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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

Factors Associated with Thirty-Day Emergency Department Revisits for Upper Gastrointestinal Bleeding: Insights from a Five-Year Retrospective Study

Üst Gastrointestinal Kanama Nedeniyle 30 Gün İçerisindeki Acil Servis Tekrar Başvurularıyla İlişkili Faktörler: Beş Yıllık Retrospektif Bir Çalışmadan Bulgular

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ABSTRACT

Aim: This study aims to identify key factors associated with 30-day emergency department (ED) revisits among patients discharged after upper gastrointestinal bleeding (UGIB), providing insights to optimize patient management and improve outcomes.

Material and Methods: A single-center retrospective cohort study was conducted at a tertiary university hospital between January 1, 2018, and December 31, 2022. Adult patients (>18 years) diagnosed with UGIB were included, while those with incomplete data or transferred to other facilities were excluded. Data on demographics, clinical features, laboratory parameters, endoscopic findings, and revisits were analyzed. Univariate and multivariate logistic regression models were used to identify predictors of UGIB-related ED revisits.

Results: Among 862 patients, the 30-day revisit rate was 19.9% (n=172), with 84 revisits related to UGIB. Female gender, malignancy, anticoagulant use, prior UGIB history, and lower discharge hemoglobin levels were identified as significant predictors of UGIB-related revisits. Patients with Forrest IA ulcers had a 42.9% revisit rate, while those with Forrest III ulcers showed a significantly lower rate of 5.5%. Erythrocyte suspension was used more frequently in the revisit group (83.3% vs. 61.2%, p<0.001), reflecting the severity of these cases.

Conclusion: UGIB-related revisits are influenced by several factors, including anticoagulant use, malignancy, prior UGIB history, and endoscopic findings. Tailored discharge planning, patient education, and risk stratification are critical to reducing revisits. Future studies should focus on prospective validation and the development of predictive models for targeted interventions.

Keywords: Upper gastrointestinal bleeding, Forrest classification, discharge planning, readmission

ÖZ

Amaç: Bu çalışmanın amacı, üst gastrointestinal kanama (ÜGİK) sonrası taburcu edilen hastalarda 30 günlük acil servis (AS) başvurularıyla ilişkili anahtar faktörleri belirleyerek hasta yönetimini optimize etmek ve sonuçları iyileştirmek için içgörüler sağlamaktır.

Gereç ve Yöntemler: Bu tek merkezli retrospektif kohort çalışması, 1 Ocak 2018 ile 31 Aralık 2022 tarihleri arasında bir üniversite hastanesinde gerçekleştirilmiştir. Çalışmaya, ÜGİK tanısı almış 18 yaş üstü erişkin hastalar dahil edilmiş, eksik verileri olan veya başka bir merkeze sevk edilen hastalar çalışmadan çıkarılmıştır. Demografik veriler, klinik özellikler, laboratuvar parametreleri, endoskopik bulgular ve başvurulara ilişkin veriler analiz edilmiştir. ÜGİK ile ilişkili AS başvurularını öngören faktörleri belirlemek için tek değişkenli ve çok değişkenli lojistik regresyon modelleri kullanılmıştır.

Bulgular: Toplam 862 hastanın %19,9'u (n=172) 30 gün içinde tekrar AS başvurusu yapmış olup, bunların 84'ü ÜGİK ile ilişkilidir. Kadın cinsiyet, malignite, antikoagülan kullanımı, önceki ÜGİK öyküsü ve taburculuk sırasındaki düşük hemoglobin seviyeleri, ÜGİK ile ilişkili tekrar başvuruların anlamlı öngörücüleri olarak belirlenmiştir. Forrest IA ülseri olan hastalarda tekrar başvuru oranı %42,9 iken, Forrest III ülseri olan hastalarda bu oran anlamlı derecede düşük olup %5,5'tir. Eritrosit süspansiyonu, tekrar başvuru grubunda daha sık kullanılmıştır (%83,3 - %61,2, p<0,001) ve bu, bu hastaların klinik durumlarının ciddiyetini yansıtmaktadır.

Sonuç: ÜGİK ile ilişkili tekrar başvurular, antikoagülan kullanımı, malignite, önceki ÜGİK öyküsü ve endoskopik bulgular dahil olmak üzere çeşitli faktörlerden etkilenmektedir. Taburculuk planlamasının kişiselleştirilmesi, hasta eğitimi ve risk sınıflandırması, tekrar başvuruların azaltılmasında kritik öneme sahiptir. Gelecekteki çalışmalar, bu bulguların prospektif doğrulamasına ve hedefe yönelik müdahaleler için öngörücü modellerin geliştirilmesine odaklanmalıdır.

Anahtar Kelimeler: Üst gastrointestinal kanama, Forrest sınıflaması, taburculuk planı, tekrar başvuru

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Introduction

Upper gastrointestinal bleeding (UGIB) constitutes a significant proportion of emergency department (ED) visits and plays a critical role in emergency medicine due to its high morbidity and mortality rates (1,2). It is characterized by bleeding originating above the ligament of Treitz, commonly presenting with symptoms such as hematemesis or melena (1). Effective management begins with stabilization, including securing intravenous access, fluid resuscitation, and oxygen support, followed by disease-specific treatments such as proton pump inhibitors, somatostatin analogs, endoscopy, and, when necessary, surgical intervention (3-5). In the United States, UGIB accounts for nearly 200,000 hospitalizations annually, with 67-81% of ED presentations resulting in admission for further evaluation and management (6). During hospitalization, efforts focus on stabilizing the patient, controlling the bleeding through medical or interventional therapies, and addressing the underlying etiology. Once stabilized and adequately managed, patients are discharged with follow-up plans that may include pharmacological therapy, such as proton pump inhibitors, and regulations to antiplatelet or anticoagulant regimens. However, despite these measures, many patients experience an elevated risk of re-bleeding or other complications after discharge, frequently leading to hospital revisits within 30 days (7). These revisits serve as critical indicators of patient safety and the quality of care provided, while also posing a substantial burden on healthcare systems (8).

Given the impact of recurrent ED visits on both patient outcomes and healthcare utilization, understanding the factors contributing to these revisits is crucial (9). This study aims to contribute to this understanding by categorizing patients with UGIB into two groups—those who experienced UGIB-related revisits to the ED and those who did not (including patients who may have revisited the ED for reasons unrelated to UGIB or did not revisit at all). By comparing these groups, the study seeks to identify the key risk factors associated with recurrent ED visits. The findings are anticipated to inform clinical decision-making, enhance discharge planning, and ultimately reduce the burden of repeat visits in this vulnerable patient population.

Material and Methods

Study design and settings

A single-center retrospective cohort study was conducted out at a tertiary university hospital emergency medicine department serving approximately 200,000 adult patients annually. Marmara University Clinical Research Ethics Committee Clinical Research Ethics Committee approved the study protocol (protocol number: 09.2023.1426; November 11, 2023), and the Declaration of Helsinki was complied with throughout the study. The study report was composed following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (10).

Study participants

All adult patients (>18 years of age) diagnosed with UGIB between January 1, 2018, and December 31, 2022, were retrospectively included in the study. UGIB was identified based on symptoms (hematemesis, melena) or indirect signs (e.g., syncope, fatigue, dizziness, anemia) evaluated during the ED presentation. For patients with multiple ED visits during the study period, only the initial visit was included in the analysis. Additionally, patients whose initial ED presentation resulted in mortality were excluded. Those with incomplete data or who were discharged against medical advice (DAMA) before completing investigations or treatment were also excluded from the study.

Data sources/measurement and variables

Data were collected from the hospital's electronic information management system, as well as from medical records and patient files. Patients were identified by screening the International Classification of Disease-10 (ICD-10) codes, specifically K92.2 (gastrointestinal bleeding). The recorded variables included demographic information (age, gender), presentation vitals (blood pressure, pulse, oxygen saturation, temperature), presenting symptoms (hematemesis, melena, syncope, hematochezia), comorbidities (hypertension, diabetes mellitus, coronary artery disease, dysrhythmia, chronic renal failure, malignancy etc.), medications (antiplatelet agents, anticoagulants, non-steroidal anti-inflammatory drugs, proton pump inhibitors, etc.), laboratory parameters (hemoglobin, platelet count, creatinine, blood urea nitrogen, international normalized ratio, etc.), whether a blood transfusion was performed, hospital length of stay, discharge status, and outcomes. The most recent hemoglobin levels prior to discharge were also recorded for analysis.

Endoscopy results were also examined. Endoscopic findings were categorized as no abnormality seen, gastritis/esophagitis/erosions, ulcers, varices, malignancy, or other findings (mallory-weiss syndrome, angiodysplasia, diverticulum, and anastomotic leakage). Ulcer findings were further classified using the Forrest classification system: active spurting bleeding (Forrest IA), active oozing bleeding (Forrest IB), non-bleeding visible vessel (Forrest IIA), ulcers with adherent clots (Forrest IIB), ulcers with red spots (Forrest IIC), or ulcers with a clean base (Forrest III) (11,12).

Hospital revisit was defined as any re-presentation to the ED within 30 days of discharge. Revisits were categorized into UGIB-related and unrelated groups. For revisits associated with UGIB, data on endoscopic procedures and patient outcomes were documented.

The primary outcome of the study was defined as an UGIB related ED revisit within 30 days of discharge.

Statistical Analysis

The SPSS (IBM Statistical Package for Social Sciences) for Windows 23.0 was used for statistical analysis. Histograms and Q-Q plot graphs were used to evaluate the distribution of data. Categorical variables are presented as numbers with percentages. Normally distributed variables were presented as mean and standard deviation, while non-normally distributed variables were presented as medians with interquartile ranges. Independent group comparisons were performed with the Student T-test, Mann-Whitney U test and Pearson-Chi Square. Statistical significance was set at $p < 0.05$. Factors influencing UGIB-related revisits were analyzed using logistic regression. Variables identified as potentially significant in the univariate regression analysis were subsequently included as independent variables in the multivariate logistic regression analysis. The results of the

regression analyses were presented as odds ratios (OR) with 95% confidence intervals (CIs).

Results

Over a five-year period, 971 patients were diagnosed with UGIB in the ED of Marmara University Pendik Training and Research Hospital. Of these, 109 patients were excluded from the study for various reasons, including transfer to another facility (n=41), DAMA (n=28), incomplete data (n=24), and duplicate visits (n=16). Consequently, a total of 862 patients were included in the final analysis. Among the study cohort, 172 patients had a revisit within 30 days, 84 of which were related to GIB. (Figure 1).

The mean age of the patients was 63.7 ± 18.2 years, with 36.1% being female. A comparison of the demographic characteristics of patients based on GIB-related revisits is presented in Table 1. Female patients, those with a history of GIB, patients with malignancy, and individuals using anticoagulant agents were found to have a higher incidence of GIB-related revisits (p=0.044, p=0.002, p<0.001, p=0.002, respectively). Conversely, patients using nonsteroidal anti-inflammatory drugs (NSAIDs) exhibited a lower frequency of GIB-related revisits (p=0.018).

The patient's vital signs and laboratory parameters at the time of presentation are detailed in Table 2. Hemoglobin levels at presentation were significantly lower in patients who experienced UGIB-related revisits than those who did not (p < 0.001). Furthermore, the final hemoglobin values obtained prior to discharge were also notably lower in the UGIB-related revisit group (p < 0.001).

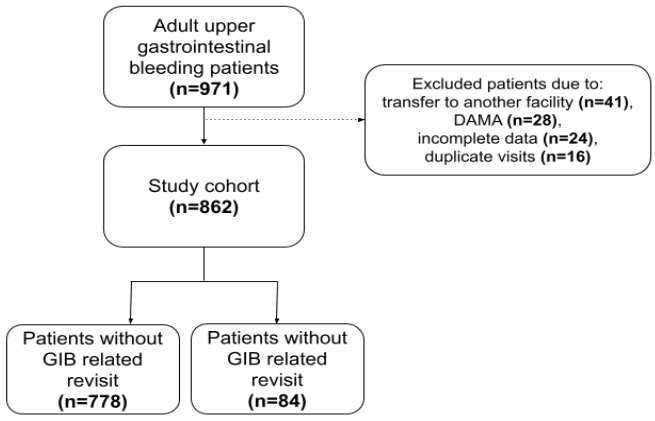

Figure 1: Flow diagram of the study

Endoscopic intervention was performed in 74% of the patients. Among these patients, ulcers (44.0 %) were the most commonly observed endoscopic finding. Table 3 provides detailed endoscopic findings and the Forrest classification of ulcers. Patients with Forrest IA ulcers had a 42.9% rate of UGIB-related revisits, whereas those with Forrest III ulcers experienced UGIB-related revisits at a significantly lower rate of 5.5%.

Erythrocyte suspension was administered to 63.3% of all patients, with higher usage observed among those with UGIB-related revisits (83.3%) compared to those without revisits (61.2%) (p < 0.001). Details on the use of other blood products, length of hospital stay, and hospital outcomes are presented in Table 4.

Characteristics, n (%)	Patients without UGIB-related revisit (n=778)	Patients with UGIB-related revisit (n=84)	All patients (n=862)	p^
Age, mean ± SD	63.6 ± 18.5	64.6 ± 16.7	63.7 ± 18.2	0.630*
Gender, female	273 (35.1)	38 (45.2)	311 (36.1)	**0.044**
Blood type				0.365
0	303 (38.9)	26 (31.0)	329 (38.2)	
A	326 (41.9)	36 (42.9)	362 (42.0)	
B	102 (13.1)	15 (12.8)	117 (13.6)	
AB	47 (6.0)	7 (13.0)	54 (6.3)	
Rh, positive	683 (87.8)	70 (83.3)	753 (87.4)	0.243
Symptoms				
Melena	506 (65.0)	57 (67.9)	563 (65.3)	0.350
Hematemesis	341 (43.8)	40 (47.6)	381 (44.2)	0.507
Hematochezia	55 (7.1)	6 (7.1)	61 (7.1)	0.980
Syncope	44 (5.7)	4 (4.8)	48 (5.6)	0.734
Comorbidities				
Hypertension	277 (35.6)	35 (41.7)	312 (63.8)	0.272
Diabetes mellitus	178 (22.9)	25 (29.8)	203 (23.5)	0.158
Dysrhythmia	76 (9.8)	7 (8.3)	83 (9.6)	0.672
Coronary artery disease	172 (22.1)	22 (26.2)	194 (22.5)	0.395
Chronic kidney disease	58 (7.5)	9 (10.7)	67 (7.8)	0.289
Liver disease	128 (16.5)	19 (22.6)	147 (17.1)	0.153
Malignancy	119 (15.3)	30 (35.7)	149 (17.3)	**<0.001**
UGIB history	248 (31.9)	41 (48.8)	289 (33.5)	**0.002**
Medication use				
Antiplatelet agent	188 (24.2)	17 (20.2)	205 (23.8)	0.422
Anticoagulant agent	156 (20.1)	29 (34.5)	185 (21.5)	**0.002**
Non-steroidal anti-inflammatory drugs	157 (20.2)	8 (9.5)	165 (19.1)	**0.018**
Proton pump inhibitors	119 (15.3)	15 (17.9)	134 (15.5)	0.538

Table 1: Comparison of the demographic data of patients based on UGIB-related revisits (n=862)
SD: Standart deviation; UGIB: Upper gastrointestinal bleeding.
^: Pearson Chi-Square Tests, *: Student-t Test,

Characteristics, n (%)	Patients without UGIB-related revisit (n=778)	Patients with UGIB-related revisit (n=84)	All patients (n=862)	p*
Systolic BP, mmHg, mean ± SD	116.8 ± 23.0	113.5 ± 23.6	116.4 ± 23.1	0.208
Diastolic BP, mmHg, mean ± SD	71.2 ± 15.3	70.2 ± 15.7	71.1 ± 15.3	0.553
Pulse, /min, mean ± SD	92.5 ± 19.1	93.3 ± 182.3	92.6 ± 19.0	0.727
Saturation, %, median (IQR)	98 (96-99)	98 (96-99)	98 (96-99)	0.244**
Hemoglobin, g/dL, mean ± SD	9.4 ± 3.0	7.8 ± 2.7	9.2 ± 3.0	**<0.001**
Hemoglobin at discharge, g/dL, mean ± SD	9.6 ± 1.9	8.8 ± 1.6	9.4 ± 1.9	**<0.001**
Platelet,10^3/mcL median (IQR)	231 (165-296)	243 (143-312)	231 (164-299)	0.729**
INR, median (IQR)	1.2 (1.1-1.4)	1.2 (1.1-1.4)	1.2 (1.1-1.4)	0.526**
Creatinine, mg/dL, median (IQR)	0.9 (0.7-1.2)	0.8 (0.7-1.3)	0.9 (0.7-1.2)	0.654**
Blood urea nitrogen, mg/dL, median (IQR)	29 (20-44)	30 (19-45)	29 (20-44)	0.838**

Table 2: Vitals and laboratory characteristics of patients with and without UGIB-related revisits
BP: blood pressure; IQR: interquartile range; UGIB: upper gastrointestinal bleeding; SD: Standard deviation. *: Student-t Test, **: Mann-Whitney U

Characteristics, n (%)	Patients without UGIB-related revisit (n=778)	Patients with UGIB-related revisit (n=84)	All patients (n=862)	p^
Endoscopy performed	582 (74.8)	57 (67.9)	639 (74.0)	0.167
Endoscopy results (n=639)				**0.004**
No abnormality seen	40 (6.9)	2 (3.5)	42 (6.6)	
Gastritis, Esophagitis, Erosions	122 (21.0)	3 (5.3)	125 (19.6)	
Ulcer	256 (44.0)	23 (40.4)	279 (43.7)	
Varices	110 (18.9)	18 (31.6)	128 (20.0)	
Malignancy	40 (6.9)	9 (15.8)	49 (7.7)	
Others[&]	14 (2.4)	2 (3.5)	16 (2.5)	
Forrest Classification (n=279)[#]				**0.004**
Forrest IA	4 (57.1)	3 (42.9)	7 (100.0)	
Forrest IB	14 (77.8)	4 (22.2)	18 (100.0)	
Forrest IIA	24 (92.3)	2 (7.7)	26 (100.0)	
Forrest IIB	23 (92.0)	2 (8.0)	25 (100.0)	
Forrest IIC	37 (92.5)	3 (7.5)	40 (100.0)	
Forrest III	154 (94.5)	9 (5.5)	163 (100.0)	

Table 3: Comparison of endoscopic findings and timing between patients with and without UGIB-related revisits
[#] Percentages in the Forrest classification row represent row percentages.
[&:] The others include Mallory-Weiss syndrome, angiodysplasia, diverticulum, and anastomotic leakage.
UGIB: Upper gastrointestinal bleeding.
^: Pearson Chi-Square Tests.

Characteristics, n (%)	Patient without UGIB-related revisit (n=778)	Patient with UGIB-related revisit (n=84)	All patients (n=862)	p^
Blood product use				
Erythrocyte suspension	476 (61.2)	70 (83.3)	546 (63.3)	**<0.001**
Platelet suspension	60 (7.7)	10 (11.9)	70 (8.1)	0.181
Fresh frozen plasma	159 (20.4)	22 (26.2)	181 (21.0)	0.219
Outcome				0.499
ED-Discharge	276 (35.5)	32 (38.1)	308 (35.7)	
Ward-Discharge	473 (60.8)	47 (56.0)	520 (60.3)	
ICU-Discharge	29 (3.7)	5 (6.0)	34 (3.9)	
Hospital length of stay, hours, median (IQR)	42 (19-96)	35 (18-100)	42 (19-97)	0.899**

Table 4: Comparison of blood product utilization and patient outcomes between patients with and without UGIB-related revisits
ED: Emergency department; ICU: Intensive care unit; IQR: interquartile range; UGIB: upper gastrointestinal bleeding.
^: Pearson Chi-Square Tests, **: Mann-Whitney U

Univariate and multivariate analyses were conducted to identify factors associated with UGIB-related revisits. The key predictors identified in the multivariate analysis included malignancy (OR: 2.531, 95% CI: 1.510–4.242, p<0.001), a history of gastrointestinal bleeding (OR: 1.711, 95% CI: 1.048–2.792, p=0.032), and the use of anticoagulant agents (OR: 1.689, 95% CI: 1.009–2.828, p=0.046). Conversely, higher hemoglobin levels at discharge were associated with a reduced likelihood of revisits (OR: 0.798, 95% CI: 0.666–0.957, p=0.015). The complete analysis and odds ratios are detailed in Table 5.

Upon detailed analysis of the 84 UGIB-related revisits, 46 patients (54.7%) underwent endoscopy. Among these, no pathology was detected in four patients, while 10 had ulcers (1 Forrest IB, 1 Forrest IIA, 8 Forrest III), 17 had varices, 12 had malignancies, and three presented with findings consistent with gastritis, esophagitis, or erosions. In terms of patient outcomes, 43 were discharged directly from the ED, 30 were admitted to the ward, 7 required ICU admission, and four died in the ED.

Variable	Univariate analysis		Multivariate analysis	
	OR (95%CI)	p*	OR (95%CI)	p*
Female gender	1.528 (0.970-2.407)	0.067	1.237 (0.768-1.992)	0.382
Age	1.003 (0.991-1.016)	0.630		
Hypertension	1.292 (0.817-2.042)	0.273		
Diabetes mellitus	1.428 (0.869-2.347)	0.160	1.234 (0.732-2.081)	0.430
Liver disease	1.484 (0.861-2.560)	0.156	1.224 (0.667-2.245)	0.514
Malignancy	3.077 (1.890-5.008)	**<0.001**	2.531 (1.510-4.242)	**0.000**
UGIB history	2.038 (1.295-3.207)	**0.002**	1.711 (1.048-2.792)	**0.032**
Anticoagulant agent use	2.102 (1.297-3.407)	**0.003**	1.689 (1.009-2.828)	**0.046**
NSAID use	0.416 (0.197-0.881)	**0.022**	0.468 (0.214-1.024)	0.057
Initial hemoglobin level[#]	0.827 (0.760-0.899)	**<0.001**		
Discharge hemoglobin level[#]	0.723 (0.616-0.848)	**<0.001**	0.798 (0.666-0.957)	**0.015**
Erythrocyte suspension use	3.172 (1.756-5.732)	**<0.001**	1.817 (0.930-3.551)	0.081
Endoscopy procedure performed	0.711 (0.437-1.155)	0.169	0.668 (0.392-1.140)	0.139
Endoscopy results (n=639)				
No abnormality seen	1.000 (Reference)	0.492		
Gastritis/esophagitis/erosions	0.492 (0.079-3.049)	0.446		
Ulcer	1.797 (0.408-7.916)	0.439		
Varices	3.273 (0.727-14.741)	0.123		
Others	2.857 (0.367-22.245)	0.316		
Malignancy	4.500 (0.914-22.147)	0.064		

Table 5: Univariate and multivariate analyses of parameters predicting UGIB-related revisits (n=862)

CI: confidence interval; UGIB: Upper gastrointestinal bleeding; NSAID: Non-steroid anti-inflammatory drugs; OR: odds ratio. Statistically significant p values are written in bold.

