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Investigation of the Efficacy of Risk Scoring Systems on Prognosis in Patients with STEMI Presenting to The Emergency Department

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Keywords: ST-elevation myocardial infarction, risk scoring systems, triage in emergency departments early warning score

Dear Editor,

I read with great interest the article titled "investigation of the efficacy of risk scoring systems on prognosis in patients with ST-elevation myocardial infarction (STEMI) presenting to the emergency department," published in volume 23 of the Eurasian Journal of Emergency Medicine in 2024 (1). This study stands out for its evaluation of the effectiveness of various risk scoring systems used in emergency departments for patients with STEMI.

The findings highlight that the Triage in Emergency Departments Early Warning score (TREWS) performs as effectively as other widely used scoring systems (TIMI, ProACS, and C-ACS) in predicting short-term mortality, even demonstrating superior performance in certain instances. Particularly the high area under the curve values for TREWS (0.847 and 0.823 for 24-hour and 28-day mortality, respectively) emphasize its potential utility in clinical emergency medicine.

However, I would like to draw attention to a few points:

Study design: The single-center design and relatively small sample size may limit the generalizability of the findings. A larger, multicenter study could help validate these results more robustly (2).

Long-term outcomes: While the study focuses on short-term mortality, the evaluation of long-term outcomes (e.g., recurrent cardiac events or quality of life) would provide valuable insights for clinicians making prognostic decisions (3).

Practicality of TREWS: Additional discussion on the practical ease of using TREWS compared to other scoring systems in the time-sensitive setting of emergency departments could further highlight its clinical relevance and applicability (4).

This study provides critical insights and valuable guidance for the management of STEMI patients in emergency settings. The robust statistical analysis and methodology lend credibility to the findings. Addressing the points above in future studies may enhance the understanding and application of these risk scoring systems.

Footnotes

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

Financial Disclosure: The author declared that this study received no financial support.

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Investigation of Associated Diseases in Acute Myocardial Infarction and Heart Failure: Metabolomic Insights

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Abstract

Aim: Cardiovascular diseases (CVDs) are among the most common causes of death world-wide. Acute myocardial infarction (AMI) and heart failure (HF) are the most common CVDs, and the development of HF after AMI is common. The aim of our study was to determine the metabolic profile in the serum of patients with AMI/HF and to correlate metabolites with comorbidities.

Materials and Methods: The study included 30 AMI and 30 HF patients admitted to Emergency Medicine Service who met the inclusion criteria. Serum samples were collected and analysed using liquid chromatography-high resolution mass spectrometry (LC-HRMS). Data were analysed using TidyMass and MetaboAnalyst.

Results: LC-HRMS analysis of AMI and HF revealed metabolites that may be directly associated with pancreatic cancer, colon cancer, renal failure and uremia. These metabolites were involved in energy metabolism, lipid metabolism, and nucleotide metabolism. In addition, the metabolite N,N-dimethyldodecylamine N-oxide was found to be elevated in HF, compared to AMI.

Conclusion: This study sheds light on metabolic changes in AMI/HF patients. It particularly highlights the metabolite relationship between cancer and kidney pathologies and CVDs. It points out that polypharmacy observed in HF may increase the accumulation of possibly hamful chemicals in the body.

Keywords: Acute myocardial infarction, cardiovascular diseases, comorbidities, heart failure, metabolomics, metabolites

Introduction

Cardiovascular diseases (CVD) are one of the leading causes of death world-wide despite advances in diagnosis and treatment (1,2). Acute myocardial infarction (AMI) and heart failure (HF) affect quality of life and impose significant economic burdens (3,4). Although the diagnosis and treatment of AMI patients have improved significantly in the last decade, AMI still remains the most important contributor to HF (5). The incidence of HF among patients hospitalised for AMI ranges from 14% to 36% (6). There are also studies reporting that this rate rises to 37.5% (7). The high mortality rate has forced researchers to look for the best way to diagnose, risk stratify, and manage patients with suspected CVDs. The most frequently studied conditions are AMI and HF (8). Therefore, circulatory biomarkers that provide easy and fast results are utilised in the diagnosis and treatment of these diseases. The most commonly used biomarkers in the diagnosis of AMI and HF are troponin T/I and N-terminal pro-brain natriuretic peptide (9,10). In addition to these classical biomarkers, the identification of new biomarkers with technological advances may facilitate the management of AMI and HF. It may also facilitate the determination of HF development after AMI.

The metabolomics method is a powerful technique that enables the determination of the metabolite profile associated with the disease state (11,12). Metabolite profiling allows a comprehensive assessment of metabolites that may change during disease progression (12,13). Therefore, it can be used to recognize altered metabolic features in diseases and to predict comorbidities. The prediction of the hospitalisation duration and survival probability

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of patients with CVD by metabolic studies highlights the importance of these studies (14). In addition, serum metabolites have been reported to improve new AMI or HF-specific risk prediction and identification of risk populations (14-16). Despite the abundance of metabolomic studies focusing individually on AMI or HF, comparative analyses between conditions are still scarce. We hypothesized that distinct metabolic profiles may characterize AMI and HF, and that specific metabolites could serve as biomarkers for HF development following AMI. Moreover, we proposed that serum metabolite signatures might aid in identifying comorbidities associated with these conditions. To investigate these hypotheses, we conducted comprehensive non-targeted metabolomic profiling of serum samples from AMI and HF patients.

Materials and Methods

The study included 30 AMI and 30 HF patients admitted to Bezmialem Vakıf University Hospital Emergency Medicine Service. Signatures were obtained from all patients for the informed consent form. Metabolomics was performed on blood samples obtained during routine examination. The AMI patient group consisted of individuals who presented to the emergency department with dyspnoea and chest pain, and were diagnosed with acute coronary artery disease after coronary angiography with more than 50% stenosis. The HF patient group consisted of individuals who presented to the emergency department with shortness of breath and chest pain, and were diagnosed with HF based on physical examination and B-type natriuretic peptide results.

Blood samples in tubes without separating gel were centrifuged at 3500 RPM for 10 minutes. Supernatants were stored at -86 °C until further processing. On the experimental day, 500 µL of thawed serum samples were transferred into a separate Eppendorf tube, followed by the addition of 1 mL of methanol. The mixture underwent centrifugation at 10,000 × g for 1 hour, after which the upper phase was carefully transferred into high-performance liquid chromatography vials. Mass spectrometry analyses were carried out using liquid chromatography, high resolution mass spectrometry on a Thermo Q Exactive instrument. Chromatographic separation was achieved under isocratic conditions with methanol as the mobile phase, employing a Fortis C18 column (3 µm particle size, 150 × 2 mm). Full-scan analysis in both positive and negative electrospray ionization modes was performed. The acquired raw mass spectrometry data were converted into mzXML and mgf formats using the open-source ProteoWizard software (17). The study was conducted in accordance with the principles of the 1964 Declaration of Helsinki. Ethics committee approval was obtained from Bezmialem Vakıf University Non-Interventional Research Ethics Committee (decision number: 2023/312, date: 22.11.2023).

Statistical Analysis

The processed data were analyzed for metabolite profiling using the TidyMass and MetaboAnalyst R packages (18,19). Metabolite annotation was based on publicly available spectral libraries, including the Human Metabolome Database, MassBank, and the North American MassBank. Pathway analysis was conducted using the Kyoto Encyclopedia of Genes and Genomes database. Differential metabolite analysis was conducted using fold change (FC) values, with a significance threshold of FC ≥Q2 or FC ≤0.5. Statistical significance was assessed through adjusted p-values (p-adjust <0.05) using the Benjamini-Hochberg correction to control for false discovery rates. Non-parametric tests, such as the Wilcoxon rank-sum test, were applied to account for non-normally distributed data. Analyses were performed using the open-source coding language R (version 4.4.0) (20).

Results

The mean age and gender of 30 AMI and 30 HF patients included in the study is presented (Table 1). Among the identified metabolite sets, those associated with pancreatic cancer exhibited the most significant enrichment, with a p value of 0.00098. This was followed by kidney disease-associated metabolites, which showed notable enrichment with a p value of 0.00131. Colorectal cancer-associated metabolites also demonstrated significant enrichment, with a p value of 0.00252. The uremia-associated metabolites had the highest p value among the identified sets (p=0.00430), indicating relatively less statistical significance compared to the other enriched pathways (Figure 1).

In this study, a set of circulating metabolites was identified in patients with AMI and HF. The detected metabolites included amino acids and their derivatives such as L-histidine, L-carnitine, DL-phenylalanine, arginine, tryptophan, and norleucine; as well as metabolites related to lipid metabolism, including sphingosine C16, glycerophosphocholine, and lauric acid diethanolamide. Additionally, compounds involved in nucleotide metabolism, such as cytosine, 5-methylcytosine, thymine, and thymidine, were detected. Energy metabolism-related metabolites, including creatinine and creatine, were also identified.

Quantitative comparison of the two patient groups demonstrated statistically significant differences in specific serum metabolites. Among these, N,N-Dimethyldodecylamine N-oxide exhibited the greatest increase in HF patients relative to those with AMI, with a 77.32-FC (p-adjust =0.0018). Conversely, the levels of Ketamine (FC =0.019, p-adjust =0.027) and its metabolite Norketamine (FC =0.035, p-adjust =0.027) were markedly reduced in the HF group

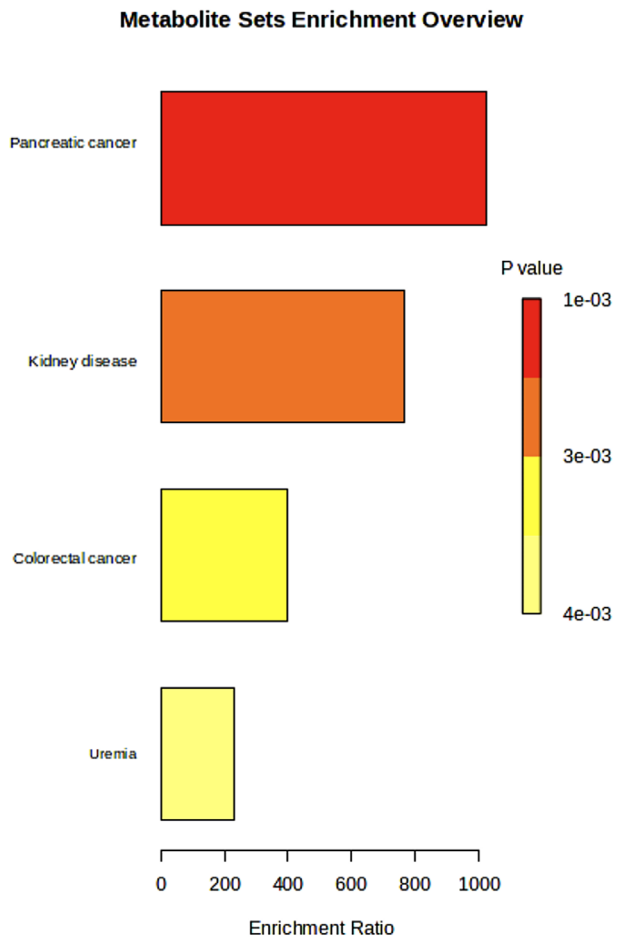

Figure 1. Metabolite set enrichment analysis

This figure presents the metabolite set enrichment analysis conducted to determine the biological relevance of identified metabolites in patients with AMI and HF. The X-axis represents the enrichment ratio, while the color scale indicates the p-value, with lower p-values signifying more significant findings. AMI: Acute myocardial infarction, HF: Heart failure

Table 1. Demographic and clinical characteristics of participants

		AMI	HF
Age	mean ± SD	59.93±14.67	65.87±12.46
	min-max	37-88	34-88
Gender		22M, 8FM	20M, 10FM

AMI: Acute myocardial infarction, HF: Heart failure, FM: Female, M: Male

(Table 2 and Figure 2).

Discussion

The important findings of our study are that common metabolites were detected in pancreatic cancer, kidney disease, colorectal cancer, and uremia, and that these may be associated with AMI-HF. In addition, the N, N-Dimethyldodecylamine N-oxide metabolite was increased in HF compared to AMI, as determined by the examination of AMI and HF metabolic profiles.

AMI and cancer have been reported to involve the same molecular pathways in disease development and progression (5,21). HF is accompanied by a broad spectrum of both cardiovascular and non-cardiovascular comorbidities (22). Recently, the relationship between HF and cancer has been questioned in many studies. In these studies, it has been reported that HF and cancer frequently overlap and evidence of a direct effect between the diseases has emerged (23-25). It has been reported that glucose, glutamine, and fatty acids can provide nutrients to meet the metabolic needs of the tumour (26). In our study of metabolic profiles, we found that metabolites detected in AMI and HF may be associated with pancreatic cancer and colorectal cancer. In particular, common nucleotide and energy metabolites such as cytosine, 5-methylcytosine, thymine, and thymidine strengthened the association between HF and both pancreatic and colorectal cancer. In light of the reported changes in cancer-related energy and nucleotide metabolism (27), our data support these metabolic trends.

The CVD mortality rate increases with decreasing estimated glomerular filtration rate (28). Renal failure is often associated with HF and worsens the patient's prognosis (29). Accurate estimation of renal function may be critical for assessing prognosis in patients with HF (30). In our study, we identified metabolites that are common in nucleotide, energy, and lipid metabolism in AMI-HF and renal disease. A large number of lipid abnormalities have been reported in patients with chronic renal failure, supporting our study results (31). In this respect, the common metabolites detected in our study may be useful in the detection of renal diseases that may accompany CVD.

Previous studies have reported various metabolites such as 9-cis retinoic acid and dehydrophytosphingosine as CVD risk biomarkers (32-34). A recent study found that serum acylcarnitine was associated with clinical symptoms and severity of coronary artery disease (35). These findings underscore the importance of metabolic alterations in the pathophysiology of CVDs. In parallel with technological advancements, the large-scale production and widespread use of organic chemicals in industry and manufacturing have significantly increased (36). In Japan, N,N-dimethyldodecylamine is included in "Class I Designated Chemical Substances", which includes compounds that may be harmful to health and ecosystems (37-39). Alkyldimethylamines, especially N,N-Dimethyldodecylamine, are widely used in many industrial products such as disinfectants, detergents, dye additives, wetting agents, antistatic agents, and textile bleaches (40,41). One study mentioned that dimethyldodecylamine may also be found in medicines (38). Polypharmacy occurs in HF

Table 2. Fold change, adjusted p-value, p-value values for annotated metabolites obtained from analysis results				
Compound name	**Fold change**	**p value**	**p value adjust**	**Adduct**
(+/-)-Norketamine	0.035205	0.00245	0.02704	(M+H)+
N,N-Dimethyldodecylamine N-oxide	77.32334	0.00005	0.00182	(M+H)+
Ketamine	0.019157	0.00188	0.02704	(M+H)+

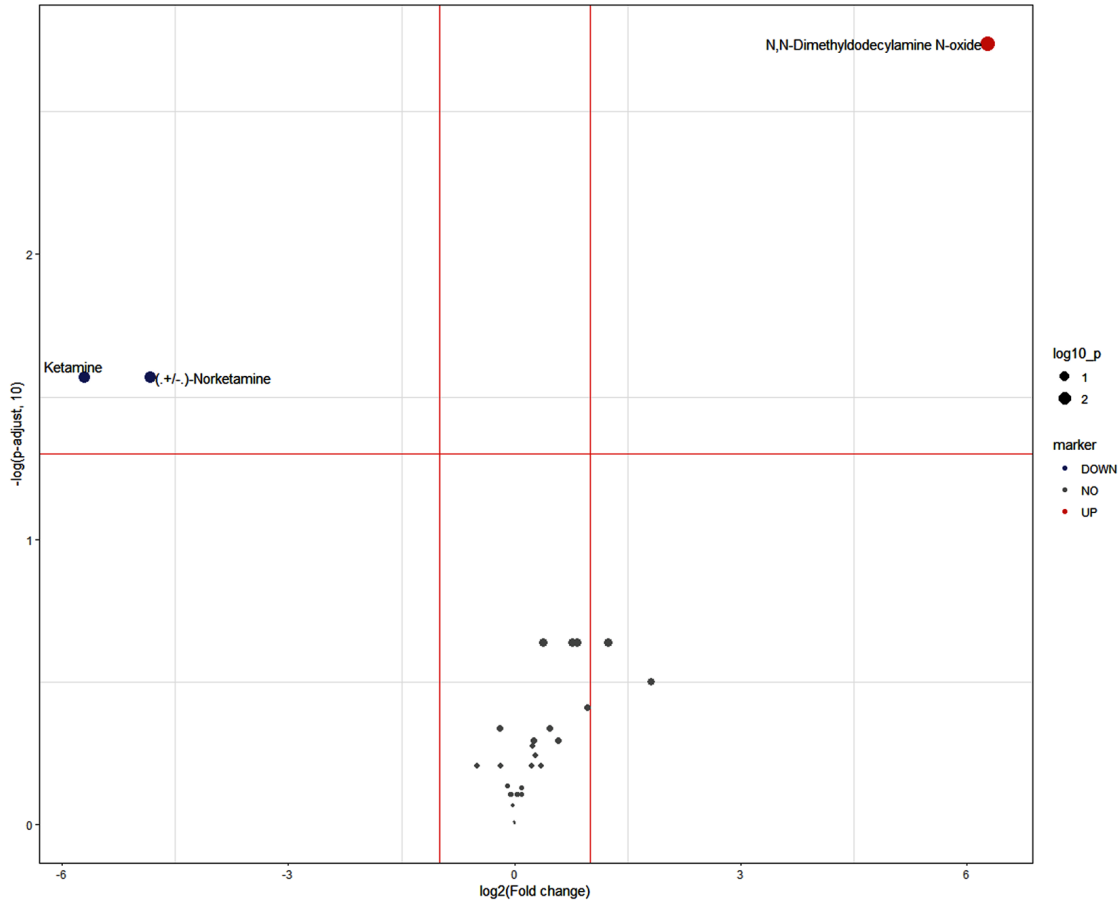

Figure 2. Volcano plot of circulating metabolites in AMI and HF patients

This volcano plot illustrates the comparative analysis of circulating metabolite levels in HF patients relative to those with AMI. The X-axis represents $\log_2$ (fold change) values, while the Y-axis denotes $-\log_{10}$ (p-adj) values. Statistically significant metabolites are color-coded: red indicates upregulated (UP) metabolites, while blue represents downregulated (DOWN) metabolites. AMI: Acute myocardial infarction, HF: Heart failure

because there are many comorbidities (42). Polypharmacy is the long-term use of 5 or more drugs (43). Dimethyldodecylamine N-oxide has been reported to have a median concentration of 29.9 ng/mL in human serum (44). In our study, we found that the concomitant use of various drugs may have caused an increase in N,N-dimethyldodecylamine N-oxide metabolite in HF. In addition, we found that serum ketamine and norcetamine metabolites were reduced in HF, compared to AMI. This result was not very plausible. This unexpected result may be because our study was a non-targeted metabolomics study.

Study Limitations

The small number of patients participating in the study, the fact that the study was conducted in a single hospital, and the absence of a control group limit our study.

Conclusion

Our results showed that nucleotide, energy, and lipid metabolites are common in AMI/HF, cancer, and kidney diseases. Detection of these metabolites may accelerate the detection and treatment of AMI and HF comorbidities. Thus, the management of AMI

and HF may become easier. In addition, excessive drug use in HF may cause harmful chemicals to accumulate in the body and complicate the treatment process.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the principles of the 1964 Declaration of Helsinki. Ethics committee approval was obtained from Bezmialem Vakıf University Non-Interventional Research Ethics Committee (decision number: 2023/312, date: 22.11.2023).

Informed Consent: Signatures were obtained from all patients for the informed consent form.

Footnotes

Author Contributions

Concept: Y.A.Ç., B.T., U.S., M.D., S.S., Design: Y.A.Ç., B.T., U.S., M.D., S.S., Data Collection or Processing: Y.A.Ç., B.T., Analysis or Interpretation: U.S., M.D., S.S., Literature Search: A.Ç., B.T., Writing: Y.A.Ç., M.D., S.S.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Keywords: ST-elevation myocardial infarction, risk scoring systems, triage in emergency departments early warning score

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However, I would like to draw attention to a few points:

Study design: The single-center design and relatively small sample size may limit the generalizability of the findings. A larger, multicenter study could help validate these results more robustly (2).

Long-term outcomes: While the study focuses on short-term mortality, the evaluation of long-term outcomes (e.g., recurrent cardiac events or quality of life) would provide valuable insights for clinicians making prognostic decisions (3).

Practicality of TREWS: Additional discussion on the practical ease of using TREWS compared to other scoring systems in the time-sensitive setting of emergency departments could further highlight its clinical relevance and applicability (4).

This study provides critical insights and valuable guidance for the management of STEMI patients in emergency settings. The robust statistical analysis and methodology lend credibility to the findings. Addressing the points above in future studies may enhance the understanding and application of these risk scoring systems.

Footnotes

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Evaluation of the Relationship between Nitric Oxide Levels and Troponin, CK, CK-Mb, and CoHB Levels in Patients Presenting to the Emergency Department with Carbon Monoxide Poisoning

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Abstract

Aim: Ischemic alterations may occur due to hypoxia following carbon monoxide (CO) poisoning. As a result, the heart, brain, and other organs experience a loss of functionality. This study aimed to evaluate the relationship between the levels of nitric oxide (NO), which may be responsible for cardiac damage, and those of troponin, creatine kinase muscle-brain (CK-MB), and carboxyhemoglobin (COHb). These are markers of cardiac damage in patients who presented to the emergency department after being exposed to CO gas.

Materials and Methods: This prospective study included 103 individuals divided into three groups: troponin-negative patients with CO poisoning, troponin-positive patients with CO poisoning, and healthy controls. The NO levels of the groups were statistically compared. The correlation between NO levels and troponin, creatine kinase (CK), CK-MB, and COHb levels was also examined.

Results: The NO value was the lowest in the troponin-positive group and the highest in the control group, with significant differences between the three groups ($p<0.001$). According to the correlation analysis, the NO level was significantly and negatively correlated with the CK and COHb levels, but not the CK-MB level ($p<0.001$). This study revealed lower NO levels in patients with CO poisoning than in healthy individuals.

Conclusions: NO levels have an inverse relationship with troponin and CK values when comparing groups categorized by troponin levels. Therefore, it is postulated that cardiac damage can be prevented by administering inhaler NO therapy together with CO therapy to patients with CO poisoning.

Keywords: Carbon monoxide poisoning, nitric oxide, troponin, carboxyhemoglobin, cardiac damage

Introduction

Carbon monoxide (CO) poisoning is one of the most frequently reported toxicological causes of death. Poisoning occurs due to the incomplete combustion of compounds that contain carbon in their structure. After inhalation, CO passes into the blood through the lungs. When CO combines with hemoglobin, carboxyhemoglobin (COHb) is formed. The concentration of oxygen within the human body decreases as it is replaced by CO, leading to insufficient oxygen transport to tissues. As a result, the heart, brain, and other organs experience a loss of functionality (1).

Due to tissue hypoxia from CO poisoning, the release of electrons from the electron chain in mitochondrial cytochromes stops. The process of oxidative phosphorylation is compromised, leading to the occurrence of cellular hypoxia. CO also binds strongly to intracellular pigments, such as myoglobin. The toxic effects of CO on myocardial myoglobin result in a decrease in cardiac muscle contraction, thereby leading to a reduction in cardiac output. Hypoxia creates ischemic alterations in tissues, which subsequently lead to an increase in troponin, creatine kinase (CK), and creatine kinase muscle-brain (CK-MB) levels (2-3).

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Nitric oxide (NO) plays an important role in regulating heart contraction, heart rate, and vascular tone. Cardiovascular diseases, such as hypertension, heart failure, ischemic heart disease, coronary artery disease, and arrhythmias, are associated with an impaired NO response (4-5). NO is of primary importance in the relaxation of coronary arteries. Furthermore, the flow-induced relaxation response in the coronary microcirculation is mediated by NO (6-7).

This study aimed to evaluate the relationship between NO levels, a potential contributor to cardiac damage, and those of troponin in patients who developed cardiac damage due to exposure to CO gas and sought medical attention in the emergency department. At the same time, an attempt was made to quantitatively reveal the relationship between CK and CK-MB values and NO values, as indicators of cardiac damage. While assessing these parameters, the correlation between the COHb values and NO values of patients with CO poisoning was also evaluated. Thus, it was investigated whether new treatment principles could be developed based on NO levels prior to the occurrence of cardiac damage in patients with CO poisoning.

Materials and Methods

Study Design and Setting

This study was conducted prospectively from September 1, 2020, to April 30, 2022, at the emergency department of a tertiary hospital (Erzurum, Health Practice and Research Hospital, Atatürk University). The study was initiated following the approval of the Ethics Committee of Atatürk Medical Faculty for Clinical Research (decision number: 53, date: 05.11.2020). Patients were accepted into the study after obtaining written informed consent from all volunteers or their relatives. Written informed consent was obtained from conscious patients, while in unconscious patients, consent was obtained in writing from their first-degree relatives. The study protocol was implemented by following the tenets of the Declaration of Helsinki.

Sample Size and Patients

The sample size of the study was calculated by using G*Power 3.1 analysis. Accepting the effect size as 0.5, the type 1 error rate as 0.05, and the power as 0.80, it was determined that a total of 90 participants (at least 30 in each group) were required. Three patient groups were formed: troponin-negative, troponin-positive, and healthy controls. A total of 30 troponin-positive and 43 troponin-negative patients presenting with CO poisoning were included in the study. Since there is no universal standard for a normal NO level, a healthy adult control group was also created, and the normal NO value was accepted as the average of the values measured in the control group. As a result, the sample consisted of 103 individuals.

Patients aged more than 18 years who were diagnosed with CO poisoning and presented to the emergency department within the first eight hours of CO exposure were included in this study. The diagnosis of CO poisoning was made based on the patients' anamnesis (medical history) and blood COHb levels above 5% (10% in smokers). The inclusion criteria of the study were as follows: being over 18 years of age, voluntary participation in the study, having a COHb level above 5 (or greater than 1 if supported by anamnesis and clinical findings), and not having a chronic disease other than hypertension. Patients excluded from the study were those aged under 18 years, those who did not volunteer to participate in the study, those with chronic diseases other than hypertension, those with other drug intoxication accompanying CO poisoning at the time of admission, pregnant women, cases in which more than eight hours had passed after CO exposure, and patients who refused treatment and follow-up. Of the total of 204 patients who presented to our emergency department with CO poisoning, 101 patients were excluded from the study because eight hours had elapsed since CO exposure, 100% oxygen therapy had been started at an external center, or due to pregnancy.

Evaluation of Patients and Data Collection

The circulation and airway scores and the Glasgow Coma Scale scores (8) of the patients were examined at the time of presentation to the emergency department, with CO poisoning.

According to this evaluation, the patients were referred to the critical care room, yellow area, or green area. Three groups were formed: the first group consisted of patients with CO poisoning who had negative troponin values (troponin-negative); the second group consisted of those with CO poisoning who had high troponin values (troponin-positive); and the third group consisted of healthy individuals without CO poisoning or chronic disease. The normal range of NO was determined based on the values measured in the control group.

