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Original Article

Prognostic significance of radiological parameters in patients with acute pulmonary embolism: a retrospective observational study

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ABSTRACT

Aims: Acute pulmonary embolism (PE) is a significant global cause of mortality. This study aimed to evaluate the prognostic relationship between radiological parameters obtained from computed tomography pulmonary angiography (CTPA) in patients with acute PE. PE is an important cause of mortality all over the world. In this study, we aimed to investigate the prognostic correlation between radiological parameters in CTPA in patients with acute PE.

Methods: This study included 227 patients diagnosed with PE who underwent CTPA upon admission to a tertiary emergency department (ED) between January 1, 2019, and July 1, 2021. We compared 24 patients (10.6%) who died with 203 patients (89.4%) who survived. Clot burden was assessed by calculating the Qanadli score (Qscore) from CTPA images. The study evaluated several radiological parameters, including the Qanadli score (Qscore), main pulmonary artery (PA) diameter, ascending aorta (AO) diameter, AO/PA ratio, right ventricular (RV) to left ventricular (LV) diameter ratio (RV/LV ratio), and inferior vena cava (IVC) reflux. Short-term mortality within one month was tracked, and mortality rates were determined accordingly.

Results: The Qscore demonstrated limited accuracy in predicting mortality, with a sensitivity of 41% and a specificity of 44% (AUC: 0.415, 95% CI 0.312–0.518, p=0.175). IVC reflux was an indicator of RV dysfunction. Compared to surviving patients, those who died exhibited a lower incidence of IVC reflux, with a statistically significant difference (p=0.047). The RV/LV and AO/PA ratios did not show significant associations with mortality. In contrast, AO and PA diameters were found to be predictors of mortality, with sensitivities of 66% and 61%, and specificities of 66% and 62%, respectively (AO: AUC 0.683, 95% CI 0.562–0.804, p=0.03; PA: AUC 0.651, 95% CI 0.514–0.788, p=0.016).

Conclusion: Overall, the study concluded that the Qscore from CTPA was not a reliable prognostic indicator of mortality in PE patients admitted to the emergency department. In contrast, the diameters of the AO and PA emerged as potential predictors of mortality.

Keywords: Pulmonary embolism, qanadli score, radiologic parametres, mortality

INTRODUCTION

Pulmonary embolism (PE) is defined as embolic occlusion of the pulmonary arterial system. It is the third leading cause of cardiovascular death, following stroke and myocardial infarction.[1,2] Acute PE is estimated to cause more than 100,000 deaths annually worldwide.[3] The majority of deaths from acute PE, exceeding 70%, occur within the first few hours to several days after onset. Mortality rates are particularly elevated within the first hour.[4] Prompt recognition of acute PE is crucial for timely diagnosis and effective treatment. Although the clinical presentation of acute PE ranges from asymptomatic cases to sudden death, approximately 81% of patients present with dyspnea, 50% with hypoxia, and 70% with tachycardia.[5] Risk stratification in patients with acute PE is essential for guiding appropriate treatment and optimizing patient management.[6] In a recent study comparing auxiliary diagnostic methods in PE, a statistical significance was found between massive involvement of computed tomography pulmonary angiography (CTPA) and echocardiography results. It has been shown that echocardiography is preferable as an auxiliary radiological method in the diagnosis of massive PE.[7] However, CTPA is the preferred initial imaging test for patients with suspected PE due to its high sensitivity and specificity.[8] According to the European Society of Cardiology PE guidelines, CTPA is recommended for patients with a high suspicion of PE, even

in cases of hemodynamic instability. Additionally, in patients with low or intermediate clinical probability, a normal CTPA result effectively rules out the diagnosis of PE without the need for further investigation.[9] Several studies have explored the potential role of CTPA as a tool for assessing patient prognosis in cases of PE.[6,10,11] Previous studies have demonstrated that right heart dysfunction and PE identified on CTPA are potential prognostic markers.[12,13] The Qanadli score (Qscore) is one of the embolic obstruction indices in CTPA that has been shown in studies to have prognostic value. Clot burden can be used to assess the presence, location, and extent of arterial occlusion.[6,13] Patients with right ventricular (RV) dysfunction are known to have a high mortality rate, even if their hemodynamics are initially stable. RV dysfunction can be used as an indicator to predict the clinical outcomes of patients with acute PE.[6]

The objective of this study was to investigate the relationship between various multidetector CTPA parameters and short-term mortality in patients with acute PE.

METHODS

This study was designed as a retrospective observational study. Patients who presented to the emergency department of a tertiary care center between January 1, 2019, and July 1, 2021, and were diagnosed with PE via CTPA were included. A total of 2,913 patients who had previously undergone CTPA were analyzed. Ethical approval for this study was obtained from Akdeniz University Faculty of Medicine Clinical Researches Ethics Committee (Date: 20/04/2022, Decision No: 2022-KAEK-266). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The requirement for informed consent was waived due to the retrospective nature of the study. Of the initial patient pool, 268 were identified with a diagnosis of acute PE, with 41 excluded based on the exclusion criteria. Ultimately, 227 patients were included in the final analysis. Inclusion criteria consisted of patients aged 18 years or older and those with a confirmed diagnosis of PE via CTPA. Patients whose CTPA parameters could not be measured due to contrast media incompatibility, as well as those with undetermined treatment or outcome criteria, were excluded from the study (Figure 1). Socio-demographic information for all patients was obtained from the hospital's information-recording system. Each patient's Wells score was calculated using clinical data and the following criteria: clinical signs of deep venous thrombosis (DVT) (3 points), pulmonary thromboembolism (PTE) as the most likely diagnosis (3 points), heart rate >100/minute (1.5 points), recent surgery or immobilization within the last month (1.5 points), history of prior DVT or PTE (1.5 points), hemoptysis (1 point), and malignancy (1 point).

Measurements of Image on CTPA

All CTPA images were acquired in the emergency department using a Toshiba ACTIVION 16 (TSX-031A, Japan) multislice CT scanner. The images were initially reviewed by an emergency physician. In cases of indeterminate image interpretation, a final decision was made after discussion and review by an emergency physician with at least 10 years of experience in chest CT for pulmonary emergencies. PE-related parameters were measured and recorded on patient data forms. CTPA cross-sectional scans were processed and analyzed to assess right heart function. The following CT landmarks were assessed: the RV to left ventricular (LV) diameter ratio (RV/LV ratio), the ratio of the main pulmonary artery (PA) diameter to the ascending aorta (AO) diameter (AO/PA ratio), the diameter of the superior vena cava (SVC), and the morphology of the interventricular septum. The widest point of the heart on the axial CT images was used to measure the diameters, including the maximum diameters of the right and left ventricles on CTPA images. Transverse sections were measured between the inner aspect of the interventricular septum and the free wall of the ventricles, perpendicular to the long axis of the heart. The RV/LV ratio was then calculated. The diameters of the main pulmonary artery and the ascending aorta were measured from transverse sections adjacent to the main pulmonary artery and right pulmonary artery, respectively, followed by the calculation of the AO/PA ratio. The diameters of the SVC and azygos vein were measured at the point where the azygos vein joins the SVC on transverse CT images. All radiological parameters are illustrated in Figure 2. The convexity of the interventricular septum bowing towards the left ventricle was also examined. Reflux into the inferior vena cava (IVC) and the reflux of contrast material into the hepatic vessels were assessed using axial images.[6]

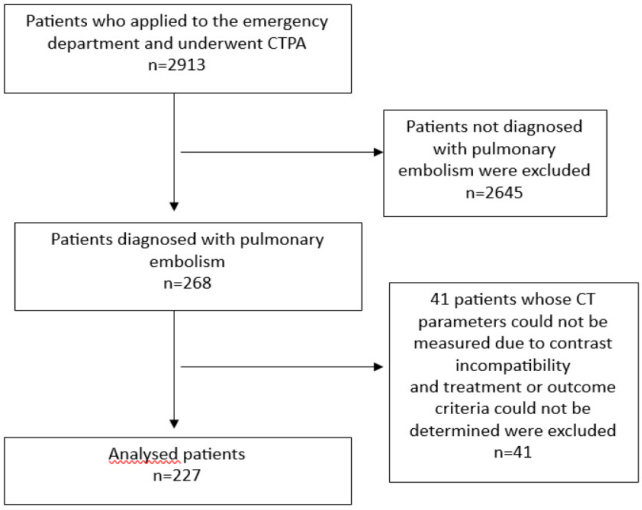

Figure 1. Patient flow chart

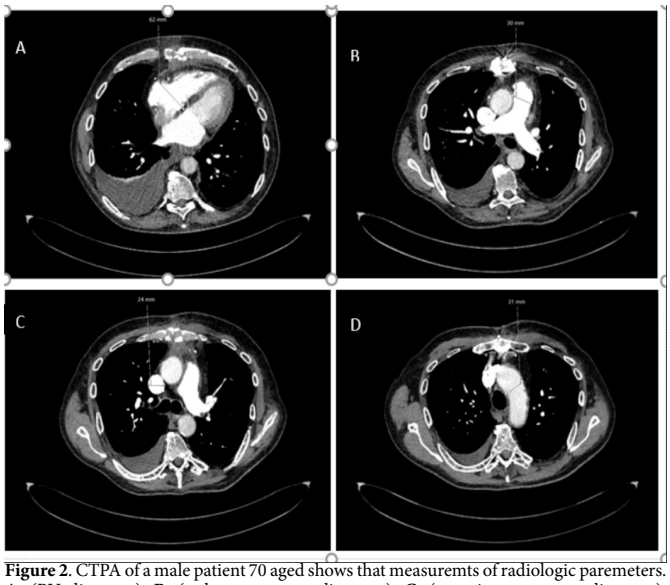

Figure 2. CTPA of a male patient 70 aged shows that measuremts of radiologic paremeters. **A.** (RV diameter), **B.** (pulmonary arter diameter), **C.** (superior vena cava diameter), **D.** (ascenden aorta diameter)

The Qanadli score was calculated using the formula (n×d)/40×100, where 'n' represents the number of segmental branches affected by the proximal thrombus in the pulmonary artery tree (ranging from 1 to 20), and 'd' denotes the degree of occlusion in the pulmonary artery (0 for no occlusion, 1 for partial occlusion, and 2 for complete occlusion).[12]

Primary Outcome

Short-term mortality was defined based on the 1-month mortality rate of the patients. To determine the 30-day mortality rate, the hospital records of all patients discharged within 30 days after PTCA were reviewed. When available, mortality information was gathered through telephone interviews with the patients. If personal interviews were not possible, mortality information was obtained directly from relatives. The patients were then classified into two groups: the survival group and the mortality group. The relationship between the measured parameters and mortality following PTCA was analyzed.

