (55,8)	2 (40)	3 (60)	106 (55,8)	0,906
	nonGR	37 (43,5)	42 (44,2)	3 (60)	2 (40)	84 (44,2)	
Use of dexmedetomidine when agitation prevents weaning	GR	76 (90,6)	81 (85,3)	0 (0)	0 (0)	168 (89,4)	0,701
	nonGR	8 (9,4)	14 (14,6)	5 (100)	5 (100)	22 (11,6)	
Non-pharmacological methods to reduce delirium	GR	58 (68,2)	72 (75,8)	3 (60)	3 (60)	136 (71,6)	0,582
	nonGR	27 (31,8)	23 (24,2)	2 (40)	2 (40)	54 (28,4)	

Abbreviations; AR-A= Anesthesiology and Reanimation Assistant, AR-S= Anesthesiology and Reanimation Specialist, IC-A= Intensive Care Assistant, IC-S= Intensive Care Specialist. Categorical variables are expressed as n and %. GR=Guideline-compliant response, nonGR=non-guideline response. Categorical variables are expressed as n and %. * $p < 0.05$ was considered statistically significant. **Chi-square test.

4. Immobility management

It was found that 89.5% of the physicians gave answers in line with the guideline in “implementing a mobilization program”. It was observed that the answers given did not vary according to medicine career. ($p > 0.05$; Table 5).

5. Sleep management

It was observed that physicians gave answers compatible with the guideline at a rate of 84.2% for “non-pharmacological interventions to improve

sleep”, 72.6% for “pharmacological interventions” and 35.3% for “use of sleep-promoting protocol” (Table 5).

When examining how the answers given were affected by the medicine career, 60% of IC-S, 62.3% of AR-A, and 20% of IC-A gave answers compatible with the guideline regarding “pharmacological interventions to improve sleep”. AR-S, on the other hand, gave answers that were more compatible with the guideline at a rate of 85.3% (adjusted $p < 0.00625$), and these results were statistically significant ($p < 0.05$; Table 5). Other answers regarding the management of sleep

Table 5. Evaluation of immobility and sleep disorder management according to medical career**

Medical career		AR-A	AR-S	IC-A	IC-S	Total	p
		n (%)	n (%)	n (%)	n (%)	n (%)	
Use of mobilization program	GR	76 (89,4)	84 (88,4)	5 (100)	5 (100)	170 (89,5)	0,732
	nonGR	9 (10,6)	11 (11,6)	0 (0)	0 (0)	20 (10,5)	
Non-pharmacological interventions to improve sleep	GR	67 (78,8)	84 (88,4)	4 (80)	5 (100)	160 (84,2)	0,248
	nonGR	18 (21,2)	11 (11,6)	1 (20)	0 (0)	30 (15,8)	
Pharmacological interventions to improve sleep	GR	53 (62,3)	81 (85,3)	1 (20)	3 (60)	138 (72,6)	0,002^{a/b}
	nonGR	31 (37,7)	14 (14,7)	4 (80)	2 (40)	51 (26,8)	
Use of sleep promoting protocol	GR	30 (35,3)	36 (37,9)	0 (0)	1 (20)	67 (35,3)	0,573
	nonGR	54 (64,7)	59 (62,1)	5 (100)	4 (80)	122 (64,7)	

Abbreviations; AR-A= Anesthesiology and Reanimation Assistant, AR-S= Anesthesiology and Reanimation Specialist, IC-A= Intensive Care Assistant, IC-S= Intensive Care Specialist. Categorical variables are expressed as n and %. GR=Guideline-compliant response, nonGR=non-guideline response. Categorical variables are expressed as n and %. *p<0.05 was considered statistically significant. **Chi-square test. b: Bonferroni correction, adjusted p<0.00625, AR-S group creating the statistical difference.

disruptions did not vary according to medical career (p>0.05; Table 5).

Situations that make the difference

In the post hoc analysis using Bonferroni correction, the adjusted p value was determined as 0.00625. Adjusted p values were calculated for each variable. The difference in the answers to the questions “Pharmacological interventions to improve sleep” and “Identification of risk factors affecting pain” resulted from the answers given by the AR-S group, whose adjusted p values gave significant results. It was found that the difference in the answers given to the question “Drugs used in addition to opioids” was due to the answers given by the AR-A and AR-S groups, whose adjusted p values gave significant results (p <0.00625). No significant results were found in the answer to the question “Use of pharmacological agents to prevent delirium”. In this case, it can be said that it is due to the answers given by the AR-A and AR-S groups, which gave the closest result to significance and had equal p values.

Discussion

Prevention and management of ICU problems are vital to optimizing the immediate and long-term recovery and outcomes of critically ill adults by minimizing distress caused by PADIS symptoms in critical patient

care. The PADIS 2018 guideline provides updated information on the prevention and management of PADIS symptoms in adult ICU patients and does so using an integrated, evidence-based, multidisciplinary ICU protocol (16). In the literature research, there are very few studies revealing physicians' attitudes in the management of PADIS symptoms. In this study, the compliance of intensive care physicians in Türkiye with the PADIS guideline in symptom management was investigated. The majority of physicians participating in the study were from the branches of anesthesiology and reanimation, and it was observed that they generally complied well with the guidelines in the management of PADIS symptoms. In pain management, a high rate of guideline compliance was noted in “protocol-based management”, “identification of risk factors”, “use of rating scales” and “use of pharmacological agents”, while a low rate of guideline compliance was observed in “participation of family members in pain assessment”, “use of vital signs”, and “ use of non-pharmacological method”. Although guideline compliance rates were high in “depth of sedation” and “sedative agent selection in non-cardiac surgery patients”, this rate remained low in “sedative agent preference after cardiac surgery”. While physicians stated very high compliance rates with the guideline in the use of “pharmacological agents” and “non-pharmacological methods” in delirium management, this rate remained low in

“identification of risk factors” and “delirium follow-up”. There were very high guideline-concordant responses in “use of mobilization program” in immobilization management. Regarding sleep management, there was high guideline compliance in “pharmacological” and “nonpharmacological interventions”, while less compliance was seen in “sleep-promoting protocols”. Although a significant relationship between medical career and guideline compliance could not be detected in general, guideline compliance was higher among physicians experienced in “use of drugs in addition to opioids” in pain management, “use of pharmacological drugs to prevent delirium” and “pharmacological interventions to improve sleep”. In addition, it was found that AR-Ss were less compliant with the guideline in “evaluation of risk factors affecting pain”. The results of this study, which was conducted only in Türkiye, emphasize the importance of clinical experience in symptom evaluation and management according to the PADIS guideline.

The SCCM recommends the routine use of valid and reliable assessment tools to monitor symptoms of pain, agitation/sedation, and delirium (3). Recent studies have also suggested that utilizing a guideline-based comprehensive questionnaire could lead to improved outcomes among critically ill adults (17,18).

This study demonstrates that attitudes towards compliance with the PADIS guideline and symptom management in the ICU change, especially as physicians' careers progress, and that this change is especially evident in the taking of pharmacological measures. These findings may guide education and policy development efforts to encourage critical care teams to be more aware of symptom management and stricter adherence to PADIS guidelines.

While studies have shown that pain and sedation assessments can be reliably conducted in brain-injured patients (19), barriers to routine implementation exist because physicians may perceive these patients as having impaired consciousness (20). In a previous study, diverse monitoring and treatment protocols were shown to be implemented for patients admitted to the

ICU based on whether they had neurological or non-neurological conditions (21). The findings in this study provide important insights into how pain management and assessment are addressed in the ICU. There were differences between AR-A, AR-S, IC-A and IC-S groups regarding pain management protocols and determination of risk factors. In pain management, guideline-compliant responses on “identification of risk factors affecting pain” and “drugs used in addition to opioids” differed significantly between different medicine career groups. This demonstrates the diversity of approaches to pain assessment and management at different stages of medical education and across different disciplines within the critical care specialty. In particular, in more experienced groups such as AR-S and IC-S, compliance with the guideline on “medication in addition to opioids” was more common. These results highlight the need to adopt guideline even in more complex pain management scenarios.

Despite physicians' dedication to pain relief, they may encounter difficulties in accurately documenting pain levels and inadvertently undertreat their patients by underestimating the severity of their pain. A common but detrimental belief is that individuals who do not show outward signs of pain do not actually experience pain that necessitates treatment. Another harmful scenario is the tendency of physicians and nurses to believe that patients frequently exaggerate their pain (22). In the PADIS 2018 guideline, it is stated that family and loved ones can be included in the pain assessment process when appropriate and when the patient cannot self-report. It was observed that the contribution of the families of critically ill adults to the pain assessment was 33.7% in the clinical practices of the physicians participating in this study. Involving patients and their families directly may be a key initial strategy in combating these detrimental beliefs and enhancing pain management practices.

Payen et al. discovered that the rates of sedation (43%) and analgesia (42%) assessments in ICUs were notably lower compared to the administration rates

of sedatives (72%) and opioids (90%) (23). This lack of compliance, resulting in excessive treatment and a lack of awareness, is concerning due to the known risks associated with sedatives and opioids and their well-documented side effects (3). Standardized assessments are essential to ensure improved alignment between the needs for analgesics and sedatives and clinical practices (24). In this study, the use of protocol-based (analgesedation) pain assessment and management program was 68.9%, and there was no significant difference between medical careers. In addition, the preference for light sedation in mechanically ventilated patients was compatible with the guideline with a rate of 64.2% and did not change with the medical career. These results emphasize that routine protocol use should be encouraged in ICUs in Türkiye to first assess patients' pain status and then evaluate the need for sedation.

Intensive care physicians' compliance with the PADIS guideline and their attitudes towards delirium management are of critical importance in the ICU (25). This study reveals the extent to which physicians comply with the recommendations of the PADIS guideline, such as routinely evaluating delirium risk factors, using scales for delirium, and using pharmacological and non-pharmacological methods. Findings demonstrated a significant difference in compliance with the PADIS guideline "use of pharmacological agents to prevent delirium" as the medical career progresses. This suggests that as career level increases, physicians comply more with the guideline on delirium prevention or prefer certain approaches. On the other hand, "routine evaluation of delirium risk factors", "delirium follow-up", "use of pharmacological/non-pharmacological methods to reduce/treat delirium" did not show a significant difference according to medical career levels. This suggests that specific delirium management practices are similar across all medical career stages.

Early mobilization and intensive care rehabilitation are important parts of the PADIS evaluation. In critically ill adults in the ICU, peripheral muscle weakness begins

very early and they lose significant amount of muscle mass (26). There are concerns among ICU staff about early mobilization since critically ill adults have various tools such as ventilators, arterial and central venous lines. Studies have shown that patients on ventilators, continuous renal replacement therapy, or extracorporeal membrane oxygenation devices can be rehabilitated safely and without serious harm (26). In this context, in the survey conducted, the rate of mobilization or rehabilitation program application in critically ill adults was 89.5%, and no significant difference was found according to medical career levels. This result shows that there is a general awareness and acceptance among physicians about the importance of early mobilization and rehabilitation. The consistent approaches of physicians at different career levels on this issue may be an indication that a standardized approach has been adopted regarding the early mobilization and rehabilitation of patients in the ICU. This consistency may play a critical role in enabling patients to achieve better clinical outcomes in the ICU and better functional status in the long term.

Sleep assessment is inherently subjective, thus it is difficult to evaluate in the ICU setting. Since communication with patients is not possible, clear information about the rest they perceive and the factors that disturb them cannot be obtained. Therefore, nighttime rest is often overlooked and forgotten by healthcare professionals. Assessing sleep in patients in the ICU is a complex duty and studies report that polysomnography is the gold standard for sleep assessment (27). Although there is no recommendation for routine use of sleep monitoring in the PADIS guideline, the rate of sleep monitoring among the physicians who participated in our survey was 72.8%. It is stated that the factors that disrupt sleep in ICU patients have been identified in many studies. These are environmental, pharmacological and mechanical ventilation-related factors (18,28). It was observed that 65.8% of the physicians participating in this study evaluated the "factors affecting sleep quality" in the ICU admission of critically ill adults. It was found that 84.2% of the physicians gave answers

in line with the guideline in “non-pharmacological method applications to improve sleep”, and this did not change between medical careers. Although the relationship between sleep disruption and important outcomes such as delirium occurrence, duration of mechanical ventilation, length of stay in the ICU and mortality has not been fully established, these results demonstrate that there is awareness of sleep disruption in the ICU.

This study offers a broad perspective regarding compliance with intensive care protocols, including different medicine career levels, but this also brings with it certain limitations. Firstly, having a wide range of participants, from assistant physicians to intensive care specialists, allows making comparisons between physicians at different career stages in terms of compliance with the guidelines. However, the fact that there are 85 anesthesia assistants, 95 anesthesia and reanimation specialists, 5 intensive care assistants and 5 intensive care specialists creates an imbalance in the sample distribution, which may affect the general validity of the results. Secondly, the single-center (national) nature of the study is another factor that limits the broad applicability of the findings. Considering that different geographical and institutional practices are possible factors that may influence guideline adherence, a multicenter (international) study design may provide more generalizable results. Thirdly, the study carries a risk of bias due to the subjectivity of physicians' evaluations of themselves and their practices. Finally, the cross-sectional design of the study limits the ability to detect cause-effect relationships and does not allow for causal interpretations of the results. Longitudinal studies over time can provide a better understanding of trends in guideline compliance and changes in practice over time. Such studies can help us examine in more detail the developments in intensive care practice and the effects of these developments on patients' recovery processes. Therefore, it may be

recommended that future research have a multicenter and longitudinal design with more homogeneous participant groups, taking into account the limitations noted in this study.

In conclusion, this study demonstrated that intensive care physicians, including anesthesiology and reanimation assistants in Türkiye, exhibited generally compatible attitudes with the PADIS 2018 guideline in the management of “pain, agitation/sedation, delirium, immobility, and sleep disruption” symptoms in critically ill adults in the ICU. Additionally, as the medicine career increased, more consistent responses were given to the guideline in the management of some symptoms. This demonstrated the importance of clinical experience in the management of critically ill adults.

Ethical approval

This study has been approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (approval date: October 12, 2023, number: 19). Written informed consent was obtained from the participants.

Author contribution

Study conception and design: MSD, MŞÇ; data collection: MSD, MŞÇ, OK, SH, SU, SH; analysis and interpretation of results: MSD, MŞÇ, OK, SH; draft manuscript preparation: MSD, MŞÇ, SU, SH. The author(s) reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Content analysis of Youtube videos related to brain death

Beyin ölümü ile ilgili Youtube videolarının içerik analizi

Sevim Şenol Karataş¹, Sait Fatih Öner¹, Oğuz Kağan Bulut¹

¹Department of Anesthesiology and Reanimation, Elazığ Fethi Sekin City Hospital, Elazığ, Türkiye

ABSTRACT

Introduction: This study aimed to evaluate the quality of information content in YouTube videos related to brain death.

Methods: A search was conducted on the YouTube video platform using the keywords “brain death” and “brain death and organ donation” on November 20, 2024. A total of 42 videos were included in the evaluation. Data regarding the number of views, likes, comments, video duration, the number of days since the video was uploaded, and the source of the video were recorded. To classify the quality of the video content, DISCERN (Quality Criteria for Consumer Health), GQS (Global Quality Scale) for evaluating educational content, JAMA (Journal of the American Medical Association) for assessing the accuracy of the video source, and USEFULNESS for determining the utility of the videos were used.

Results: Among the analyzed videos, 25 (59.52%) were uploaded by physicians. Sixteen videos (38.10%) were rated as having very low educational quality, 13 (30.95%) provided partially sufficient information about the video source, 16 (38.10%) were of low information quality, and 13 (30.95%) were found to be of low usefulness. The quality scores of videos uploaded by physicians were significantly higher compared to other groups.

Discussion and Conclusion: The quality and educational value of YouTube videos related to brain death are low. Therefore, it is crucial that videos accessed through YouTube and other social media platforms are supervised by experts in the field to ensure accurate and useful information.

Keywords: brain death, organ donation, YouTube

ÖZ

Giriş ve Amaç: Bu çalışma, beyin ölümü ile ilgili YouTube videolarındaki bilgi içeriğinin kalitesini değerlendirmeyi amaçlamıştır.

