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Beyond the Scan: Laboratory Investigations in Infant Head Trauma

✉ Rohit Kumar Varshney

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Keywords: Pediatric head trauma, biomarkers, abusive head trauma

Head trauma in children aged 0-2 years represents a diagnostic challenge requiring comprehensive evaluation beyond neuroimaging alone. While computed tomography (CT) dominates diagnostic approaches, laboratory investigations provide critical prognostic information and aid in detecting occult injuries. This editorial examines the essential role of laboratory testing in emergency department assessment of this vulnerable population.

Infants under two years cannot verbalize symptoms, presenting with non-specific manifestations such as vomiting, lethargy, or irritability that may mask life-threatening intracranial hemorrhage. Abusive head trauma remains undiagnosed in approximately 30% of initial presentations (1). The Pediatric Emergency Care Applied Research Network criteria achieve high sensitivity (100%) but modest specificity (53.8%), indicating that many children undergo unnecessary imaging while others with significant injury escape detection (1). One of the articles published in the current issue states that increased severity of head trauma is associated with greater reductions in hemoglobin and hematocrit levels, and elevated glucose levels. Moreover, these laboratory parameters may serve as useful indicators of prognosis and mortality risk in pediatric patients with moderate to severe head trauma.

Laboratory investigations complement imaging by revealing physiologic derangements, metabolic dysfunction, and systemic complications independent of structural lesions on CT scans. These findings fundamentally alter clinical management and prognostic assessment.

Hemoglobin concentration demonstrates remarkable prognostic significance in pediatric head trauma. Studies show that hemoglobin levels correlate inversely with injury severity and outcomes, with lower values predicting mortality and neurologic disability (1). The “delta-hemoglobin ratio” proportional change from admission to nadir hemoglobin independently predicts poor neurologic outcomes. Age-specific thresholds include delta-hemoglobin decrease exceeding 30.7% in infants 0-6 months and -20.6% in 6-12 month-olds (1).

The Pittsburgh Infant Brain Injury score (PIBIS), a validated clinical prediction rule incorporating hemoglobin <11.2 g/dL, achieves 93.3% sensitivity for detecting brain injury in well-appearing infants (1). Hemoglobin measurement serves as a surrogate for cerebral oxygen delivery in the context of impaired autoregulation characteristic of developing brains.

Coagulopathy represents both a consequence of severe brain injury and a critical determinant of outcome. Prospective studies reveal that 22% of children with severe traumatic brain injury demonstrate disseminated intravascular coagulation (2). Tissue factor released from injured brain parenchyma triggers systemic coagulation cascade activation, manifesting as hematoma expansion the leading cause of neurologic deterioration in the first 24-48 hours (2).

Coagulation abnormalities possess particular diagnostic significance in abusive head trauma. Research demonstrates that 54% of abused children with parenchymal brain damage exhibit prothrombin time (PT) prolongation, compared to only 20%



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without parenchymal injury (2). Among fatalities from abuse, 94% display PT prolongation. Critically, these abnormalities develop acutely following injury rather than representing pre-existing hemorrhagic diatheses a distinction with profound protective and legal implications (2).

Serum biomarkers represent a paradigm shift in traumatic brain injury diagnosis. The US Food and Drug Administration approved the Banyan Brain Trauma Indicator in 2018 the first blood-based diagnostic tool measuring glial fibrillary acidic protein and ubiquitin C-terminal hydrolase-L1 (3). These proteins, released following neuronal and glial cell damage, achieve 100% sensitivity and 67% specificity for detecting clinically important traumatic brain injury in children including those under 2 years (3).

Notably, biomarker elevations occur even in children with normal CT scans, detecting microscopic axonal injury invisible to conventional neuroimaging. This finding challenges the traditional “CT-positive” versus “CT-negative” dichotomy, revealing a continuum of neuronal damage with potential implications for cognitive development and post-concussive symptoms (3). Cost-effectiveness analyses indicate biomarker screening becomes economically advantageous when test cost remains below \$308.96, with favorable cost-effectiveness ratios compared to additional CT imaging (3).

Admission blood glucose concentration provides independent prognostic information. Hyperglycemia (glucose >200 mg/dL) correlates with injury severity and unfavorable outcomes, with persistent elevation beyond 48 hours showing strong association with mortality and neurologic disability (2). Elevated glucose exacerbates ischemic brain injury through lactate accumulation, oxidative stress, and cerebral edema formation. Protocols maintaining tight glycemic control (glucose ≤100 mg/dL) demonstrate reduced intracranial pressure and improved functional outcomes (2).

Hyponatremia occurs in 13-20% of hospitalized pediatric head trauma cases, typically from syndrome of inappropriate antidiuretic hormone secretion or cerebral salt-wasting syndrome (2). Distinguishing between these entities proves clinically critical: syndrome of inappropriate antidiuretic hormone secretion requires fluid restriction while cerebral salt-wasting demands aggressive sodium repletion. Hyponatremia predicts poor neurologic outcomes independent of injury severity, likely through exacerbation of cerebral edema (2).

Systematic screening for injuries beyond the clinically apparent proves essential in suspected child abuse. Occult abdominal trauma occurs in 2-10% of physically abused children, presenting

with subtle findings (4). Measurement of hepatic transaminases (aspartate aminotransferase and alanine aminotransferase) and pancreatic enzymes identifies occult liver and pancreatic injuries with high positive predictive value (4).

Current recommendations advocate screening all children under 2 years with suspected abusive injuries using complete blood count, hepatic transaminases, pancreatic enzymes, coagulation studies, and urinalysis (4). Transaminase elevations above 80 IU/L warrant abdominal imaging to exclude solid organ injury (4). Alarming, screening rates remain low only 20-51% of eligible children undergo appropriate testing, yet 41% of screened children yield positive results identifying previously unsuspected injuries (4).

Optimal utilization of laboratory investigations requires integration with clinical findings and imaging within coherent decision-making frameworks. For well-appearing infants within 24 hours of reported minor trauma, PIBIS scores guide neuroimaging decisions. When non-accidental trauma enters the differential, comprehensive laboratory evaluation becomes mandatory (5). Detection of coagulopathy or transaminase elevation triggers additional imaging and subspecialty consultation.

For children with confirmed intracranial injury, serial hemoglobin measurements enable calculation of delta-hemoglobin ratios for prognostic stratification. Glucose monitoring maintains optimal ranges targeting 100-150 mg/dL. Daily electrolyte assessment identifies hyponatremia requiring intervention.

The evaluation of head trauma in children aged 0-2 years demands comprehensive assessment integrating clinical evaluation, neuroimaging, and laboratory investigation. Hemoglobin dynamics predict mortality and disability. Coagulation abnormalities herald hematoma expansion and provide forensic evidence. Biomarkers detect brain damage invisible to CT. Glucose and electrolyte derangements offer modifiable therapeutic targets. Screening panels identify occult injuries.

Conclusion

Professional societies should update clinical practice guidelines recommending laboratory screening protocols stratified by age and injury mechanism. Healthcare systems should invest in point-of-care testing infrastructure and electronic decision support tools facilitating appropriate utilization. For the vulnerable infant whose injury severity may be masked by normal imaging, laboratory investigation provides essential context that can alter outcomes and protect the most vulnerable among us.

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Investigation of the Relationship of SCUBE-1 and VAP-1 Levels on Diagnosis, Prognosis and Clinical Results in Patients with Pulmonary Thromboembolism Diagnosis in Emergency Department

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Abstract

Aim: Acute pulmonary thromboembolism (APT) is a life-threatening disease. The aim of this study is to investigate the relationship between the diagnosis and prognosis of alternative biomarkers such as signal peptide-CUB-EGF domain-containing protein 1 (SCUBE-1) and vascular adhesion protein-1 (VAP-1) in the diagnosis of clinically suspected acute APT.

Materials and Methods: Patients diagnosed as APT in emergency department were included in the study. Patients with acute ischemic disease, liver failure, renal failure, pregnancy, active malignancy and/or history of known APT were excluded from the study. A control group was formed from healthy volunteers at similar age and sex. SCUBE-1 and VAP-1 levels were studied from serum samples taken from the patient and control groups.

Results: Serum SCUBE-1 levels were 7.60 (6.22-71.05) ng/mL in the patient group and 23.79 (5.08-118.28) ng/mL in the control group ($p<0.001$). Serum VAP-1 levels were 1.07 (0.20-24.36) ng/mL in the patient group and 9.31 (0.21-25.98) ng/mL in the control group ($p<0.001$). Both serum levels of SCUBE-1 and VAP-1 were significantly lower in the patient group. There was no correlation between both biomarkers with Wells rules, revised Genova score, Pulmonary Embolism Severity index (PESI) sPESI and early mortality risk.

Conclusion: Serum SCUBE-1 and VAP-1 levels were found to be useful in the diagnosis of APT. However, both biomarkers are not successful in predicting prognosis. In the light of these data; it can be said that studies with larger patient subgroups are needed in order to enter into clinical use in terms of diagnosis and prognosis of serum levels of SCUBE-1 and VAP-1 in patients with APT.

Keywords: Acute pulmonary thromboembolism, emergency department, SCUBE-1, VAP-1

Introduction

Acute pulmonary thromboembolism (APT) is a major health problem that significantly threatens human life (1). The disease often presents with non-specific clinical symptoms, and diagnosis relies heavily on clinical suspicion. Definitive diagnosis is achieved through ventilation/perfusion (V/Q) scintigraphy or thorax computed tomography angiography (CTA) (2). However, these

methods require radiation and contrast exposure, which may not be feasible in all patients. Among laboratory tests, D-dimer is widely used to exclude acute pulmonary thrombosis rather than confirm it, due to its low specificity (3). Given these limitations, there is a strong clinical need for alternative, non-invasive, and more specific diagnostic biomarkers.

The non-specificity of the clinical picture, the fact that the diagnosis depends on the experience of the physician, and the



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necessity of exposure to radiation and contrast material for the definitive diagnosis have revealed the necessity of alternative diagnostics for APT. Signal peptide-CUB-EGF domain-containing protein 1 (SCUBE-1) is a cell surface glycoprotein stored in platelet alpha-granules and released upon platelet activation. It also originates from endothelial cells under inflammatory or hypoxic conditions, highlighting its relevance in acute vascular events (4,5). SCUBE-1 contributes to thrombus formation and has been studied in diseases such as myocardial infarction and ischemic stroke. Vascular adhesion protein-1 (VAP-1) also known as amine oxidase copper-containing 3, is a transmembrane glycoprotein with dual functionality as an adhesion molecule and an enzyme. It mediates leukocyte adhesion, rolling, and transmigration during inflammation. A soluble form is also released into the circulation, suggesting systemic effects in inflammatory states (6-8).

These two biomarkers were selected for this study due to their direct roles in the pathophysiology of APT: SCUBE-1 in platelet aggregation and thrombogenesis, and VAP-1 in endothelial inflammation and immune cell recruitment. SCUBE-1, by reflecting acute platelet activity, may offer advantages over D-dimer in terms of specificity. Although VAP-1 has primarily been evaluated in chronic inflammatory diseases, its endothelial involvement in acute inflammation makes it a candidate for further study in acute thromboembolic events (6,8,9).

However, the temporal kinetics of VAP-1 as a relatively novel biomarker such as its rise, peak, and normalization times during acute inflammatory conditions remain unclear, which may limit its early diagnostic utility (10). The aim of this study was to investigate the serum levels of SCUBE-1 and VAP-1 in patients diagnosed with APT in the emergency department and to evaluate their potential diagnostic and prognostic value.

Materials and Methods

Study Design and Selection of Patient and Control Group

The study was prospectively planned. Patients who presented to the emergency department of our hospital between 01.01.2019 and 30.06.2019 and were diagnosed with APT by contrast-enhanced CTA were included in the study. A group of healthy volunteers, matched for gender, age, and exclusion criteria, was formed for comparison with the patients with APT included in the study. Demographic data, clinical probability scores (Wells' criteria, revised Geneva score), simplified Pulmonary Embolism Severity index (sPESI), and early mortality risk score (in 30 days) of the patients were recorded.

In the power analysis (G*Power 3.1.9.7 package program), a minimum (min) sample size of 16 was determined for each of the control and patient groups for 99% power with an effect size of 1.62 at a 95% significance level.

Inclusion criteria for the study were defined as being older than 18 years of age, presenting to the emergency department, and being diagnosed with acute APT by contrast-enhanced CTA. Exclusion criteria of the study: acute ischemic disease, liver or advanced heart failure, disease, pregnancy, active malignancy, hematological disease, and a known history of APT.

Determination of Serum SCUBE-1 and Serum VAP-1 Levels

5 mL of blood taken from the peripheral veins of the patients was placed in a biochemistry tube and centrifuged at $3000 \times g$ (core NF800, REF: Z10.NF 800). After centrifugation, the serum part of the blood was separated, placed in an eppendorf tube, and stored in an ultra-deep freezer (NUAIRE, Serial No: 9394248) at -80°C until the study day. Before starting the study, the ELISA kits kept at $2-8^{\circ}\text{C}$, and the samples kept in an ultra-deep freezer at minus 80°C were brought to room temperature. Serum SCUBE-1 and VAP-1 levels in the samples were determined using the Human Scube1 ELISA kit (SunRed, Cat: 201-12-5378) and the Human SVAP-1 ELISA kit (SunRed, Cat. No: 201-12-2134). While the sensitivity for the Human Scube1 ELISA kit is 0.852 ng/mL , the measurement range is $1-300\text{ ng/mL}$; the sensitivity for the Human SVAP-1 ELISA kit is 0.185 ng/mL , and the measurement range is $0.2-60\text{ ng/mL}$.

Statistical Analysis

Data were analyzed with IBM SPSS v23. The normality of quantitative data was analyzed using the Shapiro-Wilk test. Mann-Whitney U test and Kruskal-Wallis tests were used to compare non-parametric data. receiver operating characteristic (ROC) analysis was performed to obtain the cut-off value. The area under the curve, as a result of the ROC analysis, was presented with a 95% confidence interval. Sensitivity, specificity, positive and negative likelihood ratios, positive and negative predictive value, and correct classification rate were calculated for the diagnostic test evaluation data. The relationship between the data was examined with the Spearman's correlation test. The chi-square test was used to analyze categorical data. Results were presented as median (min to maximum), frequency (n), and percentage (%). The significance level was accepted as $p < 0.05$. Our study received ethics approval from the Ondokuz Mayıs University Clinical Research Ethics Committee (decision number: OMÜ KAEK 2019/26, date: 14.05.2019). The Clinical trial number obtained for the study is NCT06525051, and it was assigned on 2024-12-10.

Results

The study included 44 patients with acute pulmonary embolism and 44 control patients with similar age, gender, and exclusion criteria, making a total of 88 patients. Demographic characteristics of the patients are shown in Table 1.

Table 1. Characteristic properties of the patients			
		Patient	Control
Female*		24 (54.5)	24 (54.5)
Age**		68.5 (22-84)	68.5 (22-84)
BMI**		29.0 (18-51)	23.3 (20-33)
Symptom*			
	Dyspnea	32 (72.7)	
	Chest pain	22 (50.0)	
	Leg swelling	17 (38.6)	
	Cough	10 (22.7)	
	Back pain	9 (20.5)	
	Altered mental status	9 (20.5)	
	Flank pain	7 (15.9)	
	Palpitation	7 (15.9)	
Vital signs**			
	Systolic blood pressure (mmHg)	120 (80-160)	
	Diastolic blood pressure (mmHg)	70 (50-100)	
	Fever (oC)	36.4 (35.0-37.6)	
	Pulse (bpm/minute)	91 (54-145)	
	Respiratory rate (/minute)	22 (13-42)	
	O ₂ saturation (%)	94.5 (70-100)	
Komorbidities*			
	Hypertension	14 (31.8)	
	Coronary artery disease	8 (18.2)	
	Diabetes mellitus	6 (13.6)	
	COPD	3 (6.8)	
	Cerebrovascular disease	3 (6.8)	
Wells' criteria**		4.5 (0-9)	
	PE likely*	31 (70.4)	
Revized geneva score**		6 (0-13)	
	PE likely*	24 (54.5)	
Right ventricular dysfunction*		29 (65.9)	
sPESI score**		1 (0-3)	
	0 point*	19 (43.2)	
	≥1 point*	25 (56.8)	

BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, PE: Pulmonary embolism, sPESI: Simplified Pulmonary Embolism Severity index, *n (%), **median (minimum-maximum)

Serum SCUBE-1 level was found to be significantly lower in the patient group compared to the control group ($p<0.001$). When the cut-off was taken at 9.00 ng/mL, the sensitivity was calculated as 75.0%, the specificity as 75.0% [area under the curve (AUC): 0.742, $p<0.001$].

Serum VAP-1 level was also found to be significantly lower in the patient group compared to the control group ($p<0.001$). When the cut-off was taken at 3.50 ng/mL, the sensitivity was calculated as 72.7% and the specificity as 77.3% [AUC: 0.737 (0.629-0.845), $p<0.001$]. Values for serum SCUBE-1 and VAP-1 are shown in Table 2, and ROC analysis is shown in Figure 1.

There was no significant difference between clinical probability scores and serum SCUBE-1 and VAP-1 levels ($p>0.05$) (Table 3). No significant difference was found between serum SCUBE-1 and serum VAP-1 for the sPESI and 30-day early mortality risk classification ($p>0.05$).

Table 2. Comparison of signal peptide CUB-EGF domain-containing protein-1 and vascular adhesion protein-1 serum parameters among the groups

	SCUBE-1 (ng/mL)	VAP-1 (ng/mL)
Patient	7.60 (6.22-71.05)	1.07 (0.20-24.36)
Control	23.79 (5.08-118.28)	9.31 (0.21-25.98)
p	<0.001	<0.001
Cut-off	9.00 ng/mL	3.5 ng/mL
Sensitivity	75.00 (59.66-86.81)	72.73 (57.21-85.04)
Spesifisity	75.00 (59.66-86.81)	77.27 (62.16-88.53)
AUC (95% CI)	0.742 (0.663-0.851)	0.737 (0.629-0.845)
p	<0.001	<0.001

SCUBE-1: Such as signal peptide-CUB-EGF domain-containing protein 1, VAP-1: Vascular adhesion protein-1, AUC: Area under the curve, CI: Confidence interval

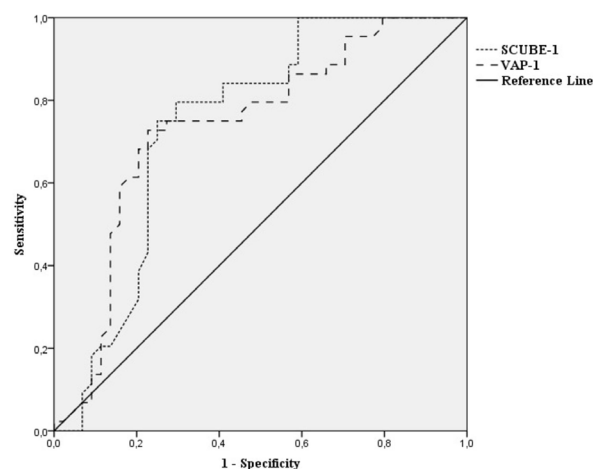


Figure 1. Receiver operating characteristics curve analysis of serum SCUBE-1 and serum VAP-1 values

SCUBE-1: Such as signal peptide-CUB-EGF domain-containing protein 1, VAP-1: Vascular adhesion protein-1

Table 3. Comparison of signal peptide CUB-EGF domain-containing protein-1 and vascular adhesion protein-1 serum parameters among clinical probability scores and predictive mortality risk scores

		SCUBE-1 (ng/mL)*	VAP-1 (ng/mL)*
Wells' criteria			
	PE unlikely (n=13)	7.60 (6.22-71.05)	1.05 (0.20-24.36)
	PE likely (n=31)	7.60 (6.22-67.75)	1.13 (0.23-24.29)
	p	0.949	0.616
Revised Geneva score			
	PE unlikely (n=20)	7.75 (6.22-68.59)	0.98 (0.20-24.36)
	PE likely (n=24)	7.45 (6.22-71.05)	1.15 (0.23-24.36)
	p	0.604	0.596
sPESI			
	0 point (n=19)	7.75 (6.22-68.59)	1.09 (0.20-23.34)
	≥1 point (n=25)	7.60 (6.22-71.05)	0.90 (0.23-24.36)
	p	0.577	0.943
Early mortality risk			
	Low risk (n=8)	8.66 (6.22-68.59)	5.29 (0.49-23.34)
	Intermediate-low risk (n=21)	7.60 (6.22-56.16)	1.05 (0.20-22.15)
	Intermediate-high risk (n=9)	7.23 (6.81-8.48)	0.65 (0.23-2.39)
	High risk (n=6)	7.72 (6.60-71.05)	3.37 (0.68-24.36)
	p	0.688	0.070

SCUBE-1: Such as signal peptide-CUB-EGF domain-containing protein 1, VAP-1: Vascular adhesion protein-1, PE: Pulmonary embolism, sPESI: Simplified Pulmonary Embolism Severity index, *median (minimum-maximum)

Table 4. Relationship between serum SCUBE-1, serum VAP-1 and demographic properties and laboratory values

	SCUBE-1		VAP-1	
	r	p	r	p-value
Age	-0.012	0.910	-0.097	0.370
Body mass index	-0.404	<0.001	-0.308	0.004
Leukocyte	-0.128	0.409	0.156	0.313
Hemoglobin	-0.192	0.211	-0.325	0.031
Platelet	0.194	0.208	0.471	0.001
Lymphocyte	0.221	0.150	0.425	0.004
Neutrophil	-0.168	0.276	-0.030	0.845
D-dimer	-0.191	0.215	-0.273	0.073
Troponin I	-0.052	0.735	-0.166	0.280
Creatine	-0.488	0.001	-0.329	0.029
pH	0.125	0.420	0.077	0.621

r: Spearman's rho correlation, SCUBE-1: Such as signal peptide-CUB-EGF domain-containing protein 1, VAP-1: Vascular adhesion protein-1

The relationship between serum SCUBE-1 and serum VAP-1 levels and demographic characteristics of the patients was evaluated with the Spearman's rho correlation test. A moderately negative correlation was found between the patients' body mass index (BMI) and serum SCUBE-1 levels, and a positive correlation with VAP-1 levels (for SCUBE-1 $r=-0.397$, $p<0.001$; for VAP-1 $r=0.337$, $p=0.001$). The relationship between serum SCUBE-1 and VAP-1 levels and the characteristics of the patients is shown in Table 4.

Discussion

APT is one of the most common cardiovascular diseases threatening human life (11). Clinical probability scores have been developed for preliminary diagnosis. Definitive diagnosis includes CTA or V/Q scintigraphy. This means exposure to radiation, contrast material, or radioactive material for patients who are suspected of having a particular diagnosis. The most important factor leading to the diagnosis is the physician's prediction and experience. Today, the number of biomarkers that can be used as an aid in diagnosis is very small. The most commonly used D-dimer is used to exclude the diagnosis because it is elevated in many diseases (3). Although clinical studies are ongoing for new biomarkers, there is no new biomarker that has been used yet. The lack of biomarkers, coupled with clinical suspicion, contributes to the burden of radiation and contrast agents in patients. Therefore, new biomarkers are needed to diagnose APT. If validated in future studies, SCUBE-1 and VAP-1 could potentially aid in early decision-making and reduce reliance on contrast-enhanced imaging, thus lowering exposure to radiation and nephrotoxic agents in select patient populations.

SCUBE-1 was first studied by Dai et al. (5) in acute myocardial infarction and ischemic stroke, and it was emphasized that it could be an indicator of thrombus. In the literature, there are studies showing that serum SCUBE-1 level increases with advanced age and decreases with obesity (12). SCUBE-1 has been studied several times in acute and chronic conditions. There are studies showing that serum levels may either increase or decrease in cases of acute thrombosis (4,13,14). There are two articles in the literature examining the relationship between APT and SCUBE-1. The first of these is a preliminary study, a study conducted with a few patients and control groups. This study consists of 11 patient groups and 23 volunteer groups (13). Another study was conducted with two groups: patients with suspected APT who applied to the emergency department, and a control group of those not considered to have APT, who also applied to the emergency department (14). The fact that each patient participates in this study and has a disease that requires admission to the emergency department precludes objective comparisons between groups. Serum SCUBE-1 levels

were significantly higher in the APT group in both studies. Our study has the potential to be a reference point, as it includes the largest number of patients and control groups in this area. In addition, the control group selected in our study consisted of healthy volunteers of similar age and gender, who did not apply to the hospital. Contrary to the other two studies, the serum SCUBE-1 level in our study was found to be significantly higher among the healthy volunteers included in the study group. This contrasts with prior studies and may stem from methodological differences, such as timing of sample collection, control group selection, and the potential consumption of biomarkers in acute thrombotic processes.

Serum SCUBE-1 level starts to rise 6 hours after activation in patients with acute platelet activation (5). This could indicate that, in acute presentations, there may be a delay in the measurable elevation of or a consumption effect due to active thrombus formation, contributing to the unexpectedly low levels. This may explain why this biomarker is not elevated enough in the serum of patients presenting with sudden dyspnea and chest pain, in this acute period. The body mass indices of patients with APT were found to be high, and high body mass indices may cause low serum SCUBE-1 levels. It is known that smoking may cause a decrease in serum SCUBE-1 level (5). The control group was composed of healthy non-smoker volunteers, whereas the patient group did not have a similar distinction applied.

Serum VAP-1 levels are biomarkers that have been studied mostly in chronic conditions (15-17). The available data on VAP-1 is limited. For example, in an acute ischemic condition, information such as when the serum level will start to rise, when it will peak, when it will begin to decline, or in which situations it will not be available in the current literature. There is one article in the literature examining the relationship between VAP-1 and APT (18). In this study, patients who underwent CTA with a pre-diagnosis of APT were included, and the serum VAP-1 level was found to be lower in patients with APT than in patients without APT. In our study group, serum VAP-1 level was higher in healthy volunteers than in the patient group. VAP-1 is a biomarker secreted in inflammatory processes; there is no information about when it will increase in acute situations. This limits its interpretability as a diagnostic biomarker in acute conditions such as APT. Further research is needed to elucidate the temporal dynamics of VAP-1 levels in acute inflammation. VAP-1 has been studied mostly in chronic diseases in the literature, and it has been found to be higher in chronic conditions (16,17).

There was no statistically significant difference between serum SCUBE-1 and serum VAP-1 levels and pulmonary embolism clinical probability scores and clinical risk classifications. Likewise, when the risk of early mortality, which predicts 30-day

mortality, and serum levels are compared, there is no statistically significant difference, although the serum levels decrease as the risk increases. Although these biomarkers were helpful in making the diagnosis, they were insufficient to evaluate the prognosis. Furthermore, no statistically significant correlation was found between these biomarkers and clinical scores or 30-day mortality. This limits their prognostic utility in current clinical practice.

Thrombosis and inflammation are now recognized as interrelated processes rather than isolated events. SCUBE-1, a molecule stored in platelet alpha-granules, plays an active role in platelet adhesion, aggregation, and thrombus formation. Its release during acute vascular injury links it directly to the coagulation cascade. Elevated SCUBE-1 levels have been reported in myocardial infarction and ischemic stroke, both of which involve platelet-rich thrombi (4,5). In contrast, VAP-1 is predominantly involved in endothelial activation and leukocyte trafficking. It facilitates the adhesion and transmigration of inflammatory cells across the vascular wall, a key step in the inflammatory response that may exacerbate thrombus formation (6-9). Therefore, the measurement of SCUBE-1 and VAP-1 together may reflect complementary aspects of the thrombo-inflammatory response seen in APT.

Despite this mechanistic relevance, the current study demonstrated lower serum levels of both SCUBE-1 and VAP-1 in APT patients compared to healthy controls. This unexpected finding may be explained by biomarker consumption during acute thrombus formation or by delayed systemic release, particularly in the very early stages of presentation. Furthermore, the lack of temporal kinetic data especially for VAP-1 limits our ability to determine the optimal time window for measurement (10). As such, while these biomarkers show biological plausibility, their clinical utility as early diagnostic markers for APT remains to be validated in larger prospective studies. In summary, SCUBE-1 and VAP-1 reflect key processes in thromboinflammation and may contribute to a more nuanced understanding of APT pathophysiology.

In a study on rats, the serum SCUBE-1 level was found to be low in obese rats (12). In our study, a low negative correlation was found between serum SCUBE-1 and VAP-1 levels with BMI. This situation was identified by our first study on humans. In addition, it has been previously shown that the serum SCUBE-1 level increases with advanced age (5). However, in our study, neither SCUBE-1 nor VAP-1 levels were found to be significantly associated with age.

Study Limitations

In biomarker studies with APT, there are many exclusion criteria to control confounding variables. This demonstrates that multiple

studies, including subgroups, are required to adapt the results to all patients with APT. Additionally, while our study was adequately powered, the relatively small sample size (n=44 per group) remains a limitation for the generalizability of the findings. Larger multi-center studies are warranted.

Conclusion

In our study, serum SCUBE-1 and serum VAP-1 levels were found to be significantly lower in patients diagnosed with APT compared to healthy controls. These findings suggest that both biomarkers may reflect thromboinflammatory processes associated with APT. Although they showed potential diagnostic value, their prognostic utility appeared limited. Given the dynamic nature of biomarker expression in acute events, further prospective, multicenter studies are needed to clarify the optimal timing, clinical applicability, and prognostic significance of SCUBE-1 and VAP-1 measurements in APT management.

Ethics

Ethics Committee Approval: Our study received ethics approval from the Ondokuz Mayıs University Clinical Research Ethics Committee (decision number: OMÜ KAEK 2019/26, date: 14.05.2019).

Informed Consent: The study was prospectively planned.

Footnotes

Authorship Contributions

Surgical and Medical Practices: İ.A., H.U.A., Ö.K.T., Concept: İ.A., H.U.A., Ö.K.T., Design: İ.A., H.U.A., Ö.K.T., Data Collection or Processing: İ.A., H.U.A., Analysis or Interpretation: İ.A., H.U.A., Ö.K.T., Literature Search: İ.A., H.U.A., Writing: İ.A., H.U.A., Ö.K.T.

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Outcome of Cardiac Arrest and Non-Cardiac Arrest Patients with Severe Acidosis in the Emergency Department: A Retrospective Cohort Study

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Abstract

Aim: We aimed to evaluate the outcome of cardiac arrest and non-cardiac arrest patients with severe acidosis admitted to the emergency department (ED) and to analyze the relationship between in-hospital mortality and clinical factors.

Materials and Methods: Patients with severe acidosis (pH <7.1) presenting to the ED were included in the study. Patients were divided according to arrest status and outcomes and analyzed accordingly.

Results: The study included 540 patients with severe acidosis. The 30-day mortality rate was 74.8% in all patients. In the non-cardiac arrest subgroup, the 30-day mortality rate was 21.4%. Non-arrest and non-survivors were more likely to be older, male, and have a higher prevalence of hypertension and coronary artery disease. Mortality was significantly higher among patients with sepsis, metabolic causes, and isolated respiratory arrest, while it was lower, in those with neurological etiologies, diabetic ketoacidosis, and seizures (p<0.05). Although no significant differences were observed in blood gas parameters, non-survivors had significantly higher lactate and creatinine levels lower hemoglobin levels (p<0.05). Univariate analysis identified advanced age, male sex, sepsis, metabolic causes, isolated respiratory arrest, hypertension, coronary artery disease, elevated partial carbon dioxide pressure (pCO₂) and creatinine, and reduced hemoglobin as significant predictors of 30-day mortality (p<0.05 for all).