The patients with CO poisoning were connected to monitors that evaluated blood pressure, respiratory rate, fever, saturation, and heart rhythm, and were placed in a security perimeter. The respiratory rate, blood pressure, pulse rate, oxygen saturation, and body temperature of the patients who were monitored in the emergency department were recorded. During this period, systemic and neurological examinations were performed. 12-lead electrocardiograms (ECGs) were taken, and the data were recorded. Levels of complete blood count, aspartate aminotransferase, alanine transaminase, arterial blood gas,

troponin, CK, CK-MB, and NO were determined as soon as possible following patient presentation. Lactate, COHb, and the presence of acidosis and alkalosis were evaluated in blood gas. The form previously prepared for patients diagnosed with CO poisoning was completed for all patients diagnosed with this condition. This form included the patient's age, gender, presentation date, emergency department protocol number, vital signs, oxygen saturation, complaints, type of CO poisoning, time since CO exposure, treatment initiation time, the presence of syncope, medical history, smoking and medication history, and arterial blood gas results. During this period, normobaric treatment (100% oxygen) was started, and hyperbaric treatment was added for those with appropriate indications. Hyperbaric treatment was planned for patients with a COHb level >25; syncope; and cardiac involvement (echocardiography findings and elevated troponin). The patients' NO levels were measured from the blood taken before hyperbaric treatment. No correlation between NO levels and hyperbaric oxygen treatment was studied. The patients were transferred to the emergency intensive care unit for follow-up.

Echocardiography was performed on the patients within the first two hours of presentation and at the 24th hour, and their ejection fraction (EF) values were measured. Cardiac changes, if any, were noted. During this process, a control ECG was taken, and any ECG changes were recorded. Echocardiography was performed by cardiologists.

Blood Collection and NO Measurement

Blood samples taken for the measurements of troponin, CK, and CK-MB levels were evaluated at the biochemistry laboratory using a Beckman Coulter AU5800 device. The data were taken from the hospital's automation system and recorded into a form. The blood samples taken for analysis of NO were transferred to 5 mL biochemistry tubes and centrifuged at 6.000 rpm for ten minutes with a Rixos 32 device. The serum obtained after centrifugation was transferred to a separate tube and stored at -80 degrees. Then, the serum was assayed collectively. A commercial enzyme-linked immunosorbent assay measurement kit (Human NO ELISA Kit, Catalog No: 201-12-1511, SunRed Biotechnology Company, China) was used to measure the NO level in the serum sample. This kit was produced for the detection of human NO levels in serum, plasma, urine, cell culture supernatant, and tissue homogenate and has a measurement range of 4-600 µmol/L, a sensitivity of 2.052 µmol/L, an intra-run precision coefficient of variation value of <10% and an inter-run precision coefficient of variation value of <12%.

Statistical Analysis

The IBM SPSS v. 20.0 (SPSS Inc., Chicago, IL, United States) program was used to analyze the data obtained. Continuous variables were expressed as mean (standard deviation) or median (interquartile range) values. Categorical data were presented as numbers (percentages). A normality analysis was performed. In the comparison between two independent groups, the independent-samples t-test was used when the normal distribution condition was met, and the Mann-Whitney U test was used otherwise. When comparing more than two independent groups and continuous variables, the ANOVA test was used for normally distributed data and the Kruskal-Wallis test for non-normally distributed data. Following ANOVA, post-hoc methods were employed using the Tukey test in cases where the variances were homogeneous and using the Tamhane T2 test in those where the variances were not homogeneous. Following Kruskal-Wallis analysis, an appropriate post-hoc test was used. However, the description of using one-way ANOVA (k-samples) may not accurately fit the context since ANOVA is not typically used as a post-hoc for Kruskal-Wallis. A p-value of <0.05 was considered significant in all statistical analyses.

Results

The study included a total of 103 patients. In the troponin-negative group, 47.7% (n=20) of the patients were female and 52.3% (n=23) were male. In the troponin-positive group, 45.2% (n=14) of the patients were female and 54.8% (n=16) were male. In the control group, 53.3% (n=16) of the patients were female and 46.7% (n=14) were male. The mean age of the entire cohort at the time of presentation was 33.44±13.82 years, and the median age was 27 (minimum: 18 - maximum: 79) years (Table 1).

Table 1 presents the patients' complaints, the presence of chest pain and syncope, the causes of CO poisoning, any ECG changes, the treatment plan, and the EF status, according to the groups.

Vital signs, pH, lactate, myoglobin values, and the EF status of the patients according to the groups are detailed in Table 2.

The comparison of the study parameters among the three groups revealed significant differences: in the COHb value between the troponin-positive group and the control group, between the troponin-negative group and the control group (p<0.001); the CK value between the troponin-positive group and the control group, between the troponin-negative group and the control group (p<0.001); the CK-MB value between the troponin-positive and troponin-negative groups (p=0.003); and the troponin value between the troponin-positive and troponin-negative groups, as well as between the troponin-negative group and the control group (p<0.001). Furthermore, the NO value significantly differed between the three groups (p< 0.001). The NO value was the lowest in the troponin-positive group and the highest in the control group (Table 3).

According to the correlation analysis, the NO level was significantly and negatively correlated with the CK and COHb levels ($p < 0.001$), but not with the CK-MB level ($p=0.265$) Furthermore, as the troponin value increased, the NO value decreased. Therefore, it can be stated that as cardiac involvement increases, the NO value decreases (Table 4).

Table 1. Demographic and clinical characteristics of the groups

		Troponin-negative (n=43, 100%)	Troponin-positive (n=30, 100%)	Control (n=30, 100%)
Age (year/mean ± SD)		32.81±11.02	39.17±18.66	28.60±9.46
Gender	Female	20 (46.5%)	14 (46.7%)	16 (53.3%)
	Male	23 (53.5%)	16 (53.3%)	14 (46.7%)
Presentation complaint	Headache	22 (51.2%)	7 (23.3%)	0 (0%)
	Dizziness	11 (25.6%)	9 (30.3%)	0 (0%)
	Fainting	1 (2.3%)	4 (13.3%)	0 (0%)
	Nausea and vomiting	8 (18.6%)	2 (6.7%)	0 (0%)
	Altered state of consciousness	1 (2.3%)	8 (26.7%)	0 (0%)
	No complaint	0 (0%)	0 (0%)	30 (100%)
Cause of CO poisoning	Stove fume	24 (55.8%)	15 (50%)	0 (0%)
	Natural gas	7 (16.3%)	7 (23.3%)	0 (0%)
	Tandoor	8 (18.6%)	1 (3.3%)	0 (0%)
	Exhaust smoke	4 (9.3%)	1 (3.3%)	0 (0%)
	Fire smoke	0 (0%)	6 (20.1%)	0 (0%)
	No known exposure	0 (0%)	0 (0%)	30 (100%)
ECG changes	Present	0 (0%)	1 (3.3%)	0 (0%)
	Not present	43 (100%)	29 (96.7%)	30 (100%)
Chest pain	Present	0 (0%)	3 (10%)	0 (0%)
	Not present	43 (100%)	27 (90%)	30 (100%)
Syncope	Present	6 (14%)	9 (30%)	0 (0%)
	Not present	37 (86%)	21 (70%)	30 (100%)
Treatment plan	Normobaric	37 (86%)	0 (0%)	0 (0%)
	Hyperbaric	6 (14%)	30 (100%)	0 (0%)
	No treatment	0 (0%)	0 (0%)	30 (100%)

SD: Standard deviation, CO: Carbon monoxide, ECG: Electrocardiogram

Table 2. Vital signs and EF status of the patients according to the groups

		Troponin-negative (n=43)	Troponin-positive (n=30)	Control (n=30)
Vital signs	GCS score (median)	15	15	15
	SBP (mmHg)	122.84±11.395	124.67±19.161	119.70±13.35
	DBP (mmHg)	69.51±8.93	67.67±9.91	66.53±9.64
	sPO_2 (%), median	97	95	98
	Pulse/min, median	80	88	80
pH, median (IQR)		7.39 (7.33)	7.38 (7.36)	7.38 (7.34)
Lactate, median (IQR)		1.4 (0.8)	3.0 (2.6)	0.950 (0.5)
Myoglobin, median (IQR)		18.4 (14.4)	31.0 (95.1)	12.5 (7.3)
EF (%), median (IQR)		60 (5)	55 (5)	60 (0)

EF: Ejection fraction, GCS: Glasgow Coma Scale, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, sPO_2: Oxygen saturation, IQR: Interquartile range

Table 3. Evaluation of the patients' NO, CK, CK-MB, troponin, and COHb levels according to the groups					
Parameter	**Group 1**	**Group 2**	**Group 3**	**p**	**Post-hoc**
NO (µmol/L)	45 (26.0)	17.5 (31.3)	110 (95)	0.000	1-2, 1-3, 2-3
Troponin (ng/LT)	2.40 (2.4)	37.0 (1875.5)	1.35 (2.7)	0.000	2-1, 2-3
CK-MB (U/L)	24 (20)	50 (101)	31 (22)	0.000	1-2
CK (U/L)	90 (75)	146 (11)	16 (9)	0.000	3-1, 3-2
COHb (%)	10.2 (15.9)	18.1 (24.3)	0.8 (0.9)	0.000	3-1, 3-2
NO: Nitric oxide, COHb: Carboxyhemoglobin, Group 1: Troponin-negative, Group 2: Troponin-positive, Group 3: Control, CK-MB: Creatine kinase muscle-brain					

Table 4. Evaluation of the relationship between NO and CK, CK-MB, COHb, and troponin in patients with CO poisoning					
	NO	COHb	Troponin	CK	CK-MB
Spearman's rank correlation	1	0-.499	0-.535	0-.537	0-.110
P		0.000	0.000	0.000	0.265
N		103	103	103	103
NO: Nitric oxide, COHb: Carboxyhemoglobin, CK-MB: Creatine kinase muscle-brain					

Table 5. Evaluation of the relationship between NO and length of hospital stay in patients with CO poisoning		
	NO	**Length of hospital stay**
Spearman's rank correlation	1	0-0.725
P		0.000
N		103
NO: Nitric oxide, Carbon monoxide (CO)		

There was an inverse correlation between the NO level and length of hospital stay in patients with CO poisoning (p=0.001). In other words, as the NO value decreased, the length of hospital stay increased (Table 5).

Discussion

In most fatalities caused by CO gas, acute myocardial damage plays an important role in increased long-term mortality. The role of NO in the regulation of heart contraction, heart rate, and vascular tone is significant. In the current study, individuals with CO poisoning who had elevated troponin levels were observed to have a significantly lower NO level compared to both troponin-negative patients and healthy controls. Furthermore, the NO value of the troponin-negative patient group was significantly lower than that of the control group. Further investigations are warranted to explore the efficacy of inhaled NO interventions as a potential measure to prevent future cardiac events and as a supplementary approach to oxygen therapy in individuals with CO poisoning, NO is considered an important intracellular and intercellular, bioactive molecule that affects various physiological and pathophysiological functions in the body, including cardiac contractility and vasodilation regulation (9). During ischemia, NO synthesis increases with increased NO synthase activity. Cardiac damage increases with cellular cytotoxicity. However, oxygenation during reperfusion facilitates delayed NO production, especially in the periinfarct region, and the conversion of NO into peroxynitrite reduces the NO level (10).

In this study, the NO level was found to be very high in the healthy adult control group, while it was the lowest in the group exhibiting elevated troponin values. The NO level also significantly differed between the troponin-negative and troponin-positive patients with CO poisoning, with lower values being detected in the latter.

In animal experiments, endothelial cells have been implicated in the development of ischemic damage. Myocardial ischemia is considered to develop after endothelial damage from CO poisoning. The disruption of the NO synthase enzyme, released from the endothelium due to endothelial damage, decreases NO synthesis. NO has an inverse correlation with ischemia-induced cardiac damage and troponin elevation (11). Similarly, in the current study, it was observed that as the NO level decreased, the troponin level of the patients with CO poisoning increased.

In a study comparing serum NO levels before and after the treatment of CO poisoning, it was found that the NO level was higher after treatment (12). This can be considered an indicator that the NO level decreases in the presence of CO exposure.

It plays an important role in regulating heart contraction, beat rate, and vascular tone. Cardiovascular diseases such as

hypertension, heart failure, ischemic heart disease, coronary artery disease and arrhythmias are associated with impaired NO response (5). Myocardial damage due to CO poisoning occurs with myocardial hypoperfusion; the CO has a toxic effect on myocardial mitochondria. Consequently, various arrhythmias, including ventricular extrasystole and fibrillation, may develop rapidly after CO exposure, without tachycardia or myocardial damage, which can affect mortality (13). In the current study, consistent with the literature, the NO level of the patients with cardiac damage was found to be lower than that of the healthy controls.

Intracellular heme protein function is affected by the partial pressure of at least three gases. These are CO, O^2 and NO. Even at low COHb levels, the CO concentration is 109 times greater than the NO concentration. CO gas binds to the heme competitively with NO. When CO binds to heme, free NO remains in the environment. This free NO has been shown to directly impair myocardial contraction (14). As the CO concentration in the environment increases, NO is expelled from heme proteins and replaced with CO (15).

CK-MB, troponin, myoglobin, and brain natriuretic peptide are the most expressed cardiac proteins in the heart muscle, and they increase after myocardial damage (16-18). The most frequently used biomarkers are troponin I, cardiovascular isoenzyme CK-MB, and CK (19-20). Icme et al. (21) reported statistically significantly higher lactate, CK-MB, and troponin I levels in patients receiving hyperbaric treatment than in those receiving normobaric treatment. In another study, Toksoy (13) detected no correlation between COHb and troponin I levels. In the same study, the mean CK level was found to be 282 U/L, and the mean CK-MB level was 27.45 U/L. In the current study, there was a negative correlation among other cardiac parameters, such as troponin, CK, and CK-MB.

The COHb level is one of the main diagnostic criteria after exposure to CO gas. CO can be produced endogenously and exogenously. In a study conducted by Toksoy (13), a statistically significant difference was found between the presentation complaints of the patients and their COHb levels. In contrast, Hampson et al. (22) found no significant correlation between presentation complaints and COHb values. Karakuzu (23), evaluating retrospective data, determined that high COHb levels did not correlate with clinical findings. Yurtseven et al. (24) detected no correlation between troponin I and COHb levels in patients with CO gas exposure and high troponin levels. In the current study, there was an inverse correlation between the NO and COHb levels, i.e., as the COHb value increased, the NO value decreased.

Study Limitations

The first limitation of our study is the very short half-life of NO, and that NO levels were not examined according to the time of presentation to the hospital in patients with CO poisoning. Moreover, several patients were transported from the incident site by ambulance, and the administration of oxygen therapy through a nasal cannula in the ambulance was a variable that influenced the NO level; however, this treatment was not included in our evaluation. Another limitation of our study is that it is a single-center study and the long-term results are unknown.

Conclusion

Patients with CO poisoning exhibit lower NO levels compared to healthy individuals. The NO level decreases further patients with high troponin levels as compared to in troponin-negative cases. Therefore, it is postulated that inhaled NO therapy in conjunction with CO therapy may serve as a preventive measure against cardiac damage in individuals exposed to CO.

Ethics

Ethics Committee Approval: The study was initiated following the approval of the Ethics Committee of Atatürk Medical Faculty for Clinical Research (decision number: 53, date: 05.11.2020).

Informed Consent: Patients were accepted into the study after obtaining written informed consent from all volunteers or their relatives.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.K.Ç., A.G., Concept: A.G., Design: B.K.Ç., A.G., Data Collection or Processing: B.K.Ç., A.G., Analysis or Interpretation: A.G., Literature Search: B.K.Ç., A.G., Writing: B.K.Ç., A.G.

Conflict of Interest: The authors declare that they have no conflicts of interest.

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Supraventricular Tachycardia Triggered by Spicy Food Consumption: A Novel Case Report and Review of Potential Mechanisms

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Abstract

Supraventricular tachycardia (SVT) is a common cardiac arrhythmia characterized by rapid heart rates originating above the ventricles. Numerous triggers, such as caffeine, alcohol, and stimulants, have been extensively reported; however, the role of dietary spices as potential triggers remains largely unexplored. Capsaicin, the active ingredient in chili peppers, acts primarily through transient receptor potential vanilloid type 1 (TRPV1) channels, exerting diverse physiological effects, including modulation of cardiovascular function. While capsaicin has documented long-term cardiovascular protective properties, its acute arrhythmogenic potential through other mechanisms remains understudied.

We report an unprecedented case of a 48-year-old male who presented with recurrent episodes of SVT triggered consistently by spicy food intake. The patient arrived at the emergency department approximately 30 minutes after spicy food consumption with a heart rate of 215 beats per minute, resistant to vagal maneuvers. Administration of intravenous adenosine successfully restored sinus rhythm. Comprehensive cardiac evaluations, including echocardiography, coronary angiography, and electrophysiological studies, revealed no underlying cardiac pathology.

Based on this case, we hypothesize a potential role for capsaicin-induced activation of TRPV4 channels, influencing cardiac contractility and arrhythmogenesis. Prior literature has primarily addressed capsaicin's interaction via TRPV1 channels, neglecting acute electrophysiological disturbances. This novel clinical scenario underscores the need for clinicians to consider spicy food consumption as a possible trigger for SVT in differential diagnosis. Further studies are warranted to clarify acute cardiac responses and electrophysiological mechanisms triggered by capsaicin and related dietary spices.

Keywords: Supraventricular tachycardia, capsaicin, TRPV channels, spicy food, arrhythmogenesis

Introduction

Spices have been utilized for various purposes throughout human history (1). Spices play a significant role in culinary cultures worldwide, influencing numerous physiological systems, from the stimulation of chemosensory receptors through taste, aroma, and pungency, to their effects on surface membranes such as skin and mucosa, and, further impacting cardiovascular, respiratory, autonomic, and metabolic functions (2). Recent experimental and clinical studies on capsaicin, the active component of chili peppers, have demonstrated its significant role in cardiac physiology and pathologies, predominantly mediated via activation of the transient receptor potential vanilloid type 1 (TRPV1) channels (3). Piperine (from black pepper) and capsaicin have exhibited positive inotropic and chronotropic effects and demonstrated cross-tachyphylaxis in isolated rat atria (4). The known cardiac mechanism of capsaicin and the physiological role of TRPV1 channels in cardiac tissues are illustrated below (Figure 1) (5).

Supraventricular tachycardia (SVT) is defined as a tachycardia originating from above the ventricles, characterized by a heart rate exceeding 100 beats per minute. SVTs are classified based

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on their origin, including sinus tachycardia, atrial tachycardia, atrioventricular nodal reentrant tachycardia, and another form of reentrant tachycardia (6). SVT is usually self-limiting and generally not life-threatening; however, prolonged episodes accompanied by syncope, chest pain, or dyspnea necessitate intervention. The presence of accessory conduction pathways contributing to SVT increases morbidity and mortality risks, warranting more aggressive treatment (7). Acute interventions include vagal nerve stimulation (8), adenosine (9), calcium channel blockers (10), beta-adrenergic receptor antagonists (8), and procainamide, whereas definitive management often involves catheter ablation (11).

Although there are publications regarding cardiac rhythm disturbances triggered by spice consumption, clinicians typically do not prioritize spices when evaluating patients presenting with such disturbances. Here, we present a previously unreported case of SVT triggered by spice consumption. The informed consent form was obtained from the patient for this case report.

Case Report

A 48-year-old male presented to the emergency department (ED) with palpitations that started approximately 30 minutes after consuming spicy food and lasted for nearly one hour without relief. Upon admission, vital signs were as follows: blood pressure 110/80 mmHg, heart rate 215 bpm, and oxygen saturation 97% on room air. The patient denied any other active complaints. Medical records revealed multiple prior ED visits with similar palpitations following spicy food intake. He reported no chronic illnesses, medication use, cardiac history, or family history of sudden cardiac death. Detailed questioning revealed no alcohol, tobacco, energy drink, or stimulant use.

Physical examination showed a Glasgow Coma scale of 15, good general appearance, normal lung auscultation, tachycardic heart rhythm, without additional sounds or murmurs, and normal findings in other systems. Initial electrocardiogram (Figure 2) demonstrated SVT [hazard ratio (HR) 215 bpm]. Following unsuccessful modified Valsalva maneuvers, intravenous adenosine administration (6 mg, then 12 mg) restored normal sinus rhythm (HR 92 bpm, Figure 3). Cardiac enzymes and blood tests were within normal limits. Cardiology consultation and bedside echocardiography revealed no abnormalities. The patient remained stable without recurrence of SVT during ED observation. He was discharged after six asymptomatic hours with advice to avoid spicy foods. Subsequent elective coronary angiography and electrophysiological studies were unremarkable.

Discussion

Various underlying factors associated with SVT have been reported, with alcohol and caffeine consumption being the most common dietary triggers. However, spicy food has not been previously documented in the literature as a potential acute precipitant of SVT episodes (12). While a limited number of studies have explored the cardiovascular implications of capsaicin the active compound in chili peppers none have directly associated it with SVT (13,14).

Previous case reports and observational studies have linked spicy food consumption to a spectrum of cardiovascular and systemic effects, including syncope, urticaria, gastrointestinal symptoms, coronary vasospasm, acute myocardial infarction, and even fatal myocardial ischemia in predisposed individuals (12,15). These findings highlight that capsaicin's bioactive role extends beyond gastrointestinal discomfort and may involve acute cardiovascular modulation.

From a mechanistic perspective, capsaicin is a potent agonist of the TRPV channels, primarily TRPV1 and, to a lesser extent, TRPV4. While TRPV1 activation has been associated with long-term cardioprotective outcomes such as nitric oxide-mediated vasodilation, antihypertensive effects, and attenuation of atherosclerosis (16), its acute effects-especially in the context of electrical conduction abnormalities-remain under-investigated. Recent preclinical studies suggest that TRPV4 channels, which are also expressed in ventricular cardiomyocytes, can influence myocardial contractility and are implicated in arrhythmogenesis through calcium influx and mechanosensitive signaling pathways.

Our hypothesis builds on these findings: capsaicin may have triggered SVT in this patient via acute TRPV4 activation, leading to intracellular calcium dysregulation and enhanced automaticity or reentry mechanisms within the atrioventricular node. This is supported by limited evidence showing acute elevations in heart rate following capsaicin ingestion, although electrophysiological studies assessing arrhythmic potential are notably lacking.

Furthermore, individual susceptibility may play a significant role. Genetic variability in TRPV channel expression, underlying autonomic tone, and pre-existing subclinical conduction abnormalities might predispose certain individuals to arrhythmic events following spicy food intake. Unfortunately, the absence of baseline Holter or electrophysiological data in this patient limits causal inference.

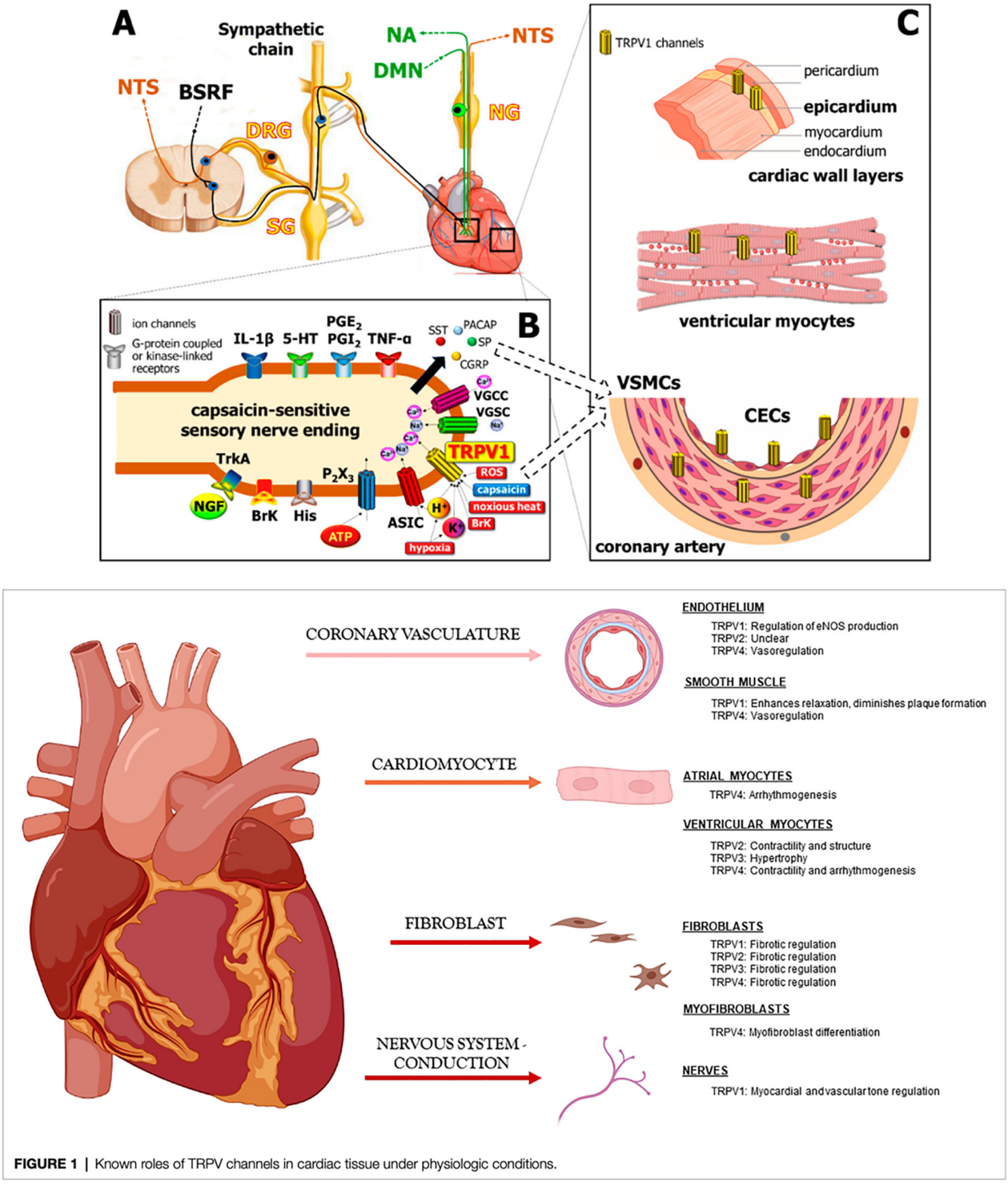

Figure 1. Known cardiac mechanism of action of capsaicin (3) and known roles of TRPV channels on cardiac tissue under physiological conditions (5)