* A logistic regression model was used for univariate and multivariate analysis to assess the predictive factors that affect UGIB-related revisits.

[#] In the correlation analysis, a high Pearson correlation coefficient (r=0.81) was observed between the initial hemoglobin level and the hemoglobin level at discharge. Therefore, only one of these parameters was included in the multivariate analysis.

Discussion

This study comprehensively analyzes the factors associated with 30-day ED revisits among patients with UGIB. The revisit rate of 19.9% observed in our cohort aligns with prior studies, which report rates ranging from 14% to 25% depending on patient populations and healthcare settings (5,13). This underscores the importance of targeted interventions to minimize recurrent presentations, thereby improving patient outcomes and reducing healthcare burdens.

A notable observation in our study was the higher frequency of UGIB-related revisits among female patients. Although the reason for this gender disparity remains unclear, it is consistent with some reports in the literature suggesting potential differences in healthcare-seeking behaviors, comorbidities, or biological factors between men and women (7). However, other studies have reported conflicting results, indicating either no significant gender differences or higher revisit rates among male patients (13). This variability highlights the need for further research to explore the interplay of gender-specific factors in UGIB-related outcomes.

Our findings also revealed a significant association between anticoagulant use and increased likelihood of UGIB-related revisits. Patients on anticoagulant therapy had a significantly higher odds ratio for revisits, consistent with previous research identifying anticoagulation as a major risk factor for recurrent bleeding (5,7). This result emphasizes the need for careful management of anticoagulant regimens in patients recovering from UGIB, particularly regarding resumption timing and dose adjustments. The American College of Gastroenterology (ACG) Clinical Guidelines recommend individualized approaches for anticoagulant therapy resumption, balancing thrombotic and re-bleeding risks (5).

Interestingly, patients using NSAIDs were found to have a lower likelihood of revisits. This observation may be related to the pathophysiology of NSAID-induced damage, which primarily affects the mucosal layer and is often effectively managed by discontinuing NSAID use and initiating protective therapies for the damaged mucosa (14). In contrast, bleeding associated with underlying chronic conditions such as malignancy or varices is often not easily or rapidly treatable, thereby contributing to recurrent bleeding episodes and higher revisit rates (9,15).

A history of gastrointestinal bleeding was another independent predictor of revisits. This finding aligns with studies suggesting that prior bleeding episodes reflect underlying vulnerabilities, such as chronic mucosal injuries or comorbidities, that predispose patients to recurrent events (7). Clinicians should closely monitor patients with such histories, employing proactive follow-up strategies and patient education to mitigate risks (5).

One of the key findings was that higher hemoglobin levels at presentation and discharge were associated with a reduced likelihood of revisits. This finding supports the notion that optimal hemodynamic stabilization before discharge plays a critical role in reducing post-discharge complications. Conversely, patients who required blood transfusion during hospitalization exhibited a higher risk of revisits. This association likely reflects the underlying severity of illness and worse clinical conditions in these patients, necessitating transfusion. The poor baseline clinical status, rather than the transfusion itself, indirectly contributes to the increased revisit risk. In clinically stable patients with good general conditions, restrictive blood transfusion strategies remain the preferred approach to minimize potential adverse effects while addressing patient needs (7,16,17).

Endoscopic findings emerged as critical factors in understanding revisit risks. Among the patients, bleeding associated with malignancy and varices was particularly notable. Subgroup analysis comparing ulcer classifications revealed that patients with Forrest I ulcers, indicative of active bleeding, had a significantly higher likelihood of UGIB-related revisits (42.9%) compared to patients with Forrest III ulcers, representing ulcers with a clean base and lower bleeding risk, which showed a significantly lower revisit rate of 5.5%. These findings emphasize the importance of tailoring follow-up plans based on endoscopic findings and warrant closer monitoring of patients with high-risk stigma and more intensive interventions to reduce the risk of recurrent bleeding. These results are consistent with previous literature emphasizing the importance of endoscopic results in predicting patient outcomes (5,12).

Finally, the observed revisit rate and its associated factors underscore broader implications for healthcare systems. Effective discharge planning, including comprehensive patient education, medication reconciliation, and follow-up arrangements, remains paramount in mitigating revisits. Studies have shown that structured post-discharge interventions significantly reduce 30-day readmissions, emphasizing the value of multidisciplinary approaches (13,18).

Limitations

This study has several limitations. First, its retrospective design may introduce inherent biases, although including five-year data strengthens its reliability and provides a broad perspective on patient outcomes. Second, the study was conducted at a single tertiary care center, which may limit generalizability. Furthermore, as a tertiary center, the patient population likely included a higher proportion of complex cases, such as malignancies, potentially skewing results. Additionally, malignancies were not subcategorized into gastrointestinal and non-gastrointestinal cancers. This limits our ability to determine whether all observed revisit risks associated with malignancies are related to gastrointestinal cancers or are also influenced by other cancer types. Future studies should explore these distinctions through subgroup analyses to clarify these associations. Another limitation was the exclusion of patients transferred to other facilities due to limited access to their complete data. Many of these patients likely required intensive care, introducing a potential selection bias that could inadvertently underrepresent the most severe cases. Lastly, while most patients returned to the same hospital for follow-up due to structured discharge plans, some may have sought care elsewhere, resulting in incomplete data on revisits (19).

Conclusion

This study identifies critical predictors of UGIB-related ED revisits, including anticoagulant use, prior bleeding history, lower hemoglobin levels at discharge, and specific endoscopic findings. These findings reinforce the need for personalized risk stratification and tailored post-discharge strategies to improve outcomes. Future research should focus on prospectively validating these findings and developing predictive models to guide clinical decision-making.

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All authors read and approved the final submitted version of the manuscript. All authors have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

The Examination of Occupational Injuries in the Emergency Department

Acil Servise Başvuran Mesleki Yaralanmaların İncelenmesi

Ercan Nalbant[1], Burak Davran[1]

ABSTRACT

Aim: While examining the demographic characteristics of injured individuals presenting to the emergency department due to occupational accidents, we also analyzed the types and mechanisms of injuries encountered based on the type of work causing the accident, assessed the adequacy of occupational safety measures, and investigated the patient burden on the emergency department caused by these cases. Emphasis was placed on the possibility of reducing the burden on the emergency department by completing the treatment of some occupational accident patients in occupational health clinics or primary care centers.

Material and Methods: We designed the study as a single-center, retrospective study. We included trauma cases who presented to the emergency department documented with occupational accident reports using the hospital automation system. Trauma patients aged 18 and above, presenting to the emergency department of a tertiary care and research hospital, were examined between January 1-2022, and December 31-2023. The study population was formed according to inclusion and exclusion criteria.

Results: Within the study, 887 patients were examined, of whom 80.8% were male. The mean age of the patients was 34 years. Penetrating-shearing instrument injury (35.4%) and blunt trauma (35.4%) were the most common injury mechanisms, with lacerations (34.6%) being the most common lesions. The upper extremities (41.3%) were the most commonly affected body regions. Furthermore, 74.7% of patients were found to belong to the group of cases treatable with simple medical interventions.

Conclusion: Based on our findings, we suggest that some of the existing diagnoses and medical interventions can be managed in occupational health clinics or primary care centers. Acting accordingly can alleviate the workload of emergency departments.

Keywords: Occupational accident, emergency department, trauma.

ÖZ

Amaç: Çalışmamız, iş kazaları nedeniyle acil servise başvuran hastaların demografik özelliklerini ve istihdamın türüyle ilişkili yaralanma türlerini ve mekanizmalarını inceledi. Ayrıca, iş güvenliği önlemlerinin etkinliğini ve bu yaralanmaların acil servis yükü üzerindeki etkisini değerlendirdik. Çalışma, belirli iş kazası vakalarının tedavisinin iş yeri veya aile hekimliği merkezlerinde tamamlanarak acil servisin yükünün hafifletilebileceğini önermektedir.

Gereç ve Yöntemler: Bu çalışma tek merkezli, retrospektif bir çalışma olarak planladı. Çalışmaya acil servise başvuran, iş kazası tutanağı tutulmuş travma vakaları dahil edildi. 1 Ocak 2022- 31 Aralık 2023 tarihleri arasında üçüncü basamak bir eğitim ve araştırma hastanesinin acil servisine başvuran 18 yaş üstü iş kazasına bağlı travma hastaları hastane otomasyon sistemi kullanılarak incelendi. Çalışma popülasyonu dâhil etme ve hariç tutma kriterlerine göre oluşturuldu.

Bulgular: Çalışma dâhilinde %80,8'i erkek 887 hasta incelenmiştir. Hastaların yaş ortalaması 34'tür. Penetrasyon-kesici alet yaralanması (%35,4) ve künt travma (%35,4) en sık yaralanma mekanizmalarıdır ve kesiler (%34,6) en sık lezyonlardır. Üst ekstremiteler (%41,3) en çok zarar gören vücut bölgeleridir. %74,7 hastanın ise basit tıbbi müdahale ile tedavi edilebilir hasta gurubunda olduğu tespit edilmiştir.

Sonuç: Verilerimiz doğrultusunda var olan tanı ve tıbbı müdahalelerin bir kısmının iş yeri hekimliği veya aile hekimliği merkezlerinde yapılabileceği tespit edilmiştir, bu doğrultuda hareket etmek acil servislerin iş yükünü azaltabilir.

Anahtar Kelimeler: İş kazası, acil servis, travma.

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Introduction

Surveillance of occupational injuries is necessary to guide educational and regulatory interventions, provide information for the development of new low-risk technologies, identify research priorities, and monitor progress towards injury reduction goals. Among various potential injuries, occupational injuries hold global significance (1).

Injuries arise from an imbalance between a wide range of biomechanical, physical, and psychological demands inherent in adverse working conditions and workers' ability to cope with them (2).

Work-related injuries and illnesses impose a significant human and economic burden on workers, employers, and society (3). The estimated economic loss caused by occupational injuries and illnesses is equivalent to %4 of the world's gross domestic product (4).

The International Labour Organization estimates that approximately 340 million occupational accidents occur worldwide each year, with an annual estimate of about 2.3 million fatalities due to occupational accidents and work-related diseases (5). According to data from the Turkish Social Security Institution (SSI), in the year 2022, 465.769 (79.1%) were male out of a total of 588.823 individuals who experienced occupational accidents, and a total of 1.517 individuals, of which 1.478 (97.4%) were male, were reported deceased (6).

Accurate public health surveillance provides estimates of the magnitude of the problem, identifies high-risk groups, guides prevention strategies, and assesses their effectiveness, making it an important component in reducing the burden of occupational injuries and illnesses (7).

The greatest cost of occupational injuries is incurred in developing countries, where the workforce is most densely concentrated. In these nations, many individuals work in hazardous industries such as agriculture, logging, and mining, where safety standards or regulations may be lacking (8).

Since most occupational injury cases present to the emergency department, research conducted in emergency departments is important for elucidating occupational injuries (9).

While eliminating occupational accidents may be challenging, many workplace accidents can be prevented with simple measures (10).

Based on the hypothesis that many existing workplace accidents are simple in nature, our aim was to reduce the workload of the emergency department by elucidating the mechanisms of occupational accidents and identifying the necessity for medical intervention. Additionally, we aimed to investigate injury mechanisms according to occupational sectors.

Material and Methods

The study was retrospectively designed by examining cases of occupational accidents presenting to the adult emergency department of Kanuni Training and Research Hospital, affiliated with the Health Sciences University, Trabzon School of Medicine. Ethical approval for the study was obtained from the relevant university ethics committee (Ethics No: 2024/88). Patients who presented to the emergency department due to occupational accidents and had an accident report filed during the 24-month study period were included. Patients under 18 years of age, those who refused emergency department treatment, and those with incomplete data in the records were considered exclusion criteria. Information regarding the type, mechanism, and organ system affected by the injury, as well as the feasibility of treatment with simple medical intervention, was obtained from the occupational accident reports (11). The need for imaging for diagnosis, as well as the treatment process and outcome of hospitalized patients, was obtained from the hospital automation system.

Statistical Anaylsis

All data obtained from the study were recorded in a Microsoft Excel file and analyzed. All analyses were conducted using Jamovi v.1.6 statistical software (The Jamovi Project (2021) Computer Software, version 1.6. Sidney, Australia). Categorical data were represented in the form of frequency (n) and corresponding percentage values. Normally distributed continuous variable data were defined as mean plus standard deviation (SD), and non-normally distributed data were defined as median and interquartile range (IQR). The assessment of distributional normality was conducted employing the Shapiro-Wilk test. Student's t-test was applied for comparing continuous variables with normal distribution, and Mann-Whitney U test was applied for variables with non-normal distribution. The chi-square test was employed to assess the association between categorical variables across different groups.

Results

Within the scope of our study, there were 983 patient admissions to the emergency department due to occupational injuries between January 1-2022, and December 31-2023. During the same period, a total of 268.130 patient admissions were recorded in our emergency department. Due to missing data in the records of 96 patients with documented occupational accident reports, they could not be included in the study. Additionally, occupational comparisons could not be made in the statistical analysis as only the professional information of 34 patients from various occupational sectors could be accessed.

Among the 887 patients who presented to the emergency department due to occupational accidents meeting the inclusion criteria, 717 (80.8%) were male, and 170 (19.2%) were female. The median age of the patients was 34 (IQR 26-44). Imaging studies were not conducted for 277 (31.2%) patients, while 355 (40%) patients underwent only X-ray examinations, and 255 (28.8%) patients underwent other imaging methods. Treatment with simple medical intervention was sufficient for 663 (74.7%) patients. Hospitalization was required for treatment in 94 (10.6%) patients, and 69 (7.8%) patients underwent surgery for various reasons. Four (0.5%) patients died due to their injuries from occupational accidents. The demographic characteristics and clinical course of the patients are summarized in Table 1.

Characteristics	All patients (n=887)
Gender	
Male, n (%)	717 (80.8)
Female, n (%)	170 (19.2)
Age (years), median (IQR)	34 (26-44)
Imaging	
None, n (%)	277 (31.2)
X-ray, n (%)	355 (40.0)
CT or MRI, n (%)	255 (28.8)
Simple Medical Intervention, n (%)	663 (74.7)
Surgical Intervention, n (%)	69 (7.8)
Hospitalization, n (%)	94 (10.6)
Mortality, n (%)	4 (0.5)

IQR: *Interquartile Range (25p, 75p),* ***CT:*** *Computed tomography,* ***MRI:*** *Magnetic resonance imaging*

Table 1. The Patients' Demographic Data and Baseline Characteristics

When examining factors affecting mortality in patients injured in occupational accidents, neither age nor gender showed an association with mortality (p=1.0 for gender (p>0.05), Fisher's exact test; p=0.105 for age (p>0.05), Mann-Whitney U test). There was an association between injuries that could not be treated with simple medical intervention and mortality compared to injuries that could be treated with simple medical intervention (p=0.004, Fisher's exact test). Among the 69 (7.78%) patients who underwent surgery, two patients died, and among the 818 (92.2%) patients who did not undergo surgery, two patients also died, indicating an association between undergoing surgery and mortality (p=0.032, Fisher's exact test). Hospitalized patients had a higher mortality rate compared to non-hospitalized patients (p=0.001, Fisher's exact test). The statistical analysis of mortality is summarized in Table 2.

Among the most common injury mechanisms encountered by victims of occupational accidents, penetrating-shearing instrument injury (314, 35.4%), blunt trauma (314, 35.4%), and fall and sprain injuries (176, 19.8%) are the most frequent forms of injury. Significant associations were found between the type of injury mechanisms and the feasibility of treatment with simple medical intervention (p=0.001, chi-square test). Additionally, the trauma mechanisms were significant in terms of hospitalization for treatment (p=0.001, chi-square test). However, there was no significant result when questioning the trauma mechanisms regarding the need for surgery (p=0.322, chi-square test). Blunt traumas, with 97 cases of injuries unresolved by simple medical intervention, constituted the most common group requiring hospitalization, while falls and sprains were the most common group requiring hospitalization. Moreover, blunt traumas were the group with the highest surgical requirement.

In 206 cases (23.2%) of occupational accident cases presenting to the emergency department, no lesions were detected, and for the 201 patients in whom no lesions were detected, a decision was made for treatment with simple medical intervention. The three most common types of lesions encountered were incisions (307, 34.6%), abrasions and ecchymosis (183, 20.6%), and fractures (134, 15.1%). When analyzed according to the type of wound, significant associations were established between the types of injuries and the feasibility of treatment with simple medical intervention (p=0.001, chi-square test), the need for hospitalization (p=0.001, chi-square test), and the need for surgical treatment (p=0.001, chi-square test). Among the group of patients who could not be treated with simple medical intervention, fractures ranked first with 132 patients, of whom 56 required hospitalization and 37 required surgical treatment.

When considering the affected body regions of patients who experienced work-related injuries, the upper extremity (366, 41.3%), lower extremity (158, 17.8%), and head-neck and face regions (142, 16%) rank as the top three. Significant associations were established between the feasibility of treatment with simple medical intervention (p=0.001, chi-square test), the need for hospitalization (p=0.001, chi-square test), and the need for surgical treatment (p=0.025, chi-square test) when compared based on the affected body region. Of the 87 upper extremity injuries that could not be treated with simple medical intervention, the highest number of patients requiring hospitalization for treatment was 28. Upper extremity traumas also ranked first in the group of patients whose treatment was completed surgically, with 36 cases. The classification of the patient population according to the need for simple medical intervention, hospitalization, and surgical treatment, along with the statistical analysis, is summarized in Table 3.

Characteristics	All patients (N=887)	Mortality	Non-Mortality	p value
Gender				
Male, n (%)	717 (80.8)	4	713	1.000^
Female, n (%)	170 (19.2)	0	170	
Age (years), median (IQR)	34 (26-44)	44.5 (37.8-53.0)	34 (26.0-43.5)	0.105*
Simple medical intervention				
Yes, n (%)	663 (74.7)	0	663	**0.004^**
No, n (%)	224 (25.3)	4	220	
Surgical intervention				
Yes, n (%)	69 (7.78)	2	67	**0.032^**
No, n (%)	818 (92.2)	2	816	
Hospitalization				
Yes, n (%)	94 (10.6)	4	90	**0.001^**
No, n (%)	793 (89.4)	0	793	

IQR: *Interquartile range (25p, 75p),* ****:*** *Mann-Whitney U test,* ***^:*** *Fisher's exact test,*

Table 2. Statistical Analysis for Mortality

Characteristics	All patients (n=887)	SMI (n=663)	Non-SMI (n=224)	p*	Hospitalization (n=94)	Non-Hospitalization (n=793)	p*	SI (n=69)	Non-SI (n=818)	p*
Trauma Mechanism, n (%)										
Penetrating-shearing instrument injury	314 (35.4)	270	44		16	298		24	290	
Blunt trauma	314 (35.4)	217	97		34	280		26	288	
Falls and sprains	176 (19.8)	108	68		36	140		18	158	
Burning	23 (2.6)	18	5		2	21		0	23	
Inhaler accident	22 (2.5)	21	1	0.001	0	22	0.001	0	22	0.322
Weight lifting	18 (2.0)	16	2		0	18		0	18	
Electric shock	9 (1.0)	5	4		4	5		1	8	
Blast and pressure	6 (0.7)	4	2		2	4		0	6	
Chemical burns	5 (0.6)	4	1		0	5		0	5	
Wound Type, n (%)										
None	206 (23.2)	201	5		3	203		0	206	
Incision	307 (34.6)	265	42		15	292		20	287	
Abrasion and ecchymosis	183 (20,6)	168	15		7	176		4	179	
Fracture	134 (15.1)	2	132		56	78		37	97	
Hematoma	38 (4.3)	27	11	0.001	4	34	0.001	1	37	0.001
Extremity amputation	12 (1.4)	0	12		3	9		5	7	
Dislocation	4 (0.5)	0	4		3	1		2	2	
Intracranial hemorrhage	1 (0.1)	0	1		1	0		0	1	
Pneumothorax	1 (0.1)	0	1		1	0		0	1	
Pulmonary contusion	1 (0.1)	0	1		1	0		0	1	
Affected Organ or System, n (%)										
None	76 (8.5)	74	2		2	74		0	76	
Head, neck, and face	142 (16.0)	106	36		19	123		6	136	
Thorax	44 (5.0)	14	30		20	24		3	41	
Abdomen	24 (2.7)	13	11		5	19		2	22	
Vertebra	9 (1.0)	7	2	0.001	0	9	0.001	0	9	0.025
Upper extremity	366 (41.3)	279	87		28	338		36	330	
Lower extremity	158 (17.8)	110	48		19	139		21	137	
Eye	66 (7.5)	59	7		0	66		1	65	
Urogenital	2 (0.2)	1	1		1	1		0	2	

*IQR: Interquartile Range (25p, 75p), *: x^2 test, SMI: Simple medical intervention SI: Surgical intervention,*

Table 3. Statistical Analysis for Simple Medical İntervention, Hospitalization, Surgical Intervention

Discussion

In our study, 717 (80.2%) were male and 170 (19.8%) were female individuals, with a median age of 34 (IQR 26-44), were victims of occupational accidents. Similar numbers were reported in a study conducted at a tertiary hospital in Denizli province in 2012, where upon examining the distribution by gender, 13.6% (n=72) were female (86.4% (n=456) were male), with a mean age of 32.7±9.7 for the entire group (12). Additionally, a study published in 2018 showed that approximately 80% of occupational accidents involved male individuals, which is consistent with the results of our study (13). Our study supports the literature in indicating that occupational accidents are more commonly observed in males.