Conclusion: Severe acidosis is associated with high 30-day mortality, particularly in cardiac arrest patients. However, non-arrest patients also exhibit considerable mortality. Advanced age, male sex, cardiovascular comorbidities, sepsis, and elevated lactate, pCO₂, and creatinine levels were identified as key predictors. Early recognition and management of these factors may improve outcomes.

Keywords: Severe acidosis, emergency, mortality

Introduction

The maintenance of blood pH within a narrow physiological range (7.35-7.45) is essential for the optimal activity of intracellular enzymes and the preservation of cellular membrane integrity (1). This homeostasis is regulated by buffer systems in conjunction with respiratory and renal mechanisms, which collectively prevent significant deviations in pH and thereby support the normal function of all cellular and organ systems (2).

Acid-base disorders are common among critically ill patients admitted to the emergency department (ED) and are observed in

97.3% of critical care areas such as the resuscitation area (3). Severe acidosis is a life-threatening emergency that is often associated with poor outcomes. Severe metabolic acidosis is typically defined as a pH level below 7.1. This condition may arise due to various etiologies, including lactate accumulation resulting from a shift to anaerobic cellular metabolism, acute or chronic renal insufficiency, systemic hypoperfusion, or hypoventilation (4).

The most significant issues linked to acidosis include hemodynamic instability, respiratory failure, renal and hepatic failure, severe infections, trauma, various metabolic disorders,



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and toxic ingestion. Consequently, acidemia has been identified as a poor prognostic factor (1). The presence of these conditions, along with the fact that acidemia is a symptom of a critical illness, explains why severe acidemia, generally (defined as a pH value below 6.8-7.0), is considered to be incompatible with life (5,6). However, there are rare reports of patients surviving even when the pH drops to as low as 6.7 (7-11). Determining the prognostic impact of severe acidemia could significantly influence critical patient care and decision-making in the initial hours of resuscitation, especially the mortality rate in this patient group is still unknown.

During cardiac arrest, tissue perfusion ceases entirely, leading to a shift toward anaerobic metabolism and the development of lactic acidosis. Following reperfusion, metabolic acidosis may further worsen. In patients with cardiac arrest, severe acidosis impairs myocardial contractility and diminishes the responsiveness to vasopressors, thereby negatively affecting resuscitation outcomes. Several studies have demonstrated that a pH level below 7.0 is associated with reduced rates of successful defibrillation and return of spontaneous circulation (12).

In non-cardiac arrest patients, severe acidosis is commonly observed in conditions such as diabetic ketoacidosis (DKA), acute and/or chronic renal failure (CRF), profound hypoxia, sepsis, and drug or alcohol intoxications (e.g., salicylates, metformin), as well as following epileptic seizures. In these cases, acidosis except in seizure-related presentations tends to develop more gradually and involves more complex pathophysiology. Although the underlying etiology may vary, a pH <7.2 in critically ill non-cardiac patients has been associated with increased mortality. However, early and targeted interventions in the ED, tailored to the specific cause, may improve patient outcomes (13). A review of the literature reveals that most existing studies have been conducted on cardiac arrest patients and within intensive care unit settings, primarily focusing on clinical and prognostic factors (5-13). This study primarily aimed to evaluate patients presenting to the ED with severe acidosis and to investigate the association between 30-day mortality and clinical factors, particularly in the subgroup of patients with non-cardiac arrest-related severe acidosis. A better understanding of the determinants of mortality in this patient population may contribute to the development of early diagnostic and therapeutic strategies in clinical practice. In this context, optimizing the clinical trajectory and treatment approaches for patients with severe acidosis represents a critical opportunity to improve patient management and outcomes.

Materials and Methods

This is a retrospective study. The Ethics Committee of University of Health Sciences Türkiye, Ankara Atatürk Sanatorium Training

and Research Hospital approved the study protocol in accordance with (decision number: 2024-BÇEK/11, date: 14.02.2024) the ethical principles of the Declaration of Helsinki and current Good Clinical Practice guidelines. Since our study was retrospective, the requirement for informed consent was waived.

Between 01.01.2021 and 01.12.2023, patients aged ≥ 18 years who were admitted to the ED of the 780-bed University of Health Sciences Türkiye, Ankara Atatürk Sanatorium Training and Research Hospital (Ankara, Türkiye) whose blood gas analysis obtained within the first hour of ED admission showed a pH value below 7.1 at least once were included in the study. Patients were excluded if they had unreliable blood gas analysis results (e.g., markedly inconsistent values in tests performed immediately before or after), lacked blood gas sampling within the first hour of admission, or had missing key parameters, lactate levels, complete blood count, international normalized ratio (INR), or biochemical values.

Demographic data, comorbidities [hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), chronic obstructive pulmonary disease, CRF, cerebrovascular disease], laboratory results (including biochemical values, venous blood gas analysis, etc.) and hospital outcomes were obtained through a retrospective review of patient files.

Patients were classified into the following categories based on the reason for admission: cardiac arrest, bleeding/trauma, intoxication, sepsis, metabolic, neurological, and unknown/other. Patients admitted with DKA and epileptic seizures were classified separately. Patients with multiple diagnoses were noted accordingly in the tables. Among non-arrest patients, those who developed severe acidosis due to DKA or epileptic seizures were evaluated separately.

Patients who were documented in the hospital records as having cardiac arrest and received cardiopulmonary resuscitation (CPR) were classified under the cardiac arrest group. Patients who did not undergo CPR and diagnosed with respiratory arrest in the system records were classified as having isolated respiratory arrest. Initially, a cohort was established comprising all patients with severe acidosis. Subsequently, a distinct subgroup of patients with severe acidosis but without cardiac arrest was identified. Statistical analyses were conducted to evaluate the factors associated with 30-day mortality in both groups.

Statistical Analysis

All data obtained throughout the study and recorded on the study form were analyzed using the IBM SPSS 20.0 statistical program (Chicago, IL, USA). The Kolmogorov-Smirnov test was used to determine whether the distribution of discrete and

continuous numerical variables followed a normal distribution. Continuous numerical variables were expressed as median interquartile range (IQR: 25-75), while categorical variables were expressed as the number of cases and percentages. Categorical variables were analyzed using the chi-square test, and continuous variables were analyzed using the Mann-Whitney U test. To identify the risk factors predicting mortality in patients with non-arrest severe acidosis, univariate regression analysis was performed. Results were considered statistically significant when $p < 0.05$.

Results

A total of 540 patients were included in the study (Figure 1). The median age was 69 years (IQR: 57-79), and 43.1% of the patients were female. Among the study population, 71.5% presented to the ED following cardiac arrest. The overall 30-day mortality rate was 74.8%.

When 30-day mortality rates were compared across all patients, those who died were significantly older and had a higher prevalence of HT and CAD, whereas DM was more common among survivors ($p < 0.05$ for all). Mortality rates were significantly elevated in patients with cardiovascular etiologies, while patients with metabolic or neurological etiologies exhibited lower mortality rates. Laboratory findings revealed that non-survivors were more acidotic and had significantly higher Partial carbon dioxide pressure (pCO_2), lactate, INR, creatinine, and potassium ($p < 0.05$ for all parameters) (Table 1).

In the non-arrest group, the 30-day mortality rate was 21.4%. Among these patients, those who died were more likely to be older and male, and have a higher prevalence of HT and CAD. Analysis of diagnostic categories revealed that mortality

was significantly higher in patients with sepsis, metabolic causes, and isolated respiratory arrest, whereas it was lower in those with neurological etiologies, DKA, and seizure-related presentations ($p < 0.05$ for all values). There were no statistically significant differences in arterial blood gas parameters between survivors and non-survivors. However, non-survivors exhibited significantly higher levels of lactate and creatinine, along with lower hemoglobin concentrations ($p < 0.05$ for all values) (Table 2).

In the subgroup of patients with non-arrest-related severe acidosis, univariate analyses were initially conducted to assess the impact of the variables listed in Table 3 on 30-day mortality. This analysis identified advanced age, male sex, presence of sepsis, metabolic causes, isolated respiratory arrest, HT, CAD, elevated pCO_2 and creatinine levels, and reduced hemoglobin as significant factors associated with increased mortality ($p < 0.05$ for all values).

Discussion

Although the adverse effects of severe acidosis are well-known, its impact on mortality and the factors influencing it remain unclear. In this study, conducted to examine the factors that may affect mortality, we identified several key variables that influence patient outcomes. The 30-day mortality rate in patients with severe acidosis was 74.8%, while the mortality rate for non-arrested patients was 21.4%. This rate was 68% in one study and 83% in another (4,5). In another study, the mortality rate for patients with a history of arrest was 90% (14). Although mortality rates are generally high, the significant survival rate observed in this patient group highlights the importance of early diagnosis of potential influencing factors and a timely treatment approach.

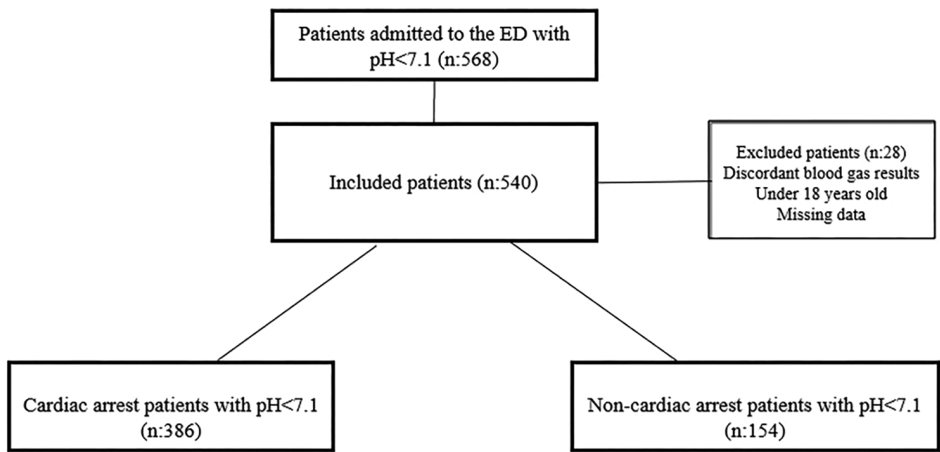


Figure 1. Flow chart of patients
ED: Emergency department

Table 1. Comparison of demographic and laboratory values of all patients according to 30-day mortality

	Survived (n=136)	Decased (n=404)	p value
Age, years, median (IQR: 25-75)	56.5 (34-70.75)	72 (62-81)	<0.001
Gender, female, (n %)	54 (39.7%)	179 (44.3%)	0.349
*Diagnosis, (n %)			
Cardiopulmonary arrest	15 (11.0%)	371 (91.8%)	<0.001
Hemorrhage/trauma	10 (7.4%)	24 (5.9%)	0.558
Intoxication	3 (2.2%)	7 (1.7%)	0.718
Sepsis	13 (9.6%)	49 (12.1%)	0.416
Metabolic	29 (21.3%)	32 (7.9%)	<0.001
Neurological	24 (17.6%)	4 (1.0%)	<0.001
Unknown	0 (0.0%)	138 (34.2%)	<0.001
Isolated respiratory arrest	9 (6.6%)	7 (1.7%)	0.007
Comorbidities, (n %)			
Hypertension	50 (36.8%)	188 (46.5%)	0.047
Diabetes	70 (51.5%)	150 (37.1%)	0.003
COPD	17 (12.5%)	75 (18.6%)	0.104
CAD	29 (21.3%)	145 (35.9%)	0.002
CRF	17 (12.5%)	27 (6.7%)	0.032
CVD	8 (5.9%)	27 (6.7%)	0.743
Malignancy	12 (8.8%)	46 (11.4%)	0.404
Laboratory, median (IQR: 25-75)			
pH	7.02 (6.93-7.06)	6.92 (6.81-7.01)	<0.001
pCO ₂ , mmHg	37.9 (25.6-54.5)	67.65 (49.22-86.47)	<0.001
HCO ₃ , mmol/L	9.4 (7.3-11.7)	9.3 (6.85-11.7)	0.661
BE, mmol/L	20.55 (16.42-24.2)	19.3 (15.3-23.5)	0.064
Anion gap, mEq/L	25.45 (18.02-31.45)	22.5 (17.27-27.52)	0.029
Lactate, mmol/L	4.74 (2.73-8.77)	9.98 (6.58-12.79)	<0.001
Hemoglobin, g/dL	14.3 (11.8-16.17)	11.8 (9.8-13.72)	<0.001
INR	1.28 (1.13-1.47)	1.53 (1.26-1.85)	<0.001
Glucose, mg/dL	218 (143.75-504.5)	236 (137-360)	0.136
Creatine, mg/dL	1.32 (1.1-1.87)	1.53 (1.21-2.3)	0.002
Potassium, mmol/L	4.94 (4.24-5.74)	5.52 (4.56-6.61)	<0.001

*Some patients were assigned more than one diagnosis, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, CRF: Chronic renal failure, CVD: Cerebrovascular disease, pCO₂: Partial carbon dioxide pressure, BE: Base excess HCO₃: Bicarbonate, INR: International normalization rate, IQR: Interquartile range

Table 2. Comparison of demographic and laboratory values of non-cardiac arrested patients according to 30-day mortality

	Survived (n=121)	Decased (n=33)	p value
Age, years, median (IQR: 25-75)	53 (31-70)	75 (68-84)	<0.001
Gender, female, (n %)	48 (39.7%)	20 (60.6%)	0.032
*Diagnosis, (n %)			
Cardiovascular disease	17 (14.0%)	8 (24.2%)	0.159
Hemorrhage/trauma	10 (8.3%)	1 (3.0%)	0.459
Intoxication	3 (2.5%)	2 (6.1%)	0.291
Sepsis	9 (7.4%)	15 (45.5%)	<0.001
Metabolic	29 (24.0%)	16 (48.5%)	0.006
Neurological	23 (19.0%)	1 (3.0%)	0.025
Isolated respiratory arrest	9 (7.4%)	7 (21.2%)	0.047
Diabetic ketoacidosis	38 (31.4%)	4 (12.1%)	0.027
Epileptic seizure	23 (19%)	0 (0.0%)	0.004
Comorbidities, (n %)			
Hypertension	44 (36.4%)	19 (57.6%)	0.028
Diabetes	67 (55.4%)	21 (63.6%)	0.395
COPD	15 (12.4%)	7 (21.2%)	0.259
CAD	26 (21.5%)	15 (45.5%)	0.006
CRF	17 (14.0%)	6 (18.2%)	0.584
CVD	7 (5.8%)	3 (9.1%)	0.447
Malignancy	10 (8.3%)	4 (12.1%)	0.501

Table 2. Continued			
	Survived (n=121)	Decased (n=33)	p value
Laboratory, median (IQR: 25-75)			
pH	7.02 (6.93-7.07)	7.03 (6.91-7.06)	0.824
pCO ₂ , mmHg	35.8 (24.55-52.6)	42.6 (30.7-60.4)	0.082
HCO ₃ ⁻ , mmol/L	9.0 (7.22-11.4)	9.8 (6.3-12.05)	0.646
BE, mmol/L	20.9 (17.25-24.6)	19.1 (15.4-25.4)	0.248
Anion gap	25.95 (18.25-31.87)	23.6 (16.8-27.8)	0.156
Lactate, mmol/L	4.25 (2.57-7.66)	6.78 (4.52-9.5)	0.041
Hemoglobin, g/dL	14.3 (11.9-16.3)	11.7 (9.5-13.35)	<0.001
INR	1.26 (1.12-1.46)	1.35 (1.17-1.65)	0.089
Glucose, mg/dL	211 (140-545.5)	217 (139.5-295)	0.359
Creatinine, mg/dL	1.33 (1.13-2.13)	2.31 (1.54-5.45)	<0.001
Potassium, mmol/L	4.97 (4.27-5.81)	5.44 (4.62-5.9)	0.174
*Some patients were assigned more than one diagnosis, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, CRF: Chronic renal failure, CVD: Cerebrovascular disease, pCO ₂ : Partial carbon dioxide pressure, HCO ₃ ⁻ : Bicarbonate, BE: Base excess, INR: International normalization rate, IQR: Interquartile range			

Table 3. Univariate regression model to predict the 30 day mortality in noncardiac arrest patients			
	Wald	p value	Odds ratio (95% CI)
Age, median (IQR: 25-75)	18.187	<0.001	1.062 (1.033-1.092)
Gender, female, (n %)	4.475	0.034	0.427 (0.194-0.939)
*Diagnosis, (n %)			
Cardiovascular disease	1.933	0.164	1.958 (0.759-5.047)
Intoxication	0.992	0.319	2.538 (0.406-15.857)
Sepsis	22.582	<0.001	10.370 (3.952-27.212)
Metabolic	7.179	0.007	2.986 (1.341-6.646)
Isolated respiratory arrest	4.851	0.028	3.350 (1.142-9.826)
Comorbidities, (n %)			
Hypertension	4.683	0.030	2.375 (1.085-5.199)
Diabetes mellitus	0.719	0.396	1.410 (0.637-3.122)
COPD	1.607	0.205	1.903 (0.704-5.143)
CAD	7.241	0.007	3.045 (1.353-6.851)
CRF	0.347	0.556	1.359 (0.489-3.779)
Malignancy	0.461	0.497	1.531 (0.448-5.235)
Laboratory, median (IQR: 25-75)			
pH	0.286	0.593	0.419 (0.017-10.124)
pCO ₂ , mmHg	3.676	0.045	1.017 (1.000-1.034)
HCO ₃ ⁻ , mmol/L	0.304	0.581	1.031 (0.924-1.151)
BE, mmol/L	1.124	0.289	0.967 (0.909-1.029)
Anion gap	1.465	0.226	0.971 (0.927-1.018)
Lactate, mmol/L	2.182	0.140	1.054 (0.983-1.131)
Hemoglobin, g/dL	12.233	<0.001	0.775 (0.672-0.894)
INR	0.167	0.683	0.962 (0.800-1.157)
Glucose, mg/dL	3.070	0.080	0.998 (0.996-1.000)
Creatinine, mg/dL	3.972	0.046	1.154 (1.002-1.328)
Potassium, mmol/L	1.520	0.218	1.230 (0.885-1.708)
*Some patients were assigned more than one diagnosis, COPD: Chronic obstructive pulmonary disease, CAD: Coronary artery disease, CRF: Chronic renal failure, pCO ₂ : Partial carbon dioxide pressure, HCO ₃ ⁻ : Bicarbonate, BE: Base excess, INR: International normalization rate, IQR: Interquartile range			

When the diagnoses of the patients were analyzed, cardiovascular mortality rates were high in the general patient group, while metabolic mortality rates were low. In the non-arrested patient group, mortality rates were significantly higher in cases of sepsis and metabolic causes compared to patients with DKA.

In one study, the primary disorder was not associated with mortality, whereas in another study, the mortality rate was found to be low in acidosis with metabolic causes (1-4). Mortality

rates in DKA have been found to be low in various studies. We believe that the relatively low mortality rate in DKA is due to the contribution of underlying secondary pathologies to the condition. The rate may have been higher in our study because cardiovascular diseases are among the common causes of death. However, early aggressive treatment in patients with suspected sepsis, among those without a history of arrest, but with severe acidosis, may serve as an important intervention to reduce mortality.

Analysis of blood gas parameters revealed that non-survivors were more acidotic and had significantly elevated levels of pCO_2 and lactate. Previous research has suggested that the severity of acidosis may be associated with patient prognosis (15). In the non-arrest subgroup, no significant differences were observed in pH or pCO_2 levels between survivors and non-survivors; however, lactate levels remained persistently elevated in those who died. Interestingly, although elevated lactate levels were also observed in patients presenting with epileptic seizures, no mortality occurred in this subgroup. This finding is consistent with a previous study reporting elevated lactate levels in seizure patients, attributed to transient anaerobic metabolism (16). Several studies have proposed that hyperlactatemia may be linked to increased mortality risk (1-14). In this context, we suggest that elevated lactate levels when interpreted in conjunction with the underlying etiology may serve as a valuable marker in guiding clinical decision-making in critically ill patients.

In the study by Gutgold et al. (4), it was reported that high CO_2 levels may be associated with mortality, while no relationship was found between pH and mortality. In another study, a high CO_2 level has been found to be associated with mortality (17). However, Allyn et al. (14) did not find a relationship between CO_2 levels and mortality. Since elevated CO_2 levels may reflect increased physiological dead space, they could indicate a prolonged duration since the onset of cardiac arrest, potentially leading to higher mortality because of irreversible tissue damage. This discrepancy may also be explained by differences in study settings, as our study was conducted in the ED, whereas the comparison study was conducted in an intensive care unit.

We found that potassium, creatinine, INR, and hemoglobin among laboratory parameters, as well as hemoglobin and creatinine in the non-arrest group, were associated with mortality. Although creatinine was found to be associated with mortality in the study by Allyn et al. (14), it was noted that explaining this relationship would be difficult. Paz et al. (5) reported that hyperkalemia could be a determinant of mortality. In a study conducted in patients diagnosed with acute renal failure, it was shown that both creatinine levels and hyperkalemia may be associated with mortality (18,19). Another study found that low hemoglobin levels could be associated with mortality (20). Therefore, we believe that high creatinine, high potassium, and low hemoglobin levels may serve as predictors of mortality in critically ill patients.

In our univariate analysis, sepsis, metabolic causes, and elevated pCO_2 levels were significantly associated with increased mortality. Advanced age was also found to be an independent predictor of mortality [odds ratio (OR): 1.062; 95% confidence interval: 1.033-1.092; $p<0.001$], which is consistent with the decline in physiological reserve and the increased burden of comorbidities

observed in older patients. When evaluated by diagnostic categories, sepsis (OR: 10.37; $p<0.001$), isolated respiratory causes (OR: 3.35; $p=0.028$), and metabolic causes (OR: 2.99; $p=0.007$) emerged as significant risk factors for mortality. The markedly high mortality observed in the sepsis group may be explained by mechanisms such as multi-organ dysfunction, cytokine storm, and lactic acidosis. These findings suggest that the systemic impact of sepsis-induced acidosis may be more devastating than that of other etiologies (21).

Among comorbid conditions, CAD was significantly associated with mortality (OR: 3.045; $p=0.007$). This finding may be attributed to reduced cardiovascular reserve and increased susceptibility to myocardial ischemia during episodes of systemic hypoperfusion. HT also emerged as a significant risk factor (OR: 2.375; $p=0.030$), suggesting that chronic vascular damage may exacerbate clinical outcomes during acute physiological stress. Regarding laboratory parameters, low hemoglobin was inversely associated with mortality (OR: 0.775; $p<0.001$). This association likely reflects impaired oxygen delivery capacity in the setting of reduced hemoglobin concentration, contributing to tissue hypoxia and adverse outcomes (22). In addition, elevated pCO_2 levels (OR: 1.017; $p=0.045$) and increased creatinine levels (OR: 1.154; $p=0.046$) were found to be significantly associated with mortality. These findings highlight the prognostic significance of respiratory failure and acute or chronic renal dysfunction, respectively (7). These findings may serve as a cautionary note in predicting mortality in patients with severe acidosis in the ED.

Study Limitations

This study has several limitations. First, its retrospective design led to instances of missing data, which may have introduced selection bias. Second, we did not subclassify the specific types of acid-base disturbances (e.g., high anion gap vs. normal anion gap metabolic acidosis), which limited our ability to draw definitive conclusions regarding the underlying etiologies. Third, overlapping primary diagnoses in some patients may have confounded outcome comparisons across diagnostic categories; for instance, a patient diagnosed with both DKA and sepsis was included in both groups, potentially distorting mortality estimates. Additionally, all blood gas samples analyzed were venous rather than arterial, precluding accurate assessment of oxygenation status. Finally, although a multivariable regression model was initially planned to identify independent predictors of mortality in non-cardiac arrest patients with severe acidosis, the analysis could not be performed due to statistical limitations. Specifically, modeling attempts resulted in perfect separation, where certain predictors (e.g., sepsis, age) nearly perfectly distinguished survivors from non-survivors. This issue, which commonly arises in small sample sizes or sparsely distributed

data, prevents reliable estimation of regression coefficients. Therefore, only unadjusted odds ratios from the univariate analysis are reported.

Conclusion

Although the majority of patients presenting to the ED with severe acidosis are those who have experienced cardiac arrest, a notable mortality rate also exists among patients with non-arrest-related severe acidosis. This study highlights that severe acidosis, particularly in the ED setting, is associated with high 30-day mortality, especially among patients presenting with cardiac arrest. However, even in the non-arrest subgroup, a substantial mortality rate of 21.4% was observed. Key predictors of mortality included advanced age, male sex, HT, CAD, sepsis, metabolic etiologies, isolated respiratory arrest, elevated pCO_2 and creatinine levels, and low hemoglobin. These findings underscore the importance of early recognition and targeted management of high-risk clinical and laboratory features to improve outcomes in patients with severe acidosis.

Ethics

Ethics Committee Approval: The Ethics Committee of University of Health Sciences Türkiye, Ankara Atatürk Sanatorium Training and Research Hospital approved the study protocol in accordance with (decision number: 2024-BÇEK/11, date: 14.02.2024) the ethical principles of the Declaration of Helsinki and current Good Clinical Practice guidelines.

Informed Consent: This is a retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Z.S.Ö., H.Ö.O., Concept: E.E., Design: E.E., Data Collection or Processing: Z.S.Ö., H.Ö.O., S.A., Analysis or Interpretation: E.E., Y.C., Literature Search: E.E., Writing: Z.S.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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Hemoglobin, Hematocrit, and Glucose Levels in Patients Aged 0-2 Years with Head Trauma Assessed in the Emergency Department

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Abstract

Aim: Head injuries are common in the pediatric population, with traumatic brain injury being a significant cause of morbidity and mortality. Assessing the clinical condition of children aged 0-2 years with head injuries is particularly challenging due to non-specific symptoms and limited communication abilities. This study aimed to investigate changes in post-traumatic levels of hemoglobin (HGB), hematocrit (HCT), and glucose, and to evaluate their potential as prognostic indicators for clinical outcomes and mortality.

Materials and Methods: This retrospective study was conducted with the approval of the Çukurova University Non-Interventional Clinical Research Ethics Committee. A total of 342 pediatric patients diagnosed with isolated moderate to severe head trauma were included. These patients were admitted to the Emergency Department of Niğde Ömer Halisdemir Training and Research Hospital between January 1, 2019, and January 1, 2022. Data were reviewed retrospectively. HGB, HCT, and glucose levels were compared based on trauma type and lesion characteristics using one ANOVA followed by Duncan's test. An independent t-test was used to compare laboratory values between patients who survived and those who did not. Statistical significance was set at $p < 0.05$. All analyses were performed using SPSS version 26.0 (IBM Corp.).

Results: Falls were the most common mechanism of injury, accounting for 161 cases (47%). Linear skull fractures were observed in 86 cases (25%). Of the total cases, 270 patients (79%) were admitted to the general ward, and 72 (21%) were admitted to the intensive care unit (ICU). A significant decrease in HGB and HCT levels, along with an increase in glucose levels, was observed in patients who died ($p < 0.001$). Similarly, these changes were significant among patients requiring ICU admission ($p < 0.001$).

Conclusion: Increased severity of head trauma was associated with greater reductions in HGB and HCT levels and elevated glucose levels. These laboratory parameters may serve as useful indicators of prognosis and mortality risk in pediatric patients with moderate to severe head trauma.

Keywords: Head trauma, hemoglobin, hematocrit, glucose, traumatic brain injury

Introduction

Head injuries are commonly encountered in pediatric emergency departments and can result in serious short- and long-term consequences. Due to their high prevalence and potentially severe outcomes, the Centers for Disease Control and Prevention have characterized traumatic brain injuries as a "silent epidemic" (1). Although trauma-related risks and complications affect all

pediatric age groups, clinical assessment is particularly challenging in children aged 0-2 years. In this age group, head injuries can range from minor trauma to skull fractures (2). Difficulties in obtaining an accurate history, limited cooperation during physical examination, and challenges in assessing the Glasgow Coma scale (GCS) complicate the evaluation process. Additionally, the risk of multiple organ injury and shock further hinders accurate clinical assessment in this vulnerable population (3).



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Computed tomography (CT) of the brain is considered the gold standard for diagnosing pediatric head trauma. However, its use involves exposure to ionizing radiation, which poses a significant concern in young children due to the associated increased lifetime risk of malignancies, including brain tumors and leukemia. This has led to diagnostic uncertainty, particularly in asymptomatic or minimally symptomatic cases, and raises concerns about overuse of imaging (4). In response, several clinical decision-making algorithms have been developed to guide CT use, including the Canadian CT Head Rule, New Orleans Criteria, NEXUS-II, National Institute for Health and Care Excellence guidelines, the Children's Head Injury Algorithm for the Prediction of Important Clinical Events, the Canadian Assessment of Tomography for Childhood Head Injury, and the Pediatric Emergency Care Applied Research Network (PECARN) criteria (5).

Among these, the PECARN criteria have shown the highest specificity for children under two years of age, with a reported sensitivity of 100% and specificity of 53%. The PECARN algorithm for this age group includes the following risk indicators: GCS ≤ 14 , altered mental status, presence of scalp hematoma in the occipital, parietal, or temporal regions, history of loss of consciousness ≥ 5 seconds, abnormal behavior as reported by a caregiver, and mechanisms of severe trauma (e.g., ejection from a motor vehicle, fatal motor vehicle collision, vehicle rollover, fall from a height greater than 3 feet (90 cm), or bicycle/motorcycle accidents without helmet use) (6). Despite the utility of PECARN and similar algorithms, they may not adequately capture early or asymptomatic presentations in young children, particularly when radiologic signs such as intracranial hemorrhage have not yet manifested (5,6).

This diagnostic limitation highlights the need for alternative, accessible, and objective biomarkers to support prognosis and clinical decision-making in this age group. Therefore, the present study investigates the relationship between hemoglobin (HGB), hematocrit (HCT), and glucose levels, which are commonly measured in emergency departments, inpatient units, and intensive care settings, and the severity of head trauma. The study also aims to evaluate the potential of these biomarkers as predictors of prognosis and mortality in children under the age of two with head injuries.

Materials and Methods

This retrospective study was conducted following the approval of the Çukurova University Non-Interventional Clinical Research Ethics Committee (decision number: 59, date: 07.04.2023). A total of 342 pediatric patients who presented to the emergency department of Niğde Ömer Halisdemir Training and Research Hospital between January 1, 2019, and January 1, 2022, and were

diagnosed with moderate to severe head trauma during their initial evaluation, were included in the review.

Exclusion criteria were as follows: the presence of additional trauma apart from head trauma, bleeding diathesis or any other bleeding disorder, acute or chronic anemia, congenital anomalies, diabetes mellitus, or hemolyzed blood samples obtained for biochemical and/or hematological analysis.

Inclusion criteria included isolated head trauma cases in children aged 0-2 years who were asymptomatic at the time of presentation to the emergency department and showed no evidence of bleeding on the initial brain CT scan.

The patients were stratified into two age groups: 0-12 months and 12-24 months. The aim was to evaluate potential differences in HGB, HCT, and glucose values across these age groups.