Yöntem ve Gereçler: 20 Kasım 2024 tarihinde YouTube platformunda “beyin ölümü” ve “beyin ölümü ve organ bağıışı” anahtar kelimeleri kullanılarak bir arama yapılmıştır. Değerlendirme için toplamda 42 video dahil edilmiştir. Videoların izlenme sayısı, beğeni sayısı, yorum sayısı, video süresi, yüklenme tarihinden itibaren geçen gün sayısı ve video kaynağına ilişkin veriler kaydedilmiştir. Video içeriğinin kalitesini sınıflandırmak için DISCERN (Quality Criteria for Consumer Health), GQS (Global Quality Scale) eğitimsel içeriği değerlendirmek için, JAMA (Journal of the American Medical Association) video kaynağının doğruluğunu değerlendirmek için ve USEFULNESS videoların faydasını belirlemek için kullanılmıştır.

Bulgular: Analiz edilen videoların 25'i (%59,52) doktorlar tarafından yüklenmiştir. On altı video (%38,10) çok düşük eğitimsel kaliteye sahip olarak derecelendirilmiş, 13 video (%30,95) video kaynağı hakkında kısmen yeterli bilgi sağlamış, 16 video (%38,10) düşük bilgi kalitesine sahip bulunmuş ve 13 video (%30,95) düşük fayda düzeyinde değerlendirilmiştir. Doktorlar tarafından yüklenen videoların kalite puanları, diğer gruplara kıyasla önemli ölçüde daha yüksek bulunmuştur.

Tartışma ve Sonuç: Beyin ölümü ile ilgili YouTube videolarının kalite ve eğitimsel değeri düşüktür. Bu nedenle, YouTube ve diğer sosyal medya platformlarından erişilen videoların doğru ve faydalı bilgi sağlanmasını garanti altına almak için alan uzmanları tarafından denetlenmesi kritik önem taşımaktadır.

Anahtar Kelimeler: beyin ölümü, organ bağıışı, YouTube

✉ Sevim Şenol Karataş • drsevimkaratas@gmail.com

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Introduction

The internet has become one of the most frequently used sources of information today due to its accessibility to a large portion of the global population and its diverse range of informational content (1). Approximately five billion people worldwide are active internet users (2). It is well-known that people regard the internet as a significant source of health information and often research their health conditions online before seeking care from healthcare institutions (3). The rapid, easy, and low-cost access to medical information online is among the primary reasons for this trend (4). According to data from the Turkish Statistical Institute (TÜİK) in 2021, 92.0% of households in Turkey had internet access, and 82.6% of individuals aged 16-74 used the internet. The rate of searching for health-related information was reported as 69.6% (5). It has been noted that internet usage in Turkey, especially for following health-related news, is remarkably high (6).

YouTube is a widely used and easily accessible website and video-sharing platform globally (7). The widespread use of YouTube has made it an important source for accessing health-related information for patients (8). However, due to the lack of a pre-upload evaluation mechanism, it can both provide benefits to users and lead to the dissemination of misleading information (9).

In the literature, there is no study analysing the videos available on the YouTube platform concerning brain death, a topic that is highly debated and requires accurate information. Therefore, this study aims to evaluate the quality and accuracy of the information content in videos related to brain death available on YouTube.

Methods

Search strategy

On November 20, 2024, a search was conducted on YouTube (Alphabet Inc., Mountain View, CA, USA)

using the terms “brain death” and “brain death and organ donation.” A total of 100 videos were initially reviewed. The exclusion criteria for this study included videos in languages other than Turkish, those with irrelevant content, videos longer than 30 minutes, duplicates, and videos with poor audio or visual quality that hindered proper evaluation.

Based on these criteria, 58 videos were excluded: 8 due to duplication, 12 because they exceeded 30 minutes in duration, 18 for being news content from newspapers or television, and 20 for containing irrelevant content. As a result, 42 videos were included for analysis (Figure 1).

The video analysis was conducted independently and simultaneously by two separate researchers.

Video evaluation

For each video, the number of views, duration, and total likes were recorded. Various tools were utilized to assess video quality: DISCERN Score: DISCERN, an effective method for evaluating the quality of health information on the internet, was employed (10). This tool consists of 12 items, assessing the reliability, quality, adequacy, and overall evaluation of the information provided about brain death. Each item was scored from 1 to 5, and a total DISCERN score was calculated. Scores were classified as follows: 51–60: Excellent, 41–50: Good, 31–40: Moderate, 21–30: Poor, 11–20: Very poor (11).

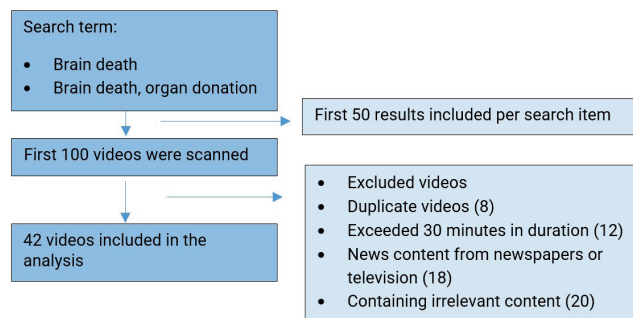


Figure 1. Selection methodology of YouTube videos

Journal of the American Medical Association (JAMA) Criteria: This scoring system includes four criteria—authorship, citation, disclosure, and currency. Videos were rated as follows: 1 point: Insufficient data on the source, 2–3 points: Partially sufficient data on the source, 4 points: Fully sufficient data on the source (12).

Global Quality Scale (GQS): GQS evaluates the educational value of videos, scoring them as: 1: Poor quality, 2: Poor quality but contains limited information for patient use, 3: Moderate quality, some information present but lacks essential details for patients, 4: Good quality, provides useful information for patients, 5: Excellent quality, highly useful for patients (13).

USEFULNESS Score: Videos were assessed for their usefulness to the target audience: 0: Not useful, 1–3: Minimally useful, 4–7: Useful, 8–10: Very useful (14).

Engagement Index = $(\text{Likes} - \text{Dislikes}) / \text{Views} \times 100$ (15).

Total interaction = $(\text{Likes} - \text{Dislikes}) + \text{Comments}$ (15).

Videos were categorized based on their sources, being classified as uploaded by physicians or non-physicians.

Statistical analysis

The Statistical Package for Social Science for Windows (SPSS) version 23.0 was used for the analysis of the data obtained in the study. Descriptive statistics, including frequency and percentage distribution analysis, minimum-maximum values, mean, and standard deviation, were employed to summarise the data. Kappa analysis was utilised to determine the inter-rater reliability among experts evaluating the YouTube videos.

The normality of the data distribution, both overall and within groups, was tested using the Shapiro–Wilk test. For the comparison of scores obtained in the study, the Kruskal–Wallis test was used when the data did

not follow a normal distribution to evaluate differences between groups. In cases where significant differences were identified between groups, the Bonferroni-adjusted Mann–Whitney U test was applied.

To examine the relationships between variables, Spearman's rank correlation (ρ) analysis was conducted. Results were considered statistically significant at a 95% confidence level ($p < 0.05$).

Ethical approval

As the videos analyzed in this study were publicly accessible and the analysis did not include any information about video titles or the personal details of the creators, and no human or animal subjects were involved, ethical approval was not required.

Results

The inter-rater reliability among experts evaluating YouTube videos was determined using Kappa analysis. The results indicated excellent agreement across all evaluations: DISCERN (Kappa = 0.976), JAMA (Kappa = 0.961), USEFULNESS (Kappa = 0.958), and GQS (Kappa = 0.967).

A total of 42 videos were analyzed. Of these, 25 (59.52%) were uploaded by physicians, while 17 (40.48%) were uploaded by non-physicians. The total number of views across all videos was 464,047. The most-viewed video had 95,732 views, and the most-liked video received 1,000 likes.

The DISCERN score was used to assess educational quality. The results revealed that: 16 videos (32.10%) were of very low quality, 9 videos (21.43%) were of good or excellent quality. Regarding the accuracy and reliability of the video source as evaluated by the JAMA criteria: 29 videos (69.05%) had insufficient data about the video source, 8 videos (19.05%) had fully sufficient data. Based on the USEFULNESS scoring system: 17 videos (40.48%) were not useful, 9 videos (21.42%) were highly useful. GQS, used to

determine educational value, indicated that: 16 videos (38.10%) were of poor quality, 7 videos (16.67%) were of excellent quality (Table 1).

The average DISCERN score was determined to be 28.81 ± 15.87 (median: 23; min-max: 12–60), while the mean JAMA score was 2.05 ± 1.04 (median: 2; min-max: 0.00–4). The average USEFULNESS score was 3.23 ± 3.64 (median: 2; min-max: 0.00–10), and the mean GQS score was 2.33 ± 1.46 (median: 2; min-max: 1–5) (Table 1).

According to Table 2, the average time elapsed since the upload of the analysed videos was 1857 ± 1197.83 days (median: 1927.50; min-max: 32–4546). The average duration of the videos was 4.95 ± 7.35 minutes (median: 2.01; min-max: 0.51–22.50). The mean number of likes was 127.10 ± 208.87 (median: 28.50; min-max: 0–1000), and the mean number of comments was 13.98 ± 43.45 (median: 0; min-max: 0–231). The average number of views was 5468.50 ± 11743 (median: 2160; min-max: 101–56140), while the mean total interaction was 138.71 ± 223.82 (median:

Table 1. Evaluation of video quality

Variables		Frequency	%
SOURCE	Physician	25	59,52
	Non-physicians	17	40,48
DISCERN Score 28.81 ± 15.87 23 (12-60)	Very poor	16	38,10
	Poor	13	30,95
	Moderate	6	14,29
	Good	1	2,38
	Excellent	8	19,05
GQS 2.33 ± 1.46 2 (1-5)	Poor quality	16	38,10
	Poor quality, limited information	11	26,19
	Moderate quality, partially useful information	6	14,29
	Good quality, provides useful information	2	4,76
	Excellent quality, highly useful information	7	16,67
JAMA Score $2,05 \pm 1,04$ 2(0.00-4)	Insufficient data regarding video source	29	69,05
	Partially sufficient data regarding video source	5	11,90
	Completely sufficient data regarding video source	8	19,05
USEFULNESS $3,23 \pm 3,64$ 2 (0,00-10)	Not useful	17	40,48
	Minimally useful	13	30,95
	Useful	3	7,14
	Very useful	9	21,42
	Total	42	100

Table 2. Evaluation of the reviewed videos

	Mean	Standard deviation	Median	Minimum	Maximum
Days elapsed since upload	1857	1197.83	1927.50	32	4546
Video duration (sec)	4.95	7.35	2.01	0.51	22.50
Total likes	127.10	208.87	28.50	0	1000
Total comments	13.98	43.45	0	0	231
Total views	5468.50	11743	2160	101	56140
Total interaction	138.71	223.82	49.50	1	1000
Engagement index	1.47	1.32	1.35	0.04	6.33

49.50; min-max: 1–1000). The average engagement index was determined to be 1.47 ± 1.32 (median: 1.35; min-max: 0.04–6.33).

When comparing the scores across video uploaders, significant differences were observed in DISCERN ($p = 0.00017$), JAMA ($p = 0.00018$), GQS ($p = 0.00095$), and USEFULNESS ($p = 0.00022$) scores. In all cases where differences were identified, the average scores of videos uploaded by the physician group were significantly higher than those uploaded by the non-physician group (Table 3). The higher scores of videos uploaded by physicians may be attributed to the content of these videos being more grounded in academic knowledge.

When examining the correlations between the scores, a moderate positive correlation was found between the number of views and DISCERN ($\rho = 0.487$), a moderately high positive correlation with GQS ($\rho = 0.547$), a moderate positive correlation with JAMA ($\rho = 0.465$), and a moderate positive correlation with USEFULNESS ($\rho = 0.393$). The positive correlation between the number of views and quality measurements suggests that the audience tends to prefer higher-quality videos. Additionally, a moderate positive correlation was observed between video duration and DISCERN ($\rho = 0.396$), while weak positive correlations were found with GQS ($\rho =$

0.346), JAMA ($\rho = 0.340$), and USEFULNESS ($\rho = 0.345$) (Table 4).

Discussion

YouTube is the second most visited website after Google (16). Its accessibility and free usage have made it a vital source of information. Since YouTube is open to all users, anyone with an account can upload videos on any topic. Health-related videos are not only uploaded by physicians but also by hospitals, medical students, healthcare companies, non-physician healthcare professionals, and patients. As a result, YouTube hosts both accurate and misleading health information (17). Patients watch videos to learn about their health conditions and also share videos describing their own experiences (18).

There are numerous studies in the literature evaluating the quality of health-related YouTube videos (19). This study evaluated YouTube videos providing information about brain death. Of the videos analyzed, 59.52% were uploaded by physicians, while the remaining were predominantly shared by individuals providing religious commentary. According to DISCERN scores, the educational quality of videos on brain death was found to be moderate. Despite the fact that most of the speakers were physicians, the low average

Table 3. Comparison of video uploaders and their scores

Variables	Physician	Non-physicians	p
DISCERN score	35.75 ± 15.77 32 (14-60)	18.89 ± 10.49 14.5 (12-51)	0.00017*
GQS	2.96 ± 1.37 2.5 (1-5)	1.39 ± 1.02 1 (1-5)	0.00095*
JAMA score	2.26 ± 0.60 2 (1-4)	1.43 ± 1.29 2 (0-4)	0.00018*
USEFULNESS	4.62 ± 3.51 4 (1-4)	2.34 ± 3.76 0 (0-10)	0.00022*
Total interaction	118.33 ± 226.90 27.5 (1-1000)	170.28 ± 252.37 60 (1-840)	0.222
Engagement index	1.10 ± 0.97 0.69 (0.04-3.55)	1.76 ± 1.35 1.80 (0.08-6.33)	0.0533

* Mann-Whitney U Test, p-value < 0.05

Table 4. Correlation comparisons among scores

Variables	DISCERN	GQS	JAMA	USEFULNESS
Total views	0.487 *0.001	0.547 *0.0001	0.465 *0.001	0.393 *0.010
Days elapsed since upload	0.057 0.721	0.158 0.315	0.245 0.173	0.246 0.170
Total likes	0.029 0.852	0.215 0.170	0.220 0.160	0.234 0.150
Total comments	0.091 0.562	0.243 0.120	0.220 0.160	0.235 0.140
Video duration (sec)	0.396 *0.010	0.346 *0.025	0.340 *0.035	0.345 *0.030
Engagement index	0.043 0.782	0.213 0.174	0.215 0.170	0.222 0.150
Total interaction	0.114 0.473	0.078 0.625	0.098 0.564	0.110 0.487

P-value; *rho = Spearman's correlation coefficient, significant at the 0.01 significance level.

DISCERN score is notable. This may be attributed to insufficient explanation of brain death diagnostic criteria and inadequate coverage of organ donation. However, all quality scoring metrics were higher for videos uploaded by physicians.

No correlation was found between daily views or likes and DISCERN, GQS, JAMA, or USEFULNESS scores. This suggests that video quality cannot be determined by the number of likes or views. Some studies indicate that the use of animations or visual effects in videos increases likes and views, regardless of content quality (20).

A weak positive correlation was identified between video duration and quality scores, likely due to longer videos providing more detailed explanations. Comment counts were not correlated with video quality, which may be because some high-quality videos do not allow comments, or because captivating speakers in videos with misleading information still attract significant comments. Furthermore, since YouTube has removed the visibility of total dislike counts, these are not reflected in total interaction scores.

Brain death and vegetative state are often confused concepts. This confusion leads families of patients with brain death to avoid organ donation, holding onto hope that the patient may recover. The biggest barrier to organ donation is the public's lack of adequate or accurate information. Educating and raising awareness about the difference between brain death and vegetative state is crucial to increasing organ donation rates. Another major barrier to organ donation is religious concerns (21). In countries like Turkey, where the majority of the population is Muslim, religious considerations play a significant role. Among the videos analyzed, only 4.76% emphasized that "the decision of the medical professional is reliable and valid," while 35.72% claimed that "brain death is not real, and organ donation is equivalent to murder as long as the heart is beating." However, Islamic teachings permit life-saving treatments, including organ transplantation. The Directorate of Religious Affairs in Turkey declared organ transplantation permissible in Islam through its 1980 decision No. 396 (22).