Penetrating-shearing tool injuries (35.4%), blunt trauma (35.4%), and fall and sprain injuries (19.8%) are common mechanisms of injury leading to admission to our emergency department. According to the study by A. Tadros et al., the most common mechanisms of injury are fall and crush injuries (13). Similarly, in a study conducted by Ruchi Bhandari et al., blunt trauma and injuries related to falls were also among the leading mechanisms of injury (14). The variation in results across different studies may be influenced by the diversity in regional occupational sectors.

Incisions (34.6%), abrasions and ecchymosis (20.6%), and fractures (15.1%) are commonly encountered types of lesions in our cases. In the study by Bhandari et al., sprains, lacerations, contusions, and fractures were also among the most frequent types of lesions, yielding similar results to our study (14).

According to our study, when considering body regions, injuries to the upper extremity (41.3%), lower extremity (17.8%), and head-neck and face regions (16%) rank as the top three. In the study by Hösükler et al., although with different proportions, the extremities and head-neck regions were among the most injured organ systems, with the upper extremity (56.9%) and head-neck (20.9%) regions being prominent (15).

In the study conducted at our tertiary hospital, 74.7% of occupational accident patients could be treated with simple medical interventions. Additionally, 31.2% of these patients did not even undergo imaging procedures. Given this, it is important for occupational accident victims to utilize primary care facilities or workplace health services before ER where the diagnosis and treatment of critical patients take precedence. This is crucial for reducing the increasing workload of healthcare professionals in emergency departments and enabling them to allocate their motivation and attention to more urgent cases.

Furthermore, out of 983 patient admissions, 96 were found to have missing data. More significantly, only 34 patients' occupational information could be accessed. Consequently, there is insufficient information about injury characteristics according to occupational types based on the identified geography. The accuracy of this data is crucial for increasing preventive measures that can be taken according to industries to prevent potential accidents and raise awareness among employees about accidents.

Conclusion

Our study supports the literature indicating that occupational accidents are observed more frequently in males. Penetrating-cutting tool injuries and blunt trauma are the main mechanisms of injury in workplace accidents. Cuts,

abrasions, bruises, and fractures are the types of lesions we commonly encounter. In our study, upper extremity, lower extremity, head, neck, and facial injuries were the most frequently encountered body regions in occupational accidents.

The registered total number of occupational accidents in Turkey, which was 430.985 in 2018, showed a rapid increase to 422.463 in 2019, 384.262 in 2020, 511.084 in 2021, and 588.823 in 2022 (6). Each year, the increase in the number of occupational accidents inevitably leads to an increase in the workload in the healthcare sector, along with an increase in societal loss of life and property. Particularly, having knowledge about regional industries such as agriculture and industrial activities will contribute to foreseeing trauma patients' conditions and shaping training activities aimed at enhancing the knowledge and skills of healthcare professionals

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

The Effect of Stroke Units on The Management of Ischemic Stroke Patients in the Emergency Department: A Retrospective 5-Year Study

Acil Serviste İskemik İnme Hastalarının Yönetimine İnme Ünitesinin Etkisi: 5 Yıllık Geriye Dönük Tarama

Cem Şimşek[1], Sedat Yanturalı[2], Dijan Tav Şimşek[1], Rıdvan Atilla[3]

ABSTRACT

Aim: Ischemic stroke is one of the leading causes of morbidity and mortality Worldwide. It is recommended to treat stroke patients in specialized care centers known as stroke units (SU). The aim of this study is to investigate the impact of the stroke unit on the treatment of stroke patients in the emergency department (ED).

Material and Methods: This retrospective observational study was performed in the emergency department of Dokuz Eylül University Faculty of Medicine Hospital. Patients aged 18 years and over with a diagnosis of ischemic stroke were included in the study. A comparison was made between the demographic characteristics, treatments given, length of stay in the emergency department and hospital, and mortality rates before and after the SU was introduced.

Results: A total of 1,546 patients were included in this study; 583 of the patients were admitted before the SU was established, and 963 were admitted after. The majority of stroke patients (56%) were male. The mean age of patients before the SU was 72±12.4 years and after SU it was 70±12.9 years. The highest number of admissions was observed in the 71-80 age group. The most common symptoms for hospital admission were weakness in arms and legs and dysarthria. Thrombolytic treatment was administered to 1.2% of ischemic stroke patients before the SU and 5.5% after the SU (p=0.00). The mean hospital length of stay was 10.7±8.3 days before the SU and 9.4±8.3 days after. Mortality was 8.6% before the SU and 6.7% after.

Conclusion: The establishment of the Stroke Unit (SU) resulted in an increased rate of thrombolytic treatment. In this study SU had no effect on mortality. Despite the increase in the number of patients, there was no change in the length of stay in the ED; however, hospital length of stay was shortened.

Keywords: Emergency department, stroke, stroke unit, ischemic stroke, thrombolytic treatment

ÖZ

Amaç: İskemik inme dünya genelinde önemli bir morbidite ve mortalite nedenidir. Tedavi sürecinin inme ünitesi olarak adlandırılan özelleşmiş bakım merkezlerinde yapılması önerilmektedir. Bu çalışmanın amacı, inme ünitesinin (İÜ) acil servisteki inme hastalarının tedavisine etkisini araştırmaktır.

Gereç ve Yöntemler: Bu retrospektif gözlemsel çalışma Dokuz Eylül Üniversitesi Tıp Fakültesi Hastanesi Acil Servisinde yapıldı. İskemik inme tanısı alan 18 yaş üstü hastalar çalışmaya dahil edildi. İnme ünitesi öncesi ve sonrası dönemde hastaların demografik özellikleri, verilen tedaviler, acil serviste ve hastanede kalış zamanı karşılaştırıldı.

Bulgular: Bu çalışmaya 1546 hasta dahil edildi. Hastaların 583'ü İÜ öncesi, 963 tanesi İÜ sonrası dönemde hastaneye kabul edildi. İnme geçiren hastaların çoğunluğu (%56) erkekti. İÜ açılmadan önceki hastaların yaş ortalaması 72±12,4 yaş; İÜ açıldıktan sonraki yaş ortalaması 70±12,9 yaş bulundu. En çok başvurunun 71-80 yaş grubunda olduğu görüldü. Hastaların hastaneye başvuru nedenleri arasında en sık kol ve bacakta güç kaybı ve konuşma bozukluğu yer almaktadır. İÜ öncesi iskemik inme hastalarının %1,2'sine, İÜ sonrası ise %5,5'ine trombolitik tedavi verilmişti. (p=0,00). İÜ öncesi ve sonrası dönemde hastanede kalış süreleri sırasıyla 10,7 ±8,3 gün ve 9,4±8,3 gün bulunmuştur. Mortalite İÜ öncesi dönemde %8,6 iken İÜ sonrası dönemde %6,7 bulundu.

Sonuç: İÜ açılmasıyla trombolitik tedavi verilme oranında artış olmuştur. İÜ'nin mortaliteye üzerine etkisi olmamıştır. Hasta sayısının artmasına rağmen hastaların acil serviste kalış süresinde değişiklik olmamış fakat hastanede kalış süresi kısalmıştır.

Anahtar Kelimeler: Acil servis, inme, inme ünitesi, iskemik inme, trombolitik tedavi

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Introduction

According to the 2022 Global Stroke Fact Sheet by the World Stroke Organization (WSO), approximately 12.2 million new stroke cases occur worldwide yearly. Of these, 7.6 million (62%) are ischemic strokes, resulting in 3.3 million stroke-related deaths annually (1). Stroke is the second leading cause of death and the third leading cause of disability globally. In Türkiye, as per the 2019 World Health Organization (WHO) report, stroke is the second most common cause of death among women and the third among men (2). In 2017 alone, 38,099 deaths in Türkiye were attributed to stroke (3).

The WHO defines stroke as the interruption of blood flow to the brain, typically caused by the rupture or blockage of blood vessels (4). The primary goal in the treatment of ischemic stroke is to eliminate the clot causing the stroke. Different treatment options, including thrombolytic, anticoagulants, antiplatelet therapy, and mechanical thrombectomy, are available (5). Thrombolitic treatment is an effective option for ischemic stroke. Intravenous recombinant tissue plasminogen activator (tPA) was approved by the United States (US) Food and Drug Administration (FDA) for the treatment of ischemic stroke in 1996(5). In Türkiye, rtPA began to be administered following its approval in 2006. Thrombolytic therapy, which requires close monitoring and carries a risk of serious complications, dedicated stroke units (SU) are necessary for its use (5). The concept of specialized SU was first proposed in the 1950s, and studies demonstrating their effectiveness in stroke care began to emerge in the 1980s (6,7). A landmark 1991 study comparing general intensive care units (ICUs) to SUs found that stroke patients benefitted more from care in SU (8). Further research comparing general and specialized ICU services revealed that patients receiving care in SUs experienced reduced mortality both during their ICU stay and in the following 18 months (9,10). Numerous meta-analyses and reviews have since confirmed that SU reduce mortality, shorten hospital stays, and improve recovery outcomes for ischemic stroke patients (10,11).

Stroke units developed earlier in other parts of the world, and their implementation in Türkiye occurred later. After the approval of rtPA in Türkiye, a SU was established in 2007 within the Neurology Clinic of Dokuz Eylul University.

The aim of this study is to assess the impact of the Stroke Unit at Dokuz Eylul University Facult of Medicine on the management of stroke patients in the ED.

Material and Methods

In this study, patients admitted to the Emergency Department of Dokuz Eylül University Hospital with a diagnosis of ischemic stroke and hospitalized in neurology, stroke unit, or intensive care unit were included. Ethical approval date and number are: Dokuz Eylul University Hospital, Izmir, 13.01.2011; 2011/01-08. A retrospective screening method was used for a total of 5 years. 19.05.2007, the date of admission of the first patient admitted to the ED as the opening of the Stroke Unit was taken as the midpoint, data was collected 2.5 years before and 2.5 years after this date. For this purpose, patients were admitted to the ED between 01.01.2005 and 31.12.2009 and were hospitalized with a diagnosis of ischemic stroke were collected. Patients admitted to the ED with ischemic stroke between 01.01.2005 and 18.05.2007 were classified as the "before SU" group; whereas patients admitted between 19.05.2007 and 31.12.2009 were classified as the "after SU" group. Hospital information of both groups of patients was retrospectively obtained from patients electronic and physical archive files. Patients' age, gender, presenting complaint, treatments given, length of stay in the emergency department, length of hospitalization, and outcome information were recorded on previously created forms. The recorded data were divided into before-SU and after-SU periods, those periods were compared. Length of stay in the emergency department was the primary outcome, with length of hospital stay, thrombolytic treatment rate and mortality were secondary outcomes.

Inclusion criteria:

i) Over 18 years old

ii) Patients admitted to the emergency department with ischemic stroke (based on diffusion-weighted MRI) between 01.01.2005 and 31.12.2009

Exclusion criteria:

i) No evidence of ischemic stroke on diffusion-weighted MR imaging,

ii) Those with missing data in their file were excluded from the study.

Statistical Analysis

The SPSS 15.0 Evaluation version was used for statistical calculations. Descriptive statistics were given as numbers and percentages for categorical variables and mean, standard deviation, median, minimum, and maximum for numerical variables. Continuous variables were compared using Student's t-test for normally distributed variables and categorical variables were compared using Chi-square (X^2) test and $p < 0.05$ was considered statistically significant.

Results

In this study a total of 1546 patients were admitted to the hospital with diagnosis of ischemic stroke. Of these, 583 (37.7%) were admitted before SU was established and 963 (62.3%) were admitted after. Of all patients diagnosed with ischemic stroke, 56% (n=867) were male and 44% (n=679) were female. There was no significant difference between groups in terms of gender before and after the establishment of the SU. 57.1% (333) males and 42.9% (250) females were admitted before SU, and 55.5% (534) males and 44.5% (429) females were admitted after SU; p=0.53). The mean age of ischemic stroke patients before and after the SU was 72±12.4 years (range: 31–103 years) and 70±12.9 years (range: 22–106 years), respectively. There was no difference in mean age between the two groups(p=0.32). The highest number of patients are in the 71-80-year age group, and there is no difference between the before and after SU groups (Figure 1).

The majority of symptoms related to ischemic stroke was associated with motor skills. The most common symptoms were limb weakness and speech impairment. The most frequent sensory symptoms were imbalance and loss of sensation. The most prevalent cognitive symptoms were altered consciousness, nausea, and vomiting. (Table 1) The distribution of symptoms and clinical findings remained similar before and after establishing the Stroke Unit (Figures 2, 3, 4).

Pathologic Findings/Complaints	Before SU, n (%)	After SU, n (%)
Motor Signs	370 (64.4)	659 (68.9)
Weakness in the arm	33 (5.7)	46 (4.8)
Weakness in the leg	14 (2.4)	21 (2.2)
Weakness in both arm and leg	143 (24.5)	287 (29.8)
Inability to walk	3 (0.5)	2 (0.2)
Inability to swallow	1 (0.2)	0 (0.0)
Facial asymmetry	31 (5.3)	48 (5.0)
Dysarthria, motor aphasia	133 (22.8)	235 (24.4)
Loss of vision, diplopia	12 (2.1)	20 (2.1)
Sensory signs	114 (19.8)	177 (18.5)
Numbness, loss of sensation	32 (5.5)	65 (6.7)
Aphasia	16 (2.7)	15 (1.6)
Dizziness, loss of balance	66 (11.3)	97 (10.1)
Cognitive signs	91 (15.8)	121 (12.6)
Alteration of conscious	69 (11.8)	93 (9.7)
Amnesia	1 (0.2)	0 (0.0)
Somnolence	1 (0.2)	3 (0.3)
Nausea, vomiting	12 (2.1)	13 (1.3)
Seizure	1 (0.2)	6 (0.6)
Arrest	0 (0.0)	1 (0.1)
General condition disorder	5 (0.9)	2 (0.2)
Syncope	2 (0.3)	3 (0.3)

Table 1. Clinical Symptoms
SU: Stroke Unit

Overall, 26.3% (403) of ischemic stroke patients were admitted to the hospital within the first three hours. Of these patients, 66.1% (1030) exhibited motor symptoms, 20.4% (316) presented with sensory symptoms, and 12.1% (187) with cognitive symptoms. Among those with motor symptoms who presented within three hours, 41.6% had limb weakness, and 36.8% had speech impairment. Of those presenting with sensory findings in the first three hours, 50.8% had dizziness and imbalance, while 29.8% experienced sensory loss. Among patients with cognitive symptoms presenting within the first three hours, 82.8% exhibited altered consciousness.

In our study, 90.8% (1393) of ischemic stroke patients received antiplatelet therapy, 5.3% (82) received anticoagulant treatment, and 3.9% (60) received thrombolytic therapy. The administration of thrombolytic therapy increased significantly after SU. Before the SU was established 1.2% (7) of ischemic stroke patients received thrombolytic therapy whereas it raised to 5.5% (53) after SU. The increase in this rate was found to be statistically significant ($\chi 2=21.352$, $p=0.00$) (Figure 5).

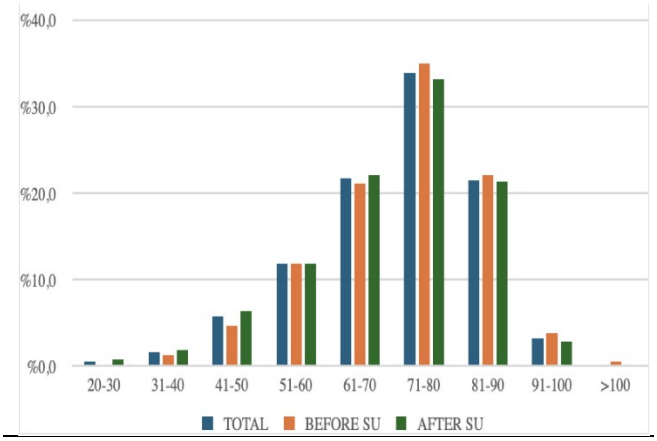

Figure 1. Ischemic stroke percentage distribution by age group

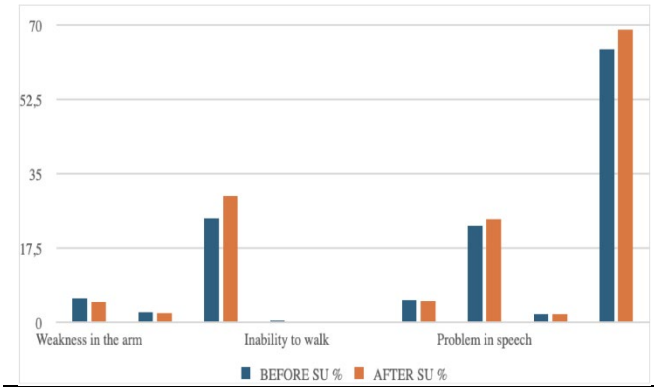

Figure 2. Motor signs before SU and after. SU:SU: stroke unit

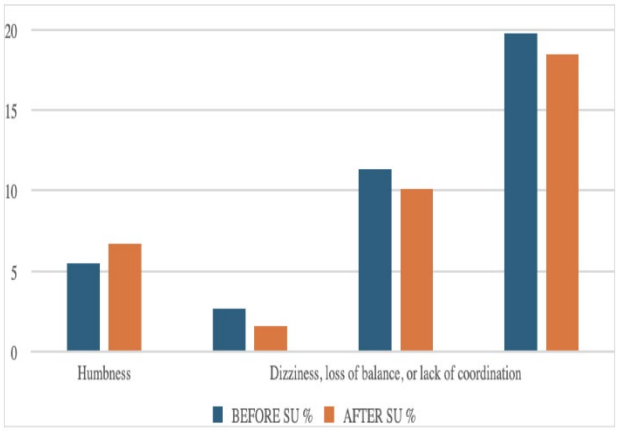

Figure 3. Sensorial signs before SU and after SU. SU: stroke unit

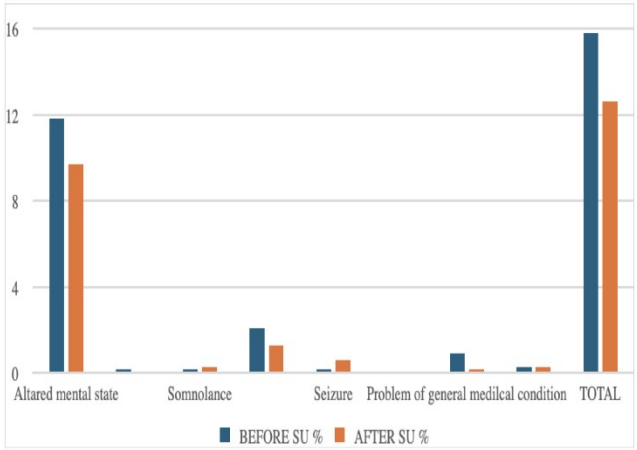

Figure 4. Cognitive signs before SU and after SU. SU: Stroke Unit

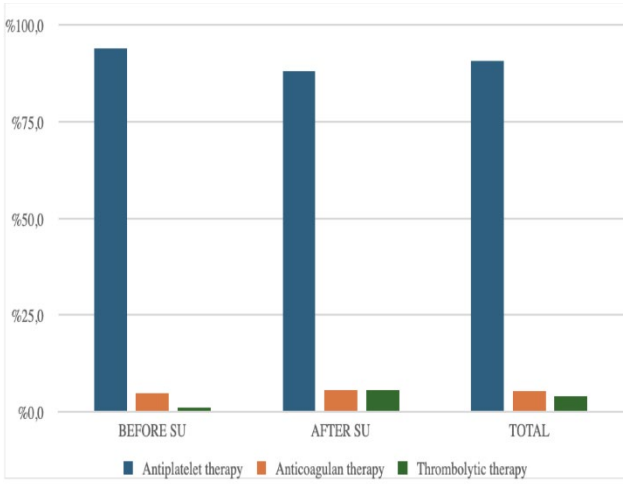

Figure 5. Treatment Before SU and After SU. SU: stroke unit

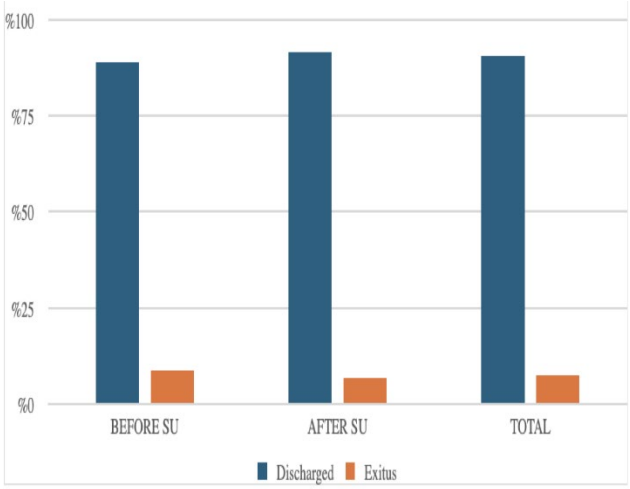

Figure 6. Before SU and after SU, hospital death and discharge rates. SU: stroke unit

Ischemic stroke patients stayed in the ED for a mean of 15.7±20.6 hours (min: 0.3; max: 360 hours). ED length of stay is 15.6±22.7 hours (min: 0.3; max: 360 hours) before SU, 15.7±19.2 hours (min: 0.7; max: 240 hours) after SU, and there was no statistical difference (p=0.93). The mean length of stay in the ED was 15.7±18.8 hours for patients receiving antiaggregant therapy, 20.5±42.5 hours for anticoagulant therapy, and 10.8±12.5 hours for thrombolytic therapy. The mean length of stay in the ED of patients receiving thrombolytics was statistically shorter than that of patients receiving anticoagulant therapy (p=0.03). The mean length of stay in the hospital for patients receiving antiplatelet therapy, anticoagulant therapy, and thrombolytic therapy was 9.8±8.2 days, 11.3±10.2 days, and 8.5±6.3 days, respectively. The differences between treatment modality and length of stay were not statistically significant (p=0.26). The mean hospital stay of the patients before SU was 10.7±8.3 days and 9.4±8.3 days after SU. The length of stay in the hospital was significantly shorter after SU (p=0.00).