Falls from a height of 3 feet (90 cm) or more were classified as high falls, while those from lower heights were categorized as

Table 1. Frequencies of the parameters and data used in the study categorized by groups

		Number (n)	Percentage (%)
Trauma type	Fall	161	47
	Traffic accident	141	41
	Fall from height	40	12
Hospitalization	Intensive care	72	21
	Neurosurgery ward	270	79
Sex	Male	164	48
	Female	178	52
Age	0-12 months	209	61
	12-24 months	133	39
Lesion	Epidural hemorrhage	65	19
	Contusion	77	23
	Subdural hemorrhage	60	18
	Subarachnoid hemorrhage	54	16
	Linear skull bone fractures (total)	86	25
	Temporal skull bone fractures	35	10.2
	Frontal skull bone fractures	27	7.8
	Parietal skull bone fractures	15	4.3
	Occipital skull fractures	9	2.6

low falls, in accordance with the PECARN criteria for children under 2 years of age.

To minimize confusion related to timing and to allow for a more accurate analysis of case distribution throughout the day, the 24-hour period was divided into three equal 8-hour intervals over the study's 3-year duration.

In the emergency department of our hospital, 2 mL of venous blood was collected for complete blood count analysis and transferred immediately into purple-capped tubes containing K2 or K3 ethylenediaminetetraacetic acid (EDTA). The tubes were gently inverted several times to ensure proper mixing of EDTA with the blood to prevent clotting. The samples were promptly sent to the hospital laboratory and analyzed using the Sysmex XN-1000 SA-01 hematology analyzer. Reference ranges in our laboratory for HGB and HCT values in children aged 0-2 years are as follows: male patients: HGB 10.1-12.5 g/dL; HCT 30.8-37.8%; female patients: HGB 10.2-12.7 g/dL; HCT 30.9-37.9%. For glucose analysis, 1 mL of venous blood was collected into a 13×10 mm serum tube specifically designed for glucose testing. The samples were analyzed in the hospital's biochemistry laboratory using a Roche Cobas C501 autoanalyzer. The reference range for glucose in both male and female patients under 2 years of age was 74-106 mg/dL.

Statistical Analysis

Normality of the HCT, HGB, and glucose data was assessed using the Shapiro-Wilk test, along with evaluations of skewness and kurtosis. The data were found to follow a normal distribution ($p>0.05$). Therefore, one-way ANOVA was employed to compare HCT, HGB, and glucose levels based on trauma type and lesion characteristics. When significant differences were detected,

the Duncan post-hoc test was used to identify group-specific differences. An independent samples t-test was applied to compare laboratory values between deceased and surviving patients.

All statistical analyses were performed using IBM SPSS Statistics version 26 (SPSS Inc., Chicago, IL, USA), and a p value of <0.05 was considered statistically significant.

Results

The most common mechanism of head trauma was falls, accounting for 161 cases (47%), while falls from a height represented the least common cause, with 40 cases (12%). Of the 342 cases, 164 (48%) were male and 178 (52%) were female. Regarding age distribution, 209 patients (61%) were in the 0-12 month group, and 133 patients (39%) were in the 12-24 month group.

The most frequently observed injury was linear skull fracture, reported in 86 cases (25%), whereas the least frequent injury was subarachnoid hemorrhage, identified in 54 cases (16%), (Table 1).

One-way ANOVA and Duncan's post-hoc test were performed, based on the evaluated parameters, to assess whether there were statistically significant differences in HGB, HCT, and glucose levels among the groups. The results indicated significant differences in HGB and HCT values according to both the type of trauma and the type of lesion.

Although glucose levels did not significantly differ based on trauma type, a statistically significant increase in glucose values was observed when grouped by lesion type. Specifically, among trauma types, the lowest HGB and HCT values were recorded in

Table 2. Mean values of hemoglobin, hematocrit, and glucose levels according to trauma type and lesion type, including groupings based on Duncan's test results

Parameter	Trauma type					p value
	Fall	Traffic accident		Fall from height		
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Hemoglobin	11.75±0.10c	10.43±0.11b		9.74±0.17a		0.01
Hematocrit	34.88±0.26c	31.52±0.29b		29.5±0.5a		0.01
Glucose	102.91±1.09	108.28±1.51		103.3±3.03		>0.05
Parameter	Lesion					
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	p value
Group	Epidural hemorrhage	Contusion	Linear skull fractures	Subarachnoid hemorrhage	Subdural hemorrhage	
Hemoglobin	10.04±0.15ab	11.95±0.13c	12.04±0.14c	9.69±0.14a	10.34±0.11b	0.01
Hematocrit	30.78±0.36b	35.41±0.32c	35.61±0.32c	29.45±0.48a	31.01±0.26b	0.01
Glucose	107.86±2.47bc	102.16±1.6ab	101.78±1.63a	109.56±2.75c	107.05±1.45abc	0.01

*Values expressed with different letters are in different groups. Letters a, b and c represent different groups

cases involving falls from height. When categorized by lesion type, cases of SAH exhibited the lowest HGB and HCT values, as well as the highest glucose levels.

HGB, HCT, and glucose values were analyzed using one-way ANOVA and Duncan's post-hoc test to evaluate potential differences based on age group, sex, and hospital ward. No statistically significant differences were found in HGB, HCT, or glucose levels when grouped by age or gender. However, when grouped according to the ward of admission, the lowest HGB and HCT values and the highest glucose levels were observed in patients admitted to the ICU. An independent samples t-test was conducted to compare HGB, HCT, and glucose levels between patients who died and those who survived. The analysis revealed statistically significant differences in all three parameters between the deceased and surviving patients. Specifically, HGB and HCT levels were significantly lower, while glucose levels were significantly higher in the exitus group.

The distribution of cases was analyzed across three eight-hour intervals within a 24-hour period. The highest number of cases, 150 (44%), occurred between 08:00 and 15:59, while the lowest, totaling 68 cases (20%), was recorded between 00:01 and 07:59.

Discussion

Head injuries represent the most common type of pediatric trauma. Despite the implementation of preventive strategies, morbidity and mortality rates remain notably high among children. It has been reported that approximately 80% of pediatric deaths due to multiple trauma involve head injuries (7). Several studies have demonstrated that the severity of head trauma correlates with changes in specific laboratory parameters, such as HGB, HCT, and glucose levels. In cases of severe head trauma, HGB and HCT levels tend to decrease, while glucose levels often increase (1,8).

Torabi et al. (9) reported that in a study involving 157 patients, 19.2% exhibited brain damage on CT scans, and glucose levels were significantly higher in those with such findings. Another study suggested that elevated blood glucose and reduced HGB and HCT levels in pediatric patients with isolated head trauma may be associated with a poorer prognosis (10). A statistically significant association has also been noted between clinical symptoms such as recurrent vomiting, decreased consciousness, and headache and abnormal brain CT findings. It was further reported that only 3.5% of asymptomatic cases demonstrated positive CT findings (11). In some cases, it may take up to 48 hours for CT abnormalities to become apparent (12).

Table 3. Mean values of hemoglobin, hematocrit, and glucose levels based on gender, age group, and ward of admission, with groupings determined by Duncan's test

Sex				
Parameter		Male	Female	p value
		Mean \pm SD	Mean \pm SD	
	Hemoglobin	11.09 \pm 0.1	10.86 \pm 0.11	0.67
	Hematocrit	32.9 \pm 0.29	32.83 \pm 0.30	0.86
	Glucose	102.83 \pm 1.16	107.33 \pm 1.31	0.71
Age group				
Parameter		0-12 months	12-24 months	p value
		Mean \pm SD	Mean \pm SD	
	Hemoglobin	11 \pm 0.11	10.93 \pm 0.12	0.68
	Hematocrit	32.85 \pm 0.28	32.89 \pm 0.30	0.94
	Glucose	106.08 \pm 1.25	103.75 \pm 1.17	0.62
Service**				
Parameter		Intensive care hospitalization	Service hospitalization	p value
		Mean \pm SD	Mean \pm SD	
	Hemoglobin	9.98 \pm 0.14	11.24 \pm 0.09	<0.001
	Hematocrit	29.89 \pm 0.40	33.66 \pm 0.22	<0.001
	Glucose	105.58 \pm 2.02	105.56 \pm 1.99	<0.001
Values expressed with different letters are in different groups. Letters a, b and c represent different groups				

Table 4. Comparison of mean glucose, hemoglobin, and hematocrit values between deceased and surviving patients

Parametre	Group		p value
	Dead patients	Surviving patients	
Hemoglobin	8.01±0.14	10.97±0.08	<0.001
Hematocrit	27.25±0.38	32.87±0.20	<0.001
Glucose	159.24±3.98	105.17±0.88	<0.001

Table 5. Distribution of cases by time of occurrence within 24-hour intervals

	Time	Number (n)	Percentage (%)
Time period of the event	08:00-16:00	150	44.01
	16:01-24:00	124	36.25
	24:01-07:59	68	20.04

Given the potential long-term risks of ionizing radiation, especially the increased risk of malignancy in pediatric populations, cautious use of CT imaging is advised in this age group (13). Several studies have indicated that repeated cranial CT scans in hospitalized children may contribute to mortality rates of up to 15% annually, and result in substantial healthcare costs due to radiation-induced malignancies (14).

Consistent with findings in the literature, this study observed that decreasing HGB and HCT levels and increasing glucose levels were associated with increasing trauma severity. In fatal cases (exitus), these changes were particularly pronounced. Cases involving high-energy trauma, such as traffic accidents or falls from heights, were associated with lower initial GCS scores and more severe clinical presentations. These patients were more likely to be admitted to the ICU. Among ICU admissions, patients who were later found to have subarachnoid hemorrhage (SAH) on follow-up CT scans exhibited more pronounced reductions in HGB and HCT, and elevated glucose levels.

These findings suggest that reductions in HGB and HCT, and elevations in glucose may be indicative of poor prognosis, increased morbidity, and higher mortality risk. Therefore, such laboratory parameters could serve as useful adjuncts in clinical decision-making and management. Furthermore, in asymptomatic pediatric patients, particularly those under 2 years of age, monitoring these parameters may reduce the need for unnecessary or repeated CT scans between the time of trauma and symptom onset potentially minimizing radiation exposure, reducing the risk of long-term complications such as malignancy, and decreasing healthcare costs.

Head trauma can lead to a variety of intracranial lesions, with traumatic SAH associated with higher morbidity and mortality rates compared to other intracranial hemorrhages. The reported mortality rate for traumatic SAH ranges from 50% to 60% (15). In line with this, our study found that patients with SAH particularly those resulting from high-energy trauma per PECARN criteria presented with more severe clinical findings, lower GCS scores, and were more frequently admitted to the ICU. In these cases, laboratory data showed greater declines in HGB and HCT and higher glucose values.

Moreover, existing studies have identified linear skull fractures as the most common lesion in pediatric head trauma (16), with the temporal and frontal bones being the most frequently affected sites (17). Our study similarly found linear skull fractures to be the most prevalent injury pattern.

Similarly, in this study, linear skull fractures were identified as the most common cranial injury, observed in 86 cases (25%). Among these, 35 cases (10.2%) involved the temporal bone, 27 cases (7.8%) involved the frontal bone, 15 cases (4.3%) involved the parietal bone, and 9 cases (2.6%) involved the occipital bone. Other documented lesions included cerebral contusions in 77 cases (23%), epidural hemorrhage in 65 cases (19%), subdural hemorrhage in 60 cases (18%), and SAH in 54 cases (16%).

Previous studies have shown gender-related differences in the incidence of pediatric head trauma, with most reporting a higher prevalence among males (18). However, in this study, females accounted for 178 cases (52%) and males for 164 cases (48%). This reversal may reflect demographic or social factors influencing healthcare-seeking behavior during the study period, such as a higher likelihood of female children being brought to the emergency department.

Research has also indicated that head trauma in children below one year of age most frequently occurs between 0 and 12 months and is primarily caused by falls (19,20). In line with this, our study found that 209 cases (61%) occurred in the 0-12 month age group, compared to 133 cases (39%) in the 12-24 month group. Falls were the leading cause of injury (161 cases, 47%), followed by traffic accidents (141 cases, 41%) and falls from height (40 cases, 12%). The high frequency of falls in this age group may be attributed to underdeveloped motor skills, increased susceptibility to environmental obstacles, and insufficient supervision by caregivers.

Several studies have explored the timing of pediatric head trauma. Some have reported peak incidence between 06:01 am and 12:00 pm (1), while others noted increased frequency between 3:00 pm and 7:00 pm (21). AlSowailmi et al. (22)

similarly reported that most cases occurred in the afternoon. Consistent with these findings, this study found that 150 cases (44.01%) occurred between 8:00 am and 4:01 pm., 124 cases (36.25%) between 4:01 pm and midnight, and 68 cases (20.04%) between midnight and 7:59 am. The higher number of daytime cases may be related to increased physical activity during waking hours, whereas lower case counts at night may correspond to longer sleep durations.

Study Limitations

It is important to note that this study is limited by its retrospective design and single-center data collection from a hospital in Niğde, which may affect the generalizability of the findings. Further multicenter studies with larger and more diverse populations are necessary to validate these results and improve clinical guidelines.

Conclusion

This study demonstrated that in children under two years of age, increasing trauma severity was associated with greater reductions in HGB and HCT levels, and elevations in glucose levels. These changes were more pronounced in patients with fatal outcomes (exitus) or those requiring ICU admission. A statistically significant association was observed between HGB, HCT, and glucose values, and poor prognosis, including increased morbidity and mortality. The majority of head trauma cases occurred between 8:00 am and 4:00 pm and were primarily caused by falls. No significant differences in HGB, HCT, or glucose levels were found when analyzed by age or gender. Further research is essential to develop predictive models, improve early diagnosis and treatment strategies, and establish standardized clinical criteria. The present study aims to contribute to the existing body of literature and serve as a reference point for future investigations.

Ethics

Ethics Committee Approval: The approval of the Çukurova University Non-Interventional Clinical Research Ethics Committee (desicion number: 59, date: 07.04.2023).

Informed Consent: This retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ö.Y., Concept: Ö.Y., Design: Ö.Y., Data Collection or Processing: Ö.Y., M.G., Analysis or Interpretation: Ö.Y., Literature Search: Ö.Y., M.G., Writing: Ö.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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Evaluation of Earthquake Victims Following the 2023 Kahramanmaraş-Türkiye Earthquake: A Multicenter Trial with 8025 Cases

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Abstract

Aim: Our multicenter study includes the largest number of earthquake victims reported in the literature, aiming to evaluate demographic data and outcomes of patients who presented to emergency departments following 2023 Kahramanmaraş, Türkiye earthquake.

Materials and Methods: Patients admitted to hospital emergency departments after the February 6, 2023 Kahramanmaraş earthquakes were retrospectively evaluated over a 22-day period. Data analyzed included age, gender, triage scales, overall health status, vital signs, laboratory and imaging results, definitive diagnoses, outcomes of patients, and emergency interventions.

Results: Of the 8025 patients reported in 18 centers, 51.2% (n=4112) were female, and the average age of the patients was 40.91±20.12. A total of 3578 people (57.6%) had a green triage tag, indicating good overall health with relatively minor injuries. Lower extremity fractures were the most prevalent finding in radiographs, accounting for 33.7% (n=663), of the cases, while cerebral hemorrhage, rib fractures, and lumbar fractures were the most common results in tomography scans. The three most common diagnoses were soft tissue trauma (n=1270; 21.1%), crush syndrome (n=932; 15.5%), and lower extremity fractures (n=851; 14.2%). Cast-splint application (n=813; 22.18%), central venous catheterization (n=393; 10.72%), and fasciotomy (n=322; 8.78%) were the primary procedures performed in the emergency departments. Out of the 1886 hospitalized patients, the orthopedics clinic received the highest number of admissions (n=600). A total of 3461 patients were discharged, and 495 died.

Conclusion: Findings of our study revealed higher rates of morbidity and mortality than in previous earthquakes, with orthopedic injuries being the most common outcome of earthquake-related trauma. We believe that establishing tent hospitals in earthquake-prone regions and surrounding provinces, constructing long-term healthcare facilities and trauma centers with emergency services, testing facilities, imaging areas, operating rooms, hemodialysis and intensive care units, employing horizontal architecture designs, and improving referral networks can help to reduce these rates.

Keywords: Earthquake, trauma, morbidity, mortality, precautions

Introduction

Throughout history, natural disasters resulting in significant loss of life and property damage have occurred in many of our country's earthquake-prone areas. Notable catastrophic events include the earthquakes in 1939 Erzincan, 1949 Karlıova, 1998 Adana Ceyhan, 1999 Gölcük, 2003 Bingöl, 2011 Van, 2020 Elazığ, and, most recently, the Kahramanmaraş earthquake on February 6, 2023, which also devastated the surrounding provinces.

In the immediate aftermath of an earthquake, disruptions frequently occur during the initial response, subsequent follow-up, and patient treatment. These challenges arise from unavailable hospital transportation routes, insufficient healthcare personnel, and limited healthcare facilities (1,2). Such difficulties became particularly evident following the large-magnitude Kahramanmaraş earthquake. The extent of injury caused by earthquakes directly influences the incidence of fatalities and life-threatening conditions such as crush syndrome, myocardial infarction, hemopneumothorax, vascular injuries, intra-abdominal injuries, pelvic injuries, and renal failure (3). Over the past century, earthquakes have

accounted for 100,000 fatalities in Türkiye (4). According to official data from April 2023, the Kahramanmaraş earthquake alone resulted in over 50,000 deaths and more than 120,000 injuries. Our study aims to contribute to the existing literature by analyzing information obtained from multiple hospitals that managed victims of the 2023 Kahramanmaraş earthquake. (Photograph 1a-e).

Materials and Methods

Ethical approval for this study was obtained from the University of Health Sciences Türkiye, Adana City Training and Research Hospital Clinical Research Ethics Committee (decision number: 2569, date: 11.05.2023). Following this approval and authorization from hospital administrations, hospital records of earthquake victims brought to emergency services after the two Kahramanmaraş earthquakes, first, with magnitude 7.7 (duration 65 seconds, depth 9.1 kilometers) at 04.17 local time, and second, with magnitude 7.6 (duration 45 seconds, depth 16.4 kilometers) at 13.24 on February 6, 2023, were reviewed. Age, gender, mode of arrival, triage rankings, general health status, vital signs, physical examination findings, laboratory and imaging results,



Photograph 1a. A patient suffering from crush trauma and subsequent compartment syndrome

definitive diagnoses, emergency interventions, hospitalized clinics, patient transport methods, consultations, and outcomes were evaluated by combining the data with records from both assigned and volunteered earthquake response teams.

Statistical Analysis

A chi-square test was used to examine the associations between two categorical variables. Descriptive statistics for categorical variables are provided as numbers and percentages. Hypotheses were evaluated bidirectionally, with p-values less than 0.05 signifying statistical significance. SPSS Windows version 24.0 (Statistical Package for the Social Sciences) by IBM Corporation in Chicago, United States, was utilized.

Results

A total of 8025 patient records were obtained from 18 different healthcare centers. Of all patients, 51.2% (n=4112) were female, and average age of patients was 40.91 ± 20.12 . More than half (59.6%, n=4446) of the patients presented to the hospital by their own means, and of these, 3578 (57.6%) patients were categorized with a green triage tag, indicating good overall health and



Photograph 1b. Patient evacuation via aircraft

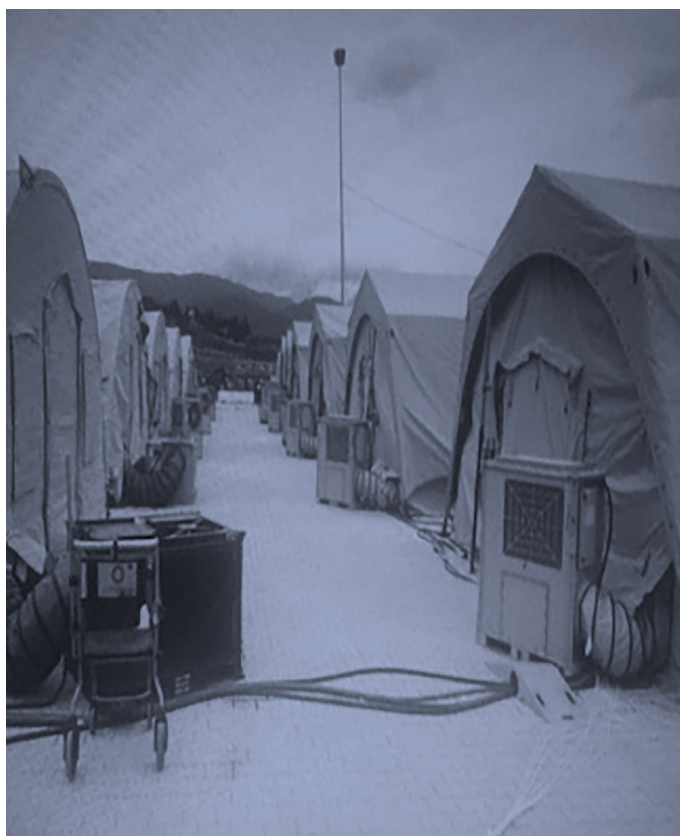
relatively minor injuries. University of Health Sciences Türkiye, Adana City Training and Research Hospital, received the highest number of patients, accounting for 11.8% (n=944) of the study population (Table 1).

Table 2 displays the summary of the patients' laboratory parameters and vital signs.

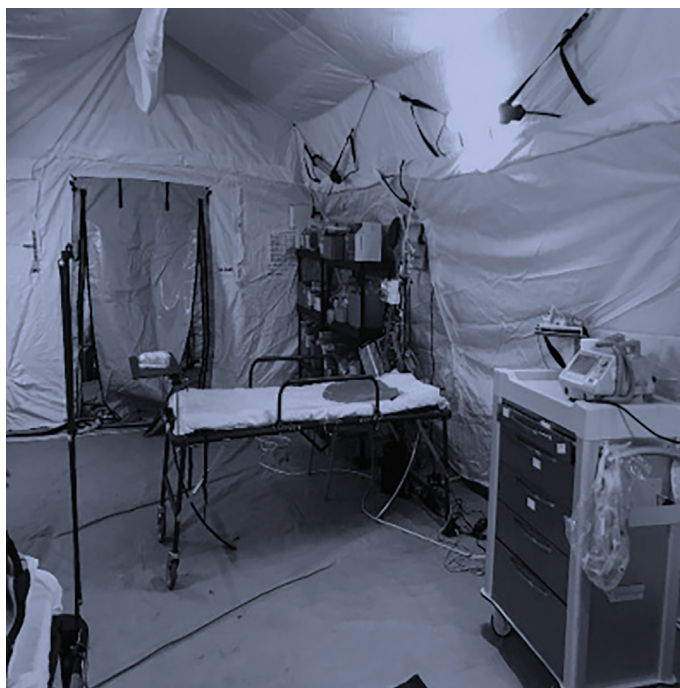
Among patients whose electrocardiographys could be obtained, 909 exhibited sinus rhythm, 197 had sinus tachycardia, and 34 presented with atrial fibrillation. Direct radiography results revealed that lower extremity fractures were the most common injuries sustained by patients, accounting for 33.7% (n=663) of findings. Pelvic fractures, rib fractures, lumbar fractures, free fluid in the abdomen, and cerebral hemorrhage were the most common injuries observed in the computed tomography results. (Table 3).

Soft tissue trauma (n=1270, 21.1%), crush injuries (n= unspecified, 15.5%), and lower extremity fractures (n=851, 14.2%) were the three most frequent diagnoses (Table 4).

The most frequent procedures performed on patients were casting-splinting (22.18%, n=813), central venous catheterization



Photograph 1c. Exterior view of a mobile field hospital



Photograph 1d. Interior view of a mobile field hospital



Photograph 1e. Photo of a severely damaged building following the earthquake

(Images taken from the archive of Ali Karakuş)

(10.72%, n=393), and fasciotomy (8.78%, n=322). Table 5 outlines all interventions performed.

Orthopedics (n=2225, 35.57%), internal medicine (n=1312, 20.98%), and neurosurgery (n=672, 10.74%) were the most frequently consulted departments by emergency department physicians. Consistent with this, these three clinics also received the highest number of admissions (Figure 1).

Transportation between healthcare facilities occurred primarily by patients' own means (38%), followed by ambulance (35%), sea vehicles (20%), and aircraft (7%). Outcomes included 495 deaths, 1,886 hospitalizations, and 3,461 discharges (Figure 2).

Discussion

The February 2023 earthquake in Kahramanmaraş, Türkiye, impacted more than 13 million individuals across a vast geographical area. Government statistics released following the event reported over 50,000 deaths and 107,000 injuries (5). In the aftermath of such catastrophic disasters, technological shortcomings and unexpected adverse outcomes can render registration systems inadequate, leading to patient information being missing or unrecorded in healthcare facilities. The ability to accurately record and maintain patient registration information, as well as medical status details, is crucial in both routine and extraordinary situations. During such disasters, healthcare centers often face impaired registration due to factors such as crowding in emergency departments, disruptions in the information recording and automation systems, and insufficient personnel. Similar issues have been observed in previous disasters, yet adequate measures were not consistently taken to establish the necessary precautions despite acknowledging the challenges of maintaining records and their critical role (6-10). Our study

Table 1. Hospitals and patient demographics: age, gender, mode of arrival, and overall health condition of patients included in the study

Healthcare center	n (%)
1. University of Health Sciences Türkiye, Adana City Training and Research Hospital	944 (11.8)
2. Mersin University Faculty of Medicine	892 (11.1)
3. Çukurova University Faculty of Medicine	771 (9.6)
4. Osmaniye State Hospital	727 (9.1)
5. Hatay Mustafa Kemal University Faculty of Medicine	714 (8.9)
6. University of Health Sciences Türkiye, Elazığ Fethi Sekin State Hospital	678 (8.4)
7. Gaziantep 25 Aralık State Hospital	548 (6.8)
8. Adıyaman University Faculty of Medicine	476 (5.9)
9. Malatya İnönü University Faculty of Medicine	467 (5.8)
10. University of Health Sciences Türkiye, Diyarbakır Gazi Yaşargil Training and Research Hospital	413 (5.1)
11. Adana Seyhan State Hospital	392 (4.9)
12. Fırat University Faculty of Medicine	283 (3.5)
13. Harran University Faculty of Medicine	217 (2.7)
14. Dicle University Faculty of Medicine	192 (2.4)
15. Gaziantep Nizip State Hospital	132 (1.6)
16. Malatya Turgut Özal University Training and Research Hospital	90 (1.1)
17. Kahramanmaraş Sütçü İmam University Faculty of Medicine	53 (0.7)
18. Çanakkale Mehmet Akif Ersoy State Hospital	36 (0.4)
Age, mean \pm SD (min-max)	40.91\pm20.12 (0-103)
Gender	
Female	4112 (5.2)
Male	3913 (48.8)
Method of arrival to hospital	
Deceased prior to arrival	438 (5.9)
By own means	4446 (59.6)
By ambulance	2524 (33.8)
Other	51 (0.7)
Overall health condition/triage tag	
Non-urgent (green)	3578 (57.6)
Less urgent (yellow)	1634 (26.3)
Urgent/life-threatening (red)	1001 (16.1)

SD: Standard deviation

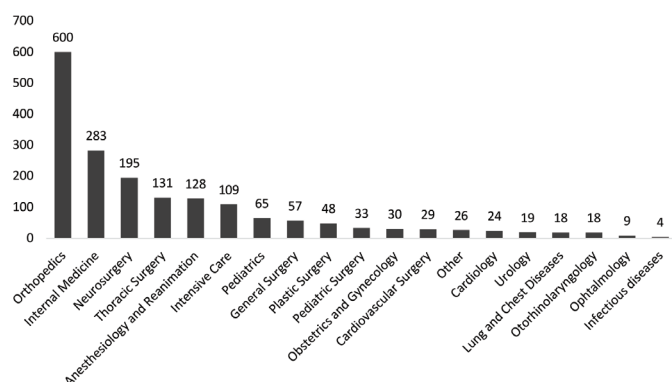
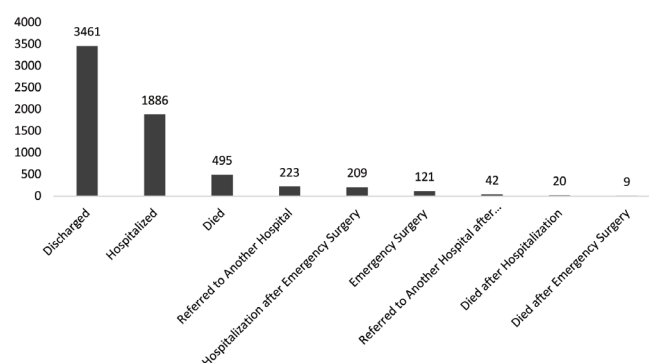
**Figure 1.** Bar graph showing the distribution of departments where patients were admitted**Figure 2.** Bar graph showing distribution of patient outcomes

Table 2. Distribution of vital signs and laboratory parameters of the patients		
	Mean ± SD	Median (min-max)
Glascow coma score	13.79±3.37	15 (3-15)
Blood pressure (systolic) (mmHg)	124.81±17.55	124 (20-220)
Blood pressure (diastolic) (mmHg)	80.02±13.2	80 (0-158)
Heart rate (bpm)	82.94±16.98	81 (0-154)
Body temperature (°C)	36.45±0.47	36.4 (26.4-39.2)
PO ₂ (mmHg)	96.61±4.08	98 (22-100)
White blood cells (x10 ⁹ /L)	14.11±7.25	12.43 (0.1-49.98)
Platelet count (x10 ⁹ /L)	261949.69±225254.02	237000 (5820-725000)
Blood urea nitrogen (mg/dL)	36.85±33.47	24.8 (1.84-279)
Creatinine (mg/dL)	1.13±1.2	0.78 (0.1-14)
Na ⁺ (mEq/L)	138.41±5.36	138 (110-189)
K ⁺ (mEq/L)	4.46±0.86	4.3 (1-14.92)
CK (U/L)	8870.21±27682.29	790 (2-344650)
CK-Mb (ng/mL)	136.18±149.96	83 (5-635)
Amylase (U/L)	131.59±277.74	58 (10-2947)
AST (U/L)	380.06±625.69	141 (0.3-6363)
ALT (U/L)	189.12±368.74	73.9 (5.5-4055)
Troponin (ng/mL)	727.78±1367.46	193 (0.11-7460)
CRP (mg/L)	103.01±93.78	96 (0-604)
Glucose (mg/dL)	150.26±112.14	112.5 (20-676)
Albumin (g/dL)	17.23±11.11	15 (2.6-36)
Calcium (mg/dL)	7.18±0.9	7.5 (5.1-8.2)
Lactate (mmol/L)	3.43±3.48	2.3 (0-21.5)
pH (blood gas)	7.34±0.12	7.37 (6-7.72)
HCO ₃ (blood gas) (mEq/L)	21.4±6.27	22.3 (0-64.2)

SD: Standard deviation, CK: Creatine kinase, CK-Mb: Creatine kinase-myocardial band, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein

across eighteen different centers highlighted these shortcomings, as data was often manually recorded on A4-sized blank papers, procedural notebooks, and patient cards. Many patients could not be properly registered at hospitals due to overcrowding in emergency departments, lack of internet connectivity, and faulty automation systems. Some records were eventually entered into the hospital automation using patient lists compiled by assigned staff members.