Statistical Analysis

Descriptive statistical analyses were performed using SPSS version 25.0 (Statistical Package for Social Sciences), with statistical significance set at $p<0.05$. Technical abbreviations were explained upon first use. The normality of the data was assessed using the Kolmogorov-Smirnov test. For continuous variables with a normal distribution, mean and standard deviation values were calculated, while median and interquartile ranges were used for non-parametric and non-normally distributed data. Chi-square and Fisher's exact tests were applied to compare categorical variables. Independent t-tests were used for normally distributed variables, and Mann-Whitney U tests for non-normally distributed variables. Logistic regression analysis was conducted to identify potential factors affecting mortality. Receiver operating characteristic (ROC) curves were analyzed, and the area under the curve (AUC) was calculated to determine optimal cut-off values for the AO and PA diameters, as well as Qscore.

RESULTS

The mean age of all patients was 59.73±16.76 years, with 127 (55.90%) being male. Dyspnea was the most common presenting complaint, reported by 155 patients (68.30%). Among the comorbid conditions examined, malignancy was present in 83 patients (36.60%). Short-term mortality analysis revealed that 24 patients (10.60%) died within one month. The mortality and survival groups were compared based on PE-related clinical parameters. The median respiratory rate was significantly higher in the mortality group compared to the survival group (30 vs. 24, $p<0.001$). The median oxygen saturation was significantly lower in the mortality group compared to the survival group (90 vs. 94, $p=0.039$). The main demographic and clinical characteristics of the patients are detailed in Table 1. This study investigated the correlation between radiological parameters and mortality in patients undergoing PTCA. The results indicated that the mean Qscore was significantly lower in the mortality group compared to the survival group (6.92±5.80 vs. 9.97±8.50, $p=0.027$). Additionally, the mortality group had significantly higher measurements of AO and PA diameters compared to the survival group (35.54±6.38 vs. 32.07±5.10, $p=0.002$, and 29.66±5.74 vs. 27.16±4.14, $p=0.049$, respectively). The incidence of IVC reflux, an indicator of RV dysfunction, was lower in the mortality group compared to the survival group, with a statistically significant difference between the two groups ($p=0.047$). The relationship between each measurement parameter in PTCA and PE and their impact on survival is presented in Table 2. Table 3 summarizes the results of the multivariate logistic regression analysis, which identified several independent factors influencing mortality, with respiratory rate showing statistical significance ($p=0.05$). Mortality cut-off values for AO diameter, PA diameter, and Qscore were calculated as 33.50, 28.50, and 5.50, respectively (Figure 3).

However, at this specific cut-off value, the Qscore did not predict mortality effectively, with a sensitivity of 41% and a specificity of 44% (AUC: 0.415, 95% CI 0.312–0.518, $p=0.175$). In contrast, the AO and PA diameters demonstrated better predictive value, with AO showing a sensitivity of 66% and specificity of 66%, and PA with a sensitivity of 61% and specificity of 62%. These reduced sensitivity and specificity values were linked to mortality (AO: AUC 0.683, 95% CI 0.562–0.804, $p=0.03$; PA: AUC 0.651, 95% CI 0.514–0.788, $p=0.016$).

Table 1. The relationship of demographic and clinical parameters with survival due to PE

Variables (n=24)	Mortality, n (%)	Survival (n=203)	p
Gender (female/male)	13 (54.2)/11 (45.8)	87 (42.9)/116 (57.1)	0.291
Age>70	12 (50)	58 (28.6)	0.320
Prior history of surgery	1 (4.2)	15 (7.4)	0.477
Prior histroy of PE	0 (0)	16 (7.9)	0.230
Malignancy	13 (54.2)	70 (34.5)	0.058
Heart failure	1 (4.2)	4 (2)	0.431
Chronic lung disease	4 (16.7)	32 (15.8)	0.550
Dyspnea	19 (79.2)	136 (67)	0.226
Palpitation	2 (8.3)	15 (7.4)	0.697
Wells score (IQR)	5.5 (4.12-5.87)	4.5 (4-5.5)	0.348
Chest pain	0 (0)	87 (100)	<0.001
Vital parameters, (IQR)			
SBP	126 (111-141)	126 (111-141)	0.330
DBP, (mean±SD)	81.21±13.062	77.77±14.403	0.237
Heart rate, beats/min;	110 (91-127)	107 (92-121)	0.784
Respiratory rate	30 (28-36)	24 (20-28)	<0.001
SpO_2	90 (81-95)	94 (88-97)	0.039

IQR: Interquartile range, * At admission, SpO_2: Blood oxygen saturation, SBP: Systolic blood pressure, PE :Pulmonary embolism , SD: Standart deviation

Table 2. The relationship between measurement parameters on CTPA and survival due to PE.

Variables	Mortality (n=24)	Survival (n=203)	p
*VCS	19.29±4.87	19.67±3.78	0.709
*Aort	35.54±6.38	32.07±5.10	0.002
*PA	29.66±5.74	27.16±4.14	0.049
*AO/PA	1.22±0.21	1.19±0.19	0.483
*LA	28.79±8.77	29.98±7.74	0.482
*RV	34.91±9.22	33.08±7.43	0.268
*LV	33.20±9.03	34.94±9.17	0.381
*RV/LV	1.12±0.40	1.01±0.38	0.183
*Qscore	6.92±5.80	9.97±8.50	0.027
βPresence of obstruction,	17 (70)	152 (74)	0.668
βSeptal bowing	1 (4.2)	9 (4.4)	0.714
βPresence of pleural effusion	11 (45.8)	66 (32.5)	0.192
βPresence of pulmonary infarction	3 (12.5)	61 (30)	0.092
βIVC reflux	4 (16.7)	10 (4.9)	0.047

*mean±SD, independent t test was used. β n (%), chi-squared and Fishear exact test was used. VCS: Superior vena cava diameter, AORT: Ascending aorta diameter (mm), PA: Pulmonary artery diameter (mm), AO/PA: Ascending aorta/pulmonary artery diameter LA: Left atrium diameter RV: Right ventricular diameter, RV/LV: Right ventricle/left ventricle diameter, Qscore: Qanadli score, IVC: Vena cava inferior, PE: Pulmonary embolism, CTPA: Computed tomographic pulmonary angiography

Table 3. Variables related to deaths at the end of the 1st month

Variables related to mortality	B±SE	OR	(%95 CI)	p
† AO	-0.070±0.049	0.933	(0.847-1.027)	0.156
† PA	-0.062±0.059	0.940	(0.837-1.055)	0.293
† Qanadli score	0.066±0.034	1.068	(0.999-1.141)	0.052
† Respiratory rate	-0.107±0.039	0.898	(0.833-0.969)	0.005
† IVF reflux	-0.291±0.723	0.748	(0.181-3.087)	0.688
† SpO_2	0.013±0.036	1.013	(0.945-1.086)	0.720

DSO:89
B±SE: Regression coefficient and standard error, **AO:** Ascending aorta diameter, **PA:** Pulmonary artery diameter **SpO_2:** Oxygene saturation

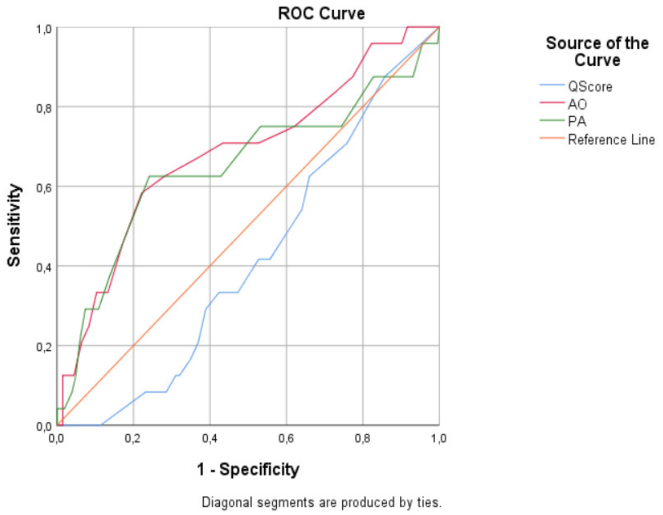

Figure 3. The prognostic accuracy of the ascending aorta (AO) diameter, main pulmonary artery (PA) and Qanadli score (Qscore) to predict mortality. The ROC curve shows that the area under the curve (AUC) revealed that the area of risk stratification, Qscore, AO, and PA diameters were 0.415 (95%CI: 0.312-0.518, p=0.175), 0.683 (95%CI: 0.562-0.804, p=0.003) and 0.651 (95%CI: 0.514-0.788,p=0.016), respectively.

DISCUSSION

This study examined the relationship between clinical and radiological parameters and short-term mortality in patients with acute PE in the emergency department. The findings revealed several simple yet useful parameters that could assist emergency physicians in the rapid and early management of acute PE, a condition with potentially fatal outcomes. Among the clinical parameters, patients with a fatal outcome were found to have lower oxygen saturation (SpO_2) and were tachypneic. Notably, respiratory rate emerged as an independent predictor of mortality. Our study demonstrated that although the Qscore, one of the radiological parameters, was associated with mortality, its low sensitivity and specificity limit its utility as a prognostic marker. The variability in the prognostic value of the Qscore reported in the literature suggests that no definitive cut-off value has been established for this score. In a study by Hefeda et al.[6] which included 32 patients with a 30-day mortality follow-up, a Qscore above 18 was identified as a predictor of mortality, though it showed a weak correlation. In a similar study by Wei-Ming Huang et al.[14] which included 201 patients with acute PE, a mean Qscore of 6.8±4.0 was not found to be significant in predicting mortality. In another study conducted by Cozzi et al.[10] including 780 acute PE patients in the emergency department, the mean Qscore was 17.6±12.7, and no prognostic relationship with short-term mortality was identified. In fact, the severity of PE is believed to be influenced not only by clot size and thrombus extension but also by the underlying cardiac condition.[15] These findings are consistent with numerous other studies and meta-analyses in the literature, and can be explained by the underlying pathophysiology.[16-18] Furthermore, the calculation of the Qanadli score, being a semi-quantitative technique, poses challenges due to its low reproducibility and high inter-observer variability. As a result, it may have limited prognostic value in the emergency department, particularly since it is often reported with a delay.