It was determined that 7.4% (115) of the patients died in the hospital and 90.6% (1431) were discharged or transferred from the hospital. The mortality rate was 8.6% (50) before SU and 6.7% (65) after. There was no statistical difference between mortality rates ($\chi 2=1.71$, p=0.19; OR:1.29 RR:1.27) and discharge rates before and after SU (χ 2=0.35, p=0.55) (Figure 6).

Discussion

Many studies have shown that SUs have positive effects on the treatment of ischemic stroke patients, the degree of dependency after discharge, and the cost of stroke (6,10) One of these specialized stroke units was established in May 2007 within the Department of Neurology at Dokuz Eylul University Hospital.

In our study, patients who applied to the Dokuz Eylül University Emergency Department and were diagnosed with ischemic stroke between January 2005 and December 2009 were retrospectively examined. It was determined that 0.6% of the patients were diagnosed with ischemic stroke and were admitted to the neurology department, intensive care unit or stroke unit. A similar rate of ischemic stroke was diagnosed and treated in the before and after SU periods.

The mean age of patients admitted due to stroke was 71.2±12.7 years in our study. There was no difference between the mean age of patients who had a stroke before and after SU. It was observed that most of the patients with ischemic stroke were between the ages of 60-90 years, in which risk factors for ischemic stroke are common. The mean age was 62 years in Kumral et al., 67.2 years in Bousser et al., and 73.2 years in Bornstein et al (12-14). In our study, the highest number of patients is in the 70-80 age group. Bousser and Hennerici et al. observed that the stroke frequency was concentrated in the age range of 65-75 years, and the results were similar to those of our study (13,14). The frequency of ischemic stroke increases with advancing age.

Although gender has not been shown to be a risk factor in ischemic stroke, in our study, men (56%) were more common than women (44%) in patients with ischemic stroke. Although Lloyd-Jones et al. (15), Rey et al. (16), and Bousser et al. (14), reached similar results to our study. However, there are also meta-analyses showing that ischemic stroke is more common in women (17). The different results obtained in the studies suggest that gender is not a risk factor for ischemic stroke.

Ischemic stroke presents with different symptoms and signs depending on the affected area. In our study, the main symptoms in patients admitted and diagnosed with ischemic stroke were loss of strength in arms and legs, speech impairment, altered consciousness, nonsensical speech, seizures, and syncope. (Table 1) As identified by Kim et al. (18), motor symptoms and speech disorders are among the key indicators of neurological impairment. Similarly, Yanagida et al. (19) highlighted the presence of hemiplegia and disartria, while Revathi et al. (20) emphasised the significance of hemiparesis, dysarthria, and dizziness as primary symptoms leading to hospital admission. Although ischemic stroke causes many different symptoms, we thought that patients are admitted to hospital primarily because of symptoms that affect their daily life, such as motor findings and speech disorders.

Approximately 25% of patients were admitted to the hospital within the first three hours. Admission in the first 3 hours, which is essential for the effectiveness of treatment, varies between 29% and 50% (21,22). It was observed that

the rate of early admission to hospitals in our country is higher than the studies in other countries. Keskin et al. (21) found that 50% of the patients, as well as Korkmaz et al. (22) found that 44% of patients were admitted to the hospital within the first 3 hours. In our study, the number of admissions to ED within the first three hours after SU increased by approximately 24% compared to the before SU period, but still, 2/3 of the patients present late and lose the chance of thrombolytic treatment. This first 3-hour period has been extended even further, and although more effective methods such as embolectomy are among the options, access to this treatment is not accessible in all regions across the country.

Antiaggregant therapy was the most commonly used treatment option for ischemic stroke, followed by anticoagulant and thrombolytic therapy. Only 60 of the patients in our study received thrombolytic therapy. Seven (11.7%) patients received thrombolytic therapy before SU, but this increased to 53 (88.3%) after SU. Thrombolytic therapy was administered to 19.3% of patients who came within the first 3 hours. Barber et al. (23) found the admission rate within the first three hours to be 27% and the thrombolytic administration rate to be 4.7%. In our hospital, the number of patients receiving thrombolytic therapy after SU increased approximately eightfold compared to before SU. Lattimore et al. (24) found similar results. The number of patients receiving thrombolytic therapy increased significantly with the opening of the SU, as expected, and this is supporting existing evidence for opening new SU centers.

The mean length of stay of ischemic stroke patients in the ED was 15.7±20.6 hours. No significant change was observed in the length of stay in the ED before and after SU. In addition, the length of stay in the ED was significantly shorter in patients receiving thrombolytic therapy. It would be appropriate to think that the reason for the lack of difference in the mean waiting time before and after the SU period is the increasing number of patients and limited bed capacity. The number of ischemic stroke patients increased approximately two-fold in the after SU period. Hospital length of stay was significantly shorter in the after-SU period; however, it had no effect on ED length of stay.

Limitations

The limitations of our study included the inability to conduct direct observations regarding the patients' medical history, presenting complaints, and physical examinations due to the retrospective nature of the study. Additionally, the changes in the patients' disability levels following their admission to the stroke unit could not be evaluated. Furthermore, the increase in the number of patients admitted to the hospital due to systemic changes in patient admission policies coincided with the period when the stroke unit was opened, which resulted in an increased number of patients being evaluated for the effectiveness of the stroke unit in the emergency department and throughout the hospital.

Conclusion

Following the establishment of the SU at Dokuz Eylul University Hospital, the rate of thrombolytic treatment increased, however, SU had no effect on mortality. Despite the increase in the number of ischemic stroke patients, there was no change in the length of stay in the ED; however, hospital length of stay was shorter.

Conflict of Interest: There is no conflict of interest between the authors in this study.

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Authors' Contribution: CS: Designing the study, data collection, interpretation of data, writing manuscript **SY**: Designing and planning study, performing critical revision **DTS**: Contributing to writing the manuscript, performing critical revision **RA**: Designing and planning study, performing critical revision.

All authors read and approved the final version of the manuscript

Ethical Approval: Ethical approval was obtained from the Dokuz Eylul University Hospital Clinical Research Ethics Committee before the study (Decision No. 2011/01-08).

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

Thiol/Disulfide Homeostasis and the Multinational Society for Supportive Care in Cancer Risk Score in Febrile Neutropenia

Febril Nötropenide Tiyol/Disülfid Homeostazı ve Kanserde Destekleyici Bakım için Çok Uluslu Derneği Risk Skoru

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ABSTRACT

Aim: This study aims to determine the use of thiol/disulphide homeostasis parameters together with procalcitonin (PCT), C-reactive protein (CRP) and Multinational Association for Supportive Care in Cancer (MASCC) risk scoring system for the prediction of prognosis and mortality in the patients with febrile neutropenia presenting to the emergency department.

Material and Methods: The study was carried out prospectively on 53 patients with febrile neutropenia and 51 healthy subjects presenting to the emergency department. Thiol/disulphide homeostasis parameters, which are oxidative stress markers, were measured through a new method developed by Erel and Neşelioğlu. PCT and CRP were also measured. Patients were grouped in to high-risk and low-risk groups in terms of prognosis and mortality through MASCC scores.

Results: Mean values of disulphide/native thiol, CRP and PCT were found to be significantly higher in the patients having febrile neutropenia (p=0.029, p<0.001 and p<0.001, respectively). Mean values of disulphide/native thiol, CRP and PCT were found to be significantly higher in the high-risk patients (p=0.038, p=0.004, and p=0.002, respectively).

Conclusion: The use of thiol/disulphide homeostasis parameters, PCT and CRP together with the MASCC system may be used for the prediction of the prognosis in the patients with febrile neutropenia.

Keywords: Febrile neutropenia, Thiol/disulphide homeostasis, oxidative stress, procalcitonin, c reactive protein

ÖZ

Amaç: Bu çalışmada, acil servise başvuran febril nötropeni hastalarında tiyol / disülfid homeostaz parametreleri ile prokalsitonin (PCT), C-reaktif protein (CRP) ve Kanserde Destekleyici Bakım için Çok Uluslu Derneği (MASCC) risk skorlama sisteminin birlikte prognoz ve mortalitenin öngörülmesi için birlikte kullanımını belirlemeyi amaçlanmaktadır.

Gereç ve Yöntem: Çalışma prospektif olarak febril nötropeni tanısı alan 53 hasta ve acil servise başvuran 51 sağlıklı birey üzerinde gerçekleştirildi. Oksidatif stres markerleri olan tiyol / disülfid homeostaz parametreleri Erel ve Neşelioğlu tarafından geliştirilen yeni bir yöntemle ölçüldü. PCT ve CRP de ölçüldü. Hastalar MASCC skorları ile prognoz ve mortalite açısından yüksek riskli ve düşük riskli gruplara ayrıldı.

Bulgular: Febril nötropeni tanısı olan hastalarda disülfid / nativ tiyol, CRP ve PCT değerlerinin anlamlı derecede yüksek olduğu bulundu (sırasıyla p = 0,029, p <0,001 ve p <0,001). Disülfid / nativ tiyol, CRP ve PCT değerlerinin yüksek riskli hastalarda anlamlı olarak yüksek olduğu bulundu (sırasıyla p = 0,038, p = 0,004 ve p = 0,002).

Sonuç: Febril nötropeni tanısı alan hastalarda prognozun öngörülmesi için tiyol / disülfid homeostaz parametreleri, PCT ve CRP'nin MASCC sistemi ile birlikte kullanılabilir.

Anahtar kelimeler: Febril nötropeni, Tiyol/disülfit homeostazı, oksidatif stres, prokalsitonin, c reaktif protein

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Giriş

Febril nötropeni, kemoterapinin iyi bilinen bir komplikasyonudur ve acil hekimleri tarafından sık görülen onkolojik acillerden biridir (1). Nötropeni hem kemoterapinin toksik etkisi hem de malign hücrelerin kemik iliğine yayılması sonucu hematopoetik hücrelerin büyümesini engellemesi sonucu gelişir. Nötrofiller, enfeksiyöz ajanlara karşı önemli bir rol oynar ve bu nedenle nötropenik hastalar enfeksiyonlara daha duyarlı hale gelir. İnvaziv enfeksiyonlar ve steril doku hasarına neden olan durumlar, inflamatuar mediatörler ve yüksek ateşle birlikte sistemik inflamasyonun artmasına yol açabilir. Malignitesi olan hastalarda yüksek ateş; enfeksiyonlar dışında malign hücre lizisi veya kemoterapinin neden olduğu mukozal hasardan kaynaklanabilir (2).

Febril nötropenide morbidite ve mortaliteye yol açan ciddi enfeksiyonları erken evrede teşhis ve tedavi etmek oldukça önemlidir. Öte yandan, bu hastalarda yetersiz klinik ve mikrobiyolojik veriler hastalığın teşhisinde ciddi sorunlara yol açar (3). Febril nötropenide basit inflamasyon parametreleri kullanılarak enfekte hastaları enfekte olmayanlardan ayırmak zor olduğundan, komplikasyonların erken tahmini için güvenilir biyolojik belirteçler gereklidir (2, 4). Bu amaçla belirli biyolojik belirteçler önerilmiş ve risk skorları ile ilişkileri incelenmiştir. Bu belirteçlerin doğruluk ve belirleyicilik değerleri genellikle küçük ölçekli, tek merkezli klinik ve laboratuvar çalışmalarıyla değerlendirilmiş ve farklı sonuçlar elde edilmiştir (5-7).

Oksidatif stres nedeniyle salınan mediatörlerin inflamasyonla birlikte birçok sistemik hastalığa neden olduğu bilinmektedir. Tiyol/disülfid homeostazı parametreleri oksidatif stresi tespit etmek için kullanılmış ve 1979'dan beri tek yönlü olarak ölçülmüştür. Erel ve Neselioğlu tarafından geliştirilen yeni bir yöntemle bu parametreler hem ayrı ayrı hem de toplu olarak ölçülebilmektedir (8). Ayrıca prokalsitonin (PCT) ve c reaktif protein (CRP); enfeksiyon ve inflamasyon sırasında salınan biyokimyasal belirteçlerdir. CRP bir akut faz reaktanıdır ve CRP seviyesi ölçümleri bakteriyel enfeksiyonların teşhisine yardımcı olmak için sıklıkla kullanılır. Viral, otoimmün, onkolojik hastalıklar ile lokal ve sınırlı enfeksiyonlar prokalsitoninde artışa neden olmadığından, bakteriyel hastalıkları bakteriyel olmayan hastalıklardan ayırmak için kullanılır (9, 10).

Araştırmacılar, febril nötropeni hastalarını sınıflandırmak ve oluşabilecek ciddi komplikasyonları ve riskleri öngörmek için yıllardır prognostik modeller geliştirmeye çalışmışlardır. 2000 yılında, risk sınıflandırması yapmak ve özellikle düşük riskli ayakta tedavi gören hastaları belirlemek amacıyla Multinational Association for Supportive Care in Cancer (MASCC) risk skorlaması yayımlandı. MASCC skoru bu tarihten itibaren en yaygın kullanılan risk skoru haline gelmiştir ve klinik uygulama kılavuzları tarafından tavsiye edilmektedir (11).

Bu çalışma, acil servise başvuran febril nötropeni hastalarında prognoz ve mortalite tahmini için MASCC risk skorlama sistemi ile birlikte tiyol/disülfid homeostazı parametreleri, PCT ve CRP'nin kullanımının yararlı olup olmadığını belirlemeyi amaçlamaktadır.

Gereç ve Yöntemler

Bu, prospektif ve tek merkezli gözlemsel bir çalışmadır. Çalışma, yıllık yaklaşık 150000 hasta başvurusu olan bir eğitim ve araştırma hastanesinin acil servisinde Temmuz-Aralık 2017 tarihleri arasında gerçekleştirilmiştir. Malignite nedeniyle son 7 gün içinde kemoterapi gören ve başvuru sırasında ateşi olan 18 yaş üstü hastalar çalışmaya dahil edildi. Enfeksiyon Hastalıkları Derneği Amerika kılavuzlarına göre, ateş, tek bir oral sıcaklık ölçümünün>38,3°C veya bir saat boyunca>38,0°C olan bir sıcaklık olarak tanımlanır. Çalışmamızda bu iki şarttan birini sağlayan hastalar ateşi var olarak kabul edildi. Çalışma süresince vücut sıcaklığı ölçümleri oral yoldan yapılmıştır. Nötropenisi olmayan hastalar çalışmadan çıkarıldı. Mutlak Nötrofil Sayısı (MNS) < 500 hücre/mm3 olan vakalar febril nötropeni kategorisine dâhil edildi. Oksidatif stres parametrelerini değiştirebilecek başka bir durumu olan hastalar (dejeneratif hastalık, diyabet mellitus, kardiyovasküler hastalık, akut böbrek yetmezliği, serebrovasküler hastalık ve malignite dışındaki kronik karaciğer hastalığı) çalışmadan çıkarıldı. Çalışma süresi boyunca acil servise başvuran bütün hastalar çalışmaya dâhil edildi. Kontrol grubu sağlıklı gönüllülerden oluşuyordu. Sağlıklı gönüllüler 18 yaşından büyük, gebelik veya emzirme döneminde olmayan, akut veya kronik hastalığı bulunmayan, kronik ilaç kullanım öyküsü olmayan ve çalışmaya katılmayı kabul eden kişiler arasından seçilmiştir. Etik onay, Ankara Yıldırım Beyazıt Üniversitesi klinik araştırmalar etik kurulundan alınmıştır (Tarih: 14/06/2017 Numara: 134). Hem hasta hem de kontrol grubu deneklerinden yazılı bilgilendirilmiş onam alınmıştır.

Araştırmacılar, katılımcıların demografik özelliklerini (yaş, cinsiyet), başvuru şikayetlerini, hastalık ve ilaç öyküsünü, acil servise başvuru sırasındaki belirtilerini ve semptomlarını standart çalışma formlarına kaydetmiştir.

Tüm hastalardan başvuru sırasında kan kültürü, tam kan sayımı, biyokimyasal parametreler, tiyol/disülfid homeostazı parametreleri (tiyol, disülfid, native tiyol, disülfid/ native tiyol, disülfid/toplam tiyol, native tiyol/toplam tiyol), CRP ve PCT seviyelerini analiz etmek için kan örnekleri alındı.

Tiyol/disülfid homeostazı parametrelerinin ölçümü için venöz kan örnekleri jelli serum ayırma tüplerinde topladıktan sonra, örnekleri on dakika boyunca 1500 rpm'de santrifüj edildi ve serumu ayrıldı. Serum örneklerini, tüm örneklerin toplanması tamamlanana kadar -80°C'de saklandı. Ardından serum örneklerini, örnek toplama işlemi tamamlandıktan sonra Ankara Atatürk Eğitim ve Araştırma Hastanesi biyokimya laboratuvarına gönderildi.

Native tiyol ve toplam tiyol yeni ve tamamen otomatik bir sistemle ölçüldü. Disülfid bağları önce sodyum borohidrit ile serbest fonksiyonel tiyol grupları oluşturmak üzere indirgendi. İndirgenmiş ve native tiyol grupları da dâhil olmak üzere tiyol grubunun tamamı, 5,5'-dithiobis-(2-nitrobenzoic) asit ile reaksiyondan sonra belirlendi. Toplam tiyol ile native tiyol arasındaki farkın yarısı dinamik disülfür miktarını vermektedir. Native ve toplam tiyollerin belirlenmesinden sonra disülfid miktarları, disülfid/toplam tiyol yüzde oranları, disülfid/native tiyol yüzde oranları ve native tiyol/toplam tiyol yüzde oranları hesaplanmıştır. (8). PCT (Roche Cobas 6000 Japonya) ve CRP (Siemens BNII, Almanya) de aynı laboratuvarda ölçüldü.

MASCC risk puanları (Tablo 1) hastaların başvurusu sırasında hesaplandı. MASCC puanı ≥ 21 olan hastalar düşük risk grubu olarak sınıflandırılırken, MASCC puanı < 21 olan hastalar yüksek risk grubu olarak kategorize edildi (11). Hasta grubu, kontrol grubu ile tiyol, disülfid, disülfid/native tiyol, disülfid/toplam tiyol, native tiyol/toplam tiyol, CRP ve PCT değerleri açısından karşılaştırıldı. Ayrıca, hasta grubu mortalite gelişen hastalar ve mortalite gelişmeyen hastalar, MASCC puanına göre yüksek riskli ve düşük riskli hastalar ve pozitif veya negatif kan kültürü olan hastalar olarak alt gruplara ayrıldı. Mortalite için 28 günlük mortalite verisi kullanıldı. 28 günlük mortalite, hastalar aranarak öğrenildi. Bu gruplar, tiyol, disülfid, disülfid/native tiyol, disülfid/toplam tiyol, native tiyol/toplam tiyol, CRP ve PCT değerleri açısından birbirleriyle karşılaştırıldı.

İstatistiksel analizler SPSS for Windows 10.0 paket programı ile yapıldı. Verilerin normallik analizleri Shapiro Wilk testi kullanılarak yapıldı. Normal dağılım gösteren veriler ortalama ± standart sapma olarak ifade edilmiş olup bu verilerde iki grup arası ortalama karşılaştırmaları Student-t testi kullanılarak yapıldı. Sonuçlar ortalama ± SD olarak sunuldu. Kategorik verilerde iki grup arası oran karşılaştırmaları için ise Pearson Ki-kare testi kullanıldı. P <0.05 istatistiksel olarak anlamlı kabul edildi. Örneklem seçimi için elverişlilik örneklemi kullanıldı.

MASCC† skor özellikleri	Ağırlık (puan)
Hastalık yükü: semptom yok veya hafif	5
Hipotansiyon yok	5
Kronik obstrüktif akciğer hastalığı yok	4
Solid tümör veya önceden mantar enfeksiyonu yok	4
Dehidratasyon yok	3
Hastalık yükü: orta derecede semptomlar	3
Ayakta tedavi durumu	3
Yaş < 60	2

Tablo 1. Kanserde Destekleyici Bakım için Çok Uluslu Derneği (MASCC) Skoru
† Kanserde Destekleyici Bakım için Çok Uluslu Derneği

Bulgular

Çalışmaya 53 hasta dâhil edildi, 11 hasta dışlama kriterlerine sahip olduğu için çalışmaya alınmadı. Hastaların 7'si diabetes mellitus, 3'ü kardiyovasküler hastalık ve 1'i serebrovasküler hastalık nedeni ile çalışmadan dışlanmıştır. Dâhil edilen 53 hastanın 32'si erkekti ve ortalama yaş 62.62±12.80 yıl idi. Kontrol grubunda 51 gönüllü vardı, bu 51 gönüllünün 23'ü erkekti ve ortalama yaş 60.25±6.86 yıl idi. Hasta grubu ile kontrol grubu arasında yaş ve cinsiyet açısından istatistiksel olarak anlamlı bir fark yoktu (sırasıyla p = 0.245 ve p = 0.169). Hasta grubunda native tiyol, toplam tiyol, disülfid, disülfid/native tiyol ve native tiyol/toplam tiyol değerleri kontrol grubuna göre istatiksel olarak anlamlı daha düşük çıkmıştır. Hasta grubu ve kontrol grubunun, tiyol/disülfid homeostazı, PCT ve CRP parametrelerinin karşılaştırmasına ait bulgular Tablo 2'de verilmiştir.