TRPV: Transient receptor potential vanilloid, NTS: Nucleus tractus solitarius, BSRF: Brainstem respiratory field, DRG: Dorsal root ganglion, SG: Sympathetic ganglion, NA: Nucleus ambiguus, DMN: Dorsal motor nucleus, NG: Nodose ganglion, IL-1B: Interleukin-1 beta, 5-HT: 5-hydroxytryptamine, PGE: Prostaglandin E, TNF-a: Tumor necrosis factor-alpha, SST: Somatostatin, PACAP: Pituitary adenylate cyclase-activating polypeptide, SP: Substance P, CGRP: Calcitonin gene-related peptide, VGCC: Voltage-gated calcium channels, VGSC: Voltage-gated sodium channels, ROS: Reactive oxygen species, BrK: Bradykinin, ATP: Adenosine triphosphate, NGF: Nerve growth factor, VSMC: Vascular smooth muscle cell, CEC: Cerebral endothelial cell

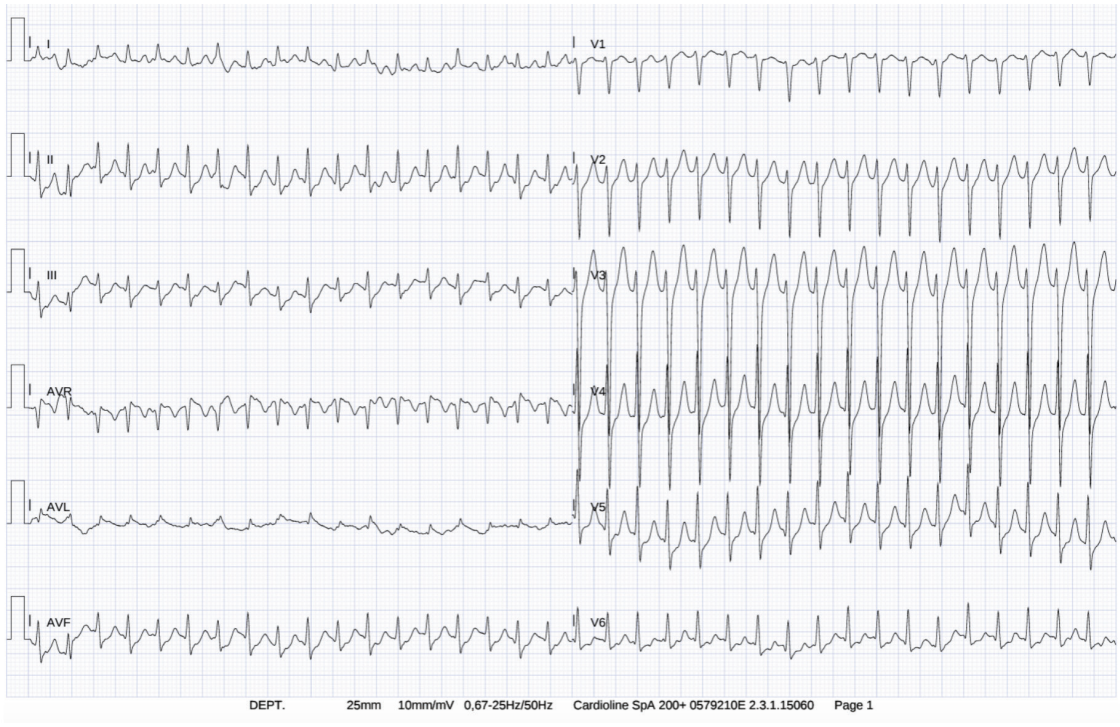

Figure 2. ECG taken at the patient's first application

ECG: Electrocardiogram, AVR: Augmented vector right, AVL: Augmented vector left, AVF: Augmented vector foot

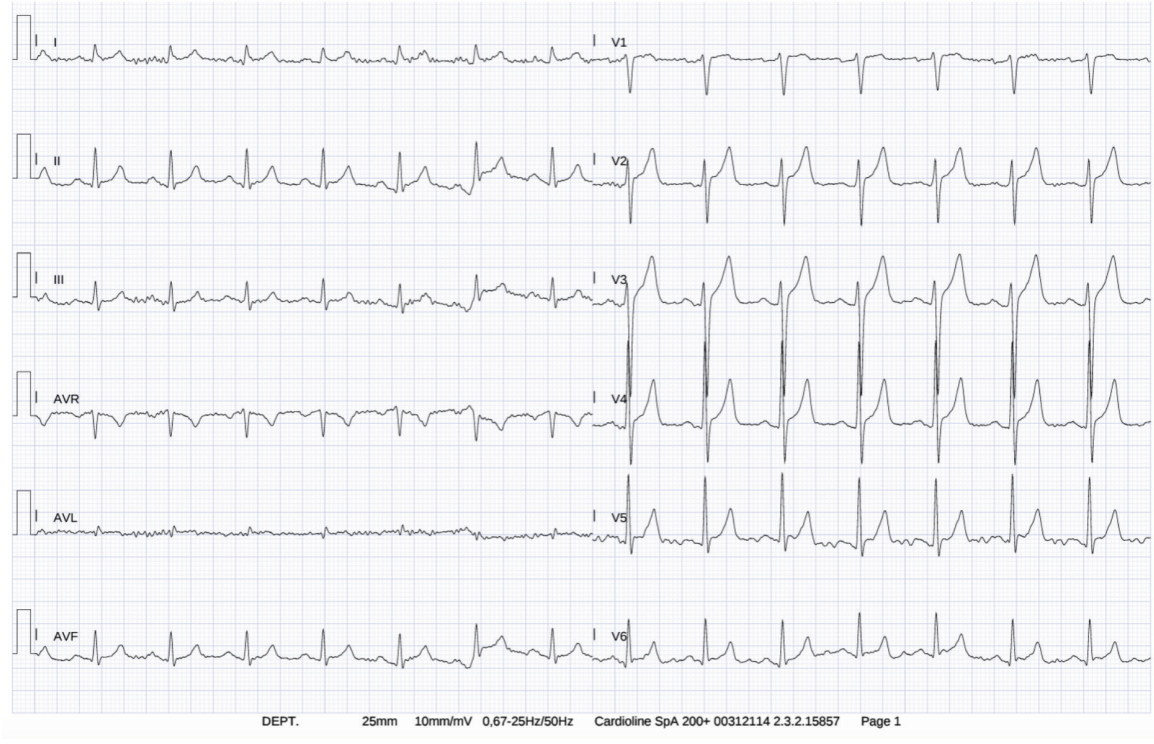

Figure 3. Control ECG taken after 6-12 mg intravenous adenosine treatment

ECG: Electrocardiogram, AVR: Augmented vector right, AVL: Augmented vector left, AVF: Augmented vector foot

Conclusion

In conclusion, this case introduces a novel and plausible trigger for SVT that has been previously overlooked in emergency clinical settings. It underscores the need for a more comprehensive dietary history in patients presenting with idiopathic arrhythmias. Future prospective studies are warranted to investigate the acute electrophysiological effects of capsaicin and delineate the specific roles of TRPV1 and TRPV4 channels in cardiac rhythm regulation.

Ethics

Informed Consent: The informed consent form was obtained from the patient for this case report.

Footnotes

Authorship Contributions

Concept: İ.K., Data Collection or Processing: K.S.K., Writing: İ.K., K.S.K.

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

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Practical and Legal Aspects of Applying Artificial Intelligence in Emergency Medicine

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Abstract

This narrative review explores current applications of artificial intelligence (AI) in emergency medicine, critically evaluates the supporting evidence, and discusses the ethical, legal, and regulatory challenges surrounding its integration into clinical practice. Peer-reviewed literature and recent systematic reviews on AI applications in emergency medicine were analyzed using a structured narrative approach. AI-driven operational forecasting, predictive modeling for patient outcomes, diagnostic support, and AI-assisted triage systems are among the domains evaluated. AI models, such as neural networks and gradient boosting machines, have demonstrated superiority over traditional triage tools in forecasting outcomes like in-hospital mortality and intensive care unit admission. AI in diagnostics has enhanced point-of-care ultrasound analysis, sepsis detection, and electrocardiogram interpretation. Operationally, AI makes it possible to predict patient volume, emergency department crowding, and resource allocation in real time. Despite these developments, there are still few prospective clinical trials confirming better patient outcomes. Algorithmic bias, a lack of transparency, automation bias, and restrictions on generalizability across clinical settings are among the main issues. Emerging regulatory frameworks like the European Union AI act and ethical and legal frameworks like the General Data Protection Regulation and Health Insurance Portability and Accountability Act are essential for directing the responsible use of AI. AI has significant potential to improve the provision of emergency care. However, ethical protections, legal compliance, integration with clinical workflows, and thorough external validation are necessary for responsible implementation. To guarantee the safe and fair implementation of AI in emergency medicine, future initiatives must concentrate on explainable AI, multicenter prospective research, and stakeholder collaboration.

Keywords: Artificial intelligence, emergency medicine, clinical decision support, triage systems, machine learning, ethical issues, legal regulation, prognostic models, diagnostic accuracy

Introduction

Emergency medicine is a high-stakes profession with inherent resource limitations, complicated patient flow, and time-sensitive decision-making. Chronic emergency department (ED) overcrowding and the Coronavirus disease-2019 pandemic have brought attention to systemic issues like long wait times, employee burnout, and poor patient outcomes (1). Artificial intelligence (AI) has become a promising tool to supplement emergency care in this context. AI systems can help with quick triage, diagnostic support, outcome prediction, and operational decision-making thanks to developments in machine learning (ML) and data analytics. In fact, AI methods have already shown potential in enhancing

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clinical decision support, medical imaging interpretation, and ED triage accuracy (1,2). From prehospital evaluation to in-hospital diagnostics, prognostication, and resource management, AI technologies are being used increasingly throughout the emergency care spectrum. AI-enabled symptom checkers can be used by patients before they arrive, and dispatch centers can use AI to streamline response logistics and triage. AI models assist in clinical decision-making during hospitalization by predicting results, analyzing diagnostics, and classifying risk. Predictive algorithms are used administratively to guide strategies for crowding mitigation, bed distribution, and staffing.

It is still difficult to integrate AI advancements into standard emergency care, despite this promise. Relatively few prospective trials have shown better patient outcomes in real-world settings, and the majority of AI applications in emergency medicine to date have come from retrospective studies or proof-of-concept models (1,2). For example, a 2020 scoping review identified 150 studies of AI in emergency care, over 82% of which were retrospective and only 2% were prospective controlled trials (2). The overall body of evidence is still small, even though about 25% of these interventions sought to improve diagnosis (particularly in imaging), and some algorithms even beat physicians in particular tasks. Before AI tools are widely used, thorough validation and an evaluation of their effects on patient-oriented outcomes are still required. This narrative review explores the main ethical, legal, and regulatory concerns related to the use of AI in emergency medicine while acknowledging both the potential and the gaps. The methodological approach, major application domains (triage, diagnostics, prognostication, resource management), ethical considerations (fairness, transparency, oversight, consent), and the legal/regulatory landscape [liability, data protection, and governance frameworks in the United States (US) and European Union (EU)] are all covered.

Triage

An important advancement in digital health is the growing availability of AI-based symptom checkers on web and mobile platforms, which provide users with real-time triage recommendations (3). These tools interpret user-provided symptoms by utilizing natural language processing (NLP) and pattern recognition algorithms recommend appropriate care-seeking actions based on perceived urgency (4). The scientific community continues to have concerns about their accuracy and safety, despite their promising potential to empower patients and manage healthcare demand (3).

Variability in these systems' performance has been brought to light by systematic reviews and comparative studies. For example, a 2020 study that looked at 22 different symptom checkers found significant variations in triage recommendations and diagnostic accuracy (3). Interestingly, the study found that both under- and over-triage rates were high, especially for conditions that require immediate attention, like myocardial infarction or stroke (3). While over-triage can unnecessarily strain emergency services, under-triage can result in delayed care for critical conditions, potentially worsening outcomes (5).

The proprietary nature of many underlying algorithms, sometimes referred to as "black boxes", presents a significant challenge in assessing and enhancing these tools (3). These algorithms might use antiquated medical guidelines or heuristics that haven't been thoroughly tested (3). It is challenging to evaluate their internal reasoning and spot any biases or limitations because of this lack of transparency.

Experts emphasize the importance of extensive validation studies and external benchmarking to ensure clinical reliability before public health initiatives or emergency medical care triage systems are widely implemented (3). Recalibration and prospective testing using patient data are ideal for this validation to preserve accuracy over time. Using ML and NLP to improve emergency room triage precision and consistency is still being studied (5). Frameworks are also being developed to reflect real-world patient circumstances in symptom assessment tool case vignettes (6). AI is being studied for clinical decision support systems, patient triage, and diagnostic support in emergency care (7). ML algorithms are also being used to predict inpatient admissions using ED triage data to improve patient flow management (8). Development of interpretable ML models for triage that address class imbalance is also underway to improve accuracy and clinical judgment (9).

More advanced AI applications are appearing in emergency dispatch. The Corti platform helps emergency call operators identify cardiac arrest-related clinical phrases, tone, and metadata using ML and real-time speech recognition. In retrospective tests, such technologies detected out-of-hospital cardiac arrest faster than human dispatchers, enabling advanced life support (10). AI simplifies triage decision-making and automatically extracts demographics and geography. Few prospective trials exist, and further study is needed to address false alarm rates, dispatcher over-reliance, and system latency before widespread adoption.

Studying the specific developments, difficulties, and factors surrounding AI-assisted triage systems is important to build on the analysis of the traditional Emergency Severity index (ESI) and the potential of AI models (like gradient boosting machines and neural networks) to improve triage accuracy.

Gradient boosting machines and neural networks can predict important outcomes such as intensive care unit (ICU) admission and in-hospital mortality better than the ESI. Studies have shown that ML models outperform the ESI in AUROC scores (11). One study using data from over 189,000 emergency patients created and validated interpretable ML models for ICU admission by comparing models based on ESI, vital signs, and a mix of vital signs, demographics, and medical history (12). Another study examined feed-forward neural networks, regularized regression, random forests, and gradient-boosted trees for predicting ICU versus non-ICU care after 24 hours of admission using 41,654 ED visits (12). These findings show that AI models can manage complex interactions between several variables, which could lead to more nuanced risk categorization than rule-based systems. The effectiveness of gradient boosting machines is demonstrated by increased research into specific ML methodologies. A study that used a gradient boosting ML model to predict early mortality in ED triage showed how useful it is of the model for enhancing patient classification (13). Extreme-Gradient-Boosting-based interpretable ML models have been used to forecast extended wait times in the ED, enabling the assessment of equity among various patient groups (14). For clinical adoption, this emphasis on interpretability is essential because it helps medical professionals comprehend the logic behind an AI's recommendation.

Even with little information available, deep-learning techniques, particularly neural networks, have demonstrated promise in identifying critically ill patients during triage (15). In time-sensitive triage situations where only preliminary information is available, deep learning's capacity to automatically extract complex features from raw data may be especially helpful. The efficiency of various ML models, such as artificial neural networks, for predicting ESI levels has also been compared (16).

The generalizability of AI models is still a major obstacle, despite the encouraging outcomes. Numerous models are trained and validated using datasets from individual institutions, which might not account for the differences in patient demographics, clinical procedures, and data gathering techniques among various emergency rooms (11). Before deployment, thorough local validation is required due to this limitation. A crucial area of study is the significance of external validation and the possibility of performance deterioration in unfamiliar settings.

Ensuring demographic fairness in AI-assisted triage is another significant challenge. Models that consistently under- or over-triage particular demographic groups, like minority populations, may result from bias in training data (14). This issue is brought to light by studies that examine differences in ED prioritization according to demographic traits even when triage acuity scores are comparable (17). When developing, assessing, and implementing models, demographic fairness must be carefully taken into account. Building equitable AI systems requires methods for assessing fairness, like those employed in the study looking at ethnic differences in wait time prediction models (14).

A number of tactics are suggested to lessen these difficulties and make it easier for AI to be used responsibly in triage. To guarantee performance and dependability, local validation of AI models within the particular context of the implementing institution is crucial (14). Incorporating human-in-the-loop supervision is also crucial. Clinical judgment should not be replaced by AI; rather, it should be seen as an aid. When needed, medical professionals should be able to override AI recommendations and offer input, to help the system improve over time.

Beyond demographic data and vital signs, multimodal data integration offers additional promise for improving AI triage accuracy. A more complete picture of a patient's condition can be obtained by using NLP to incorporate unstructured data from electronic health records (EHR), such as doctor notes and past medical information (18). In addition to data gathered at the triage point, studies have investigated the use of ML predict hospital admission at triage based on patient history (19).

Building interpretable AI models is also essential to encouraging adoption and trust among medical professionals. Clinicians can validate a recommendation based on their medical expertise when they understand why a model makes a specific prediction. There is still research being done on interpretable ML models for triage prediction (12).

Diagnostics

Advances in medical imaging, data synthesis, deep learning, and specialist tools like electrocardiogram (ECG) and sepsis tools affect pre-hospital and ED emergency diagnosis. Emergency medicine's high stakes and time limits demand fast and accurate diagnosis to improve patient outcomes (20). ED triage and outcome prediction using ML and AI are major areas of focus. ML models are being created to predict hospital admission and mortality using triage data as such as patient history, vital signs, and nursing notes (21). To reduce subjectivity in conventional systems like the ESI, a deep learning approach that uses electronic medical records (EMRs) has been proposed to improve ED triage accuracy (22). Comparisons of ML models with classical ESI show promising clinical outcome prediction (11). NLP is essential for extracting meaningful information from unstructured text data in triage notes and improving prediction accuracy (23).

Emergency diagnosis requires medical imaging. In hemodynamically unstable patients who may not be candidates

for computed tomography pulmonary angiography, point-of-care ultrasound is increasingly employed to diagnose large pulmonary embolism (24). AI models are also being studied for real-time ultrasound picture interpretation in emergency settings like the extended focused assessment with sonography in trauma test to improve diagnostic precision and decision-making (25). Multimodal AI systems that use metadata and ocular images, for primary diagnosis and eye emergency triage, show the potential of combining data sources for diagnostic efficiency (25).

Emergency cardiac diagnosis requires ECG analysis. AI and deep learning models, notably convolutional neural networks (CNNs), are revolutionizing ECG analysis by automating high-precision arrhythmia identification (25). ML algorithms using 12-lead ECGs are being developed to predict acute mortality in ED patients (25). Acute coronary syndrome patients need quick ECG acquisition at triage, and clinical prediction methods in tablet apps are being studied to accelerate this process (26). Bedside assays for high-sensitivity troponin I are also being compared to central laboratory analysis to determine if they can quickly diagnose acute myocardial infarction (27). Sepsis is life-threatening, and delayed treatment increases mortality; therefore, ED triage must discover it early (28). ML improves sepsis triage detection before lab results (28).

Data synthesis, which integrates multimodal data from physiological signals, EMRs, and medical imaging, is boosting diagnostic accuracy (29). Hybrid deep learning architectures using CNNs, recurrent neural networks, and transformer models are being studied for multimodal data fusion in healthcare diagnostics (29). To reduce ED overcrowding and improve resource allocation, deep learning is being used to analyze heterogeneous medical data to predict patient criticality and identify the appropriate clinical departments (30).

Despite advances, emergency AI-driven diagnostic tools are still challenging to implement. These include addressing the medicolegal implications of deploying AI in high-risk scenarios, ensuring AI model interpretability and fairness, and undertaking clinical validation studies (31). To ensure successful incorporation into healthcare workflows, clinician views on AI in emergency triage must be considered (31). Multidisciplinary panels must be used to investigate diagnostic errors in EDs to improve patient safety (32).

Prognostication

Emergency medicine uses AI for prognostication, or patient outcome prediction from structured data. In high-acuity, fast-paced settings like the ED, AI-driven predictive models can help doctors identify patients at risk of deterioration, ICU admission, protracted hospitalization, or death. These techniques improve early risk categorization for faster interventions, triage, and resource allocation.

ML algorithms can predict clinical worsening using preliminary ED data including vital signs, lab results, and patient demographics. Algorithms can predict in-hospital cardiac arrest, mechanical ventilation, major trauma transfusions, and infection, or septic shock. AI techniques for early sepsis identification that combine lab measurements and dynamic vital sign trajectories to provide real-time risk scores have garnered attention. Some models outperform rule-based systems in retrospective validations with AUROC values close to 0.90 (33). A meta-analysis of prognostic AI in emergency settings found that ML models outperformed conventional risk stratification methods in predicting hospital admission and short-term death (34). Many of these models are "early warning systems" that detect clinically stable patients who could decompensate in hours. Several health organizations are using AI-based early warning capabilities in their ED information systems to flag high-risk patients for clinical reassessment or escalation.

Translation into clinical practice is problematic. The generalizability of predictive AI models is often limited by their training setting. One often reported proprietary sepsis prediction system utilized in numerous hospitals performed worse than earlier reports, exhibiting low sensitivity and inappropriate calibration in external validation cohorts (35). This mismatch emphasizes the need for external validation and post-deployment monitoring. Audits, recalibrations, and impact analyses should be done regularly to detect performance drift and maintain clinical relevance.

Another issue is automation bias—physicians may overuse algorithmic risk rankings instead of clinical judgment. AI results should be considered as supporting data, not as final instructions. The doctor must interpret prognostic AI by combining contextual knowledge of the patient's presentation with the algorithm's detection of subtle, data-driven risk patterns.

Despite these shortcomings, prognostic AI could transform emergency treatment. Due to their ability to assess high-dimensional, temporally linked data, models can detect early signs of deterioration as such as hemodynamic microtrends or subtle laboratory abnormalities that humans cannot. These insights can reduce unnecessary outcomes, personalize monitoring intensity, and improve patient disposition decisions (ED discharge vs. observation vs. ICU stay). Future efforts should

focus on explainable AI (XAI) frameworks that integrate easily into ED procedures and provide interpretable risk estimates. Research priorities include prospective, multicenter trials to determine how AI-informed prognostication influences clinician judgment, patient outcomes, and health system performance.

AI is increasingly employed to improve clinical decision-making and operational efficiency in EDs, which often have congestion, resource constraints, and unpredictable patient surges. Dynamic capacity planning using AI-based forecasting, scheduling, and logistics systems may improve patient flow, reduce waits, and employee burnout for emergency medicine administrators.

Predictive Forecasting and Capacity Planning

AI demand forecasting is among its most advanced operational uses. ML models trained on historical ED data, including chief complaints, patient arrival times, seasonal trends, weather data, and public event calendars, can effectively anticipate hourly or daily patient loads. These short-term estimates enable proactive personnel, space, and bed modifications. If an AI tool predicts a high-volume day after a major athletic or meteorological event, clinical directors can plan extra staff or pre-open surge capacity units. A recent study shows that AI-based ED crowding forecasts improve throughput and reduce left without being seen (36). Heuristic-based models do not.

Triage vitals, presenting complaint, first labs, and imaging can also be used by AI to predict patient-level length of stay (LOS). This aids downstream bed planning, transfer prioritization, and real-time patient streaming. In high-occupancy settings, LOS prediction helps estimate discharge rates more precisely, which helps manage bed turnover (37).

Staff Scheduling and Workload Balancing

AI can help schedule staff by recognizing demand trends and matching staffing to expected acuity and volume. Dynamic scheduling algorithms can identify understaffed periods, optimize shift timing, and ensure the right skill mix of attending physicians, residents, and nurses during peak hours. In one application, AI-driven dashboards predicted ED crowding eight hours in advance and recommended real-time staffing adjustments, enhancing throughput and employee satisfaction (38).

AI is being studied for real-time ambulance dispatch optimization. AI algorithms can use prior EMS data, traffic patterns, and projected ED congestion to route ambulances to facilities with the correct acuity and capacity. This could reduce ED offload and transport delays, which cause system bottlenecks (39).

Inventory and Supply Chain Optimization

AI helps with supply forecasting and logistics in emergency care, in addition to managing staff and beds. Based on historical and current data, algorithms can forecast trends in resource consumption, such as the use of tPA in stroke or the need for transfusions in trauma. By using these insights, hospitals can better stock equipment, drugs, and blood products, minimizing shortages during surges and cutting waste during lulls. This type of predictive logistics is particularly useful in high-stakes situations like disaster response or mass casualty incidents (40).

Implementation Considerations

Even with promising pilot results, a number of crucial elements must come together for AI to be successfully implemented in ED operations:

Data integration: In order to access real-time data feeds, AI systems must easily interface with current hospital command centers, admission-discharge-transfer systems, and EHR.

Interpretability: The results of operational AI must be clear and intelligible. To trust and follow predictions and recommendations, clinicians and administrators must comprehend the reasoning behind these predictions and recommendations.

Stakeholder buy-in: Frontline employees' and administrative leadership's participation is crucial. To prevent resistance or unintentional disruption, tools must be co-designed with users in mind and customized to local workflows.

Small but significant gains in ED LOS, patient satisfaction, and clinician workload distribution have been shown in early trials of AI-supported operational systems (41). Scalable and validated AI tools for capacity management are set to become just as important as clinical algorithms in promoting patient-centered, resilient emergency care, as the demand on emergency services continues to increase.

Ethical Considerations in the Use of AI in Emergency Medicine

AI in emergency medicine could boost efficiency and outcomes, but ethical issues must be addressed to ensure patient safety. AI ethics must be built on fairness, openness, human monitoring, and informed consent. This is because EDs treat vulnerable patients under time and budget constraints.

Fairness and bias are fundamental ethical dilemmas. If trained on unrepresentative datasets or structural inequities, AI models may unintentionally exacerbate care disparities. If training data show that women have historically underreported cardiac symptoms, a triage algorithm may continually underestimate

risk in female patients. In rural or resource-constrained contexts, algorithms based on metropolitan university hospital data may perform poorly. Variable measurement, algorithm design, and data sampling biases might worsen healthcare inequities and discriminatory treatment. To solve this problem, datasets must be representative and diversified, and models must use fairness requirements or employ bias correction methods, such as resampling or reweighting, to ensure fairness. After deployment, institutions should evaluate demographic subgroup AI performance and establish redress processes for inequalities. Finally, equitable results for all groups served are as crucial as technical performance. Transparency matters too. Many powerful AI models, especially deep learning-based ones, are "black boxes" that predict without explanation. Emergency clinicians must understand, contextualize, and question AI-generated recommendations to make rapid choices based on limited data. XAI provides a partial solution by producing interpretable outputs such as feature attribution scores or visual explanations like diagnostic image heatmaps. These arguments improve clinician trust, accountability, and decision-making. The EU General Data Protection Regulation (GDPR) and the impending AI act require individuals to have access to relevant information about automated judgments, making explainability in high-risk AI systems increasingly critical. Clarity and usability must be balanced in practice; too comprehensive an explanation can overwhelm doctors, while an explanation that is too simple will not impart meaningful information. Understanding that hypotension and altered mental status triggered a triage signal can help make care decisions in the high-pressure ED without delaying action.

Clinician autonomy and oversight are also ethical requirements. AI should complement human decision-making, not replace it. Doctors may overuse AI results and trust AI advice without adequate critical thinking, raising concerns about automated bias. This can be troublesome if the model is used outside its intended scope or if AI recommendations clash with clinical intuition. Over time, uncritical AI use can cause "moral deskilling," leading to medical practitioners losing confidence in their judgment. AI systems reduce this risk by incorporating human-in-the-loop protections that let doctors change or question outcomes. Clinicians should have final-say over high-stakes care decisions per institutional policy. Certain AI platforms require clinicians to disclose their reasoning for rejecting or approving algorithmic advice to encourage reflection and discourage mindless acceptance. Regulators are codifying these expectations as the EU AI act requires human oversight for high-risk medical AI systems. Emergency medicine regulations may require human providers to verify AI triage scores or diagnostic signals before acting.