This study analyzed only the top 50 most relevant videos for each search term on a fixed date. YouTube content is dynamic, with new videos being uploaded

every minute. Different results may emerge with newly added videos. Increasing organ donation requires providing accurate information, as knowledge is one of the most improvable factors in this area (23). Factors influencing organ donation decisions should be identified, and healthcare education programs should be organized to enhance organ donation rates (24). These programs should be tailored to the cultural structure, religious beliefs, and knowledge level of the community and should be planned in a clear and comprehensible manner (25). Sharing stories of individuals who have continued their lives through organ transplantation may also be beneficial (26). Physicians, religious leaders, celebrities, and politicians, who significantly influence societal behaviours, should use social media to disseminate accurate information to broader audiences. Proper communication of the concept of brain death is expected to increase the number of organ donors (27).

Conclusion

Health-related content on YouTube and other social media platforms should be monitored by experts to ensure the dissemination of accurate and reliable information. Existing YouTube content on brain death is inadequate. Preparing and uploading higher-quality, informative, and visually appealing videos on this subject could be beneficial.

Ethical approval

As the videos analyzed in this study were publicly accessible and the analysis did not include any information about video titles or the personal details of the creators, and no human or animal subjects were involved, ethical approval was not required.

Author contribution

Study conception and design: SFÖ; data collection: SŞK, OKB; analysis and interpretation of results: SŞK, OKB; draft manuscript preparation: SŞK, SFÖ. The

author(s) reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Reliability and validity of the Turkish version of the Chelsea critical care physical assessment tool (CPAx-TR)

Chelsea yoğun bakım fiziksel değerlendirme aracı'nın (CPAx-TR) Türkçe versiyonunun güvenilirliği ve geçerliği

Mehmet Burak Uyaroğlu¹, Esra Pehlivan², Gamze Koyutürk³, Kürşat Nuri Baydilli⁴, Hakan Parlak⁵

¹Department of Physiotherapy, Vocational School of Health Services, Fenerbahçe University, İstanbul, Türkiye

²Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, University of Health Sciences, İstanbul, Türkiye

³Department of Ergotherapy, Faculty of Health Sciences, İstanbul Topkapı University, İstanbul, Türkiye

⁴Department of Biostatistics and Medical Informatics, Faculty of Medicine, University of Health Sciences, İstanbul, Türkiye

⁵Department of Anesthesiology and Reanimation, Faculty of Medicine, İstinye University, İstanbul, Türkiye

ABSTRACT

Objective: Assessing physical function in Intensive Care Unit(ICU) patients is essential for clinical decision-making. The Chelsea Critical Care Physical Assessment Tool(CPAx) is a validated instrument developed to evaluate functional status. This study aimed to cross culturally adapt the CPAx into Turkish and examine its validity and reliability.

Materials and Methods: The tool was translated into Turkish using forward-backward translation and administered to 60 ICU patients. For the reliability analysis, internal consistency was evaluated using Cronbach's alpha coefficient. The construct validity of the CPAx was tested by factor analysis. The criterion validity was performed using the correlation between the CPAx and the Physical Function ICU Test (PFIT).

Results: The internal consistency of the tool was found to be high and Cronbach's alpha value was calculated as 0.960. All item-total score correlations were above 0.30. Exploratory Factor Analysis revealed that all items were grouped into a single factor. In Confirmatory Factor Analysis, the model showed good fit (CMIN/df=1.207;CFI=0.993;NFI=0.959;GFI=0.907; RMSEA=0.059). Furthermore, the correlation analysis with P-FIT revealed a strong positive relationship ($r=0.892$; $p<0.001$).

Conclusion: It has been determined that the CPAx-TR shows acceptable levels of validity and reliability in evaluating functionality in ICU patients.

Keywords: critical care, functionality, reliability, validity

ÖZ

Amaç: Yoğun bakım ünitelerinde (YBÜ), hastaların fonksiyonel durumunu değerlendirme klinik karar verme açısından kritik roldedir. Chelsea Kritik Bakım Fiziksel Değerlendirme Aracı (CPAx), YBÜ hastalarında fonksiyonel durumu değerlendirmek için geliştirilmiş, geçerliliği kanıtlanmış bir araçtır. Çalışmanın amacı; CPAx aracının Türkçeye kültürlerarası uyarlamasını yapmak ve yoğun bakım hastalarında geçerlik ve güvenilirliğini değerlendirmektir.

Gereç ve Yöntem: Çeviri ve geri çeviri yöntemi ile Türkçe'ye uyarlanan araç, yoğun bakım ünitesinde yatan 60 hastaya uygulanmıştır. Güvenirlik analizi kapsamında, iç tutarlılık Cronbach's alpha katsayısı ile değerlendirilmiştir. Yapı geçerliği kapsamında ise, CPAx aracı ile Fiziksel Fonksiyon YBÜ Testi (P-FIT) arasında Pearson korelasyon analizi yapılmıştır.

Bulgular: Aracın iç tutarlılığı yüksek bulunmuş, Cronbach's alpha değeri 0,960 olarak hesaplanmıştır. Madde-toplam puan korelasyonlarının tamamı 0,30'un üzerinde çıkmıştır. Açımlayıcı faktör analizi sonucunda, tüm maddelerin tek faktörde toplandığı görülmüştür. Doğrulayıcı faktör analizinde modelin iyi uyum gösterdiği belirlenmiştir (CMIN/df=1,207; CFI=0,993; NFI=0,959; GFI=0,907; RMSEA=0,059). Ayrıca, P-FIT ile yapılan korelasyon analizinde güçlü bir pozitif ilişki bulunmuştur ($r = 0.892$; $p < 0.001$).

Sonuç: CPAx-TR'nin YBÜ hastalarında işlevselliği değerlendirmede kabul edilebilir düzeyde geçerlik ve güvenilirlik gösterdiği tespit edilmiştir.

Anahtar kelimeler: fonksiyonellik, güvenilirlik, geçerlik, kritik bakım

✉ Mehmet Burak Uyaroğlu • mburakuyaroglu@gmail.com

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Telif hakkı © 2025 Yazar(lar). Türk Yoğun Bakım Derneği tarafından yayımlanmıştır. Açık erişimli bu makale, orijinal çalışmaya uygun şekilde atıfta bulunulması koşuluyla, herhangi bir ortamda veya formatta sınırsız kullanım, dağıtım ve çoğaltmaya izin veren [Creative Commons Atf Lisansı \(CC BY\)](#) ile dağıtılmıştır.

Introduction

Decreased muscle strength and neuromuscular disorders, functional impairments, organ and system dysfunctions because of prolonged mechanical ventilation (MV), immobilization, and inactivity are severe problems among patients treated in the Intensive Care Unit (ICU) and may be followed by adverse effects including Post Intensive Care syndrome (PICS) and mortality (1,2). Studies have shown that after admission to the ICU, muscle atrophy is rapid and reaches 17.7% in the lower extremities and 13.2-16.9% in the upper extremities within the first 10 days (3,4). Prolonged ICU stay increases the risk of Intensive Care Unit-Acquired Weakness (ICU-AW), characterized by symmetrical and systemic atrophy of limb and respiratory muscles (5). However, immobilization also affects the cardiac system and studies has been reported that prolonged supine position causes dysregulation of blood volume in the peripheral circulation and a 20% decrease in cardiac workload (6). Muscle atrophy process that develops in the ICU can also lead to the chronic physical and psychological problems after discharge. Patients with an ICU stays exceeding 72 hours have been shown to have poor ambulation performance with cardiopulmonary dysfunction, muscle weakness and malnutrition after ICU discharge (7). A study shown that reduced walking speed, difficulties with stair climbing, and challenges in performing independent activities such as dressing in discharged ICU patients (8).

The evaluation of physical function status in the ICU is crucial for identifying patients' functional impairments, determining individualized treatment plans, and monitoring the effectiveness of the applied interventions (9). Performing adequate and timely measurements, along with implementing early rehabilitation as appropriate, can contribute to increased success rates in ventilator weaning, reduce lengths of stay in both the ICU and hospital, facilitate earlier discharge,

and enhance the quality of life during and post-ICU admission (10,11). Assessing the physical functional status and of ICU patients can be difficult due to cognitive dysfunction, existing cognitive impairment, coma, oversedation/analgesia and nutrient disorders (12,13). In this context, the existing scales used should provide the specificity required by ICU conditions. Several tools have been developed and are clinically utilized to evaluate physical function and activity in critically ill ICU patients, including the Functional Independence Measure (14), PFIT (15), Barthel Index (16), Modified Rankin Scale (17), Functional Status Score for the ICU (11), Karnofsky Performance Status Scale (11), 4P Score (18), Glasgow Coma Scale(GCS) (19), Disability Rating Scale (17), and Chelsea Critical Care Physical Assessment(CPAX) (20).

The CPAX tool has been designed specifically to evaluate physical functions in ICU patients (20,21). The CPAX is comprised of ten domains: respiratory, cough, moving within the bed, supine to sitting on the edge of bed, dynamic sitting, standing balance, sit to stand, transferring from bed to chair, stepping, and grip strength. In contrast to other questionnaires assessing ICU patients, this tool additionally evaluates the respiratory status and grip strength domains. Grip strength is an indicator of the strength of the peripheral muscles (22). In addition, the fact that most ICU patients receive ventilatory support may leads to the catabolism process in diaphragm muscle, thereby increasing immobilization (23). Therefore, evaluating these parameters in ICU patients is essential, as it offers a more comprehensive understanding.

Chelsea Critical Care Physical Assessment Tool, initially developed in the UK, also has Swedish, Norwegian, German, Danish, South African and Chinese versions available (20,21,24-30). However, this tool remains untested in a Turkish ICU patient and has yet to be used in an ICU. The aim of the study is to evaluate the reliability and validity of the Turkish version of the CPAX in ICU patients.

Material Method

This is a methodological study with a prospective, single-arm design. This study aimed to evaluate the validity and reliability of the Chelsea Critical Care Physical Assessment (CPAx) tools. After the cross-cultural adaptation and translation process, the reliability and validity of the Turkish version of the tool were investigated. Prior to the study, contact was made via email with Evelyn Corner, and permission was granted to adapt the tool.

Cross-cultural adaptation and translation process

We employed a cross-cultural adaptation approach in the translation process, following the guidelines outlined by the International Test Commission and World Health Organization (WHO). to ensure cultural relevance and accuracy (31,32). In the first step, The CPAx was independently translated from English to Turkish by two bilingual Turkish translators without prior knowledge, each translating separately from the other (33). Subsequently, three physiotherapists and an ICU consultant reviewed and compared the translations to identify and resolve any inconsistencies, leading to the creation of a draft Turkish version. Then, Two bilingual translator, were unaware of the purpose of translation, retranslated the edited Turkish version into English. As a final step, the original tool was compared with the back-translated English version, and adjustments were made as needed. Afterward, the revised version reviewed and approved by a professional translator.

Participants

Data were collected from Jan 2021 to Jan 2022 in the Istinje University Hospital, General Medical ICU. To determine a sample size in scale development or adaptation studies, it is generally advised to include 5 to 10 participants per item (34). Therefore, 60 patients were included in the study. Inclusion criteria for the study were individuals admitted to the ICU with critical illnesses, aged over 18 ages, Glasgow Coma Scale (GCS) total score greater than 11 point and ICU stay longer than 48 hours. Exclusion criteria included the

presence of unstable fractures, limb deformities or dysfunctions, Myasthenia Gravis or neuromuscular dysfunction, and a diagnosis of COVID-19.

Ethical considerations

Ethical approval was received from the Ethics Committee of Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital (2021-70). Written informed consent was obtained from participants or their first-degree relatives. The study is registered at Clinicaltrials.gov (NCT04811638).

Data collection

Patient data, including medical histories, diagnosis, age, sex, use of the cigarette and alcohol, and GCS (19), RASS (35) and APACHE II (36) scores were recorded.

Physical Function ICU Test (PFIT)

Physical Function ICU Test is a tool introduced by Skinner et al. in 2009 to assess endurance, strength, and functional levels in ICU patients (15). The Turkish reliability of the test was adapted on major abdominal surgery by Avcı et al. in 2019 (37). The test includes sit-to-stand, cadence, muscle strength of bilateral shoulder flexion, and bilateral knee extension subitems. Knee flexion and shoulder extension strength are assessed using the Oxford grading (0-5) system. Each section is scored between 0 and 3, and a total score is calculated. The original scale's internal consistency coefficient ranges from 0.996 to 1 (15,38).

Chelsea Critical Care Physical Assessment (CPAx) tool

Developed by Corner et al. in 2013, the tool based on a 6-point Guttman Scale (20,21). It is a tool that combines visual and numerical elements and assessing ten physical function parameters, ranging from total dependence to independence. It evaluates not only physical function and mobility but also respiratory function and cough ability, and grip strength. A total score between 0 and 50 can be

calculated, where 0 indicates total dependence and 50 represents complete independence (20,21).

Data analysis

Statistical analyses were performed using IBM SPSS statistics version 22 and IBM SPSS AMOS version 25. The normal distribution of the continuous variables was tested using the Shapiro-Wilk test. Internal consistency was measured using Cronbach’s alpha statistical test. In the Cronbach α test, the acceptable level of high-reliability of the tool was determined to be greater than 0.80, and in addition, the item-total correlation values were required to be greater than 0.30 (39,40). Correlations between the P-FIT scores were measured using the Spearman rank (p) correlation coefficient (41). In confirmatory factor analysis (CFA), the fit indexes and their cut-off values for appropriate fit were given as Table 1 (42). In the exploratory factor analysis, a factor loading greater than 0.45 and a variance explanation rate exceeding 50% were required as criteria. The Type I error rate in our analysis was set at 5%.

Results

The clinical and demographic status of the patients in this study are presented in Table 2. The study included sixty critically ill patients admitted to the ICU, with a mean age of 68.30 ± 12.06 years; 38 (63.3%) were male and 22 (36.7%) females. The mean value of the APACHE II score was 21.52 ± 7.21 . The mean GCS score was 11.88 ± 3.50 and the mean RASS score was -0.23 ± 1.22 . The average duration of ICU stay

Table 1. The range of acceptable fit indexes

	Good Fit	Acceptable Fit
CMIN/DF	$0 < \text{CMIN/DF} \leq 2$	$0 \leq \text{CMIN/DF} \leq 3$
CFI	$0.97 \leq \text{CFI} \leq 1.00$	$0.95 \leq \text{NNFI} \leq 0.97$
NFI	$0.95 \leq \text{NFI} \leq 1.00$	$0.90 \leq \text{NFI} \leq 0.95$
GFI	$0.95 \leq \text{GFI} \leq 1.00$	$0.90 \leq \text{GFI} \leq 0.95$
RMSEA	$0 \leq \text{RMSEA} \leq 0.05$	$0.05 \leq \text{RMSEA} \leq 0.10$

CMIN/DF, Chi-square statistic divided by degrees of freedom; CFI, Comparative Fit Index; NFI, Normed Fit Index; GFI, Goodness-of-Fit Index; RMSEA, Root Mean Square Error of Approximation.

Table 2. Patients’ demographic and clinical characteristics

	n (%)	
Sex		
Male	38 (63.3)	
Female	22 (36.7)	
Diagnosis		
Pneumonia	9 (15)	
COPD	16 (26.7)	
Urosepsis	2 (3.3)	
Respiratory failure	12 (20)	
Hyperkalemia	1 (1.7)	
Subdural Hematoma	2 (3.3)	
Pulmonary Edema	5 (8.3)	
Intracranial Hematoma	5 (8.3)	
Gastrointestinal Perforation	1 (1.7)	
Liver Failure	2 (3.3)	
Lung Resection	1 (1.7)	
Deterioration of General Condition	1 (1.7)	
Pleural Effusion	3 (5)	
Medical History		
Present	50 (83.3)	
Absent	10 (16.7)	
Family History		
Present	49 (81.7)	
Absent	11 (18.3)	
Surgical History		
Present	36 (60)	
Absent	24 (40)	
Smoking status		
Current Smoker	17 (28.3)	
Non-smoker	28 (46.7)	
Former Smoker	15 (25)	
Ventilatory Support Type		
Invasive	23 (38.3)	
Non-invasive	37 (61.7)	
Discharge status		
Discharge	36 (60)	
Transfer to another unit	9 (15)	
Exitus	15 (25)	
	$\bar{x} \pm \text{SD}$	Med (min/max)
Age (years)	68.30 ± 12.06	71 (32/84)
APACHE II (admission)	21.52 ± 7.21	21 (5/38)
GCS	11.88 ± 3.50	13 (3/15)
RASS	-0.23 ± 1.22	0 (-5/1)
ICU Admission (day)	7.68 ± 4.96	6.5 (2-22)

COPD, Chronic Obstructive Pulmonary Disease; APACHE II, Acute Physiology And Chronic Health Evaluation II; GCS, Glasgow Coma Scale; RASS, Richmond Agitation-Sedation Scale; ICU, Intensive Care Unit
 n, Sample size; %, Percentage; \bar{x} , Mean; SD, Standard Deviation; Med, Median; Min, Minimum; Max, Maximum

was 7.68 ± 4.96 days. Among the primary diagnoses, COPD was the most common, followed by pneumonia. Additionally, 50 participants had a history of chronic disease, and 49 had a family history of chronic illness. A total of 36 participants had a history of surgical procedures. Upon ICU discharge, 36 (60%) patients were discharged home, 9 (15%) were transferred to other units, and 15 (25%) exitus.