	Hasta grubu (n=53)	Kontrol grubu (n=51)	p değeri*
Native tiyol (µmol/L)	258,27 ± 81,36	429,13 ± 50,82	<0,001
Toplam tiyol (µmol/L)	289,82 ± 79,84	471,61 ± 53,33	0,001
Disülfit (µmol/L)	15,61 ± 9,31	21,29 ± 7,39	0,001
Disülfit/native tiyol	0,071 ± 0,065	0,050 ± 0,018	0,029
Disülfit/total tiyol	0,057 ± 0,041	0,045 ± 0,015	0,057
Native tiyol/total tiyol	0,884 ± 0,084	0,909 ± 0,030	0,046
CRP (mg/L)	144,58 ± 101,29	4,00 ± 1,28	<0,001
PCT (ng/ml)	12,82 ± 12,64	5,76 ± 2,33	<0,001

Tablo 2. Hasta grubu ile kontrol grubunun ortalama Tiyol/disülfid homeostaz parametreleri, CRP† ve PCT‡ düzeyleri açısından karşılaştırılması

*Student-t test

†: C Reaktif Protein

‡: Prokalsitonin

Mortalite olan hastalarda native tiyol, toplam tiyol, disülfid/native tiyol, disülfid/toplam tiyol ve native tiyol/toplam tiyol değerleri kontrol grubuna göre istatiksel olarak anlamlı daha düşük çıkmıştır. Mortalite gelişen ve gelişmeyen hastaların, tiyol/disülfid homeostazı parametreleri, PCT ve CRP parametrelerinin karşılaştırılması Tablo 3'te verilmiştir.

	Mortalite olan (n=11)	Mortalite olmayan (n=42)	p değeri*
Native tiyol (µmol/L)	224,71 ± 80,86	293,13 ± 67,00	0,002
Toplam tiyol (µmol/L)	261,04 ± 80,77	319,70 ± 68,20	0,006
Disülfit (µmol/L)	17,85 ± 10,44	13,29 ± 7,47	0,073
Disülfit/native thiol	0,095 ± 0,081	0,046 ± 0,029	0,007
Disülfit/total thiol	0,071 ± 0,050	0,042 ± 0,024	0,012
Native tiyol/Toplam tiyol	0,854 ± 0,101	0,915 ± 0,047	0,007
CRP (mg/L)	166,08 ± 115,20	122,26 ± 80,76	0,115
PCT (ng/ml)	20,31 ± 32,83	3,92 ± 8,96	0,018

Tablo 3. Mortalite olan ve mortalite olmayan hastalarda tiyol/disülfit homeostaz parametreleri, CRP† ve PCT‡ düzeylerinin karşılaştırılması

*Student-t test, †: C Reaktif Protein, ‡: Prokalsitonin.

MASCC puanına göre yüksek riskli hastalarda native tiyol, toplam tiyol, disülfid/native tiyol, değerleri düşük riskli hastalara göre istatiksel olarak anlamlı daha düşük çıkarken,

CRP ve PCT daha yüksek çıkmıştır. MASCC puanına göre yüksek ve düşük riskli hastaların, tiyol/disülfid homeostazı, PCT ve CRP parametrelerinin karşılaştırılması Tablo 4'te verilmiştir.

	Yüksek Risk(n=40)	Düşük Risk(n=13)	p değeri*
Native tiyol (µmol/L)	241,89 ± 77,23	308,68 ± 75,19	0,012
Toplam tiyol (µmol/L)	274,51 ± 75,76	336,93 ± 76,06	0,018
Disülfit (µmol/L)	16,09 ± 9,54	14,12 ± 8,73	0,497
Disülfit/native tiyol	0,079 ± 0,071	0,047 ± 0,033	0,038
Disülfit/total tiyol	0,062 ± 0,044	0,042 ± 0,028	0,070
Native tiyol /toplam tiyol	0,874 ± 0,090	0,915 ± 0,054	0,058
CRP (mg/L)	163,34 ± 104,08	86,85 ± 66,87	0,004
PCT (ng/ml)	15,95 ± 28,35	0,92 ± 1,78	0,002

Tablo 4. MASCC[§] skoruna göre Tiyol/disülfit homeostazı, CRP† ve PCT‡ parametrelerinin karşılaştırılması

*Student-t test, †: C Reactive Protein, ‡: Prokalcitonin, §: Kanserde Destekleyici Bakım için Çok Uluslu Derneği.

Pozitif kan kültürü sonucu çıkan hastalarda CRP ve PCT değerleri negatif kan kültürü sonucuna sahip hastalar göre istatiksel olarak anlamlı daha yüksek bulunmuştur. Pozitif ve negatif kan kültürü olan hastaların, tiyol/disülfid homeostazı, PCT ve CRP parametrelerinin karşılaştırılması Tablo 5'te verilmiştir.

Laboratuvar belirteçleri	Negatif kan kültürü n=17	Pozitif kan kültürü n=36	p değeri*
CRP (mg/L)	191,23 ± 110,52	122,55 ± 90,02	0,034
PCT (ng/ml)	27,80 ± 38,16	4,93 ± 11,02	0,027
Native tiyol (µmol/L)	245,39 ± 98,88	264,36 ± 72,42	0,486
Disülfit (µmol/L)	13,92 ± 8,40	16,41 ± 9,71	0,346
Toplam tiyol (µmol/L)	273,23 ± 94,60	297,65 ± 72,00	0,355
Disülfit/native tiyol	0,074 ± 0,081	0,070 ± 0,058	0,863
Disülfit/total tiyol	0,059 ± 0,047	0,056 ± 0,039	0,806
Native tiyol /toplam tiyol	0,881 ± 0,095	0,885 ± 0,080	0,880

Tablo 5. Kan kültürü pozitif ve negatif olan hastalarda tiyol/disülfit homeostazı, CRP† ve PCT‡ parametrelerinin karşılaştırılması

*Student-t test, †: C Reaktif Protein, ‡: Prokalsitonin.

Tartışma

İnflamasyonun ön planda olduğu hastalıklarda, oksidatif stres mediatörlerinin artışı ile ilişkili olarak proinflamatuar sitokinlerin üretiminde artış gözlenir. Tiyol/disülfid homeostazı da oksidatif stres belirteçlerinden biridir. Bozulmuş tiyol/disülfid dengesi, diyabet mellitus, kardiyovasküler hastalıklar, romatoid artrit, kronik böbrek yetmezliği, kanser, Alzheimer hastalığı ve Parkinson hastalığı gibi çoğu inflamatuar hastalığın oluşumunda rol oynar (12). PCT, inflamatuar ve enfeksiyöz vakaların tanısında kullanılan ve c hücrelerinden salınan spesifik bir belirteçtir (13). Yüksek PCT seviyeleri, enfeksiyonun şiddeti ile ilişkilidir ve şiddetli enfeksiyonlar, sepsis ve çoklu organ disfonksiyon sendromu (MODS) olan hastaların izlenmesinde de kullanılabilir. Yukarıda belirtilen tüm nedenlerden dolayı, PCT bakteriyel ve non-bakteriyel inflamasyonun ayırıcı tanısında güvenilir bir belirteç olarak kabul edilir (10). CRP, neredeyse tüm mikrobiyal enfeksiyonlar ve inflamatuar durumlarda sitokinler salındıktan sonra akut faz reaktanı olarak salgılanan bir biyokimyasal belirteçtir (9).

CRP ve PCT'nin inflamatuar belirteçler olarak yaygın kullanımına ve bazen tutarsız sonuçlarına rağmen, PCT, sistemik enfeksiyonları olan febril nötropenik hastalar üzerindeki son çalışmalarında tanısal ve prognostik bir belirteç olarak öne çıkmıştır (14). Wu ve arkadaşları tarafından yapılan bir meta-analiz, CRP ve PCT'nin febril nötropenik hastalarda şiddetli enfeksiyonların erken tanısı için kullanılma olasılığını değerlendirmiştir (15). PCT ve CRP'ye rağmen, enfeksiyonun şiddeti ve ölüm riski hala doğru bir şekilde tahmin edilememektedir. Bu nedenle, yeni belirteçler aranmaktadır (16).

Wenneras ve arkadaşları tarafından yapılan bir çalışmada, PCT ve CRP değerleri, kanıtlanmış veya kanıtlanmamış enfeksiyonlar ve şiddetli inflamasyonu olan tüm febril nötropenik hastalarda normal aralığın üzerinde bulunmuştur. En güçlü parametre olarak enfekte hastalarda PCT değerleri daha yüksek ölçülmüştür. CRP, enfekte hastalarda daha düşük oranda yüksek kaydedilmiştir (2). Benzer şekilde, Ruokonen ve arkadaşları tarafından yapılan çalışmada, enfeksiyonu olan veya bakteriyemili nötropenik hastalarda ölçülen PCT değerleri, kaynağı belirsiz düşük ateşi olan nötropenik hastalardan daha yüksek bulunmuştur (17). Çalışmamızın verileri de febril nötropenik hastalarda PCT ve CRP açısından benzer sonuçlar vermiştir. Çalışmamızda, febril nötropenili hastalarda disülfid/native tiyol oranı kontrol grubuna göre daha yüksek bulunurken, disülfid, native tiyol, toplam tiyol ve native tiyol/toplam tiyol değerleri daha düşük ölçülmüştür. İki grup arasında disülfid/toplam tiyol oranı açısından bir fark kaydedilmemiştir. Bulgularımız, tiyol/disülfid homeostazının sepsis olan hastalarda araştırıldığı bir çalışma ile uyumlu bulunmuştur (18).

Febril nötropeni hastalarında mortalite oranları literatürde %4 ile %24 arasında değişen oranlarda bulunmuştur (19-21). Çalışmamızdaki mortalite oranı yaklaşık %25 idi. Literatürde, Massaro ve arkadaşları, PCT'nin mortaliteyi öngörmede iyi bir belirteç olmadığını bildirmiştir (22), ancak onkolojik acillerde erken prognostik bir belirteç olarak kullanıldığında PCT'nin kısa süreli mortaliteyi gösterebileceğini belirten bazı çalışmalar da mevcuttur. Başka bir çalışmada, febril nötropenik hastalık, özellikle bakteriyemi nedeniyle ölen hastalarda CRP ile mortalite arasındaki ilişkinin, enfeksiyon dışı nedenlerle ölenlere göre daha güçlü olduğu bulunmuştur (23). Çalışmamızda, disülfid/native tiyol, disülfid/toplam tiyol ve PCT değerleri ölen hastalarda daha yüksek ölçülürken, native tiyol, toplam tiyol ve native tiyol/toplam tiyol ortalama değerleri aynı grupta daha düşük kaydedilmiştir. Ölen ve hayatta kalan hastalar arasında

disülfid ve CRP değerleri açısından fark bulunmamıştır. Ayar ve arkadaşlarının, sepsis olan çocuklarda yaptığı çalışmada, ölen ve sağ kalan hastalar arasında bu tiyol/disülfid homeostazı parametreleri açısından fark bulunamamıştır (24). PCT değerleri, mortaliteyi öngörme açısından literatürdeki çalışmalara uygundur. Yüksek disülfid/native tiyol, disülfid/toplam tiyol ve düşük native tiyol, toplam tiyol ve native tiyol/toplam tiyol değerleri, febril nötropenide mortalite tahmini için PCT ile birlikte değerli belirteçler olarak kullanılabilir.

Risk sınıflamaları, hangi hastaların ayakta tedavi göreceğine karar vermek ve febril nötropenik hastalarda ciddi komplikasyonları önlemek için kullanılır (25). MASCC skoru, febril nötropeninin yönetimi için birçok çalışmada güvenilir olduğu gösterilen ve klinik uygulamalarda yaygın olarak kullanılan, %71 duyarlılık ve %91 pozitif prediktif değere sahip, risk yönetimi temelli bir skorlama sistemidir. MASCC skoruna göre düşük riskli hastalarda erken taburculuk ve ayakta tedavi, yaşam kalitesini artırır ve nazokomiyal enfeksiyonları azaltır. MASCC skorunun düşük riskli hastaları belirlemek için kullanılabilecek maliyet etkin ve güvenli bir yöntem olduğu gösterilmiştir (26). Literatürde MASCC ile PCT ve CRP arasındaki ilişkiyi gösteren birçok çalışma olmasına rağmen, MASCC ile tiyol/disülfid homeostazı parametrelerini karşılaştıran bir çalışma bulunmamaktadır. Combariza ve arkadaşları, MASCC risk skoru ve ortalama CRP değerinin kombinasyonunun, nötropenik ateşi olan hastalarda ilk 5 gün içinde yüksek mortalite riskini başarılı bir şekilde teşhis ettiğini bildirmiştir (27). Uys ve arkadaşları, çalışmalarında PCT ve CRP değerlerinin MASCC risk skoruna göre düşük riskli ve yüksek riskli hastalarda risk sınıflaması ile anlamlı bir şekilde ilişkili olduğunu (en güçlü korelasyon) belirtmişlerdir (28). Ahn ve arkadaşları tarafından yapılan çalışmada, yüksek riskli MASCC skoru ve PCT yükselmesinin kombinasyonu, bakteriyemi ve septik şok tespiti için güçlü bir prediktör olarak bulunmuştur (29). Çalışmamızda, MASCC risk skoruna göre yüksek riskli hastalarda PCT ve CRP seviyeleri yüksek bulunmuş olup, literatürle uyumludur. Literatüre ek olarak, yüksek riskli hastalarda disülfid/native tiyol seviyeleri yüksek, native tiyol ve toplam tiyol seviyeleri ise düşük bulunmuştur. MASCC risk skoruna göre yüksek riskli ve düşük riskli hastalar arasında disülfid, disülfid/toplam tiyol ve native tiyol/toplam tiyol değerleri açısından fark bulunmamıştır. MASCC ve PCT ile CRP arasındaki korelasyonu araştıran farklı çalışmalar bulunmasına rağmen, Pubmed veri tabanında 'thiol' 'dissulphide' ve 'febrile neutropenia' anahtar kelimeleri kullanılarak yapılan literatür taramasında MASCC risk skoru ile tiyol/disülfid homeostazı arasındaki ilişkiyi gösteren bir araştırmaya ulaşılamamış olup çalışmamız bu konuda yapılan ilk çalışmadır.

Kan kültürlerinin nispeten düşük tanısal performansı nedeniyle febril nötropeninin nedenini belirlemek zordur. Viscoli ve arkadaşları tarafından yapılan bir çalışmada, febril nötropenide bakteriyemi sıklığı %29 olarak tespit edilmiştir (30). Literatürde, pozitif kan kültürü olan hastalarda yüksek PCT ve CRP seviyelerini gösteren çalışmalar da bulunmaktadır (31,32). Çalışmamızda, pozitif kültür sonuçlarına sahip hastalarda PCT ve CRP değerleri yüksek bulunmuş olup, literatürdeki verilerle benzerdir. Tiyol/disülfid homeostazı parametreleri ile kültür sonuçları arasında anlamlı bir ilişki bulunmamıştır.

Kısıtlılıklar

Çalışmamızın popülasyonu, özellikle düşük risk grubundaki hasta sayısı açısından diğer çalışmalardan daha küçüktür. Çalışmamızın daha fazla sayıda hasta ile tekrarlanması ve daha kesin sonuçlara ulaşılması mümkündür.

Sonuç

Yaptığımız literatür taramasına göre çalışmamız, febril nötropeni tanısı almış hastalarda tiyol/disülfid homeostazı parametreleri ile PCT ve CRP ve MASCC skorlama sistemi arasındaki ilişkiyi analiz eden ilk araştırmadır. Febril nötropeni hastalarının farklı prognostik gruplarında tiyol/disülfid homeostazı parametrelerinin anlamlı derecede farklı olduğunu gözlemledik ve ileri çalışmalarla bu markörlerin acil servise başvuran febril nötropeni hastalarının prognostik değerlendirilmesinde kullanılabileceğine inanıyoruz.

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

The Relationship Between CRP Levels and Hospitalization, Discharge, Readmission and Mortality Rates of Geriatric Patients Presenting to the Emergency Department

Acil Servise Başvuran Geriatrik Hastaların CRP Düzeyi ile Hastaneye Yatış, Taburculuk, Yeniden Başvuru, Mortalite Oranları Arasındaki İlişki

Yusuf Kantar [1], Necmi Baykan [2], Funda İpekten [3], Melih İmamoğlu [4]

ABSTRACT

Aim: This study aims to investigate the association between C-reactive protein (CRP) levels and outcomes such as hospitalization, discharge, readmission, and mortality in geriatric patients (aged 65 and over) presenting to the emergency department for non-traumatic reasons.

Material and Methods: CRP levels were retrospectively analyzed from blood tests taken during routine diagnostic and therapeutic processes for patients over 65 years of age who presented to the emergency department of a secondary state hospital for non-traumatic reasons between January 1, 2023, and June 30, 2023. Patients were categorized into five CRP level groups (5-50 mg/L, 51-100 mg/L, etc.) and evaluated for their medical history, complaints, hospitalization status, consultation requests, and mortality.

Results: Patients with CRP levels between 5-100 mg/L were more frequently diagnosed with non-infective causes, while CRP levels over 101 mg/L were predominantly associated with infective causes. A statistically significant association was found between elevated CRP levels and increased rates of hospitalization and mortality ($p < 0.001$).

Conclusion: A significant relationship was observed between CRP levels and the rates of consultation and hospitalization in geriatric patients admitted to the emergency department for non-traumatic reasons. Additionally, elevated CRP levels were strongly associated with increased mortality rates among hospitalized patients. The findings indicate that CRP levels exceeding 101 mg/L were associated with infectious diagnoses and poor outcomes, highlighting the need for close monitoring of these patients. CRP levels should be considered an integral part of the decision-making process in geriatric emergency patients.

Keywords: Geriatric patient, CRP levels, mortality, emergency department

ÖZ

Amaç: Bu çalışma, travmatik olmayan sebeplerle acil servise başvuran 65 yaş ve üzeri geriatrik hastalarda C-reaktif protein (CRP) düzeyleri ile hastaneye yatış, taburculuk, yeniden başvuru ve mortalite gibi sonuçlar arasındaki ilişkiyi araştırmayı amaçlamaktadır.

Gereç ve Yöntemler: 1 Ocak 2023 ile 30 Haziran 2023 tarihleri arasında, travmatik olmayan sebeplerle bir ikinci basamak devlet hastanesi acil servisine başvuran 65 yaş üstü hastalardan rutin tanı ve tedavi süreçleri sırasında alınan kan testlerinden elde edilen CRP düzeyleri retrospektif olarak analiz edilmiştir. Hastalar beş farklı CRP düzey grubuna (5-50 mg/L, 51-100 mg/L vb.) ayrılmış ve tıbbi geçmişleri, şikayetleri, hastaneye yatış durumları, konsültasyon talepleri ve mortalite sonuçları değerlendirilmiştir.

Bulgular: CRP düzeyleri 5-100 mg/L arasında olan hastalar daha sık enfektif olmayan nedenlerle tanı alırken, CRP düzeyleri 101 mg/L ve üzerinde olan hastaların çoğunlukla enfektif nedenlerle tanı aldığı gözlemlenmiştir. Yükselmiş CRP düzeyleri ile artmış hastaneye yatış ve mortalite oranları arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur ($p < 0,001$).

Sonuç: Travmatik olmayan sebeplerle acil servise başvuran geriatrik hastalarda CRP düzeyleri ile konsültasyon ve hastaneye yatış oranları arasında anlamlı bir ilişki gözlemlenmiştir. Ayrıca, yüksek CRP düzeylerinin hastaneye yatırılan hastalar arasında artan mortalite oranları ile güçlü bir şekilde ilişkili olduğu tespit edilmiştir. Bulgular, CRP düzeylerinin 101 mg/L'yi aşması durumunda enfektif tanılar ve olumsuz sonuçlarla ilişkili olduğunu göstermekte ve bu hastaların yakından izlenmesi gerektiğini vurgulamaktadır. CRP düzeyleri, geriatrik hastaların acil servislerdeki karar verme süreçlerinde önemli bir faktör olarak değerlendirilmelidir.

Anahtar Kelimeler: Geriatrik hasta, CRP düzeyleri, mortalite, acil servis

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Introduction

C-reactive protein (CRP) is produced in response to inflammation, with elevated levels indicating systemic involvement. As an acute-phase protein, CRP levels can rise rapidly after tissue damage or infection and gradually decline as the inflammatory process resolves (1). CRP is initially produced at sites of inflammation and infection in a monomeric form, referred to as monomeric CRP (mCRP). It is synthesized in many cells such as hepatocytes, smooth muscle cells, endothelium and macrophages. Although CRP is considered to be an indicator of infection and cardiac events, there is increasing evidence that it provides significant support to the host in inflammatory processes such as complement pathway, phagocytosis, apoptosis and release of cytokines (2).

CRP levels can rise significantly during inflammatory processes, including rheumatologic diseases, cardiovascular events, and infections (3). As an acute-phase protein, CRP levels increase rapidly in response to inflammation, with changes of at least 25% observed during such events. However, when the stimuli cease, CRP values gradually decrease over 8-18 hours, reflecting its half-life. In seemingly healthy individuals, several factors such as age, weight, gender, and smoking status can also influence CRP levels (4). As a non-specific marker of systemic inflammation, CRP is associated with higher mortality and worse clinical outcomes in elderly patients, particularly in vascular events like intracranial hemorrhage, ischemic stroke, and coronary disorders (5). As the inflammatory response evolves with aging, it is further complicated by the presence of multiple comorbidities and disabilities. This makes it challenging to assess the clinical significance of serum CRP levels in older adults with acute infections, especially considering age-related changes in immunity and cytokine production (6).

While CRP is a well-established marker of inflammation, its utility in predicting clinical outcomes such as hospitalization rates and mortality in geriatric patients presenting with non-traumatic conditions is under-explored. This study aims to address this gap by investigating the correlation between CRP levels and patient outcomes in this population. Previous studies have demonstrated the predictive value of CRP in infectious and non-infectious conditions in younger populations. However, its association with outcomes such as hospitalization and discharge decisions in geriatric patients, particularly in emergency settings, warrants further investigation. We hypothesize that elevated CRP levels in geriatric patients are significantly associated with increased hospitalization rates, readmission within seven days, and higher mortality.

Material and Methods

In this study, CRP levels from routine blood tests taken during the diagnosis and treatment of patients over 65 years old who presented to the emergency department (ED) of a secondary state hospital for non-traumatic reasons between January 1, 2023, and June 30, 2023, were retrospectively analyzed. CRP levels of the patients were compared with discharge, readmission, hospitalization and mortality as variables.