AI complicates informed consent, which has long been a cornerstone of moral medical practice. AI in treatment should be explained to patients, especially if it affects their decision-making. AI tool discussions in the ED are often infeasible due to time constraints, unconscious patients, and possibly lethal scenarios. These instances fall under emergency informed consent exceptions in US and European law. We should be transparent about AI's contribution wherever possible. Hospitals may employ signage, general consent forms, or institutional regulations to disclose AI systems for clinical decision-making. Hospitals should notify patients after AI significantly affects a diagnosis or treatment plan, especially without human review. Hospitals might adopt a strategy of "ogoing informed transparency" to ensure that patients are aware of AI use, even if particular disclosures are not possible during an urgent visit. Transparency is crucial when AI programs are experimental or make judgments without human input, such as EMS routing. Formal study methods or separate permission may be ethical in certain cases, although clarity on the context of 'separate permission' is advised.

Legal and Regulatory Issues

A thorough grasp of current frameworks and new regulations is necessary to navigate the substantial legal and regulatory challenges associated with the integration of AI into emergency medicine. Although AI has the potential to improve productivity and patient care, its application is limited by a complicated framework that includes liability, data protection, and regulatory supervision (42).

Laws pertaining to privacy and data protection are a major concern (43,44). The Health Insurance Portability and Accountability Act (HIPAA) in the US establishes guidelines for safeguarding private patient health data (44). Regarding the use and disclosure of protected health information, HIPAA places duties on covered entities (healthcare clearinghouses, health plans, and providers) and their business associates. HIPAA compliance is crucial when AI systems handle patient data, necessitating strong administrative and technical safeguards to guarantee data security and privacy (45).

Even more stringent regulations are enforced by the GDPR of the EU (46) which gives people broad control over their personal data, including the ability to access, amend, and remove data as well as the ability to object to processing (47). Strict adherence to the principles of data minimization, purpose limitation, and transparency in algorithmic processing is required for the

GDPRs application to AI in healthcare (46). Obtaining appropriate patient consent for data usage, establishing clear data governance policies, and ensuring adequate anonymization or pseudonymization of data used for AI training and deployment are among the legal challenges in this area (48).

Another crucial legal issue is liability, and another is accountability (49,50). The advent of AI complicates traditional medical malpractice law, which holds healthcare organizations and individual practitioners accountable for careless acts (50). Determining who is at fault—the doctor, the healthcare facility, or the AI developer—when an AI system causes a negative outcome is a complex legal matter (49). The "learned intermediary" doctrine, which holds that AI is a decision-support tool and that the doctor is ultimately in charge of assessing AI recommendations and reaching clinical conclusions, is frequently invoked in current legal viewpoints (50). Physicians are required by this doctrine to use their own clinical judgment and evaluate AI systems' output critically (50).

However, product liability law becomes more important as AI systems in emergency medicine become more self-sufficient and require less human intervention (51). The AI developer or manufacturer may be held accountable if damage is caused by an error in the warnings, design, or manufacturing of the AI system. This puts the AI product itself front and center instead of the doctor's actions. There are particular legal difficulties in establishing a flaw in a sophisticated, self-learning AI system, such as establishing causation and pinpointing the precise part or algorithm that caused the damage (49). Globally, the legal frameworks pertaining to liability protection and AI service businesses are changing, with various jurisdictions investigating potential solutions (52).

The US Food and Drug Administration (FDA) and the US, through the proposed AI act, are playing important roles in the ongoing development of regulatory pathways for AI in healthcare. In recognition of the need for frameworks that can adjust to the iterative nature of AI development and learning, the FDA has started to develop regulatory approaches for medical devices that use AI. High-risk AI applications in healthcare are subject to strict requirements for conformance assessment, risk management, data governance, and human oversight (53,54). The EU AI act, a comprehensive regulatory framework for AI, classifies AI systems according to their risk level. The goal of these regulatory initiatives is to guarantee the ethical, safe, and efficient use of AI in clinical settings; however, developers and healthcare providers face compliance challenges as a result of these changing regulations (50).

Additional legal factors include the possibility of algorithmic bias producing discriminatory results, the need for transparency and explainability in AI decision-making to foster trust and support legal scrutiny, and intellectual property rights pertaining to AI algorithms and datasets (53). For AI to improve patient care in emergency medicine while reducing potential risks, legal and regulatory frameworks must change to keep up with the technology's advancements. These frameworks must address concerns of safety, ethics, and accountability (43)

Conclusions and Implications

AI, with its innovative capabilities to support triage, diagnosis, prognostication, and operational management, is rapidly transforming emergency medicine. AI tools are already being used in various ways, from clinical decision support systems and predictive analytics platforms to AI-supported emergency dispatch systems and patient-facing symptom checkers. According to preliminary assessments, these technologies have the potential to improve patient flow in emergency rooms, decrease the time it takes to treat critical conditions, and increase diagnostic accuracy, all of which can help address enduring issues like overcrowding, a lack of resources, and a heavy clinical burden. Although encouraging, the current body of evidence is still inconclusive. There have been little prospective validation or randomized clinical trials that verify improvements in patient outcomes, and the majority of published studies to date are retrospective. Premature or careless adoption of AI systems, if not thoroughly evaluated, risks unforeseen consequences, like missed diagnoses, skewed decision-making, or a decline in patient trust. If AI is to be used in emergency situations in a way that is both safe and moral, then key issues like algorithmic bias, lack of explanation, and variable integration with clinical workflows need to be carefully considered. Stakeholders in the clinical, research, ethical, and regulatory domains must consider several implications. First, to evaluate the practical effects of AI tools, there is an urgent need for thorough and methodologically sound research, especially multicenter prospective studies. Meaningful outcomes such as mortality, complication rates, patient satisfaction, and system-level efficiency should be included in these studies in addition to accuracy metrics. To identify deterioration over time and guarantee continued safety and relevance, systems for continuous performance monitoring and model recalibration should be put in place concurrently. Second, the deployment of AI must continue to revolve around ethical implementation. This means creating inclusive, equitable, and transparent systems with datasets that reflect a range of demographics and use cases. When implementing AI, hospitals should make sure that emergency personnel are properly trained in AI literacy and

that system design incorporates human oversight. Before new tools are put into use, institutional review boards or AI ethics committees may be crucial in ensuring that they are in line with ethical requirements and clinical needs. Third, it's crucial to navigate the constantly changing legal and policy landscape. Precise liability standards are required to maintain clinician trust and establish accountability in the event of AI-related harm. GDPR and HIPAA compliance, among other privacy laws, must be proactively incorporated into system architecture rather than being an afterthought. Crucially, legal frameworks ought to develop in tandem with technological advancements, providing safeguards without impeding responsible advancement. Last but not least, successful AI integration in emergency medicine will require interdisciplinary collaboration. To guarantee that AI systems are not only technically sound but also clinically beneficial, morally sound, and socially acceptable, clinicians, data scientists, engineers, ethicists, and legislators must collaborate from the very beginning of development. While working with legal experts can help anticipate and mitigate risks related to consent, bias, and accountability, involving frontline users in the design process can help ensure that tools are in line with the complex realities of the ED.

Conclusion

Considering all factors, AI holds immense potential to improve the promptness, precision, and fairness of emergency care. However, achieving this potential will require more than just technological advancement; it will also require our shared dedication to evidence-based development, ethical responsibility, and operational and legal preparedness. When used carefully, AI can be a strong ally of emergency physicians, complementing human knowledge rather than taking its place and ultimately helping to create a more secure, responsive, and compassionate emergency care system.

Ethics

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Footnotes

Author Contributions

Concept: T.B., I.S., L.S., Design: T.B., I.S., E.F.V., L.S., Data Collection or Processing: I.S., M.P., L.S., Analysis or Interpretation: T.B. I.S., E.F.V., M.P., F-X.D., A.L., L.S., Literature Search: T.B. I.S., M.P., F-X.D., A.L., L.S., Writing: T.B. I.S., E.F.V., M.P., F-X.D., A.L., L.S.

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Cerebral Fat Embolism Syndrome-case Report

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Abstract

Fat embolism syndrome (FES) is an uncommon complication, typically presenting with respiratory insufficiency following orthopedic trauma. The condition is referred to as cerebral FES (CFES) when neurological symptoms dominate, which is an even rarer form of FES. We present a case of a 21-year-old male who was brought to the emergency department with lower extremity fractures following a traffic accident. The patient experienced a sudden decline in consciousness and developed confusion during his follow-up. An echocardiogram performed in the emergency room revealed hyperechogenic structures in heart chambers, and subsequent magnetic resonance imaging scan showed multiple infarct areas, leading to a diagnosis of CFES. The diagnosis of CFES is challenging due to the non-specific nature of the symptoms and the frequent normality of computed tomography scans. High clinical suspicion is crucial in patients with orthopedic injuries who experience sudden neurological decline.

Keywords: Fat embolism, orthopedic trauma, cerebral fat embolism syndrome

Introduction

Fat embolism syndrome (FES) is a rare complication, typically presenting with respiratory insufficiency following orthopedic trauma (1). Diagnostic criteria for FES were first established by Gurd in 1970 and later modified by Wilson, becoming widely used. He proposed that the diagnosis of FES be established by the simultaneous identification of at least two major clinical findings or one major and four minor clinical findings. The major criteria encompass respiratory insufficiency, neurological disturbances, and petechial rash. Minor criteria include the detection of fat globules in urine or sputum, renal dysfunction, jaundice, retinal changes, pyrexia, tachycardia, unexplained alterations in platelet (PLT) count or hematocrit, and the presence of fat macroglobulinemia (2,3). Other classifications include Lindeque's classification, which focuses on respiratory symptoms, and Schonfeld's classification, which develops a scoring system. The Schonfeld classification is organized so that Petechiae are 5 points, Chest X-ray changes (diffuse alveolar infiltrates) are 4 points, hypoxemia is 3 points, fever (>38 °C), tachycardia (>120 bpm), tachypnea (>30 bpm), and confusion are each given one point (2,4). Regardless of the classification system, the classic presentation includes a triad of respiratory distress, petechial rash, and neurological changes (3). When neurological symptoms dominate, the condition is referred to as cerebral FES (CFES) (5). Early recognition is crucial, especially in orthopedic trauma patients showing sudden neurological decline. Diagnosing CFES is challenging due to the lack of universal criteria, relying instead on clinical assessment and the patient's medical history (6).

Case Report

A 21-year-old male was brought to the emergency medicine department complaining of back and leg pain after a traffic accident. There is no history of drug use other than psychiatric medication. Upon arrival at the emergency depeartment, his vital signs were stabile and glaskow coma scale is scrored 15. conscious, oriented-cooperative, pupillar isochoric, infrared +/+. Abdominal and respiratory examinations are normal. No obvious pathology was observed in the cranial nerve examination. Multiple bone fractures were present in the right lower extremity; muscle strength was not clearly assessed; no obvious muscle strength loss was observed in other extremities. The patient's imaging shows right femur, fibula and tibial shaft fractures (Figure 1), lung

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contusion, and C6 corpus fracture. No pathological findings were observed in abdominal imaging. No pathological findings were present in the laboratory results obtained during admission to the hospital. Toxicology results were normal. Laboratory data showed a drop in hemoglobin (HGB) during its follow-up at emergency department (HGB: 15.1 g/dL, first HGB: 16.6 g/dL). Also, during his intensive care unit stay, he was reported to have a petechial rash, mostly on the anterior surface of his trunk. There was a decrease in PLT count (PLT: 85K/uL) and a drop in HGB (HGB: 10.1 g/dL, after orthopedic surgery HGB: 14.3 g/dL, reference range: 12-18 g/dL).

The patient, who did not need urgent surgery by the thoracic and neurosurgery departments, had a long-leg splint applied to his right lower extremity and was monitored according to the operation plan, with a Philadelphia neck collar attached. During the follow-up, the patient's vital signs remained stable. Approximately 11-12 hours after admission, he suddenly developed confusion and agitation followed by a rapid decline in the level of consciousness. Thereupon, an emergency bedside ultrasound was performed. Upon the detection of thrombus-like structures at Echo (Figure 2), computed tomography (CT) and diffusion magnetic resonance imaging (MRI) were performed. According to diffusion MRI (Figure 3), focal areas were observed in the localization of both basal ganglia, some of which restrict linear moderate diffusion, and these areas were in the millimeter dimension. In addition, a focal area restricting diffusion in millimeter dimensions was observed in the right half of the pons. Focal area restricting linear moderate diffusion at the

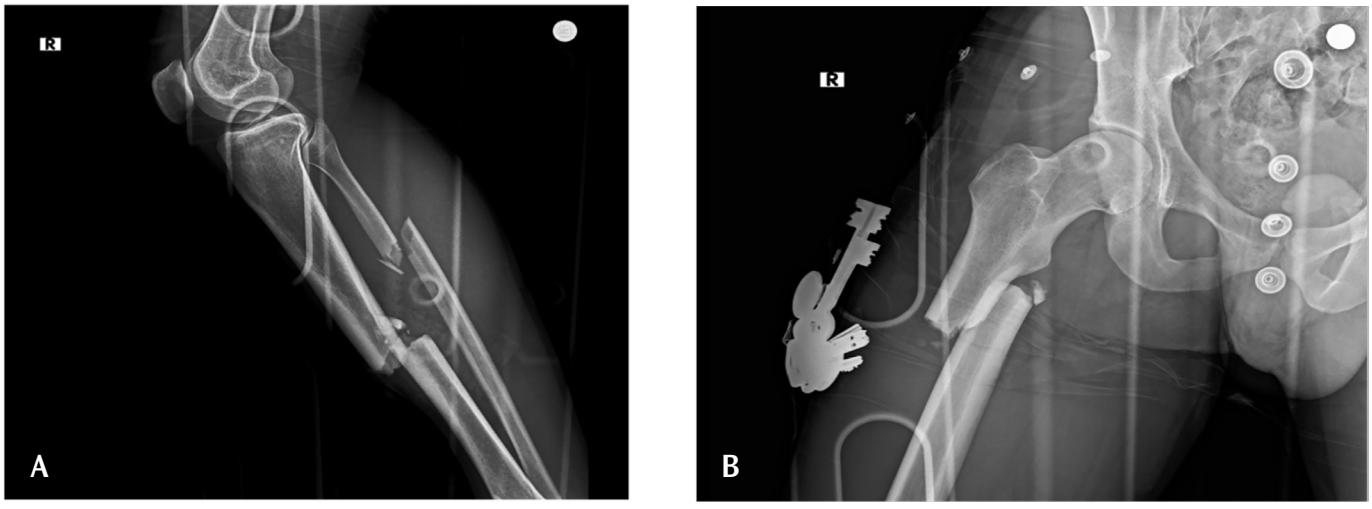

Figure 1. (A) Femur shaft fracture, (B) Fibula and tibial shaft fractures

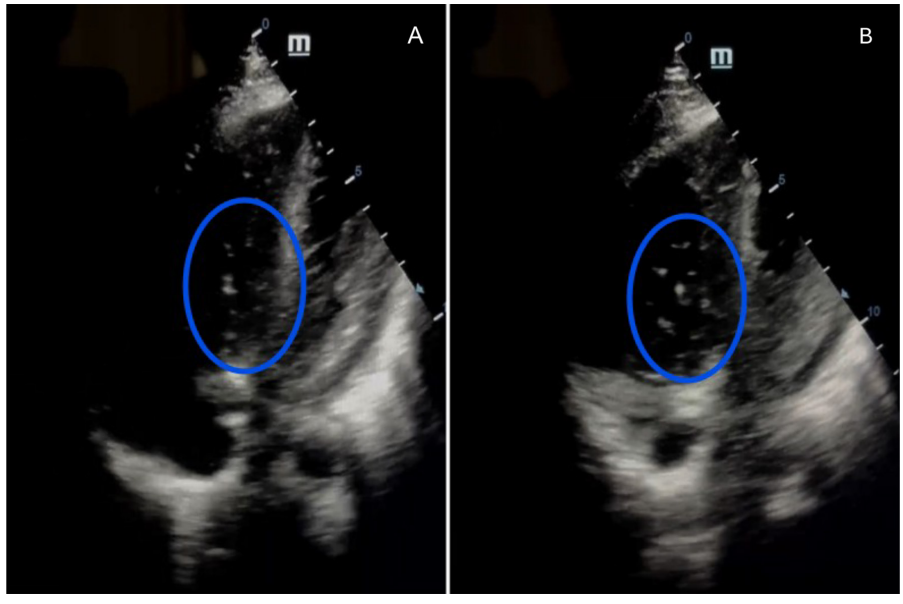

Figure 2. (A, B) Thrombus-like structures highlighted by blue circles on echocardiography

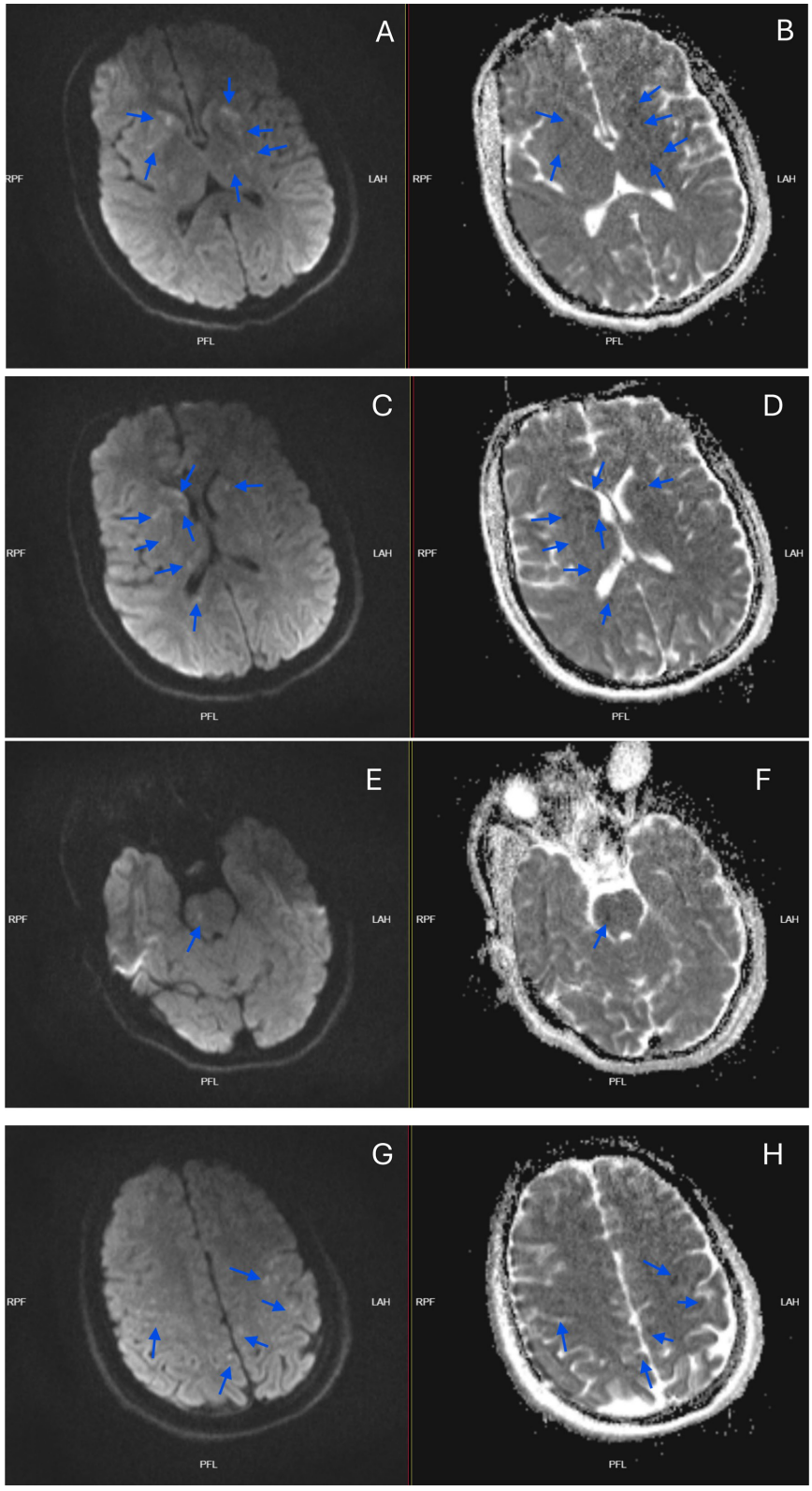

Figure 3. Multiple infarct areas on MRI (starfield pattern). Axial diffusion-weighted imaging (DWI) and corresponding apparent diffusion coefficient images (A–H), demonstrating areas of diffusion restriction indicated by blue arrows

MRI: Magnetic resonance imaging, RPF: Right posterior frontal, PFL: Posterior fronto-lateral, LAH: Left anterior hemisphere

cortical level was observed at the centrum semiovale level, and focal areas restricting diffusion in millimeter size in the frontal and parietal lobes on the left were also observed. MRI findings are consistent with a starfield pattern suggestive of cerebral fat embolism. There is no hemorrhage on CT. Additionally, the patient developed desaturation and underwent a pulmonary CT angiography to rule out pulmonary pathologies, but pulmonary embolism was detected. According to the report, a smear-like effusion was observed in both hemithoraxes, and nonspecific density increases were observed in the dependent segments. With supportive treatment; intensive care follow-up was planned with a preliminary diagnosis of fat embolism.

Discussion

FES is an uncommon disorder primarily characterized by respiratory insufficiency, often arising as a complication following orthopedic trauma (1). Typically presenting within 1-2 days following trauma involving long-bone fractures or orthopedic surgery, it manifests as a petechial rash, progressive respiratory insufficiency, and declining mental status (7). Only a small subset of patients, comprising 0.9% to 2.2%, subsequently develops FES, which is classically characterized by a triad of respiratory symptoms, petechial rash, and alterations in mental status (6). The diagnosis of FES is predominantly clinical; however, the Gurd and Wilson criteria, as well as the Schonfeld fat embolism index, remain two of the most widely utilized and validated diagnostic frameworks (4). In our case, the patient fulfilled 3 major criteria of the Gurd and Wilson Criteria for FES: respiratory distress and petechial rash and neurological symptoms as altered mental status, along with minor criterias, drop in HGB (from 16.6 to 10.1 g/dL), thrombocytopenia (85 K/uL) and according to the Schonfeld fat embolism index, the patient met the following criteria: petechial rash (5 points), and confusion(1 point).

The term "CFES" is used to describe cases where neurological symptoms are the predominant features (5). CFES is a rare variant of FES characterized by isolated neurologic symptoms including ischemic and hemorrhagic strokes, seizures, convulsive and non-convulsive status epilepticus, autonomic impairment, acute encephalopathy, and coma (1,6). Literature reviews and case reports have shown that CFES is common in men with bilateral femur fractures in their early 30s (8).

This diagnosis should be considered in trauma patients with long bone fractures who were found to have confusion or focal neurologic deficits. CFE should also be considered in patients with a history of remote trauma, as in this case, who present with new-onset neurologic symptoms (8).

The hypothesized mechanism is that fat globules enter arterial circulation either through an intracardiac shunt such as a patent foramen ovale, or, more commonly, micro globules filter directly through lung capillaries to reach arterial circulation (6).

MRI utilizing either diffusion-weighted imaging or susceptibility-weighted imaging sequences offers the greatest sensitivity for confirming the diagnosis (9,10). While there are no pathognomonic imaging findings, the "starfield pattern" observed on MRI is the most prevalent and recognized manifestation of CFES (11). This imaging finding is also consistent with the MRI findings in our case, further supporting the possibility of CFES in our patient.

Also, in the study by Maghrebi et al. (12), transthoracic echocardiography showed the "snowstorm" appearance of numerous hyperechoic particles in the inferior vena cava. Bedside echocardiographic evaluation in our patient demonstrated hyperechoic structures suggestive of thrombus formation. There are no definitive or specific treatments of FES; therefore, management is entirely supportive (9).

Considering the multifactorial etiology of FES, early operative fixation of long bone fractures is argued to reduce the incidence of FES, although it cannot be prevented in all patients (13,14).

In our case, we discussed a patient who was admitted to the hospital as a result of a traffic accident and who developed a change in consciousness during follow-up. Based on the clinical, laboratory, and imaging findings, differential diagnoses, such as diffuse axonal injury, disseminated intravascular coagulation, and intraparenchymal, subdural, or epidural hemorrhages, should be considered in trauma patients presenting with altered mental status. However, cerebral fat embolism was considered the more likely diagnosis in our case.

Conclusion

The diagnosis of CFES is challenging due to the non-specific nature of the symptoms and the frequent normal results of CT scans. High suspicion should be maintained in patients with orthopedic injuries who exhibit sudden neurological decline. There are no universal diagnostic criteria for CFES, making the diagnosis dependent on the patient's medical history and clinical manifestations (6).

Ethic

Informed Consent: Written informed consent was obtained from the patient for publication of this case and related images.

Footnotes

Author Contributions

Surgical and Medical Practices: D.A., B.P., H.A.Y., Ö.F.D., Concept: D.A., B.P., Design: D.A., H.A.Y., Data Collection or Processing: M.B.E., B.C., Analysis or Interpretation: M.B.E., B.C., Literature Search: M.B.E., Writing: M.B.E., B.P.

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Retrospective Analysis: The Effect of the Seasonal Changes on the Frequency of Urinary System Stone Operations

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Abstract

Aim: Urolithiasis is a multifactorial disease influenced by various factors, including climate and seasonal changes. While climatic effects on stone formation have been studied, seasonal variations in urinary stone surgeries remain underexplored. To investigate the seasonal variation in the frequency of urinary stone surgeries over a three-year period and assess potential seasonal influences on surgical incidence and emergency department visits.

Materials and Methods: A retrospective review of 841 urinary stone surgeries and 509 transurethral resections of the prostate (TUR-P) procedures (as controls) performed between January 2018 and December 2020 was conducted. Procedures were categorized by meteorological seasons. Statistical analysis was performed using chi-square tests to evaluate differences in seasonal distribution.

Results: Urinary stone surgeries showed a significant seasonal variation, with the highest frequency in summer (27.8%) and the lowest in spring (19.3%) ($p<0.05$). No similar seasonal trend was observed in TUR-P procedures. The majority of patients were female (66.0%) with a mean age of 49.7 years. The ureter and kidneys were the most common locations of stone formation. Most patients underwent ureterorenoscopy, and postoperative DJ stenting was frequent (79.5%). Residual stones and complications were infrequent.

Conclusion: The findings demonstrate a statistically significant increase in urinary stone surgeries during summer, suggesting seasonal influences on disease manifestation. These results highlight the importance of heightened clinical awareness and preventive measures, particularly during warmer months, to reduce the burden of urinary stone disease and emergency department visits.