According to the ESC PE Guidelines, mild RV dilatation, defined as an RV/LV ratio above 0.9, is observed in over 50% of hemodynamically stable patients. Its clinical significance is minimal, and it is associated with low risk.[9] However, studies in the literature suggest that an RV to LV ratio greater than 1 is associated with poorer outcomes.[19-21] In our study, no significant correlation was found between the RV/LV ratio and mortality. Similar findings have been reported in the literature. For example, a study by Araoz et al.[22] found no significant association between an increased RV/LV ratio and poor 30-day outcomes. In contrast, our study found that the presence

of IVC reflux was significantly associated with mortality when compared to the survivor group, though it was not identified as an independent factor affecting mortality. Nonetheless, previous studies have demonstrated that both IVC reflux and an RV/LV ratio exceeding 1.2 are indicative of poor prognosis.[6] In a study conducted by Ghaye et al.[16] involving 82 patients, both the RV/LV ratio and the presence of IVC reflux were significantly different between the mortality and survival groups. Additionally, this study demonstrates that the diameters of the AO and PA, two radiological parameters associated with PE, may predict mortality above specific thresholds. There is limited literature on the prognostic correlation of radiological parameters in PE. Ghaye et al.[16] conducted a study comparing the relationship between AO and PA diameters in CTPA with respect to mortality predictors in the mortality and survival groups. In the mortality group, the mean diameters of the aorta and pulmonary artery were 36.1±4.5 mm and 32.2±3.8 mm, respectively. In contrast, the ascending aorta diameter was significantly greater in the survival group, though it has been shown to predict mortality with low sensitivity and specificity. However, no significant relationship between PA diameter and mortality could be demonstrated.[16]

Limitations

The first limitation of this study is its single-center, retrospective design. Secondly, the challenges associated with calculating the Qscore may have influenced the results. We recommend that future researchers conduct large cohort studies to enhance clinical efficiency by minimizing operator errors through the use of various semi-automated and artificial intelligence software.

CONCLUSION

In conclusion, this study demonstrated that the Qscore is not a reliable prognostic parameter for predicting mortality in PE patients in the emergency department. In contrast, the diameters of the AO and PA are associated with mortality, albeit with low sensitivity and specificity.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval for this study was obtained from Akdeniz University Faculty of Medicine Clinical Researches Ethics Committee (Date: 20/04/2022, Decision No: 2022-KAEK-266).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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An oxidative stress biomarker in acute kidney injury: intra-erythrocyte glutathione

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ABSTRACT

Aims: The aim of the study is to determine intra-erythrocyte glutathione, which is thought to be a more specific and sensitive biomarker apart from the biomarkers traditionally used in the diagnosis of acute kidney injury (AKI), which causes high mortality and morbidity, and is also an oxidative stress marker.

Methods: The study was conducted with 51 volunteers who developed AKI and were diagnosed in the emergency department, and 51 volunteers who applied to the emergency department green triage coded area and did not have AKI. Both groups consisted of individuals between the ages of 18-65, who had a history of diabetes mellitus, who were pregnant, and those who applied to the hospital due to trauma were not included in the study. Demographic characteristics, complete blood count tests at admission, biochemical tests and intra-erythrocyte glutathione and its derivatives were compared in the patient and control groups.

Results: Gender distribution was equal between the groups in the study (p=1,000). Serum urea and serum levels were found to be higher in the patient group compared to the control group. Total glutathione and glutathione disulfide amounts were found to be higher in the patient group, and the native glutathione amount was lower than the control group (p<0.001).

Conclusion: With the results obtained in our study, intra-erythrocyte glutathione and its derivatives in acute kidney injury can be used for diagnostic purposes, since more standardized results can be obtained in AKI than conventional markers. The available data should be supported by more comprehensive studies and considering the limitations of our study.

Keywords: AKI, glutathione, oxidativestress

INTRODUCTION

Acute kidney injury (AKI), defined as a reduction in the kidney's capacity for excretion and filtration over days or weeks, results in the accumulation of waste products that are normally cleared by the kidneys. AKI can manifest asymptomatically, observable only through changes in laboratory parameters, or present as more severe clinical conditions involving alterations in circulating volume, electrolyte disturbances, and/or acid-base imbalance, leading to high morbidity and mortality.[1,2]

In emergency settings, AKI diagnosis spans a wide spectrum, from asymptomatic clinical presentations to mild symptoms such as nausea, vomiting, fatigue, and loss of appetite, and more severe conditions such as uremic encephalopathy, which can cause loss of consciousness.[2]

Serum creatinine, a traditional laboratory marker used in the diagnosis and early treatment of AKI, has been found to lack sufficient sensitivity and specificity due to variations in factors such as age, sex, race, and muscle mass. This has prompted the search for novel biomarkers. In critical illness, the most commonly measured markers of oxidative stress include isoprostanes, hydroxynonenal, lipid peroxides, chlorinated compounds, oxidized glutathione, nitrated and oxidized proteins, and malondialdehyde identified as thiobarbituric acid-reactive substances.[3]

This study aimed to assess intracellular erythrocyte glutathione, an oxidative stress biomarker, as a potentially more specific and sensitive biomarker compared to traditional markers in the diagnosis of AKI, which is associated with high mortality and morbidity.

METHODS

The study was carried out with the permission of Ethical Committe Ankara Bilkent City Hospital Clinical Researches

Ethics Committee No. 1 (Date: 01.12.2021, Decision No: 2173). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study was conducted prospectively as an observational cross-sectional analysis of patients presenting to the Emergency Medicine Clinic at Ankara Bilkent City Hospital.

The study included patients aged 18-65 diagnosed with AKI as the case group and volunteers aged 18-65 presenting to the green triage zone of the emergency department without AKI as the control group. Patients with acute infections, diabetes mellitus, pregnancy, or trauma-related emergency department visits were excluded from both groups.

The diagnosis of AKI was established based on at least a 1.5-fold increase in the patient's serum creatinine level from the baseline, a reduction in glomerular filtration rate (GFR) by at least 25%, and/or a urine output less than 0.5 ml/kg/hour or anuria.

A total of 51 patients meeting the inclusion criteria for AKI and 51 volunteers without AKI were included in the study as the control group.

Statistical Analysis

All analysis was performed using IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY: IBM Corp). The normality of continuous numerical variables was assessed using the Shapiro-Wilk test. Data with normal distribution were presented as mean±standard deviation and 95% confidence intervals, while data without normal distribution were presented as median (min-max).

The Mann-Whitney U test was used for the comparison of non-normally distributed variables between two independent groups, and the Independent Samples t-test was applied for normally distributed variables. Comparisons of categorical variable ratios were performed using Pearson Chi-Square or Fisher's Exact tests, as appropriate.

Receiver operating characteristics (ROC) analysis was used to determine diagnostic predictive values such as sensitivity and specificity. A p-value <0.05 was considered statistically significant.

RESULTS

Our study included a total of 51 patients diagnosed with AKI and 51 individuals without AKI as the control group. The mean age of the patient group was 59 years, consisting of 25 male and 26 female participants, whereas the control group had a mean age of 43 years, also consisting of 25 male and 26 female participants.

The study groups were compared using biochemical blood tests. The mean blood urea levels were 121 mg/dl in the patient group and 36 mg/dl in the control group, demonstrating a statistically significant difference (p<0.001). For serum creatinine levels, the mean value was 3.1 mg/dl in the patient group and 0.8 mg/dl in the control group, also revealing a statistically significant difference (p<0.001). The glomerular filtration rate (GFR) was compared between the groups, with the mean GFR being 24 ml/min/1.73 m^2 in the patient group and 100 ml/min/1.73 m^2 in the control group, showing a statistically significant difference (p<0.001) (Table 1).

The comparison of native glutathione levels between the groups showed a mean value of 601.639 µmol/L in the patient group and 685.447 µmol/L in the control group, with a statistically significant difference (p<0.001). The total glutathione levels were also significantly different, with a mean value of 1766.060 µmol/L in the patient group and 1413.104 µmol/L in the control group (p<0.001). Furthermore, the mean disulfide level was 44.480 µmol/L in the patient group and 31.961 µmol/L in the control group, indicating a statistically significant difference (p<0.001) (Table 2).

In comparisons of glutathione levels normalized to hemoglobin (Hgb), the mean total glutathione per Hgb was calculated as 133.353 µmol/L in the patient group and 124.376 µmol/L in the control group, with a statistically significant difference (p<0.001). The native glutathione per Hgb was 44.394 µmol/L in the patient group and 60.454 µmol/L in the control group, again showing a statistically significant difference (p<0.001). The mean disulfide per Hgb was 44.480 µmol/L in the patient group and 31.961 µmol/L in the control group, with a statistically significant difference (p<0.001) (Table 3).