Using discharge summaries and ICD-10 codes obtained from the HIS system, patients were categorized into two main categories: infectious and non-infectious causes. Data were collected by recording the information accessed through the hospital HIS system on pre-prepared forms. Patients under 65 years of age or those presenting with traumatic injuries were excluded from the study. Additionally, patients with missing data or incomplete records in the hospital HIS system were also excluded.

CRP levels were categorized based on clinically relevant thresholds used in previous studies and were classified into five groups: 5-50, 51-100, 101-150, 151-200, and >200 mg/L. These categories were selected to capture significant variations in CRP levels commonly associated with different clinical outcomes in geriatric patients.

Ethical approval for the study was obtained from the Karadeniz Technical University Faculty of Medicine Ethics Committee (Approval Date: November 8, 2023; No: 2023/200). Due to the retrospective nature of the study, patient consent was waived. All patient data were anonymized to ensure confidentiality.

The sample size was determined using G Power analysis, with an effect size of 0.3, a significance level of 0.05, and a power of 80%. The analysis indicated that a minimum of 133 patients were required to achieve sufficient statistical power for the study. In the statistical analysis, the data were uploaded to SPSS 23.0 (Chicago, USA) and analyzed.

The conformity of the data to normal distribution was evaluated by histogram, Q-Q graphs and Shapiro-Wilk test. For normally distributed variables, mean and standard deviation were used as descriptive statistics. For non-normally distributed variables, median (1st quartile-3rd quartile) values were reported. In qualitative variables, numbers and percentages were used as descriptive statistics. The Pearson χ^2 test and Fisher's exact test were used to compare qualitative variables due to the categorical nature of the data. These tests were selected to determine statistically significant associations between CRP levels and clinical outcomes, such as hospitalization and mortality. Significance level was accepted as $p<0.05$.

Results

Patients over 65 years of age admitted to the emergency department for non-traumatic reasons within a 6-month period were retrospectively screened. A total of 647 patients were initially screened for the study. However, 142 patients were excluded due to being trauma patients or having missing data in hospital records. Ultimately, 505 patients were included in the final analysis. G Power analysis indicated that a minimum of 133 patients would be required to achieve sufficient statistical power, meaning that the analyses were conducted with a sample size well above the required threshold. Of the 505 patients included in the study, 52.7% were female, and the mean age was 77.6 years (Table 1). Hypertension (42.6%) and chronic obstructive pulmonary disease (20.2%) were the most common underlying conditions (Table 2). A significant proportion (29.3%) of patients had no chronic disease (Table 2), indicating a subgroup with fewer comorbidities but still at risk for elevated CRP levels.

When the complaints of the patients presenting to the ED were categorized, the most common complaints were shortness of breath (28.9%), abdominal pain (10.3%), and

nausea and vomiting (9.3%) (Table 2). Based on anamnesis, physical examination, and investigations, the clinical conditions of the patients were categorized into infective and non-infective causes. Diagnoses such as pneumonia, urinary tract infection, upper respiratory tract infection, and gastroenteritis were categorized as infective causes, while acute myocardial infarction, cerebrovascular events, and muscle and joint pain were included in the non-infective category. Accordingly, 41.6% of the cases were determined to have infective causes, and 58.4% were classified as non-infectious. It was observed that 55.8% of the patients in both groups had CRP levels between 5 and 50 mg/L (Table 3).

Female	266 (52.7)
Male	239 (47.3)
Mean Age	77.63±8.53
Vital Signs	
Body temperature (°C)	36.57±0.64
Pulse rate (/min)	93.13±20.02
Systolic blood pressure (mmHg)	132.97±30.73
Diastolic blood pressure (mmHg)	76.78±15.95
Saturation (%)	93.42±5.27
Blood Test Results	
Hemoglobin	12.33±2.06
White Blood Cell	9.1 (7.1-11.8)
Neutrophil	6.8 (4.7-9.4)
Platelet	210.0 (168.0-265.5)

Table 1. Demographic characteristics, vital signs and blood test results of the patients
Data are expressed as mean±standard deviation, median (1st quarter-3rd quarter) and n(%).

When CRP levels were compared according to the diagnostic categories, it was observed that patients with CRP levels between 5 and 100 mg/L were mostly diagnosed with non-infective conditions, while those with CRP levels between 101 and 200 mg/L, and those with levels above 200 mg/L, were more commonly diagnosed with infective causes. As CRP levels increased, the likelihood of receiving an infective diagnosis also increased, and this relationship was found to be statistically significant ($p < 0.001$) (Table 3).

Medical History	**n (%)**
Hypertension	215 (42.6)
Chronic Obstructive Pulmonary Disease	102 (20.2)
Coronary Artery Disease	102 (20.2)
Diabetes Mellitus	98 (19.4)
Alzheimer's	41 (8.1)
Chronic Renal Failure	30 (5.9)
Malignancy	24 (4.8)
Cerebrovascular Disease	18 (3.6)
Other	6 (1.1)
No Disease in Medical History	148 (29.3)
Complaints	**n (%)**
Shortness of breath	146 (28.9)
Abdominal Pain	52 (10.3)
Nausea Vomiting	47 (9.3)
Cough	31 (6.1)
Fatigue	25 (5.0)
Chest Pain	23 (4.6)
Change of Consciousness	23 (4.6)
Dizziness	22 (4.4)
Nutrition Disorder	18 (3.6)
Diarrhea	18 (3.6)
Headache	17 (3.4)
Muscle Joint Pain	16 (3.2)
Dysuria	15 (3.0)
High Fever	15 (3.0)
Speech Impairment	9 (1.8)
Sore Throat	9 (1.8)
Lack of strength	5 (1.0)
Syncope	4 (0.8)
Palpitations	4 (0.8)
Bleeding	5 (1.0)

Table 2. Medical history of the cases and complaints at presentation to the emergency department

CRP LEVEL (mg/L)	**5-50**	**51-100**	**101-150**	**151-200**	**>200**	***p***
Diagnosis	**n (%)**	**n (%)**	**n (%)**	**N (%)**	**n (%)**	
Infective causes (n=210)	77 (27.3)	47 (44.3)	34 (59.6)	31 (81.6)	21 (95.5)	
Non-infectious causes (n=295)	205 (72.7)	59 (55.7)	23 (40.4)	7 (18.4)	1 (4.5)	
Consultation Status						
Consultation requested (n=175)	59 (20.9)	35 (33.0)	32 (56.1)	29 (76.3)	20 (90.9)	<0.001
No consultation requested (n=330)	223 (79.1)	71 (67.0)	25 (43.9)	9 (23.7)	2 (9.1)	
Outcome of first presentation to the ED						
Discharged patients (n=374)	239 (84.8)	80 (75.5)	35 (61.4)	18 (47.4)	2 (9.1)	<0.001
Hospitalized patients (n=131)	43 (15.2)	26 (24.5)	22 (38.6)	20 (52.6)	20 (90.9)	
Finalization of patients hospitalized from the ED						
Discharged (n=118)	47 (39.8)	28 (23.7)	15 (12.7)	16 (13.6)	12 (10.2)	0.002
Mortality cases (n=24)	3 (12.5)	2 (8.3)	9 (37.5)	4 (16.7)	6 (25.0)	
Diagnostic categories of patients with mortality						
Infective causes (n=21)	1 (33.3)	2 (100.0)	8 (88.9)	4 (100.0)	6 (100.0)	0.061
Non-infectious causes (n=3)	2 (66.7)	0 (0.0)	1 (11.1)	0 (0.0)	0 (0.0)	

Table 3. Outcome status of hospitalized patients according to CRP levels and diagnoses of patients with mortality
CRP: C-Reactive Protein **ED:** Emergency Department

Of the cases included in the study, 54.9% were admitted to the ED as outpatients, and 43% were brought by ambulance. Only four patients (0.8%) were referred to the ED from another outpatient clinic within the hospital, and seven patients (1.4%) were referred from another hospital. A majority of the patients, 74.1% (374), were discharged from the ED, while 25.9% (131) were hospitalized at the first presentation. Among the hospitalized patients, 72.5% (95) were admitted to the ward, and 27.5% (36) were admitted to the intensive care unit (ICU). Of the discharged patients, 18.7% (70) were readmitted to the hospital within seven days. Among those readmitted, 24.3% (14) were hospitalized during the second admission.

When CRP levels were compared with hospitalization status, it was observed that higher CRP levels were associated with a greater likelihood of hospitalization. Specifically, only 15.2% of patients with CRP levels between 5 and 50 mg/L were hospitalized, while 90.9% of those with CRP levels above 200 mg/L required hospitalization. This association between higher CRP levels and increased hospitalization rates was found to be statistically significant ($p < 0.001$) (Table 3).

When post-hospitalization CRP values of patients who were hospitalized at the first admission were examined, it was observed that 63.4% did not show an increase in CRP. Similarly, when the CRP levels at the second admission of patients who were discharged from the ED and readmitted within 7 days were examined, 57.1% did not show an increase in CRP levels.

When the consultation status of the patients admitted to the ED was analyzed, it was found that consultation was requested for 175 patients. A statistically significant association was observed between higher CRP levels and an increased likelihood of consultation requests. Specifically, 90.9% of patients with CRP levels above 200 mg/L required consultation, compared to only 20.9% of patients with CRP levels between 5 and 50 mg/L ($p < 0.001$) (Table 3).

The average length of hospital stay for patients hospitalized for both infective and non-infective reasons was 7 days. Of these patients, 79.7% were discharged, 16.2% died, and 4.1% were transferred to another hospital.

The total number of patients who were hospitalized at the first presentation to the ED and after the second presentation within seven days was 142. Of these patients, 118 were discharged, while 24 died. Among the patients who died, 79.2% had CRP levels higher than 101 mg/L at the first presentation. In contrast, 63.5% of the discharged patients had CRP levels below 100 mg/L. This significant difference in CRP levels between discharged patients and those who died indicates a strong association between higher CRP levels and increased mortality ($p = 0.002$) (Table 3). Additionally, among the patients who died, 87.5% had infective causes, and 85.7% had CRP levels above 101 mg/L at the time of admission (Table 3).

Discussion

Elevated CRP levels were first identified in the 1980s. However, the lack of a control group in earlier studies limited the ability to make definitive judgments about the usefulness of CRP in detecting infections in elderly patients (7). Years later, Cox et al. demonstrated that elevated CRP levels on admission to a geriatric ward were significantly associated with a higher prevalence of clinically detected infections (8). Our study confirms the association between elevated CRP levels and poor clinical outcomes in geriatric patients presenting to the emergency department for non-traumatic reasons. These findings extend previous research by demonstrating that CRP levels not only correlate with infection severity but also serve as predictors of hospitalization and mortality in this population. These results suggest that routine CRP measurement could improve risk stratification and management decisions in the emergency setting.

Christ et al. found that the most common presenting complaint of geriatric patients admitted to the ED was altered consciousness (9). In contrast, our study identified shortness of breath as the most common presenting complaint, with altered consciousness ranking seventh. This difference may result from variations in patient populations across study centers.

Singler et al. reported a mean fever of 37.3°C in geriatric patients admitted to the hospital, while Simonetti et al. found normal fever measurements in 36% of pneumonia patients (10,11). In our study, the mean temperature was 36.5°C. This could be due to the inclusion of patients without infection and the slower febrile response in geriatric patients compared to younger populations.

In the study by Hogart et al., a CRP cutoff of 40 mg/L was suggested for geriatric patients suspected of having an infection (12). Sierra et al. proposed a cutoff of 80 mg/L in septic patients, irrespective of age (13). Wester et al. showed that CRP cutoffs varied depending on the microorganism involved (14). In our study, patients with CRP levels above 101 mg/L were more commonly diagnosed with infectious causes. Additionally, patients with CRP levels above 150 mg/L had a higher likelihood of hospitalization. These findings suggest that CRP levels exceeding 100 mg/L warrant careful evaluation for infection, while CRP levels above 150 mg/L should raise concerns about hospitalization. The higher cutoff levels observed in our study may be due to the inclusion of both hospitalized and discharged patients, unlike other studies that focused solely on hospitalized patients.

Short-term elevations in CRP have been linked to mortality in sepsis, as shown by Ryu et al., and in community-acquired pneumonia, as reported by Viasus et al. (15,16). In 1986, Cox et al. were the first to report that pneumonia patients who died had significantly higher CRP levels at the time of hospital admission compared to those who survived (8). Our study is consistent with these findings, showing that CRP levels above 100 mg/L are strongly associated with infectious diagnoses and increased mortality. However, unlike previous studies that focused exclusively on hospitalized patients, our research includes patients discharged from the ED. This provides a broader perspective on how CRP levels can be utilized in decision-making, particularly at the initial presentation in the emergency setting.

Limitations

This study has several limitations. First, its retrospective design may introduce selection bias and limit the ability to

infer causality. Additionally, the study was conducted at a single center over a limited time period, which may affect the generalizability of the findings. The exclusion of patients with incomplete data and the lack of detailed information about prescribed treatments at discharge may have influenced the results, particularly in relation to the causes of readmissions. The reasons for readmission were not explored in detail, and it is possible that different factors may have contributed to readmissions beyond CRP levels alone. Furthermore, the classification of patients into infectious and non-infectious groups was based on clinical diagnoses, which could introduce variability in classification. Other factors, such as comorbidities, vital signs, and medications prescribed at discharge, could have affected CRP levels at both initial and repeat presentations. This study did not perform ROC analysis to determine optimal CRP cutoff values, and the chosen thresholds were based on previous literature. More comprehensive prospective, multicenter studies, incorporating ROC analysis, are needed to validate these findings and establish more precise CRP thresholds for clinical decision-making in geriatric populations.

Conclusion

In conclusion, a statistically significant relationship was observed between CRP levels measured in patients over 65 years of age admitted to the emergency department for non-traumatic reasons and the rates of emergency department consultation and hospitalization. When mortality rates among hospitalized patients were assessed, a significant association was observed between increasing CRP levels and mortality. This study highlights the significant association between elevated CRP levels and key clinical outcomes, such as hospitalization, consultation rates, and mortality, in geriatric patients presenting to the emergency department for non-traumatic reasons. Additionally, CRP levels should be considered an integral part of the decision-making process in geriatric emergency patients. CRP values exceeding 150 mg/L should raise concern for potential infection and the need for hospitalization. Moreover, patients with CRP levels over 101 mg/L should be closely monitored for adverse outcomes, as they are at higher risk for readmission and mortality.

Given the strong correlation between CRP levels and adverse outcomes, incorporating CRP measurements into routine clinical assessments in the emergency department could significantly improve the identification of high-risk geriatric patients. This would allow for earlier interventions, better resource allocation, and potentially improved patient outcomes.

Future research should explore the underlying mechanisms by which CRP levels are elevated in non-infectious conditions and further evaluate their prognostic significance. Additionally, prospective studies evaluating the role of CRP in guiding therapeutic interventions, such as the use of antibiotics or other treatments in the emergency department, could further refine its clinical utility.

Overall, CRP remains a valuable biomarker in the management of geriatric patients, providing crucial insights into patient prognosis and aiding in the timely delivery of appropriate medical interventions. Its continued use in emergency settings can play a vital role in optimizing patient outcomes and improving the quality of care.

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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA MAKALESİ

Evaluating the Real-World Impact of Desk-Based Disaster Preparedness: A Case Study of the Covid-19 Pandemic

Masa Başı Afet Hazırlık Süreçlerinin Sahadaki Etkilerinin Değerlendirilmesi: COVID-19 Pandemisi Örneği

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ABSTRACT

Aim: The aim of this study is to evaluate the effectiveness of disaster management and preparedness activities based on the experience of compliance with the pandemic plan in a university hospital.

Material and Methods: The study was designed as a descriptive, cross-sectional investigation. A total of 645 employees from various professional groups working at a university hospital voluntarily participated in the study. The data were collected using a survey method. The Awareness Level Regarding the Pandemic Process Questionnaire was distributed via email. Descriptive statistics were calculated, and for the analysis of numerical variables, the "Student's t-test" was used if the variables were normally distributed, while the "Mann Whitney U test" was applied if the distribution was non-normal. For categorical variables, the "chi-square test" was employed.

Results: Survey completion rates were higher among nurses, while the lowest response rates were observed among other healthcare personnel. The proportion of employees with moderate or higher knowledge of the institution's pandemic plan was found to be 85%, whereas the rate of those with a high level of knowledge was 57%. Knowledge of the pandemic plan was significantly higher among women, those who received direct information, individuals informed by the infection control committee, participants in online training sessions, those aware of how to access procedure and guideline information, and employees who had previously participated in various in-hospital informational sessions or drills. Overall, it was observed that a majority of the survey respondents were well-acquainted with the hospital's pandemic plan.

Conclusion: Regular information sessions are crucial for updating knowledge and maintaining motivation. The disaster preparedness process, which is among the institutional priorities, will facilitate a comprehensive and effective response practice in real disaster situations when organized in accordance with its intended purpose.

Keywords: Disasters, disaster management, online training, hospital disaster preparedness

ÖZ

Amaç: Bu çalışmanın amacı, bir üniversite hastanesinde pandemi planına uyum deneyimine dayalı olarak afet yönetimi ve hazırlık faaliyetlerinin etkinliğini değerlendirmektir.

Gereç ve Yöntemler: Çalışma, tanımlayıcı ve kesitsel bir araştırma olarak tasarlanmıştır. Çalışmaya, üniversite hastanesinde çalışan çeşitli meslek gruplarından toplam 645 çalışan gönüllü olarak katılmıştır. Veriler, anket yöntemiyle toplanmıştır. Pandemi Süreci ile İlgili Farkındalık Düzeyi Anketi, e-posta yoluyla dağıtılmıştır. Tanımlayıcı istatistikler hesaplanmış, sayısal değişkenlerin analizinde, normal dağılım gösteren değişkenler için "Student's t-test" kullanılmış, normal dağılım göstermeyen değişkenler için ise "Mann Whitney U testi" uygulanmıştır. Kategorik değişkenler için ise "ki-kare testi" kullanılmıştır.

Bulgular: Anketi tamamlayanların oranı, hemşireler arasında daha yüksek bulunmuş, en düşük yanıt oranı ise diğer sağlık personelinde gözlemlenmiştir. Kurumun pandemi planı hakkında orta veya yüksek düzeyde bilgi sahibi olan çalışanların oranı %85 bulunurken, yüksek düzeyde bilgiye sahip olanların oranı %57 olmuştur. Pandemi planı bilgisi, kadınlar, doğrudan bilgi alanlar, enfeksiyon kontrol komitesinden bilgi alanlar, çevrimiçi eğitimlere katılanlar, prosedür ve kılavuz bilgilerine nasıl erişileceğini bilenler ve daha önce hastane içi bilgilendirme oturumlarına veya tatbikatlara katılanlar arasında anlamlı derecede daha yüksek bulunmuştur. Genel olarak, anketi yanıtlayanların çoğunluğunun hastanenin pandemi planı hakkında iyi bir bilgiye sahip olduğu gözlemlenmiştir.

Sonuç: Düzenli bilgilendirme oturumları, bilgilerin güncellenmesi ve motivasyonun sürdürülmesi için kritik öneme sahiptir. Kurumsal öncelikler arasında yer alan afet hazırlık süreci, amacına uygun şekilde organize edildiğinde, gerçek afet durumlarında kapsamlı ve etkili bir müdahale pratiği sağlanacaktır.

Anahtar Kelimeler: Afetler, afet yönetimi, çevrimiçi eğitim, hastane afet hazırlığı.

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Introduction

The importance of disaster preparedness is often discussed after disasters occur. However, there is no standardized definition for the scope and methodology of the disaster preparedness process. In many countries, national regulations have established minimum standards for dealing with disasters. Hospitals' ability to respond rapidly and effectively is crucial in disaster situations. The completion of preparations and raising awareness beforehand are critical for defining roles and ensuring efficient resource use, minimizing chaos and risks.

Mayner and Arbon (2015) examined 110 definitions of disaster to identify the most consistent one, defining it as an event causing widespread harm to a community that exceeds its ability to cope (1). The Centre for Research on the Epidemiology of Disasters (CRED) categorizes pandemics among biological disasters (CRED, 2024) (2). According to the World Health Organization (WHO), a pandemic is defined as an outbreak that occurs globally or in a very large geographical area, crossing international borders, and usually affecting a large number of people (3). On March 11, 2020, the WHO declared COVID-19 as a pandemic, marking the first pandemic caused by a coronavirus in history (4).

When examining the chronology of pandemic preparedness in Turkey, it is noted that the process began in 2004, and the National Pandemic Preparedness Plan was published in 2006 (5). On April 13, 2019, the Presidency published a decree on "Global Influenza Pandemic" detailing the necessary measures for public institutions to take in the event of a pandemic that could affect the majority of the population (6). The decree emphasized the importance of protecting public health, preparing emergency intervention mechanisms, and training and protecting healthcare workers.

However, preparedness plans alone do not ensure successful execution during a disaster. Key factors such as internal communication, information flow, authority, decision-making, coordination, and ongoing review of command structures are crucial for effective implementation (7).

The first pandemic preparedness plan at Hacettepe University Hospitals was enacted in February 2014 under the title “Respiratory Infectious Diseases Pandemic Action Plan (8).” In March 2017, it was updated to the “Hacettepe University Hospitals Pandemic Action Plan (9).” Various revisions were made over time regarding procedural flows, algorithms, and the names of instructions. In line with global developments, the "COVID-19 (2019-nCoV Disease) Infection Control Directive" was added, and on March 2, 2020, the pandemic action plan was finalized (10). Following the detection of the first COVID-19 case in Turkey, the Pandemic Action Plan and the Hospitals’ Disaster Plan were activated at Hacettepe University Hospitals on March 11, 2020 (12).

The awareness, knowledge, adherence to the pandemic plan, and challenges faced during its implementation at Hacettepe University Hospitals have not been evaluated. Existing studies mainly assess healthcare workers' preparedness for potential pandemics and their perceptions (13). However, following an actual pandemic, it is essential to treat the experience as a drill, document it, and conduct evidence-based evaluations to guide process improvements and interventions at the institutional level. This study aims to evaluate the effectiveness of disaster management and preparedness activities based on the experience of adherence to the pandemic plan at a university hospital.