Alternative solutions for recording system malfunctions should be developed to avoid such issues in the future, and patient information systems should be organized well in advance of unforeseen disasters. Future improvements may include placing wristbands with identifying information, ensuring patient registration cards are easily accessible and readily available in adequate numbers, providing sufficient communication equipment and base stations, and enhancing hospital recording systems and data networks to manage the increased demand. Part

of the healthcare staff should be specifically assigned to handle patient data, especially in the initial hours and days following a disaster. Patient cards or pre-made paper frameworks should contain all relevant data about the patient, including name, identifying information, address, physical findings, diagnosis, treatment, and outcomes.

Beyond immediate property damage and casualties, earthquakes can result in a variety of acute and chronic conditions. Injuries sustained after an earthquake are usually caused by falling objects or being trapped under rubble. The most common traumatic complications in the immediate aftermath of earthquakes include head traumas, lower extremity injuries, and crush syndrome, a complication characterized by development of renal failure after crushing trauma (1,4,8,11). According to the study of Ceylan et al. (6), spinal injuries, crush injuries, open and closed fractures, soft tissue injuries, and compartment syndrome were the most frequent orthopedic injuries following an earthquake.

Table 3. Distribution of radiological imaging results

	n (%)
Direct radiography	
Fracture on skull radiograph	33 (1.7)
Vertebra fracture	27 (1.4)
Rib fracture	24 (1.2)
Pneumothorax	21 (1.1)
Hemothorax	11 (0.6)
Hemopneumothorax	30 (1.5)
Pelvic fracture	120 (6.1)
Fracture of upper extremity	323 (16.4)
Fracture of lower extremity	663 (33.7)
Other imaging findings	717 (36.4)
Head CT	
Cerebral hemorrhage	79 (25)
Fracture	43 (13.6)
Cerebral hemorrhage and fracture	16 (5.1)
Other intracranial pathologies	178 (56.3)
Thorax CT	
Rib fracture	111 (26.8)
Pneumothorax	56 (13.5)
Hemothorax	31 (7.5)
Hemopneumothorax	43 (10.4)
Pericardial effusion	16 (3.9)
Other thoracic findings	157 (37.9)
Spine CT	
Cervical spine fracture	21 (5.3)
Thoracic spine fracture	56 (14)
Lumbar spine fracture	169 (42.2)
Sacral spine fracture	26 (6.5)
Other spinal trauma findings	128 (32)
Abdominal CT	
Spleen laceration	25 (8.9)
Liver laceration	12 (4.3)
Diaphragm injury	40 (14.3)
Free intraperitoneal fluid	47 (16.8)
Other intra-abdominal injuries	156 (55.7)
Pelvic CT	
Pelvic fracture	125 (47.9)
Other pelvic trauma findings	136 (52.1)
CT: Computed tomography	

Another study conducted on Great Hanshin earthquake survivors identified spinal injuries, extremity fractures, and pneumothorax as common injuries (12). Fractures of the upper and lower extremities were reported to be the most common diagnoses in the study of Keskin et al. (1), which included 532 patients. Many other studies have also highlighted the significance of crush syndrome and acute renal failure associated with it (13-18). Acute compartment syndrome is another significant complication of earthquake-related trauma, with reported incidences varying from 1.36 to 16.6% (19). If left untreated, acute compartment syndrome can result in lifelong problems, including limb loss in severe cases. Consistent with the previous research, lower extremity fractures, crush syndrome, and soft tissue damage were the most common diagnoses in our study. Patients who developed crush syndrome and acute renal failure underwent emergent hemodialysis. Some patients required transfer to nearby institutions in the initial days following the earthquake due to an increase in orthopedic and surgical emergencies and limited operating room availability.

The primary objective of emergency physicians following catastrophic events is to focus on patients with a high likelihood of survival and administer appropriate treatments as soon as possible. Initial management of earthquake survivors includes airway assessment, cardiopulmonary resuscitation, fluid therapy, wound cleansing, tetanus prophylaxis, symptomatic approach, and administration of antibiotics and analgesics. Additional treatments and interventions include emergency fasciotomy, hemodialysis, cast-splint placement, and extremity elevation (15,19). The most frequently administered treatments and performed procedures documented in our study included airway management, cardiopulmonary resuscitation, fluid therapy, tetanus prophylaxis, painkiller administration, plaster splint placement following a symptomatic approach, and emergency fasciotomy.

Among the most significant challenges posed by earthquakes are organizational issues observed both within and between hospitals, as well as issues related to the disaster's epicenter. Following the initial response, a strategic approach with appropriate referral and transportation processes should be implemented without delay (1,2,15). Emergency helicopter transportation has been shown to be particularly successful for patients in this context, given the road network congestion following the earthquake (12). During the aftermath of the 2023 Kahramanmaraş earthquake, patient transfer times were prolonged due to a large number of earthquake victims, limited laboratory capacity, damaged airport roads, traffic jams, and hospital overcrowding in neighboring provinces. Attempts were made to use the İskenderun seaport to transport patients to Mersin and other districts. Many patients

Table 4. Distribution of the most common five diagnoses

	Diagnosis					Total n (%)
	I	II	III	IV	V	
Acute abdominal pain	79	9	0	0	0	88 (1.5)
Crush syndrome	905	27	0	0	0	932 (15.5)
Acute kidney injury	89	140	2	0	0	231 (3.9)
Hemothorax	41	23	7	0	0	71 (1.2)
Hemopneumothorax	208	72	23	0	0	303 (5.1)
Fracture of upper extremity	352	183	41	5	1	582 (9.7)
Fracture of lower extremity	489	217	110	31	4	851 (14.2)
Vascular trauma	38	12	6	2	1	59 (1)
Cerebral hemorrhage	171	23	9	8	1	212 (3.5)
Spinal injury	233	35	33	13	6	320 (5.3)
Pelvic injury	101	40	11	4	1	157 (2.5)
Pneumomediastinum	9	0	3	0	0	12 (0.2)
Amputation	2	0	0	0	0	2 (0.1)
Compartment syndrome	19	0	8	0	0	27 (0.4)
Multitrauma	3	0	0	0	0	3 (0.1)
Soft tissue injury	1267	3	0	0	0	1270 (21.1)
Vertebral fracture	10	0	0	0	0	10 (0.2)
Rib fracture	15	0	0	0	0	15 (0.3)
Other	821	26	5	0	0	852 (14.2)

Table 5. Distribution of procedures administered to patients

	Applied procedure					Total n (%)
	I	II	III	IV	V	
Central venous catheterization	391	2	0	0	0	393 (10.72)
Amputation	109	49	0	0	0	158 (4.31)
Reduction of dislocated joints	208	40	3	0	0	251 (6.85)
Fixation of fractures	136	98	29	0	0	263 (7.17)
Fasciotomy	196	49	56	21	0	322 (8.78)
Casting-splinting	611	140	46	14	2	813 (22.18)
Suturing	287	21	5	4	2	319 (8.7)
Chest tube placement	177	47	13	3	1	241 (6.57)
Thoracotomy	11	4	3	0	1	19 (0.52)
Craniotomy	14	2	2	5	0	23 (0.63)
Laparotomy	28	16	3	2	0	49 (1.34)
Hemodialysis	89	70	27	5	6	197 (5.37)
Other	420	33	7	4	0	464 (12.66)
Cardiopulmonary resuscitation	102	42	2	0	0	146 (3.98)
Emergent delivery	6	2	0	0	0	8 (0.22)

were able to transport themselves to another hospital during the immediate post-disaster period. Patient transfers were significantly improved after establishing airplane and helicopter ambulance services.

Over the past three decades, earthquakes have caused an estimated 1 million fatalities worldwide. China recorded the largest number of fatalities in 1556, with 830,000 deaths. Türkiye has lost more than 100,000 people to earthquakes during the last century (4). Research suggests that 85-95% of patients can be saved within the first 24-28 hours with the proper interventions. Death rates following earthquakes tend to increase over the following years. The 1995 Hanshin-Awaji earthquake resulted in 6,434 fatalities, predominantly due to thoracic trauma and severe crush injuries. Meanwhile, the 2011 Japan earthquake and tsunami caused an estimated 10,000 to 18,500 deaths (9,12,15,20). While hypovolemia and vital organ damage were the most common causes of mortality in the initial 48 hours following an earthquake, acute renal failure, sepsis, multiorgan failure, and myocardial infarction were identified as the leading causes of death within the first week (1). In the immediate aftermath of the disaster, a lack of available patient records led to some pre-hospital deaths being processed through the emergency room. Most deceased individuals were later moved to the hospital morgue or to established wards within hours. The majority of earthquake-related fatalities resulted from severe vascular injuries, hypovolemia, hypoxia, thoracic or intra-abdominal organ damage, and crush injuries from being buried under the debris. For those admitted to hospital, sepsis and multiorgan failure were the main causes of death. The most valuable lesson learned from earthquakes is that timely preparation is the most effective approach for reducing death and injury. To achieve this goal, seismic studies should be conducted before designing and constructing earthquake-resistant public structures, residential areas, and healthcare facilities.

Study Limitations

While our study represents the largest case series on earthquake-related trauma reported to date, it has several limitations. Data collection was challenging due to infrastructure failure, which may have led to inaccuracies in manually recorded patient information. Heterogeneity across 18 healthcare centers may have introduced variability in practices, and focusing solely on emergency department presentations means the study doesn't capture individuals who died at the scene. Finally, the limited 22-day follow-up, means long-term outcomes were not assessed.

Conclusion

Earthquakes belong to the group of disasters in which preventive measures are essential to avoid catastrophic outcomes. To reduce

the number of fatalities and injuries, physicians and healthcare workers should learn from past incidents and proactively implement strong security measures. Our study revealed higher morbidity and fatality rates compared to those reported in previous earthquakes. Rapid deployment of field hospitals is essential at the onset of an earthquake to minimize mortality and morbidity rates and traumatic complications. Construction efforts should include permanent hospitals with horizontal architectural design and equipped with comprehensive departments including emergency services, testing facilities, imaging centers, operating rooms, and intensive care units. The number of trauma hospitals and intensive care units needs to be increased, and referral networks improved, in both earthquake-prone areas and low-risk neighboring provinces. Similar scenarios occurred during previous disasters, but a lack of sufficient precautions meant the outcomes remained largely unchanged. It is crucial to learn from these traumatic experiences to avoid past mistakes.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the University of Health Sciences Türkiye, Adana City Training and Research Hospital Clinical Research Ethics Committee (decision number: 2569, date: 11.05.2023).

Informed Consent: This is retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: All authors, Concept: A.K., A.A. Ö.Y., Design: A.K., A.A. Ö.Y., Data Collection or Processing: All authors, Analysis or Interpretation: Ö.Y., M.K. B.K., Literature Search: Ö.Y., M.K. Writing: Ö.Y., M.K.

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Prognosis Assessment in Emergency Department via Nutritional and Muscle Measurements for Home Health Care Patients

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Abstract

Aim: This study examined the relationship between the factors contributing to emergency department visits for patients who receive home health care services and the density and area of the pectoralis major muscle.

Materials and Methods: In this study, the relationship between demographic data, mini nutritional assessment form data, scores, malnutrition situation, pectoralis major muscle density and area measured on thoracic tomography and prognosis of patients receiving home health care who applied to the emergency department between January and December 2023 was examined.

Results: A total of 220 patient files were found that met the study criteria. The mean screening score of all patients and the mean malnutrition indicator score indicated a risk of malnutrition. In the Ex-group, pectoralis major muscle density (especially on the right side) and area (especially on the left side) were significantly lower, respectively. Pectoralis major muscle density and area measurements of patients with sarcopenia in both sexes were significantly lower compared to control subjects.

Conclusion: The contribution of the pectoralis major muscle to daily living activities is limited, which may lead to a more pronounced occurrence of sarcopenia in patients who are bedridden and immobile for extended periods. Moreover, monitoring the decline in area and density within this muscle group is crucial for accurately predicting prognosis.

Keywords: Emergency department, pectoralis major muscle, prognosis, home healthcare

Introduction

Many studies have thoroughly explored the challenges and health implications associated with the rising elderly population, directly resulting from increased life expectancy. An effort has been made to investigate how reducing muscle volume due to ageing affects healing time for diseases, treatment responses, complications, and survival rates.

Nutrition is crucial for effective muscle building. Hormonal changes associated with ageing, chronic diseases, and long-

term medication use significantly decrease muscle anabolism and increase catabolism. Furthermore, factors such as reduced mobility, insufficient protein intake, and malnutrition from unbalanced and inadequate diets directly contribute to pronounced muscle loss in older adults. It is imperative to address these issues to maintain muscle health as we age. In this group, muscle breakdown and reduced muscle function are evident among individuals with significant mobility limitations who can walk with support and depend on others for food and toileting (1). Older adults who are bedridden, require assistance to



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walk, and depend on others for daily activities often experience significant muscle loss. These issues must be prioritised to ensure enhanced support and improved quality of life for this vulnerable population.

Research illustrates that ageing is associated with decreased muscle mass and increased intramuscular fat accumulation. These factors contribute to elevated levels of pro-inflammatory cytokines, which are linked to a heightened risk of metabolic and cardiovascular diseases (2,3). Decreased muscle density is linked to functional loss, leading to longer hospital stays in intensive care patients and worse outcomes for cancer patients (4,5). Sarcopenia, often seen in elderly patients with malnutrition, reduces infection resistance, slows recovery, and causes frequent long-term hospitalisations. Muscle weakness also heightens the risk of falls. The dislocation and fracture of the hip can result in significant adverse effects, such as heightened medication usage and a diminished quality of life for patients (6). In patients who are bedridden or have limited mobility, the prognosis is typically poor due to the exacerbation of chronic diseases, decreased muscle strength, and prolonged infection duration (7). Malnutrition weakens respiratory muscles and alters lung structure, raising the risk of pulmonary infections and negatively impacting lung function. In an experimental study, rats were subjected to a ten-day fasting diet. The findings indicated that malnutrition led to an expansion of the alveolar spaces, reduced surfactant production, and the development of shortness of breath. These results underscore the significant impact of nutritional deprivation on respiratory function (8).

The pectoralis major muscle (PMM) is located in the anterior region of the chest. Its primary function is to connect the ribcage to the arm and scapula. Although it does not function directly as a respiratory muscle, it provides support during inspiration (9,10). Studies show that internal skeletal muscle strength can be evaluated with PMM measurement and can be a prognostic factor for disease outcomes (11).

This study examined the relationship between the factors contributing to emergency department (ED) visits for patients who receive home health care services and the density and area of PMM, where PMM refers to (define PMM if not previously defined). We focused on clinical outcomes in this patient group by providing precise prognostic assessments. Our efforts emphasise implementing structured rehabilitation and nutrition programs to prevent or mitigate muscle loss and enhance muscle quality.

Materials and Methods

Patient Selection

This study involved a retrospective review of patient files of patients who presented to the ED, possessed home health care records, and underwent thorax computed tomography (CT) imaging. Furthermore, we analyzed how all collected data impacted mortality during the hospital stay.

Patients who were not registered with home health care services, did not have a thoracic CT, did not complete an Mini Nutritional Assessment (MNA) form, presented due to trauma, or died in the ED were excluded from the study (Figure 1).

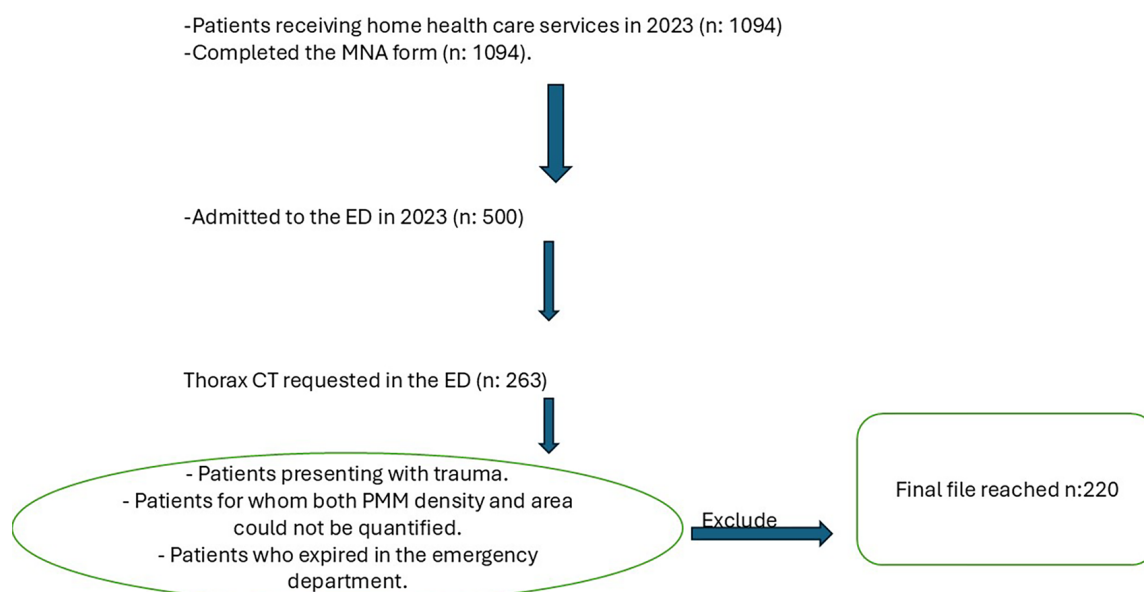


Figure 1. Study inclusion and exclusion criteria

PMM: Pectoralis major muscle, ED: Emergency department, CT: Computed tomography

For the study, demographic data, diagnosis, dependency classification (such as bedridden, dependent on others for toilet or food), service they were admitted to if hospitalised, duration of hospital stay, and outcomes for those who received home health services and applied to the ED between January 1, 2023, -and December 31, 2023, were noted. This information was combined with data from MNA forms recorded in the home health services archive. This study was approved by the Kırklareli University Faculty of Medicine Ethics Committee (decision number: P202400017/4-date: 29.05.2024). The study was conducted in accordance with the Declaration of Helsinki. Due to the retrospective nature of the study, informed consent was not obtained. However, we ensured the privacy and confidentiality of the patients' data.

Data Classification

The MNA form is a screening test designed for geriatric patients. It comprises two key components: screening and assessment. There are six questions in the screening score section:

- 1- Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties? (0 point (p)= severe decrease in food intake, 1 p= moderate decrease in food intake, 2 p= no decrease in food intake)
- 2- Weight loss during the last 3 months (0p = weight loss greater than 3 kilogram (kg), 1p= does not know, 2p= weight loss between 1 and 3 kg, 3p= no weight loss)
- 3- Mobility (0p= bed or chair bound, 1p= able to get out of bed/ chair but does not go out, 2p= goes out)
- 4- Has suffered psychological stress or acute disease in the past 3 months? (0p= yes, 2p= no)
- 5- Has neuropsychological problems? (0p= severe dementia or depression, 1p= mild dementia, 2p= no psychological problems)
- 6- Body mass index (BMI) (0p= BMI less than 19, 1p= BMI 19 to less than 21, 2p= BMI 21 to less than 23, 3p= BMI 23 or greater) is questioned and noted.

The highest score that can be obtained from this section is 14. Scores between zero and 7 indicate that individuals are "malnourished"; scores between 8 and 11 suggest that individuals are "at risk of malnutrition"; and scores between 12 and 14 indicate that individuals are in "normal nutritional status." If a score of 11 or below is received from this section, the assessment section will be started.

The purpose of the assessment score section is to calculate the individuals' "malnutrition indicator score." The assessment consists of 12 sections, and the maximum score is 16:

- 1- Lives independently (not in nursing home or hospital) (1p= yes, 0p= no)
- 2- Takes more than 3 prescription drugs per day (0p= yes, 1p= no)
- 3- Pressure sores or skin ulcers (0p= yes, 1p= no)
- 4- How many full meals does the patient eat daily? (0p= 1 meal, 1p= 2 meals, 2p=3 meals)
- 5- Selected consumption markers for protein intake (yes or no answers were recorded for consuming eggs/legumes 2 or more times a week, at least 1 serving of dairy products per day, and meat/fish/white meat every day (0p= if the number of yes is 0/1, 0.5p= if the number of yes is 2, 1p= if the number of yes is 3)
- 6- Consumes two or more servings of fruit or vegetables per day (1p= yes, 0p= no)
- 7- How much fluid (water, juice, coffee, tea, milk...) is consumed per day? (0p= less than 3 cups, 0.5p= 3 to 5 cups, 1p= more than 5 cups)
- 8- Mode of feeding (0p= unable to eat without assistance, 1p= self-fed with some difficulty, 2p= self-fed without any problem)
- 9- Self view of nutritional status (0p= views self as being malnourished, 1p= is uncertain of nutritional state, 2p= views self as having no nutritional problem)
- 10- In comparison with other people of the same age, how does the patient consider his or her health status? (0 points = not as good, 0.5 points= does not know, 1 point= as good, 2 points= better)
- 11- Mid-arm circumference (MAC) in cm (0p= MAC less than 21, 0.5p= MAC 21 to 22, 1p= MAC greater than 22)
- 12- Calf circumference (CC) in cm (0p= CC less than 31, 1p= CC 31 or greater)

The malnutrition indicator score is determined based on the scores acquired from these two sections. In this section, three different score ranges are used to define patients regarding nutrition. According to these ranges, if the test score is below 17, the patient is "malnourished." If the score is between 17 and 23.5, the patient is at risk of malnutrition. If the score is between 24 and 30, the patient is considered to have a "normal nutritional status" (12).

Thoracic Tomography Evaluation

Thorax CT examinations were performed using Siemens Healthineers Somatom go.now (Erlangen, Germany), a model device with 32 detectors, a slice thickness of 3 mm, and a dose

of 110 kV. Measurements were made on a radiology workstation called "Radiant".

The areas and densities of the PMM were measured by a radiologist with 15 years of experience.

The area of the PMM was measured manually by drawing a polygonal region of interest on a single axial image of the CT scan just above the aortic arch. PMM contours were determined and measured. Area measurements were made in all patients included in the study.

Right and left pectoral muscle density was measured at the same level (Figure 2). Muscle density measurement was performed only on images obtained without a contrast agent. Density measurement was not performed on contrast-enhanced scans. Additionally, images showing artefacts were excluded; density measurements were not conducted.

The right and left PMM areas were measured (in cm²), and the density was calculated in Hounsfield units.

Statistical Analysis

The analysis was conducted to determine the statistical significance of the relationships among patients' nutrition types, nutritional adequacy, weight and muscle loss, and the duration and prognosis of the disease.

The descriptive statistics of the data included the mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The distribution of variables was measured by Kolmogorov-Smirnov and Shapiro-Wilk tests. The independent sample t-test was used to analyse quantitative independent data

with a normal distribution, and the Mann-Whitney U test was used to analyse data with a non-normal distribution. The chi-square test was used in the analysis of qualitative independent data. The SPSS 28.0 program was used in the analyses. When the chi-square test conditions were not met, the Fisher's exact test was used. In all tests, a p-value of less than 0.05 was considered statistically significant.

Results

A total of 220 patient files were found that met the study criteria. 54.1% of the patients were female, and the mean age was 79.0 ± 12.0 years. 37.7% of the patients were bedridden or chair-bound. A severe decrease in nutrition was detected in 8.6% of them, and a decrease of more than three kilograms in weight was detected in 9% of them, in the last three months. There were no patients in nursing homes or hospitals. 10.9% of the patients had pressure sores. Seven point seven percent stated that they ate at most one meal a day. It was determined that 45.4% did not consume enough protein, 52.2% consumed less than 2 servings of fruit/vegetables per day, and 33.7% consumed less than 3 glasses of liquid per day. 15.4% of the patients thought they were malnourished. 28.1% thought their health was not good compared to their peers. Thirty-five percent were dependent on someone else to eat. The mean screening score of all patients was 9.4 ± 2.5 , and the mean malnutrition indicator score was 19.3 ± 4.7 points, which indicates they are at risk of malnutrition. PMM (right) density and area average was low in all patients. The most frequently diagnosed disease groups in the ED were related to lung, musculoskeletal, and cardiac diseases. It was

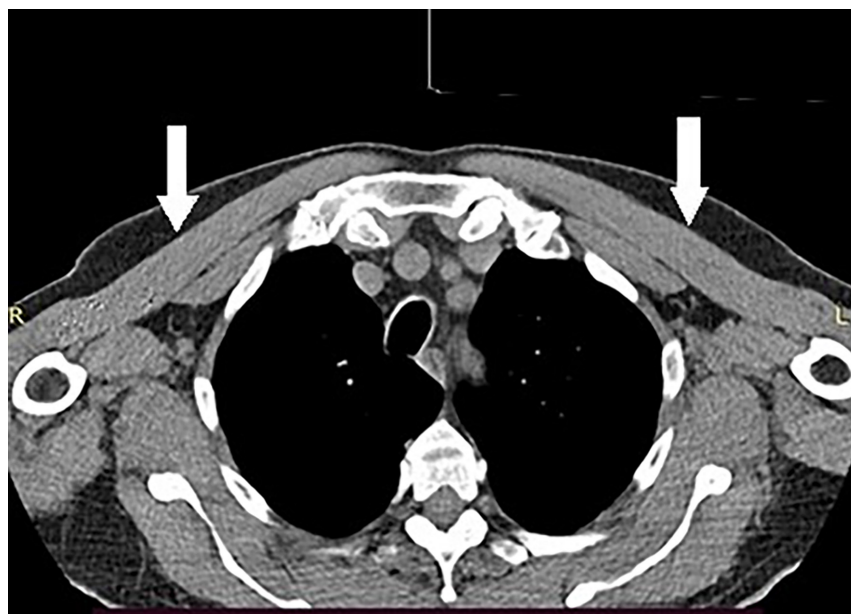


Figure 2. White arrows indicate right and left pectoralis major muscles

determined that 41.4% of the patients were admitted to the ward from the ED, and 22% of these patients expired in the ward (Table 1).

When the patients were examined according to their hospitalization status, the prevalence of inpatient treatment was higher in female patients ($p=0.024$). PMM density (especially on the right side) was significantly lower in the hospitalized group than in the other group ($p<0.001$). The PMM area (particularly the left side) was lower in the hospitalized group than in the other group; however, the difference was not statistically significant ($p=0.241$). Screening, assessment, and total malnutrition indicator scores were found to be low in both groups. The rate of hospitalization due to problems related to electrolyte disorders and neurological diseases was higher compared to other

conditions ($p=0.000/0.007$). The ex-rate was significantly higher in the hospitalized group than in the other group ($p=0.000$) (Table 2).

When patients were analysed according to their prognosis, the death rate of female patients was higher than that of male patients ($p=0.049$). In the Ex-group, PMM density, especially on the right side ($p=0.019$), and area, especially on the left side ($p=0.005$), were significantly lower than in the other group. Screening ($p=0.524$), assessment ($p=0.689$), and malnutrition indicator scores ($p=0.968$) were low in both groups, but there was no difference between the groups. The hospital stay of patients with ex was longer than that of the other group, but there was no statistically significant difference between the groups ($p=0.514$) (Table 3).

Mean PMM density ($p<0.001$) and total PMM area ($p=0.003$) were significantly higher in men than women. The malnutrition score was considerably lower in men than in women ($p=0.036$). PMM area measurements of patients with sarcopenia in both sexes were significantly lower than those of patients without sarcopenia ($p=0.027/0.033$). Scores screening ($p=0.023/0.024$) and malnutrition scores of patients with sarcopenia in both genders were significantly lower than those of patients without sarcopenia ($p=0.001/0.000$) (Table 4).

Discussion

This study provides compelling evidence that PMM density and area are inversely related to mortality rates. Additionally, it highlights that a reduction in PMM density is associated with a greater likelihood of patients receiving inpatient treatment.

It's essential to consider other factors for a more accurate assessment (13). The determination of area and density using imaging methods for internal skeletal muscles, such as PMM, produces more precise results.

Men inherently possess more muscle mass than women, which is a primary reason why sarcopenia is observed more markedly in women (14). While malnutrition affects both sexes, the greater muscle mass in men significantly enhances their prognosis. This explains why female patients in this study showed significantly lower muscle area and density compared to males, indicating sarcopenia.

Sarcopenia is defined as progressive muscle loss. It may develop due to age, loss of activity, diseases, and nutrition (15). Drummond et al. (16) observed impaired muscle signalling in individuals who were sedentary for 7 days, despite amino acid supplementation for basal muscle protein synthesis. The evidence indicates that sarcopenia and muscle deterioration

Table 1. Demographic characteristics of patients and MNA form results

Age, years, mean \pm SD	79 \pm 12.0
Gender, n (%)	
Female	119 (54.1)
Male	101 (45.9)
PMM density (HU), mean \pm SD	
Right	46.6 \pm 11.5
Left	45.3 \pm 12.1
PMM area (cm ²), mean \pm SD	
Right	9.4 \pm 5.0
Left	9.3 \pm 5.3
Screening score	9.4 \pm 2.5
Assessment	9.8 \pm 3.6
Malnutrition indicator score	19.3 \pm 4.7
Diagnosis in the ED, n (%)	
Pulmonary disease	73 (33.2)
Electrolyte disorders	17 (7.7)
GIS	23 (10.5)
GUS	18 (8.2)
Cardiac disease	29 (13.2)
Musculoskeletal disease	40 (18.2)
Neurological disease	20 (9.1)
The outcome in the ED, n (%)	
Discharge from ED	128 (58.1)
Hospitalization	92 (41.8)
Length of stay, days, mean \pm SD	15.1 \pm 18
Outcome in the service, n (%)	
Discharge	71 (77.1)
Ex	21 (22.9)

SD: Standard deviation, GIS: gastrointestinal system, GUS: genitourinary system, HU: Hounsfield unit, PMM: Pectoralis major muscle, ED: Emergency department, MNA: Mini Nutritional Assessment

Table 2. Results of patients’ hospitalization status			
	Discharge from ED (n=128)	Hospitalization (n=92)	p value
Age, median (min-max)	79.0 (21.0-98.0)	82.0 (51.0-96.0)	0.105
Gender, n (%)			
Female	61 (47.7)	58 (63.0)	0.024
Male	67 (52.3)	34 (37.0)	
PMM density (HU), mean ± SD			
Right	49.9±10.1	42.7±11.9	<0.005
Left	47.7±11.2	42.4±12.6	<0.005
PMM area (cm²), median (min-max)			
Right	8.9 (0.6-33.1)	8.1 (1.9-31.3)	0.318
Left	9.0 (0.0-28.5)	7.6 (1.6-34.3)	0.241
Screening score, median (min-max)	9.0 (1.0-14.0)	10.0 (3.0-14.0)	0.120
Assessment, median (min-max)	10.5 (2.0-16.0)	8.8 (1.0-16.0)	0.144
Malnutrition indicator score, median (min-max)	20.0 (9.0-29.0)	19.8 (8.0-29.0)	0.770
Mortality			
No	128 (100.0)	71 (78.3)	<0.005
Yes	0 (0.0)	21 (21.7)	
SD: Standard deviation, HU: Hounsfield unit, PMM: Pectoralis major muscle, ED: Emergency department			

SD: Standard deviation, HU: Hounsfield unit, PMM: Pectoralis major muscle, ED: Emergency department

Table 3. Prognosis of patients			
	Survived (n=199)	Exitus (n=21)	p value
Age, median (min-max)	81 (21.0-98.0)	83.0 (66.0-94.0)	0.226
Gender, n (%)			
Female	104 (52.0)	15 (71.4)	0.049
Male	96 (48.0)	6 (28.6)	
PMM density (HU)			
Right, mean ± SD	47.4±11.2	40.5±12.2	0.019
Left, median (min-max)	46.7 (14.6-80.5)	40.8 (6.8-60.3)	<0.005
PMM area (cm²), median (min-max)			
Right	8.8 (0.6-33.1)	6.6 (3.0-11.7)	0.011
Left	8.8 (0.0-34.3)	6.2 (2.8-13.2)	0.030
Screening score, median (min-max)	10.0 (1.0-14.0)	10.0 (6.0-13.0)	0.524
Assessment, median (min-max)	9.5 (1.0-16.0)	9.3 (4.0-14.0)	0.689
Malnutrition indicator score, median (min-max)	20.0 (8.0-29.0)	19.5 (12.0-26.5)	0.968
Length of stay, days, median (min-max)	10.0 (1.0-60.0)	9.0 (1.0-150.0)	0.514
SD: Standard deviation, HU: Hounsfield unit, PMM: Pectoralis major muscle			

SD: Standard deviation, HU: Hounsfield unit, PMM: Pectoralis major muscle

can quickly become irreversible for patients who are bedridden for prolonged periods. To significantly improve outcomes, it is crucial to initiate radical changes in both nutrition and mobility from day one, including implementing passive exercises. Taking these steps early can make a profound difference in recovery. Furthermore, sarcopenic obesity arises when muscle tissue is lost at a faster rate than fat tissue during sarcopenia. Excess fat tissue within the muscle causes lower density readings in CT. Koçyiğit et al. (17) demonstrated that elderly patients with sarcopenic

obesity exhibited lower scores on the MNA and showed greater susceptibility to infections compared to their peers. This study establishes that the elevated hospitalisation and death rates among patients with PMM area and low density are directly linked to immune system disorders caused by sarcopenia and sarcopenic obesity (18).