Keywords: Urolithiasis, seasonal variation, urinary stone surgery, summer incidence, hydration, endourological procedures

Introduction

Urolithiasis is a multifactorial disease characterized by the formation of calculi in the kidney, ureter, bladder, or urethra. It is a common cause of emergency department visits, most frequently presenting as renal colic; an acute and severe flank pain that often radiates to the groin and may be accompanied by hematuria and dysuria. The prevalence of renal colic varies globally, ranging between 5% and 15%, depending on geographical, environmental, genetic, and lifestyle-related factors (1). Recurrence rates are as high as 50%, and the incidence is significantly higher in men (2).

Numerous factors contribute to the development of urinary stones, including race, gender, body mass index, dietary patterns, fluid intake, and climate. Certain "stone belt" regions have been identified at regional and global levels, where the incidence of urolithiasis is disproportionately high. For instance, populations in the Western Hemisphere demonstrate elevated prevalence rates (approximately 5-9% in Europe, 12% in Canada, and 13-15% in the United States, particularly in the southeastern states) compared to those in the Eastern Hemisphere, where rates are generally lower (1-5%) (3,4). A well-known high-risk region is the so-called Afro-Asian stone belt (5), which spans from Egypt, Saudi

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Arabia, Sudan and the UAE to Kuwait, Iran, Pakistan, Thailand, India and the Philippines, with prevalence figures ranging from 4% to 20% in various studies (6). Climatic and seasonal factors have gained increasing attention due to their potential impact on hydration status and metabolic processes involved in stone formation. In hot and arid environments, increased perspiration and insensible water loss lead to reduced urinary volume and increased solute concentration, which promote crystal formation. Moreover, greater exposure to sunlight stimulates vitamin D synthesis, which may result in hypercalcemia—a known risk factor for calcium-based stones. These mechanisms suggest that urinary stone incidence may vary with seasonal changes, particularly in warmer months when dehydration is more likely.

Although the relationship between climate and urolithiasis has been previously examined, few studies have focused specifically on seasonal variation in the frequency of stone-related surgical interventions. Moreover, much of the existing literature on this topic is several decades old and may not accurately reflect current population dynamics or environmental trends. The primary aim of this study is to determine whether a seasonal pattern exists in the surgical management of urolithiasis by comparing the frequency of urinary stone operations across different seasons. The findings may help inform preventive strategies, guide future etiologic research, and provide insights into potential seasonal influences on clinical practice.

Materials and Methods

Between 1 January 2018 and 31 December 2020, a total of 841 urinary stone surgeries and 509 transurethral resections of the prostate (TUR-P) procedures—selected as the control group—were retrospectively reviewed and classified according to the four meteorological seasons: spring (March–May), summer (June–August), autumn (September–November), and winter (December–February). TUR-P cases were chosen as the control group based on the assumption that, unlike urinary stone disease, benign prostatic hyperplasia and its surgical treatment are not influenced by environmental or seasonal factors. This comparison aimed to determine whether the incidence of urinary stone surgeries demonstrated a seasonal trend beyond general surgical activity. This study was reviewed and approved by the Ethics Committee of Bezmialem University for the application titled "Retrospective Analysis: The Effect of Seasonal Changes on the Frequency of Urinary System Stone Surgeries" during the 11th Interventional Research Committee meeting, with unanimous approval (decision number: E-54022451-050.05.04-19936, date: 25.05.2021). All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics, version 22.0, a widely used software package in biomedical research. The primary statistical method for categorical variables was the chi-square test, used to assess associations between groups and determine whether observed differences were statistically significant. A p value of <0.05 was considered indicative of statistical significance.

Results

A total of 841 urinary stone operations performed between January 1, 2018, and December 31, 2020, were evaluated. The seasonal distribution of these procedures was as follows: 19.3% (n=162) in spring, 27.8% (n=234) in summer, 26.3% (n=221) in autumn, and 26.6% (n=224) in winter. In the control group, consisting of 509 patients who underwent TUR-P during the same period, the seasonal distribution was 15.9% (n=81) in spring, 22.2% (n=113) in summer, 29.7% (n=151) in autumn, and 32.2% (n=164) in winter. According to the comparative analysis, the rate of urinary stone operations was significantly higher in summer than in spring (27.8% vs. 19.3%, $p<0.05$). Additionally, the rate of urinary stone operations in summer was significantly higher than the rate of TUR-P operations in the same season (27.8% vs. 22.2%, $p<0.05$). The association between surgical procedure type and seasonal distribution was analyzed using the Pearson chi-square test, indicating a statistically significant difference in seasonal distributions between the two groups ($\chi^2=10.640$, $p=0.014$).

The mean age of the study population was 49.7±15.8 years, with a predominance of female patients (66.0%). The most common stone locations were the ureter (45.9%) and the kidney (44.1%). The majority of patients underwent Type 3 surgery (83.8%), followed by Type 4 (8.7%). Left-sided stones (54.0%) were slightly more frequent than right-sided stones (46.0%) among patients with laterality data (n=767). Hydronephrosis was present in 54.8% of the patients at diagnosis. Flank pain (75.1%) was the most common presenting symptom, followed by nausea/vomiting (5.5%) and urinary retention (5.5%). More than half of the patients (58.1%) had a history of previous stone disease, and 27.5% had undergone prior stone surgery. Preoperative extracorporeal shock wave lithotripsy (ESWL) was reported in 7.6%, while only 0.4% required postoperative ESWL. Residual stones were observed in 8.3% of the cases. A preoperative DJ stent was placed in 12.6% of patients, whereas postoperative DJ stents were used in 79.5%. Comorbidities were present in 34.6% of patients. Postoperative complications (fever, bleeding, infection, organ injury) were rare, occurring in only 1.1% of the patients. The mean stone size was

212.5±257.8 mm², and the mean creatinine level was 1.12±0.81 mg/dL. The mean symptom duration prior to presentation was 16.4±12.9 days, and the mean hospital stay was 2.05±2.54 days (Table 1).

Discussion

In this study, patients who underwent surgery for urinary system stones in our clinic over approximately three years, were retrospectively analysed to investigate whether seasonal temperature variations influence the frequency of urinary stone surgeries. Our results demonstrated a statistically significant increase in urinary stone surgeries during the summer months, with a corresponding decline in spring. In contrast, the seasonal distribution of TUR-P procedures, selected as a control group, remained relatively stable and was not significantly elevated in summer. These findings suggest a potential association between seasonality and the incidence of symptomatic or obstructive urinary stone disease requiring surgical intervention.

The observed summer peak in stone surgeries is consistent with existing evidence indicating that warm weather and dehydration may play a crucial role in stone formation and symptomatic presentation (7). Several pathophysiological mechanisms may explain this relationship. High ambient temperatures during summer months increase insensible water loss through perspiration, leading to reduced urine output and increased urinary solute concentration—key factors in promoting crystallization and stone formation. Additionally, enhanced sunlight exposure may lead to increased vitamin D synthesis and calcium absorption, potentially raising urinary calcium levels and promoting calcium-based stones (8,9). Geographical studies have similarly identified higher stone disease prevalence in hot, arid regions, often referred to as “stone belts”. Our findings support this climate-stone link and extend it to surgical outcomes, emphasizing that environmental factors may not only influence stone formation but also the clinical burden on healthcare systems during warmer months. It is noteworthy that despite global warming and climate shifts, seasonal patterns in stone-related hospital visits and procedures remain evident, reinforcing the relevance of weather-related risk factors.

The demographic and clinical characteristics of our study population provide additional context for the observed seasonal variation. The majority of the patients were female, with a mean age of approximately 50 years. While stone disease has traditionally been more common in men, our data showed a higher proportion of female patients. This finding may reflect changing dietary and lifestyle patterns, as recent studies suggest a narrowing of the historical sex disparity in stone disease prevalence (10). Flank pain was the most frequently reported

Table 1. Demographic and clinical characteristics of patients undergoing urinary stone surgery

Variable	Value
Age (years), mean ± SD	49.7±15.8
Sex, n (%)	
Male	286 (34.0%)
Female	555 (66.0%)
Stone location, n (%)	
Renal	371 (44.1%)
Ureteral	386 (45.9%)
Bladder	73 (8.7%)
Urethral	11 (1.3%)
Type of operation, n (%)	
Percutaneous nephrolithotomy	59 (7.0%)
Open nephrolithotomy	4 (0.5%)
Ureterorenoscopy	705 (83.8%)
Cystolithotripsy	73 (8.7%)
Laterality (n=767), n (%)	
Right	353 (46.0%)
Left	414 (54.0%)
Hydronephrosis, n (%)	
Present	461 (54.8%)
Absent	380 (45.2%)
Presenting symptom, n (%)	
Flank pain	632 (75.1%)
Hematuria	40 (4.8%)
Nausea/vomiting	46 (5.5%)
Dysuria	36 (4.3%)
Urinary retention	46 (5.5%)
Others	41 (4.8%)
Previous stone history, n (%)	
Yes	489 (58.1%)
No	352 (41.9%)
Previous stone surgery, n (%)	
Yes	231 (27.5%)
No	610 (72.5%)
Residual stone, n (%)	
Yes	70 (8.3%)
No	771 (91.7%)
Preoperative DJ stent, n (%)	
Yes	106 (12.6%)
No	735 (87.4%)
Postoperative DJ stent, n (%)	
Yes	669 (79.5%)
No	172 (20.5%)
Comorbidities, n (%)	
None	550 (65.4%)
≥1 comorbidity	291 (34.6%)
Postoperative complication, n (%)	
Yes	9 (1.1%)
No	832 (98.9%)
Stone size (mm²), mean ± SD	212.5±257.8
Symptom duration (days), mean ± SD	16.4±12.9
Hospital stay (days), mean ± SD	2.05±2.54

SD: Standard deviation

presenting symptom, and the most common stone locations were the ureter and kidney. More than half of the patients (58.1%) had a history of previous stone disease, consistent with the high recurrence rates reported in the literature. Therefore, it is recommended that individuals with urinary stone disease undergo regular follow-up visits in the urology outpatient clinic at specified intervals. Most patients underwent ureterorenoscopy, and over 79% received a postoperative DJ stent, reflecting a preference for endourological management strategies in current clinical practice. Residual stones and postoperative complications were infrequent, suggesting effective perioperative planning and surgical proficiency (11).

Study Limitations

Despite the robustness of the dataset, this study has several limitations. First, its retrospective design precludes establishing causality. Second, meteorological variables such as temperature, humidity, and sunlight exposure were not included in the analysis, which could have provided more detailed insights into seasonal effects. Additionally, the study was conducted at a single institution, potentially limiting the generalizability of the findings to regions with different climates, healthcare systems, or patient demographics. Future research incorporating environmental data, multi-center collaboration, and prospective designs may yield a more comprehensive understanding of the seasonal dynamics of urinary stone disease. Moreover, preventive strategies—such as hydration education during high-risk seasons—should be evaluated for their potential to reduce symptomatic presentations and surgical burden.

Conclusion

In conclusion, our study found a statistically significant increase in urinary stone surgeries during summer months, suggesting a seasonal influence on disease manifestation. These findings underscore the need for heightened clinical awareness and preventive strategies during warmer seasons to reduce the morbidity and healthcare resource utilization associated with urinary stone disease.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Bezmialem University (decision number: E-54022451-050.05.04-19936, date: 25.05.2021). All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: This is a retrospective study.

Footnotes

Author Contributions

Surgical and Medical Practices: B.D., A.İ., F.G., S.A., Y.Ö.İ., Concept: B.D., Design: B.D., A.İ., F.G., Data Collection or Processing: M.E.D., Analysis or Interpretation: M.E.D., Literature Search: S.A.A., F.G., S.A., Writing: B.D., S.A.A.

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

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Evaluation of Survival Rates and Associated Factors After Cardiopulmonary Resuscitation

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Abstract

Aim: The aim of this study was to determine survival rates in patients who underwent cardiopulmonary resuscitation (CPR) and to evaluate related demographic characteristics, clinical findings, and laboratory results.

Materials and Methods: Data from 620 patients who were transported by ambulance to the emergency department while receiving CPR were retrospectively analysed. Demographic characteristics, clinical findings, laboratory values, and time variables were recorded. Factors associated with survival were evaluated using the chi-square test, independent samples t-test, correlation analysis, and logistic regression analysis.

Results: The median age of the 620 patients included in the study was 67 years (IQR: 54-79), and 64.52% (n=400) were male. 95.32% (n=591) of the calls received by the emergency call centre originated from the region. 98.55% of patients (n=611) lived in urban areas. The one-month survival rate after CPR was found to be 12.42%. Successful resuscitation was achieved in 7.90% of these patients (n=49). In multivariate logistic regression analysis, pH ≤6.817 (OR: 37.39, 95% CI: 14.48-96.52, p<0.001), PO_2 (OR: 0.990, 95% CI: 0.984-0.996, p=0.002), platelet count (OR: 0.99, 95% CI: 0.99-1.00, p=0.034), neutrophil-to-lymphocyte ratio (OR: 0.83, 95% CI: 0.72-0.94, p=0.004), basophil count (OR: 0.18, 95% CI: 0.06-0.55, p=0.002), and MCHC (OR: 1.01, 95% CI: 1.01-1.01, p<0.001) were identified as significant independent predictors of mortality. The combined model incorporating pH and PO_2 demonstrated excellent discriminative ability with an AUC of 0.923 (95% CI: 0.875-0.971), sensitivity of 97.8%, and specificity of 83.1% at a cut-off probability of 0.700.

Conclusion: This study demonstrated that arterial blood gas findings (particularly pH ≥6.817 and PO_2 ≤45.5 mmHg) and certain hematological markers (platelet, neutrophil-to-lymphocyte ratio, basophil) have high diagnostic value in predicting mortality after cardiac arrest.

Keywords: Cardiopulmonary resuscitation, survival, platelet/lymphocyte ratio, neutrophil/lymphocyte ratio, predictive factors

Introduction

Cardiac arrest is defined as the cessation of systemic circulation following the termination of the heart's mechanical activity (1). Cardiopulmonary resuscitation (CPR) is a vital intervention in cardiac arrest and increases the likelihood of survival when performed successfully (2). However, post-CPR survival rates vary worldwide and are often below the desired level (3).

The literature reports survival rates of 8% after out-of-hospital cardiac arrest in European countries, while this rate reaches 10-12% in the United States. A study conducted in the United States in the case of in-hospital cardiac arrests found that the survival rate was approximately 25% (4,5). Recent literature reports that these rates have improved over the years (6,7). A study conducted in Türkiye found that the survival rate after out-of-hospital cardiac arrest was 6.9% (8).

Identifying the factors that influence survival rates is crucial for improving the effectiveness of CPR, various factors that may affect survival after cardiac arrest have been identified. These include age, the location and time of cardiac arrest, the occurrence of ventricular fibrillation, and ventricular tachycardia defined as shockable rhythms, diagnosis of cardiac arrest, the time to initiation of basic life support, and the time to defibrillation (9,10).

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Recently, the effect of hematological parameters and inflammatory markers on prognosis after cardiac arrest has also been investigated (11-13). Hematological parameters such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), which are indicators of the systemic inflammatory response, have been reported to have prognostic value in various cardiovascular diseases (14,15). These parameters are gaining importance in clinical practice as low-cost, easily accessible biomarkers that can be calculated from routine laboratory tests.

The pathophysiological process following cardiac arrest is complex and involves many components, including ischemia-reperfusion injury, systemic inflammatory response syndrome, multiple organ failure, and permanent neurological damage (16,17). In this process, changes in hematological parameters can reveal both the severity of the damage and the body's potential for self-repair. In particular, changes in the activities of leukocyte subpopulations can provide valuable information about the severity of the systemic inflammatory response and patient prognosis (18,19).

The aim of this study is to evaluate the survival rates of patients who underwent CPR at the scene and the related demographic, clinical, and laboratory factors. The findings obtained may contribute to the identification of practical and effective biomarkers that can be used in early prognostic assessment after CPR.

Materials and Methods

This retrospective cohort study included 620 patients who underwent CPR between January 2020 and December 2022. The study was conducted with the approval of the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (desicion number: E-10840098-772.02-3157, date: 01.07.2021).

Demographic characteristics (age, gender), clinical findings (level of consciousness, respiratory status, pulse rate), laboratory values, and time variables (command response time, station response time, transport time, intervention time, time to hospital arrival) were recorded.

Level of consciousness was assessed in three categories: conscious, confused, and unresponsive. Respiratory status was analysed in seven categories: normal, rapid, superficial, irregular, shortness of breath, none. Pulse status was assessed in four categories: normal, arrhythmic, thready and no pulse.

Laboratory values were assessed using venous and arterial blood samples taken upon patient admission. Parameters: white blood cell (WBC, 10^3/µL), red blood cell (RBC, 10_2/µL), hemoglobin (HGB, g/dL), hematocrit (HCT, %), platelet (PLT, 10^3/µL), neutrophil (NEUT, 10^3/µL), lymphocyte (LYMPH, 10^3/µL), monocyte (MONO, 10^3/µL), eosinophil (EO, 10^3/µL), basophil (BAS, 10^3/µL), creatinine (mg/dL), aspartate aminotransferase (AST, U/L), alanine aminotransferase (ALT, U/L), C-reactive protein (CRP, mg/L), and blood gas values (pH, PO_2 in mmHg, PCO_2 in mmHg) were included. Derived parameters such as the NLR and PLR were also calculated.

Successful CPR is defined as the restoration of spontaneous circulation and the recovery of sustained vital functions in a patient who has experienced cardiac arrest or respiratory arrest.

Long-term success: patients who survived for more than 24 hours were considered successful. Complete success: defined as 30-day survival and good neurological status (20).

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) version 25.0 software was used for data analysis. Continuous variables are expressed as arithmetic distributed data, while categorical variables are expressed as frequency and percentage distributions.

The Shapiro-Wilk test was used to assess the normal distribution of the data. The Student's t-test was used to compare the quantitative data of two groups showing normal distribution. Pearson's chi-square analysis was used to compare frequencies. The relationship between survival and continuous variables was evaluated using Pearson correlation analysis.

Logistic regression analysis was used to determine the factors affecting survival. For the combined predictive model, pH and PO_2 values were first evaluated as continuous variables in Univariate logistic regression. Subsequently, optimal cut-off values for pH (≤6.817) and PO_2 (≤45.5 mmHg) were determined using receiver operating characteristic (ROC) curve analysis with Youden's index (sensitivity + specificity - 1) to maximize both sensitivity and specificity. These dichotomized variables, along with other significant hematological parameters, were then entered into a multivariate logistic regression model using the enter method. The predicted probabilities from the final model were used to construct a ROC curve, and the optimal cut-off probability (0.700) for mortality prediction was determined using Youden's index. The level of statistical significance was set at $p<0.05$.

Table 1. Demographic characteristics of patients

Gender, n (%)	
Female	220 (35.48)
Male	400 (64.52)
Region, n (%)	
Inland	591 (95.32)
External	29 (4.68)
Place of residence, n (%)	
Urban	611 (98.5)
Rural	9 (1.45)
Age, years, median (min-max)	67 (54-72)

Results

The median age of the 620 patients included in the study was 67 years (IQR: 54-79), and 64.52% (n=400) were male. 95.32% (n=591) of the calls received were made from within the region. 98.55% (n=611) of the patients lived in urban areas. Fully successful CPR was achieved in 7.90% (n=49) of these patients (Tables 1, 2).

12.10% of patients (n=75) had respiratory disease, 1.77% (n=11) had trauma due to a fall, 0.65% (n=4) had heart disease, 0.65% (n=4) had oncological disease, and 0.48% (n=3) had internal disease.

pH and PO_2 values were very low in deceased patients (p<0.001). PCO_2 values were similar in surviving and deceased patients (p=0.186). WBC, PLT, PLT/LYMPH ratio, BAS, MCV, and PCT were significantly lower in deceased patients (MCV: p=0.003, others: p<0.001). HGB, PLT/NEUT ratio, EO, MCH, MCHC, and PDW values were significantly higher in deceased patients (PLT/NEUT: p=0.038, other values: p<0.001) (Table 3).

In Univariate logistic regression analysis, the parameters with a significant effect on mortality were pH, pH ≤6.817 group variable, PO_2, and PO_2 ≤45.5 group variable, RBC, HGB, HCT, PLT, NEUT, LYMPH, PLT/LYMPH, NEUT/LYMPH, EO, BAS, MCV, MCH, MCHC, and PDW (Table 3).

In the multivariate logistic regression analysis, the mortality risk was 37.39 times higher in the pH ≤6.817 group (reference group: pH >6.817), [95% confidence interval (CI): 14.48-96.52, p=0.001].

For every 1-unit increase in values, the mortality risk is increased by 1% for PO2, 0.5% for PLT, 17% for NEUT/LYMPH, 82% for BASO, and 1% for MCHC (Table 3).

At a cut-off probability of 0.700 for the combined predictive model (pH + PO_2), the sensitivity of the predicted probabilities was 0.978, specificity was 0.831, positive predictive value was 0.976, and negative predictive value was 0.842 (Table 4).

The mortality prediction model, with an area under the curve (AUC) value of 0.923 (95% CI: 0.875-0.971), demonstrated significantly better performance than the pH and the PO_2 (DeLong test: p=0.017 for both) (Figure 1).

Table 2. Clinical characteristics of patients

Triage code, n (%)	
Yellow	15 (2.42)
Red	561 (90.48)
Black	44 (7.1)
Level of consciousness, n (%)	
Conscious	32 (5.17)
Confused	13 (2)
Unconscious	575 (92.7)
Pupils, n (%)	
Normal	66 (10.63)
Anisocoric	7 (1.08)
Fixed dilated	219 (35.52)
Isochoric	2 (0.36)
Myotic	18 (2.88)
Mydriatic	21 (3.41)
No response	287 (46.31)
Respiratory, n (%)	
Normal	18 (2.86)
Rapid	1 (0.19)
Superficial	7 (1.14)
Irregular	14 (2.29)
Shortness of breath	14 (2.29)
None	566 (91.24)
Skin, n (%)	
Normal	55 (8.91)
Cyanotic	321 (51.87)
Pale	217 (34.94)
Sweaty	17 (2.67)
Hyperemic	2 (0.36)
Icteric	2 (0.36)
Dry	6 (0.89)
Pulse, n (%)	
Normal	40 (6.53)
Arrhythmic	23 (3.73)
Filamentous	19 (2.99)
Not in use	538 (86.75)

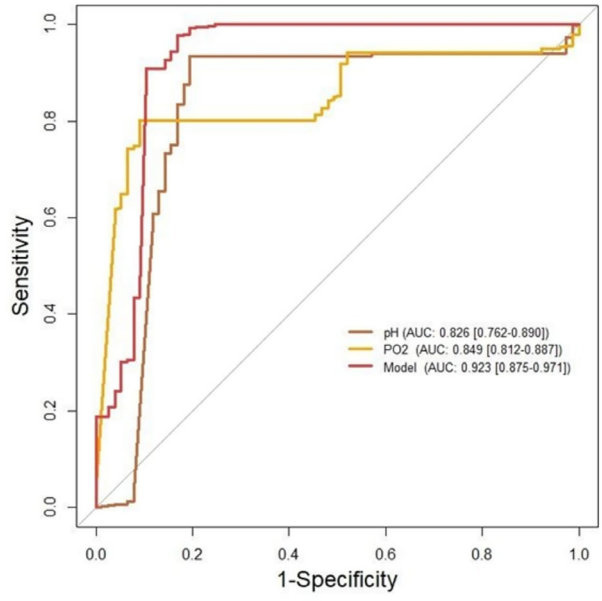

Figure 1. Receiver operating characteristic curves for mortality prediction using pH, PO_2, and the combined model (pH + PO_2)
AUC: Area under the curve

Table 3. Results of logistic regression analysis for mortality prediction using laboratory parameters						
	Univariate logistic regression analysis			Multivariate logistic regression analysis		
	Odds ratios	95% CI	p value	Odds ratios	95% CI	p value
pH	13.75	4.46-42.36	**<0.001**	-	-	-
pH ≤6.817	58.21	30.16-112.35	**<0.001**	37.39	14.48-96.52	**<0.001**
PCO_2	1.00	1.00-1.00	0.809	-	-	-
PO_2	0.990	0.986-0.993	**<0.001**	0.990	0.984-0.996	**0.002**
PO_2 ≤45.5	40.28	18.01-90.09	**<0.001**	-	-	-
WBC	1.00	0.99-1.00	0.369	-	-	-
RBC	1.64	1.29-2.09	**<0.001**	-	-	-
HGB	1.02	1.01-1.02	**<0.001**	-	-	-
HCT	1.07	1.04-1.10	**<0.001**	-	-	-
PLT	0.98	0.98-0.99	**<0.001**	0.99	0.99-1	**0.034**
NEUT	0.97	0.96-0.98	**<0.001**	-	-	-
LYMPH	1.03	1.02-1.05	**<0.001**	-	-	-
PLT/NEUT	0.96	0.91-1.01	0.116	-	-	-
PLT/LYMPH	0.91	0.89-0.93	**<0.001**	-	-	-
NEUT/LYMPH	0.75	0.70-0.81	**<0.001**	0.83	0.72-0.94	**0.004**
MONO	1.00	0.98-1.03	0.855	-	-	-
EO	1.60	1.28-1.99	**<0.001**	-	-	-
BAS	0.05	0.02-0.13	**<0.001**	0.18	0.06-0.55	**0.002**
MCV	1.05	1.01-1.08	**0.009**	-	-	-
MCH	1.39	1.24-1.56	**<0.001**	1.16	0.97-1.39	0.098
MCHC	1.01	1.00-1.01	**<0.001**	1.01	1.01-1.01	**<0.001**
MPV	1.13	0.88-1.44	0.340	-	-	-
PCT	0.94	0.74-1.20	0.632	-	-	-
PDW	2.39	1.52-3.75	<0.001	1.52	0.96-2.39	0.074

PLT: Platelet, NEUT: Neutrophil, LYMPH:Lymphocyte, WBC: White blood cell, RBC: Red blood cell, HGB: Hemoglobin, HCT: Hematocrit, MONO: Monocyte, EO: Eosinophil, BAS: Basophil, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, MPV: Mean platelet volume, PCT: Plateletcrit, PDW: Platelet distribution width

Table 4. Diagnostic performance of pH, PO_2, and the combined model (pH + PO_2)			
	Combined model (pH + PO_2)	pH	PO_2
AUC (95% CI)	0.923 (0.875-0.971)	0.826 (0.762-0.890)	0.849 (0.812-0.887)
Cut-off point	0.700	6.817	45,500
Sensitivity	0.978	0.934	0.801
Specificity	0.831	0.805	0.909
Positive predictive value	0.976	0.971	0.984
Negative predictive value	0.842	0.633	0

AUC: Area under the curve, CI: Confidence interval

Discussion

This study aimed to investigate the effect of sociodemographic, clinical, and laboratory parameters on mortality in patients undergoing CPR during cardiac arrest monitoring. A retrospective analysis of 620 patients revealed the role of arterial blood gas parameters and hematological biomarkers in predicting mortality risk.