Material and Methods

This study was designed as a descriptive cross-sectional study. The researchers used a questionnaire to collect data for the study, which included participants’ demographic characteristics, the areas they worked in during the pandemic, and their knowledge regarding the pandemic process.

The study population consisted of all academic, auxiliary healthcare personnel, and administrative staff working at Hacettepe University’s Adult, Pediatric, and Oncology Hospitals.

Following the declaration of the pandemic in March 2020, a survey titled “Awareness Level of Personnel Working at Hacettepe University Hospitals Regarding the COVID-19 Pandemic Process” was prepared to measure the knowledge of active personnel regarding the pandemic process. Personnel who had not worked actively for more than a year (due to reasons such as maternity leave, unpaid leave, military service, or administrative leave) were excluded from the study. The survey form was sent electronically, and a reminder was sent one week later.

During the pandemic, various departments at Hacettepe University Hospitals, including the Infection Control Committee and Nursing Management, provided training both face-to-face and through practical demonstrations. Disaster preparedness documents were shared via email and text messages, online programs on personal protective equipment were broadcasted, and training modules were made available. Specifically, three online training programs were developed.

The study questionnaire asked participants about their demographic characteristics, the areas in which they worked during the pandemic, and their general knowledge of the pandemic process and the pandemic plan at Hacettepe Hospitals, using a Likert scale for responses. Ethical approval was obtained from the Ethics Committee of Hacettepe University with approval number 35853172-900 and approval 16/06/2020.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics 21.0 software (IBM Corp., 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). Categorical variables are presented as frequencies or percentages, and continuous variables are presented as mean ± standard deviation and median (minimum-maximum) values. One-way analysis of variance (ANOVA) and Pearson correlation analysis were used to compare the individual and professional characteristics of employees with their knowledge of and resources related to the pandemic. The chi-square test was used for comparing two categorical variables, while the non-parametric Mann-Whitney U test was applied for continuous variables. A statistical significance level of $p<0.05$ was considered.

Results

At the time of the study, there were 5748 staff members in academic and administrative titles at Hacettepe University Hospitals. Staff on administrative leave and those with less than one year of work experience were excluded from the study. As a result, 1036 individuals did not meet the inclusion criteria, and a questionnaire was sent to 4712 individuals. A total of 645 individuals (13.6%) completed the survey. The largest group of respondents were nurses (23.4%), followed by administrative staff (10.4%), academic staff (10.0%), auxiliary support staff (8.6%), and other healthcare professionals (4.9%).

The distribution of average age, gender, length of employment, and job titles of the 645 respondents is shown in Table 1. Of the respondents, 241/645 (39.1%) had worked in COVID-19 units and/or areas providing outpatient services. A total of 446/640 (69.7%) staff members received direct information about the pandemic. Among those who received direct information, 77.5% were trained by the Infection Control Committee, and 49.7% received training from Hospital Management/Quality Coordination (Table 2).

Considering participants with intermediate or high levels of knowledge, the knowledge levels for social distancing (99.3%), personal protective equipment (PPE) (99.2%), hand hygiene (99.0%), surgical mask usage (98.8%), hair-beard regulations (97.5%) were very good. Knowledge of name tags (86.5%) and N95 masks (90.1%) was at a good level. Knowledge of inpatient isolation (83.7%), patient transfer (79.1%), and sample transportation (73.4%) was at an intermediate-to-good level, while knowledge about accessing psychological support (62.3%) and psychological support for children (67.5%) was at an intermediate level (Table 3).

Characteristics n (%)	**Results (n=645)**
Age (years) Mean (SD)	36.5 (8.9)
Female gender n (%)	445 (68.9)
Years of employment n (%)* 0-5	
0-5	187 (29.0)
6-10	101 (15.7)
11-20	244 (37.9)
≥ 21	112 (7.3)
Job description n (%)**	
Academic staff	151 (23.5)
Nurse	227 (35.4)
Other healthcare staff	56 (8.7)
Administrative staff	124 (19.3)
Support staff	83 (12.9)

Table 1. Demographic Characteristics of the Staff
*n=644, **n=641

The knowledge of the pandemic plan of Hacettepe University Hospitals was reported by 642 participants. 24.8% of participants fully knew the plan, 32.9% knew it, 27.1% knew it at an intermediate level, 8.4% did not know it, and 6.9% had no knowledge of it (Table 3). A total of 544 (84.7%) participants had intermediate or higher knowledge of the pandemic plan. When comparing participants' job locations and their knowledge of the Hacettepe University Hospitals' pandemic plan, the highest knowledge level was found among nurses (91.1%), followed by auxiliary staff (82.9%), academic staff (82.0%), administrative staff (81.9%), and technical staff (76.7%), with intermediate or higher knowledge levels.

Characteristics n (%)	**Results (n=645)**
Unit Worked in During the Pandemic:	
COVID ward/clinic	241 (39.6)
Non-COVID ward/clinic	173 (28.4)
Operating room	132 (21.7)
Administrative departments	21 (3.4)
Other	42 (6.9)
Knowledge of the Concept of Pandemic Before COVID-19 n (%)	524 (81.6)
Participation in Drills Before COVID-19 n (%)	39 (6.0)
Direct Information Regarding the Pandemic n (%)	446 (69.1)
Source of Pandemic Training Information (n=446)	195 (43.7)
Infection Control Committee only	71 (15.9)
Hospital management only	27 (33.8)
Infection Control Committee and Hospital management	27 (6.0)
Departmental Head of the unit worked	2 (0.4)
Other	
PPE online training viewing n (%)	
All of it	357 (55.8)
Some of it	107 (16.7)
None	176 (27.5)
Knowledge of access to pandemic plan instructions, procedures, and guidelines n (%)	544 (85.7)

Table 2. Staff Knowledge and Awareness Regarding the Pandemic
PPE: Personal Protective Equipment

Higher levels of knowledge regarding the Hacettepe University Hospitals' pandemic plan were found among female participants (p=0.016), those who had received direct information about the pandemic plan (p<0.001), those who received pandemic information from the Infection Control Committee (p=0.004), those who had attended online pandemic training (p<0.001), those who had previously participated in any drills (p=0.023), and those who were familiar with procedures/instructions (p<0.001) (Table 4). There was no significant difference in knowledge of the pandemic plan between staff working in the COVID-19 unit (83.6%) and those working in other areas (85.0%). Furthermore, no significant difference was found based on participants' age, length of employment, or knowledge of the pandemic plan (p>0.05).

Discussion

On March 11, 2020, the World Health Organization declared the COVID-19 pandemic due to the SARS-CoV-2 infection. At the same time, the Hacettepe Hospital Pandemic Action Plan and Hospital Disaster Plan were activated. As part of these efforts, informational and training sessions were initially held for academic staff, healthcare personnel, and other administrative staff at the hospital. During these sessions, preventive measures against the pandemic, diagnostic, treatment, and management algorithms set by the Ministry of Health, algorithms established by Hacettepe Infection Control Units, and appropriate usage methods for personal protective equipment were shared regularly with all hospital employees. By June 2020, when this survey was conducted, the Infection Control Committee had conducted 17 training

	n (%)				
	I don't know at all	I know a little	I know moderately	I know	I know completely
Hacettepe Knowledge of the pandemic plan	44 (6.9)	54 (8.4)	174 (27.1)	211 (32.9)	159 (24.8)
Ministry of Health pandemic plan	27 (4.2)	42 (6.6)	158 (24.6)	242 (37.8)	172 (26.8)
Hand hygiene knowledge	3 (0.5)	3 (0.5)	8 (1.3)	54 (8.4)	572 (89.4)
Social distancing knowledge	3 (0.5)	1 (0.2)	5 (0.8)	44 (6.8)	591 (91.8)
Name badge knowledge	56 (8.7)	31 (4.8)	50 (7.8)	79 (12.3)	426 (66.4)
Hair-beard knowledge	6 (0.9)	10 (1.6)	27 (4.2)	58 (9.0)	540 (84.2)
Personal protective equipment knowledge	4 (0.6)	1 (0.2)	23 (3.6)	92 (14.3)	523 (81.3)
Surgical mask knowledge	6 (0.9)	2 (0.3)	16 (2.5)	83 (12.9)	534 (83.1)
N95 mask knowledge	33 (5.1)	31 (4.8)	59 (9.2)	113 (17.6)	407 (63.3)
Inpatient isolation knowledge	59 (9.2)	46 (7.1)	83 (12.9)	137 (21.3)	319 (49.5)
Transfer knowledge	80 (12.5)	54 (8.4)	127 (19.8)	151 (23.6)	229 (35.7)
Sample transportation knowledge	115 (17.9)	56 (8.7)	90 (14.0)	164 (25.5)	217 (33.8)
Psychological support knowledge	174 (27.1)	68 (10.6)	139 (21.7)	102 (15.9)	159 (24.8)
Child support knowledge	93 (21.9)	45 (10.6)	80 (18.9)	75 (17.5)	132 (31.1)

Table 3. Staff Knowledge Level Regarding Pandemic Plan and Personal Protection

	Pandemic knowledge exists	No pandemic knowledge	p
Age (years), n (SD)	36.7 (9.6)	36.1 (8.7)	0.57
Female gender, n (%)	385/535 (71.9)	58/97 (59.7)	0.016
Direct information received, n (%)	404/542 (74.5)	40/95 (42.1)	<0.001
Information received from the Infection Control Committee, n (%)	320/405 (79.0)	25/42 (59.5)	0.004
PPE online training watched, n (%)	419/541 (77.4)	44/96 (45.8)	0.001
Participation in drills, n (%)	38/544 (6.9)	1/98 (1.0)	0.023
Knowledge of access to pandemic plan instructions, procedures, guidelines, n (%)	490/537 (91.2)	52/95 (54.7)	<0.001

Table 4. Knowledge of the Pandemic Plan of Hacettepe University Hospitals

sessions, the Hospital Quality Coordination had 11, and the Adult Hospital Chief Medical Officer had 6, along with 20 sessions from other units, all focused on reminding employees about new flow charts, necessary precautions, and protection measures.

No study has yet assessed hospital staff's knowledge level regarding informational meetings. This study aimed to measure hospital employees' understanding of the pandemic plan during the pandemic. A total of 645 employees (13.6% response rate) from Hacettepe University Hospitals completed the survey. Nurses were more likely to participate, while other healthcare personnel showed the lowest engagement. Among the respondents, 85% had an average or higher level of knowledge about the hospital's pandemic plan, with 57% demonstrating good knowledge. Knowledge was higher among women, those who received direct information, those informed by the Infection Control Committee, those who participated in online training, those aware of where to access procedures/instructions, and those who had participated in drills.

Labrague et al. (2017) conducted a systematic review of disaster preparedness among nurses between 2006-2016. The study found that prior disaster training led to better individual preparedness and that training and drills were critical for disaster response. It also highlighted the importance of first aid and infection control training for disaster readiness. However, despite knowing that their institutions had disaster preparedness documents, many nurses were unaware of specific protocols or where to access the documents, and a quarter had not read them. Previous studies on the effectiveness of disaster preparedness training have indicated that such training does not sufficiently increase disaster knowledge and awareness (13). For example, a study by Almukhlifi et al. (2021) assessed disaster preparedness among emergency service workers and found that most employees were inadequately prepared (14). Similarly, a systematic literature review by Williams et al. (2008)(15) found that disaster preparedness training was ineffective in improving knowledge and skills related to disaster intervention. Cotanda et al. (2016)

evaluated disaster preparedness training in a pediatric emergency department and concluded that while the training increased knowledge, there was no improvement in responses to practical situations. These results suggest that theoretical knowledge may not always translate directly into practical application (16). Although written instructions are crucial, hands-on online training programs are highly valuable for helping individuals understand the process. Bartley et al. (2007) found that a training video based on disaster drill images contributed to improving knowledge among assistant doctors (17). Our study also shows that employees who participated in online training programs had a better understanding of the pandemic plan process. Therefore, it may be important to include more visual and online training programs in future improvements.

In parallel, a randomized controlled trial by O'Connell (2021) conducted in a children's hospital with various professional groups found that digital training achieved greater success in reaching its goals and had higher satisfaction among participants (18).

In our study, only 6% of participants had previously participated in any drills, which is a low percentage. The World Health Organization's Health Emergency and Risk Management (EDRM) Framework (19) emphasizes the critical importance of preparedness and readiness for disasters, and recommends including disaster planning, development, and implementation in disaster coordination algorithms. According to the Hospital Disaster and Emergency Management Regulation (2020)(20), hospitals are required to conduct at least one desk-based and one field exercise annually with different scenarios. However, participation in drills is voluntary. Our study showed that having participated in a drill resulted in better knowledge and understanding of the general pandemic plan. This suggests that hospital management should place more emphasis on drills after the pandemic period (21).

During the pandemic, participants were highly knowledgeable about essential preventive measures such as hand hygiene, social distancing, and the use of surgical and N95 masks. The high level of knowledge among hospital staff is promising, as they serve as role models for the public. Notably, no significant difference was observed between those working in COVID wards/clinics and those in other units, nor did professional experience significantly impact knowledge levels. Moreover, pandemic management extends beyond disease control to include the psychological well-being of healthcare workers. Understandably, concerns about personal and family health were prevalent, particularly in the early stages of the pandemic. In this study, knowledge about psychological support for employees and their children was among the lowest. Despite expert-led informational efforts, a gap remains, highlighting the need for further initiatives in this area.

Limitations

One of the significant limitations of this study is the response rate to the survey. Although approximately 650 employees were reached, and the distribution of roles was relatively similar, only 14% of the total staff participated in the survey. It is likely that individuals with more knowledge of the pandemic plan were more inclined to complete the survey. Therefore, it can be assumed that the level of knowledge about the pandemic plan might be lower across the entire staff group.

Conclusion

The results of this survey indicate that the majority of participants were well-informed about the hospital's pandemic plan. Both healthcare workers and administrative staff, as well as auxiliary health service workers, demonstrated a good level of knowledge regarding protective measures such as the use of personal protective equipment, hygiene rules, and social distancing. Managing the pandemic is also a psychological process, and employees require further information and guidance in this regard. It has been found that it would be beneficial to provide direct information, preferably through the Infection Control Committee, alongside online briefings during the training process. Regular informational meetings could play a crucial role in updating employees' knowledge and maintaining their motivation. In this regard, organizing the disaster preparedness process in line with institutional priorities will ensure comprehensive and effective response capabilities in actual disaster situations.

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CASE REPORT / OLGU SUNUMU

Delayed and Atypical Neuroleptic Malignant Syndrome Following Extended-Release Injectable Aripiprazole Use

Uzun Salınımlı Enjekte Edilebilir Aripripazol Kullanımını Takiben Gecikmiş Ve Atipik Nöroleptik Malign Sendrom

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ABSTRACT

Aim: Neuroleptic malignant syndrome (NMS) is an uncommon but life-threatening condition associated with antipsychotic medications that interfere with central dopaminergic pathways. While typically linked to high-potency antipsychotics like haloperidol, atypical antipsychotics such as aripiprazole can also induce NMS. The syndrome is characterized by hyperthermia, autonomic instability, altered mental status, and muscle rigidity, though atypical cases may lack some of these hallmark features. We aim to present an NMS case presented with delayed atypical symptoms following extended-release injectable (ERI) aripiprazole.

Case Presentation: A 40-year-old female patient with bipolar disorder and major depression arrived at the emergency department complaining of decreased mental clarity, difficulty with swallowing solid food, and impairments in communication and mobility who received ERI aripiprazole 40 days prior to admission. Despite lacking rigidity, she exhibited motor jerks, autonomic instability, and a delayed elevation in creatine kinase levels. NMS was diagnosed after excluding other causes, but the patient deteriorated rapidly, developing acute renal failure, cardiovascular instability, and malignant arrhythmia, which led to death.

Conclusion: This case highlights the potential for delayed and atypical presentations of NMS with ERI aripiprazole, emphasizing the need for clinicians to maintain a high index of suspicion for NMS, even when typical symptoms like rigidity are absent.

Keywords: Neuroleptic malignant syndrome, antipsychotic agents, aripiprazole

ÖZ

Amaç: Nöroleptik malign sendrom (NMS), santral dopaminerjik yolaklar üzerine etkili antipsikotik ilaçlarla ilişkili nadir görülen ancak yaşamı tehdit eden klinik bir durumdur. Genellikle haloperidol gibi yüksek etkili klasik antipsikotiklerle ilişkilendirilirken, aripiprazol gibi atipik antipsikotikler de NMS'ye neden olabilir. Sendrom, hipertermi, otonomik instabilite, değişen mental durum ve kas rijiditesi ile karakterizedir, ancak atipik vakalarda bu belirgin özelliklerden bazıları eksik olabilir. Uzun etkili enjektabl (USE) aripiprazol kullanımı sonrası gecikmiş atipik semptomlarla gelen bir NMS olgusunu sunmayı amaçladık.

Olgu Sunumu: Olgumuzda bipolar bozukluğu ve majör depresyonu olan ve uzun salınımlı enjektabl (USE) aripiprazolden sonra atipik NMS gelişen 40 yaşında bir kadın vakasını sunuyoruz. Rijiditesi olmamasına rağmen, motor atımlar, otonomik instabilite ve kreatin kinaz seviyelerinde gecikmeli yükselme meydana gelen hastada NMS, diğer nedenler dışlandıktan sonra teşhis edildi, ancak hastanın kliniği hızla kötüleşti; akut böbrek yetmezliği, kardiyovasküler instabilite ve malign aritmi hastanın ölümüyle sonuçlandı.

Sonuç: Bu vaka, USE aripiprazol kullanımı ile NMS'nin gecikmiş ve atipik semptomlarla başvurma potansiyelini vurgulayarak, rijidite gibi tipik semptomlar olmasa bile klinisyenlerin NMS'ye karşı yüksek bir şüphe barındırmaları gerektiğinin altını çizmektedir.

Anahtar Kelimeler: Nöroleptik malign sendrom, antipsikotikler, aripiprazol

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Introduction

With a 0.02% to 3.2% incidence rate, neuroleptic malignant syndrome (NMS) is an uncommon but potentially fatal condition linked to the use of antipsychotic medications that affect central dopaminergic neurotransmission. NMS can lead to a 10%-55% mortality rate (1). Dopamine antagonist exposure, altered mental status, rigidity, hyperthermia, and autonomic instability are typical diagnostic criteria for NMS. Other symptoms that may be present include diaphoresis, tachycardia, mutism, tachypnea, cardiovascular lability, and incontinence, with no apparent underlying neurological, metabolic, infectious, or other cause (2). We present a case of a patient who developed NMS in an atypical and delayed fashion following the administration of extended-release injectable aripiprazole.

Case Presentation

A 40-year-old female patient arrived at the emergency department complaining of decreased mental clarity, difficulty with swallowing solid food, and impairments in communication and mobility. Her medical history included hypothyroidism, hypertension, generalized anxiety disorder, and most recently, bipolar illness and major depression. Hence, she was prescribed lithium 1200 mg daily, venlafaxine 300 mg daily, bupropion 150 mg daily, and aripiprazole 200 mg monthly on a regular basis. Her oral aripiprazole 20 mg/day therapy was changed to 200 mg intramuscular extended-release aripiprazole 40 days prior to admission. The patient's next of kin informed our team that the patient's symptoms began following her second dose ten days ago, progressively deteriorated over time, and reached their peak within the past three days. She denied infectious symptoms, unusual food or drug intake, and random unprotected sexual intercourse. Initial vital signs were noted as; Glasgow Coma Scale Score 13/15 (E3V4E6), blood pressure 153/99 mmHg, pulse rate 103/bpm, temperature 36.8 °C, oxygen saturation 99%, respiratory rate 28/pm. On physical examination, the patient was disorganized, only responded with single words, and opened her eyes in response to verbal stimuli. There was no evidence of rigidity. With painful stimuli, all extremities had 4 points out of 5 on the muscle power scale. Upon admission, there were noticeable jerks in the left arm and right leg.

Her antipsychotic medications were discontinued, and intravenous hydration was started. According to her laboratory results, there was no evident pathology related to infection causes or electrolyte-metabolic abnormalities. Lithium blood level was within the therapeutic range. Serum creatinine kinase levels were the only laboratory parameter that changed noticeably. The measured blood creatinine kinase result was 284 U/L (with a reference cutoff of 145 U/L). Thoracic and abdominal computer tomography (CT) scans reported no evidence of an infection. Central imaging (non-contrast brain CT scan and diffusion-weighted magnetic resonance imaging) revealed no evidence of pathology. The electroencephalogram test showed intermittent slowing. Biperiden hydrochloride 10 mg was administered via IV route for suspected extrapyramidal adverse reaction resulting in automatic motor activity in the extremities. 10 mg of diazepam was administered via IV route to relieve the motor activity in the setting of a focal seizure to whom motor activity persisted following the biperiden hydrochloride.

Repeated laboratory tests resulted in creatinine: 2.2 mg/dl (initial 0.81 mg/dl), blood urea nitrogen (BUN): 32 mg/dl, K: 4.4 mEq/L, pH.7.24, base excess (BE): -5, HCO3: 22 mmol/L, lactate: 1.7, creatinine kinase : 483 U/L, no increase in the acute phase reactants. Intravenous hydration continued.

At the 30th hour of admission, 38.3°C and 38.5°C fever measurements were documented. In addition to applying a cold compress along with administering an intravenous dose of 1 gram of paracetamol, the patient also underwent repeat laboratory testing and blood cultures. Ceftriaxone for prophylaxis was initiated. No evidence of infection was present in the laboratory tests.

Contrast-enhanced brain magnetic resonance imaging (MRI) was performed to detect space-occupying lesions and central system infection due to the patient's state of somnolence and the development of nonsensical speech. 10 mg of intravenous midazolam was given before the MRI in order to minimize motor activity and provide sedation. The contrast-enhanced cranial MRI, which was obtained at 48th hours of admission revealed no signs in favor of intracranial mass or encephalitis.