This study demonstrated that the mean MNA score of all patients receiving home health care indicates a significant risk of malnutrition. The results show that patients lack adequate

Table 4. Analysis of sarcopenia presence by gender

	Female		p value	Male		p value
	Sarcopenia (+)	Sarcopenia (-)		Sarcopenia (+)	Sarcopenia (-)	
BMI (kg/m²), n (%)						
Underweight	7 (5.9)	-		10 (9.9)	-	
Normal	-	19 (16)	0.409	-	12 (11.9)	0.409
Overweight	93 (78,2)	-		79 (78.2)	-	
PMM density (HU), mean ± SD	85.0±22.6	97.2±20.2	0.202	98.4±15.5	105.1±20.7	0.265
Total PMM area (cm²), median (min-max)	10.3 (5.6-18.4)	15.7 (0.6-61.1)	0.027	14.6 (5.7-24.8)	19.5 (5.1-64.0)	0.033
Screening score, median (min-max)	8.0 (1.0-11.0)	10.0 (3.0-14.0)	0.023	7.5 (4.0-11.0)	10.0 (4.0-14.0)	0.024
Malnutrition indicator score, median (min-max)	13.5 (9.0-20.5)	21.0 (8.0-28.0)	0.001	13.3 (9.0-21.5)	19.0 (9.0-29.0)	<0.005
BMI: Body mass index, SD: Standard deviation, HU: Hounsfield unit, PMM: Pectoralis major muscle						

and balanced nutrition. Limited movement further contributes to the inevitable onset of sarcopenia in these individuals. Malnutrition, similar to sarcopenia, also leads to impairment of the T-cell response, alterations in macrophage function and activity, and a decline in type IV hypersensitivity reactions. The increasing average age is particularly associated with an risk of serious infections due to a decline in immune system function, consequently raising the risk of sepsis (19). Pneumonia is the most common cause of death in elderly patients (20). This study demonstrates that a substantial proportion of patients who died had electrolyte disorders. While we could not definitively determine if these disorders arose as a consequence of pneumonia, it is evident that most patients experienced issues directly related to lung pathology. The ageing process leads to an increase in sarcopenia, which significantly impairs respiratory reflexes, including coughing. Furthermore, low PMM density and area play a important role in the development of pneumonia (21,22). We believe that the factor contributing to this situation is the generally low muscle mass and density observed within the patient population we examined. It is essential to strengthen the PMM to ensure that the respiratory reflex remains highly effective (23).

Study Limitations

The principal limitation of this study is its reliance on retrospective data from a single institution. Certain data may have been inaccessible. Additionally, because only the records of patients presenting to the ED and undergoing non-contrast thorax CT scans were evaluated, definitive conclusions cannot be generalized to all patients receiving home healthcare services. Nonetheless, considering that the data were derived from the sole hospital situated in the city center—the largest hospital in the province—the findings possess considerable relevance.

Conclusion

The contribution of PMM to daily living activities is limited, which may lead to a more pronounced occurrence of sarcopenia in patients who are bedridden and immobile for extended periods. Relying solely on measurements of exoskeletal muscles can lead to misunderstandings when identifying sarcopenia. This muscle group can be quantified via CT scans obtained in the ED, thereby potentially assisting in prognostic prediction.

Ethics

Ethics Committee Approval: This study was approved by the Kırklareli University Faculty of Medicine Ethics Committee (decision number: P202400017/4-date: 29.05.2024). The study was conducted in accordance with the Declaration of Helsinki.

Informed Consent: Due to the retrospective nature of the study, informed consent was not obtained.

Footnotes

Author Contributions

Surgical and Medical Practices: O.G., L.T., E.P.S., Concept: O.G., D.V.K., L.T., G.A., E.P.S., Design: O.G., L.T., E.P.S., Data Collection or Processing: L.T., E.P.S., Analysis or Interpretation: O.G., G.A., E.P.S., Literature Search: D.V.K., G.A., Writing: O.G., D.V.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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Evaluation of Trauma Severity Scores in Electric Scooter Related Injuries

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Abstract

Aim: Our study aimed to identify injuries related to electric scooters (e-scooters) in the emergency department (ED) and to compare trauma severity scores.

Materials and Methods: This prospective, single-center study was conducted during the 3-month summer period between June 1 and August 31, 2023, on adult and pediatric patients who presented to the ED with e-scooter-related injuries. ROC analyses were performed for the injury severity score (ISS), revised trauma score (RTS), and trauma and injury severity score (TRISS).

Results: A total of 106 patients were included, with a mean age of 21.5 years (interquartile range: 15–39.5), and 69.8% (n=74) were male. The three most commonly injured areas in patients admitted to the ED with e-scooter injuries were the head (50.9%, n=54), knee (34.9%, n=37), and forearm-elbow (26.4%, n=28). The median ISS of patients admitted to the intensive care unit was higher than that of patients admitted to the ward or discharged (NISS: 18 vs. 2), whereas the median RTS and TRISS values were lower (RTS: 7.64 vs. 7.84; TRISS: 4.39 vs. 5.72). The median ISS of deceased patients was higher than that of surviving patients (ISS: 29 vs. 2), while the RTS and TRISS values were lower (RTS: 7.11 vs. 7.84; TRISS: 3.48 vs. 5.72). The TRISS (area under the curve =0.991) had the highest discriminatory ability in predicting mortality (p<0.001). When the TRISS was ≤4.47, the sensitivity for predicting mortality was 100%, specificity 96.97%, positive predictive value 70%, negative predictive value 100%, positive likelihood ratio 33, and negative likelihood ratio 0.0.

Conclusion: E-scooter-related injuries were common among young people and males. The most frequent injury sites were the head, knee, and forearm–elbow region. The TRISS was the most successful score in predicting mortality in e-scooter-related injuries.

Keywords: E-scooter, injury severity score, revised trauma score, trauma and injury severity score

Introduction

Due to advantages such as fast transportation, affordability, compactness, and portability, the use of electric scooters (e-scooters) has increased in recent years, both worldwide and in Türkiye. The convenience provided by e-scooters has also brought with it some safety issues (1). The rapid increase in the use of e-scooters worldwide has led to a increase in injuries. Various studies have shown that orthopedic injuries related to e-scooter accidents often occur in the head and extremities and that they are high-energy, serious injuries. Failure to use helmets and protective equipment leads to serious e-scooter-related injuries

(2). In Türkiye, individuals over the age of 15 can use e-scooters, and there is no requirement to wear protective gear or have a driver's license when using them. In Türkiye, the speed limit for e-scooters is set at 25 km/h, and riding on sidewalks and carrying more than one person is prohibited (3). In the US, the population-adjusted incidence of e-scooter-related injuries rose from 1.53 per 100,000 people in 2014 to 9.22 per 100,000 people in 2019, with the head being the the most common site of injury (4,5).

Traumatic injuries are a significant cause of morbidity and mortality, particularly among young adults and adolescents. The varying mortality rates reported at different trauma centers highlight the potential for differing trauma severity and the



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importance of scoring traumatic injuries (6). Various scoring systems exist, such as the injury severity score (ISS), revised trauma score (RTS), and trauma injury and severity score (TRISS), based on the anatomical location and characteristics of injuries or specific physiological parameters. The RTS is calculated using parameters such as the glasgow coma scale (GCS), systolic blood pressure (SBP), and respiratory rate. In contrast, the ISS is calculated by summing the squares of the highest abbreviated injury score (AIS) values in the three most severely injured body regions. The TRISS is computed using the ISS and RTS scores. These scoring systems have their strengths and weaknesses in the emergency department. Simple models offer ease of use, while more complex models offer higher accuracy (7).

Our study aimed to identify e-scooter-related injuries in the emergency department of University of Health Sciences Türkiye, Kayseri City Hospital, a tertiary care hospital, and to compare trauma severity scores.

Materials and Methods

Type of Research and Ethics

Our study was designed as a descriptive, prospective, single-center study. The study was conducted at the Emergency Medicine Clinic of University of Health Sciences Türkiye, Kayseri City Training and Research Hospital after obtaining approval from the Clinical Research Ethics Committee of the same institution (decision number: 890, date: 22.08.2023). The study was conducted in accordance with the Helsinki Declaration.

Study Design and Population

Our study was conducted on adult and pediatric patients with e-scooter-related injuries who visited the emergency department during the 3-month summer period between June 1, 2023, and August 31, 2023. Written consent was obtained from all patients or their families. All patients were informed about the study, and consent was obtained from the patients themselves and their parents or guardians.

Of the 122 eligible patients, 106 were included in the study. A total of 16 patients were excluded, including 12 patients who did not give consent and four patients who were brought in with out-of-hospital cardiac arrest (Figure 1).

Statistical Analysis

The obtained data were statistically analyzed using the IBM SPSS 27 (Statistical Package for Social Sciences). The Kolmogorov-Smirnov or Shapiro-Wilk test was used to determine whether the distributions of the variables were normal. Data for continuous variables were presented as mean, standard deviation, or median and interquartile range (IQR) or minimum-

maximum values, depending on whether they followed a normal distribution. Categorical variables were presented as percentages and frequencies. Since the variables did not follow a normal distribution in comparisons between two groups, the Mann-Whitney U test was used. ROC analyses were performed for the ISS, RTS, and TRISS. In addition, the ROC curves of these parameters were compared. Descriptive statistics such as area under the curve (AUC) (ROC curve), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, negative likelihood ratio, and 95% confidence interval were provided. Statistical significance was set at $p < 0.05$.

Trauma Score Formulas

1. ISS: Calculated based on the three most severely injured body regions according to the AIS (6).

$$ISS = X^2 + Y^2 + Z^2$$

2. RTS: $RTS = 0.9368 \text{ (GCS)} + 0.7326 \text{ (SBP)} + 0.2908 \text{ (coded respiratory rate)}$ (7).

3. TRISS: $b = b^0 + b^1(RTS) + b^2(ISS) + b^3(\text{age index})$ (8-10).

Results

The average age of patients was 21.5 (IQR: 15-39.5, min: 1, max: 81) years, and 69.8% (n=74) were male and 30.2% (n=32) were female. In addition, 33% (n=35) of patients were under the age of 18. Fifteen patients (14.2%) were under 10 years of age and

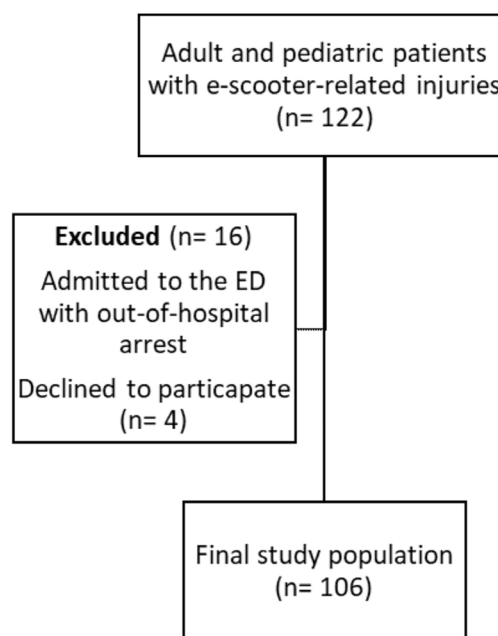


Figure 1. Flow chart of patients included in the study
ED: Emergency department

had ridden the e-scooter with someone older than themselves. One patient was one year old. None of the patients was wearing helmets or protective gear. The three most commonly injured areas among patients admitted to the emergency department due to e-scooter injuries were the head (50.9%, n=54), knee (34.9%, n=37), and forearm and elbow regions (26.4%, n=28) (Figure 2). While 12.3% (n=13) of the patients were admitted to the intensive care unit (ICU), 87.7% (n=93) were admitted to the ward. 6.6% (n=7) of the patients died; two died in the emergency department and five in the hospital.

Statistically significant differences were found among ISS, RTS, and TRISS scores and ICU admission (p-values: <0.001, <0.003, and <0.001, respectively). The median ISS scores of patients admitted to the ICU were higher than those of patients admitted to the ward or discharged (NISS: 18 vs. 2), while the median RTS and TRISS scores were lower (RTS: 7.64 vs. 7.84 and TRISS: 4.39 vs. 5.72) (Table 1).

Statistically significant differences were found between ISS, RTS, TRISS scores, and their relationship with mortality (p-values <0.001). The median ISS scores of deceased patients were higher than those of surviving patients (ISS: 29 vs. 2), while the median RTS and TRISS scores were lower (RTS: 7.11 vs. 7.84; TRISS: 3.48 vs. 5.72) (Table 1).

According to the results of the ROC analysis of continuous measurements in terms of mortality, the ability of ISS, RTS, and TRISS scores to predict mortality was found to be statistically significant, (p-values<0.001). Accordingly, patients with ISS >13, RTS ≤7.55, and TRISS ≤4.47 were found to have a higher probability of death. The TRISS score (AUC=0.991) had the highest discriminatory ability in predicting mortality (p<0.001). When the TRISS score was ≤4.47, the sensitivity for predicting mortality was 100%, specificity was 96.97%, PPV was 70%,

NPV was 100%, positive likelihood ratio was 33, and negative likelihood ratio was 0.0. ROC analyses and curves for predicting mortality using the scores are shown in Table 2 and Figure 3. Additionally, in the pairwise comparisons of ROC curves for mortality, no statistically significant difference was found in the AUC values of the measurements for the ISS, RTS, and TRISS scores (p-values were p=0.119 for ISS vs. RTS, p=0.316 for ISS vs. TRISS, and p=0.085 for RTS vs. TRISS).

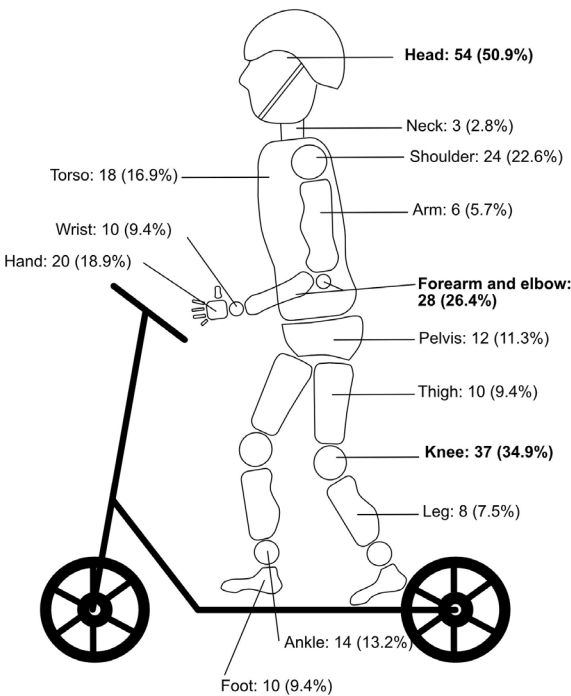


Figure 2. Distribution of injury locations among patients with e-scooter-related injuries
E-scooter: Electric scooter

Table 1. Comparison of variables in terms of ICU admission and mortality							
Variable	Total (n=106)	Non-ICU (n=93)	ICU (n=13)	p	Survive (n=99)	Death (n=7)	p
Age, years	21.5 (15-39.5)	21 (16-34.5)	41 (9-64.5)	0.234	22 (16–39)	17 (11-57)	0.775
Male, %	74 (69.8)	66 (71)	8 (61.5)	0.526*	70 (70.7)	4 (57.1)	0.429*
Heart rate, beats/min	90 (82.8-99)	90 (82.5-98.5)	88 (82.5-107.5)	0.889	90 (82-98)	86 (84-113)	0.524
SBP, mmHg	120 (110-131)	120 (110-130)	132 (122.5-154)	0.019	120 (110-130)	136 (86-100)	0.275
DBP, mmHg	79.5 (70-82)	78 (70-82)	82 (74.5-88.5)	0.079	80 (70-82)	79 (64-112)	0.744
SpO ² , %	99 (97.8-99)	99 (98-99)	99 (95.5-100)	0.941	99 (98-99)	99 (94-100)	0.854
ISS, median (IQR)	2 (2-9)	2 (1-5)	18 (17-27.5)	<0.001	2 (1-5)	29 (17-41)	<0.001
RTS, median (IQR)	7.84 (7.84-7.84)	7.84 (7.84-7.84)	7.64 (7.33-7.84)	0.003	7.84 (7.84-7.84)	7.11 (6.61-7.84)	<0.001
TRISS, median (IQR)	5.72 (5.14-5.81)	5.72 (5.47-5.80)	4.39 (3.29-5.26)	<0.001	5.72 (5.47-5.80)	3.48 (2.23-3.86)	<0.001

*Fisher's exact test was used, and other p-values were calculated using the Mann-Whitney U test.
ICU: Intensive care unit, IQR: Interquartile range, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SpO²: Peripheral capillary oxygen saturation, ISS: Injury severity score, RTS: Revised trauma score, TRISS: Trauma and injury severity score

Table 2. ROC analysis results for mortality prediction

	AUC (p value)	Cut-off	Sensitivity (95% CI)	Specificity (95% CI)	LR+	LR–	PPV	NPV
Mortality - ISS	0.978 (<0.001)	>13	100 (59-100)	91.9 (84.7-96.4)	12.4	0.0	46.7	100
Mortality - RTS	0.837 (<0.001)	≤7.55	71.43 (29-96.3)	95.96 (90-98.9)	17.68	0.30	55.6	97.9
Mortality-TRISS	0.991 (<0.001)	≤4.47	100 (59-100)	96.97 (91.4-99.4)	33	0.0	70	100

AUC: Area under the curve, CI: Confidence interval, LR+: Positive likelihood ratio, LR–: Negative likelihood ratio, PPV: Positive predictive value, NPV: Negative predictive value, ISS: Injury severity score, RTS: Revised trauma score, TRIS: Revised trauma score, TRISS: Trauma and injury severity score

Discussion

Demographic studies of e-scooter-related injuries have shown that patients are in their thirties and two-thirds are male (11–13). In our study, slightly more than two-thirds of patients were male, and the median age was 21.5 years, which was lower than in other studies.

E-scooter-related injuries are more serious because people do not use protective gear. Bloom et al. (14) looked at 248 patients with e-scooter-related injuries and found that only 3% wore helmets. In a study, it was reported that the most common reasons for motorcycle riders not to use a helmet were the weight of the helmet, heat and suffocation, neck pain, and the restriction of head and neck movements (15). In our study, none of the patients who came in with e-scooter injuries wore helmets. This result shows the importance of monitoring e-scooter users and the necessity of using protective equipment.

Störmann et al. (12) found that the upper and lower extremities were most commonly injured in patients presenting with e-scooter-related injuries, while Clough et al. (16) reported that both head and extremity injuries were most common. In our study, the most common injuries were to the head, knee, and forearm, elbow region. The importance of helmet, knee pad, and elbow pad use was emphasized in our study.

Studies on multiple-trauma patients have investigated the predictive value of trauma scores, frequently comparing ISS, RTS, and TRISS scores (7,9,17,18). A study conducted in France showed that e-scooter injuries are similarly severe as those resulting from bicycles or motorcycles (19). In a recent study involving 426 patients with multiple trauma, where ISS and RTS scores were also examined, the TRISS score was found to have the best performance in determining mortality (AUC: 0.93, sensitivity 97.1%, and specificity 76.7%) (20). Similarly, in our study, the TRISS score (AUC=0.991) had the highest discriminatory ability in predicting mortality, with a sensitivity of 100% and a specificity of 97%. In the study by Efeoglu Sacak et al. (21), the AUC value of the RTS score in predicting mortality in multitrauma patients was found to be excellent at 0.92, but in our study, it was good at 0.84.

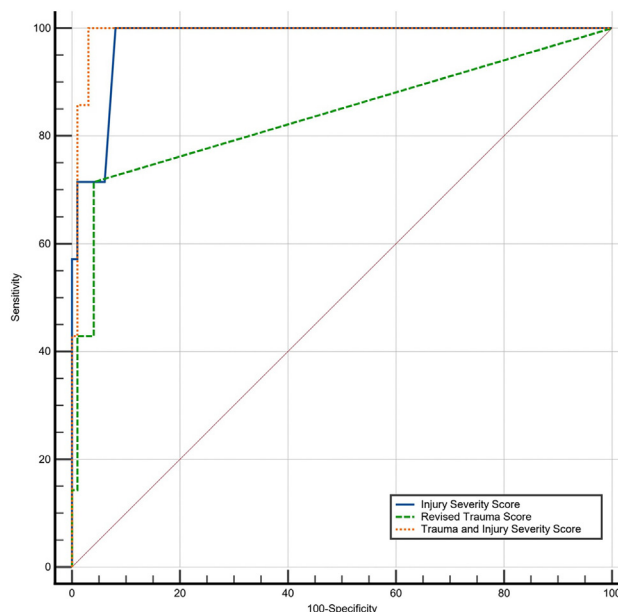


Figure 3. ROC curves of scores in terms of mortality

The main limitation of our study was that it was conducted over a 3-month period and at a single-center. Another limitation was the small number of patients. However, our study in our country that emphasizes the importance of trauma scores in e-scooter injuries and is forward-looking. We believe that more comprehensive studies evaluating trauma scores are needed during this period of increasing e-scooter use.

Study Limitations

The study is limited by its single-center focus and short-term duration. Secondly, the inclusion of patients consecutively while the principal investigator was in the emergency room may have created a sampling bias. Another limitation is the small number of patients. Our study did not evaluate pediatric and adult patients separately. Lastly, patients who visited the emergency department in cardiopulmonary arrest were not included in the study, which may have partially led to a spectrum bias.

Conclusion

In general, injuries related to e-scooters were common among young people and males. The most common injury sites were the head, knee, and forearm-elbow region. TRISS was the most successful score in predicting mortality in injuries related to e-scooters.

Ethics

Ethics Committee Approval: The study was conducted at the Emergency Medicine Clinic of University of Health Sciences Türkiye, Kayseri City Training and Research Hospital after obtaining approval from the Clinical Research Ethics Committee of the same institution (decision number: 890, date: 22.08.2023). The study was conducted in accordance with the Helsinki Declaration.

Informed Consent: Written consent was obtained from all patients or their families.

Footnotes

Author Contributions

Surgical and Medical Practices: R.K.S., Concept: R.K.S., T.Ş., Design: R.K.S., T.Ş., Data Collection or Processing: N.B., Analysis or Interpretation: İ.T., Literature Search: M.B., Writing: R.K.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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From Public Access Defibrillator to Personal Access Defibrillator: Proposal of Prompts to Optimize Automated External Defibrillation Use by Laypeople

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Abstract

Aim: This study aimed to assess whether integrating additional prompts to the automated external defibrillator (AED) interface could reduce common errors among untrained laypeople.

Materials and Methods: An observational before-after design was employed. The Control group (pre-cohort) consisted of 36 participants from previous research, whereas the after cohort included 36 participants with similar characteristics. All participants were evaluated in a simulated out-of-hospital cardiac arrest (OHCA) scenario. After one minute of chest compressions, an AED was used to deliver shock. In the follow-up cohort, a smartphone provided voice prompts encouraging proper chest compressions and advising against removing the pads or turning off the AED.

Results: In the Control group, six participants turned off the AED ($p=0.010$), and four removed the pads ($p=0.040$), while none in the after-cohort group made these errors. Regarding other mistakes, no participants in the after cohort performed compressions in the stomach (two participants in the Control group), two participants did not find the sticky part of the pads (three in the Control group), and two placed the pads in the wrong place (four in the Control group).

Conclusions: Simple voice prompts during the 2-minute interval between AED analyses improved the performance of untrained laypeople in a simulated OHCA scenario.

Keywords: Bystander, cardiopulmonary resuscitation, chest compressions, hands-off time; no-flow time, training

Introduction

The use of an automated external defibrillator (AED) is the third link of the chain of survival (1); it is crucial in the public and expert assistance of out-of-hospital cardiac arrest (OHCA), especially in cardiac arrests (CAs) with shockable rhythms. In these events, early use of AED can triple the chances of survival with good neurological outcomes (2).

The assistance of a CA should not be limited to healthcare professionals, as bystanders also play an essential role in initiating life support manoeuvres that could increase the survival rates of OHCA patients (3). This is the rationale for training the community in basic life support (BLS) and AED use skills (4).

AEDs are designed for laypeople to use safely without prior training. They typically feature two main buttons: one to turn



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on or off and the other to deliver a shock, which is activated only when the AED detects a shockable heart rhythm after analyzing the electrocardiogram. Additionally, AEDs should offer clear visual and auditory instructions to guide users through the defibrillation process, signalling when to administer a shock on the basis of the analyzed rhythm.

However, in practice, some barriers may interfere with optimal use of public defibrillation. In this sense, previous research from our group revealed that naïve laypeople found some relevant problems while using AEDs tested under simulated scenarios, which suggests that the proper use of the device might be less intuitive (5,6). We observed severe or critical errors, such as turning off the AED or removing the pads immediately after an AED shock.

To address these issues, adding prompts to current AED sound messages has been proposed (6). These prompts include 1) “active” advice, given every 30 seconds during the 2-minute chest compression period after a shock, and 2) “reactive” advice, triggered by user errors (i.e., prompting, “Are you sure that the AED is no longer needed?” when the user tries to turn off the AED).

We hypothesize that adding specific active advice on the AED during the 2-min chest compression period between any AED rhythm analysis would improve laypeople’s AED performance in terms of potential efficacy. The objective of this study was to analyse whether this improvement in AED function was associated with fewer inappropriate actions, namely, using the AED incorrectly: 1) turning off the AED and 2) removing the pads after shock.

Materials and Methods

Study Design and Ethics

This study followed a before-after design (Figure 1). The study received ethical approval from the Bioethics Committee of the University of Santiago de Compostela on 19 December 2019. In accordance with the institutional policy of the committee, no numerical ethical approval code is issued for research projects. Therefore, while the study was formally approved, there is no associated approval number. The ethical review process was duly completed, and the committee confirmed that the study met all relevant scientific, ethical, and methodological standards.

Population

A convenience sample of 72 university students participated in this study. The inclusion criterion was not having previously undergone any BLS training. Written informed consent was

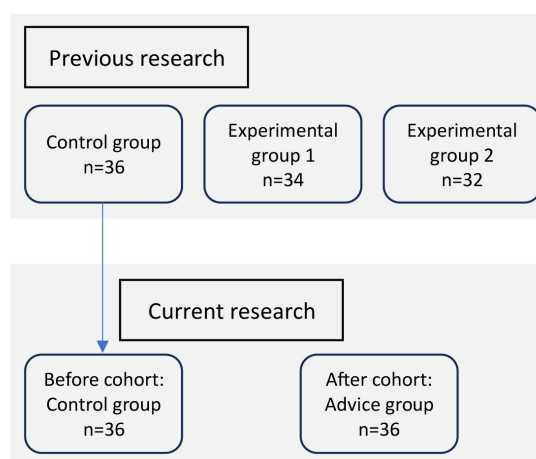


Figure 1. Flow-chart of the before-after design

obtained from all participants, who stated that they were participating voluntarily and that they could withdraw at any stage of the research.

Pre-intervention

The participants in the “before” cohort (Control group) of this study were 36 individuals extracted from previous research by our team (6). In this research, 102 university students with no prior BLS training were involved, then split into three groups: one Control group (without intervention) and two experimental groups that received two hours of BLS training. Finally, all the participants were exposed to an OHCA simulation scenario with the aim of comparing the no-flow time between groups. Of those 36 participants who composed the Control group, six had to be excluded from the final analysis because they turned off the AED, and four had to be excluded because pads were removed after AED shock during the tests (6).

Intervention

Thirty-six university students were invited to participate in the “after” cohort (advice group) of the present study. None of them had previously participated in any type of BLS training. They were exposed to the same OHCA simulated scenario as the previous cohort. The only change between the preintervention and intervention stages was the implementation of active advice during AED use.

In the OHCA scenario, all participants had to use an AED Trainer 2 (Laerdal). As this device does not emit any prompts during the 2 minutes of cardiopulmonary resuscitation (CPR) between AED analyses, a smartphone was used in the intervention cohort to simulate the voice prompts for active advice during the BLS and AED scenarios, as explained in the BLS assessment subsection.

BLS Assessment

Both cohorts were evaluated by means of a standard OHCA simulated scenario, as described in our previous research (6). In brief, participants were placed in front of a mannequin torso and told that a person had collapsed while crossing a crosswalk. They were then asked, “What would you do?”. After that, proficiency in performing the BLS protocol was checked. 1) checking safety; 2) assessing response; 3) opening the airway and checking breathing; 4) alerting the emergency medical services; 5) sending for an AED; 6) starting CPR; and 7) using the AED. The simulated scenario required the delivery of a shock, for which an AED was provided after 1 min of chest compressions. The AED was programmed to recommend two shocks but not a third one, since the casualty was presumed to be breathing spontaneously at that moment.

The AED used in the simulation was AED Trainer 2 (Laerdal, Norway). This type of AED, after shocking and recommending chest compressions, does not provide any prompt during the two minutes between heart rhythm analyses. To simulate active advice from the AED, an audio recording previously recorded by a smartphone was relayed during the 2-min CPR. The voice note was relayed just after the shocking messages shown in Table 1. The participants were told that they should interpret the messages from the smartphone to determine if they were prompted by the AED.

The manikin (Laerdal, Norway) used was a torso able to provide real-time feedback on compression and ventilation quality. The manikin was connected to a Simpad SkillReporter, which was not shown to the participants at any time.