A study published in 2024 observed that 67.5% of out-of-hospital cardiac arrest cases were in patients over 65 years of age (21).

The median age of the patients included in the study was 67 years (IQR: 54-79), and 64.5% were male, supporting that cardiac arrest is more common in older individuals and males (22). This finding is consistent with the literature showing that cardiovascular risk factors increase with age and are more prevalent in males.

98.5% of patients lived in urban areas indicates that intervention at the scene was faster. However, our study found no significant difference in positively affecting survival rates after CPR. This indicates that the effectiveness of CPR should not be evaluated based solely on geographical location.

The successful resuscitation rate is only 7.9%, and a study reported in the literature indicates that out-of-hospital cardiac arrest survival rates are 9% in Europe, 6% in North America, 11% in Australia, and 2% in Asia (23). Our findings are consistent with international values.

Recent evidence from the 2024 update of the Utstein Out-of-Hospital Cardiac Arrest Reporting Template provides an important context for interpreting survival rates (24). The updated guidelines emphasise the importance of standardised reporting and risk adjustment for key Utstein factors such as age, gender, location of arrest, and bystander status. When evaluated against these current standards, our observed survival rate reflects the complex interaction of multiple prognostic factors.

A key finding from recent research shows that cardiac arrest survival rates deteriorated significantly during the coronavirus disease 2019 pandemic, with survival rates falling significantly in 2020 and remaining below pre-pandemic levels (25). This temporal context is particularly relevant to our study period (2020-2022) and suggests that the survival rates we observed may reflect both traditional prognostic factors and pandemic-related healthcare system challenges.

Although there were variations between countries, a generally low survival rate was observed. Possible reasons include delayed intervention, failure to recognise cardiac arrest, or serious comorbidities before cardiac arrest. Since 95% of calls were due to medical reasons, with 12% of these being respiratory system diseases, it indicates that acute respiratory decompensation plays a significant role in the development of cardiac arrest.

In our study, analyses of laboratory data revealed that arterial blood gas parameters, particularly pH and PO_2 values, were the strongest predictors of mortality. In Univariate and multivariate logistic regression analyses, the mortality risk was 37.4 times higher in patients with pH ≤6.817. This finding indicates that metabolic acidosis developing after arrest is incompatible with life. von Auenmueller et al. (26) specifically investigated the value of arterial blood gas parameters for predicting mortality in out-of-hospital cardiac arrest survivors, and reported that pH and lactate were the most relevant parameters because they were strongly and independently associated with mortality.

Hypoxaemia was found to be similarly an independent predictor of mortality, with the mortality rate increasing dramatically below PO_2 ≤45.5 mmHg. These findings support the critical role of oxygenation in resuscitation success and the need to integrate early arterial blood gas measurements into clinical decision support systems (27).

Hematological parameters also yielded noteworthy results. PLT counts were significantly higher in survivors, and each unit increase in PLT levels was associated with a 0.5% reduction in mortality risk. This demonstrates that microvascular dysfunction and systemic inflammation following cardiac arrest can be monitored via hematological markers (28).

In particular, the PLT/LYMPH ratio and NEUT/LYMPH ratio provide information about the nature of the inflammatory response. The increase in mortality with a decrease in the NEUT/LYMPH ratio suggests that suppression of the immune response after cardiac arrest may be an indicator of poor prognosis. This finding is consistent with studies showing that immune functions play an important role in the early period after cardiac arrest (29).

The inverse relationship between BAS and mortality, and the significant difference in EO values, are also noteworthy. These findings may reflect the immunomodulatory effects of the granulocyte series and suggest that some hematological parameters may represent the disruption of immune balance after arrest. High erythrocyte indices such as MCH and MCHC likely reflect the compensatory response to hypoxic stress and oxygen-carrying capacity after arrest, and this is consistent with the literature (30).

In our study, the predictive power of the model was also evaluated using ROC analysis. The AUC value of the model including the pH and PO_2 parameters was found to be 0.923 (95% CI: 0.875-0.971). This high AUC value indicates that the model has a strong discriminatory power in predicting mortality.

Specifically, when using a threshold value of 0.700, the sensitivity and specificity of the model were calculated as 97.8% and 83.1%, respectively. This performance may provide significant advantages in clinical practice for early prognosis determination (31).

Study Limitations

The main limitations of this study are its retrospective nature and the absence of certain clinical variables (CPR duration, witness to cardiac arrest).

Conclusion

In conclusion, this study demonstrated that arterial blood gas findings (particularly ≤6.817 and PO_2 ≤45.5 mmHg) and certain hematological markers (PLT, NEUT/LYMPH ratio, BAS) have high diagnostic value in predicting mortality after cardiac arrest. These findings are promising as they can be used in early triage and clinical decision-making processes. Prospective and multicentre studies could strengthen the integration of these parameters into clinical practice.

Ethics

Ethics Committee Approval: The study was conducted with the approval of the İstanbul Medipol University Non-Interventional Clinical Research Ethics Committee (desicion number: E-10840098-772.02-3157, date: 01.07.2021).

Informed Consent: This retrospective study.

Footnotes

Author Contributions

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

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

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The Effect of Delirium Knowledge Level Among Intensive Care Patients' Relatives on Family Care Satisfaction: A Cross-Sectional Study

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Abstract

Aim: Delirium affects 20-80% of intensive care unit (ICU) patients and significantly impacts family members' psychological well-being and care satisfaction. However, the relationship between family members' delirium knowledge and their satisfaction with ICU care remains understudied. This study investigated the association between ICU patients' relatives' delirium knowledge levels and their care satisfaction, while identifying key predictors of family satisfaction.

Materials and Methods: This cross-sectional study was conducted between January and April 2024 at Turgut Özal Medical Center, Malatya, Türkiye. The study included 305 family members of ICU patients hospitalized for ≥48 hours. Participants were recruited using convenience sampling from four ICUs (internal medicine, coronary, neurology, and medical oncology). Data collection instruments included: Caregiver Characteristics Form, Caregiver Intensive Care Delirium Knowledge Questionnaire-Turkish Version (CIDKQ-T), and Family Satisfaction in the Intensive Care Unit scale (FS-ICU-24). Statistical analyses included descriptive statistics, Pearson correlation coefficient/Spearman's rank correlation, and multiple linear regression.

Results: Participants demonstrated moderate delirium knowledge (CIDKQ-T mean: 11.62±2.54, range: 0-21) and moderate ICU care satisfaction (FS-ICU-24 mean: 52.14±14.48, range: 0-100). Strong positive correlations were found between delirium knowledge and all FS-ICU-24 dimensions: total satisfaction ($r=0.60$, $p<0.001$), care satisfaction ($r=0.45$, $p<0.001$), decision-making satisfaction ($r=0.53$, $p<0.001$), and information satisfaction ($r=0.48$, $p<0.001$). Multiple regression analysis ($R^2=0.36$, $F(7.142) = 12.85$, $p<0.001$) identified delirium knowledge as the strongest predictor of family satisfaction ($\beta=0.42$, $p<0.001$), followed by university education ($\beta=0.31$, $p=0.002$), presence of neurological disease ($\beta=0.28$, $p=0.004$), and female gender ($\beta=0.25$, $p=0.008$). Longer hospitalization (10-13 days) negatively affected satisfaction ($\beta=-0.22$, $p=0.018$).

Conclusion: Family members' delirium knowledge significantly predicts their ICU care satisfaction, explaining 36% of the variance in satisfaction scores. These findings support implementing structured delirium education programs for families as part of family-centered ICU care protocols.

Keywords: Delirium knowledge, intensive care unit, family satisfaction, patient relatives

Introduction

Intensive care units (ICUs) constitute specialized clinical environments dedicated to the continuous monitoring and management of critically ill patients utilizing advanced technology and a multidisciplinary team approach. These units are indispensable for patients necessitating intensive medical and nursing support (1,2). Patients within ICUs encounter substantial physiological and psychological stressors, which markedly elevate their susceptibility to delirium. Delirium is a neurocognitive disorder characterized by acute onset, fluctuating course, and impairments in attention, awareness, and cognition (3,4). It ranks among the most prevalent complications in ICUs, with reported incidence rates varying from 20% to 80%, and even higher frequencies observed in patients undergoing mechanical ventilation (3-5).

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The detrimental clinical outcomes associated with delirium are extensively documented; it is known to prolong hospitalization, elevate mortality risk, and contribute to long-term cognitive impairment (6,7). Affected patients often require extended periods of mechanical ventilation, experience heightened rates of complications, and demonstrate reduced functional independence following discharge. Significantly, the repercussions of delirium extend beyond the patient, profoundly impacting their family members (2,3).

Family members witnessing their loved ones exhibiting symptoms such as altered consciousness, agitation, disorientation, and uncharacteristic behavioral changes frequently endure intense psychological distress and uncertainty (8,9). These experiences can precipitate anxiety, depressive symptoms, and post-traumatic stress among relatives (10). Particularly, individuals lacking adequate understanding of delirium may misinterpret these manifestations, leading to feelings of helplessness and apprehension. This can subsequently impair communication and erode trust between families and healthcare providers, adversely affecting overall satisfaction with the ICU experience (11,12).

Emerging research underscores a positive correlation between the level of knowledge families possess about delirium and their reported satisfaction with care received in the ICU (13,14). When relatives comprehend the etiology and clinical features of delirium, they are better equipped to participate meaningfully in the care process and engage in more effective communication with healthcare staff (10,11). Educational and awareness-raising initiatives have demonstrated efficacy in reducing family anxiety and enhancing their capacity to navigate the ICU experience (2,15). Consequently, providing accurate and comprehensive information concerning delirium is paramount—not solely for improving patient outcomes but also for safeguarding the psychosocial well-being of families and their satisfaction with healthcare services (6,16).

A review of contemporary literature indicates a relative paucity of studies comprehensively investigating the relationship between family members' knowledge of delirium and their satisfaction with ICU care (17,18). Much of the existing research focuses on general ICU experiences, often lacking a detailed examination of the unique psychosocial burden imposed by delirium on families (8,18). Given its distinct clinical trajectory and associated uncertainties, delirium presents a specific emotional and psychological challenge for family caregivers, differentiating it from other ICU complications.

In light of these considerations, this study concurrently assesses the knowledge levels of ICU patients' family members regarding delirium and their satisfaction with the care provided. The outcomes are anticipated to furnish a foundation for developing targeted educational strategies, foster active family involvement in delirium management, and reinforce patient- and family-centered care approaches. Furthermore, the study explores demographic and clinical factors influencing this relationship and identifies significant predictors of family care satisfaction.

Materials and Methods

Study Design

This investigation was conceived as a cross-sectional study, conducted over a four-month period from January to April 2024 at the Turgut Özal Medical Center, affiliated with Malatya Turgut Özal University, in Malatya, Türkiye.

Sample and Setting

The study population comprised family members of patients hospitalized in the internal medicine, coronary, neurology, and medical oncology ICUs of the aforementioned medical center. The final sample included 305 family members of patients who had been admitted to the ICU for a minimum of 48 hours. Sample size determination was performed using G*Power 3.1 software, specifying an effect size of 0.50, a statistical power of 95%, and an alpha significance level of 0.05. This calculation yielded a minimum required sample size of 305 participants, consistent with parameters derived from prior correlation studies examining analogous relationships (9,16).

Inclusion Criteria:

- Age 18 years or older
- Primary caregiver designation for an ICU patient hospitalized for ≥48 hours
- Minimum of three separate visits to the patient during the ICU stay
- Demonstrated ability to comprehend and complete the study questionnaires
- Provision of voluntary informed consent to participate

Exclusion Criteria:

- Presence of visual, auditory, or cognitive impairments that would preclude completion of the questionnaires
- History of a prior psychiatric diagnosis potentially influencing responses
- Inability or unwillingness to provide informed consent

Data Collection Tools

Caregiver Characteristics Form: This instrument was developed by the research team following an extensive review of relevant

literature. It was designed to capture participants' socio-demographic details (e.g., age, gender, educational background) and attributes related to their caregiving role (e.g., relationship to the patient, prior caregiving experience).

Caregiver Intensive Care Unit Delirium Knowledge Questionnaire-Turkish Version (CIDKQ-T): The CIDKQ was developed by Krewulak et al. (19) to quantify caregivers' knowledge concerning delirium in ICU patients. The Turkish adaptation and validation of this tool was subsequently performed by Erbay Dallı and Kelebek Girgin (20), who reported a test-retest reliability coefficient of 0.81. The questionnaire encompasses 21 items distributed across three subscales: risk factors (10 items), management practices (6 items), and symptoms (5 items). Respondents select from "Yes," "No," or "I don't know" options. Correct responses are assigned 1 point, while incorrect or "I don't know" responses receive 0 points. Total scores range from 0 to 21, with higher scores indicative of greater knowledge about delirium.

Family Satisfaction in the Intensive Care Unit (FS-ICU-24): FS-ICU-24 is a validated instrument initially developed by Heyland and Tranmer (21), and later refined by Wall et al. (22), designed to systematically evaluate family members' satisfaction with care provided in the ICU. The validity and reliability of the Turkish version were established by Tastan et al. (23). The scale comprises 24 items organized into two primary domains: satisfaction with care (14 items) and satisfaction with decision-making (10 items). Responses are recorded on a 5-point Likert scale. Higher scores correspond to higher levels of satisfaction. In the current study, Cronbach's alpha values were calculated as 0.96 for the overall scale, 0.96 for the care subscale, 0.82 for the decision-making subscale, and 0.92 for the information subscale.

Data Collection Process

Data acquisition was conducted through face-to-face interviews administered by the researchers. Participants completed the Caregiver Characteristics Form, the CIDKQ-T, and the FS-ICU-24 under researcher supervision to ensure clarity and comprehensiveness of responses.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics version 28.0. Descriptive measures, including frequencies, percentages, means, and standard deviations, were calculated to summarize the study variables. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess data normality, while relationships between variables were examined through Pearson correlation coefficient or Spearman's rank correlation analyses, as appropriate. Multiple linear regression analysis was subsequently conducted to identify the key predictors of family satisfaction with ICUs. Statistical significance was defined as a p-value less than 0.05 for all analyses.

Ethical Considerations

This study received approval from the Non-Interventional Clinical Ethics Committee of İnönü University (desicion number: 2024-6/1, date: 14.01.2024). Formal institutional permission was also obtained from the administration of the Turgut Özal Medical Center. The research was conducted in strict adherence to the principles outlined in the Declaration of Helsinki. All participants were comprehensively informed about the study's purpose, scope, and procedures, and their participation was entirely voluntary. Written informed consent was obtained from each individual prior to enrolment. The confidentiality of all collected information was rigorously maintained, and data were used exclusively for scientific purposes.

Results

Among the 305 participating family members, 190 (62.3%) were female. The mean age of participants was 48.98±7.05 years. The largest proportion of participants (n=135, 44.3%) fell within the 31-41 age range. The majority reported being married (64.1%), having attained a high school education (45.3%), and having income levels that approximately matched their expenses (43.0%). In terms of relationship to the patient, children constituted the largest group (37.7%). A significant majority of participants (68.9%) reported no prior experience with patient care. Regarding the primary diagnoses of the hospitalized patients, cardiovascular diseases were most prevalent (32.1%), while oncological diseases were least common (13.8%). Analysis of hospitalization duration indicated that 40% of patients remained in the ICU for a period of 10-13 days (Table 1).

On the FS-ICU-24, the mean total satisfaction score was 52.14±14.48. Examination of the subscale scores revealed means of 54.78±19.0 for the care subscale, 49.07±18.48 for the decision-making subscale, and 16.91±16.13 for the Information subscale. Performance on the CIDKQ-T yielded a mean total score of 11.62±2.54. Subscale analysis showed mean scores of 6.62±1.5 for risk factors, 3.56±0.5 for management practices, and 1.94 ± 0.2 for symptoms (Table 2).

A robust positive correlation was identified between the total score on the FS-ICU-24 and the total score on the CIDKQ-T ($r=0.60$, $p<0.001$). Significant positive correlations were also observed between the FS-ICU-24 care subscale and the CIDKQ-T risk factors subscale ($r=0.461$, $p<0.001$), the CIDKQ-T practices subscale ($r=0.484$, $p<0.001$), and the CIDKQ-T symptoms subscale ($r=0.471$, $p<0.001$).

Furthermore, significant positive relationships were found between the FS-ICU-24 decision-making subscale and the CIDKQ-T risk factors subscale (r=0.401, p=0.001), the CIDKQ-T practices subscale (r=0.493, p=0.001), and the CIDKQ-T symptoms subscale (r=0.516, p=0.001).

Table 1. Socio-demographic characteristics of the participants

Variables	Number	Percentage (%)
Gender		
Male	115	37.7
Female	190	62.3
Age groups		
20-30	90	29.5
31-41	135	44.3
42-52	80	26.2
Marital status		
Married	157	64.1
Single	88	35.9
Educational level		
Elementary school graduate	98	32.1
High school graduate	138	45.3
University graduate	69	22.6
Level of income		
Income is lower than expenses	93	30.5
Income equals expenses	131	43.0
The income of the organization is higher than its expenses	81	26.5
Degree of closeness with the patient		
Wife	50	16.4
Parent	68	22.3
Child	115	37.7
Sibling	72	23.6
Previous patient care experience		
Yes	95	31.1
No	210	68.9
Diagnosis of patients in intensive care units		
Cardiovascular diseases	98	32.1
Respiratory system diseases	69	22.6
Neurological diseases	46	15.1
Oncological diseases	42	13.8
Infections	50	16.4
Length of hospitalization		
3-6 days	56	18.4
6-9 days	71	23.2
10-13 days	122	40.0
14 or more days	56	18.4
Average age	48.98±26.5	

Similarly, significant positive correlations were detected between the FS-ICU-24 information subscale and the CIDKQ-T risk factors subscale (r=0.437, p<0.001), the CIDKQ-T practices subscale (r=0.526, p<0.001), and the CIDKQ-T symptoms subscale (r=0.501, p<0.001) (Table 3).

Multiple linear regression analysis identified several factors as statistically significant predictors of family care satisfaction among ICU patients' relatives [F (7,142)=12.85, p<0.001)]. The regression model explained 36% of the variance in the dependent variable (R^2=0.36, adjusted R^2=0.34). The most substantial predictors were identified as the level of knowledge about delirium (β=0.42, p<0.001; standardized β=0.38) and attainment of a university-level education (β=0.31, p=0.002; Standardized β=0.28). The presence of a neurological disease in the patient (β=0.28, p=0.004) and being female (β=0.25, p=0.008) also demonstrated significant positive relationships with satisfaction. Conversely, a patient's hospitalization duration of 10-13 days was associated with a negative effect on care satisfaction (β=-0.22, p=0.018). Demographic factors such as younger age (20-30 years age group; β=0.18, p=0.032) and being the child of the patient (β=0.15, p=0.045) exhibited weaker, yet statistically significant, positive effects. Multicollinearity diagnostics (VIF values all being <5) and the Durbin-Watson statistic (1.98) confirmed that the underlying assumptions of the regression model were not violated. These results underscore the critical influence of delirium knowledge and educational background on family care satisfaction (Table 4).

Discussion

This research investigated the knowledge levels concerning delirium among relatives of patients receiving treatment in ICU and explored its relationship with their satisfaction. The finding that 62% of participants were female aligns with existing literature, which consistently shows that caregiving

Table 2. Mean scores of the participants on the scales

Scale names	Mean ± SD	Min-max
Intensive care family satisfaction scale total score	52.14±14.48	0-100
Care subdimension	54.78±19.0	0-100
Decision making subdimension	49.07±18.48	0-100
Knowledge subdimension	16.91±16.13	0-100
Intensive care delirium knowledge level test for caregivers total score	11.62±2.54	0-21
Risk factors sub-dimension	6.62±1.5	0-10
Applications sub-dimension	3.56±0.5	0-6
Symptoms subscale	1.94±0.2	0-5

SD: Standard deviation

responsibilities disproportionately fall on women. Studies frequently indicate that women assume more active roles in patient care and are typically designated as primary caregivers (18,24,25). This observation reinforces the significant role gender plays in healthcare dynamics and supports the notion that women are more frequently engaged in the intensive care process. The concentration of participants (44.3%) within the 31 to 41-year age range suggests that adults in this age group are particularly likely to be involved in ICU caregiving. The overall mean age of 48.98±7.05 years indicates that the relatives of ICU patients are generally middle-aged. This implies that the demographic plays a crucial role as caregivers and that age is a factor influencing active participation in care processes (18,26). The high proportion of married individuals (64.1%) suggests that spousal and family support networks are instrumental in the caregiving process. Married individuals may have access to greater emotional and practical support, which constitutes an important resource for coping with stress (24,25). Additionally, the finding that 68.9% of participants had no prior patient care experience highlights potential knowledge gaps and uncertainties that could exacerbate anxiety during the care process. This underscores the vital importance of providing information and support specifically tailored to novice caregivers.

The predominance of children (37.7%) as the primary relatives involved indicates that the responsibility for caring for ICU patients often falls to the younger generation. This finding suggests a shifting dynamic where children are playing an increasingly important role in intensive care processes. Analysis of patient diagnoses revealed that cardiovascular diseases were most common (32.1%), reflecting the high prevalence of these conditions in ICUs and their frequent requirement for complex and prolonged care. In contrast, oncological diseases had the lowest representation (13.8%), suggesting that cancer patients may require or receive intensive care less frequently. This points to potentially different care dynamics and trajectories for oncology patients, who often have distinct treatment needs and health challenges (24-26).

Previous studies have generally reported that caregiver scores on delirium knowledge tests like the CIDKQ-T tend to be at or below average levels (27-30). This indicates that while caregivers may possess basic awareness, they often lack comprehensive knowledge about delirium. Studies utilizing the FS-ICU-24 scale typically report average total satisfaction scores ranging from moderate to high (15,28), suggesting that families are generally satisfied with ICU care. When examining subscales, the "care" subscale often receives the highest scores, implying that families are particularly satisfied with the direct medical and nursing care provided (27). Conversely, scores on the "information" and "decision-making" subscales are frequently lower, indicating that families may feel less informed about their relative's condition and less involved in care decisions (27). These patterns may vary based on healthcare system structures, cultural contexts, and methodological differences across studies conducted in different regions (26,27). Nonetheless, these consistent trends highlight

Table 3. Correlations between FS-ICU-24 and CIDKQ-T scales and subscales

	"FS-ICU-24 care subscale	FS-ICU-24 decision making subscale	FS-ICU-24 knowledge subscale	FS-ICU-24 total score
CIDKQ-T total score	r=0.450, p=0.000*	r=0.528, p=0.001*	r=0.477, p=0.000*	r=0.600, p=0.000*
CIDKQ-T risk factors subscale	r=0.461, p=0.000*	r=0.401, p=0.001*	r=0.437, p=0.000*	r=0.506, p=0.000*
CIDKQ-T applications subscale	r=0.484, p=0.000*	r=0.493, p=0.001*	r=0.526, p=0.000*	r=0.456, p=0.000*
CIDKQ-T symptoms subscale	r=0.471, p=0.000*	r=0.516, p=0.001*	r=0.501, p=0.000*	r=0.541, p=0.000*

*Spearman's correlation p<0.05. CIDKQ-T: Caregiver Intensive Care Unit Delirium Knowledge Questionnaire-Turkish version, FS-ICU-24: Family Satisfaction in the Intensive Care Unit

Table 4. Factors predicting family care satisfaction in relatives of intensive care unit patients

Independent variables	β	Stand. error	p-value	95% CI	Stand. β	VIF
Delirium knowledge level	0.42	0.08	<0.001	0.26-0.58	0.38	1.20
Education level (university)	0.31	0.07	0.002	0.17-0.45	0.28	1.15
Gender (female)	0.25	0.06	0.008	0.13-0.37	0.22	1.10
Age group (20-30 years)	0.18	0.05	0.032	0.03-0.33	0.16	1.08
Degree of closeness (child)	0.15	0.04	0.045	0.07- 0.23	0.14	1.05
Length of hospitalization (10-13)	-0.22	0.05	0.018	-0.32-0.12	-0.20	1.12
Presence of neurological disease	0.28	0.06	0.004	0.16-0.40	0.25	1.18

β: Beta, CI: Confidence interval, VIF: Variance inflation factor

the need to promote family-centered care practices, ensure adequate information provision and emotional support for families, and actively involve them in decision-making processes within ICUs to enhance overall satisfaction (10,25). Therefore, the current findings reinforce the necessity for continued efforts to improve family satisfaction in ICU settings.

The strong positive correlation identified between the total scores of the FS-ICU-24 and the CIDKQ-T ($r=0.60$, $p<0.001$) demonstrates that ICU patients' relatives' knowledge level is directly associated with their satisfaction with the care experience. This aligns with literature suggesting that adequate information about the ICU process positively influences family members' perceptions of care quality and facilitates their psychosocial adjustment (13,14). Conversely, insufficient information is known to exacerbate feelings of stress, anxiety, and uncertainty among relatives, thereby negatively impacting overall satisfaction levels (28).

The significant correlations between the FS-ICU-24 care subscale and the various CIDKQ-T subscales (risk factors, applications, symptoms) indicate that relatives' understanding of the critical illness process directly affects their perception of care quality. Studies consistently emphasize that families require comprehensive information to comprehend their relative's condition and that transparent information-sharing practices are strongly linked to care satisfaction (13,28). Specifically, providing sufficient details regarding disease management, treatment protocols, and symptom control enables family members to collaborate more effectively with the healthcare team (14,27).

The positive relationships between the FS-ICU-24 decision making subscale and the CIDKQ-T subscales suggest that as relatives' knowledge increases, so does their participation in decision-making processes. Literature confirms that involving family members in decisions is critical from both ethical and psychosocial perspectives (24,26). Active participation reduces feelings of uncertainty and strengthens their sense of responsibility and engagement in their loved one's treatment journey (10,25,26). Moreover, being well-informed allows families to make more considered choices regarding invasive interventions, palliative care options, and end-of-life preferences (28).

The significant correlations between the FS-ICU-24 information subscale and the CIDKQ-T subscales underscore that the quantity and quality of information provided to relatives enhances their satisfaction with healthcare services and their confidence in the process. Prior research has shown that consistent and clear communication from healthcare professionals reduces anxiety and stress levels among patients' families (15,25). Effective information-sharing also supports informed decision-making by relatives, leading to more positive ethical and clinical outcomes (28,29).

The multiple linear regression analysis revealed several key factors influencing the care satisfaction of ICU patients' relatives. The model's explanation of 36% of the variance indicates that the examined variables substantially impact satisfaction. Most notably, the level of knowledge about delirium ($\beta=0.42$, $p<0.001$) emerged as the strongest predictor, suggesting that enhancing family awareness could markedly improve satisfaction. This finding accentuates the pivotal role of the knowledge of relatives in the ICU experience (30,31). Educational attainment ($\beta=0.31$, $p=0.002$) was another significant factor, with university-educated individuals reporting higher satisfaction; which likely reflects the positive influence of education on information processing and engagement with healthcare processes.