At the 50th hour of admission, a fever of 38.3 °C was documented again. A lumbar puncture was performed.

Along with the recurrent motor activities on the extremities, the patient’s GCS score has deteriorated; consequently, she required an RSI with IV midazolam 0.15 mg/kg and IV 0.8 mg/kg rocuronium. As hypotension occurred and persisted, noradrenaline infusion was initiated with 0.1 mcg/kg/min dosing, titrated to 0.25 mcg/kg/min.

The cerebrospinal fluid (CSF) culture showed no signs of bacterial or fungal colonization, and the laboratory findings revealed the following: glucose 131 mg/dL (concurrent blood glucose level 201 mg/dL), protein 38 mg/dL, LDH 62 U/L, and Cl 141 meq/L. Peripheral blood cultures revealed gram (+) clustered cocci and gram (-) bacillus colonization. Although bacterial infection was not considered in the foreground, intravenous treatment with meropenem and vancomycin was initiated. As the following culture typing analysis resulted afterwards, gram (+) clustered cocci colonization was reported more likely as a contamination (coagulase [-] Staphylococcus spp.), and gram (-) bacillus colonization was reported as Acinetobacter lwoffii and Acinetobacter calcoaceticus, which are sensitive to meropenem.

The patient was transferred to the intensive care unit (ICU) at the 66th hour of ER admission. The patient's jerks continued upon admission to the intensive care unit, and their body temperature rose to 38°C. Control test results showed a substantial rise in CK (3556 U/L) and creatinine (3.64 mg/dL) which was accompanied by acidemia and anuria, therefore the patient was taken under dialysis. As the patient's need for vasopressors increased following hemodialysis, IV vasopressin was added with an infusion rate of 0.04 IU/min. Fever persisted during the ICU stay. Soon after, cardiovascular instability further led to malignant arrhythmia and eventually cardiac arrest. Written informed consent was obtained from the next of kin.

Discussion

NMS is a rare but potentially lethal complication of antipsychotic medications. Typical, high-potency antipsychotics such as haloperidol are among those most likely responsible; however, reports have linked a variety of drug classes, including low-potency and atypical antipsychotics, as well as antiemetic drugs that block dopaminergic receptors, to NMS (2,3).

Central dopaminergic receptor blockage is the pathogenic mechanism causing autonomic instability, hyperthermia, and parkinsonian symptoms such as rigidity (4). It is believed that central dopaminergic receptor inhibition at the hypothalamus results in hyperthermia and autonomic instability, whereas central receptor blockade in the nigrostriatal pathways causes parkinsonian-type symptoms such as rigidity (2,4). Aripiprazole is an atypical antipsychotic that acts as a partial agonist at the dopamine D2/D3/D4 receptors, in contrast to the antipsychotics that have stronger D2 blockage. It additionally features concurrent partial agonist action at serotonin 5-HT1A receptors and antagonist activity at 5-HT2A receptors (2,5).

There is no specific diagnostic test for NMS. A comprehensive history, physical examination, and laboratory results, such as increased creatine kinase (more than 1000 IU/L), can assist confirm the clinical diagnosis in individuals with suspected NMS (6). In a consensus study conducted in 2010 aiming to diagnose NMS using the Delphi method, diagnostic criteria were determined by the consensus of a committee consisting of 11 psychiatrists, 2 anesthesiologists, 2 emergency specialists, and 2 neurology specialists (Table 1) (7). A higher score is associated with the diagnosis, although the exact threshold number remains undetermined (7). The latest DSM-V criteria were also published a table of similar criteria for the diagnosis of NMS (8). Table 2 shows the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) diagnostic criteria for NMS; including administration of a dopamine-blocking agent in the prior 72 hours, hyperthermia, rigidity, and altered level of consciousness (major criteria), and the presence of at least 2 of the following signs: tachycardia, diaphoresis, urinary incontinence, tachypnea, blood pressure fluctuations, elevated creatine kinase (CK) level, and leukocytosis, after exclusion of other causes (8). Leukocytosis with a left shift, electrolyte imbalances, elevated liver function tests, increased creatinine, and myoglobinuria due to rhabdomyolysis are other nonspecific laboratory findings (2).

The dosing and time frame between antipsychotic use and the onset of NMS is unique. Prior NMS history, high antipsychotic dosages, parenteral administration, recent or abrupt dose increases, switching antipsychotics, dehydration, and concurrent use of lithium, anticholinergic drugs, and antidepressants are risk factors for NMS (2).

Diagnostic criterion	Priority score*
Exposure to dopamine antagonist, or dopamine agonist withdrawal, within past 72 hours	20
Hyperthermia (>100.4°F or >38.0°C on at least 2 occasions, measured orally)	18
Rigidity	17
Mental status alteration (reduced or fluctuating level of consciousness)	13
Creatine kinase elevation (at least 4 times the upper limit of normal)	10
Sympathetic nervous system lability, defined as at least 2 of the following: • Blood pressure elevation (systolic or diastolic ≥25 percent above baseline) • Blood pressure fluctuation (≥20 mmHg diastolic change or ≥25 mmHg systolic change within 24 hours) • Diaphoresis • Urinary incontinence	10
Hypermetabolism, defined as heart-rate increase (≥25 percent above baseline) AND respiratory-rate increase (≥50 percent above baseline)	5
Negative work-up for infectious, toxic, metabolic, or neurologic causes	7

Table 1. Neuroleptic malignant syndrome diagnostic criteria: Expert panel consensus
No threshold score has been defined and validated for us in making a diagnosis of NMS.
* The mean priority score indexes each criterion according to its relative importance in making a diagnosis of NMS according to an expert panel.
Adapted from Gurrera et al. (7)

Diagnostic criteria of NMS based on DSM-V (9)	
Major symptoms	Rigidity Hyperthermia (>38.0°C, measured minimum 2 times orally) Diaphoresis Exposure to dopamine antagonist within 72 h prior to the beginning of symptoms
Minor symptoms	Autonomic nervous system: Tachycardia (rate > 25% above baseline), hypertonia (>25% above baseline or with fluctuation), sialorrhea, urinary incontinence, pallor, tachypnea (>50% above baseline), dyspnea Mental status: Altered consciousness: qualitative (delirium); quantitative (stupor to coma) Motor symptoms: Tremor, akinesia, dystonia, myoclonia, trismus, dysarthria, dysphagia Laboratory findings: ↑Leukocytes, ↑CK, ↑Myoglobin, ↑Catecholamines, ↑Creatinine, ↓Fe, metabolic acidosis, hypoxia
Exclusion criteria	The above-named symptoms are not due to another substance or a neurological or other general medical condition

Table 2. Diagnostic criteria of NMS based on DSM-V
NMS, Neuroleptic malignant syndrome; DSM, Diagnostic and Statistical Manual of Mental Disorders.

For our patient, the calculated Delphi score was 73. Although there is no specific reference test, it has been observed that a high score correlates with the diagnosis. According to DSM-V, although NMS can be diagnosed, the absence of rigidity and initial CK elevation may make diagnosis challenging. Although the literature suggests that rigidity is a major criterion for diagnosis, a study by Gurrera et al. reported that its sensitivity was measured as 69% (10). The atypical NMS phenotype was anticipated to present with increased nausea and vomiting, lower creatine kinase peaks, less autonomic instability, and hyperthermia, as well as less severe and shorter NMS episodes. However, in our patient, clinical signs were delayed (mental status change), rigidity was absent, cardiovascular lability and CK increase followed by rhabdomyolysis, which emerged on the 3rd day of admission and 13th day of first complaints. The literature and our case suggest that, even at the possibility of reduced specificity, the absence of one or more of the primary components of NMS shall be disregarded when making a diagnosis of NMS in atypical cases. Clinical strategies for managing NMS during its acute phase include identifying potential symptoms, excluding differential diagnoses, ceasing antipsychotic medication, and putting both pharmaceutical and non-pharmacological therapies into practice.

After performing the appropriate tests for the central nervous system and metabolic reasons, no abnormality was identified in our patient. Investigations such as brain imaging and lumbar puncture are used to exclude other causes for altered mental status such as neurological disease and infection. EEG showed slowed activity and excluded epileptic seizures. The patient had no suicidal ideation, side effects of his medications were monitored and there was no evidence of intoxication. Lithium levels were also monitored within the therapeutic range. Serotonin syndrome (associated with the use of serotonergic agents) was another differential in this case, but the patient did not exhibit autonomic features, such as hyperhidrosis and diarrhea, or muscular signs, such as hyperreflexia and myoclonus, which are typical of this syndrome. According to the blood culture typing results, which were reported 1 week after the sample was taken, Acinetobacter lwoffii and A. calcoaceticus growth were detected in the blood. Although there was no risk factor for opportunistic infection in the patient, it is still unknown whether this situation is due to colonization or infection. Although acinetobacter species growth in the blood culture may be the cause of persistent fever and other symptoms, since the patient's reason for application was progressively increasing central symptoms for the last 10 days and there was no growth in the CSF culture, it was thought that the cause of the symptoms would not be primarily bloodstream infection. However, as soon as the culture result was obtained, the patient was started on meropenem without waiting for the typing. The susceptibility to meropenem of A. lwoffii and A. calcoaceticus was confirmed after all.

Frequent monitoring and supportive care are necessary to prevent complications such as acute renal failure, acute respiratory failure, arrhythmias, myocardial infarction, seizures, and sepsis. It is essential to administer intravenous fluids to maintain a euvolemic state and to prevent fever (2). Pharmacological interventions aim to reduce muscle rigidity, reverse the dopaminergic blockade, and control agitation or behavioral disturbance, which can be component of the underlying psychiatric disorder or a response to the NMS itself (3).

Dantrolene (1-2.5 mg/kg intravenously, up to 10 mg/kg/day), a direct-acting skeletal muscle relaxant, is often used in adults with NMS and has been reported to decrease rigidity and hyperthermia. When used at large doses, there is an elevated risk of hepatotoxicity (2).

It is also possible to use amantadine, a weak, noncompetitive N-methyl-D-aspartate receptor antagonist (100 mg orally to a maximum of 200 mg every 12 hours), and bromocriptine, a D2 agonist (2.5 mg through nasogastric tube every 6-8 hours, up to 40 mg/day). Benzodiazepines have been demonstrated to reduce mortality and are useful in providing muscle relaxation and managing agitation or behavioral disturbance (11).

Dantrolene sodium could not be administered to the patient because it was not available in the emergency department and, therefore administered in the intensive care unit. We believe that the diagnosis is strengthened by the fact that the patient's symptoms improved as benzodiazepines were administered, and that during follow-ups in intensive care, CK levels were higher than 3000 U/L.

Conclusion

This case is an example of NMS with atypical and delayed signs, associated with ERI aripiprazole. We should emphasize that NMS may develop as a complication of aripiprazole ERI formulations.

The delayed onset and the absence of major symptoms of NMS in our patient are atypical features that complicate the management. Therefore, clinicians should be aware that NMS is heterogeneous in onset, presentation, and progression.

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Informed Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review in this journal.

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REVIEW / DERLEME

Airway Management in Trauma Cases in Emergency Department

Acil Serviste Travma Hastalarında Havayolu Yönetimi

Volkan Arslan

ABSTRACT

Trauma patients constitute a significant proportion of emergency department admissions. It is vital to have sufficient knowledge and experience in airway management of these patients. Choosing the most appropriate method for each patient may be the most challenging step for the practitioner. In particular, the fact that some generalizations are not supported by sufficient literature information makes this choice difficult. In this article, the options that can be used in airway management of trauma patients will be discussed.

Keywords: Airway, trauma, emergency department

ÖZ

Travma hastaları acil servis başvurularının önemli bir kısmını oluşturmaktadır. Bu hastaların havayolu yönetiminde yeterli bilgi ve tecrübeye sahip olmak hayati önem taşımaktadır. Her hasta için en uygun yöntemin seçilmesi uygulayıcıyı en çok zorlayacak basamak olabilir. Özellikle de bazı genel kanıların yeterli literatür bilgisi ile desteklenmiyor olması bu seçimi zorlaştırmaktadır. Bu yazıda travma hastalarının havayolu yönetiminde kullanılabilecek seçenekler tartışılacaktır.

Anahtar Kelimeler: Havayolu, travma, acil servis

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Introduction

Trauma patients constitute a significant proportion of emergency department admissions. Trauma is still the most common cause of death under the age of 45 worldwide (1). In the United States of America, there are 37 million annual emergency department visits due to trauma. Approximately 2.6 million of these patients require hospitalization (2).

Airway has a special importance in the management of trauma patients. Airway management is the first step of classical trauma intervention in order to ensure airway patency and to continue breathing (1, 3). In airway management of trauma patients, as in other patients, there is a spectrum ranging from a simple airway opening maneuver to endotracheal intubation and even surgical airway techniques(4-9). Bhoi et al. showed that 13.25% of the patients intubated in the emergency department were trauma patients (10). Levitan et al. stated that 1800 major trauma patients were evaluated in a center where approximately 50000 patients were seen annually and 658 patients needed intubation during a 3-year study (11).

All trauma patients may reasonably be classified as having a potentially difficult airway due to their injury profiles. This creates the need for emergency physicians to keep their knowledge of airway management in this patient group constantly updated. This article will attempt to summarize airway management in trauma patients.

Airway Opening Maneuvers

The conventional wisdom is that the head-tilt chin-lift maneuver can not be used in cervical trauma, but there is insufficient evidence in the literature to support this. Due to concerns that it may mobilize cervical vertebrae and exacerbate existing injury, especially in patients with trauma affecting the spinal canal, only the jaw trust maneuver is recommended in this patient group. However, it is not possible to show how much of the spinal damage in patients with cervical trauma is due to the initial trauma and how much is secondary to airway opening maneuvers. Therefore, there is insufficient evidence to show that the head-tilt chin-lift maneuver causes secondary damage. Nevertheless, the maneuver recommended for trauma patients at the level of expert opinion is the jaw trust maneuver. Of course, it should be kept in mind that the cervical vertebrae may be mobilized during jaw trust and caution should be exercised (12-17).

Face Mask/ Preoxygenation

The use of a face mask can be problematic, especially in maxillofacial injuries. Alternative methods of oxygenation should also be considered. The possibility that the mask may not fit the face properly and/or the mask may cause secondary damage due to trauma should be considered. Another respiratory support method that may pose a problem due to mask use is non-invasive ventilation. If it is thought that the patient needs non-invasive mechanical ventilation support, it is necessary to choose the appropriate type of mask (8, 18-20).

If it is decided to intubate the patient, the preoxygenation stage should be decided by considering maxillofacial trauma and skull base fractures. Especially in skull base fractures, using high-flow oxygen during the preoxygenation phase is not recommended because it may cause/increase pneumocephalus. It is controversial whether apneic oxygenation can be used in these patients (5, 6, 13, 19-21).

Supraglottic Devices

Supraglottic devices are important tools used in airway management. Although they are seen as a part of rescue oxygenation in emergency services, they provide important advantages before hospitalization. As it is known, recent publications recommend the use of supraglottic devices instead of endotracheal intubation, especially during intervention in the field. This situation seems logical as it will save time for the limited health personnel to direct their efforts to other tasks. Although there is no different recommendation for trauma patients, it should be remembered that the mouth opening should be sufficient and there should be no upper airway obstruction for the insertion of supraglottic devices. However, there are no publications showing the superiority of any supraglottic device over another. Therefore, practitioners can use the supraglottic device available to them (19, 22-24).

Endotracheal Intubation

Endotracheal intubation can be considered as the most preferred method in airway management. At least it would not be wrong to say that it is the most popular. It is a difficult process to manage and requires experience for all patients. The success of intubation is measured by advancing the tube through the vocal cords with the minimum number of attempts as well as the absence of complications. Current literature suggests that even when an endotracheal tube is placed correctly in a single attempt, if complications develop, the procedure may be considered a failure. Considering that patient management is a whole and that the general condition of the patient may deteriorate further due to intubation-related complications, this perspective aligns with the holistic goals of patient management. It should not be forgotten that our goal is not only the placement of the tube. Our aim is to improve the clinical condition of the patient (3, 4, 8, 9, 12, 13, 16, 19, 25).

In various studies, hypotension is the most common complication of endotracheal intubation. Especially the high likelihood of multiple trauma patients being in hypovolemic shock forces the practitioner to be even more careful in this regard. The current state of hypovolemia puts all trauma patients in the physiologic difficulty class in terms of intubation. Therefore, if a trauma patient is to be intubated,

appropriate fluid and/or transfusion therapy should be provided for peri-intubation optimization (3, 4, 19, 23).

The development of metabolic acidosis in trauma patients is another condition that makes the intubation process physiologically difficult. After intubation, ventilator adjustment should be made considering the patient's compensatory respiratory effort. Rapid disruption of this compensation by the physician may lead to serious problems.

Another condition that makes intubation of trauma patients difficult is cervical movement limitation. This condition, which can be listed under the heading of anatomical difficulties, exists spontaneously in all trauma patients. In the current literature, there is insufficient evidence of secondary injury caused by endotracheal intubation. Nevertheless, the classical approach advocates that neck movements should be avoided during the procedure. In some cadaveric studies, the cervical canal distance was measured by direct radiography and it was questioned whether there was any change in this distance with neck movements. Although some change was noted in some studies, it is not known whether this change is sufficient to cause damage. In a study of patients requiring cervical stabilization due to trauma, there was no evidence of increased damage secondary to intubation. Of course, due to the technical difficulty of investigating the subject, it is unlikely that the discussion will be concluded in the near future (12, 14, 16, 17).

Intubation Aids (Stylet, Bougie)

Intubation assist devices include the stylet and the bougie. The stylet shapes the intubation tube, making it easier to guide. There have been numerous studies on the benefits of both. Both the stylet and the bougie have been separately compared with direct laryngoscopy and have been shown to improve first pass success. It may be advisable to use one of these two assist devices, especially in trauma patients. However, there are not enough studies comparing these two devices with each other. Which one is preferred should be decided based on the technical equipment available to the practitioner and the algorithm determined by the clinic (4, 10, 13, 19, 23-25).

Videolaryngoscope

Videolaryngoscopy has taken its place in our lives with an increasing rate of use. In various publications, videolaryngoscopy is compared with direct laryngoscopy. In trauma patients, it is said that the use of videolaryngoscopy significantly increases the first pass success. While the patient was intubated in an average of 1;1 attempts with videolaryngoscope, it is stated that this number increases to 3.2 when direct laryngoscopy is used in trauma patients. In another study, it was observed that the first pass success rate was 1/16 when direct laryngoscopy was used in intubation of trauma patients, while this rate increased to almost 100% when videolaryngoscopy was used. The increase in the number of intubation attempts seems to be directly proportional to the increase in complication rates. Therefore, if adequate technical equipment is available, videolaryngoscope should be the first choice for intubation of trauma patients (3-5, 9, 17, 19, 26).

Except for the first pass success, it has been commented that videolaryngoscope will reduce cervical mobilization and accordingly reduce the possibility of secondary injury. Although there are not enough studies for this, it would not be wrong to interpret that there will be less cervical mobilization due to easier visualization of the vocal cords (5, 8, 19, 20, 26).

Unfortunately, there is no answer to the question of which videolaryngoscope we should prefer. The practitioner can use any device provided in line with the preferences of the clinic (19).

Manual In-Line Stabilization

Although the cervical collar worn in trauma patients is a recommended aid for cervical vertebra stabilization, it is seen as a tool that complicates airway management. In order to continue cervical stabilization and to get rid of the negative effects of the cervical collar, a technique called “manual in line stabilization (MILS)”, which can be translated as manual fixation, is used in trauma patients. However, there are reports that this technique also has negative effects on intubation success. It is argued that the first pass success decreases in patients using the MILS technique. In addition, some publications state that the use of a cervical collar also decreases the first pass success and argue that the collar should be removed. On the other hand, removal of the cervical collar is thought to affect cervical stabilization badly (15, 27, 28).

Front of Neck Access (FONA)

It is known that the need for a surgical airway is a very common situation in emergency practice. However, every emergency physician must master this practice. Although it is rare, this intervention is life-saving when there is no other option. Surgical airway may be required in trauma patients, especially in maxillofacial trauma. In the study by Levitan et al. only 2 trauma patients needed surgical airway in 3 years (11).

It should be kept in mind that this procedure may become somewhat more difficult in trauma patients. Trauma-related deformities or problems such as bleeding/hematoma around the trachea may make localization of the cricothyroid membrane difficult. Therefore, the practitioner who will approach the anterior neck in trauma patients must be trained and experienced in this field. The easiest way to

provide adequate training for this rare condition is model and/or cadaver practice. As with all other interventional procedures, practice is essential for surgical airway (6, 7, 19, 20, 29).

In cases where the cricothyroid membrane may be difficult due to problems in trauma patients, it may be appropriate to use ultrasonography to solve this difficulty. With ultrasonography, the cricothyroid membrane can be localized noninvasively and the procedure can be continued. It would not be wrong to include ultrasonography device in the surgical airway materials in trauma patients because it will both speed up and reduce possible complications (19).

Awake Intubation

Unfortunately, flexible intubation is not a widely used technique in emergency clinics. Both the cost of the device and the time-consuming application of the technique and the fact that other alternatives, which are often applied more rapidly than this procedure, are preferred in intubations performed in emergency departments seem to explain this situation.

In trauma patients, there are not enough studies on this technique known as awake intubation or flexible intubation. Therefore, it is not possible to objectively evaluate the possible pros and cons of the method (9, 13, 15, 19, 24).

Awake intubation also requires practitioner practice. If it is among the airway management preferences of the clinic, it is obvious that practical trainings should be organized at appropriate intervals.

Conclusion

Although there are various studies addressing airway management in trauma patients, there is no definitive recommendation in the literature. The inadequate level of evidence of the existing recommendations is evidence of the need for more studies in this field.

Nevertheless, it would not be wrong to suggest that the choice should be made in line with the injury mechanisms and clinical condition of trauma patients, the experience of the practitioner and the technical facilities of the clinic. Of course, repeating theoretical and practical trainings at regular intervals and increasing the practitioner experience can be presented as another recommendation.

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