Table 1. Biochemical blood analysis of patient and control groups

	Groups										
	Control					Patient					
	Mean	SD	Med	%25	%75	Mean	SD	Med	%25	%75	p-value
Urea	36	14	34	28	44	121	65	103	77	139	<0.001*
Creatinine	0.8	0.2	0.8	0.7	1.0	3.1	1.9	2.4	1.9	3.4	<0.001*
GFR	100	24	99	86	119	24	13	23	15	31	<0.001*

*Mann Whitney-U test, **Independent Samples-t test, SD: Standard deviation, GFR: Glomerular filtration rate

Table 2. Total glutathione, native glutathione, and disulfide analysis in patient and control groups

	Groups										
	Control					Patient					
	Mean	SD	Med	%25	%75	Mean	SD	Med	%25	%75	p-value
Native glutathione	685.447	253.891	674.880	538.017	747.918	601.639	210.257	576.870	456.960	719.460	<0.001*
Total glutathione	1413.104	314.131	1347.005	1198.131	1659.711	1766.060	245.268	1697.250	1599.693	1842.020	<0.001*
Disulfide	363.828	140.299	341.084	260.913	451.096	582.211	169.923	583.934	509.846	670.025	<0.001**

*Mann Whitney-U test, **Independent Samples-t test, SD: Standard deviation

Table 3. Glutathione and disulfide levels per hemoglobin in patient and control groups

	Groups										
	Control					Patient					
	Mean	SD	Med	%25	%75	Mean	SD	Med	%25	%75	p-value
Native Glutathione per Hgb	60.454	22.871	57.403	44.393	72.380	44.394	13.680	42.417	33.315	52.364	<0.001**
Total Glutathione per Hgb	124.376	32.685	119.762	98.512	146.196	133.353	28.417	126.637	111.394	152.194	<0.001*
Disulfide per Hgb	31.961	13.573	27.986	22.079	41.944	44.480	16.238	42.610	34.071	53.821	<0.001*

*Mann Whitney-U test, **Independent samples-t test, SD: Standard deviation, Hgb: Hemoglobin

DISCUSSION

AKI has an incidence rate of 18% among hospitalized patients and 0.25% in the general population. While the mortality rate for uncomplicated AKI is 5-10%, this figure can rise to 40-90% in intensive care settings, highlighting AKI as a significant public health problem.[3,4]

In our study, we prospectively analyzed data from 51 patients diagnosed with AKI or chronic kidney disease exacerbated by AKI who presented to the Emergency Department of Ankara Bilkent City Hospital, along with 51 patients without AKI confirmed by laboratory tests.

The gender distribution in both the patient and control groups was equal. The mean age of the patient group was 51 years, while the control group had a mean age of 43 years. The higher mean age of the patient group may be attributed to the selection of the control group from the green triage zone.

Serum creatinine, traditionally used in the diagnosis and early treatment of AKI, has been found to lack adequate sensitivity and specificity due to variations related to age, gender, race, and muscle mass. Consequently, alternative biomarkers have been explored. Commonly measured oxidative stress markers in critical illness include isoprostanes, hydroxynonenal, lipid peroxides, chlorinated compounds, oxidized glutathione, nitrated and oxidized proteins, and malondialdehyde, a thiobarbituric acid-reactive substance.[3]

Glutathione, the most abundant intracellular antioxidant molecule, is synthesized in all eukaryotic cells, primarily in the liver. It plays a critical role in scavenging free radicals, reducing oxidized products, and protecting biomolecules from the harmful effects of reactive oxygen species.[5-7] Conditions that result in cellular stress disrupt protein stabilization and cause lipid peroxidation, leading to the formation of reactive oxygen species. Due to its high metabolic activity, the kidney is one of the organs most affected by oxidative stress.[8]

An animal study demonstrated that renal glutathione (GSH) levels decreased following ischemic injury. Furthermore, administration of N-acetylcysteine increased GSH levels and alleviated AKI.[9]

In our study, oxidative stress was evaluated by measuring total glutathione, native glutathione, and glutathione disulfide levels. Results indicated that the mean disulfide and total glutathione levels were statistically higher in the patient group compared to the control group, whereas the native glutathione levels were significantly higher in the control group than in the patient group.

A study by Otal et al.[10] in Ankara in 2018, involving 42 patients diagnosed with AKI and treated with hemodialysis in the emergency department, along with 45 controls, reported that native glutathione, disulfide, and total glutathione levels were higher in the control group. However, the ratio of disulfide to total glutathione and native glutathione was found to increase in favor of disulfide in AKI patients. The same study demonstrated that these ratios decreased after hemodialysis compared to pre-dialysis levels.

Similarly, a study conducted by Ayar et al.[11] in Ankara between 2015 and 2017, involving 20 pediatric patients with AKI and 39 healthy controls, showed that the median total glutathione and native glutathione levels were significantly lower in the AKI group compared to the control group.

When comparing the results of our study to the literature, it is evident that our findings support previous research.

CONCLUSION

AKI is a clinical condition diagnosed in emergency departments and associated with high morbidity and mortality. Our findings demonstrate that native glutathione levels decrease while glutathione disulfide levels increase in AKI. These parameters may serve as potential biomarkers for AKI, particularly when serum creatinine levels, influenced by various factors, are insufficient for diagnosis. However, considering the limitations of our study, further research with larger sample sizes is required.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethical Committe Ankara Bilkent City Hospital Clinical Researches Ethics Committee No. 1 (Date: 01.12.2021, Decision No: 2173).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Management of hypertensive emergencies in the emergency department: presenting complaints and outcomes

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ABSTRACT

Aims: This study aimed to evaluate the clinical features, management strategies, and outcomes of patients presenting with hypertensive conditions to the emergency department (ED). The findings aim to contribute to the epidemiological profiling of hypertensive emergencies and enhance management practices in EDs.

Methods: A retrospective, observational study was conducted at Ankara Etlik City Hospital ED between September 16 and September 23, 2024. Patients aged ≥18 years with a blood pressure (BP) ≥140/90 mmHg were included. Pregnant, postpartum, or breastfeeding women and those with incomplete data were excluded. Data were collected on demographics, clinical features, comorbidities, diagnostics, treatments, and outcomes. Statistical analysis involved descriptive and comparative methods, with significance set at $p<0.05$.

Results: The study included 111 patients (61 females, 55%; 50 males, 45%) with a mean age of 56.36 years. Among them, 10 patients (9.9%) required hospitalization, while 100 (90.1%) were discharged. The mean systolic and diastolic BP were 163.7 mmHg and 89.3 mmHg, respectively. Common presenting symptoms included headache (14.4%), chest pain (5.5%), and hematuria (1.8%), while 10.8% were asymptomatic. Hospitalization rates were significantly higher in female patients ($p=0.012$). However, no significant associations were found between BP values, diagnostic interventions, or treatments and hospitalization outcomes.

Conclusion: The study highlights the challenges in managing hypertensive patients in EDs, especially those without target organ damage. While female patients showed higher hospitalization rates, factors like BP levels and diagnostic interventions did not correlate with outcomes. Further multicenter and prospective studies are needed to explore these findings and develop individualized, evidence-based approaches for hypertensive patient care in EDs.

Keywords: Hypertension, emergency department, hypertensive crisis, management

INTRODUCTION

Hypertension is a leading modifiable risk factor for vascular diseases, including cardiovascular and cerebrovascular conditions. Despite its widespread prevalence, many individuals with hypertension remain undiagnosed, and among those diagnosed, blood pressure (BP) control is often suboptimal.[1,2] The existing literature provides detailed recommendations and evidence for managing hypertension in outpatient settings and offers clear guidance for patients presenting to the emergency department (ED) with hypertensive crises. However, there is limited guidance for managing patients who present to the ED with significantly elevated BP without a hypertensive emergency.[3,4] Studies indicate that nearly half of patients presenting to the ED exhibit hypertension, regardless of the presence or absence of new or worsening target organ damage.[5]

The management of hypertension in the ED can be categorized into two main groups: asymptomatic severe hypertension and significantly elevated BP with evidence of new or worsening target organ damage. Management strategies for cases involving target organ damage are more clearly defined and supported by higher-quality evidence.[6] However, there is currently no consensus on the optimal treatment strategies for patients presenting to the ED with hypertension but without target organ damage.[7] Moreover, aggressive treatment strategies may impair perfusion and negatively impact patient outcomes. Approximately one-third of patients receiving intravenous antihypertensive therapy are reportedly treated inappropriately.[8] These findings highlight the need for further research to improve ED practices in this area.

In this study, we aimed to evaluate the clinical characteristics, management strategies, and outcomes of patients presenting to the ED with hypertensive conditions. We hope the data obtained will contribute to defining the epidemiological profile of hypertensive emergencies and improving the management of these cases in ED settings.

METHODS

Study Design

This study was designed as a retrospective and observational analysis. It included patients presenting with elevated blood pressure to the Emergency Department (ED) of Ankara Bilkent City Hospital between September 16, 2024, and September 23, 2024. Ethical approval for this study was obtained from the Ankara Etlik City Hospital Ethics Committee (Date: 25/09/2024, Decision No: AEŞ-BADEK-2024-888). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Participants

Patients aged 18 years and older with a blood pressure of 140/90 mmHg or higher at the time of presentation were included in the study. Pregnant, postpartum, or breastfeeding women, as well as patients with incomplete data, were excluded. Both male and female patients were included to form a heterogeneous population.

Data Collection

Patient records were screened using the Hospital Information Management System (HIMS) with the keyword "hypertension." Eligible patients meeting the inclusion criteria were identified. Data were collected on demographic characteristics, clinical features, comorbidities, diagnostic tests performed, and treatment outcomes.

Inclusion Criteria

- Age ≥18 years
- Presentation to the ED within the specified dates
- Blood pressure at presentation of at least 140/90 mmHg

Exclusion Criteria

- Pregnant, postpartum, or breastfeeding women
- Patients with incomplete data

Evaluation Parameters

- **Demographic characteristics:** Age, gender
- **Clinical features and physical examination findings:** Presenting complaints
- **Comorbidities:** Pre-existing conditions and medications used
- **Diagnostic tests:** ECG, computed tomography, blood tests
- **Outcomes:** Discharge, hospitalization

Statistical Analysis

The collected data were analyzed using descriptive and comparative statistical methods. Categorical variables were presented as frequencies and percentages, while numerical variables were expressed as mean±standard deviation for normally distributed data, or median (min–max) for non-normally distributed data. Normality was assessed using the Kolmogorov-Smirnov test. Comparisons were conducted using Chi-square and Mann-Whitney U tests. ROC analysis was performed to determine optimal cut-off points, with $p<0.05$ considered statistically significant. All analyses were performed using IBM SPSS version 25.0.