The significant positive effects associated with the presence of a neurological disease ($\beta=0.28$, $p=0.004$) and female sex ($\beta=0.25$, $p=0.008$) suggest that satisfaction levels may be higher in contexts where family-centered care is emphasized and where comprehensive information and support are provided to relatives (30,32). The adoption of a family-centered approach in the neurology ICU where the study was conducted may have contributed to this finding by better informing and supporting relatives.

The identification of female gender as a factor increasing care satisfaction may be linked to observed tendencies among women to engage more deeply in the care process and communicate more effectively with healthcare providers. As supported by existing literature, women often assume a more active role in patient care, enabling them to navigate the ICU experience more consciously and derive greater satisfaction from the services received (21,31). The negative effect associated with a hospitalization duration of 10–13 days ($\beta=-0.22$, $p=0.018$) suggests that prolonged ICU stays may contribute to caregiver burnout and heightened stress, ultimately reducing satisfaction levels (28,32).

The analysis also indicated that younger age (20-30 years) and being the child of the patient had statistically significant, though relatively modest, positive effects on care satisfaction. The potentially greater comfort younger individuals have with digital information resources, their ability to communicate effectively with staff, and their possibly more flexible expectations could contribute to higher reported satisfaction in this group (24,30). The positive effect associated with being the patient's child may be explained by the strong emotional bonds children often have with their parents, leading to heightened emotional investment and consequently higher satisfaction when their expectations for support and care are met (28,32).

This study establishes a strong positive association between knowledge of delirium and family satisfaction among relatives of ICU patients ($r=0.60$, $p<0.001$). Regression analysis identified delirium knowledge as the foremost predictor of satisfaction ($\beta=0.42$), alongside education level, gender, and the presence of neurological disease. These results strongly advocate for the development and implementation of structured education and support programs targeted at family members.

Study Limitations

Several limitations of this study should be acknowledged when interpreting its findings. The cross-sectional design precludes the establishment of causal relationships between family members' knowledge of delirium and their care satisfaction. As the research was conducted within a single tertiary care center, the generalizability of the results to other healthcare institutions or different cultural contexts may be limited. The reliance on self-reported questionnaires introduces the potential for recall bias and social desirability bias. Furthermore, the absence of data pertaining to the actual incidence and severity of delirium among the patients may have influenced the perceptions and experiences reported by family members. Future investigations employing multicenter, longitudinal designs and incorporating objective clinical metrics are warranted to validate and extend upon these findings.

Conclusion

This cross-sectional study demonstrates that knowledge levels regarding delirium among relatives of intensive care patients are generally inadequate and that this deficit exerts a significant negative impact on family care satisfaction. The findings indicate that improving awareness and understanding of delirium represents a key modifiable factor capable of enhancing satisfaction with care.

Our results support the necessity of integrating standardized educational modules on delirium for families into routine ICU protocols and fortifying family-centered care frameworks with specific components addressing delirium management. Specifically, targeted educational programs focusing on delirium prevention, recognition, and management are anticipated to yield higher care satisfaction scores.

For future research, randomized controlled trials are recommended to evaluate the causal nature of this relationship and to assess the generalizability of these findings across diverse clinical and cultural settings.

Ethics

Ethics Committee Approval: This study received approval from the Non-Interventional Clinical Ethics Committee of İnönü University (desicion number: 2024-6/1, date: 14.01.2024). Formal institutional permission was also obtained from the administration of the Turgut Özal Medical Center.

Informed Consent: Voluntary informed consent was provided for participation.

Footnotes

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Investigation of the Relationship Between Serum Subfatin Levels and Clinical Outcome in Patients with Transient Ischemic Attack in the Emergency Department

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Abstract

Aim: We hypothesized that lower serum subfatin levels at admission might be associated with a higher risk of subsequent stroke in transient ischemic attack (TIA) patients. Therefore, this study aimed to examine the relationship between baseline subfatin levels and the occurrence of new cerebrovascular events at 28 and 90 days.

Materials and Methods: Patients who were admitted to the emergency department and diagnosed with TIA between 01.04.2022 and 31.03.2023 were studied prospectively.

Results: A total of 141 volunteers (71 patients and 70 controls) who met the criteria were included in the study. The median subfatin level of the patients was 1.51 [interquartile range (IQR): 25-75: 1.27-1.71] and the median subfatin level of the control group was 1.62 (IQR: 25-75: 1.13-2.32). There was a statistically significant association between coronary artery disease (CAD) and stroke development at 28 and 90 days [($p<0.05$), ($p<0.05$)]. Median subfatin levels were numerically lower in patients who experienced stroke within 28 and 90 days compared to those without subsequent stroke; however, these differences did not reach statistical significance ($p>0.05$). Therefore, no definitive conclusion can be drawn regarding the prognostic role of subfatin in this cohort.

Conclusion: CAD was significantly associated with stroke occurrence at both 28 and 90 days, underscoring its role as a major predictor of adverse outcome in TIA patients. We also found that although subfatin levels were lower in patients who had a stroke within 28 and 90 days compared to patients who did not have a stroke, there was no statistically significant difference between them.

Keywords: Emergency department, transient ischemic attack, subfatin, stroke

Introduction

Transient ischemic attack (TIA) is defined as a clinical picture of sudden onset and neurological deficits resulting from a transient decrease in blood flow to a specific area of the brain. It usually resolves spontaneously within 24 hours and is distinguished from stroke by these characteristics (1). However, the risk of stroke is significantly higher in individuals with TIA compared to the general population. The risk of stroke within the first 48 hours of TIA varies between 10-15% and this rate increases even more in the first week (2). Therefore, early evaluation, risk assessment and clinical follow-up of patients

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with TIA is critical to prevent more serious complications such as stroke (3).

In recent years, inflammation, oxidative stress and vascular dysfunction have been recognized to play important roles in the pathophysiology of TIA and stroke. In this context, the effects of adipokines (adipose tissue-derived hormones) on the central nervous and cardiovascular systems are of increasing interest (4). Adipokines are involved in various biological processes associated with cardiovascular diseases, obesity and metabolic syndrome. One adipokine, subfatin (C1q/tumor necrosis factor-related protein 13), is involved in many metabolic processes such as energy homeostasis, inflammation and insulin sensitivity. It has also been reported that subfatin levels may be associated with atherosclerosis and cardiovascular diseases (5). However, the relationship between subfatin levels and risk factors for TIA and stroke has not been fully elucidated and research on this subject is limited.

Investigating the possible effects of subfatin on the process of brain ischemia may contribute to the prediction of stroke risk in patients with TIA. It is thought that subfatin levels may affect neuroinflammation, oxidative stress, and endothelial dysfunction, processes that play critical roles in ischemic events (6). Therefore, examining the association of biomarkers such as subfatin with stroke risk may contribute to the identification of individuals at high risk after TIA and the development of strategies that can guide the management of these patients. This study aimed to investigate the relationship between subfatin levels and the clinical outcome of patients with TIA.

Materials and Methods

Place, Time and Type of Study

This study was conducted in the emergency department of University of Health Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital with the approval of the clinical research ethics committee with the (desicion number: 2011-KAEK-25 2022/03-08, date: 23.1.2011), patients with a final emergency department diagnosis of TIA were prospectively analyzed.

Inclusion and Exclusion Criteria

Inclusion Criteria

Patient group;

1. Patients over 18 years of age,
2. Patients with normal radiologic imaging results,
3. Patients who gave consent to the study by themselves or their relatives were included.

In the control group, patients over 40 years of age, who had no comorbidities, and gave consent to the study, were included.

Exclusion Criteria in the Study

Patient group;

1. Patients younger than 18 years of age,
2. Patients who did not give consent to the study,
3. Patients with infarction detected on radiologic imaging,
4. Patients with bleeding detected on radiologic imaging,
5. Patients with a mass detected on radiologic imaging,
6. Pregnant patients,
7. Those with previous cerebrovascular disease were not included in the study.

In the control group, those under 40 years of age, pregnant women, and those with any comorbidities were excluded.

Work Plan

A standardized study data entry form was created for the data of the patients included in the study. Demographic information (age, gender), height, weight, body mass index, date of presentation to the emergency department (ED), vital signs (fever, respiratory rate in minutes, fingertip oxygen saturation in room air and with oxygen supplementation, systolic blood pressure), data such as diastolic blood pressure, complaints at admission, chronic diseases, medications and radiologic imaging, and the patient's outcome in the ED (discharge, admission, intensive care unit admission, excitus, treatment refusal) were recorded. In addition, patients or their relatives were contacted on days 28 and 90 and asked whether they had a new stroke attack. After the study was completed, the data in the study forms obtained were saved in electronic format for statistical analysis.

Laboratory Studies

Complete blood count, serum electrolytes (Na, Cl), renal function tests (blood urea nitrogen and creatinine), cardiac troponin, international normalized ratio levels were obtained from the patients participating in the study. To study METRNL (subfatin) level, 3 mL blood samples were collected into aprotinin tube (tube containing 500 KIU aprotinin to protect blood pretolysis).

Blood samples were allowed to clot for 30 minutes and then centrifuged at 3000 rpm for 10 minutes at room temperature. The serum obtained was portioned and stored at -80 degrees Celsius for subfatin level studies.

Human METRNL levels were determined by ELISA method in the biochemistry laboratory of S University of Health Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital. The ELISA kit used was Shanghai Biotechnology Co. Brand, produced in Yunnan, People's Republic of China, and the unit for Human METRNL is ng/mL. Baoshan, Romer, ChroMate 4300 ELISA reader, manufactured in Getzdersof /Austria, was used. ELISA method was performed according to the kit procedure as follows:

- Standards were prepared as recommended in the procedure. For this study, double standards and double blinds were used in each kit.
- 50 µL of the blind and standards were added to the appropriate wells. Then 40 µL of sample sera were added to the appropriate wells.
- Then 10 µL of biotin-METRNL antibody was added to the sample wells.
- 50 µL of Str-HRP-Conjugate Reagent was added to the standard and sample wells. No HRP solution was added to the blinds. The wells were then covered with a cover plate, shaken gently and incubated in an oven at 37 °C for 60 min.
- After removing from the oven, the sample was emptied. Then, 350 µL of 30 times diluted washing solution was added to each well and washed 5 times.
- After washing, 50 µL of cromogen A solution was added to each well. Then 50 µL of choromogen B solution was added to each well in dim light. The wells were covered with a cover plate, shaken gently and incubated in the dark at 37 °C for 10 min in an oven.
- The reaction was terminated by adding 50 µL of stop solution to each well. Measurement was performed at 450 nm on a ChroMate-4300 microplate reader.

Statistical Analysis

IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp. Armonk, NY: USA. Released 2012) package program was used for statistical analyses. Descriptive statistics were expressed as mean ± standard deviation, median and range and/or interquartile range (IQR) for numerical variables, while categorical variables were expressed as number of cases and (%). Kolmogorov-Smirnov test was used for normality distribution of the data. Levene's test was used to determine whether the assumption of homogeneity of variances was met. The significance of the difference between the groups in terms of continuous numerical variables for which parametric test statistical assumptions were met was examined by Student's t-test. Significance of the difference in terms of continuous numerical variables for which parametric test statistical assumptions were not met was evaluated by Mann-Whitney U test. Kruskal-Wallis test was used for comparisons of three or more groups. Pearson correlation analysis was used to evaluate the relationships between parametric distributed data and Spearman's correlation analysis was used to evaluate the relationships between non-parametric distributed data. Fisher's exact test was used to analyze whether there was a relationship between categorical variables. $P<0.05$ was considered statistically significant. Results were given at 95% confidence interval.

Results

A total of 141 volunteers, including 71 patients and 70 controls, who met inclusion criteria were included in the study. The mean age of the patient group was 64.15±13.11 years and the mean age of the control group was 50.13±11.20 years. Forty-one (57.7%) of the patient group and 50 (71.4%) of the control group were male. It was found that 58 (81.7%) of the patients had comorbidities and the most common comorbidities were hypertension (n=35, 49.3%) and diabetes mellitus (n=26, 36.6%). Stroke developed within 28 days in 12 (16.9%) and within 90 days in 14 (19.7%) patients (Table 1).

The median subfatin level of the patients was 1.51 (IQR: 25-75: 1.27-1.71) and the median epicardial adipose tissue thickness was 0 mm (IQR: 25-75: 0-0.6), while the median subfatin level of the control group was 1.62 (IQR: 25-75: 1.13-2.32) and the median epicardial adipose tissue thickness was 0.3 mm (IQR: 25-75: 0.2-0.4).

While there was no statistically significant difference between the median subfatin levels of the patient group and the control group ($p>0.05$), the median epicardial adipose tissue thickness was found to be statistically significantly different ($p<0.001$) (Table 2).

In the analysis performed to determine the relationship between gender, comorbidities, medication use, electrocardiogram (ECG) findings, antiaggregant and anticoagulant use and stroke development in 28 days, a statistically significant relationship was found between coronary artery disease (CAD) and stroke development in 28 days ($p<0.05$). The stroke rate within 28 days was higher in patients with CAD (Table 3).

In the analysis performed to determine the relationship between gender, comorbidities, medication use, ECG findings, antiaggregant and anticoagulant use and stroke development in 90 days, a statistically significant relationship was found between CAD and stroke development in 90 days ($p=0.005$).

Table 1. Clinical and demographic information		
Patient group age (years)*		64.15±13.11
Control group age (years)*		50.13±11.20
Patient group gender#	Male	41 (57.7)
	Female	30 (42.3)
Control group gender#	Male	50 (71.4)
	Female	20 (28.6)
Comorbidities#		58 (81.7)
Comorbidities#	Hypertension	35 (49.3)
	Diabetes mellitus	26 (36.6)
	Coronary artery disease	18 (25.4)
	Arrhytmia	2 (2.8)
	Malignity	2 (2.8)
	Valvular diease	2 (2.8)
	Congestive heart failure	1 (1.4)
	Asthma/COPD	4 (5.6)
	Chronic kidney disease	1 (1.4)
	Others	16 (22.5)
Use of medication for comorbidity#		52 (73.2)
Antiaggregant drug use#		19 (26.8)
Anticoagulant drug use#		2 (2.8)
Electrocardiography findings #	Normal sinus rhythm	52 (73.2)
	Atrial fibrillastion	9 (12.7)
	Left bundle branch block	6 (8.5)
	Others	4 (5.6)
Emergency department outcome#	Admission	67 (94.4)
	Others	4 (5.6)
Stroke within 28 days		12 (16.9)
Stroke within 90 days		14 (19.7)
Total number of patients#		71 (100)

#n (%), *Mean ± SD, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation

The rate of stroke within 90 days was found to be higher in patients with CAD (Table 4).

In the analysis performed to investigate whether there was a difference between subfatin levels and stroke status of the patients within 28 and 90 days, no statistically significant difference was found between subfatin levels and stroke status of the patients within 28 and 90 days (Table 5).

Discussion

Stroke is one of the leading causes of mortality and morbidity worldwide. TIA is a real neurological emergency due to the increased risk of stroke in patients after TIA. Many imaging methods and scoring systems are used to assess the risk of stroke after TIA. There are studies showing that these diagnostic methods are inadequate (2). In this study, we evaluated the effectiveness of serum subfatin level in determining the risk of stroke after TIA.

Hypertension is the most common comorbid disease in participants diagnosed with TIA. In our study, 81.7% of the patients had comorbid diseases and the most common comorbid disease was hypertension with a rate of 49.3%. In the study conducted by Wilson et al. (7) hypertension was found to be the most common comorbid disease with 73.5%. In a study by Kapral et al. (8) hypertension was found to be the most common comorbid disease with a rate of 66%. Our findings in this regard are consistent with other studies in the literature.

Table 2. Clinical and laboratory data of participants			
Variables	**Patient group**	**Control group**	**p value**
Age, years[&]	64.15±13.11	50.13±11.20	**<0.001**[*]
Subfatin level[ε]	1.51 (1.27-1.71)	1.62 (1.13-2.32),	>0.05[#]
Height, cm[&]	166.65±8.20	170.79±7.80	**=0.002**[*]
Weight, kg[&]	74.76±14.50	77.64±12.33	>0.05[*]
BMI[&]	26.85±4.33	26.55±4.37	>0.05[*]
Fever, C[ε]	36.2 (36.2-36.4)	36.3 (36.2-36.5)	>0.05[#]
Pulse /mi [&]	85.82±11.81	78.83±7.58	**<0.001**[*]
SBP mm/Hg[&]	145.48±22.55	127.30±6.20	**<0.001**[*]
DBP mm/Hg[&]	83.42±15.32	77.96±7.37	**=0.008**[*]
Oxygen saturation[ε]	97 (96-98)	97 (96-98)	>0.05[#]
Respiratory rate /min[ε]	14 (13-15)	12 (12-13)	**<0.001**[#]
Epicardial adipose tissue thickness/mm	0 (0-0.6)	0.3 (0.2-0.4)	**<0.001**[#]
Left ventricle end – systolic diameter/cm	3.68±0.70	2.80±0.28	**<0.001**[*]
Left ventricle end – diastolic diameter/cm	4.59±0.55	4.38±0.37	**<0.05**[*]
Left atrium diameter/cm	3.49±0.38	3.32±0.28	**=0.003**[*]
Ascending aorta diameter/cm	3.38±0.30	3.22±0.29	**=0.002**[*]
Ejection fraction[ε]	55 (50-60.0)	60 (60-60)	**<0.001**[#]
$ABCD^2$ score[ε]	4 (3-5)		
Leukocyte count[&]	8871.1±2649.9		
Neutrophil count[&]	5649.0±2217.9		
Lymphocyte count[ε]	2350 (1580-3140)		
MPV[&]	10.61±1.25		
Platelet count[&]	244940±76574		
INR[ε]	0.97 (0.89-1.08)		
Glukose/mg/dL	122 (103-143)		
Sodium/mmol/L	138.46±2.64		
Clor/mmol/L	104,62 ±3.49		
BUN/mg/dL	17 (13-23)		
Kreatinin/U/L	0.89 (0.68-1.07)		
Troponin/ng/L	4.80 (1.87-10.05)		

[ε]Median IQR (25-75), [&]Mean ± SD, [*]Student t-test, [#]Mann-Whitney U test, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MPV: Mean platelet volume, BUN: Blood urea nitrogen, INR: International normalized ratio, SD: Standard deviation, IQR: Interquartile range

This may be due to the fact that hypertension disrupts the endothelial structure and leads to atherosclerosis formation.

In our study, there was a statistically significant association between CAD and stroke development at 28 and 90 days. In the study by Amarenco et al. (9) taking those without CAD as reference, the age- and sex-adjusted risk ratio of vascular events was 2.10 (0.63-6.96) for asymptomatic coronary stenosis <50%, 4.36 (1.35-14.12) for asymptomatic coronary stenosis ≥50% and 6.86 (2.15-21.31) for known CAD (9). Another study by Robinson et al. (10) also found an increased risk of stroke in patients with a history of CAD. The findings of our study are consistent with the literature.

In untreated TIAs, the risk of stroke at 3 months can reach up to 20%. Most of this risk occurs in the first 10 days, especially in the first 2 days (2,11,12). Observational data show that rapid clinical diagnosis and immediate preventive measures reduce the 3-month stroke risk by up to 80% (13). In a multicenter study in which patients with suspected TIA or mild stroke were rapidly triaged, evaluated and treated, the 3-month stroke risk was found to be approximately 5% (12). In some studies, the risk of

Table 3. Fisher's exact test of variables with stroke within 28 days						
Variables			**Stroke within 28 days**		**Total**	**Fisher's exact test**
			No	**Yes**		
Gender	Female	n (%)	25 (83.3)	5 (16.7)	30 (100)	p>0.05
	Male	n (%)	34 (82.9)	7 (17.1)	41 (100)	
Accompanying disease	No	n (%)	12 (92.3)	1 (7.7)	13 (100)	p>0.05
	Yes	n (%)	47 (81.0)	11 (19.0)	58 (100)	
Hypertension	No	n (%)	30 (83.3)	6 (16.7)	36 (100)	p>0.05
	Yes	n (%)	29 (82.9)	6 (16.1)	35 (100)	
Coronary artery disease	No	n (%)	47 (88.7)	6 (11.3)	53 (100)	p<0.05
	Yes	n (%)	12 (66.7)	6 (33.3)	18 (100)	
Diabetes mellitus	No	n (%)	37 (82.2)	8 (17.8)	45 (100)	p>0.05
	Yes	n (%)	22 (84.6)	4 (15.4)	26 (100)	
Congestive heart failure	No	n (%)	58 (82.9)	12 (17.1)	70 (100)	p>0.05
	Yes	n (%)	1 (100)	0	1 (100)	
Arrhytmia	No	n (%)	57 (82.6)	12 (17.4)	69 (100)	p>0.05
	Yes	n (%)	2 (100)	0	2 (100)	
COPD/asthma	No	n (%)	55 (82.1)	12 (17.9)	67 (100)	p>0.05
	Yes	n (%)	4 (100)	0	4 (100)	
Malignity	No	n (%)	57 (82.6)	12 (17.4)	69 (100)	p>0.05
	Yes	n (%)	2 (100)	0	2 (100)	
Chronic renal failure	No	n (%)	58 (82.9)	12 (17.1)	70 (100)	p>0.05
	Yes	n (%)	1 (100)	0	1 (100)	
Valvular heart disease	No	n (%)	57 (82.6)	12 (17.4)	69 (100)	p>0.05
	Yes	n (%)	2 (100)	0	2 (100)	
Others	No	n (%)	48 (87.3)	7 (12.7)	55 (100)	p>0.05
	Yes	n (%)	11 (68.8)	5 (31.3)	16 (100)	
Medication use	No	n (%)	17 (89.5)	2 (10.5)	19 (100)	p>0.05
	Yes	n (%)	42 (80.8)	10 (19.2)	52 (100)	
Antiagregant	No	n (%)	45 (86.5)	7 (13.5)	52 (100)	p>0.05
	Yes	n (%)	14 (73.7)	5 (16.3)	19 (100)	
Anticoagulant	No	n (%)	57 (82.6)	12 (17.4)	69 (100)	p>0.05
	Yes	n (%)	2 (100)	0	2 (100)	
Electrocardiography	Normal sinus rhythm	n (%)	43 (82.7)	9 (17.3)	52 (100)	p>0.05
	Atrial fibrillation	n (%)	9 (100)	0	9 (100)	
	Left bundle branch block	n (%)	4 (66.7)	2 (33.3)	6 (100)	
	Others	n (%)	3 (75.0)	1 (25.0)	4 (100)	
Total		n (%)	59 (83.1)	12 (16.9)	71 (100)	

COPD: Chronic obstructive pulmonary disease

an acute ischemic stroke after TIA varies between 3.5%-10% in the first 2 days and 9.2%-17% in the first three months (14-17). In our study, the stroke rate was 16.9% within 28 days and 19.7% within 90 days. The reason why these rates were partially high may have been due to post-discharge treatment non-compliance and existing comorbidities in these patients.

Subfatin is an adipokine that has been discovered in recent years and is thought to play a role in various metabolic and inflammatory processes. This protein secreted by adipose tissue plays important roles in many disease processes such as obesity, diabetes and cardiovascular diseases. It has also been suggested that subfatin may be involved in vascular inflammation, endothelial dysfunction and atherosclerotic processes. In a study

Table 4. Fisher's exact test of variables with stroke within 90 days						
Variables			**Stroke within 90 days**		**Total**	**Fisher's exact test**
			No	**Yes**		
Gender	Women	n (%)	24 (80.0)	6 (20.0)	30 (100)	p>0.05
	Men	n (%)	33 (80.5)	8 (19.5)	41 (100)	
Accompanying disease	No	n (%)	12 (92.3)	1 (7.7)	13 (100)	p>0.05
	Yes	n (%)	45 (77.6)	13 (22.4)	58 (100)	
Hypertension	No	n (%)	30 (83.3)	6 (16.7)	36 (100)	p>0.05
	Yes	n (%)	27 (77.1)	8 (22.9)	35 (100)	
Coronary artery disease	No	n (%)	47 (88.7)	6 (11.3)	53 (100)	p<0.05
	Yes	n (%)	10 (55.6)	8 (44.4)	18 (100)	
Diabetes mellitus	No	n (%)	36 (80.0)	9 (20.0)	45 (100)	p>0.05
	Yes	n (%)	21 (80.8)	5 (19.2)	26 (100)	
Congestive heart failure	No	n (%)	56 (80.0)	14 (20.0)	70 (100)	p>0.05
	Yes	n (%)	1 (100)	0	1 (100)	
Arrhytmia	No	n (%)	55 (79.7)	14 (20.3)	69 (100)	p>0.05
	Yes	n (%)	2 (100)	0	2 (100)	
COPD/asthma	No	n (%)	53 (79.1)	14 (20.9)	67 (100)	p>0.05
	Yes	n (%)	4 (100)	0	4 (100)	
Malignity	No	n (%)	55 (79.7)	14 (20.3)	69 (100)	p>0.05
	Yes	n (%)	2 (100)	0	2 (100)	
Chronic renal failure	No	n (%)	56 (80.0)	14 (20.0)	70 (100)	p>0.05
	Yes	n (%)	1 (100)	0	1 (100)	
Valvular heart disease	No	n (%)	55 (79.7)	14 (20.3)	69 (100)	
	Yes	n (%)	2 (100)	0	2 (100)	p>0.05
Others	No	n (%)	47 (85.5)	8 (14.5)	55 (100)	p>0.05
	Yes	n (%)	10 (62.5)	6 (37.5)	16 (100)	
Medication use	No	n (%)	17 (89.5)	2 (10.5)	19 (100)	p>0.05
	Yes	n (%)	40 (76.9)	12 (23.1)	52 (100)	
Antiagregant	No	n (%)	44 (84.6)	8 (15.4)	52 (100)	p>0.05
	Yes	n (%)	13 (68.4)	6 (31.6)	19 (100)	
Anticoagulant	No	n (%)	55 (79.7)	14 (20.3)	69 (100)	p>0.05
	Yes	n (%)	2 (100)	0	2 (100)	
Electrocardiography	Normal sinus rhythm	n (%)	42 (80.8)	10 (19.2)	52 (100)	p>0.05
	Atrial fibrillation	n (%)	8 (88.9)	1 (11.1)	9 (100)	
	Left bundle branch block	n (%)	4 (66.7)	2 (33.3)	6 (100)	
	Others	n (%)	3 (75.0)	1 (25.0)	4 (100)	
Total		n (%)	57 (80.3)	14 (19.7)	71 (100)	

COPD: Chronic obstructive pulmonary disease

Table 5. Analysis of the variables with subfatin levels				
Variables		**N**	**Subfatin level#**	**p value***
Stroke within 28 days	No	59	1.53 (1.23-1.73)	>0.05
	Yes	12	1.45 (1.33-1.58)	
Stroke within 90 days	No	57	1.51 (1.22-1.72)	>0.05
	Yes	14	1.47 (1.38-1.61)	

*Mann-Whitney U test, #Median interquartile range (25-75)

by Cavli et al. (18) investigating obesity/insulin resistance and subfatin levels, a significant relationship was found between low serum subfatin levels and obesity/insulin resistance. In another study by Köse et al. (19), the relationship between subfatin and preeclampsia was investigated and serum subfatin level was found to be significantly lower in preeclampsia patients compared to the control group. In the study by Demir et al. (20) investigating the relationship between ischemic stroke and serum subfatin level, no significant relationship was found. In the study by Yilmaz et al. (21) investigating subfatin levels in patients with acute coronary syndrome, subfatin levels were found to be lower in patients with non-ST elevation myocardial infarction and ST elevation myocardial infarction compared to the control group (21). In a study by Albayrak et al. (22), subfatin levels were found to be lower in patients with cerebral ischemia, intracerebral hemorrhage and subarachnoid hemorrhage compared to the control group.