Outcomes

The primary outcome was the number of participants who were able to complete the scenario without turning off the AED or removing the pads from the chest of the manikin. The secondary outcomes included other AED use errors, which were not directly influenced by active advice, such as incorrect tablet allocation or not finding the sticky part of the pads. In addition, the compression fraction was recorded and analysed as a secondary outcome, defined as the percentage of time during which

participants were performing chest compressions: 1) during the complete scenario, 2) from the start of chest compressions, 3) from the start of chest compression to the third analysis, and 4) from providing the AED to the third AED analysis.

The results from the BLS and chest compressions, and ventilation quality variables were registered as controls to verify that confounding variables did not influence primary or secondary outcomes.

Statistical Analysis

Categorical variables related to primary outcomes and the BLS sequence were described as absolute and relative frequencies. The compression fraction and CPR quality variables are expressed as medians with interquartile ranges (IQRs). Frequencies were analysed with the chi-square test, while continuous variables were analysed with the Mann-Whitney U test. Statistical analyses were performed with IBM SPSS Statistics v.25 for Macintosh. A significance level of $p<0.05$ was considered for all analyses.

Results

Demographics

Data from the 72 participants were analysed, regarding the mistakes made during AED use. The compression fraction was analyzed only for those participants who completed the OHCA scenario. Table 2 shows the demographic data of the whole sample and of those participants who completed the OHCA scenario. Demographics are presented in this way because the analysis was performed using the data of the whole sample and the participants who completed the scenario.

No significant differences were found in the proportion of females between the groups or in the time spent by each group to complete the OHCA scenario ($p>0.05$ in both analyses). The participants in the advice group were slightly younger than the participants in the Control group ($p<0.05$).

Primary Outcomes

The primary outcomes were the participants who turned off the AED or removed the pads from the chest of the manikin. All the errors associated with AED use are shown in Table 3.

Table 1. Voice advice embedded in the AED procedure		
Type of advice	Time related	Text/message
Active	After shocking	Perform chest compressions; push hard and fast in the center of the chest. Do not remove the pads
Active	After 30 seconds	Remember to maintain chest compressions: push hard and fast in the center of the chest
Active	After 60 seconds	Continue with chest compressions until next advice and do not turn-off the AED at any moment
Active	After 90 seconds	Remember to maintain chest compressions: push hard and fast in the center of the chest
AED: Automated external defibrillator		

No participants from the advice group turned off the AED or removed the pads during the OHCA simulation, whereas 10 Control group participants made some of these mistakes ($p=0.001$).

Secondary Outcomes

The secondary outcomes were the errors that were not directly influenced by the active advice and the compression fraction. Table 3 shows no significant differences between the groups in terms of errors related to not finding the sticky part of the pads and incorrect allocation of pads.

Regarding compression fraction, this variable was registered in four-time intervals, and the results are shown in Table 4. Although a trend toward an increase in the compression fraction was observed at all intervals in the advice group, no significant differences were found.

Controls

The BLS sequence proficiency and chest compression quality in the control and advice groups are shown in Additional file 1,

Tables 1 and 2. The BLS sequence performance was poor in both groups, with less than half of the participants able to correctly perform most of the steps. Only significant differences between groups were observed in the starting chest compressions step [Control group: 10 participants (52.6%); advice group: 28 participants (90.3%); $p=0.002$].

With respect to the quality of chest compressions, no differences in the number of compressions performed, median compression depth, median compression rate, or percentage of correct chest compressions by hand position were found between groups. The median compression depth was shallower than the 50 mm recommended by the European Resuscitation Council Guidelines 3 in both groups [Control group: 33 mm (IQR: 26-46); advice group: 36 mm (IQR: 26-42)]. Although the median compression rate was between 100 and 120 $\text{com}\cdot\text{min}^{-1}$, the first quartile was lower than 100 $\text{com}\cdot\text{min}^{-1}$ in both groups (Control group median: 110 $\text{com}\cdot\text{min}^{-1}$; IQR: 85-126; advice group median: 103 $\text{com}\cdot\text{min}^{-1}$; IQR: 80-117).

Table 2. Sample demographics

	Whole sample		Participants who completed the scenario	
	Control group (n=36)	Advice group (n=36)	Control group (n=19)	Advice group (n=32)
Female ^a	23 (63.9)	25 (69.4)	13 (68.4)	23 (71.9)
Age ^b in years	21 (21-21)	20 (19-21)	21 (21-21)	20 (19-21)
Time to complete the scenario ^b in s	--	--	555 (520-592)	525 (504-560)

^a: Absolute frequencies (relative frequencies), ^b: median (interquartile range)

Table 3. Errors registered within AED use

Error	Control group (n=36)	Advice group (n=36)	Chi-square
Turning-off the AED	6 (16.7)	0 (0)	0.011
Removing the pads	4 (11.1)	0 (0)	0.040
Compressions on the stomach	2 (5.6)	0 (0)	No sig.
Not finding the sticky part of the pads	3 (8.3)	2 (5.6)	No sig.
Wrong pads allocation	4 (11.1)	2 (5.6)	No sig.

AED: Automated external defibrillator

Table 4. Chest compression fraction showed as median (IQR)

Interval	Control group (n=19)	Advice group (n=32)	Mann-Whitney U test
Complete scenario	52.0 (43.0-58.0)	58.0 (49.0-62)	No sig.
From starting compressions	63.4 (52.7-68.9)	65.5 (58.7-69.4)	No sig.
From compressions to the third analysis	66.9 (57.2-74.0)	70.2 (61.1-76.1)	No sig.
From providing the AED to the third analysis	61.6 (49.9-70.0)	65.4 (55.7-71.5)	No sig.

AED: Automated external defibrillator, IQR: Interquartile range

Discussion

AEDs have been designed to be applied quickly and with minimum advice both by health professionals and the public (3), but our study has shown that simple audio prompts may even enhance AED function.

In 1995, the American Heart Association published the first statement of public access defibrillation (PAD), with the goal of increasing early defibrillation in patients with OHCA (7). For instance, significant efforts have been made to increase public awareness and make AEDs more accessible. Some strategies to improve bystander defibrillation rates include deploying publicly available AEDs, implementing citizen responder programs, or dispatching mobile AEDs (8), including the use of drones to deliver AEDs, which is a hot topic of research (9-11). However, there is still a low rate of bystander defibrillation (12) even in states where onsite availability of AEDs is mandatory (13,14), with regional variability in AED accessibility (15). In addition, although most OHCA occur at home, AEDs are not available 24/7. A study performed in Canada reported that AEDs are available only 44% of the time, mainly from 10:00 am to 4:30 pm (15). Consequently, bystander defibrillation is even less common in patients experiencing OHCA at home (16).

Almost three decades after the first statement of PAD, the goal of significantly increasing bystander defibrillation has not been achieved. Brooks noted that instead of working around the technology, an AED technology that has barely changed in recent decades, we should consider changing it (17). Thus, it is necessary to focus not only on technological factors but also on human factors to increase awareness, knowledge, and competencies that allow laypeople to perform CPR and use AED during OHCA. Brooks advocates shifting the paradigm from public access defibrillators to personal access defibrillators, while developing new models that are more affordable and ultraportable (17). In addition, it was assumed that AEDs are easy to use and that anyone without training can successfully use them. However, according to simulated studies, this might be only partially true, as laypeople find it difficult to solve OHCA simulated scenarios that require the use of AED (5,6), even with the assistance of a dispatcher (18).

Our study revealed that only the implementation of simple active messages during a two-minute period of chest compressions between AED analyses was sufficient to increase the number of participants who successfully solved the simulation scenario (from 52.8% in the Control group to 88.9% in the advice group). The active messages reduced critical mistakes that could prevent the delivery of a shock in a real-life situation, such as turning off the AED or removing the pads. This approach involves

simple messages every 30 seconds encouraging laypeople to keep compressing the chest, since the 2 min between AED analyses might be perceived as much longer, making the silence uncomfortable and resulting in uncertainty about what to do during that time (5).

The implementation of active messages or new prompts in the current functions of the AED could be considered feasible measures to change the paradigm mentioned above. In the design of a teaching-learning process, it is important to consider the characteristics, motivations, and capacities of the students. If the goal is to increase bystander AED use, it is necessary to adapt new models and their functions to the public, in addition to public initiatives. Previous research has recommended changing from the current AED to an automated intelligent external defibrillator (AiED), in which not only the active messages assessed in the present study are recommended but also reactive messages (e.g., "Are you sure that the AED is no longer needed?" If the device is attempting to turn off) (5,6). Other advice was proposed, for example, to activate the paediatric mode and to place the pad (19).

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Study Limitations

This study is not free of limitations. A before-after design was chosen, which could introduce potential confounding factors inherent to this type of methodology. However, control variables revealed that both arms of the study were comparable. Although the simulation scenarios try to be as realistic as possible, there are psychological variables that are not present. For instance, the pressure to assist in real CA the fear of failure or other emotional factors might influence the results, which means that our results cannot be directly extrapolated to real OHCA patients. Future studies should provide further evidence to corroborate our findings, as this study was carried out on a specific sample, which limits its generalizability.

Conclusion

The implementation of simple active voice prompts during the 2-min interval between consecutive AED analyses improved the performance of laypeople in a simulated OHCA scenario. None of the participants made critical mistakes, such as turning off the AED or removing the pads during the simulation, which meant that more participants successfully completed the scenario.

Ethics

Ethics Committee Approval: The study received ethical approval from the Bioethics Committee of the University of Santiago de Compostela on 19 December 2019. In accordance with the institutional policy of the committee, no numerical ethical approval code is issued for research projects. Therefore, while the study was formally approved, there is no associated approval number. The ethical review process was duly completed, and the committee confirmed that the study met all relevant scientific, ethical, and methodological standards.

Informed Consent: Written informed consent was obtained from all participants, who stated that they were participating voluntarily and that they could withdraw at any stage of the research.

Footnotes

Authorship Contributions

Concept: C.A-G., Design: C.A-G., A.C.F., A.R.N., Data Collection or Processing: C.A-G., A.C.F., C.P.D., C.G.R., Analysis or Interpretation: C.A-G., Literature Search: C.A-G., Writing: C.A-G., A.C.F., C.P.D., C.G.R., A.R.N.

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Does Lactate Dehydrogenase Act as an Early Warning System Predicting Mortality in Trauma Patients?

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Abstract

Aim: Trauma is one of the most prevalent causes of death and disability in middle age, and early diagnosis and treatment are critical in minimizing mortality and morbidity. Lactate dehydrogenase (LDH) is an indicator of inflammation in many diseases. We aim to present this study, in which we measure the power of LDH to show us mortality in the blood sample taken at the first examination in trauma patients, in the light of the literature.

Materials and Methods: Trauma patients of emergency medicine department between November 2020 and November 2021, were analyzed. Trauma mechanism, consultations, mortality-morbidity, and scoring were evaluated retrospectively.

Results: The glasgow coma scale (GCS), injury severity score (ISS), and new injury severity score (NISS) values of the patients were 14.58 ± 1.76 (95% confidence interval: 14.43-14.73), 14 (0-76), and 18 (0-101) respectively. The data for leukocytes, hemoglobin, platelets, glucose, aspartate aminotransferase (AST), and LDH were significantly different between the control and patient groups. The comparison of leukocyte, hemoglobin, glucose, creatinine, AST, and LDH data between the survivors and the deceased in the patient group revealed a statistically significant difference. ROC analysis was then applied to evaluate these markers in the non-surviving patients. ISS, NISS, GCS, alanine aminotransferase, AST and LDH were found to be significant.

Conclusion: LDH elevation, which is studied between routine procedures, may be beneficial for physicians working in the periphery both in patient referral and in making an early operation decision. Thus, we believe that mortality and morbidity will decrease with the use of LDH, a cost-effective marker.

Keywords: Trauma, LDH, radiology, mortality, emergency service

Introduction

In addition to being the leading cause of death in patients under 45 years of age, trauma is associated with complications and late death (1). Among these complications, multiple organ dysfunction syndrome (MODS) is the most common and causes a significant increase in mortality (2,3). Therefore, initiating effective treatment early in trauma patients requires identifying patients at high risk of developing MODS. This approach is at the forefront of reducing victimization resulting from trauma.

In recent years, several studies have investigated trauma-related mortality and its predictors in emergency settings in Türkiye. A study comparing falls from height and traffic accidents, reported that trauma mechanism significantly influences mortality rates, underlining the need for mechanism-based prognostic tools (4).

Another study focusing on pediatric trauma emphasized the importance of early physiological markers in identifying high-risk patients in the emergency department (5). Additionally, mortality predictors in traffic accidents were explored in a study



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that highlighted the potential role of simple parameters for early prognostication (6). In light of these national findings, our study aims to evaluate whether lactate dehydrogenase (LDH)—a low-cost and routinely available biomarker—could serve as an early predictor of trauma severity and mortality in adult patients.

Serum LDH is a low-cost test that is included in the regular procedures requested during a hospital admission evaluation. As a result, it could be an appropriate marker for physicians to use in determining the prognosis of trauma patients without incurring additional costs or requiring additional time or blood samples. LDH is a cytoplasmic enzyme that is found in every major organ, including the brain, lung, liver, and heart (7). Serum LDH levels are thought to be an indicator of inflammation and the extent of tissue damage. (8-13). The object of this retrospective study was to examine the association between mortality in trauma patients and serum LDH concentration.

Materials and Methods

Patients and Methods

Five hundred fourteen cases of trauma patients, who were admitted to the emergency medicine clinic between November 2020 and November 2021, were analyzed. Trauma mechanism, consultations, mortality-morbidity and scoring were evaluated retrospectively. As the control group, 130 people who underwent non-traumatic routine control were included in the study. Approval was obtained from the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (decision number: 2022-16-01; date: 15.08.2022).

Inclusion and Exclusion Criteria

In this retrospective study, patients whose laboratory values were assessed later and whose glasgow coma scale (GCS), injury severity score (ISS), and new injury severity score (NISS) values were recorded at admission to the emergency department were included.

Patients with trauma or malignancy (liver, lung, and hematological malignancy) who were using anticoagulant drugs were removed from the study.

Patients who came for non-traumatic routine control were included as the control group, while patients with malignancies (liver, lung, and hematological malignancies) and those using anticoagulant drugs were left out of the study.

Statistical Analysis

The normal distribution analysis was performed by considering the data in the study: Five parameters [Skewness-Kurtosis, standard deviation (Std)/mean, Q-Q plots, histogram, and Shapiro-Wilk test]. Normally distributed parameters with sufficient data were shown as mean \pm Std, and the independent samples t-test

was applied for pairwise comparisons. The median (minimum-maximum) Mann-Whitney U test was used for groups that did not have enough data or did not have a normal distribution. The chi-square test was applied to analyze the frequency of categorical data. The ROC curve was developed by examining the sensitivity and specificity of diagnostic tests. A multiple logistic regression analysis was performed with risk factors for estimating mortality. In the study, a significance level of $\alpha=0.05$ was used, and a p-value less than α was considered significant.

Results

In this study, there were 514 individuals in the patient group, and the mean age was 39.88 ± 13.45 [95% confidence interval (CI): 37.85-41.91]. Of the patients, 161 were female, and 353 were male. The GCS, ISS, and NISS values of the patients were 14.58 ± 1.76 (95% CI: 14.43-14.73), 14 (0-76), and 18 (0-101), respectively.

Leukocyte, hemoglobin, platelet, glucose, aspartate aminotransferase (AST), and LDH data revealed statistically significant differences between the control and patient groups. Creatinine and alanine aminotransferase (ALT), data did not reveal any statistically significant distinctions between the control and patient groups ($p>0.05$). While patient group leukocyte data increased by 20% relative to control group data, patient group hemoglobin data decreased. The patient group had greater levels of glucose, blood urea nitrogen, AST, and LDH than the control group (Table 1).

The mortality frequency observed in those who underwent surgery (2), was statistically significantly different from the expected mortality frequency (8.5) ($p<0.001$). There is no substantial difference between expected and observed mortality rates for other causes of trauma (Table 2).

The observed frequency of death (2) of patients who received neurosurgery consultation was statistically different from the expected frequency of death (6) ($p=0.007$). The observed death frequency of patients who received pediatric surgical consultation (3) was different from the observed death frequency in another group, and this difference was statistically significant ($p=0.022$). No statistically significant differences were found between the expected and observed death frequencies of patients who received other consultations ($p>0.05$).

There was a statistically significant difference in the comparison of leukocyte, hemoglobin, glucose, creatinine, AST, and LDH data between the survivors and the deceased in the patient group. The p-values were 0.006, 0.027, 0.015, 0.031, $p<0.001$, and $p<0.001$, respectively (Table 3).

Table 1. Comparison of control and patient group data.

	Control (n=130)	Patient (n=514)	p value
Leukocyte	10190 (4650-30950)	12030 (1175-53580)	<0.001
Hemoglobin	13.25±1.89	12.68±2.21	0.007
Platelet	253.50 (66-491)	245 (16-862)	0.034
Glucose	103 (63-436)	117 (33-678)	<0.001
Blood urea nitrogen	27 (6-148)	31 (3-470)	<0.001
Creatinin	0.73 (0.41-3.47)	0.76 (0.33-3.89)	0.127
Alanine aminotransferase	18 (6-266)	20 (6.00-1396)	0.254
Aspartate aminotransferase	24 (13-371)	29 (8-1058)	0.001
Lactate dehydrogenase	252 (43-870)	270 (105-3166)	0.016

Data are presented as mean ± SD or median (minimum-maximum)

Table 2. Comparison of trauma mechanisms patients who survived and those who died

	Survival n=503	Died n=11	p value
Surgery			
No	108 (21.5)	9 (81.8)	<0.001
Yes	395 (21.5)	2 (18.2)	
Gunshot wound			
No	488 (97)	11 (100)	1.000
Yes	15 (3)	0 (0)	
Stab wound			
No	448 (89.1)	10 (90.9)	1.000
Yes	55 (10.9)	1 (9.1)	
Falls			
No	342 (68)	10 (90.9)	0.186
Yes	161 (32)	1 (9.1)	
Traffic Accident			
No	343 (68.2)	5 (45.5)	0.188
Yes	160 (31.8)	6 (54.5)	
Falling from Height			
No	436 (86.7)	9 (81.8)	0.649
Yes	67 (13.3)	2 (18.2)	
Judicial Case			
No	275 (54.7)	9 (81.8)	0.122
Yes	228 (45.3)	2 (18.2)	
Data are presented as n (%).			

The leukocyte, glucose, AST, ALT and LDH frequencies, categorized as normal and abnormal according to clinical cut-off values, were statistically significant. The p-value was respectively: p=0.011, p=0.021, p=0.002, p<0.001, and p<0.001.

Table 3. Comparison of blood values between patients who survived and those who died

	Survival	Died	p value
Leukocyte	11870 (1175-40650)	17280 (7930-53580)	0.006
Hemoglobin	13 (3-18)	9.20 (6.30-14.90)	0.027
Platelet	245 (16-862)	222 (105-437)	0.312
Glucose	117 (33-421)	158 (73-678)	0.015
BUN	31 (3-470)	24 (14-73)	0.134
Creatinin	0.75 (0.33-3.20)	0.85 (0.63-3.89)	0.031
Alanine aminotransferase	20 (6-1143)	169 (11-1396)	0.002
Aspartate aminotransferase	29 (8-675)	241 (16-1058)	<0.001
Lactate dehydrogenase	267 (105-1900)	1036 (232-3166)	<0.001

The sensitivity and specificity values of risk factors are shown in Table 4. The ROC curve of ALT, AST and LDH is shown in Figure 1, and ISS, NISS and GCS are shown in Figure 2.

ROC analysis was then applied to evaluate these markers in the non-surviving patients. ISS [area under the curve (AUC): 0.843, 95% CI: 0.709-0.977, p<0.001], NISS (AUC: 0.874, 95% CI: 0.750-0.998, p<0.001) GCS (AUC: 0.937, 95% CI: 0.834-1.000, p<0.001), ALT (AUC: 0.773, 95% CI: 0.587-0.960), AST (AUC: 0.808, 95% CI: 0.636-0.980, p<0.001) and LDH (AUC: 0.896, 95% CI: 0.782-1.000) were found to be significant (Table 4).

To this end, we analyzed LDH and GCS characteristics in binary logistic regression models. LDH was revealed to be the most important parameter in defining the mortality rate of patients in a multiple binary logistic regression analysis. (Table 5). The predictive power of the model was measured using Nagelkerke's R² coefficient. In terms of longevity, this model is 99.49% accurate and 45.46% accurate in predicting death (Table 3). There is a 59.1% variance explained in the probability of death according to the Nagelkerke's R² value (Table 5).

Discussion

In this study, we found that leukocytes, hemoglobin, platelets, glucose, AST, and LDH serum values increased with trauma and were closely related to survival among patients. In the ROC analysis performed between these blood values, GCS and LDH reached the best sensitivity and specificity. This analysis also included trauma scoring systems such as ISS, NISS, and GCS. LDH was found to be more effective in determining mortality in the binary regression analysis performed among these groups.

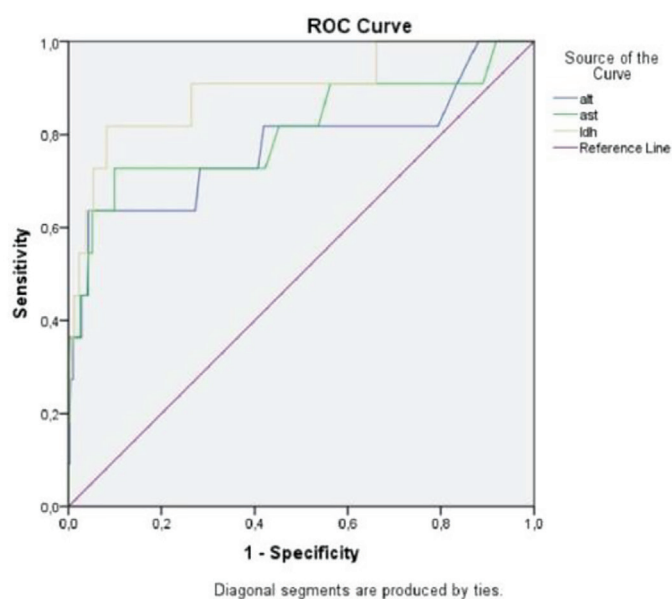


Figure 1. Chart showing ROC analysis of ALT, AST, and LDH

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, LDH: Lactate dehydrogenase

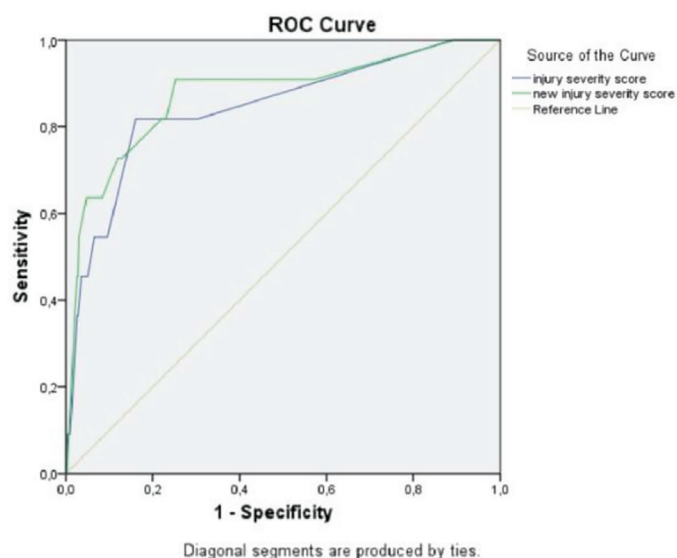


Figure 2. Chart showing ROC analysis of ISS and NISS

ISS: Injury severity score, NISS: New injury severity score

Table 4. ROC curves of risk factors

Risk factor	AUC (95% CI)	Cut-off value	p value	Sensitivity	Specificity
Injury severity score	0.843 (0.709-0.977)	23.5	<0.001	0.818	0.839
New injury severity score	0.874(0.750-0.998)	24.5	<0.001	0.909	0.748
Glasgow coma scale	0.937 (0.834-1.000)	14.5	<0.001	0.909	0.911
Alanine aminotransferase	0.773 (0.587-0.960)	144.5	0.002	0.636	0.957
Aspartate aminotransferase	0.808 (0.636-0.980)	109.5	<0.001	0.727	0.901
Lactate dehydrogenase	0.896 (0.782-1.000)	621	<0.001	0.818	0.919

AUC: Area under the curve, CI: Confidence interval, ROC: Receiver operating characteristic

Table 5. Multiple logistic regression analysis of risk factors on mortality

	B	SE	Wald	DF	Sig.	Exp (B)	95% CI for exp (B)	
							Lower	Upper
LDH	0.003	0.001	12.04	1	0.001	1.003	1.001	1.005
GCS	-0.436	0.098	19.734	1	0	0.647	0.534	0.784
Constant	-0.36	1.213	0.001	1	0.976	0.965		
Model summary								
Step	-2 Log likelihood	Cox and Snell R-square	Nagelkerke's square	Step				
1	44.395	0.131	0.591	1				
	Observed		Predicted					
			Mortality					
	Mortality		No	Yes				
		No	99.49%	0.51%				
		Yes	54.54%	45.46%				

LDH: Lactate dehydrogenase, GCS: Glasgow coma scale, SE: Standard error, B: Regression coefficient, DF: Degrees of freedom, CI: Confidence interval

LDH accelerates the process 14 times, by catalyzing the coordinated interconversion of pyruvate to lactate and nicotinamide adenine dinucleotide (NADH) to NAD⁺ (14,15).

As a result, the increasing lactate level will be closely correlated with the rise in LDH levels. The transfer of a hydride ion from NADH to pyruvate, at carbon C2 of pyruvate, furthers the chemical process. The initial stage in the molecular process is the binding of NADH to enzymes. This binding involves a large number of residues in the active site. When NADH binds, it helps lactate bind by interacting with the LDH residues. LDH-NAD⁺-lactate and LDH-NADH-pyruvate are two tertiary complexes that are created when a hydride moves quickly in both directions simultaneously (16). In our study, we think elevated LDH is the underlying cause of higher LDH levels and mortality in patients compared to the control group.

LDH is considered a marker of tissue damage following trauma. In cases of acute trauma, LDH levels generally increase within the first 48 hours, and this elevation can be used as an important parameter in evaluating patient prognosis. Specifically, the increase in LDH levels within 48 hours after admission to the intensive care unit demonstrates high sensitivity and specificity in predicting mortality (17). In chronic trauma processes, however, LDH levels require longer-term monitoring. For example, in patients who have suffered an acute ischemic stroke, elevated LDH levels at hospital admission serve as an independent indicator of prognosis and long-term mortality risk (18). These findings highlight the potential of LDH as a prognostic biomarker in both acute and chronic trauma processes.

In our study, we aimed to investigate the potential role of serum LDH levels measured at the initial admission of trauma patients in assessing the risk of mortality and morbidity. In this context, we believe that the use of LDH as a prognostic marker in both acute and chronic trauma processes may contribute to clinical practice.

The relationship between trauma, inflammation, and tissue injury constitutes a cornerstone of clinical practice. LDH has emerged as a significant biomarker in the evaluation of these processes. LDH is an enzyme present in various tissues and organs, released into the bloodstream as a result of cellular damage. Therefore, its serum levels are considered an indicator of inflammation and tissue injury (19). The association between LDH and inflammation has been highlighted in several studies. Particularly in severe inflammatory conditions such as sepsis, elevated serum LDH levels can be used to determine patient prognosis. For instance, one study reported that high LDH levels in septic patients were associated with poor prognosis (20). Among the systemic effects of trauma are not only inflammation

and tissue damage but also organ dysfunction. LDH may aid in the evaluation of these systemic effects. For example, one study found that elevated LDH levels were associated with organ dysfunction (21). In conclusion, LDH may be used as an important biomarker in the assessment of inflammation, tissue damage, and the systemic effects of trauma. Its role in these processes can contribute to clinical practice and assist in determining patient prognosis.

Both the activity of LDH and the concentration of global actin in the blood were observed to rise after trauma, as was previously reported by Hazeldine et al. (14) In cases with a fatal outcome, we discovered that LDH was considerably greater than that in the control group. LDH activity in serum samples was also compared between patients with isolated traumatic brain injury (TBI) and healthy controls, and it was observed that patients with TBI had greater LDH levels.

Since the serum concentration of LDH isoenzymes reflects tissue-specific pathological conditions, the quantification of LDH is of clinical interest (22). Their studies found that it was high in pericardial and peritoneal fluids (23), metastatic melanoma and fast-growing cancers (24,25), and this was associated with apparent inflammation. Hazeldine et al. (14) determined in their study that trauma may be the initiation of inflammation in the body. Therefore, we attribute the cause of the high LDH in the trauma patients in our study, especially in the deceased patients, to the inflammation that developed as a result of the trauma.

Study Limitations

This study has several limitations. Its retrospective and single-center design limits the generalizability of the findings. The relatively small sample size may have reduced statistical power. LDH was measured only at admission, without evaluating dynamic changes over time. This single time-point measurement restricts the ability to capture temporal fluctuations that could provide a more accurate prognostic assessment, as serial measurements are known to yield more valid and reliable results when evaluating prognostic biomarkers. Additionally, comparisons with other established biomarkers (e.g., C-reactive protein, lactate, procalcitonin) were not performed. The heterogeneity in trauma types and exclusion of critically ill patients referred to tertiary centers may have influenced mortality outcomes. Moreover, detailed data regarding the type and extent of injury (e.g., crushing, penetrating, or burn trauma) were not consistently available due to the retrospective nature of the study, limiting our ability to assess their specific impact on LDH levels. Therefore, future prospective, multicenter studies with serial LDH measurements and comprehensive trauma classification are warranted to better elucidate LDH's prognostic value in trauma patients.

Conclusion

In our study, which determined that surgical intervention reduces mortality in appropriate patients, we found that LDH elevation—measured upon initial admission—was associated with trauma severity and mortality. Given its routine availability and low-cost, LDH may serve as an accessible early indicator in trauma triage, especially in peripheral or resource-limited settings. However, considering the limitations of single-time-point measurement, we propose that this study should be regarded as a preliminary investigation suggesting a potential link between LDH and trauma outcomes. Future prospective studies incorporating serial LDH measurements are necessary to determine whether LDH can reliably predict mortality and morbidity in trauma patients.

Ethics

Ethics Committee Approval: Approval was obtained from the University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk and Research Hospital Clinical Research Ethics Committee (decision number: 2022-16-01; date: 15.08.2022).

Informed Consent: This retrospective study.

Footnotes

Author Contributions

Surgical and Medical Practices: F.T., M.K., Concept: S.E.Ç., F.T.T., M.K., Design: S.E.Ç., K.A.T., Data Collection or Processing: F.T.T., F.T., Analysis or Interpretation: S.E.Ç., K.A.T., M.K., Literature Search: S.E.Ç., F.T.T., Writing: S.E.Ç., K.A.T., M.K., F.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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Cholesterol, Urea Nitrogen, CRP, And IL-4 as Independent Predictors for Severe Acute Pancreatitis: A Retrospective Study

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Abstract

Aim: To investigate the expression and correlation between laboratory indicators, such as urea nitrogen, cholesterol, and inflammatory markers in patients with severe acute pancreatitis (AP) within 24 hour of admission and provide new insights for the early identification of severe acute pancreatitis (SAP).