The item-total correlation for all sub-items was above 0.30. The Cronbach's alpha was found to be 0.960 and it was determined that CPAX-TR has internal consistency (Table 3).

The results of the factor analysis for construct validity showed that all factor loadings were above 0.800. The tool, consisting of 9 items, was grouped into a single factor, explaining 76.973% of the total variance (Table 4).

To examine multiple fit indices for the confirmatory factor analysis of CPAX. The CMIN/DF value was 1.207, the GFI was 0,907, the NFI was 0.959, and the RMSEA was 0.059 (Table 5).

To assess criterion validity, the correlation coefficient between scales CPAX and PFIT was examined to determine their relationship. A statistically significant, strong positive correlation was identified between CPAX and PFIT ($r = 0.892, p < 0.001$) (Table 6).

Discussion

This is the first study to conduct a translation and cross-cultural adaptation of the CPAX into Turkish version and to examine its reliability and validity. The CPAX was translated and cross-culturally adapted from the English into the Turkish ICU patients. Our findings demonstrate that the CPAX-TR has high reliability and validity for ICU population and that

Table 3. Reliability of the Turkish CPAX

Item	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted	Cronbach's Alpha
Respiratory	0.757	0.959	0.960
Cough	0.802	0.957	
Moving Within The Bed	0.823	0.956	
Supine to Sitting on the Edge of Bed	0.843	0.955	
Dynamic Sitting	0.844	0.955	
Standing Balance	0.901	0.953	
Sit to Stand	0.899	0.953	
Transferring from Bed to Chair	0.879	0.953	
Stepping	0.819	0.956	

Table 4. The exploratory factor analysis results: eigenvalues of factors, factor loadings and variance amounts explained by the factors

Component	Factor loading	Factor	Initial Eigenvalues			Extraction Sums of Squared Loadings		
			Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	0.800	1	6.928	76.973	76.973	6.928	76.973	76.973
2	0.836	2	0.753	8.364	85.337			
3	0.858	3	0.470	5.226	90.563			
4	0.878	4	0.241	2.679	93.242			
5	0.880	5	0.218	2.426	95.668			
6	0.928	6	0.139	1.550	97.218			
7	0.928	7	0.100	1.114	98.332			
8	0.916	8	0.085	0.945	99.277			
9	0.864	9	0.065	0.723	100.000			

Table 5. The values of fit indexes of confirmatory factor analysis

Fit Indexes	Value	Status
CMIN/DF	1.207	Good Fit
CFI	0.993	Good Fit
NFI	0.959	Good Fit
GFI	0.907	Acceptable Fit
RMSEA	0.059	Acceptable Fit

CMIN/DF, Chi-square statistic divided by degrees of freedom; CFI, Comparative Fit Index; NFI, Normed Fit Index; GFI, Goodness-of-Fit Index; RMSEA, Root Mean Square Error of Approximation.

Table 6. Criterion validity results of CPAX

		PFIT
CPAX	r	0.892
	p	<0.001**

r, correlation coefficient; **p <0.001

statistically significant correlations of strong were present between CPAX-TR and P-FIT.

In the original CPAX version, the Cronbach's alpha value was determined to be 0.798, and the intraclass correlation coefficient (ICC) of 0.988 within a 95% confidence interval (20,21). Similarly, in the cultural adaptation and test-retest studies of the Swedish version, the ICC was 0.970, with Kappa values were observed to range between 0.88 to 0.98 (27). In the study of the Norwegian version, the ICC was reported as 0.990 within a 95% confidence interval (28). For the Chinese version, the Cronbach's alpha was found to be 0.930, with test-retest reliability of 0.902 and Kappa values ranging from 0.839 to 0.845 (30). In the German version, the Cronbach's alpha was above 0.7, and the ICC was greater than 0.8 (25,26). For the Danish version the ICC was 0.996 within a 95% confidence interval, with Kappa values ranging from 0.914 to 0.995 (24). In our study, in which we evaluated the Turkish version of the tool, the Cronbach's alpha was determined to be 0.960. Our findings are consistent with previous validation studies, indicating that the CPAX-TR scale demonstrates high homogeneity and internal consistency.

As a result of the factor analysis applied for CPAX-TR, the number of items in the tool decreased from 10 to

9. These 9 items were grouped into a single factor. For CPAX-TR, the explained total variance was 76,973%. According to these results, it was observed that the items grouped under a single factor were sufficient to explain physical function (43,44). In addition, the lowest factor loading of all items was 0.800, which is above the acceptable level of 0.45 (43,44). For the construct validity of a scale to be appropriate, 'the fit indices' examined in CFA should meet the acceptable level (45,46). According to the results, the CMIN/df value was found to be 1.207, with CFI = 0.993, NFI = 0.959, GFI = 0.907, and RMSEA = 0.059. Among these values, CMIN/df, CFI, and NFI indicate a good fit, while GFI and RMSEA show an acceptable fit (42). In conclusion, the CPAX-TR showed good construct validity.

Regarding criterion validity, in the original version developed, a moderate to strong positive correlation was found between the CPAX score and the MRC score (p<0.001), GCS score (p<0.001), sedation score (p<0.001), peak cough flow (p=0.006), and AusTOM score (p<0.001) (20). In Chinese version, correlation between MRC score and CPAX-Chi coefficient was 0.60 (p<0.001) for researcher A and 0.65 (p<0.001) for researcher B in the assessment of ICU-AW (30). Furthermore, the Chinese version demonstrated strong content validity. The item-level content validity index (I-CVI) ranged from 0.889 to 1, and the scale-level content validity index (S-CVI) was calculated as 0.955 (30). In our study, a strong positive correlation was found between the CPAX-TR score and the P-FIT score (p<0.001), suggesting that the tool reliably assessment of physical function status in ICU.

The Turkish adaptation of the CPAX offers a robust and objective means of assessing functional status in ICU settings. It holds significant potential for both clinical practice and research, particularly in enabling ICU professionals to monitor patient recovery and inform treatment strategies.

This study has several limitations. The most significant limitation is that it is a single-center study. Due to practical constraints, follow-up tools could not apply

to patients, which made a test-retest reliability analysis impossible. In future studies, conducting the inter-rater and test-retest reliability analysis is recommended. Additionally, the 'absence to grip strength protocol' limitation observed in the original version is also applicable to our study. Thirdly, the 'CPAx does not account such as exercise tolerance or walking distance' limitation noted in the German version is also apply to CPAX-TR.

Conclusion

In summary, the findings of this study suggest that the CPAX-TR is a reliable and valid tool for assessing the physical functions and activities of patients with critical illness in the ICU. The CPAX-TR can be regarded as a valuable measurement tool for healthcare professionals in the ICU to evaluate physical and respiratory function and to plan and establish goals for early rehabilitation and treatment within a multidisciplinary team. Future studies should focus on exploring the minimum clinically important change as well as the predictive validity and reliability of the CPAX tool should be investigated in more intensive care units and units with critically ill patients in Turkey.

Ethical approval

This study has been approved by the Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital Clinical Research Ethics Committee (approval date: January 14, 2021, number: 2021,70). Written informed consent was obtained from the participants.

Author contribution

Study conception and design: MBU, EP, GK; data collection of data: MBU, GK, HP; analysis and interpretation of results: MBU, EP, KNB; draft manuscript preparation: MBU, EP, GK; critical revision of the manuscript : MBU, EP, GK. The authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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2. Basamak hastanede yoğun bakım uzmanının verimliliğe etkisinin retrospektif olarak değerlendirilmesi

Retrospective evaluation of the effect of intensive care specialist on productivity in a 2nd level hospital

Murat Güneş¹, Kazım Rollas², Nimet Şenoğlu³

¹Gümüşhane Devlet Hastanesi, Erişkin Yoğun Bakım Kliniği, Gümüşhane, Türkiye

²İzmir Tepecik Eğitim ve Araştırma Hastanesi, Yoğun Bakım Kliniği, İzmir, Türkiye

³İzmir Bakırçay Üniversitesi Çiğli Eğitim ve Araştırma Hastanesi, Anestezi Yoğun Bakım Kliniği, İzmir, Türkiye

ÖZ

Giriş: 3.Basamak hastanelerde yoğun bakım (YB) uygulamaları tam zamanlı çalışan YB ekibi ile yürütülürken, 2. Basamak hastanelerde çoğunlukla açık tip YB olmaktadır. Bu çalışmada 2. Basamak yoğun bakımda YB uzmanının görev almasının sağlık bakımında gözlenen olumlu sonuçların verilerle değerlendirilmesi araştırılmıştır.

Gereç ve Yöntem: Gümüşhane Devlet Hastanesi 2. basamak yoğun bakımında yatan hastalar geriye yönelik incelendi. Ekim 2020- 2021 (YB uzmanı olmayan dönem) ile Ekim 2021-2022 (YB uzmanı olan dönem) yılları arasındaki non-covid hastalar karşılaştırıldı. Hastalar yaş, cinsiyet, post operatif olup olmadığı, ek hastalıklar, APACHE 2 skoru, malignite, yatış günü, servise transfer, il dışı sevk ve yoğun bakım mortalitesi yönünden karşılaştırıldı.

Bulgular: Ekim 2020-2021 dönemindeki 142 hastanın 127'si, Ekim 2021-2022 dönemindeki 402 hastanın 212 'si çalışmaya alındı. YB uzmanı olan dönemde post-operatif hasta oranının daha yüksek olduğu, yatış süresinin düşük olduğu saptandı. YB uzmanı olan dönemde hastaların ortalama yatış günü ve yoğun bakım mortalitesi anlamlı olarak azdı ($p<0,001$). YB uzmanı olan dönemde servise hasta devir sayısı anlamlı olarak fazlaydı. YB uzmanı olan dönemde il dışı sevk oranı anlamlı olarak düşüktü ($p<0,001$)

Sonuç: 2.Basamak hastanelerde YB uzmanının görev alabileceği, daha aktif ve etkin yoğun bakım uygulamaları yanında, yerinde sağlık hizmetlerinin mümkün olabileceği kanaatine vardık. Ülkemizde YB uzman hekimlerinin 2. veya 3. basamak hastanelerin her ikisinde de aktif olarak süreçlerde rol alması ve buralarda yoğun bakımların geliştirilmesi önemlidir.

Anahtar kelimeler: yoğun bakım uzmanı, 2. Basamak hastane, 2. Basamak yoğun bakım, 3. Basamak yoğun bakım, yoğun bakım mortalitesi, yatış günü, sevk

ABSTRACT

Introduction: While intensive care practices in 3rd level hospitals are carried out by a full-time intensive care team, 2nd level hospitals, there is mostly open type intensive care. In this study, the evaluation of the positive results observed in health care by employing an intensive care (ICU) specialist in a 2nd level ICU was investigated.

✉ Murat Güneş • muratgunes_294@hotmail.com

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Bu çalışma TYBD 22.Ulusal Yoğun Bakım Kongresinde sözlü bildiri olarak sunulmuştur.

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Materials and Methods: Patients hospitalized in the 2nd level intensive care unit of Gümüşhane State Hospital were retrospectively examined. Non-covid patients from the period between October 2020-2021 (period without an ICU specialist) and October 2021-2022 (period with an ICU specialist) were compared. Patients were compared in terms of age, gender, post-operative status, comorbidities, APACHE 2 score, malignancy, hospitalization day, transfer to the service, out-of-province referral, and intensive care mortality.

Results: 127 of 142 patients in the October 2020-2021 period and 212 of 402 patients in the October 2021-2022 period were included in the study. It was determined that the number of post-operative patients was higher and the length of stay was lower in the period when there was an ICU specialist. The average hospitalization day and ICU mortality of the patients were significantly less in the period when there was an ICU specialist ($p<0.001$). The number of patient transfers to the service was significantly higher in the period when there was an ICU specialist. The rate of out-of-province referrals was significantly lower in the period when there was an ICU specialist ($p<0.001$).

Conclusion: We came to the conclusion that intensive care specialists can work in 2nd level hospitals and that on-site health services are possible in addition to more active and effective intensive care practices. In our country, it is important for intensive care specialist physicians to actively take part in the processes in both 2nd and 3rd level hospitals and to develop intensive care units there.

Keywords: intensive care specialist, 2nd level hospital, 2nd level ICU, 3rd level ICU, ICU mortality, day of admission, referral

Giriş

Kritik hastalık insidansının artması, tıpta medikal tedavideki ilerlemeler ve artan yaşlı nüfus popülasyonu nedeniyle ülkemizde ve dünyada yoğun bakım (YB) yatak ihtiyacı gün geçtikçe artmaktadır (1,2). 3. Basamak hastanelerde YB düzeni belirli protokol çerçevesindedir. Kapalı tip YB düzeninde hastalar, YB hekimleri ve asistanlardan oluşan bir ekip tarafından takip edilmektedir (3,4). Birden fazla organ sisteminin etkilendiği kritik hasta grubunda YB konusunda yeterlilik ve devamlılık önem arz etmektedir. 2. Basamak hastanelerde açık tip YB düzeni olduğundan, diğer bir ifadeyle hastaların her birinden sorumlu ve tam zamanlı çalışan herhangi bir YB hekimi olmadığından, farklı uzmanlık dallarından hekimler hastalarının takip ve tedavilerini burada gerçekleştirmektedir. Ancak ilgili branş hekimlerinde organ yetmezliği bulunan ve durumu ağırlaşma ihtimali olan kritik hastalarda tedavi ve takipten kaçınma gözlenmektedir. Bu tüm sağlık sistemini etkilemekte, tüm branşlarda artmış iş yüküne ve artmış sevk oranlarına neden olmaktadır. Yoğun bakım ünitesinde (YBÜ) tedavisi tamamlanan hastaların servise devirlerinde de benzer nedenlerle direnç olmakta ve hastaların yatış günü uzayabilmektedir. Bu çalışmada gözlemsel olarak saptanan bu sorun, sunulan yoğun bakımın gelişimsel süreçleri açıklandı ve öncesi sonrası verilerinin karşılaştırılarak yorumlanması ile objektif veriler ışığında konunun tartışılması sağlandı. Böylece

YB uzmanının getirdiği düzen ve verimlilikle ilgili veriler retrospektif olarak değerlendirilerek YB uzmanının olmadığı dönem ile karşılaştırılması amaçlandı.