RESULTS

Our study included a total of 111 patients, of whom 61 were female and 50 were male. The mean age of the patients was 56.36 years. By the end of the follow-up period, 10 patients (9.9%) were hospitalized, while 100 patients (90.1%) were discharged. The mean systolic blood pressure (SBP) of the patients at presentation was 163.7 mmHg, and the mean diastolic blood pressure (DBP) was 89.3 mmHg.

Among the patients, 12 (10.8%) presented to the emergency department (ED) with elevated blood pressure without any symptoms, 16 (14.4%) had headaches, 6 (5.5%) experienced chest pain, 2 (1.8%) had hematuria, and 75 (67.5%) presented with symptoms not suggestive of target organ damage (Table 1).

Table 1. Demographic and clinical characteristics of patients presenting to the emergency department with hypertension

Age (mean) years		56.36
Sex n (%)	Female	61 (55%)
	Male	50 (45%)
Hospitalization n (%)	Yes	11 (9.9%)
	No	100 (90.1%)
Blood pressure (mean) n (%)	Systolic blood pressure	163.7 mmHg
	Diastolic blood pressure	89.3 mmHg
Admission symptom n (%)	Asymptomatic	12 (10.8%)
	Headache	16 (14.4%)
	Chest pain	6 (5.5%)
	Hematuria	2 (1.8%)
	Other symptoms	75 (67.5%)

The mean age of discharged patients was 56.2±15.1 years, while the mean age of hospitalized patients was 57.6±22.0 years, with no statistically significant difference between the groups (p=0.850). Regarding the gender distribution of hospitalizations, 90% of hospitalized patients were female, whereas 51% of discharged patients were female. Women had a significantly higher hospitalization rate compared to men (p=0.012).

The median systolic blood pressure (SBP) was 160.50 mmHg in the discharged group and 160.0 mmHg in the hospitalized group, with no significant difference observed between the groups (p=0.407). Similarly, the diastolic blood pressure (DBP) was 89.4±13.8 mmHg in the discharged group and 88.3±12.4 mmHg in the hospitalized group, with no significant difference (p=0.810, 95% CI: -7.55 to 9.65).

In terms of clinical assessments, there was no significant difference between the groups in the following parameters:

- Positive physical examination findings (8% vs. 9.1%, p=1.000)
- Laboratory tests ordered (62.0% vs. 63.6%, p=1.000)
- Chest X-rays obtained (28.0% vs. 36.4%, p=0.727)
- Brain CT scans performed (14.0% vs. 0.0%, p=0.353)
- ECG performed (28.0% vs. 9.1%, p=0.283)

Similarly, no significant difference was found regarding whether any treatment was administered in the ED between discharged and hospitalized patients (p=0.332) (Table 2).

Table 2. Factors affecting hospitalization in patients presenting to the ED with hypertension

Variables		Discharge n (%)	Hospitalization n (%)	p-value/(95 CI%)
Age		56.2±15.1	57.6±22.0	0.850/(-16.25 - 13.62)*
Gender	Female	51 (51.0)	10 (90.9)	**0.012****
	Male	49 (49.0)	1 (9.1)	
SBP (mmHg)		160.50 (152.2-176.0)	160.0 (146.0-167.0)	0.407***
DBP (mmHg)		89.4±13.8	88.3±12.4	0.810/(-7.55 – 9.65)*
Positive physical findings		8 (8)	1 (9.1)	1.000**
Laboratory testing ordered		62 (62.0)	7 (63.6)	1.000**
X-Ray		28 (28.0)	4(36.4)	0.727**
Brain CT		14 (14.0)	0 (0.0)	0.353**
ECG performed		28 (28.0)	1 (9.1)	0.283**
Any treatment administered		63 (54.5)	5 (45.5)	0.332**

*Independent sample t test, Mean±SD, **Fisher exact test, n(%), ***Mann-Whitney U test, Median (25-75%), SBP: Systolic blood pressure, DBP: Diastolic blood pressure, CT: Computed tomography, ECG: Electrocardiography

DISCUSSION

In our study, we retrospectively examined the demographic and clinical characteristics as well as the management strategies of patients presenting to the ED with hypertension. Hypertension is a prevalent condition in the general population and is a significant modifiable risk factor for severe complications, including cardiovascular and cerebrovascular diseases. Despite its prevalence, no clear consensus exists regarding the management of patients presenting to the ED with elevated blood pressure but without target organ damage. Our findings demonstrated that factors such as age, blood pressure values, laboratory results, and imaging studies were not associated with hospitalization outcomes in patients presenting with non-emergency hypertension. However, gender was significantly associated with hospitalization rates, with female patients being more likely to be hospitalized, highlighting the need for further investigation in this area.

The mean age of our study population was 56 years, with 55% being female. A review of the literature shows that the age distribution in similar studies varies between 50 and 75 years.[9] This variation could be attributed to differences in preventive healthcare strategies in different countries. For instance, the mean age of patients presenting with hypertension to the ED was found to be 76 years in a study conducted in France, compared to 49 years in a similar study in Burkina Faso.[10,11] Unlike most studies focusing on hypertensive crises (SBP >180 mmHg, DBP >120 mmHg), our study included patients with a hypertension diagnosis based on the Joint National Committee (JNC 8) guidelines (BP >140/90 mmHg).[12] This inclusion criterion may have excluded younger patients with transient or secondary causes of elevated blood pressure (e.g., pain), potentially contributing to the lower mean age observed in our study.

Our findings also revealed a higher proportion of female patients. Similar trends have been reported in studies by Pierin et al.[13] (57%), Mandi et al.[10] (37%), and Guiga et al.[11] (55%). Pinna et al.[14] also reported comparable results, demonstrating that men with hypertensive crises were less likely to be aware of their hypertension diagnosis, used medications less regularly, and were at higher risk for adverse outcomes. Women were found to have higher mean SBP and age. Other studies also emphasize the predominance of female patients presenting to the ED with hypertensive crises.[9,15] However, no evidence in the existing literature indicates worse outcomes or higher hospitalization rates among female patients. While our gender-related findings align with the literature regarding proportions, the differences in hospitalization and clinical follow-up outcomes may stem from our study's limited sample size and timeframe. The exclusion of patients with incomplete data and the short study period may limit the generalizability of our results.

Regarding presenting symptoms, most patients were found to have elevated blood pressure incidentally during their ED visit for other reasons, while some presented solely for asymptomatic hypertension. Symptomatic cases predominantly reported neurological or cardiac symptoms. We believe patient education could help reduce unnecessary ED visits for incidental hypertension. The literature supports the role of patient education in improving outcomes and reducing unnecessary hospital visits.[16,17] Studies on hypertensive crises show results consistent with our findings.[14,15,18] The primary distinction of our study from existing literature is the inclusion of all cases of elevated blood pressure, not just hypertensive crises.

Limitations

Our study has several limitations. First, as a retrospective analysis, it is inherently susceptible to selection and information bias due to incomplete or missing data. Patients with incomplete records were excluded to minimize this, which may have affected the generalizability of our findings. Second, the limited sample size and short timeframe may not fully represent the broader population of hypertensive patients presenting to EDs. Lastly, confounding factors such as comorbidities, medication adherence, and socioeconomic status were not comprehensively analyzed, which may have influenced the observed gender differences in hospitalization rates.

CONCLUSION

This study underscores the complexity of managing hypertensive patients in the ED, particularly in the absence of target organ damage. By broadening the inclusion criteria to encompass all hypertensive presentations, our study contributes to the literature and emphasizes the importance of individualized, evidence-based approaches for hypertensive patients in emergency care. Further prospective and multicenter studies are recommended to validate these findings and explore underlying gender-specific disparities.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval for this study was obtained from the Ankara Bilkent City Hospital Ethics Committee (Date: 25/09/2024, Decision No: AEŞ-BADEK-2024-888).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

Measuring emergency medicine physicians' knowledge levels about their legal responsibilities in interventional procedures: a cross-sectional study

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ABSTRACT

Aims: As the number of emergency department (ED) patients increases, medical-legal lawsuits also increase. Doctors must have medicolegal knowledge. Interventional procedures are frequently performed in EDs. Our study aims to evaluate emergency physicians' knowledge, attitudes, and behaviors regarding their medical-legal responsibilities regarding frequently performed interventional procedures.

Methods: This is a prospective questionnaire study in a single center. The questionnaires were answered via Google® Form. Participants were asked questions about their demographic characteristics and education levels. The study was applied to physicians working in the ED from October 10 to 20, 2023.

Results: A questionnaire was sent to 155 physicians. One hundred forty-three responded to the questionnaire. Most participants (88%) were found to have received training on interventional procedures performed in the ED, but their level of knowledge about their legal responsibilities during interventional procedures was lower (18.2%). It was observed that specialist physicians and faculty members had better awareness of interventional procedures in the Postgraduate Emergency Medicine (PEM) training program than assistant physicians ($p<0.001$). As age and professional experience increased, the training received and awareness levels increased ($p<0.001$).

Conclusion: Specialists and faculty members have higher legal knowledge, while assistant physicians face difficulties in fulfilling their legal responsibilities. Findings highlight the need for early legal education in emergency medicine for their legal responsibilities in invasive procedures.

Keywords: Interventional procedures, legal responsibility, emergency department

INTRODUCTION

Every patient who comes to the emergency department (ED) tends to perceive their situation as urgent and assume that it is a top priority. While emergency service applications in Turkey were approximately 92 million in 2016, they were approximately 130 million in 2021.[1] As EDs fill daily, it can be difficult for doctors to gauge the urgency of each case accurately. Although ED physicians are responsible for diagnosing and treating patients quickly, without error and harm, they must also comply with their medical and legal obligations and ensure compliance with legal regulations.[2] Malpractice has long been a topic of interest to ED physicians and the legal community. According to a data analysis containing records of 40,916 closed malpractice cases covering all US states from 1991 to 2005, Emergency medicine was the 15th most likely to be involved in litigation among 25 medical specialties.[3] Studies have associated emergency medicine with a moderate risk of malpractice, with litigation frequency approximately equal to the average for all specialties and fewer than average physician claims resulting in compensation.[3,4] Malpractice cases are quite stressful and involve long stages.[5]

Physicians working in ED have legal responsibility in their practices, especially when making urgent decisions that may affect patients' lives. All healthcare professionals are expected to adhere to established standards of care, clinical guidelines,

and protocols.[6] They must also comply with current standard practices in line with legal regulations and malpractice rules. Several key principles associated with patient safety and positive treatment outcomes include obtaining informed consent from patients, effective provider-patient communication, and maintaining accurate and comprehensive medical records.[7,8]

With the increasing number of malpractice cases in medical law, all physicians must understand their legal responsibilities and rights and act accordingly. This study aims to evaluate the knowledge, attitudes, and behaviors of physicians working in EDs regarding their medical and legal responsibilities while performing interventional procedures.