Materials and Methods: A retrospective study was conducted on patients with AP admitted between January 2022 and December 2022. According to the revised atlanta classification, patients were categorized into the mild acute pancreatitis (MAP) group (N=112) and the moderately severe acute pancreatitis/severe acute pancreatitis (MSAP)/SAP group (N=45). Clinical data were compared between two groups. Univariate and multivariate logistic regression analyses were performed to identify independent risk factors for severe AP. The predictive value of the model was assessed using the area under the ROC area under the curve (AUC).

Results: Compared with the MAP group, The MSAP/SAP group exhibited significantly higher proportions of fatty liver, diabetes, and hypertriglyceridemia, along with elevated levels of cholesterol, fibrinogen, urea nitrogen, bilirubin, neutrophil-to-lymphocyte ratio, C-reactive protein, D-dimer, interleukin-4, interleukin-6, and interleukin-10 ($p<0.05$). The multivariate logistic regression analysis revealed that cholesterol [odds ratio (OR): 1.278, 95% confidence interval (CI): 1.085-1.562, $p=0.007$], urea nitrogen (OR: 1.478, 95% CI: 1.203-1.976, $p=0.002$), C-reactive protein (OR: 1.016, 95% CI: 1.006-1.027, $p=0.002$), and interleukin-4 (OR: 2.151, 95% CI: 1.470-3.564, $p<0.001$) were the independent risk factors for early severe AP. The AUC of the combined prediction model incorporating these four factors was 0.932 (95% CI: 0.884-0.979), demonstrating a sensitivity of 97% and a specificity of 75%. It exhibited superior diagnostic efficacy compared to any single indicators and the commonly used BISAP scoring system.

Conclusion: This study identified cholesterol, urea nitrogen, C-reactive protein, and interleukin-4 as significant independent risk factors for the early development of severe AP. A novel predictive model was developed incorporating these four biomarkers, which demonstrated superior diagnostic efficacy compared with any single indicator and the conventional BISAP score. This model assists clinicians with a simple, objective, and powerful tool for early risk stratification of AP patients within 24 hour of admission.

Keywords: Urea nitrogen, cholesterol, CRP, IL-4, acute pancreatitis, ROC

Introduction

Acute pancreatitis (AP) is an acute life-threatening inflammatory disease characterized by abnormal activation of pancreatic enzymes, leading to autodigestion of the pancreas and injury to surrounding organs. As one of the most common causes of acute abdomen, AP can trigger systemic inflammatory response

syndrome and multiple organ dysfunction syndrome in the early stage, with mortality rates reaching 20-30% (1,2). Based on disease severity, AP is classified as mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP) (1). Early Identification of MSAP and SAP remains crucial yet challenging for improving patient survival.



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At present, no standardized and universally accepted assessment system exists in clinical practice for evaluating the severity of AP, as each available scoring method has its own advantages and limitations (3,4). Laboratory indicators are still under investigation due to their objectivity and reproducibility. biochemical parameters, such as blood urea nitrogen (BUN), and cholesterol (CHO), have been reported to correlate with AP severity in previous studies (5,6). The inflammatory cascade is recognized as a key pathophysiological mechanism of AP (7), and inflammatory markers, such as C-reactive protein (CRP) (8) and [interleukin (IL)], (7), have also been confirmed to be associated with disease severity. However, few studies have evaluated the predictive potential of combining routine biochemical indicators with inflammatory markers, including cytokines, for the early identification of severe AP. In this study, changes in clinical indicators across various severities of AP were analyzed, and the predictive value of integrating biochemical and inflammatory markers for severe AP was investigated; aiming to provide a reliable reference for the early diagnosis and timely intervention.

Materials and Methods

Research Participants

Total of 157 patients with AP diagnosed and treated between January 2022 and December 2024 were included in this study. Of these, 112 were classified as MAP and 45 as MSAP/SAP.

Patients were included if they met the following study inclusion criteria: 1) Met the diagnostic criteria specified in section 1.3 of Chinese guidelines for the diagnosis and treatment of AP (2021) (1); 2) Were stratified by AP severity according to the revised Atlanta classification (9): MAP patients assigned to the Mild group, and MSAP/SAP patients assigned to the Severe group; 3) Aged >18 years; 4) Underwent relevant examinations, including abdominal computed tomography, ultrasound, and laboratory testing within 24 hour after admission. Laboratory tests included bilirubin (BIL), CHO, BUN, creatinine (CREA), uric acid (URIC), neutrophils-to-lymphocytes ratio (NLR), platelet-to-lymphocyte ratio (PLR), CRP, fibrinogen (FIB), D-dimer (DD), interleukin-2 (IL-2), IL-4, IL-6, IL-10, tumor necrosis factor- α (TNF- α), interferon- γ (IFN- γ), and glycosylated hemoglobin type A1c (HbA1c); 5) had complete medical records.

Patients were excluded if they met the following study exclusion criteria: 1) Having recurrent or chronic pancreatitis; 2) Having tumors, pregnancy, or severe pre-existing organ dysfunction prior to disease onset.

Ethics Approval and Consent to Participate

Case data were collected from the electronic medical record system of Yixing People's Hospital, for retrospective analysis of

patients with AP. The study was approved by the ethics committee of Yixing People's Hospital, which waived the requirement for informed consent based on the following considerations: (1) All data were de-identified prior to analysis, with direct identifiers such as name, ID number, and contact information removed; and (2) The research involved minimal risk to participants, as no additional interventions or contact with patients were required. The informed consent was obtained from all patients and their families, and the study was approved by the hospital's medical ethics committee. This study was approved by the Medical Ethics Review Committee of Yixing People's Hospital (decision number: 2025 141-01, date: 15.09.2025).

Statistical Analysis

Data analysis was performed using SPSS 26.0. Continuous variables with normal distribution were expressed as ($\bar{X} \pm S$), and the LSD-T test was used for comparison. Abnormally distributed data were presented as [M (P25, P75)], and the Mann-Whitney U test was applied to determine intergroup differences. Spearman's correlation test was used to evaluate the correlation among variables. Categorical variables were expressed as count and percentage, and the chi-square test was used to compare the rates between two groups. Multivariate analysis was performed using a logistic regression model, and the discriminative ability of the model was assessed by calculating the area under the ROC curve area under the curve (AUC). P-value<0.05 was considered statistically significant.

Results

Comparison of the Clinical Data in AP Patients with Different Severities

As presented in Table 1, a total of 157 AP patients were included, comprising 112 cases in the MAP group and 45 cases in the MSAP/SAP group. No significant differences were observed between the two groups in terms of gender, age, body mass index, or prevalence of hypertension ($p>0.05$). The distribution of etiologies significantly varied between the two groups. Biliary AP was the most common subtype in the MAP group (56.25%), whereas hypertriglyceridemic AP predominated in the MSAP/SAP group (53.66%). In addition, the proportions of patients with fatty liver or diabetes were significantly associated with AP severity. Laboratory tests indicated that levels of CHO, FIB, BUN, BIL, NLR, CRP, DD, IL-4, IL-6, and IL-10 were significantly higher in the MSAP/SAP group compared with those in the MAP group ($p<0.05$). However, there are no significant differences in indicators, such as HbA1c, aspartate aminotransferase, CREA, URIC, PLR, IL-2, IFN- γ , and TNF- α , between the two groups ($p>0.05$).

Variable	MAP (N=112)	MSAP/SAP (N=45)	$\chi^2/Z/T$	p
Sex			1.175	0.278
Female	58 (51.79%)	19 (42.22%)		
Male	54 (48.21%)	26 (57.78%)		
Age	55.88±17.96	51.13±16.17	1.54	0.125
BMI (Kg/M ²)	24.90±4.06	24.79±3.96	0.115	0.908
Etiology			7.082	0.029
Biliary	63 (56.25%)	16 (35.56%)		
Hypertriglyceridemia	29 (25.89%)	21 (53.66%)		
Else	20 (17.86%)	8 (17.78%)		
Hypertension			1.181	0.277
No	75 (66.96%)	26 (57.78%)		
Yes	37 (33.04%)	19 (42.22%)		
Fatty liver			6.674	0.01
No	77 (68.75%)	21 (46.67%)		
Yes	35 (31.25%)	24 (53.33%)		
Diabetes			5.69	0.017
No	92 (82.14%)	29 (64.44%)		
Yes	20 (17.86%)	16 (36.36%)		
HbA1c (%)	6.05 (5.5, 8.00)	5.80 (5.45, 7.65)	-0.524	0.6
BIL (Mmol/L)	16.95 (11.92, 27.92)	14.62 (8.59, 19.72)	-2.166	0.03
CHO (Mmol/L)	5.03±2.27	7.48±5.41	-4.007	0
AST (IU/L)	26.75 (16.95, 153.50)	41.71 (19.50, 70.15)	-0.082	0.935
BUN (Mmol/L)	5.24±2.84	7.48±5.41	-3.346	0.001
CREA (Mmol/L)	74.04±88.30	92.34±71.70	-1.236	0.218
URIC (Mmol/L)	306.94±120.47	342.52±132.48	-1.626	0.106
NLR (%)	6.34 (4.13, 9.90)	15.20 (6.44, 22.05)	-3.952	0
PLR (%)	195.61±119.92	238.06±171.12	-1.763	0.08
CRP (Mg/L)	22.99 (8.28, 91.06)	123.47 (53.26, 167.03)	-4.115	0
FIB (G/L)	3.86±1.17	4.52±1.41	-3.02	0.003
DD (Mg/ML)	876 (526, 1391)	3373 (1946, 6813)	-6.941	0
IL-2 (Pg/ML)	1.11 (0.47, 1.77)	0.75 (0.09, 1.35)	-0.257	0.797
IL-4 (Pg/ML)	0.98 (0.73, 1.55)	2.18 (1.06, 7.10)	-4.767	0
IL-6 (Pg/ML)	12.75 (5.45, 47.71)	101.76 (36.74, 208.68)	-6.429	0
IL-10 (Pg/ML)	1.51 (0.91, 2.50)	7.02 (5.17, 15.73)	-6.318	0
TNF-A (Pg/ML)	10.28±9.91	8.39±13.40	0.969	0.334
IFN- γ (Pg/ML)	13.26±17.77	9.75±9.04	1.261	0.209

BMI: Body mass index, HbA1c: Hemoglobin A1c, BIL: Bilirubin, CHO: Cholesterol, AST: Aspartate aminotransferase, BUN: Blood urea nitrogen, CREA: Creatinine, URIC: Uric acid, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, CRP: C-reactive protein, FIB: Fibrinogen, DD: D-dimer, IL: Interleukin, TNF-A: Tumor necrosis factor-alpha, IFN- γ : Interferon-gamma, MAP: Mild acute pancreatitis, MSAP/SAP: Moderately severe acute pancreatitis/severe acute pancreatitis, Z/T: Z test/T tes

Screening the Independent Predictors and Developing a Model for Severe AP

Using AP severity (MAP: 0, MSAP/SAP: 1) as the dependent variable, 13 clinical indicators, including etiology, fatty liver, diabetes, BIL, CHO, BUN, NLR, CRP, FIB, DD, IL-4, IL-6, and IL-10,

That were significantly associated with AP severity were involved in the univariate analysis. As presented in Table 2, multivariate analysis identified CHO, BUN, CRP, and IL-4 as independent predictors of AP severity ($p<0.05$)

Table 2. Multivariate logistic regression analysis of the risk factors for severe acute pancreatitis

Variable	B	OR	Wald	p	OR (95% CI)
Etiology	0.333	0.726	0.210	0.647	1.395 (0.336, 5.792)
Fatty liver	1.303	1.033	1.589	0.207	3.679 (0.486, 27.871)
Diabetes	-0.700	1.039	0.453	0.501	0.497 (0.065, 3.807)
CHO (Mmol/L)	0.245	0.091	2.694	0.007	1.278 (1.085, 1.562)
BUN (Mmol/L)	0.391	0.124	3.155	0.002	1.478 (1.203, 1.976)
FIB (G/L)	0.529	0.482	1.201	0.273	1.697 (0.659, 4.368)
BIL (Mmol/L)	0.027	0.017	2.694	0.101	1.028 (0.995, 1.062)
NLR (%)	0.129	0.064	4.001	0.050	1.138 (1.003, 1.291)
CRP (Mg/L)	0.016	0.005	3.061	0.002	1.016 (1.006, 1.027)
DD (Mg/ML)	0.000	0.000	2.044	0.153	1.000 (1.000, 1.000)
IL-4 (Pg/ML)	0.766	0.225	3.410	<0.001	2.151 (1.470, 3.564)
IL-6 (Pg/ML)	0.002	0.002	0.586	0.444	1.002 (0.998, 1.005)
IL-10 (Pg/ML)	-0.079	0.051	2.407	0.121	0.924 (0.836, 1.021)
Constant	-7.409	1.556	-4.761	<0.001	-

CHO: Cholesterol, BUN: Blood urea nitrogen, FIB: Fibrinogen, BIL: Bilirubin, NLR: Neutrophil-to-lymphocyte ratio, CRP: C-reactive protein, DD: D-dimer, IL: Interleukin, OR: Odds ratio, CI: Confidence interval, B: Beta coefficient

Table 3. Multivariate logistic regression analysis of the risk factors of severe acute pancreatitis

Variable	AUC (95% CI)	Sensitivity	Specificity	Youden	Cut-off	p
BUN (Mmol/L)	0.643 (0.543-0.742)	40.00%	86.61%	0.389	7.545	0.005
CHO (Mmol/L)	0.587 (0.472-0.702)	35.60%	92.86%	0.256	7.705	0.059
CRP (Mg/L)	0.762 (0.658-0.866)	72.70%	71.43%	0.442	81.85	<0.001
IL-4 (Pg/ML)	0.742 (0.650-0.834)	71.10%	69.60%	0.481	1.870	0.047
BISAP	0.719 (0.628-0.811)	48.50%	78.60%	0.271	1.50	<0.001
Prediction Model	0.932 (0.884-0.979)	97.00%	75.00%	0.720	0.178	<0.001

AUC: Area under the curve, CI: Confidence interval, BUN: Blood urea nitrogen, CHO: Cholesterol, CRP: C-reactive protein, IL: Interleukin, BISAP: Bedside index of severity in acute pancreatitis

Validation of the Prediction Model

Model Discrimination

As shown in Table 3 and Figure 1, the AUC of the combined prediction model was 0.932 (95% confidence interval (CI): 0.884-0.979), with the cut-off value of 0.178, the sensitivity of 97%, and the specificity of 75%. Its performance surpassed that of individual risk factors and the commonly used BISAP scoring system, indicating that the prediction model exhibited high discriminative power.

Discussion

AP is a complex disease characterized by multiple etiologies, variable disease courses, lack of targeted drug therapies, and difficulty in early prediction of its progression, resulting in a high mortality rate. The global incidence of AP ranges from 4.9 to 73.4 per 100,000 population, with approximately 20% of patients progressing to severe AP accompanied by a 20% mortality rate

(1,10-12). Supportive therapy, integrated traditional Chinese and Western medicine therapy, and minimally invasive surgical intervention are common treatment modalities for AP, and the selection of treatment strategies depends on the severity of AP (2). Therefore, early prediction of severe AP is crucial for guiding clinical treatment decisions and improving patient prognosis.

In this study, the clinical data and laboratory indicators of patients with different severities of AP were compared. The independent risk factors were assessed, and their predictive values for identifying early severe AP patients were explored. The results revealed that hypertriglyceridemia, fatty liver, diabetes, BIL, CHO, BUN, NLR, CRP, FIB, DD, IL-4, IL-6, and IL-10 were influential factors for severe AP; while CHO, BUN, CRP, and IL-4 were noted as independent risk factors for severe AP. The discriminative performance of the model was validated by comparing the AUC values with those of individual predictors and the commonly used BISAP scoring system.

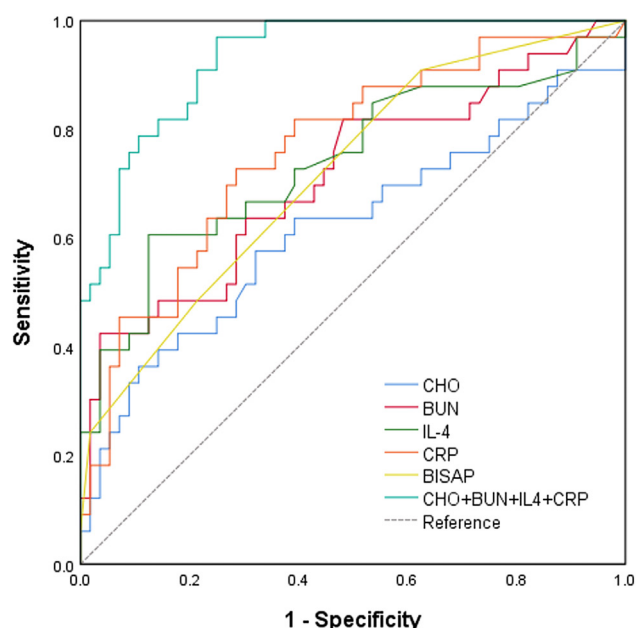


Figure 1. The ROC of the risk factors

CHO: Cholesterol, BUN: Blood urea nitrogen, IL: Interleukin, CRP: C-reactive protein, BISAP: Bedside index of severity in acute pancreatitis

CHO has multiple biological effects. As an essential component of cell membranes, it maintains structural integrity, supports membrane homeostasis, and facilitates signal transduction and material transport. It also serves as an indicator for steroid hormones, such as glucocorticoids, and acts as a metabolic regulator of lipid and glucose homeostasis (6,13). Excessive CHO can trigger inflammatory responses through Toll-like receptor 4 (TLR4) and NOD-like receptor pyrin domain-containing protein 3 (NLRP3) activation (6). Previous research has demonstrated that TLR4 plays a remarkable role in pancreatic injury (14), primarily by activating NF-Kb and upregulating the expression level of NLRP3. NLRP3 subsequently activates pro-inflammatory cytokines (E.G., ILs) leading to their release (15). Inhibition of NLRP3 inflammasome activation has been shown to significantly attenuate pancreatic injury and systemic inflammation (16). Clinically, elevated CHO level (>240 mg/dL) within 24 hour of admission has been identified as an independent risk factor for severe AP (17). Consistently, the present study revealed that CHO level within 24 hour of admission was significantly higher in the MSAP/SAP group compared with that in the MAP group. The cut-off value of CHO for predicting severe AP was 7.705 mmol/L (297.95 mg/dL; conversion factor: 38.67); consistent with previous reports above.

BUN is an integral component of classic scoring systems for predicting severe AP, such as APACHE II And BISAP. Specifically,

in the BISAP scoring system, BUN level exceeding 25 mg/dL (8.93 mmol/L, conversion factor 2.8) can contribute 1 point to the assessment of severe AP risk. Results from large-scale multicenter cohort studies demonstrated that early changes in BUN could accurately predict AP outcomes, with BUN measurement within 24 hours of admission recognized as the most valuable single routine parameter for the early prediction of severe AP (18). Yang et al. (19) further confirmed that BUN level within 48 hour of admission was optimal for predicting persistent organ failure in AP. However, a meta-analysis conducted by Wang et al. (20), which included studies on BUN measurements at different time points, failed to identify BUN's predictive value for severe AP. These findings suggest that the predictive utility of BUN depends heavily on strict timing of measurement. Consistent with Wu et al. (18) findings, the BUN level within 24 hour of admission in the MSAP/SAP group was significantly higher than that in the MAP group, and BUN was noted as an independent risk factor for the progression of AP to severe condition. However, the cut-off value derived from univariate analysis (7.545 mmol/L) and the corresponding ROC sensitivity were lower than the BISAP criteria. These results demonstrate that although BUN alone provides early warning value for severe AP, its predictive power is limited, highlighting the need for combination with other indicators.

CRP is an acute-phase reactive protein synthesized by the liver and is commonly used as a non-specific inflammatory marker. Its predictive role in severe AP remains controversial, mainly due to variability in measurement timing, threshold selection, and clinical applicability. On one hand, since CRP synthesis depends on hepatic function, its reliability may be compromised in patients with alcoholic or obesity-related AP; on the other hand, because CRP peaks 24–48 hour after inflammation onset, it may be less appropriate for very early prediction (21,22). Both Stirling et al. (23) and the Chinese guidelines for the diagnosis and treatment of Aps (2021) (1) indicated that a CRP level exceeding 150 mg/mL suggested severe AP, while the former specified that the test should be conducted within 48 hour after admission, and the latter recommended the testing time as 72 hour following the onset of AP. studies by Walker et al. (24), Rao et al. (25), and He et al. (26) support Stirling et al. (23) timing, although they propose different thresholds. Wu et al. (21) further stratified patients by measurement time (≤ 48 H, 48 H–7 days, ≥ 7 days), and found that timing did not significantly affect the predictive value of CRP for severe AP. In the present study, CRP was measured within 24 hours of admission, with a predictive threshold of 81.85 mg/L, which is lower than guideline recommendations. Moreover, the 25th percentile of CRP in patients who progressed to severe AP within 24 hour was only 53.26 mg/L. These findings demonstrate that earlier measurement at a lower threshold may hold greater clinical value for early prediction of severe AP.

IL-4 is an anti-inflammatory cytokine. Previous studies have demonstrated that following pancreatic injury, IL-4 promotes The polarization of M2a macrophages via IL-4 receptor signaling, thereby promoting pancreatic repair and regeneration (27). The polarization and subtype diversity of macrophages play a pivotal role in this process (12,27-29). Macrophages, which exhibited similar cellular phenotypes in patients with mild and severe AP and represented the most prominently altered immune cells during AP, exhibited distinct functional effects via cytokine secretion, with variations in cytokine expression levels measured between the recovery and severe phases (29,30). Both clinical and experimental studies have supported the notion that The excessive inflammatory response in AP arises from a dynamic imbalance between anti-inflammatory and pro-inflammatory factors (27,31). In severe AP, overexpression and subsequent exhaustion of IL-4 can lead to immunosuppression, complications, and organ damage, making elevated IL-4 levels a marker of poor prognosis (31). In the present study, IL-4 level in the MSAP/SAP group was significantly higher than that in the MAP group, demonstrating that the development of severe AP may promote the polarization of M1 macrophages toward M2a cells. however, due to the exhaustion of IL-4, its anti-inflammatory effect was remarkably diminished or even abolished. Notably, no counteracting pro-inflammatory cytokines were identified in this study.

Clinical data analysis identified four laboratory indicators (CHO, BUN, CRP, and IL-4) as independent predictors of early severe AP. All four were derived from routine blood tests, providing a more convenient and objective alternative to complex scoring systems.

Study Limitations

However, this study has several limitations. firstly, as a retrospective study, the inclusion of observational indicators was limited, potentially leading to the omission of other risk factors. Secondly, as a single-center study, the study restricted the extrapolation of its findings. Thirdly, when the cost-benefit ratio exceeded 0.7, fluctuations in the decision curve analysis curve were intensified, and further validation of the model still requires data from a larger sample of cases. Fourthly, AP has substantial long-term impacts, even mild cases carry risks of recurrence, progression to chronic pancreatitis, and complications involving endocrine and exocrine insufficiency. Follow-up surveys on readmission rates were limited by variability in measurement methods and small numbers of positive cases, restricting further analysis of risk factors. previous studies by Wu et al. (27) and Yue et al. (28) have highlighted the importance of dynamic cytokine monitoring. The present study analyzed serum cytokine concentrations only at admission, precluding assessment of their real-time significance during disease progression and recovery.

Conclusion

In conclusion, the present study identified CHO, BUN, CRP, and IL-4 as significant independent risk factors for the early development of severe AP. A novel predictive model was developed using four readily available biomarkers, demonstrating superior diagnostic efficacy (AUC: 0.932, Sensitivity: 97%, Specificity: 75%) compared with any single indicator and the conventional BISAP score. This model assists clinicians with a simple, objective, and effective tool for the early risk stratification of AP patients within 24 hours of admission. Despite the limitations of a single-center, retrospective design, the combined biomarker panel showed promising performance for optimizing timely interventions and improving patient prognosis. Future large-scale, prospective studies are warranted to validate these findings and explore the underlying molecular mechanisms.

Ethics

Ethics Committee Approval: This study was approved by the Medical Ethics Review Committee of Yixing People's Hospital (desicion number: 2025 141-01, date: 15.09.2025).

Informed Consent: The informed consent was obtained from all patients and their families, and the study was approved by the hospital's medical ethics committee.

Footnotes

Author Contributions

Concept: Y.C., Design: Y.C., Y.H., Data Collection or Processing: J.M., G.Q., Analysis or Interpretation: Y.H., Literature Search: G.Q., Writing: Y.C., Y.H.

Conflict of Interest: No conflict of interest was declared by the authors.

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Availability of Supporting Data

The data that support the findings of this study are available on request from the corresponding author.

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Use of Artificial Intelligence in Pulmonary Embolism Prediction

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Abstract

Aim: The purpose of this study was to use artificial intelligence to predict the risk of pulmonary embolism (PE) in patients with suspected PE admitted to the emergency room based on physical examination, laboratory, and clinical probability prediction scores without computed tomography angiography.

Materials and Methods: A comprehensive analysis was conducted on a total of 156 individuals who were admitted to the emergency room with PE. Seventy-eight patients were diagnosed with PE through anamnesis, physical examination, clinical likelihood prediction scores, investigations, and imaging. These patients were then included in the PE group. The data set includes gender, age, shock index, vital signs, complaints at arrival to the emergency department, comorbidities, medications used, medical history, radiological examinations, presence of deep vein thrombosis, electrocardiography, echocardiography findings, Wells score, Geneva score, PERC score, and laboratory tests performed.

Results: The average age of the patients in the study was 69.46 ± 15 years. Dyspnea was the most prevalent presentation, affecting 88 patients (56.4%). The most prevalent comorbidities were hypertension in 52 patients (33.1%), cancer in 51 patients (32.7%), and coronary artery disease in 35 patients (22.4%). The Wells score, D-dimer, low partial carbon dioxide pressure, and tachycardia were discovered to be important factors in the diagnosis of PE. Statistically significant parameters were investigated using a multilayer perceptron artificial intelligence model. The diagnosis of PE was correct with 96% accuracy and 89% specificity.

Conclusion: According to the findings of our study, a thorough review of the patient's anamnesis, physical examination, laboratory and imaging data, and the application of scores are all crucial in the diagnosis of PE. Furthermore, it was determined that artificial intelligence can be used to diagnose PE before using imaging modalities.

Keywords: Artificial intelligence, diagnostic algorithm, pulmonary embolism

Introduction

Venous thromboembolism (VTE) consists of deep vein thrombosis (DVT) and pulmonary embolism (PE). PE is a clinical condition that occurs when a thrombus passes from the venous circulation to the pulmonary arteries and clots. The clinical presentation varies from asymptomatic to fatal. For this reason, it is difficult to determine the true incidence of PE. Nevertheless, the incidence has increased over the years (1). PE is a critical condition that, along with myocardial infarction and stroke, is among the leading causes of cardiovascular-related death (2). PE-related

mortality may vary depending on the patient's age, comorbid diseases, disease burden, and duration of effective treatment. Thirty-day all-cause mortality in patients with PE is 6.6%. PE-related seven-day mortality was 1.1%, while thirty-day mortality was 1.8% (3). The annual cost of PE to the European Union countries was found to be 8.5 billion Euros, including indirect costs such as pre-hospital prevention, in-hospital treatment, and post-hospital care. Both the aging of the population, the increase in incidence, and the decrease in mortality will increase the financial burden of VTE events on governments in Europe and other countries of the world (4).



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Although PE is a common disease, there are no pathognomonic findings or diagnostic tests. For this reason, the clinician should be the primary authority for making the diagnosis. It is difficult for the clinician to diagnose the disease as it has a wide range of clinical presentations, from asymptomatic to fatal outcomes. It is emphasized that PE can be fatal if there are delays in diagnosis and treatment (5). The relatively high prevalence of PE makes it a common and potentially life-threatening disease (6). Early diagnosis of PE is crucial, as even patients with minor symptoms are at risk of recurrent PE (7). Currently, the gold standard diagnostic method is computed tomography-pulmonary angiography (CTPA) (8). Because of the risks associated with CTPA, including contrast agent allergy, contrast nephropathy, radiation exposure, and economic reasons, diagnostic algorithms have been proposed and clinical probability prediction scores have been developed to diagnose PE before imaging (9-15). Two of these scores are the Wells Clinical score and the Geneva score. The Wells clinical score is a widely recognized and validated tool for assessing the clinical probability of PE. It includes physical findings and risk factors such as DVT, lack of alternative diagnoses, tachycardia, immobilization or recent surgery, history of DVT or PE, hemoptysis, and malignancy (16). To help diagnose PE, the Geneva score, like the Wells score, is a standardized tool to help determine the clinical probability of PE based on several criteria, including heart rate, clinical signs of DVT, hemoptysis, and previous PE or DVT (17).

With the increasing awareness of PE among physicians and the increasing availability of diagnostic tests and imaging, the need to avoid unnecessary tests has become evident. The aim was to avoid complications of the tests and to reduce the excessive cost and length of hospitalization. For this purpose, they defined “pulmonary embolism exclusion criteria (PEEC).” It is a rule based on clinical criteria to exclude this condition in patients suspected of having it. The PEEC rule aims to prevent unnecessary additional testing in low-risk patients by assessing whether patients have certain clinical characteristics. Besides all these algorithms, only D-dimer has been validated as a biomarker to aid in the decision to exclude PE. Although not specific for PE, elevated white blood cell count, serum lactate dehydrogenase (LDH), C-reactive protein (CRP), aspartate aminotransferase (AST), and increased sedimentation rate may be detected. The diagnosis of PE plays a critical role in the management of this life-threatening condition, alongside the use of many methods and algorithms. The use of advanced imaging techniques such as CTPA and the application of algorithms, together with a high index of suspicion and rapid intervention, is essential in providing a timely and accurate diagnosis that can significantly affect patient outcomes. In this study, our aim is to investigate the feasibility of using artificial intelligence (AI) approaches in the diagnosis of PE; to identify

possible risk factors; and to ensure that CTPA, the gold standard in the diagnosis of PE, is used in appropriate patients based on AI findings.

Materials and Methods

The appropriateness of this study was approved by the İnönü University Scientific Research and Publication Ethics Committee with (decision number: 2022/45, date: 20.04.2022). In addition, the study was supported by İnönü University Scientific Research Projects Unit with project number 3002.