Materyal-Metod

Trabzon Kanuni Eğitim ve Araştırma Hastanesi etik kurulu onayı alındıktan sonra Gümüşhane Devlet Hastanesi YBÜ'de yatan non covid hastalar geriye yönelik incelendi. Bu çalışmada öncelikle YB uzmanının göreve başlamasıyla ilgili YBÜ'nün 3. Basamak olması için gereken fiziki ve ekipman koşulları ile 7-24 nöbetçi hekim olması sağlandı. Hastalar yoğun bakıma mesai saatinde YB uzmanı adına, mesai saati dışında YB endikasyonu koyan konsültan hekim adına yatırıldı. Ertesi gün mesai saati içinde konsültan hekimlerin üzerindeki hastalar YB uzmanına aktarıldı. Ekim 2020-2021 (YB uzmanı olmayan dönem) ile Ekim 2021-2022 (YB uzmanı olan dönem) döneminde YBÜ'de yatan hastalar bilgisayar sistemi üzerinden geriye yönelik tarandı. Hastalar yaş, cinsiyet, post operatif olup olmaması, ek hastalıklar (diyabet, hipertansiyon, kalp yetmezliği, astım, kronik obstrüktif akciğer hastalığı (KOA), serebrovasküler hastalık, demans, koroner arter hastalığı, kronik böbrek hastalığı, kronik karaciğer hastalığı), Acute Physiology and Chronic Health Evaluation Score 2 (APACHE 2), malignite olup olmaması yönünden incelendi. Hastaların ortalama yatış günü, post operatif hastaların ortalama yatış günü, servise transfer oranı, YBÜ'den il dışı sevk oranı

ve yoğun bakım mortalitesi geriye yönelik incelenerek karşılaştırıldı. Ayrıca belirtilen zaman dilimlerinde YB ihtiyacı nedeniyle acil servisten yapılan il dışı sevk oranı karşılaştırıldı. 18 yaşından küçük olanlar çalışma dışı bırakıldı.

İstatistik

Verilerin normal dağılımı Shapiro-Wilk testi ile değerlendirildi. Sürekli değişkenlerde, normal dağılım gösteren veriler izlendiğinden ortalama ve standart sapma kullanıldı. Kategorik değişkenler sayı ve yüzde olarak bildirildi. Sürekli değişkenlerin parametrik test varsayımlarını karşılaması nedeniyle Student's t test kullanıldı. Kategorik değişkenler için gruplar arasında karşılaştırma amacıyla verilerin özelliğine göre Chi-Square veya Fisher' exact test kullanıldı. Verilerin istatistiksel analizi, Statistical Package for Social Science for Windows (SPSS) 16 programı ile çalışılmıştır. $P < 0.05$ değeri istatistiksel olarak anlamlı kabul edildi.

Bulgular

Ekim 2020-2021 arasında YBÜ'de yatan 142 hastanın 127'si, Ekim 2021-2022 arasında YBÜ'de yatan 402 hastanın 212'si çalışmaya alındı.

Hastaların demografik özellikleri Tablo 1'de gösterildi ve istatistiksel olarak bir fark saptanmadı. YB uzmanı olan dönem YB uzmanı olmayan döneme göre kıyaslandığında hastaların post operatif olma oranı istatistiksel olarak daha fazla saptandı ($p < 0,001$) (Tablo 1). Post operatif hastaların ortalama yatış günü istatistiksel olarak daha azdı ($p < 0,001$) (Tablo 1).

Hastalar ek hastalıkları yönünden incelendiğinde diyabet, hipertansiyon, KOAH ve demans oranı YB uzmanı olan dönemde YB uzmanı olmayan döneme göre istatistiksel olarak daha fazla saptandı ($p < 0,001$) (Tablo 2). APACHE 2 skoru YB uzmanı olmayan dönemde istatistiksel olarak daha fazla saptandı ($p < 0,03$) (Tablo 2). Malignite oranı açısından iki dönem arasında istatistiksel bir fark saptanmadı ($p < 0,32$) (Tablo 2).

Tablo 1. Hastaların demografik özellikleri, post operatif hastaların dağılımı ve ortalama yatış günü

Parametreler (n (%) veya ortalama±SD)	Ekim 20-21 (n=127)	Ekim 21-22 (n=212)	p değeri
yaş	78 ±15	77 ±15	0,46
cinsiyet (kadın n (%))	58 (45,7)	106 (50)	0,5
Post operatif hastalar	12 (9,4)	55 (25,9)	<0,001
Post operatif hastaların yatış günü	18 (17)	5,6 (10)	<0,001

Tablo 2. APACHE 2 oranı, ek hastalıklar ve malignite yönünden hastaların dağılımı

Parametreler (n(%) veya ortalama±SD)	Ekim 20-21 (n=127)	Ekim 21-22 (n=212)	p değeri
APACHE 2	36 ±10	33 ±7,7	0,03
Diyabet	24 (19)	108 (50,8)	<0,001
Hipertansiyon	46 (36)	144 (67,9)	<0,001
Kalp yetmezliği	35 (27,6)	75 (35,4)	0,15
KOAH	25 (19,7)	72 (34)	<0,001
Astım	12 (9,4)	11 (5,2)	0,24
Serebrovasküler hastalık	46 (36,2)	68 (32,1)	0,47
Demans	24 (19)	73 (34)	0,003
Koroner arter hastalığı	19 (15)	46 (21)	0,15
Kronik böbrek yetmezliği	10 (7,9)	27 (12,7)	0,2
Kronik karaciğer hastalığı	0 (0)	3 (1,4)	0,29
Malignite	14 (11)	16 (7,5)	0,32

Hastaların ortalama yatış günü ve yoğun bakım mortalitesi YB uzmanı olan dönemde anlamlı olarak azdı ($p<0,001$) (Tablo 3). YB uzmanı olan dönemde servise devredilen hasta oranı anlamlı olarak fazlaydı ($p<0,001$) (Tablo 3). YBÜ'den il dışı sevk oranı açısından iki dönem arasında istatistiksel bir fark saptanmadı ($p 0,56$) (Tablo 3).

YB uzmanı olmayan dönemde 54.001 acil başvurusundan 562 il dışı sevk varken YB uzmanı olan dönemde 73.338 acil başvurusundan 531 sevk oldu. YB uzmanı olan dönemde acil servisten il dışı sevk oranı anlamlı olarak azdı ($p<0,001$).

Tartışma

Emeğin ve kaynağın yoğun şekilde kullanıldığı YBÜ'lerinde kalite performansına odaklanmak ve kalite süreçlerini yönetmek önemlidir. YBÜ'lerde yüksek kalite ve uygun maliyetli performans elde etmek isteniyorsa YB uzmanlarına görev ve sorumluluk verilmelidir. Bu çalışmadaki veriler ışığında YB alanında yetişmiş insan gücüyle birlikte hastanenin genel işleyişinde ve üretilen işlerin niteliğinde iyileşme ile birlikte bölgedeki hasta sevklerinin belirgin oranda azalması, daha özellikli ameliyatların yapılabilmesinin sağlanması mümkün olmuştur. YB uzmanları, hastaların bakım kalitesinin iyileştirilmesinde önemli rol oynarlar. Bakım modelleri, iş yükü ve güvenlik konularında uygun öneriler geliştirilmesinde ve uygulanmasında etkindirler (5). Son yıllarda YB uzmanlarının sayısındaki artış, hastalar için daha iyi sonuçlara ve daha verimli kaynak kullanımına yol açmıştır (6). YB performansının ölçülmesindeki temel konulardan biri hekim katkısıdır. Bu amaçla "YB'da kalma süresi" gibi süreç ve "mortalite oranı" gibi sonuç ölçümleri kullanılmaktadır

(7). Hastaların YB uzmanı tarafından takip edildiği ünitelerde bakım kalitesi ve verimlilik, primer doktorları tarafından takip edildiği ünitelere göre daha yüksektir. Tam zamanlı çalışan YB uzmanları, mortaliteyi, YB'da kalış süresini, komplikasyonları ve hatta maliyetleri azaltmada daha etkili olabilir. Mekanik ventilasyonun başlanması ve sürdürülmesi, weaning sürecinin yönetilmesi, sedasyon uygulamaları, enfeksiyon yönetimi ve beslenmenin standartlaştırılmış protokoller ile sağlanması YB'da kalış sürelerini dolayısı ile de maliyeti azaltabilir (6). Hastaneler ve farklı YBÜ'ler arasında işleyiş ve hasta sonuçları arasında özellikle Amerika'da geniş bir yelpaze vardır (8). YBÜ'ler arasında bu kadar değişkenlik olması farklı hekimlerin görev yapmasıyla açıklanabilmektedir. YBÜ'de kritik hastaların YB uzmanı tarafından takip edilmesi hastane maliyetlerini, yatış süresini ve mortaliteyi azalttığı gösterilmiştir (9) Açık tip YBÜ'de YB uzmanının konsültan olduğu durumlarda mortalitenin azaldığını gösteren çalışmalar literatürde mevcuttur (10,11). Bununla birlikte Pronovost ve ark. yaptığı meta analizde YB uzmanının zorunlu konsültan olduğu yüksek yoğunluklu bakımda, zorunlu konsültan olmadığı düşük yoğunluklu gruba göre hasta sonuçları daha iyi çıkmıştır (9). Levy ve ark. Yaklaşık 100 hastanenin toplam 123 YBÜ'de yaptığı çalışmada YB uzmanının takip ettiği hasta gruplarında mortalite %40 a varan oranda azalmıştır (12). Ülkemizde 3. Basamak hastanelerde YB hizmeti belirli hekim grubu tarafından ekip halinde yürütülmektedir. Ancak 2. Basamak hastanelerde böyle bir ekip olmadığından YB düzeni açık tip olmakta ve her hastane lokal çözümlerle düzen sağlamaya çalışmaktadır. Özellikle hekim sirkülasyonunun fazla olduğu mecburi hizmet bölgelerinde YB düzeni bireylere bağlı olmakta,

Tablo 3. Hastaların yoğun bakım mortalitesi, servise devir, ortalama yatış günü ve YBÜ'den sevk yönünden dağılımı

Parametreler (n (%) veya ortalama±SD)	Ekim 20-21 (n=127)	Ekim 21-22 (n=212)	p değeri
Mortalite	112 (88)	94(44)	<0,001
Yoğun bakım mortalitesi	95 (74,8)	87 (41)	<0,001
Servise devir	8 (6,3)	111 (52,4)	<0,001
Ortalama yatış günü	16 ±25	7,5 ±12	<0,001
Yoğun bakımdan il dışı sevk	6 (4,7)	7 (3,3)	0,56

mevcut kişiler değiştiğinde düzen değişebilmektedir. Bu durumdaki küçük YBÜ'lerin daha az ciddiyetteki hastalara hizmet etmeye başladığı dikkati çekmiştir (13). Bizim çalışmamızda YBÜ basamağının 3'e çıkarılmasının ve kapalı tip olmasının sonuçları incelendiğinde yoğun bakım mortalitesi YB uzmanı olan dönemde istatistiksel olarak az saptandı (Tablo 4). YB basamağının artması post operatif 3. Basamak YB ihtiyacı olacak hastaların mevcut hastanede opere olmasına imkan tanıdı ve YB'ye yatan post operatif hasta sayısı YB uzmanının olduğu dönemde daha fazlaydı (Tablo 1). Ameliyat sonrası hastaların ortalama yatış günü YB uzmanı olan dönemde istatistiksel olarak daha azdı (Tablo 1).

Ülkemizde YB yan dalı olan anesteziyoloji ve reanimasyon, iç hastalıkları, genel cerrahi, göğüs hastalıkları, nöroloji ve enfeksiyon hastalıkları anadalında uzmanlık eğitimi alan asistan hekimler, YB eğitimi ile ilgili rotasyonlarını eğitim kliniğinde yapmakla yükümlüdür. Böylece sahada görev yapan anadal hekimi kendi branşını ilgilendiren hastayı değerlendirirken kritik hastayı tanımak ve tedavisinin YB'de yapılması gerekliliği ile ilgili resmi görüş bildirebilir. Bunlar dışında asistanlığı döneminde kendi branşının YBÜ'lerinde sıkça mesai harcayan kardiyojoloji, kalp damar cerrahisi, beyin cerrahisi ve göğüs cerrahisi gibi bölümlerde çalışan hekimler de kendi alanlarıyla alakalı kritik hastayı tanıyabilir ve YB takibi ile ilgili görüş bildirebilir. YB uzmanı, ilgili branşlar tarafından YB ihtiyacı saptanmış hastaların tedavisini YBÜ'de devam ettirmekle yükümlü olup YB uzmanına konsültasyon ile müracaat edilmesi genelde başka YBÜ'deki hastalar için olmaktadır (14). Acil servise başvuran ya da serviste kötüleşen kritik hastaların hepsi için YB uzmanı tarafından değerlendirme istenmesi artmış iş yüküne neden olabilir. YB çalışanları, hasta grubunun karmaşıklığı, kaynak sıkıntısı, iş yükü yoğunluğu nedeniyle potansiyel olarak tükenmişlikle karşı karşıyadırlar. Tükenmişlik sendromunda olan hekimlerin daha az üretken, daha fazla hataya eğilimli ve sağladıkları bakım kalitesinin de daha düşük olduğu izlenir. Bu nedenle, tükenmişliği azaltmaya yönelik önleyici tedbirler

verimliliği, güvenliği artırır, kalitenin ve performansın iyileştirilmesinde etkilidir (15). YB uzmanının 24 saat süreyle yoğun bakım ünitesinde kalmasının, sadece gündüz kalmasıyla karşılaştırıldığında mortaliteyi değiştirmedeği bildirilmektedir (16, 17).

Açık tip YBÜ'lerde hastalar konsültan hekim adına yatmaktadır. Bu durum kritik hastanın sorumluluğunu almak istemeyen hekimlerde YB'ye hasta yatırmak konusunda dirence neden olabilmektedir. YB'ye kabulde gecikme veya erken/mesai dışı taburculuğun ise hastane yatış gününde uzama ve hastane mortalitesinde artışa neden olduğu bilinmektedir (18,19). YBÜ'lere acil servis dışındaki servislerden kabul edilen hastaların tedavileri sona erdikten sonra tekrar geldikleri servislere nakledilmeleri, acil servisten gelenlerin ise birincil hastalıklarıyla ilgili veya konsültasyonun sürdürülmüş olduğu servislere naklinin sağlanması gereklidir (20). Klinik pratikte bu kuralların işleminde tüm dünyada olduğu gibi ülkemizde de sorunlar oluşmakta ve YB yatakları servis nakillerindeki gecikmeler nedeniyle akılcı kullanılamamaktadır (21). Bu durum hastane ve YB maliyetlerini artırmaktadır. Hastaneye giriş yapan hastaların %5'ini YBÜ'ye kabul edilen hastalar oluşturmasına karşın, bu üniteler hastane masraflarının %20-25'ini teşkil etmektedir (22). Kahn ve ark. Yaptıkları bir çalışmada YBÜ'de son günün ortalama maliyetin 397 dolar olduğunu, hastane servisinde bir sonraki günün maliyetinin 279 dolar olduğunu; bu nedenle, YBÜ' de kalış süresinin 1 gün azaltılmasının, sadece o hastanın tüm hastane harcamalarının % 0.2'si kadar bir maliyet tasarrufu yapılabildiğini bildirmişlerdir (23). Basamağını artırdığımız YB düzeninde; hastaların yatışı mesai saati içinde YB uzmanı adına, mesai saati dışında YB endikasyonu koyan konsültan hekim adına yapıldı. Ertesi gün mesai saati içinde konsültan hekimlerin üzerindeki hastalar YB uzmanına aktarıldı. Bu durum hekimlere yoğun bakıma hasta yatırmak konusunda güven verdi. İç içe geçmiş organ yetmezlikleri ile YBÜ'ye alınan ve tedavisi tamamlanan hastaların hangi servise devir edileceği ile ilgili karmaşa hastayı yoğun bakıma yatıran konsültan hekimini bilindiğinden ortadan kalkmış oldu. Böylece

YB uzmanı olan dönemde hastaların servise transfer oranını arttı ve ortalama yatış günü istatistiksel olarak daha azdı (Tablo 3). YBÜ'nün 3. Basamak olması ve hekimler arasındaki artmış işbirliği nedeniyle kritik hastaların acil servisten il dışı sevk oranı YB uzmanı olan dönemde istatistiksel olarak daha azdı.

Sonuç

2. Basamak hastanede YB uzmanı olan dönemde YBÜ basamağının 3'e çıkarılması acil servisten il dışı sevk oranını azalttı. Kapalı tip düzen izlenmesi YB mortalitesini azalttı. Ameliyat sonrası 3. Basamak YB ihtiyacı olacak hastaların mevcut hastanede opere olabileceği sağlandı. YB uzmanının hastaları sahiplenmesi anadal hekimlerinde mesai saatleri dışında YBÜ'ye hasta yatırmak konusunda motivasyon sağladı. Hekimler arasındaki işbirliği ve adalet duygusu tedavisi tamamlanan hastaların servise transferini kolaylaştırdı. Böylece hastaların YBÜ'deki ortalama yatış günü azaldı. Edindiğimiz tecrübenin açık tip YB düzeni olan kliniklerde YB uzmanlarına yol göstereceği kanaatindeyiz. Benzer çalışmalarla ve oluşturulacak protokollerle ülkemizde YB verimliliğini artıracak daha fazla çalışmaya ihtiyaç vardır.