METHODS

Ethics

The study was conducted between October 1-20, 2023, among assistant physicians, specialist physicians, and faculty members working in a tertiary hospital's ED. The hospital handles approximately 2000 ED patients daily, including referrals from surrounding areas, with full surgical and interventional capabilities. Ethical approval was obtained from the Ankara Bilkent City Hospital No. 1 Clinical Researches Ethics Committee (Date: 12/09/2023, Decision No: E1-23-4013). Participants were informed about the study and assured confidentiality, and consent was collected through an online form integrated with a Google® Form system. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Participant Selection

There were 155 physicians working in this hospital's ED. Physicians working in the ED were asked to participate in the Google survey form online, and an informed consent form was sent online. Physicians working in the ED (assistant physicians, specialists, faculty members) who agreed to participate in the study filled out the survey form. Participants were classified according to academic title, PEM education, and professional experience.

Data Collection

In the survey-based study, answers to questions other than the participants' demographic data were classified as multiple options. The authors created the questions after reviewing the literature. The language of the survey questions is Turkish.
The questionnaire items were categorized as follows:

- Information on interventional procedures
- Previous administrative and legal actions
- Understanding of complications vs. malpractice
- Views on informed consent
- Informed consent form effectiveness
- Safe storage of consent forms
- Knowledge of PEM training
- Legal responsibility awareness

Statistical Analysis

Data analysis was performed using IBM SPSS version 23.0. Continuous variables are presented as mean±standard deviation (mean±sd), median, and range, while categorical variables are shown as numbers and percentages. The Shapiro-Wilk test (Kolmogorov-Smirnov test when n>50) assessed normality. The independent sample t-test was used to compare two independent groups when normality and variance homogeneity (evaluated with the Levene test) were met; otherwise, the Mann-Whitney U test was applied. Comparisons of more than two groups were done using the Kruskal-Wallis test, followed by the Dunn test with Bonferroni correction if significant. Categorical variables were compared using Pearson's chi-square or Fisher's Exact tests as needed. A p-value <0.05 was considered statistically significant.

RESULTS

There were 155 physicians working in this hospital's ED. One hundred forty-three of these physicians agreed to participate in the study and were included in it. A total of 143 participants, 84.6% of whom were assistant physicians.

Demographic Data

The study participants were predominantly male (59.4%). The average age was 30.9±6.5 years, ranging from 24 to 32, and the average professional experience was 5.9±6.3 years. Most of the participants (84.6%) were assistant physicians, 7.7% were specialist physicians, and 7.7% were faculty members. Regarding their specialization training, 44.8% of participants trained at city hospitals, 39.2% at training and research hospitals, and 16.1% at university hospitals (Table 1).

Tablo 1. Socio-demographic characteristics of the participants

	n	%
Age (years) (n=142)		
Mean±SD*	30.9±6.5	
Median (min-max)	29 (24-58)	
Gender (n=143)		
Female	58	40.6
Male	85	59.4
Academic title (n=143)		
Assistant physician	121	84.6
Specialist	11	7.7
Faculty member	11	7.7
The institution where specialization training was received (n=143)		
University Hospital	23	16.1
Training and Research Hospital	56	39.2
City Hospital	64	44.8
Professional experience (years) (n=142)		
Mean±SD*	5.9±6.3	
Median (min-max)	4 (1-35)	

SD: Standart deviation, Min-max: Minimum-maximum

Answers of the Participants

Table 2 shows the questionnaire and the response rates given by the participants. Most participants (88%) stated they received training on interventional procedures in the ED. However, the rate of those who thought they had sufficient knowledge about the legal responsibilities, obligations, and legal regulations regarding interventional procedures was 18.2%. The rate of those who believed they had enough knowledge about the distinction between complications and malpractice was 40.1%. The rate of those who said that the concepts of complication and malpractice cause them to hesitate when performing interventional procedures on patients was 31.5%.

Tablo 2. Table of questionnaire-based questions and answers given by participants and their rates

	Answers	n	%
Have you received training on interventional procedures performed in the emergency department? (n=142)	Yes	125	88.0
Where did you receive in-service training regarding interventional procedures performed in the emergency department? (n=143)	Workshop	6	4.2
	Symposium	18	12.6
	Course	56	39.2
	Congress	38	26.6
	Education received at the institution where you work	120	83.9
Do you know enough about your legal responsibilities, obligations, and legal regulations regarding interventional procedures performed in the emergency department? (n=143)	Yes	26	18.2
Do you think compulsory liability insurance for malpractice (related to medical malpractice) protects the physician in a legal situation in interventional procedures performed in the emergency department? (n=142)	Yes	19	13.4
Do you think you know enough about the distinction between complications and malpractice? (n=142)	Yes	57	40.1
Do the concepts of complication malpractice cause you to act hesitantly when performing interventional procedures on the patient? (n=143)	Yes	45	31.5
Do you obtain informed consent before invasive procedures in the emergency department? (n=143)	I take before every ıntervention	24	16.8
	Sometimes	112	78.3
	Never	7	4.9
How do you obtain informed consent in the emergency department? (n=141)	Verbal	26	18.4
	Written	115	81.6
Do you believe that informed consent protects you from legal proceedings? (n=143)	Yes	38	26.6
Are there any procedures that can be performed in the emergency department without informed consent? (n=143)	Yes	130	90.9
Do you think that written informed consent forms inform patients sufficiently? (n=143)	Yes	32	22.4
Do you think it would be safer and more accessible if informed consent forms were read and signed electronically (SMS, etc.)? (n=140)	Yes	109	77.9
Do patients and their relatives who read informed consent forms avoid medical procedures? (n=143)	Yes	18	12.6
Who do you think is more reliable to keep the signed informed consent forms? (n=142)	Ministry of Health	56	39.4
	Institution you work for	60	42.3
	The physician him/herself	14	9.9
How do you think it is more reliable to keep signed informed consent forms? (n=143)	Electronic environment	45	31.5
	Printed file	3	2.1
	Both of them	92	64.3
Do you know what interventional procedures you are qualified to perform? (n=143)	Yes	60	42.0
Did you receive training on interventional procedures during your postgraduate emergency medicine training? (n=142)	Yes	44	31.0
Do you find the training you received on interventional procedures during your postgraduate emergency medicine education sufficient? (n=141)	Yes	73	51.8
Have you read any additional resources other than the training program regarding your legal responsibilities for interventional procedures performed in the emergency department? (n=143)	Yes	36	25.2
Which conditions were you aware of for a medical intervention you performed in the emergency room to be considered legal? (n=143)	Informing the patient and obtaining consent	123	86.0
Which articles are you aware of regarding the conditions under which patient consent for invasive procedures to be performed in the emergency department must be obtained in order to legally protect you? (n=143)	Informing about all the conditions and possible consequences of the treatment	126	88.1
Does the physician have an obligation to apply all new methods in interventional procedures to be performed in the emergency department? (n=142)	Yes	33	23.1

Knowledge of Legal Responsibilities

Many participants indicated that they did not know their legal responsibilities regarding ED procedures (n=117). This knowledge varied significantly between groups according to academic title, educational institution, and professional experience (p<0.001) (Table 3). When asked from whom they preferred to learn about their legal responsibilities, there was a significant difference between the answers according to the academic title, with more assistant physicians (n=91) preferring physicians with legal training (p=0.047).

Tablo 3. Comparison of participant information regarding interventional procedures performed in the emergency department, including academic title, institution where specialist training was received, and professional experience distribution

Questionnaire-based questions	Academic title			p	Institution where specialized training was received			p	Professional experience	
	Assistant physician	Specialist	Faculty member		University Hospital	Training and Research Hospital	City Hospital		Median, years	p
	n (%)	n (%)	n (%)		n (%)	n (%)	n (%)			
Have you received training on interventional procedures performed in the emergency department?[a]	103 (82.4)	11 (8.8)	11 (8.8)	0.165	23 (18.4)	51 (40.8)	51 (40.8)	0.037	4	0.012
Do you know enough about your legal responsibilities, obligations, and regulations regarding interventional procedures performed in the emergency department?[a]	9 (34.6)	9 (34.6)	8 (30.8)	<0.001	11 (42.3)	11 (42.3)	4 (15.4)	<0.001	2	<0.001
Do you think it would be more helpful to learn from whom about your legal responsibilities, obligations, and legal regulations during interventional procedures performed in the emergency department?[b]	91 (82.7)	8 (7.3)	11 (10.0)	0.047	17 (15.5)	43 (39.1)	50 (45.5)	0.996	4	0.275

[a]: The "yes" answers in the center were placed in the table, [b]: The most common answer from the participants, "A medical doctor with legal education", was included in the table

Malpractice and Complications

When comparing their views on complications and malpractice, many participants with more years of experience felt they had sufficient knowledge to distinguish between complications and malpractice (p=0.034). Participants with more professional experience also reported more significant hesitation to perform procedures due to concerns about complications and malpractice (p=0.009, p=0.030) (Table 4).

Participants' Answers to Questions on Knowledge Level about Interventional Procedures in the Postgraduate Emergency Medicine Education Program

Experts and faculty members were significantly more likely to be aware of the interventional procedures they were authorized to perform under the emergency medicine training program (p<0.001). Similarly, those with more years of experience (median 5 years) were more likely to answer "yes" (p<0.001). When asked if they had received training about interventional procedures in the PEM training program at their institution, specialists and faculty members again answered "yes" (n=6, n=7)) significantly more often (p=0.028), and the likelihood increased with experience (p=0.001) (Table 5).