Dataset

In this study, 156 patients admitted to the Department of Emergency Medicine of İnönü University Faculty of Medicine Turgut Özal Medical Center from 13.10.2022-14.10.2024, with PE symptoms, were prospectively analyzed. Adult patients presenting to the emergency department with PE symptoms were included in the study. Pediatric patients under 18 years of age, as well as pregnant and recently delivered patients, were excluded. Anamnesis, physical examination, computerized order tracking system (COTS), and laboratory tests were evaluated. All patients underwent bolus-tracking pulmonary angiography, the gold standard imaging method in PE. Seventy-eight patients were diagnosed with PE and then enrolled in the PE group. The 78 patients with alternative diagnoses in whom PE was ruled out were enrolled as the control group. In the medical records of patient admissions, the admission number, name-surname, gender, age, shock index, vital signs (temperature, pulse, systolic and diastolic blood pressures, saturation values), complaints at presentation to the emergency department, comorbidities, medications used, medical history, radiological examinations, presence of DVT, electrocardiography (ECG), echocardiography findings [ejection fraction (EF)], pulmonary artery pressure (PAP), right ventricular volume (RVV), Wells score, Geneva score, PERC score, laboratory tests hemoglobin, hematocrit, mean cellular volume, monocyte count, platelet, activated partial thromboplastin time, international normalized ratio values, CRP, prothrombin time, platelet distribution width, erythrocyte distribution width, liver enzymes [alanine aminotransferase, AST, creatine kinase (CK), CK myocardial band, renal function tests [blood urea nitrogen (BUN) and creatinine], total protein, albumin, LDH, triglycerides, cholesterol, low-density lipoprotein (LDL), blood gas parameters (pH, PCO₂, PO₂, lactate, HCO₃), D-dimer, fibrinogen, pro-brain natriuretic peptide, procalcitonin (PCT), high sensitivity troponin (HS troponin), PCT triglycerides, total cholesterol, high-density lipoprotein (HDL-cholesterol), LDL-cholesterol, plasmin, vitamin K, fibrinopeptide A, factor V Leiden, and protein S were examined.

Artificial Intelligence

AI is increasingly being integrated into various aspects of healthcare, revolutionizing the field and providing new opportunities for better patient care and outcomes. AI applications in healthcare cover a wide range of areas, from diagnosis and treatment to administrative tasks and patient engagement. Machine learning (ML) techniques such as support vector machines, neural networks, and deep learning have been instrumental in leveraging structured and unstructured data to improve decision-making in healthcare (18). In the field of medical imaging, AI has played an important role in improving diagnostic accuracy and treatment strategies. ML algorithms have been used to predict outcomes and help analyze medical images such as magnetic resonance imaging and computed tomography scans, leading to improved diagnostic capabilities (19). The integration of AI into healthcare has been positively received by both patients and healthcare professionals, highlighting the potential benefits of AI in improving healthcare delivery and patient outcomes (20). However, it is crucial to ensure the interpretability and ethical use of AI in healthcare to protect patient safety and data privacy (21). Overall, the development of AI in healthcare holds great promise for transforming the sector, increasing diagnostic accuracy, improving treatment outcomes, and optimizing healthcare delivery processes.

Statistical Analysis

Data analysis was performed using IBM® SPSS® Statistics (version 25 for Windows, IBM Corporation, Armonk, New York, USA). Shapiro-Wilk test, histogram distribution, and skewness-kurtosis parameters were used for normality analysis. Descriptive statistics are presented as mean \pm standard deviation for variables with normal distribution, median (minimum-maximum) for variables with non-normal distribution, and count of cases and (%) for nominal variables. The chi-square test and the Fisher's exact test were used to analyze the relationship between categorical variables. In the evaluation of the relationship between continuous variables, the Mann-Whitney U test was used if the variables were nonparametric, and the Student t test was used if the variables were parametric. Results were considered statistically significant for $p < 0.05$.

AI Modeling

The multilayer perceptron (MLP) artificial neural network model was used with the variables that were statistically different between the PE and control groups. Gradient descent was used as the optimization function for the model. 70% of the data was used in the training of the model, while 30% was used in the testing phase.

Results

Biostatistical Analysis

The mean age of the patients included in the study was 69.46 ± 15 years. Of the patients, 79 were male (50.6%) and 77 were female (49.4%). When the presenting complaints of the patients were analyzed, 88 patients (56.4%) presented with dyspnea, 11 patients (7.1%) with palpitations, 8 patients (5.1%) with chest pain, 4 patients (2.6%) with syncope, 3 patients (1.9%) with hemoptysis, and 40 patients (25.6%) with other reasons. The general data of the patients included in the study are shown in Table 1.

Table 1. The descriptive statistics of all patients

	Mean \pm SD	Minimum-Maximum
Age (years)	69.46 \pm 15	27-98
Vital signs		
Systolic blood pressure	133.31 \pm 25.7	77-264
Diastolic blood pressure	80.58 \pm 15.21	36-130
SaO ₂	89.10 \pm 8.38	40-100
Heart rate	93.68 \pm 20.64	54-161
Fever	36.27 \pm 0.24	36-37.2
	Count (n)	Percent (%)
Gender		
Female	77	49.4
Male	79	50.6
Hospital application complaint		
Palpitations	11	7.1
Shortness of breath	88	56.4
Chest pain	8	5.1
Hemoptysis	3	1.9
Syncope	4	2.6
Other	40	25.6
Comorbidity		
DM	12	7.7
HT	52	33.3
CAD	35	22.4
COPD	21	13.5
CHF	23	14.7
CRF	7	4.5
SVE	4	2.6
Malignite	51	32.7
DVT	26	16.7
PE	9	5.8
Other	63	40.4

DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, CRF: Chronic renal failure, SVE: Serobrovascular events, DVT: Deep vein thrombosis, PE: Pulmonary embolism, SD: Standard deviation, EA-EY: Minimum-highest, TA: Tension arterial, SaO₂: Saturation

The mean age of the patients with PE was 68.48 ± 13.4 years, while the mean age of our control group was 70.44 ± 13.4 years. In the PE group, 45 patients (57.7%) were female and 33 patients (42.3%) were male. In the control group, 32 patients (41%) were female and 46 patients (59%) were male. The comparison of risk factors for PE and control groups is given in Table 2.

According to Table 2, when PE patients were compared with the control group, PE patients were more likely to be female ($p=0.037$), and complaints such as palpitations ($p=0.005$) and shortness of breath ($p=0.001$) were more common. In terms of vital signs, PE patients had lower systolic and diastolic blood pressure

Table 2. The comparison of risk factors for PE by group categories (PE, control)

	Group		p value
	PE (n=78)	Control (n=78)	
	Mean \pm SD	Mean \pm SD	
Age (years)	68.48 ± 16.4	70.44 ± 13.4	0.605
Vital signs			
Systolic blood pressure	124.83 ± 26.58	141.69 ± 22.08	<0.001
Diastolic blood pressure	75.94 ± 16.06	85.16 ± 12.85	<0.001
SaO ₂	89.33 ± 6.89	88.88 ± 9.66	0.594
Heart rate	99.89 ± 21.59	87.55 ± 17.77	<0.001
Fever	36.28 ± 0.26	36.27 ± 0.22	0.990
Gender			
Female	45 (57.7)	32 (41.0)	0.037
Male	33 (42.3)	46 (59.0)	
Hospital application complaint	Count (%)	Count (%)	
Palpitations	10 (12.8)	1 (1.3)	0.005
Shortness of breath	34 (43.6)	54 (69.2)	0.001
Chest pain	6 (7.7)	2 (2.6)	0.147
Hemoptysis	2 (2.6)	1 (1.3)	0.506
Syncope	3 (3.8)	1 (1.3)	0.311
Other	21 (29.5)	19 (24.4)	0.714
Comorbidity			
DM	12 (15.4)	0 (0)	<0.001
HT	19 (24.4)	33 (42.3)	0.017
CAD	10 (12.8)	25 (32.1)	0.004
CRF	1 (1.3)	6 (7.7)	0.117
SVE	1 (1.3)	3 (3.8)	0.620
Malignite	29 (37.2)	22 (28.2)	0.232
DVT	24 (30.8)	2 (2.6)	<0.001
PE	6 (7.7)	3 (3.8)	0.495
Other	33 (42.3)	30 (38.5)	0.624

DM: Diabetes mellitus, DVT: Deep vein thrombosis, HT: Hypertension, CAD: Coronary artery disease, CRF: Chronic renal failure, PE: Pulmonary embolism, SaO₂: Saturation, SD: Standard deviation, SVE: Serobrovascular events

($p<0.001$) and higher heart rate ($p<0.001$). Comorbidities such as diabetes ($p<0.001$), coronary artery disease ($p=0.004$), and DVT ($p<0.001$) were more common in PE patients. These data suggest that PE patients differ from the control group in terms of certain demographic and clinical characteristics. The examination of cardiac markers in our study between PE patients and the control group is given in Table 3.

According to Table 3, in ECG findings, normal sinus rhythm was found to be 65.4% in PE patients while 74.4% in the control group, and this difference was not statistically significant ($p=0.222$). Syncope or tachycardia was 17.9% in the PE group and 6.4% in the control group, and this difference was significant ($p=0.028$). There were no significant differences between the groups in terms of atrial fibrillation, block, and other ECG findings.

When EF were analyzed, mean EF, was not statistically significant between PE and control groups ($p=0.069$). The mean of PAP was also similar between the groups ($p=0.545$). RVV was 29.5% in the PE group and 18.4% in the control group, and this difference was not statistically significant ($p=0.108$). These data show that ECG and EF of PE patients had some differences compared to the control group, but most of these differences were not statistically significant. The results of the statistical analysis of the utility scores used in PE estimation are given in Table 4.

The results of hemogram, coagulation, and blood gas parameters of the patients in PE and control groups are given in Table 5.

According to Table 5, the coagulation parameter D-dimer and the blood gas parameter PaCO₂ were statistically different

Table 3. The examination of cardiac markers in our study in terms of PE patients and control group

	Group		p value
	PE (n=78)	Control (n=78)	
	Count (%)	Count (%)	
ECG			
NSR	51 (65.4)	58 (74.4)	0.222
ST	14 (17.9)	5 (6.4)	0.028
AF	7 (9.0)	12 (15.4)	0.221
BLOK	6 (7.7)	2 (2.6)	0.147
S1Q3T3	0 (0)	1 (1.3)	0.316
Other	2 (2.6)	4 (5.1)	0.405
Echocardiography	Mean \pm SD	Mean \pm SD	
EF	57.37 ± 7.01	55.85 ± 8.13	0.069
PAP	32.98 ± 10.93	34.32 ± 12.55	0.545
	Count (%)	Count (%)	
RVV	23 (29.5)	14 (18.4)	0.108

ECG: Electrocardiography, AF: Atrial fibrillation, EF: Ejection fraction, NSR: Normal sinus rhythm, PAP: Pulmonary artery pressure, RVV: Right ventricular volume, SD: Standard deviation, ST: Sinus tachycardia, PE: Pulmonary embolism

between the groups. D-dimer was found to be high in the PE group, while PaCO_2 was found to be low. The descriptive statistics of the biochemical parameters between the groups included in the study are shown in Table 6.

According to Table 6, statistically significant differences were observed in some parameters in the biochemistry analysis between PE patients and the control group. BUN levels were significantly lower in PE patients (26.72 ± 18.63) compared to

the control group (32.40 ± 22.70 , $p=0.020$). CK level was higher in the PE group (194.77 ± 650.76) compared to the control group (120.02 ± 151.06 , $p=0.038$). Total protein level was lower in PE patients (6.23 ± 1.11) than in the control group (6.60 ± 0.83 , $p=0.023$). Similarly, albumin level was lower in PE patients (3.39 ± 0.64) compared to the control group (3.63 ± 0.54 , $p=0.013$). CRP level was higher in the PE group (7.51 ± 6.94) compared than the control group (6.02 ± 7.92 , $p=0.015$). In addition, triglyceride levels were significantly higher in PE patients (136.74 ± 91.60) compared to the control group (112.69 ± 59.70 , $p=0.020$). These findings reveal that there are significant differences in the biochemical profiles of PE patients compared to the control group. The comparison of coagulation factors in PE and the control group is given in Table 7.

On the other hand, in this study, the effect of PE on 3-month mortality was examined, revealing 34 (43.6%) patients in the PE group and 19 (24.4%) patients in the control group died within 3 months. 3-month mortality in the PE group was significantly higher than in the control group ($p<0.05$).

Table 4. Examination of useful scores in PE prediction

	Group		p value
	PE	Control	
	Mean \pm SD	Mean \pm SD	
Shock index	0.82 ± 0.25	0.62 ± 0.12	<0.001
Wells score	5.73 ± 4.20	0.66 ± 0.95	<0.001
Geneva score	4.20 ± 2.96	2.11 ± 2.20	<0.001

PE: Pulmonary embolism, SD: Standard deviation

Table 5. Comparison of hematologic parameters in PE and control groups

	Group		p value
	PE	Control	
	Mean \pm SD	Mean \pm SD	
Hemogram			
HGB	12.41 ± 2.30	12.40 ± 2.64	0.945
MCV	86.80 ± 9.64	85.89 ± 7.61	0.296
HCT	38.48 ± 6.75	38.04 ± 7.88	0.717
PLT	223.94 ± 124.97	245.46 ± 115.99	0.326
PDW	11.98 ± 4.44	11.63 ± 2.12	0.420
Monocyte	0.90 ± 1.17	0.94 ± 1.31	0.838
RDW	17.0 ± 6.93	17.41 ± 10.18	0.714
Coagulation			
APTT	31.18 ± 20.68	35.97 ± 24.62	0.089
PT	19.35 ± 16.69	17.06 ± 12.76	0.481
INR	1.62 ± 2.30	1.38 ± 0.79	0.490
Fibrinogen	361.02 ± 164.41	396.51 ± 179.27	0.468
D-dimer	8.78 ± 7.99	2.49 ± 2.54	<0.01
Blood gas			
Ph	7.39 ± 0.13	7.38 ± 0.08	0.344
PaCO_2	34.79 ± 11.60	39.96 ± 18.28	0.027
PaO_2	65.38 ± 36.31	55.71 ± 24.63	0.162
HCO_3	22.99 ± 9.68	23.08 ± 8.94	0.916
Lactate	2.70 ± 2.72	2.82 ± 3.65	0.589

APTT: Activated partial thromboplastin time test, HCO_3 : Bicarbonate, HCT: Hematocrit, INR: International normalized prothrombin time, MCV: Mean corpuscular erythrocyte volume, PE: Pulmonary embolism, PLT: Platelet, PDW: Platelet distribution width, RDW: Erythrocyte distribution width, PaCO_2 : Partial carbon dioxide pressure, PaO_2 : Partial oxygen pressure, Ph: Potential hydrogen, PT: Prothrombin time, SD: Standard deviation, HGB: Hemoglobin

Table 6. The comparison of biochemical parameters in PE and control groups

	Group		p value
	PE	Control	
	Mean \pm SD	Mean \pm SD	
Biochemistry			
Creatinine	1.18 ± 0.58	1.52 ± 1.63	0.234
BUN	26.72 ± 18.63	32.40 ± 22.70	0.020
LDH	531.89 ± 1320.29	412.57 ± 357.75	0.207
CK	194.77 ± 650.76	120.02 ± 151.06	0.038
CK-MB	37.48 ± 73.75	31.68 ± 35.51	0.828
Total protein	6.23 ± 1.11	6.60 ± 0.83	0.023
Albumin	3.39 ± 0.64	3.63 ± 0.54	0.013
ALT	50.03 ± 164.60	67.16 ± 191.92	0.766
AST	64.34 ± 192.95	69.64 ± 149.98	0.578
Pro-BNP	4102.11 ± 6775.67	6472.31 ± 10494.64	0.983
Procalcitonin	1.10 ± 3.90	3.43 ± 14.85	0.486
CRP	7.51 ± 6.94	6.02 ± 7.92	0.015
Troponin	109.54 ± 376.94	207.31 ± 856.01	0.632
Triglycerides	136.74 ± 91.60	112.69 ± 59.70	0.020
Total cholesterol	175.25 ± 52.31	160.27 ± 42.33	0.135
LDL-cholesterol	107.65 ± 38.86	97.12 ± 29.52	0.110
HDL-cholesterol	38.93 ± 11.58	39.73 ± 16.24	0.944

ALT: Alanine transaminase, AST: Aspartate transaminase, CK: Creatinine kinase, CK-MB: Creatinine kinase myocardial band, LDH: Lactate dehydrogenase, LDL-cholesterol: Low-density lipoprotein, HDL-cholesterol: High-density lipoprotein cholesterol, Pro-BNP: ProBrain natriuretic peptide, PE: Pulmonary embolism, SD: Standard deviation, BUN: Blood urea nitrogen, CRP: C-reactive protein

AI Modeling

To classify PE, a MLP artificial neural network model was created in which the variables that were statistically different between PE and the control group were used as the independent variables. Gradient descent was used as the optimization function for the model. The performance metrics of the classification model are given in Table 8.

Considering the performance metrics obtained in Table 8, the MLP classification model is quite successful in classifying PE and control groups. Figure 1 shows the graph of the variable importance values obtained from the MLP model, where the most important variables in classifying PE are displayed in order. As a result of the MLP model created according to Figure 1, Wells score and D-dimer were found to be the two important variables in predicting PE.

	Group		p value
	PE	Control	
	Mean \pm SD	Mean \pm SD	
Fibrinopeptide A	28.26 \pm 27.16	20.29 \pm 15.92	0.129
Protein S	79.44 \pm 89.64	84.74 \pm 114.92	0.917
Coagulation factor 5	98.99 \pm 59.62	99.30 \pm 74.59	0.996
Vitamin K	312.67 \pm 334.77	237.04 \pm 182.20	0.862
Plasminogen	835.50 \pm 1354.78	613.63 \pm 357.08	0.337

PE: Pulmonary embolism, SD: Standard deviation

Discussion

The mean age of the PE group was 68.48 \pm 16.4 years; the female rate was 57.7%, and the most common presenting complaint was dyspnea. Palpitation was a significant symptom in the PE group. Diabetes mellitus and DVT were significantly higher in the PE group, whereas hypertension and coronary artery disease were significantly higher in the control group. Among the vital signs, tachycardia and low mean systolic and diastolic blood pressure were significant in PE. We found both Wells and Geneva scores to be significant in the diagnosis of PE. When we compared the scores, the specificity and sensitivity of the Wells score were higher compared to another scoring method. An increasing shock index is significant for the diagnosis of PE. Low PaCO₂ in blood gas was a significant finding in patients with PE. Elevated D-dimer, elevated CRP, triglycerides, and low BUN, total protein, and albumin were significant in the diagnosis of PE. In addition, fibrinopeptide A, factor 5, protein S, vitamin K, and plasminogen from the thrombophilia panel were not significantly associated with PE.

Performance metrics	Value	95% confidence interval
Accuracy	0.96	0.88-1.00
Sensitivity	1.00	0.78-1.00
Specificity	0.89	0.52-0.99
F1-score	0.97	0.90-1.00
MCC	0.91	0.80-1.00
G-mean	0.97	0.90-1.00

MCC: Matthews's correlation coefficient, PE: Pulmonary embolism

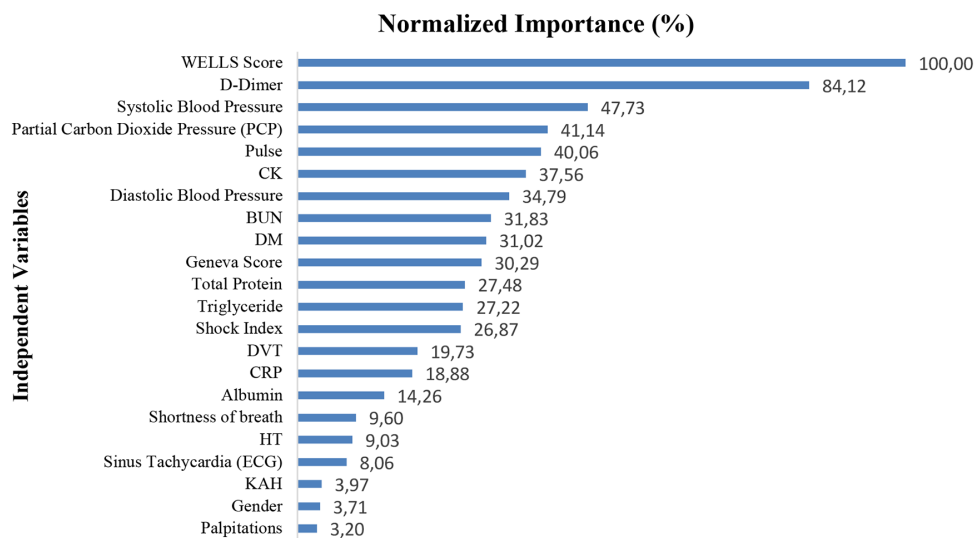


Figure 1. The variable significance based on MLP estimation model

MLP: Multilayer perceptron, CK: Creatine kinase, BUN: Blood urea nitrogen, DM: Diabetes mellitus, DVT: Deep vein thrombosis, CRP: C-reactive protein, HT: Hypertension, KAH: Coronary artery disease

When the mean age of PE patients was analyzed, it was found that Wells et al. (9) had a mean age of 50.5 ± 18.4 years, van der Hulle et al. (11) had a mean age of 53 ± 18 years, Le Gal et al. (15) had a mean age of 60.6 ± 19.4 years, Roy et al. (22) had a mean age of 52 ± 18.5 years, and Penaloza et al. (23) had a mean age of 63.9 years. In the present study, the mean age of the PE group was 68.48 ± 16.4 years, and the mean age of the control group was 70.44 ± 13.4 years. No significant difference was found between them. The female rate was 62.7% in Wells et al (9), 62% in van der Hulle et al. (11), 58.2% in Le Gal et al. (15), 60.8% in Roy et al. (22), and 62% in Penaloza et al. (23). In this study, consistent with the literature, the percentage of females in the PE group was found to be 57.7%, while the percentage of males was 42.3%. Many studies have demonstrated the relationship between tachycardia and PE (24-26). The significantly higher rate of tachycardia in the PE group is compatible with the literature.

PE is most often a complication of DVT. According to the literature, the rate of DVT in patients diagnosed with PE varies between 21% and 37%. Even in patients with suspected PE, if the lower extremity Doppler USG is positive, anticoagulant treatment can be started without the need for further examination (27). In the current study, the detection rate of DVT in the PE group was found to be significantly higher than in the control group. As a result, the relationship between PE and DVT is similar to that described in the literature.

Upon examining studies comparing the diagnostic accuracy of the most commonly used scoring systems (KOTS, Wells, and modified Geneva), it was found that the diagnostic accuracy of the Wells score was higher than that of the modified Geneva and simplified Geneva. In the studies of Shen et al. (17) and Wong et al. (28), the specificity and sensitivity of the Wells score were found to be significantly higher than the modified Geneva score. In the current study, it was found that high Wells and Geneva scores were significant in the diagnosis of PE. In this respect, the study aligns with previous literature in its methodological approach.

Thrombophilia is a inherited risk factor for VTE. Factor V Leiden deficiency and protein C deficiency are two additional common causes. Depending on the characteristics of the population selected in studies, the thrombophilia detection rate is between 10-50% (29). In this study, we measured Factor V Leiden, fibrinopeptide a, protein s, vitamin K, and plasminogen levels in accordance with the thrombophilia panel. In our study, no significant difference was found in these parameters between the PE group and the control group. The reason why thrombophilia is not significant, unlike in the literature, is what we think is due to the high average age of the patient population in the study. Additionally, it would be appropriate to perform a thrombophilia

examination by waiting 3-6 weeks after the diagnosis of PE, but this situation could not be achieved.

D-dimer is the fibrin breakdown product resulting from the destruction of thrombus formed during thrombolytic events (30). With acute PE, D-dimer level increases. Studies have shown that high D-dimer levels have HS, but low specificity in VTE. It has a high negative predictive value as it excludes.

VTE events with >95% sensitivity in ambulatory patients and in patients with low or medium COTS, unless the latter have any comorbidities. While sensitivity with high positive predictive value has low specificity, sensitivity with high negative predictive value has high specificity. it is more meaningful in excluding PE rather than making a diagnosis (31). In a meta-analysis study, in the preliminary diagnosis of PE, the D-dimer test was found to be high in 94% of the patients and normal in 6%. In our study, consistent with the literature, the positive predictive value of D-dimer in the diagnosis of PE was found to be significantly high.

There are publications on the use of BUN levels for predicting mortality in PE-patients. In a study conducted in our country, the relationship between a BUN value of 34.5 mg/dL at the time of diagnosis and mortality in patients diagnosed with acute PE, and treated aggressively with t-PA, was found to be significant with 85% sensitivity and 91% specificity (32). In another study, the ratio of BUN to serum albumin (B/A) was investigated to predict the mortality of patients hospitalized in the intensive care unit with a diagnosis of PE. This study showed that as the B/A ratio increases, the intensive care mortality of PE patients also increases (33). In the study, the BUN value at the time of admission was found to be significantly higher in the control group. Since the current study attempts to diagnose rather than predict mortality, there are no similar studies in the literature. More studies are needed on this subject.

Aujesky et al. (34) investigated the benefits of using CRP in combination with KOTS in diagnosing PE and concluded that while a CRP value >5 mg/dL was significant in excluding PE when combined with low KOTS, CRP alone could not exclude PE. Roumen-Klappe et al. (35), also reported that CRP increased in PE. A study comparing D-dimer and CRP levels in the diagnosis and exclusion of PE found that a standard CRP test using a cut-off level of 5 mg/dL can be used alone or in combination with KOTS to safely exclude PE (36). In the current study, the CRP value was significantly higher in the PE group compared to the control group. Considering similar studies in the literature, we think that elevated CRP, combined with COTS at medium to high risk, may be meaningful. However, we believe that studies with a larger number of patients are needed on this subject.

When the studies investigating the use of AI in the diagnosis of PE were examined, Müller-Peltzer et al.'s (37) study found common false positives originating from soft tissue and pulmonary vein in diagnosing PE with AI. In their study, Li et al. (38), Douillet et al. (39) stated that AI with ML algorithms will be a future tool to guide the physician regarding suspected acute PE. With the modeling obtained, it was observed that PE was classified with very high success and possible risk factors were obtained. According to the variable importance values obtained by modeling, Wells score and D-dimer were identified as the most important risk factors. With the current study, it has been shown that AI can be used in PE prediction, in line with the literature. In terms of better evaluation of the results of our study and the usability of AI in the clinic, we think that further studies with a larger number of patients are needed.

Study Limitations

The first limitation of our study is that the accuracy of the presented AI model was not tested prospectively. The second limitation is that the patients diagnosed with PE or alternative diagnoses were not examined in the survey. The contribution to the survey of the AI model that emerged as a result of the study could not be examined. Another limitation is that it is not known whether the clinicians who collected the qualitative data of the study were trained extensively about PE. Another limitation is that the study was conducted in a single center and with a limited number of patients. Therefore, it is recommended that the study be repeated in a multicenter study with a larger number of patients and conducted by clinicians who have standard knowledge about PE and its exclusion. That the AI model be studied prospectively in diagnosis and that the patients diagnosed be followed up in the survey.

Conclusion

As a result, in the diagnosis of PE, the importance of evaluating patients' anamnesis, physical examination, laboratory and imaging findings well and using scores has been determined. However, it has been determined that AI can be used before imaging methods are requested in the diagnosis of PE.

Ethics

Ethics Committee Approval: The appropriateness of this study was approved by the İnönü University Scientific Research and Publication Ethics Committee with (decision number: 2022/45, date: 20.04.2022).

Informed Consent: In this study, 156 patients admitted to the Department of Emergency Medicine of İnönü University Faculty

of Medicine Turgut Özal Medical Center from 13.10.2022-14.10.2024, with PE symptoms, were prospectively analyzed.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.S., M.G.T., Concept: M.S., M.G.T., H.Y., Design: M.S., M.G.T., Z.K., Ş.Y., Data Collection or Processing: M.S., H.Y., Z.K., Ş.Y., Analysis or Interpretation: M.G.T., H.Y., Z.K., Ş.Y., Literature Search: M.S., M.G.T., Writing: M.S., M.G.T.

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Informatics in Emergency Medicine During the Era of Artificial Intelligence

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Dear Editor,

The concept of informatics has recently gained prominence in the domains of health and medicine. The implementation of this concept and its associated computer science technologies, particularly in emergency medicine, is progressively expanding in our clinics and scientific research. This condition is likely to grow increasingly prevalent. This essay aims to examine these topics and engage the interest of physicians and researchers in this domain.

The basis of these conceptions is knowledge directly. The main objective of the term is not knowledge of a particular subject, but rather knowing of knowledge its own. The human thirst for knowledge and information began with its existence. Humanity has pursued the storage and transmission of information since its inception. The burgeoning human heritage, technical progress, and particularly the evolution of computer science have generated substantial prospects for this endeavor. A new era of information and information science, known as the information age, has commenced. This adventure advances at an astonishing rate. This discovery introduced the term informatics into our life. The genesis of this notion, whose precise roots remain uncertain, is thought to be a fusion of the terms “information” and “automatic.” The term informatics, introduced in the 1950s, encompasses the processes of gathering, classifying, processing, recording, and subsequently retrieving and disseminating information for utilization as required. This term can be defined as a multidisciplinary science intricately linked to engineering

disciplines, information science, and technology, particularly computer science and software development. The COVID-19 pandemic has led to the pervasive integration of informatics across several medical domains, making such a statement perhaps accurate (1-3). Owing to the substantial progress in Informatics during the aforementioned stages, each stage is evolving into a distinct concept.

It is unsurprising that informatics has integrated with the health and medicine sector at an appropriate speed for this advancement. Health informatics (HI) is a medical discipline that encompasses the aggregation of biomedical data and information, aids in the facilitation of problem-solving and decision-making processes, and employs modern information technology. Its function in the healthcare sector is characterized by the application of computer and information science principles for the advancement of preventive, therapeutic, and rehabilitative health services. HI, which seeks to improve health outcomes and service quality by technological advancements, is employed by several stakeholders, including physicians, healthcare professionals, insurance firms, governmental institutions and politicians (4-6).

Emergency medicine, as a medical specialty focused on delivering the most efficient and prompt healthcare with limited resources, is a distinctive field regarding HI. The interaction between this area and information technology can accurately be characterized as emergency medical informatics (EMI), warranting its designation as an independent course subject (7). The escalating integration of information technologies in EMI



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and emergency departments (ED) has sparked debate regarding the role of machine learning (ML) and artificial intelligence (8). These technologies facilitate swift analysis of extensive data sets and enhance patient-centered decision-making processes, a topic of increasing relevance in recent years. In the discipline of emergency medicine, numerous technologies are utilized across pre-hospital, hospital, and first aid environments, including cloud computing for big data storage, data mining, blockchain, the Internet of Things, wearable technologies for patient data tracking, telemedicine, smartphone applications, virtual reality for educational purposes, and comprehensive digital patient records that integrate these elements. The significance of EMI and the associated information technologies becomes evident when evaluating their roles in diminishing resource consumption and expenses, forecasting preliminary diagnoses and enhancing diagnostic precision, attaining individualized and sensitive health objectives, improving access to healthcare services, reducing medical errors and complications, and facilitating more efficient deployment of healthcare professionals and facilities, alongside the resultant quality of service outcomes (9,10). Considering the excessive use of ED and the challenges of managing critical, geriatric, sensitive patient groups with ED; the use of these technologies in ED becomes even more valuable.

In conclusion, despite raising troubling circumstances and apprehensions regarding data security, our society is rapidly digitalizing, with technological advancements increasingly permeating human existence at all times. Simultaneously, from the standpoint of HI and emergency medicine, emergency medical intelligence seems to be a domain susceptible to rapid and unanticipated advancements, presenting challenges in keeping pace, although it remains an exhilarating and innovative field of endeavor. EMI and information technologies not only improve patient care quality and service efficiency but also seem capable of producing innovative solutions for ED congestion and other ED issues. This implies the capacity to affect health policies. This underscores the demand for a heightened focus on medical

informatics education within medical and emergency medicine residency training programs, alongside the imperative to foster researchers' interest in this domain.

Footnotes

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