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Çalışma konsepti ve tasarımı: MG; veri toplama: MG, KR; sonuçların analizi ve yorumlanması: KR; makaleyi hazırlama: MG, NŞ. Yazar(lar) sonuçları gözden geçirmiş ve makalenin son halini onaylamıştır.

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Family needs, psychological distress and social support in the intensive care unit: a cross-sectional study

Yoğun bakım ünitesinde yatan hasta ailelerinin gereksinimleri, psikolojik sıkıntıları ve sosyal destek düzeylerinin incelenmesi

Songül Duran¹, Yüksel Can Öz², Esin Eşdoğan^{2,3}

¹Care of Elderly Program, Health Services Vocational College, İzmir Democracy University, İzmir, Türkiye

²Department of Psychiatric Nursing, Faculty of Health Sciences, Kocaeli University, Kocaeli, Türkiye

³Kocaeli University Health Sciences Institute, Kocaeli, Türkiye

ABSTRACT

Objectives: The aim of the study was to determine the relationships between sociodemographic factors related to the needs of individuals and family needs, psychological distress and social support.

Methods: A Personal Information Form, Critical Care Family Needs Inventory (CCFNI), Kessler Psychological Distress Scale (K10-PDS), and Multidimensional Scale of Perceived Social Support (MSPSS) were used to collect data.

Results: The domains in which the participants were determined to have the greatest degree of need were information (38.45±5.23) and support (32.04±7.05). Participants with low education level and who visited their patients more frequently than once a week had significantly higher scores on the information, assurance, proximity, and comfort subscales. The participants had high K10-PDS (25.77±9.99) and MSPSS (68.62±15.54) scores. There was a significant positive relationship between the CCFNI and MSPSS scores of the participants ($r=0.400$).

Conclusions: The family members of intensive care patients were determined to have a high degree of need and high levels of psychological distress. It is extremely important for health professionals to support the family and include them in the care process. Increasing the quality of care for the patient and providing psychological relief to the family will increase the quality of care.

Keywords: critical care, intensive care, family needs, psychological distress, social support

ÖZ

Giriş ve Amaç: Bu çalışmanın amacı yoğun bakımda hastası olan aile üyelerinin gereksinimlerini, psikolojik sıkıntı ve sosyal destek düzeylerini ve aile gereksinimleri ile ilişkili faktörleri araştırmaktır.

Yöntem ve Gereçler: Tanımlayıcı ve kesitsel tipteki bu çalışma, Şubat-Ağustos 2023 tarihlerinde bir hastanenin yoğun bakım servisine ziyarete gelen aile üyeleri ile gerçekleştirildi. Araştırmaya 166 kişi alındı. Araştırmada anket formu, Yoğun Bakım Ünitesindeki Hastaların Yakınları için Gereksinim Ölçeği, Kessler Psikolojik Sıkıntı Ölçeği ve Çok Boyutlu Algılanan Sosya Destek Ölçeği kullanıldı.

Bulgular: Araştırmada aile üyelerinin en çok gereksinim duyduğu alanlar bilgi (38.45±5.23) ve destek altboyutu (32.04±7.05) olmuştur. Eğitim düzeyi düşük olanlarda eğitim düzeyi yüksek olanlara kıyasla; hastasını haftada bir kereden fazla ziyaret edenlerde haftada bir kereden daha az sıklıkta ziyaret edenlere göre bilgi, güvenlik/yakınlık, destek konfor puanı eğitim düzeyi yüksek olanlara kıyasla daha yüksek düzeyde bulunmuştur ($p < 0.001$). Aile üyelerinin psikolojik sıkıntı puanı (25.77±9.99) ve sosyal destek puanı (68.62±15.54) yüksek düzeyde saptanmıştır. CCFNI ile MSPSS arasında pozitif yönde bir ilişki olduğu ($r = 0.40$, $p < 0.001$) belirlenmiştir.

Tartışma ve Sonuç: Araştırmada ailelerin gereksinimleri ve psikolojik distress düzeyleri yüksek düzeyde saptanmıştır. Ailelere düzenli olarak eğitimler verilmesi gerektiği ve ruhsal yönden sıkıntı düzeyi yüksek olanların uzman desteğine yönlendirilmesi gerektiği düşünülmektedir. Türkiye’de yoğun bakım ünitesinde yatan hastaların aile üyelerine yönelik kapsamlı bakım programları geliştirilmelidir.

Anahtar kelimeler: yoğun bakım, aile ihtiyaçları, psikolojik sıkıntı, sosyal destek

✉ Songül Duran • songul.duran@gmail.com

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Telif hakkı © 2025 Yazar(lar). Türk Yoğun Bakım Derneği tarafından yayımlanmıştır. Açık erişimli bu makale, orijinal çalışmaya uygun şekilde atıfta bulunulması koşuluyla, herhangi bir ortamda veya formatta sınırsız kullanım, dağıtım ve çoğaltmaya izin veren [Creative Commons Atf Lisansı \(CC BY\)](#) ile dağıtılmıştır.

Introduction

The family members of intensive care patients are exposed to several stressors that may lead them to feel defenseless. Family members find the physical environment of intensive care units and the intensive care provided unfamiliar, and they may experience worry and fear due to the life-threatening condition of their relatives, unfamiliar technologies at these units, and multiple strangers circulating in the unit (1-3). This may be distressing and exhausting for family members, and symptoms of anxiety, depression, and post-traumatic stress symptoms may persist for three months or longer (1,4,5). In a study, it was observed that family members had moderate to high levels of psychological distress symptoms that negatively affected them and the patient (2). These psychological symptoms can impact caregivers' ability to interact with the clinical team, their long-term psychological health, and their ability to help the patient manage their condition after discharge from hospital (6). When clinicians recognize this, long-term negative outcomes such as complicated grief and major depression in family members can be prevented (7). Supporting the family is essential in order to alleviate the distress experienced by the family (8,9). Studies emphasize that families of patients in intensive care should be included in the care (10,11).

Understanding the needs of the family members of patients at the hospital, especially those in intensive care units (ICUs), is the key to providing comprehensive and effective support for this group of individuals (12). Meeting the needs of families of patients in intensive care, reducing distress, reducing tension between family and staff, and giving staff greater attention to patients' needs will lead to better outcomes (13,14). High-quality intensive care unit service should also consider the needs of family members (15,16). The family members of ICU patients have various needs, such as information, flexible ICU visiting hours, hope, and assurance (17-19). Studies over the past five years have confirmed that when family members' needs are met, their decision-making capacity increases and

symptoms of post-traumatic stress disorder decrease (10,20). Family-centered care reduces psychological disorders in family members, increases patient satisfaction, and improves communication between the family member and healthcare personnel (17,21). Patient and family-centered care (PFCC) emphasizes the importance of the family as a major source of support and considers the involvement of family members in all aspects of the patient's health care (22). Dignity and respect, information sharing, patient and family participation, and collaboration in care (11,23) are key elements in this care. Both patients and family members can benefit psychologically from this care (24,25). At this point, health professionals need to systematically support the patient's family and see them as a central collaboration partner, and only in this way can the expectations of both the patient and the family be met (24,26). Nurses who have close contact with families are in an ideal position to better understand and prevent psychological distress among family members whose loved ones are treated in intensive care (2,27,28). During visiting hours, family members should be allowed to participate in patient care under the supervision and support of nurses (3). Nurses can identify stressors and early signs that negatively affect family members and provide support to them (2). Furthermore, it is recommended that nurses plan interventions to reduce family members' anxiety (29).

Social support was listed among the coping strategies used by the family members of patients hospitalized in ICUs because of critical conditions (30). Social support has been defined as an important buffer and resource for families under stress (31). Perceived social support may be categorized as informational (providing appropriate information to help the individual), emotional (positive expressions of attention and listening), or instrumental (material help or help in daily responsibilities) support (32). Social support helps individuals cope with problems, increases their satisfaction, and raises their quality of life (29). Investigating the sources of social support

for family members (29), as well as their needs, may improve the quality of patient care in ICUs.

In the literature that following a relative's admission to the intensive care unit, the needs of family members should be determined and collaborative relationships between healthcare providers and families should be facilitated (33,34). This research is important in terms of determining the current situation and planning the necessary interventions. Defining the situation and determining the needs of families can be effective in the support and care interventions that can be provided to families. In addition, determining the psychological distress levels of families will guide the psychosocial interventions that can be applied. Here, it is important to learn and emphasize the functionality of the social support mechanism, which is a protective factor for families. In Türkiye, there is no standard care practice in intensive care that focuses on the patient's family. Families can only see their patients during patient visits and receive limited information from healthcare personnel. Understanding the needs of families provides guidance for nurses, physicians, and other members of the care team in designing interventions to assist families. This study aimed to identify the needs of families of patients in ICUs, the psychological distress and social support levels of these families, sociodemographic factors associated with their needs, and the relationships between family needs, psychological distress, and social support.

Research question:

What are the relationships between the sociodemographic factors related to the needs of individuals and the family needs, psychological distress and social support?

Methods

Study design

This study was conducted with a descriptive and cross-sectional design. Descriptive studies are

also important because they often provide the first important clues about the possible determinants and course of a disease (35). In cross-sectional survey studies, the universe and sample are large. Different variables are measured at once (36). For this reason, this method was chosen in this study.

Setting

The hospital where the study data was collected is located in the city center and serves a population of 376 thousand and has a capacity of 318 beds, 38 of which belong to tertiary. Anesthesia and reanimation intensive care unit. The nurse-to-patient ratio is 2:1 for level 3 intensive care patients. The service where the research was conducted is the 30-bed Anesthesia and reanimation intensive care unit. In this intensive care unit, the relatives of the patients are informed both verbally and in writing. The doctor is responsible for this. As a standard, the relatives of the patient who is admitted are first informed verbally and then their written consent is obtained. The individual differences of the informants do not affect the study because all informants provide the same information and use the same information text.

Participants

The length of stay of patients in the hospital varies since it is a tertiary intensive care unit. A total of 60 nurses works in the service. One of the researchers works as a nurse in the clinic where the data was collected and carried out the data collection process. The purpose of the study was explained to the families and their consent was obtained from those who agreed to participate in the study.

The inclusion criteria were being a first-degree relative of a patient hospitalized in the ICU (spouse, parent, child or sibling), being at least 18 years of age, having a patient who completed their first 24 h in the ICU, and agreeing to participate in the study. This group was included in the study because it was thought that first-degree relatives responsible for patient care may

experience more distress than other relatives. The sample of the study excluded individuals who did not agree to participate, those who were family members of patients who had not completed the first 24 h of their ICU stay or whose patient was hospitalized in intensive care at least six months ago (as family members who have patients in the ICU for durations longer than six months adjust to the process, their needs and expectations may vary), and those who filled out the data collection forms incompletely. The first 6 months in the intensive care unit have been associated with higher anxiety and stress (37).

The sample calculation of this study was conducted by employing the sampling method in known states of the universe (38). To examine the prevalence of the event in sample calculation, the formula used to determine the number of individuals to be included in the sample was used.

The number of patients admitted to hospital is an average of 1160 people per year. When the deviation to be made by the prevalence of the event is applied to the formula, 166 individuals were included in the sample. <https://www.calculator.net/> site, the universe is 1160, the frequency of the event is 10%, the confidence interval is 95%, and the margin of error is 5%, the sample is 124. Considering the possibility of incomplete filling of the scales, the study was completed with 166 people. Cohen's *d* was used to determine effect sizes: small ($d \leq 0.2$), medium ($d \approx 0.5$), or large ($d \geq 0.8$) effects (39). Post hoc power analysis was performed using independent groups *t*-test analysis with a 95% confidence interval and a significance level of $p = 0.05$. The power analysis showed that this study was sufficiently powered (Effect size = 0.67). It is done to determine whether the sample size is sufficient or how powerful the study is to test the hypothesis. The post-hoc power analysis was performed with the data of the study. At the end of the study, the power was 0.99, when the effect size, *p* value, and sample size were 0.67, 0.05, and 166, respectively.

Data collection

One of the researchers explained the objectives of this study to the participants visiting their family members in the ICU and obtained their informed consent. Data were collected between February and August 2023. The purpose of the study was explained to family members who came to visit the patient. Individuals who met the inclusion criteria for the study were asked to fill out the forms.

Measurement instruments

Personal information form

This form included questions on the demographic characteristics of the participants, such as age, gender, and education level, and other questions on variables, such as their frequency of visiting the hospital and their experience in caregiving.

Critical care family needs inventory (CCFNI)

The original form of the scale was developed by Molter (40), and its validity and reliability were tested in Turkish by Büyükçoban et al. (41). Each item of the scale has Likert-type response option scored in the range of 1-4. Higher scores reflect a higher degree of need. Although the overall Cronbach's alpha internal consistency coefficient of the scale was reported as 0.93, the coefficients of its subscales varied from 0.83 to 0.92. The minimum and maximum possible scores on the scale are 40 and 160 (41). The scale consists of five subscales: information (e.g., 'To know exactly what is being done for the patient'), assurance/proximity (e.g., 'To feel close to the patient'), support/comfort (e.g., 'To feel accepted by the hospital staff'). In this article, the alpha value of the scale was found to be 0.91.

Kessler psychological distress scale (K10)

The scale, developed by Kessler et al. (42), was adapted to Turkish by Altun et al. (43). It includes 10 items about non-specific psychological distress and measures the degree of depressive symptoms within the last four weeks and those that are experienced

at the moment. (e.g., How often have you felt the following about yourself this month: extremely tired, irritable, etc. for no apparent reason?...). It is a 5-point Likert-type scale where each item has response options varying from 1 (none of the time) to 5 (all of the time). The minimum and maximum possible scores on the scale are 10 and 50. Higher scores are interpreted as higher levels of psychological distress. The scale score is evaluated according to the minimum and maximum score range that can be obtained from the scale. The internal consistency coefficient of the scale was reported to be 0.95 (43). In this article, the alpha value of the scale was found to be 0.79.

Multidimensional scale of perceived social support (MSPSS)

MSPSS was developed by Zimet et al. (44). and adapted to Turkish by Eker et al. It is a 7-point Likert-type scale that consists of 12 items and 3 subscales indicating sources of social support: family, friends, and significant others (45). (e.g., My family (e.g., my mother, father, spouse, children, siblings) tries to help me.) In Eker and Arkar's study, it was found that the scale had high consistency levels with reliability coefficients ranging between 0.80-0.95 (45). In this article, the alpha value of the scale was found to be 0.96.

Statistical analysis

The collected data were analyzed using the SPSS software package (version 25.0, SPSS Inc., Chicago, IL, USA). The independent variables of the study were calculated with frequency. Mean and Standard Deviation were used as the basic statistical terms of the scales. Normality of the data was checked with the Kolmogorov-Smirnov test.

Pearson correlation coefficient (r) and independent t tests were used to test relationships and correlations. Comparison of independent variables and scale scores was calculated using One way ANOVA analysis and Tukey test. The effect sizes of the mean differences were calculated using Eta-squared (46).

The level of significance was set at 0.05.

Ethical considerations

Approval was received from the university's ethics committee (Ethics number: 2023-16, Date: 23.02.2023) (Ethic number (IRB number.): 2023-16, Date: 23.02.2023). Informed consent forms were obtained from the participants. All procedures of the study complied with standards for human participation research (e.g., the Declaration of Helsinki).

Results

Participant characteristics

Table 1 shows the socio-demographic characteristics of the participants. This study included family members of patients hospitalized in the ICU, and 166 participants filled out the data collection forms (response rate: 95%). While 60.2% of the participants were female, 38% had undergraduate or higher degrees. It was determined that 50.6% of the participants were not cohabiting with their patients. The percentage of participants who were residing in the city where the hospital is located was 72.3%. The mean age of the participants was mean=42.14 (SD=16.80), while 66.2% of them visited their patients more frequently than once a week (Table 1).