Additional Legal Resources and Professional Experience

In addition to training in interventional procedures in PEM, residents were less likely to have access to legal resources (n=99) (p<0.001). As participants gained more professional experience, the need for additional resources increased (p<0.001). As experience increased, participants were more aware of the legal criteria for performing medical interventions in the ED; they felt they had the appropriate competence to perform the intervention (p=0.027). Furthermore, experienced physicians were more likely to agree that they were responsible for implementing all new methods of interventional procedures in the ED (p=0.005) (Table 6).

DISCUSSION

Medical malpractice has been extensively studied worldwide, particularly in developed countries, for nearly half a century. This multifaceted issue, encompassing ethical, legal, medical, educational, and managerial dimensions, has gained traction in Turkey in recent years, sparking discussions and a search for solutions.[9]

Key findings revealed that participants from university hospitals and those with more experience were more likely to report receiving procedural training. Specialists and faculty members with extensive experience believe that professional liability insurance offers legal protection during interventional procedures. Assistant physicians were less confident in distinguishing between complications and malpractice. While the level of knowledge regarding legal responsibilities in interventional procedures does not show a significant difference between the institutions where physicians received

Tablo 4. Comparison of participants' views on the concepts of complication and malpractice in interventional procedures performed in the emergency department in terms of academic title, institution where specialization training is received, and professional experience distribution

Questionnaire-based questions	Academic title				Institution where specialized training was received				Professional experience	
	Assistant physician	Specialist	Faculty member		University Hospital	Training and Research Hospital	City Hospital	p		
	n (%)	n (%)	n (%)	p	n (%)	n (%)	n (%)		Median, years	p
Do you think compulsory liability insurance for malpractice (related to medical malpractice) protects the physician in a legal situation in interventional procedures performed in the emergency department?[a]	8 (42.1)	5 (26.1)	6 (31.6)	<0.001	**8 (42.1)**	**9 (47.4)**	**2 (10.5)**	**<0.001**	**9.0**	**<0.001**
Do you think you know enough about the distinction between complications and malpractice?[a]	42 (73.7)	9 (15.8)	6 (10.5)	0.034	11 (19.3)	23 ((40.4)	23 (40.4)	0.816	4.0	0.219
Regarding the distinction between complication and malpractice, do the concepts of complication and malpractice cause you to hesitantly when performing interventional procedures on the patient? Do you think you have enough knowledge?[a]	39 (86.7)	2 (4.4)	4 (8.9)	0.009	8 (17.8)	16 (35.6)	21 (46.7)	0.068	**3.0**	**0.030**

[a]: The "yes" answers in the center were placed in the table

Tablo 5. Comparison of the participant's knowledge about the post-graduate emergency medicine interventional procedure education program in terms of academic title, institution where specialization training was received, and distribution of professional experience

Questionnaire-based questions	Academic title				Institution where specialized training was received				Professional experience	
	Assistant physician	Specialist	Faculty member		University Hospital	Training and Research Hospital	City Hospital			
	n (%)	n (%)	n (%)	p	n (%)	n (%)	n (%)	p	Median, years	p
Do you know what interventional procedures you are qualified to perform?[a]	43 (71.7)	9 (15.0)	8 (13.3)	<0.001	12 (20)	28 (46.7)	20 (33.3)	0.064	5.0	<0.001
Did you receive training on interventional procedures during your postgraduate emergency medicine training?	31 (70.5)	6 (13.6)	7 (15.9)	0.028	9 (20.5)	17 (38.6)	18 (40.9)	0.756	5.0	0.001
Do you find the training you received on interventional procedures during your postgraduate emergency medicine education sufficient? [a]	60 (82.2)	7 (9.6)	6 (8.2)	0.690	12 (16.4)	27 (37.0)	34 (46.6)	0.869	4.0	0.082

[a]: The "yes" answers in the center were placed in the table

Tablo 6. Comparison of the participants' awareness of their legal responsibilities regarding interventional procedures performed in the emergency department in terms of academic title, institution where specialized training was received, and professional experience distribution

Questionnaire-based questions		Academic title				Institution where specialized training was received				Professional experience	
		Assistant physician	Specialist	Faculty member	p	University Hospital	Training and Research Hospital	City Hospital	p	Median, years	p
		n (%)	n (%)	n (%)		n (%)	n (%)	n (%)			
Have you read any additional resources besides the training program regarding your legal responsibilities for interventional procedures performed in the emergency department?[a]		22 (61.1)	6 (16.7)	8 (22.2)	<0.001	11 (30.6)	13 (43.0)	12 (33.3)	0.020	7	<0.001
Which conditions were you aware of for a medical intervention you performed in the emergency room to be considered lawful? Informing the patient and obtaining consent	Informing the patient and obtaining consent	103 (83.7)	19 (8.1)	10 (8.1)	0.712	21 (17.1)	50 (40.7)	52 (42.3)	0.326	4.0	0.133
	Having the authority to provide medical intervention	90 (83.3)	8 (7.4)	10 (9.3)	0.529	21 (17.1)	42 (38.9)	45 (41.7)	0.132	4.0	0.027
	The intervention must be aimed at legally prescribed purposes	52 (80.0)	7 (10.8)	6 (9.2)	0.354	12 (18.5)	28 (43.1)	25 (38.5)	0.379	5.0	0.007
	The intervention must comply with the rules of medical science	94 (83.9)	7 (6.3)	11 (9.8)	0.111	19 (17.0)	43 (38.4)	50 (44.6)	0.849	4.0	0.160
Is the physician obligated to apply all new methods in interventional procedures in the emergency department?[a]		24 (72.7)	4 (12.1)	5 (15.2)	0.080	6 (18.2)	14 (42.4)	13 (39.4)	0.739	5.0	0.005

a: The "yes" answers in the center were placed in the table

their specialist training, it was revealed that experts with more experience have significantly higher levels of knowledge in this field. As experience grew, participants were more likely to consult additional resources on legal responsibilities and felt that new developments in emergency medicine should be adopted.

Our findings show that physicians specializing in university hospitals have higher education and awareness about interventional procedures than those trained in training, research, and city hospitals. This situation is supported by Bilge et al.[10] who compared the level of education regarding interventional procedures between university and research hospitals and found higher education rates in university settings. It is compatible with similar studies, Arvier et al.[11] He emphasized the need for more training in emergency room procedures in line with our results. In addition, City Hospitals have the highest number of patient admissions and a relatively higher clinical workload. The hospital's high patient load and expanded treatment services may hinder educational opportunities. According to the results of our study, while planning the academic activities of Assistant Physicians studying in City Hospitals, the aim should be to increase their knowledge level about legal liabilities in interventional procedures.

In our study, assistant physicians thought that they did not know the difference between malpractice and complications. This is consistent with previous studies showing persistent uncertainty among physicians regarding these concepts.[11] Most physicians in our study admitted hesitancy in performing interventional procedures due to concerns about complications leading to malpractice. Similarly, Başer et al.[12] reported that 71.6% of family physicians avoid procedures with high complication rates. Additionally, Hiyama et al.[13] They found that physicians with more than nine years of experience tended to avoid risky procedures, indicating a relationship between experience and procedure avoidance. In our study, the mean duration of professional experience was 5.9 years, and there was no significant difference between it and the avoidance of invasive procedures. A study evaluated physicians' legal knowledge about informed consent and confidentiality, and the lowest level of knowledge was found in emergency physicians.[14] Future studies involving more comprehensive physician groups are needed to determine whether this situation is due to the difference in working conditions between gastroenterologists and emergency physicians or the duration of professional experience.

According to a study by Skiba et al.[15] in which Australian assistant doctors participated, doctors must be more aware of their legal responsibilities regarding informed consent. In another study, it is understood from the answers given by assistant doctors to education questions that assistant doctors need to receive adequate training regarding their legal responsibilities and that their level of knowledge needs to be higher. Medical education in all branches throughout Türkiye is carried out according to a specific curriculum. Based on our results, planning to teach physicians legal responsibilities in the emergency medicine basic training program in the earlier years would be more beneficial. In addition, the increase in faculty members' legal education can increase awareness about the legal responsibilities of physicians. As a matter of fact, in the literature, medical education processes are dynamically evaluated and rearranged according to changing conditions.[16,17]

Moreover, our study revealed that only one-quarter of participants sought additional resources beyond the prescribed training program to educate themselves on their legal responsibilities concerning interventional procedures in the ED. This discrepancy is further supported by a statistically significant difference in age distribution between participants who sought additional resources and those who did not, indicating a tendency for assistant physicians to neglect supplementary learning materials. Odabaşı et al.'s[18] study revealed that 72.5% of physicians lacked awareness of the articles within the TCK related to their criminal responsibilities, with 80.9% indicating a lack of training in this area. These findings parallel our own, indicating a shared concern: physicians do not understand their legal obligations.

Given these legal intricacies, it emphasizes the importance of physicians seeking supplementary resources beyond standard training programs to acquaint themselves with their legal duties. Incorporating such knowledge into their medical practices is essential for navigating the complex legal landscape and upholding the highest standards of care and accountability. In addition, while providing basic emergency medicine training to assistant physicians, their legal responsibilities and the need to obtain consent before procedures should be explained at the beginning of their training. In this way, the doctor and the patient will be protected from bad experiences that may occur in the future.

Limitations

Our study cannot be generalized because it was conducted in Turkey and was a single center. In addition, there were fewer faculty members and specialists in the physician groups than in the assistant physicians, which may reduce the robustness of certain statistical analyses. Future studies should consider this difference and aim for more comprehensive assessments that include a larger pool of physicians across multiple centers. It is also important to recognize that participants' knowledge and perceptions of legal responsibilities may not fully reflect actual conditions. Factors such as individual experiences and educational backgrounds may influence responses and make it difficult to obtain an objective assessment.

CONCLUSION

This study highlights the essential role of legal knowledge and preparation among emergency physicians who perform interventional procedures. Our findings reveal significant differences in legal awareness across experience levels, academic titles, and educational institutions. Faculty members with more experience had significantly greater knowledge of their legal responsibilities, highlighting the need for structured legal education in emergency medicine education. Associate physicians, who comprised the majority of participants, demonstrated less confidence in distinguishing between malpractice and complications. Malpractice concerns also appear to deter some physicians from performing high-risk procedures, potentially impacting patient care. The findings highlight the importance of integrating comprehensive legal education early into graduate emergency medicine education to prepare physicians better to address the legal aspects of their practice. This education should explain complications and malpractice, informed consent, and liability protections. We recommend further research with larger, more diverse physician groups across multiple sites to develop strategies for legal education in emergency medicine.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval was obtained from the Ankara Bilkent City Hospital No. 1 Clinical Researches Ethics Committee (Date: 12/09/2023, Decision No: E1-23-4013).

Informed Consent

All participants signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

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Priapism a rare side effect of cilostazol

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ABSTRACT

We present the case of priapism associated with cilostazol. A rare side effect of cilostazol on the genitourinary system. Priapism is a long-lasting erection that occurs without sexual arousal or stimulation. It can cause irreversible damage on penis. Therefore, urgent treatment is required. Priapism can be treated with aspiration, intracavernous injection or, as in our case, with surgical ligation.Priapism is a common side effect of phosphodiesterase 5 inhibitors. However, this situation is very rare for cilostazol, one of the phosphodiesterase 3 inhibitors.

Keywords: Phosphodiesterase 3 inhibitor, priapism, leukocytosis, thrombocytosis, aspiration

INTRODUCTION

Priapism is a prolonged erection of penis. It is an unwanted, painful erection of the penis that lasts more than four hours and is unrelated to sexual desire.[1] It occurs when there is a problem with the blood flow to penis, and this can be caused by blood diseases, penis injury, certain medications, penile cancer and alcohol or drug use.[2] Drug-induced priapism comprises about 30% of cases. The drugs most frequently implicated are psychotropic drugs (phenothiazines and trazodone), antihypertensives (mainly prazosin) and heparin. Recently, the intracavernosal injection of vasoactive drugs (papaverine and phentolamine) has been described in patients treated for impotence. With the exception of heparin, an alpha-adrenergic blocking mechanism has been suggested in the priapism-inducing action of these drugs. A significant number of anecdotal case reports link priapism and drugs, and it is possible that certain cases of idiopathic priapism could be reclassified if accurate pharmacological anamnesis were to be performed.[3]

To our knowledge, this case is about priapism, one of the very rare side effects of cilostazol.

Cilostazol is a quinolone derivative primarily used to treat intermittent claudication due to peripheral vascular disease. Cilostazol is also indicated for secondary prevention in patients with a history of transient ischemic attacks or non-cardioembolic ischaemic stroke. Cilostazol improves walking distance by promoting vasodilation and antiplatelet activity with inhibition of phosphodiesterase III and subsequent increases in available cAMP.[4]

Common side effects of cilostazol are chest pain, pounding heartbeats, fever, chills, sore throat, mouth sores; or easy bruising, unusual bleeding.[5] Additionally, there are few reports of cilostazol induced nephrotoxicity.[6,7]

However, priapism is not one of the common known effects of cilostazol. This side effect of the drug is very rare and we have not come across any reported cases.

Priapism must be considered an urological emergency. Surgical procedures are the most preferred treatment for this condition but, in selected cases, drug treatment seems to be an alternative approach.[3]

CASE

In August 2024, a 75-year-old male patient with a history of angiography, bypass benign prostatic hyperplasia, and hypertension came to the emergency room with a complaint of priapism. The patient had a complaint of priapism and dysuria that had been ongoing for 2 days. He was using the following drugs: clopidogrel, lasix, spironolactone, trazodone, carvedilol, pitavastatin, acetylsalicylic acid. The patient also stated that he started taking a drug called cilastazol 10 days ago. His physical examination was normal. His blood pressure was 135/73, His body tempature was 36,7°C, and his heart rhythym was 75 beats per minute.

As seen in the Table blood sample results were normal except for thrombocytosis and leukocytosis.

The patient was consulted to urology and hematology deparments. The patient had no history of using any additional medication other than cilostazol in the last month. Therefore the use of the drug cilostozol was discontinued. Leukocytosis and thrombocytosis were seen as side effects of the drug,

Table. Blood tests throughout patient hospital stay

Blood tests	Day 1	Day 2	Day 3
wbc	16.2 K/µL	17.8 K/µL	17.6 K/µL
neu	10.9 K/µL	13.8 K/µL	13.08 K/µL
hb	11.4 g/dl	9.2 g/dl	9.2 g/dl
plt	12.1 K/µL	1177 K/µL	1002 K/µL

however, hematology called the patient for a later clinic check-up for detailed investigation.

A focused urology exam reviewed an erected penis with evidence of ischemia. Therefore, it was decided to perform aspiration.

Aspiration was performed by the urologist from the roots of the corpus cavernosum. Patient's priapism persisted despite aspiration and the procedure was interrupted because the patient exhibited hypotensive symptoms such as cold sweat and blurred vision during the procedure. The patient was treated with 1000 ml of normal saline solution as an IV bolus. When the patient's vital signs returned to the normal range, the patient was monitored and the aspiration procedure was continued. The aspiration process took almost 3 hours. A large amount of blood was discharged from the glans penis. The hemogram value decreased by 2 units, but the penis still did not become completely flaccid. Therefore the patient was scheduled for surgery and admitted to the urology service.

After the operation, the patient's penis became flaccid and the patient was subsequently discharged on the following day.

DISCUSSION

Drugs that generally cause priapism are phosphodiesterase type 5 (PDE5) inhibitor. PDE5 inhibitors, including sildenafil and tadalafil, are widely used for the treatment of erectile dysfunction, pulmonary arterial hypertension, and certain urological disorders. This group of drugs causes the blood vessels in the penis to dilate, increasing blood flow and facilitating erections.[8]

Prazosin is an alpha blocker and increases the risk of priapism by dilating blood vessels. However, this risk is quite low.

Heparin is an anticoagulant and in rare cases increases the risk of priapism by changing blood flow.

Phenothiazines increase the risk of priapism when taken in high doses due to their effects such as dopamine blockade.

As a result, the drugs with the highest risk of priapism are phenothiazines, followed by PDE5 inhibitor. Prazosin and heparin carry a lower risk.

But in our case the drug that caused the side effect was cilostazol. Cilostazol, like another anticoagulant drug such as heparin, may cause priapism.

Cilostazol; primarily used in the treatment of intermittent claudication, is a 2-oxyquinolone derivative that works through the inhibition of phosphodiesterase III and related increases in cyclic adenosine monophosphate (cAMP) levels. However, cilostazol has been implicated in a number of other basic pathways including the inhibition of adenosine reuptake, the inhibition of multidrug resistance protein 4, among others. It has been observed to exhibit antiplatelet, antiproliferative, vasodilatory, and ischemic-reperfusion protective properties (Figure). As such, cilostazol has been investigated for clinical use in a variety of settings including intermittent claudication, as an adjunctive for reduction of restenosis after coronary and peripheral endovascular interventions, and in the prevention of secondary stroke.[2]

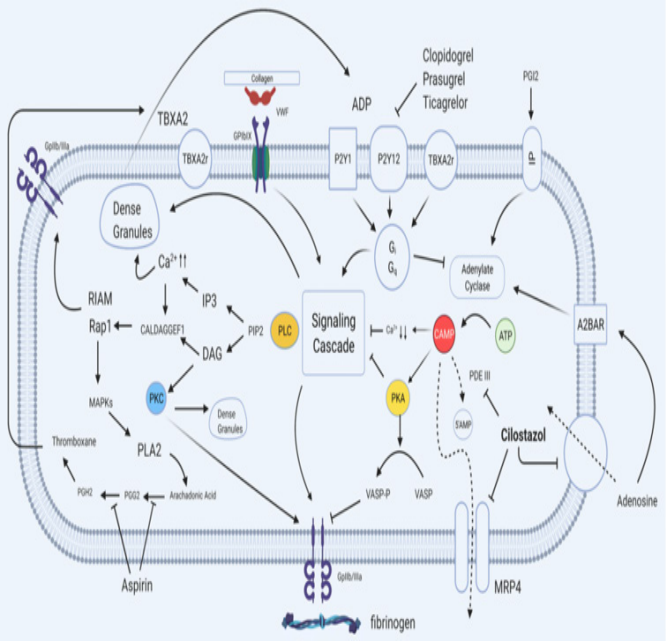

Figure. Illustration of platelet activation signaling cascade and the impact of cilostazol[7]

In our case, the patient had started using cilostazol approximately 10 days ago due to claudication.

A common complaint is intermittent claudication, characterised by pain in the legs or buttocks that occurs with exercise and which subsides with rest. Cilostazol has been shown to be of benefit in improving walking distance in people with intermittent claudication secondary to peripheral arterial disease.[9]

Cilostazol is a generally well-tolerated oral medication. The most common side effects of cilostazol are headache, diarrhea, and palpitations.[10]

Also It can induce tachycardia, tachyarrhythmia, and hypotension, thrombocytopenia or leukopenia.[11,12] Also rarely can cause nephrotoxicity.[6,7]

This case shows us that cilostazol causes erectile dysfunction even though it is a phosphodiesterase 3 inhibitor.

Cilostazol may increase the risk of priapism under 4 conditions:

1-Personal health problems, especially issues related to vascular health and blood flow.
2-Genetic and biological factors can affect a person's susceptibility to side effects from medications.
3-Combining it with medications that affect blood and blood flow may increase the risk of priapism.
4-High doses and long-term use of the drug is also one of the factors that increase the risk.

CONCLUSION

Based on our case, we may draw the conclusion that, cilostazol may cause priapism. When we disgusted with the cardiovascular surgery department, he said that such cases were rare but an expected side effect. Therefore, before starting

treatment, side effects should be considered. Patients should be informed about possible side effects.

Priapism requires immediate treatment and can cause permanent damage to penis if left untreated. If it lasts longer than 36 hours, scarring and permanent erectile dysfunction will likely occur. Therefore emergency treatment should be applied to patients developing priapism. We may rarely encounter such cases in the emergency department, which is why we wanted to present this case to you.

ETHICAL DECLARATIONS

Informed Consent
The patient signed and free and informed consent form.

Referee Evaluation Process
Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Financial Disclosure
The authors declared that this study has received no financial support.

Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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