Scale scores of the participants

Table 2 shows the average scores of the participants on the scales. The participants had a mean total Critical Care Family Needs Inventory score of mean=135.51(SD=18.49) (high level), while their mean subscale scores were mean=38.45(SD=5.23) for information, mean=20.89(SD=3.08) for assurance, mean=24.12±3.84 for proximity, mean=32.04(SD=7.05) for support, and 19.99±3.36 for comfort. The mean K10 score of the participants was mean=25.77(SD=9.99). According to the scores, the participants had potentially moderate levels of psychological distress. The participants had a mean total MSPSS score of mean=68.62(SD=15.54) (high level), whereas their mean subscale scores were mean=22.39(SD=5.89) for the family dimension,

mean=22.50±5.79 for the friend dimension, and mean=23.72(SD=4.96) for the significant other dimension (Table 2).

Table 1. Sociodemographic characteristics of participants (n=166)

Characteristics	n	%
Gender		
Female	100	60.2
Male	66	39.8
Education level		
Primary school	50	30.1
Secondary school	53	31.9
High school or higher level	63	38.0
Cohabiting with their patients		
Yes	82	49.4
No	84	50.6
Residing in the city where the hospital is located		
Yes	120	72.3
No	46	27.7
Frequency of visiting the patient		
More than once a week	110	66.2
Less than once a week	56	33.8
	Mean	Standard Deviation
Age	42.14	16.80

Table 2. Mean scores of participants in critical care family needs inventory, kessler psychological distress scale and the multidimensional scale of perceived social support scale (n=166)

Scales	Mean ± SD
Critical Care Family Needs Inventory	135.51±18.49
Information	38.45±5.23
Assurance	20.89±3.08
Proximity	24.12±3.84
Support	32.04±7.05
Comfort	19.99±3.36
Kessler Psychological Distress Scale	25.77±9.99
The Multidimensional Scale of Perceived Social Support Scale	68.62±15.54
Family	22.39±5.89
Friend	22.50±5.79
Significant other	23.72±4.96

Abbreviation: SD, standard deviation

Comparisons of the Critical Care Family Needs Inventory scores of the participants based on their sociodemographic characteristics

Table 3 shows the relationship between the Critical Care Family Needs Inventory score according to the socio-demographic characteristics of family members. Among the Critical Care Family Needs Inventory subscales, significantly higher information, assurance, proximity, and comfort scores were found among the participants who were high school graduates compared with those who had university degrees and among those who visited their patients more frequently than once a week compared with those who visited their patients less frequently than once a week. The size of the mean differences was moderate (eta squared = .077) for the difference between educational levels. And also the size of the mean differences was moderate (eta squared = .054) for the difference between frequency of visiting the patient.

The subscale Critical Care Family Needs Inventory scores of the participants did not vary significantly based on whether the patient lived in the same city as the hospital, gender, or whether the caregiver lived with their patient.

Relationships between Critical Care Family Needs Inventory, Kessler Psychological Distress Scale, and Multidimensional Scale of Perceived Social Support scores of participants

Table 4 shows the correlation between the scales. A positive and statistically significant relationship was identified between the Critical Care Family Needs Inventory and MSPSS scores of the participants. On the other hand, no significant relationship was found between their Critical Care Family Needs Inventory and Kessler Psychological Distress Scale scores (Table 4).

Table 3. Comparing critical care family needs inventory levels in terms of socio-demographic characteristics of the participants (n=166)

Characteristics	Information	Assurance	Proximity	Support	Comfort
	Mean ± Standart Deviation	Mean ± Standart Deviation	Mean ± Standart Deviation	Mean ± Standart Deviation	Mean ± Standart Deviation
Gender					
Female	38.39±5.31	20.99±2.97	24.09±3.66	32.21±6.24	20.24±3.16
Male	38.54±5.13	20.75±3.25	24.16±4.11	31.80±8.17	19.62±3.64
	p=0.852	p=0.636	p=0.900	p=717	p=247
Education level					
Primary school (50)	38.28±5.46	20.14±3.33	23.62±4.76	30.88±6.40	19.90±3.37
Secondary school (53)	40.43±3.93	22.05±2.54	25.60±2.43	33.84±8.48	21.0±3.09
High school or higher level (63)	36.92±5.51	20.52±3.04	23.26±3.67	31.46±5.95	19.22±3.40
	p=0.01 2 > 3	p=0.003 2>1, 3	p=0.002 2>1,3	p=071	p=017 2>3
Cohabiting with their patients					
Yes	38.54±5.54	20.96±3.27	24.19±3.86	32.42±6.10	19.90±3.44
No	38.35±4.94	20.83±2.89	24.04±3.84	31.67±7.89	20.08±3.29
	p=0.814	p= 0.787	p=0.805	p=0.496	p=730
Frequency of visiting the patient					
More than once a week (110)	39.35±4.91	21.52±2.80	24.80±3.70	32.50±6.55	20.40±3.37
Less than once a week	36.67±5.42	19.66±3.25	22.78±3.77	31.16±7.92	19.19±3.22
	p=0.002	p=0.000	p=0.001	p=0.249	p=0.29
Residing in the city where the hospital is located					
Yes	38.54±5.54	20.96±3.27	24.19±3.86	32.42±6.10	19.90±3.44
No	38.35±4.94	20.83±2.89	24.04±3.84	31.67±7.89	20.08±3.29
	p=0.814	p=0.787	p=0.805	p=496	p=0.730

* p< .005

Table 4. Correlations with the critical care family needs inventory, kessler psychological distress scale and the multidimensional scale of perceived social support scale

		Critical Care Family Needs Inventory	Psychological Distress Scale	The Multidimensional Scale of Perceived Social Support Scale
Psychological Distress Scale	r	-0.076	1	-0.023
	p	0.331		0.771
The Multidimensional Scale of Perceived Social Support Scale	r	0.400*	-0.023	1
	p	0.001	0.771	

* p< .001

Discussion

The participants in this study had a mean total Critical Care Family Needs Inventory score at a high level, a high MSPSS score, and a moderate level of psychological distress. Secondary school graduates

had higher information, assurance, proximity and comfort scores than high school graduates. Those who visited their patients more often than once a week had higher information, Assurance, Proximity, and Comfort scores. A positive and statistically significant relationship was identified between the Critical Care

Family Needs Inventory and MSPSS scores of the participants.

One of the first steps in providing appropriate care to intensive care patients and their families is the accurate assessment of their needs (26). The family members of intensive care patients who participated in this study had a mean total CCFNI score of mean=135.51(SD=18.49), as well as high mean scores on all CCFNI subscales, which indicated a high degree of need. The greatest degrees of need among the participants were found to be in the domains of information and support. Coşkun and Kol found a high mean comfort subscale score among family members (47). In another study, it was stated that families with patients in intensive care needed to be supported by healthcare personnel (48). As opposed to the results of this study, Elsayed et al. reported that family members had the greatest degree of need in the domains of assurance and anxiety reduction (49). Kang et al. (50). also found that the greatest degree of need among families was in the domain of assurance, followed by the domain of information. According to Salameh et al. (12), families had the greatest degree of need in the assurance domain. Meneguín et al. (33), on the other hand, reported that the highest scores of families were in the proximity domain. Haave et al. (27) observed that families were less satisfied with the information they received and their decision-making processes. A previous study revealed that family members needed information about the current status of their patients (3). Chang et al. (31) stated that most first-degree family caregivers needed to discuss the medical situation (79.3%), obtain information about the treatment of the condition (51.7%), and receive psychological support (24.1%). Although the needs of families vary according to the research results, the high level of needs shows that healthcare personnel working in these clinics should be more sensitive to family needs. Since the family's inability to participate in care and lack of support cause psychological distress in families, the benefit of including the family in the care process, the importance of communicating with family members, and the need to support

the family with psycho-education are emphasized (51). Intensive care unit nurses play a key role in supporting families by providing them with a sense of assurance and helping them cope with experiences they find distressing (52). Family members describe the support they receive from ICU nurses as very important to them in terms of coping with the situation and understanding what is going on (27). According to the results of this study, it may be beneficial to inform those who lack information about the needs of their families and to provide support in this direction to those who lack social support.

Although the contexts in which families have needs differed in different studies, the findings that these families have a high degree of need show that the healthcare personnel working at these clinics should be more perceptive of these needs. Because inadequate family involvement and support are associated with familial problems and negative psychological health outcomes during ICU care, it was recommended to involve the family in the care process, communicate with the family members with a structured approach, and provide family support through psychoeducation programs (51). Intensive care nurses play a crucial role in supporting families to provide them with a sense of assurance and help them cope with experiences that they find distressing (52). Family members of ICU patients defined the support they received from ICU nurses as highly important for them to cope with their situation and understand what was happening (27). Considering the results obtained in different studies, it could be beneficial for nurses to provide information to families according to their areas of need. In addition, including the patient and family in the intensive care team will positively affect the patient's quality of care in the post-discharge period.

In this study, according to their scores, the participants had potentially moderate levels of psychological distress. In another study, family members of patients in the ICU were found to have high levels of psychological distress (72% had anxiety symptoms, 45% had depressive symptoms, and 42% had both)

(19) Olabisi et al. (53). reported that the rate of stress in family members with patients in the ICU was 10%. Kang et al. (50). determined that family members of patients were psychologically in distress. In another study, it was discovered that family members with critical patients in the ICU had high levels of anxiety, depression, and stress, and there were moderate to severe symptoms of psychological distress that negatively affected both the patient and their family (2). It was observed that family members of ICU patients had high levels of anxiety and moderate levels of perceived social support and satisfaction with the ICU (29). The results of our study were similar to those in literature. Patient families are anxious about their patients hospitalized in the ICU, and they may have worries regarding the critical state of these patients. Families experiencing these negative emotions can be psychologically relieved if nurses inform them at regular intervals and support them when needed. Providing family members with skills for coping with stress may be beneficial in reducing psychological distress. As a method of coping with stress, the nurse can provide breathing and relaxation exercise training, use social support factors, and apply meditation, yoga and peer support training. In addition, involving the family in the care process provides comfort and support for the patient and benefits the family member as it creates a feeling of contributing to the patient's healing process (25). Strategies such as establishing therapeutic communication with the family, informing the family about the patient's condition, allowing family members to be with the patient during the procedures, and flexible visitation policies also help families overcome this stressful situation (14). Health policies should include families in intensive care patient care protocols and interventions should be implemented according to the needs of families as a routine care procedure.

The participants of this study, who were high school graduates, had significantly higher CCFNI scores in the domains of information, assurance, proximity, and comfort in comparison to the participants who had university degrees. In contrast, Baltalı et al. (2022)

reported that family needs did not vary depending on education level (54). Salameh et al. (2020), on the other hand, found that the need for assurance, proximity, and support increased in the group with high education levels (12). Elsayed et al. stated that family members with low education levels had an increased need for information (49). According to the report by Terzi et al. as education levels increased, the CCFNI subscale (information, assurance, proximity, and comfort) scores also increased (55). In the study performed by Alsharari et al. family members with high levels of education considered the domains of assurance, proximity, and information in the context of CCFNI (18). Lower health literacy of low-educated participants may have led to this result. The planning of education programs by nurses prioritizing individuals with low education levels may be beneficial to this group of individuals. Additionally, supporting digital literacy can also help these individuals.

In our study, the participants who visited their patients in the ICU more frequently than once a week had significantly higher CCFNI assurance, proximity, and information subscale scores. Elsayed et al. found that the social support need score was higher in people who visited their patients for the first time (49). Alsharari et al. reported that the frequency of hospital visits did not affect the needs of family members (18). Visiting the patient frequently may have increased the needs of the participants of this study in this context by promoting their desire to constantly check the status of the patient. This suggests that more frequent visitors developed higher emotional involvement, which may have led to increased anxiety. It is important to give sufficient information to the family members of the patient, answer their questions, and try to support them in their areas of need at every patient visit. Since the workload of intensive care units is high, sufficient healthcare personnel must be employed so that nurses can spare time for these. Structured family education programs be introduced in ICUs to alleviate distress. Authorities that determine health policies and hospital managers should support personnel recruitment to increase the number of

nurses per patient. Supporting the patient's relative makes it easier for both the family and the patient to adapt to the post-discharge process.

In this study, a positive significant relationship was identified between the CCFNI and MSPSS scores of the participants. In another study conducted with patient relatives, MSPSS scores were found to be negatively associated with anxiety, depression, burnout, hostility, and psychological distress (56). Terzi et al. stated that family members who reported having someone who supported them had higher scores on the CCFNI subscales (55). Another important need for families of intensive care patients is their need for support that will help them manage this stressful situation better and make their expectations about the progress of intensive care patients more reasonable (57). In a study conducted in Taiwan, it was determined that most families with patients in the intensive care unit needed information about the patient's medical condition and treatment and extra support such as psychological support (31). In another study conducted with family members who had patients in the intensive care unit, it was found that having low/moderate levels of perceived social support was associated with higher stress level and lower family satisfaction (32). This study shows that there is a significant relationship between the social support received by the families of patients and their family needs. This finding indicates that social support of patients' families plays a critical role in meeting family needs. This is a protective factor for both the patient and the caregiver. Peer support programs could help address family distress. It may also be beneficial to make families aware of existing social support resources and enable them to benefit from them.

In this study no significant relationship was found between their Critical Care Family Needs Inventory and Kessler Psychological Distress Scale scores. This finding suggests that qualitative studies should be conducted on how families feel when their needs are not met. With in-depth interview techniques, both the factors affecting families' needs and the

factors affecting their psychological distress can be determined.

Limitations

One of the limitations of this study was its descriptive cross-sectional design. This research does not have a methodology of establishing cause and effect relationships. Another limitation was that the intensive care patients whose family members were included in the study were not categorized or analyzed based on their different illnesses. The needs of family members may differ depending on the type of illness and its severity. Future studies are recommended to include analyzes of different diagnoses. Another limitation of the study is the lack of questions about the relationship between the patient and the family, the duration of the patient's stay in the clinic, and the patient's comorbidities. The sample consisted of individuals who could be reached and agreed to participate in the study. Individuals with very high psychological distress or who could not be reached were not included in the study. This was another limitation of the study. The study could have been enriched with qualitative interviews to explore why participants had specific needs. Since the study was conducted in a single hospital, results may not represent all ICU settings in Türkiye.

Conclusion

This study showed that family members who had patients hospitalized in the intensive care unit needed support mostly in the areas of information and support, experienced potentially moderate levels of psychological distress, and had high levels of perceived social support. It was determined that as the education levels of the participants decreased and as their frequency of visiting their patients increased, their needs also increased. A positive and significant relationship was identified between family needs and perceived social support levels. Meeting the needs of family members will increase the quality of patient care. It is believed that the most significant and largely unmet needs of family members should

be constantly assessed, and these needs should be met by intensive care nurses. Including family members as part of the treatment team in the care process will positively affect the quality of care. It is recommended that special studies be conducted with family members. In addition, improving the number of healthcare personnel in healthcare institutions can directly positively affect care.

Ethical approval

This study has been approved by the Kocaeli Derince Training and Research Hospital Clinical Research Ethics Committee (approval date: February 23, 2023, number: 2023-16). Written informed consent was obtained from the participants.

Author contribution

Study conception and design: SD, YCÖ, EE; data collection: EE; analysis and interpretation of results: SD; draft manuscript preparation: SD, YCÖ, EE. The author(s) reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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An unexpected consequences of severe rhabdomyolysis induced by Plasmodium Vivax: Acute respiratory failure with preserved renal function

Amira Aishah Che Ani¹, Winnie Li-Xue Chiang¹, Nur Najmi Abdul Halim¹, Chee-Kong Wong²

¹Department of Anaesthesiology and Critical Care, Hospital Tuanku Fauziah, Ministry of Health Malaysia, Perlis, Malaysia

²Department of Internal Medicine, Hospital Tuanku Fauziah, Ministry of Health Malaysia, Perlis, Malaysia

ABSTRACT

We described a case of a previously healthy young man with Plasmodium vivax induced severe rhabdomyolysis with a creatinine kinase (CK) level of 812,000 U/L leading to acute respiratory failure and subsequent weaning failure. Mix infections with Plasmodium falciparum were ruled out by polymerase chain reaction (PCR) and other causes including trauma, heat exhaustion, autoimmune diseases, inflammatory myopathy, drugs, and infections such as leptospirosis and COVID-19 were excluded. He presented with respiratory distress requiring intubation and ventilatory support. There was no heart or lung pathology, fever, metabolic acidosis, anaemia, or drop in consciousness level upon presentation. Extubation was attempted twice during the first week of admission, however, respiratory failure ensued after each attempt requiring reintubation in which one of the episodes was complicated by lung collapse. The respiratory distress upon presentation and failed extubation episodes were attributed to respiratory muscle weakness secondary to severe rhabdomyolysis. He was successfully extubated after almost two weeks of admission. Despite the extremely high CK level, renal function was unexpectedly preserved without the need for renal replacement therapy. To the best of our knowledge, this is the first reported case of severe rhabdomyolysis induced by P. vivax leading to respiratory failure but with preserved renal function. This case highlights that P. vivax infection can cause severe rhabdomyolysis and consequently acute respiratory failure due to muscle weakness. Awareness of such complications will guide clinicians' decisions for timely initiation and weaning from mechanical ventilation, hence avoidance of associated complications.

Keywords: rhabdomyolysis, Plasmodium Vivax, respiratory insufficiency, ventilator weaning

Introduction

Rhabdomyolysis as a complication of malaria infection is typically associated with *Plasmodium falciparum* but is rarely linked to *Plasmodium vivax* (1). While severe rhabdomyolysis commonly results in life-threatening acute renal failure (2), its association with acute respiratory failure is uncommon (3,4). This report presents a case of rhabdomyolysis due to *P. vivax* infection leading to acute respiratory failure requiring ventilatory support and subsequent weaning failure, despite preserved renal function.

Case Report

A 24-year-old Bangladeshi male with no known medical history presented to the emergency department with a 5-day history of worsening abdominal and chest pain, progressive shortness of breath, a 2-day history of dark-coloured urine and a 1-month history of intermittent fever and abdominal discomfort. He denied any recent medication use, illicit drugs intake, or recent travel. There were no episodes of vomiting, diarrhoea, jaundice, or weight loss.

✉ Amira Aishah Che Ani • miranomey@yahoo.com

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Telif hakkı © 2025 Yazar(lar). Türk Yoğun Bakım Derneği tarafından yayımlanmıştır. Açık erişimli bu makale, orijinal çalışmaya uygun şekilde atıfta bulunulması koşuluyla, herhangi bir ortamda veya formatta sınırsız kullanım, dağıtım ve çoğaltmaya izin veren [Creative Commons Atıf Lisansı \(CC BY\)](#) ile dağıtılmıştır.

On examination, he was alert but profusely diaphoretic, afebrile, tachypnoeic (respiratory rate: 34 breaths/minute), hypertensive (BP: 160/111) and tachycardic (HR: 115 beats/minute). Oxygen saturation was 100% on room air. Chest X-ray was unremarkable. Abdominal examination revealed generalised tenderness with hepatosplenomegaly; the abdomen was soft, non-distended, and without guarding.

Initial biochemical analysis was notable for severe rhabdomyolysis, with markedly elevated creatinine kinase (CK) at 812,000 U/L, CKMB >2,000 ng/ml, aspartate transaminase (AST) 12,593 U/L, alanine transaminase (ALT) 4,361 U/L and lactate dehydrogenase (LDH) 9,945 U/L (Table 1). Urine spectrometry was positive for myoglobin and haemoglobin. Renal function remained within normal limits. Other relevant tests included mildly elevated total bilirubin, negative hepatitis B/C and HIV serologies, low serum paracetamol level, and a negative COVID-19 rapid test. Troponin I was 11 ng/L with no ischaemic changes on ECG. The *Leptospira* agglutination test was negative.

Given the presence of hepatosplenomegaly and his country of origin, malaria was suspected. Peripheral blood film microscopy confirmed *P. vivax* infection with a parasite count of 1,670/59 μ L. Glucose-6-phosphate dehydrogenase (G6PD) was normal, and treatment with intravenous artesunate and oral primaquine was initiated per local protocol. There was no evidence of anaemia or thrombocytopenia on admission.

He was admitted to the intensive care unit (ICU) for respiratory support with high-flow nasal cannula (60L/min, FiO₂ 0.4) to reduce the work of breathing. Aggressive intravenous fluid resuscitation and urine alkalinisation were initiated for rhabdomyolysis. N-acetylcysteine (NAC) infusion was started due to transaminitis. Despite these measures, his respiratory distress worsened, and he required intubation after 20 hours in the ICU. This occurred in the absence of hypoxia, sepsis, pulmonary findings, or positive fluid balance. On day 2, malarial polymerase chain reaction (PCR) confirmed mono-infection with *P. vivax*

(parasite count: 0/90 μ L). On day 3, he developed acute haemolytic anaemia, with haemoglobin decline and elevated reticulocytes count (5.9%). Peripheral blood smear confirmed haemolysis; iron study was normal.

An initial attempt to extubation on day 5 to Venturi mask (FiO₂ 60%) failed within hours due to hypercapnic respiratory failure (arterial blood gas: pH 7.17, PaCO₂ 95 mmHg, PaO₂ 142 mmHg, bicarbonate 27.6, SaO₂ 99%), necessitating reintubation. A second extubation on day 8 was followed by desaturation after sips of clear fluid. Chest X-ray revealed total right lung collapse, and urgent bronchoscopy identified presence of a large amount of thick secretions occluding the right bronchial tree. Following the second failed extubation, respiratory muscle weakness was suspected. Neurological examination revealed proximal (shoulder girdle) weakness with otherwise normal findings. Intravenous immunoglobulin (IVIg) was initiated empirically for possible inflammatory myositis. Myositis antibody panel, ANA, complement levels (C3/C4), thyroid function, and HbA1c were all within normal limits. Cultures of blood, urine, and tracheal aspirate were negative.

His CK level declined progressively with supportive therapy, and his respiratory status improved in parallel. Successful extubation was achieved once CK level has dropped significantly from peak values (Figure 1). Renal function remained preserved throughout, and renal replacement therapy was not required. Repeat blood films confirmed parasitic clearance. He was extubated to non-invasive ventilation (NIV) on day 12 and subsequently transitioned to conventional oxygen therapy. He was discharged well on day 15 of hospitalisation.

Discussion

P. vivax is the most prevalent species of malaria outside sub-Saharan Africa (5). While historically considered to cause benign disease, emerging evidence demonstrated that *P. vivax* infection can

Table 1. Summary of investigation result throughout admission

	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15
Hb (g/dL)	14.7	13.0	10.7	10.8	10.0	10.3	10.6	9.4	9.3	7.9	7.4	9.2	10.10	10.7	11.5
WBC (10 ³ /uL)	14.44	13.12	9.31	9.34	9.44	10.57	12.44	10.26	12.18	10.68	10.43	10.94	11.1	13.96	9.81
Plt (10 ³ /uL)	268	287	225	232	236	256	274	218	265	275	278	288	347	388	356
Na (mmol/L)	128	136	136	136	140	139	140	138	142	143	142	140	139	137	137
K (mmol/L)	5.1	4.0	4.0	3.4	3.1	4	3.7	3.9	3.0	3.1	2.9	3.7	3.9	3.6	3.2
Ur (mmol/L)	6.0	8.2	8.2	9.1	10.3	9.6	10.5	10.2	8.1	9.7	10.1	9.1	8.6	8.3	6.2
Cr (umol/L)	54	31	31	43	40	33	46	38	32	30	36	32	41	34	35
CK (U/L)	812000	>160000	>160000	124378	72267	105907	-	40275	18927	-	4478	2055	1047	891	-
TB (umol/L)	23	15	15	15	13	12	10	12	9	9	11	8	27	8	-
ALT (U/L)	4361	3496	2774	2172	1720	1506	1297	1243	1015	749	744	577	479	382	-
ALP (U/L)	128	-	114	104	99	99	92	93	93	102	110	92	82	98	-
AST (U/L)	12593	7190	5249	3376	2177	2407	1906	1646	1016	593	468	269	180	-	-

Hb = haemoglobin, WBC = white blood cell, Plt = platelet, Na = sodium, K = potassium, Ur = urea, Cr = creat, Alb = albumin, TB = total bilirubin, ALT = alanine transaminase, ALP = alkaline phosphatase, AST = aspartate transamina.

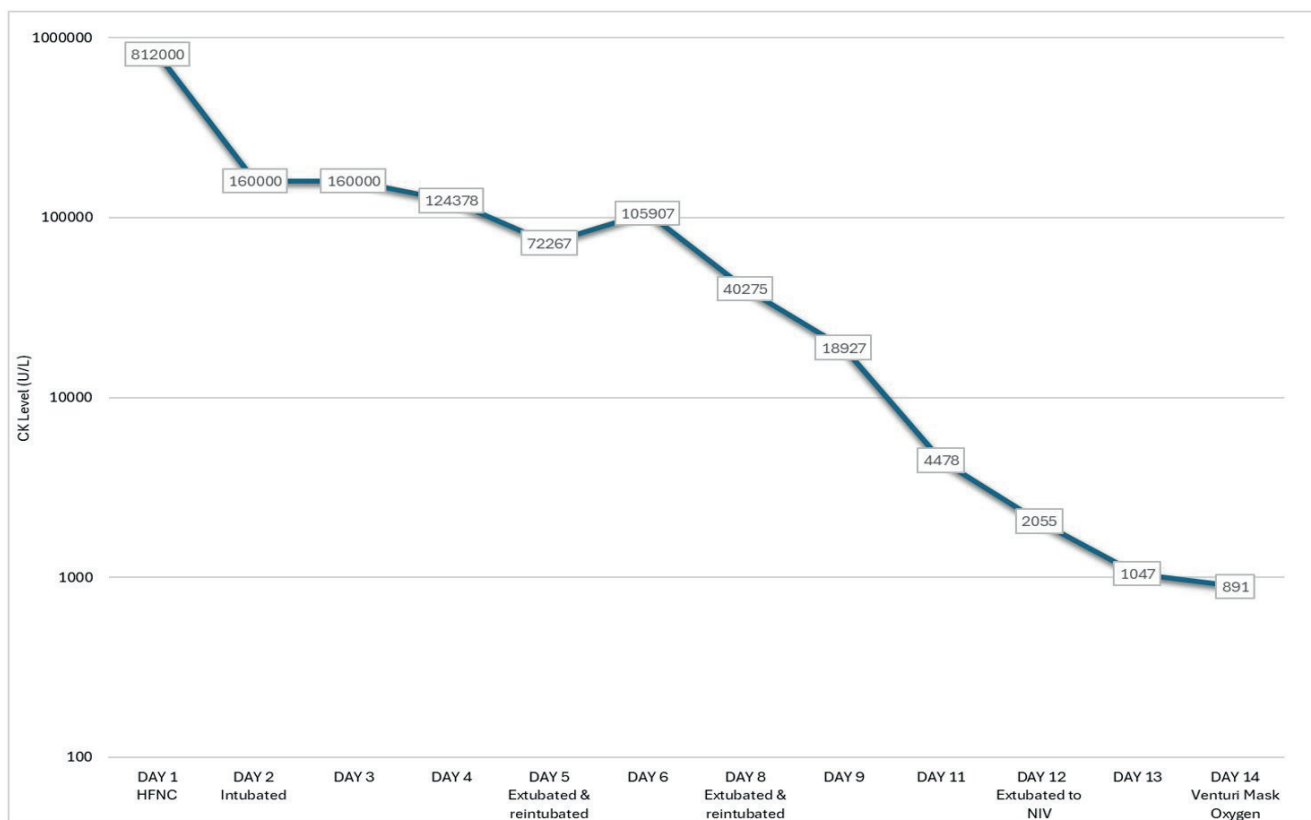


Figure 1. Trend of CK levels during ICU admission in relation to ventilatory support

CK: Creatine kinase, ICU: Intensive care unit.

result in significant morbidity and mortality (6). Rhabdomyolysis, characterised by the breakdown of skeletal muscle with the release of myoglobin, sarcoplasmic proteins, and electrolytes into the circulation (7), is a rare complication of malaria and has been primarily reported in association with *P. falciparum* (1). To date, only two cases of *P. vivax*-associated rhabdomyolysis have been reported in literature. One occurred in a patient with myoadenylate deaminase deficiency (MADD) (8). Although muscle biopsy was not performed in our patient to exclude MADD, the absence of hallmark features such as exercise intolerance fatigability, and recurrent myalgia (9), along with its low prevalence (1-2%) in Caucasians (10), makes it unlikely in our Bangladeshi patient.

The second case reported rhabdomyolysis exacerbated by anti-malarial treatment (primaquine and chloroquine) (11). In contrast, our patient presented with markedly elevated CK levels (almost 300 times higher than the second reported case), prior to the initiation of any antimalarial therapy, suggesting that *P. vivax* infection itself was the likely trigger, confirmed by PCR. Other common causes such as trauma, heat exhaustion, autoimmune diseases, inflammatory myopathy, drugs, and other relevant infections were excluded, further supporting this hypothesis.

Interestingly, while both previously reported cases progressed to acute kidney injury requiring renal replacement therapy, our patient's renal function remained preserved despite the extremely elevated CK. Early aggressive intravenous hydration, urine alkalinisation, and the patient's young age may have played a protective role (12). Additionally, we hypothesise that the administration of NAC—initiated for presumed malarial hepatopathy based on marked transaminase elevation (13), may have contributed to renal protection. NAC possesses antioxidant properties and has been shown in preclinical studies to attenuate rhabdomyolysis-induced renal injury, although human data remain limited (14).

While renal involvement is a well-recognised complication of severe rhabdomyolysis, respiratory

failure secondary to muscle involvement is less frequently reported and often underappreciated. As illustrated in this case, the need for mechanical ventilation and two failed extubation attempts were attributed to respiratory muscle weakness, despite normal pulmonary auscultation, absence of pneumonia or acute respiratory distress syndrome, and preserved neurological status at the time of ICU admission.

At the time of initial intubation, there were no signs of hypoxaemia, altered mental status, metabolic acidosis, sepsis, or significant anaemia—commonly reported contributors to respiratory distress in malaria (15). During both extubation attempts, the patient had passed spontaneous breathing trials, had a Richmond and Agitation-Sedation Scale (RASS) score of +1, was haemodynamically stable, and not on sedative agents. Pulmonary mechanics and secretion burden were considered acceptable. Nonetheless, extubation failed. First was due to hypercapnic respiratory failure, and later due to a right lung collapse, the latter attributed to retained secretions. Neurological examination performed after the second failed extubation revealed proximal weakness with preserved distal strength and no bulbar deficits. Although myositis panel was negative, empirical IVIG was administered in case of inflammatory myopathy. No infectious, autoimmune, or metabolic contributors were identified.

There are limited reports of rhabdomyolysis from other infectious causes leading to respiratory failure (3,4), but to our knowledge, this is the first report of *P. vivax*-associated rhabdomyolysis presenting with respiratory muscle weakness and failure requiring prolonged mechanical ventilation. The pathogenesis may involve systemic inflammation, oxidative stress, and microvascular sequestration of infected red cells in muscle capillaries (16). A direct cytopathic effect of *P. vivax* on muscle tissue has also been postulated (11).

Importantly, myalgia—often absent in up to 50% of rhabdomyolysis cases (17) was not reported by our patient. This may lead clinicians to underestimate the

extend of muscle involvement, including respiratory musculature. In our case, overt weakness only became apparent upon closer examination following failed extubation attempt. Anticipating respiratory failure in patients with severe rhabdomyolysis can guide decisions around timing of extubation. Literature suggests muscle regeneration typically begins within 3-5 days post-injury and peaks around 2 weeks (18). Extubation attempts on days 5 and 8 may have been premature, whereas sustained success was achieved only nearly two weeks, aligning with expected recovery time.

Conclusion

P. vivax infection can present with severe rhabdomyolysis and respiratory failure due to muscle weakness, even in the absence of renal impairment. Clinician awareness of this rare but significant complication is crucial, as early recognition may inform ventilator management and optimise extubation timing, ultimately improving patient outcomes.

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Ethical approval

This study has been approved by the Ministry of Health Malaysia Medical Research & Ethics Committee (approval date: April 3, 2024, number: 24-00632-AX7). Written informed consent was obtained from the participants.

Author contribution

Study conception and design: AACA; data collection: AACA, WLXC; draft manuscript preparation: AACA, WLXC; Constructive criticism of manuscript: CKW. Finalizing manuscript draft: NNAH. The author(s) reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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