In our study, although no significant difference was found between the plasma subfatin values of the patients and their stroke status on days 28 and 90, the mean serum subfatin values of the patients who had a stroke were lower than the mean serum subfatin values of the patients who did not have a stroke.

In conclusion, no significant relationship was found between serum subfatin levels and stroke in patients diagnosed with TIA in the ED. While a decrease in subfatin level poses a risk for conditions such as inflammation, endothelial damage and plaque formation, the lack of statistical difference in subfatin levels between the patient group and the control group in our study may be explained by the fact that no pathology was detected on imaging in the patient group diagnosed with TIA. The fact that serum subfatin levels were found to be low in clinical conditions such as obesity, insulin resistance and preeclampsia, which have been previously reported in the literature, suggests that this molecule may be used as a negative acute phase reactant in the future. More significant results may be obtained as the research on subfatin accumulates. Our study contributes to the literature as being the first study investigating the relationship between TIA and subfatin levels.

Study Limitations

The single-center nature of our study restrained the number of patients included. In addition, the relatively short follow-up duration of the patients, such as stroke status on days 28 to 90, may have prevented a clear demonstration of the relationship between subfatin and TIA. As control group formed with healthy individuals without known comorbidities, mean age of the control group was significantly lower than that of patient group. This is also one of the limitations of our study.

Conclusion

In our study, we found that CAD increased the risk of stroke in patients with TIA. We also observed that there was no significant difference between the subfatin levels of the patient and control groups. Finally, there was no significant difference between the subfatin levels measured at the time of admission in patients with TIA who had a stroke within 28 and 90 days and those who did not. Further research, conducted in a multi – center design, with larger patient groups and a longer follow – up period is needed on this inquiry.

Ethics

Ethics Committee Approval: This study was conducted in the emergency department of University of Health Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital with the approval of the clinical research ethics committee with the (desicion number: 2011-KAEK-25 2022/03-08, date: 23.1.2011).

Informed Consent: Patients who gave consent to the study by themselves or their relatives were included.

Footnotes

Author Contributions

Surgical and Medical Practices: S.Ç., M.Y., Y.İ., O.Ö., Z.E., K.H., A.Z., Concept: S.Ç., M.Y., M.O.A., Y.İ., O.Ö., Ö.F.D., K.H., A.Z., Design: S.Ç., M.Y., Y.İ., H.K., O.Ö., Z.E., Ö.F.D., D.Y., A.Z., Data Collection or Processing: S.Ç., M.Y., M.O.A., Z.E., Ö.F.D., D.Y., A.Z., Analysis or Interpretation: S.Ç., M.Y., M.O.A., Y.İ., H.K., Ö.F.D., D.Y., Literature Search: S.Ç., M.Y., O.Ö., Z.E., D.Y., K.H., Writing: S.Ç., M.Y., M.O.A., Y.İ., Z.E., K.H., A.Z.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Quantitative Assessment of Lung and Infiltration Volumes on Chest CT for Predicting Clinical Severity and Mortality in Viral Pneumonia: Insights from COVID-19 Experience

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Abstract

Aim: This study aimed to evaluate the relationship between lung volume, infiltration volume, and percentage of involvement with laboratory findings, hospitalization status, and mortality in patients with pneumonia.

Materials and Methods: This retrospective and observational study was conducted on 125 patients who presented to the emergency department between January and June 2021 and had pulmonary infiltration detected on chest computed tomography. The patients' lung volume, infiltration volume, and percentage of involvement were assessed along with laboratory parameters, hospitalization level, and mortality status.

Results: Among the 125 patients included, 56.8% were male and 43.2% were female, with a mean age of 49.8±14.4 years. Severity categories were as follows: mild in 85 (68.0%), moderate in 23 (18.4%), and severe in 17 (13.6%) patients. The mean total lung volume was 3034.4±1271.9 mL overall, 3398.7±1346.7 mL in the mild group, and 2192.9±466.8 mL in the severe group ($p<0.001$). The mean infiltration volume was 271.4±309.3 mL overall, 97.2±77.9 mL in the mild group, 456.7±162.9 mL in the moderate group, and 891.9±231.1 mL in the severe group ($p<0.001$). Mortality rates were 1.2% in the mild group, 30.4% in the moderate group, and 70.6% in the severe group, showing a direct association between mortality and the severity of involvement ($p<0.001$). Age, severity of involvement, C-reactive protein (CRP), and troponin levels were positively correlated with mortality.

Conclusion: In pneumonia cases, reduced lung volume, increased infiltration volume, and a higher percentage of lung involvement are predictive of mortality. Additionally, elevated CRP and troponin levels show a significant correlation with both the percentage of involvement and mortality.

Keywords: Emergency department, lung volume, pneumonia, involvement volume, mortality, COVID-19

Introduction

The chest imaging features associated with this lethal disease are crucial for achieving accurate and early diagnosis of coronavirus disease 2019 (COVID-19) (1). However, accurately predicting the impact of a disease on a patient's life, which includes both the likelihood of mortality and the severity of the illness, can be difficult. This can result in a variety of outcomes, including the absence of symptoms and severe and potentially fatal consequences. The diagnostic approach is based on a combination of factors, including a patient's history of exposure, clinical features, reverse transcription polymerase chain reaction (RT-PCR) testing, chest X-ray (CXR), and computed tomography (CT) of the thorax (2).

Microbiological testing, specifically real-time polymerase chain reaction (RT-PCR) or sequencing methodologies, is the gold standard for COVID-19 verification. Samples from the respiratory tract are used to conduct these procedures (3). CXR can be employed as the initial imaging method in COVID-19 pneumonia because it is simpler to clean the device, allows for bedside application, and contains lower radiation doses. Nevertheless,

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its sensitivity is lower than that of CT because low densities are challenging to detect and may be considered normal in the early stages (4). The chest CT is employed as a diagnostic instrument for COVID-19 patients to evaluate the severity of the disease, identify diagnostic challenges, and select the most suitable treatment approach. COVID-19 pneumonia is frequently characterized by bilateral multifocal peripheral ground-glass opacities, as evidenced by a chest CT scan (5). In comparison to RT-PCR, chest CT imaging may provide a more reliable, convenient, and rapid method for the diagnosis and evaluation of COVID-19 (6).

The detailed examination of tomographic imaging, which has made a significant contribution to diagnosis and treatment, has been necessary over time. Hospitals are able to prioritize medical efforts, particularly when human resources are scarce, by classifying the severity of COVID-19 in at-risk patients. Numerous studies have developed severity score systems to evaluate the extent of COVID-19 pulmonary involvement (7-10). Although these scores enhanced the assessment of COVID-19 severity, they were not without their limitations. They require time due to their complexity. Evaluation is difficult, due to the extensive scoring in specific scores that range from 20 to 40 regions. Secondly, the right lung is larger than the left lung in overall size, not in terms of chambers or segments. Dedicated software and a trained operator are necessary even for quantitative methodologies that quantify pneumonic lesion volume (11,12).

This study aimed to illustrate the influence of this involvement percentage (IP) on clinical and mortality outcomes in light of the previous findings. This was achieved by calculating the ratio of the involvement volume to the total volume of the patient's lung in a more consistent manner, irrespective of the segment, lobe, or side.

Materials and Methods

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and with the consent of the Institutional Ethics Committee (protocol code: 129, date: 15.03.2021) prior to its commencement.

Study Design and Data

This retrospective and observational study was conducted in the emergency department of a tertiary training and research hospital between January 1 and June 30, 2021. During this period, a total of 2911 consecutive adult patients (≥18 years) who underwent both RT-PCR testing for SARS-CoV-2 and chest CT at their initial emergency department presentation were screened for eligibility.

According to the World Health Organization definition, only patients with a positive RT-PCR result were considered confirmed COVID-19 cases. Therefore, RT-PCR–negative patients were excluded prior to eligibility assessment. Subsequently, a series of exclusion criteria were applied to ensure data consistency and homogeneity of the study population.

Hospitalization level (general ward vs. intensive care unit) and mortality outcomes were extracted from the institutional electronic medical record system and verified with patient follow-up documentation. Quantitative CT parameters—including lung volume (LV), infiltration volume (IV), and [IP = (IV/LV) × 100]—were recorded for each patient. For interpretability, LV was categorized as 1000-2000, 2000–3000, 3000-4000, and >4000 mL, and IP was used to classify involvement severity (IS) as mild (0-15%), moderate (15-30%), and severe (>45%).

Inclusion and Exclusion Criteria

Patients aged 18 years or older with a positive RT-PCR test result for SARS-CoV-2 and evidence of parenchymal infiltration on chest CT—manifesting as ground-glass opacity and/or consolidation—were included in the study. Only those with complete demographic, laboratory, imaging, and outcome data were eligible for analysis. Patients were excluded if they had a negative RT-PCR result for SARS CoV-2 (n=1387), no parenchymal infiltration on CT (n=534), or incomplete or poor-quality imaging and/or missing laboratory data, including cases with motion artifacts or inadequate CT coverage (n=428). Additionally, individuals with known chronic comorbidities such as chronic obstructive pulmonary disease, congestive heart failure, malignancy, or chronic kidney disease (n=268), as well as those under 18 years of age (n=45) or duplicate/repeat hospital admissions (n=37), were excluded from the analysis.

After applying all exclusion criteria, 1.212 RT-PCR–positive patients remained eligible for inclusion. From this refined cohort, 125 patients were consecutively included according to the predefined inclusion criteria until the target sample size was reached (Figure 1). This approach ensured that cases were selected consecutively and without arbitrary sampling, thereby representing a clinically and temporally unbiased subset of COVID-19 pneumonia patients during the study period.

Power Analysis

Prior to analysis, a sample size justification was performed using G* Power version 3.1. The primary endpoint was in-hospital mortality, with quantitative CT metrics (IV and IP) as the main predictors. A logistic regression framework was adopted, assuming:

Two-tailed α=0.05

Statistical power (1-β)=0.80

Expected effect size [odds ratio (OR) ≈ 1.8 per SD change in IP]

Anticipated mortality rate=15-20%, consistent with prior emergency department data

Based on these assumptions, the minimum requisite sample size was calculated to be between 110 and 130 individuals, which corresponds to our final cohort of 125 patients. A post hoc power analysis utilizing the observed area under the ROC curve [area under the curve (AUC) =0.92, where IV predicted mortality] confirmed a power exceeding 0.90, hence validating the statistical sensitivity for the study's primary purpose. The study population and sample size were considered methodologically sound and aligned with established norms for retrospective observational research.

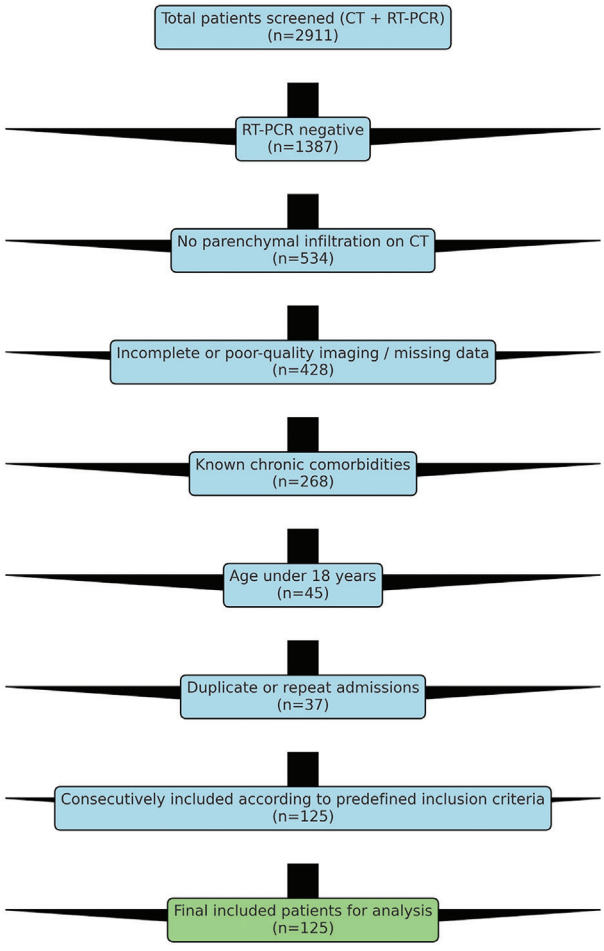

Figure 1. Patient selection flow diagram

CT: Computed tomography, RT-PCR: Reverse transcription polymerase chain reaction

Laboratory Analysis

Laboratory data were obtained from the institutional electronic medical record system, including white blood cell (WBC) count, creatinine (CRE), alanine aminotransferase, aspartate aminotransferase (AST), C-reactive protein (CRP), and troponin (TRP) values for each case. Complete blood count analyses were performed using the Sysmex DI-60 Hematology Analyzer (Sysmex Corp., Kobe, Japan), and biochemical parameters were measured with the Beckman Coulter AU-680 Automated Chemistry Analyzer (Beckman Coulter, Inc., Fullerton, CA, USA). All hematologic and biochemical results were processed and reported within approximately 45-60 minutes after sample collection.

CT Imaging and Volume Calculation

All chest CT exams were conducted using a Siemens SOMATOM Edge 128-slice multidetector CT scanner (Siemens Healthcare GmbH, Erlangen, Germany). Scans were conducted in the supine position during a single inspiratory breath-hold. The imaging settings included collimation of 128 × 0.6 mm, a rotation duration of 1.0 s, a pitch of 0.8, a tube voltage of 120 kVp, and automatic tube current modulation. Image reconstruction was executed with a 5 mm slice thickness and a 3 mm interval, utilizing a high-resolution reconstruction kernel (B70f). The CTDIvol measured 4.3 mGy, and the DLP was 175 mGy·cm.

All volumetric analyses were performed using Siemens Syngo software. Employing the VB30 workstation, utilizing the "lung analysis" and "MM reading" modules for semi-automated three-dimensional segmentation. The lung parenchyma algorithm automatically segmented each lung according to voxel density distribution. Subsequent to automatic segmentation, the radiologist meticulously adjusted the contours to exclude significant arteries, bronchi, and pleural effusions as required.

The IV was measured using a voxel-based density thresholding method, wherein all lung voxels within the attenuation range of –750 to –300 hounsfield units (HUs) were classified as exhibiting inflammatory involvement (ground-glass opacity or consolidation). The software automatically calculated for each patient:

LV: The aggregate volume of aerated lung parenchyma (in mL).

IV: The total volume of voxels designated as infiltration within the specified HU range (in mL).

IP is determined using the formula, IP = (IV/LV) x100, which indicates the fraction of lung parenchyma impacted by inflammation.

All measures were conducted by two radiologists who have 10 years of expertise in thoracic imaging and who were unaware

of the clinical results. To guarantee intra-observer reliability, each segmentation and volume extraction was conducted twice, one week apart, and the mean data were utilized for statistical analysis. Inter-observer variability was not evaluated, as the complete dataset was examined by a single reader adhering to the defined workflow methods.

After volumetric analysis, the LV, IV and [IP = (IV/LV) × 100] were automatically calculated and recorded for each patient. To facilitate clinical interpretation, LV values were categorized into four subgroups (1000-2000 mL, 2000-3000 mL, 3000-4000 mL, and >4000 mL). Based on the IP values, the IS was classified as mild (0-15%), moderate (15-30%), and severe (>45%). Hospitalization and mortality data were obtained from the institutional electronic medical records and patient follow-up forms.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range) according to their distribution, while categorical variables were expressed as counts and percentages. Group comparisons were made using the Student's t-test or Mann-Whitney U test for continuous variables and the χ^2 test for categorical variables. To identify factors associated with disease severity and mortality, univariate logistic regression analyses were first performed. Variables with p<0.05 in the univariate analysis were subsequently entered into a multivariate logistic regression model to control for potential confounding effects. The variables tested included age, TRP, WBC count WBC, CRP, LV, IV, and IP. Results were expressed as ORs) with 95% confidence intervals (CIs). Model performance was further assessed using ROC curve analysis, and the AUC values, were calculated to evaluate the predictive accuracy of quantitative CT parameters for mortality. A two-tailed p-value<0.05 was considered statistically significant.

Results

The mean age of the 125 patients [71 (56.8%) male, 54 (43.2%) female] included in the study was 49.78±14.40 years and there were 85 (68.0%) mild, 23 (18.4%) moderate, 17 (13.6%) severe cases in the IS groups. It was observed that IS increased with increasing age (p<0.001). The increase in CRP and TRP levels also showed a significant relationship with IS (p<0.001). While LV was determined to be 3034.37±1271.86 ml in all cases, it was 3398.71±1346.68 ml in the mild group and 2192.87±466.78 mL in the severe group (p<0.001). In the IV evaluation, the mean IV value of the cases was 271.42±309.34 ml. In the mild group, it was 97.17±77.93 mL; in the moderate group, 456.73±162.91 mL; and in the severe group, 891.99±231.09 mL (p<0.001). IP values were 3.44±3.31, 19.71±3.71, and 40.80±6.59 in the groups, respectively (p<0.001) (Table 1).

When variables were evaluated according to mortality status, the mean age in the mortality group was 62.30±12.29 years (p<0.001). High CRP and TRP levels were also significantly associated with mortality (p<0.001). In the mortality group, LV was 2441.22±1057.59 ml (p<0.017). IV and IP were 743.99±331.16 mL and 33.01±12.61 % in the mortality group and 181.41±207 (21) mL and 7.42±9.59% in the survival group. Both were significantly higher in the mortality group (p<0.001) (Table 2).

Table 1. Age, laboratory and involvement data according to the severity of involvement

		Involvement severity			
	All patients n (%): 125 (100)	**Mild n (%): 85(68.0)**	**Moderate n (%): 23 (18.4)**	**Severe n (%): 17 (13.6)**	**p value***
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	
Age (year)	49.78±14.40	45.34±11.92	59.83±16.03	58.35±13.43	<0.001
WBC (10^3/UL)	7.26±3.75	6.47±2.65	7.64±3.20	10.66±6.51	0.027
CRE (mg/dL)	0.89±0.58	0.90±0.66	0.92±0.38	0.87±0.37	0.429
ALT (IU/L)	33.60±27.99	35.27±28.31	38.56±33.15	18.59±7.95	0.035
AST (IU/L)	43.93±32.31	44.14±26.91	56.52±51.19	25.82±10.61	0.014
CRP (mg/dL)	67.12±68.13	44.72±52.01	104.64±46.79	128.35±100.47	<0.001
TRP (ng/L)	20.33±95.86	4.83±3.68	8.38±8.26	114.03±245.45	<0.001
LV (mL)	3034.37±1271.86	3398.71±1346.68	2309.86±652.50	2192.87±466.78	<0.001
IV (mL)	271.42±309.34	97.17±77.93	456.73±162.91	891.99±231.09	<0.001
IP (%)	11.52±13.79	3.44±3.31	19.71±3.71	40.80±6.59	<0.001

*: Kruskal Wallis test, SD: Standart deviation, WBC: White blood cell, CRE: Creatinine, ALT: Alanine aminotransferase, AST: Aspartat aminotransferase, CRP: C-reactive protein, TRP: Troponin LV: Lung volume IV: Involvement volume IP: Involvement percentage

When the variables were evaluated for IS, no significance was found between gender and IS (p=0.180). In the severe group, 11 (64.7%) patients of 17 patients had LV between 2000-3000 mL, and 6 (35.3%) had LV between 1000-2000 mL. In the severe group, there was no patient with LV over 3000 mL. In the moderate group, there was no patient who had LV<4000 (p<0.001). In the mild group, there was no patient followed up in intensive care. Thirteen (56.5%) in the moderate group and 12 (70.6%) in the severe group were followed up in intensive care (p<0.001). Mortality was observed in 1 (1.2%) mild, 7 (30.4%) moderate, and 12 (70.6%) severe group cases, and increased with the severity of involvement (p<0.001) (Table 3).

Age, IS, CRP, and TRP revealed a strong positive correlation with mortality. While a strong negative correlation was determined between LV and mortality, a weak negative correlation was observed between AST and mortality (Table 4).

Table 2. Age, laboratory and involvement data according to mortality status

Mortality			
	No n (%): 105 (84.0)	**Yes n (%): 20 (16.0)**	**p value***
	Mean ± SD	**Mean ± SD**	
Age (year)	47.39±13.56	62.30±12.29	<0.001
WBC (10^3/UL)	6.65±2.60	10.45±6.49	0.053
CRE (mg/dL)	0.91±0.62	0.85±0.34	0.798
ALT (IU/L)	36.21±29.68	19.95±7.58	0.053
AST (IU/L)	47.15±34.09	27.00±9.69	0.005
CRP (mg/dL)	56.06±56.08	125.18±94.11	<0.001
TRP (ng/L)	5.08±3.59	100.43±227.74	<0.001
LV (mL)	3147.35±1282.11	2441.22±1057.59	0.017
IV (mL)	181.41±207.21	743.99±331.16	<0.001
IP (%)	7.42±9.59	33.01±12.61	<0.001

*: Mann-Whitney U tes test, SD: Standart deviation, WBC: White blood cell, CRE: Creatinine, ALT: Alanine aminotransferase, AST: Aspartat aminotransferase, CRP: C-reactive protein, TRP: Troponin LV: Lung volume IV: Involvement volume IP: Involvement percentage

Table 3. Evaluation of the involvement severity in gender, lung volume, hospitalization and mortality groups

		Involvement severity				
		Mild	**Moderate**	**Severe**	**All patients**	**p value***
		n (%)	**n (%)**	**n (%)**	**n (%)**	
Gender lung volume hospitalization mortality						
	Male	50 (58.8)	15 (65.2)	6 (35.3)	71 (56.8)	0.180
	Female	35 (41.2)	8 (34.8)	11 (64.7)	54 (43.2)	
	1000-2000	10 (11.8)	7 (30.4)	6 (35.3)	23 (18.4)	
	2000-3000	32 (37.6)	13 (56.5)	11 (64.7)	56 (44.8)	<0.001
	3000-4000	18 (21.2)	3 (13.0)	0 (0)	21 (16.8)	
	4000<	25 (29.4)	0 (0)	0 (0)	25 (20.0)	
	Inpatient service	85 (100)	10 (43.5)	5 (29.4)	100 (80.0)	<0.001
	Intensive care	0 (0)	13 (56.5)	12 (70.6)	25 (20.0)	
	No	84 (98.8)	16 (69.6)	5 (29.4)	105 (84.0)	<0.001
	Yes	1 (1.2)	7 (30.4)	12 (70.6)	20 (16.0)	
	Total	85 (100)	23 (100)	17 (100)	125 (100)	

*: Chi-square test

In the univariate logistic regression analysis, several clinical and radiological parameters—including age, TRP, CRP, IV, and IP— were found to be significantly associated with both disease severity and mortality ($p<0.05$ for each). When these variables were further evaluated in the multivariate logistic regression model, age, TRP, and IP remained independent predictors of mortality ($p<0.05$), whereas other factors lost statistical significance after adjustment for potential confounders. Among quantitative CT parameters, IP demonstrated the strongest independent association with mortality, indicating that a higher percentage of parenchymal involvement was linked to worse clinical outcomes (Table 5).

Table 4. Correlation of mortality status with variables

	Mortality	
	r	**p value***
Age	0.373	0.001
Gender	0.016	0.861
LV	-.210	0.019
IS	0.637	<0.001
WBC (10^3/UL)	0.174	0.053
CRE (mg/dL)	0.023	0.799
ALT (IU/L)	-0.174	0.052
AST (IU/L)	-0.255	0.004
CRP (mg/dL)	0.340	<0.001
TRP (ng/L)	0.362	<0.001

*Spearman's rho correlation, IS: Involvement severity, LV: Lung volume, WBC: White blood cell, CRE: Creatinine, ALT: Alanine aminotransferase, AST: Aspartat aminotransferase, CRP: C-reactive protein, TRP: Troponin

According to ROC curve analysis, the optimal cut-off values for affected volume and LV to predict mortality were identified with a threshold of 45%, yielding 97.1% sensitivity and 95.0% specificity for affected volume (AUC: 0.920; 95% CI: 0.847-0.992, $p<0.001$) and 81.9% sensitivity and 78.1% specificity for LV (AUC: 0.331; 95% CI: 0.213-0.450, $p=0.017$). (Figure 2). An IP cut off of 45% on initial chest CT predicted mortality with high accuracy (AUC: 0.92, $p<0.001$). Clinically, patients exceeding this threshold were substantially more likely to require ICU admission, suggesting that this level of pulmonary involvement may represent a critical threshold for early escalation of care.

Discussion

Pneumonia cases are frequently presented to the emergency department and are an important cause of morbidity and mortality. In pneumonia cases, the clinical course and prognosis can be affected by many factors, such as the patient's age, additional diseases, and the agent of pneumonia. Although there may be no infiltration on CT in pneumonia, we thought that the area of pulmonary involvement in cases with infiltration may also affect the clinical course. This study was motivated by the hypothesis of both LV and IV affecting the clinical outcome of cases of an atypical viral pneumonia, such as COVID-19. While evaluating these, we also had the opportunity to assess the relationship between some laboratory parameters and infiltration and clinical outcome.

Table 5. Univariate and multivariate regression analysis of involvement severity and mortality according to variables

		Univariate			Multivariate		
		OR	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Involvement severity	Age	0.445	0.020-0.870	**0.040**	0.551	0.017-0.912	**0.012**
	TRP	1.404	1.280-1.528	**<0.001**	1.392	1.261-1.613	**0.016**
	WBC	0.938	0.667-1.199	**<0.001**			
	CRP	1.113	0.954-1.271	**<0.001**			
	LV	2.141	1.834-2.448	**<0.001**			
	IV	0.876	0.806-0.946	**<0.001**			
	IP	0.878	0.829-0.927	**<0.001**	0.893	0.852-1.011	**<0.001**
Mortality	Age	1.079	1.038-1.121	**<0.001**	1.080	1.004-1.161	**0.039**
	TRP	1.216	1.103-1.340	**<0.001**	1.180	1.030-1.353	**0.017**
	WBC	1.249	1.102-1.415	**<0.001**			
	CRP	1.013	1.006-1.021	**0.001**			
	LV	0.999	0.999-1.000	**0.030**			
	IV	1.006	1.004-1.008	**<0.001**			
	IP	1.147	1.090-1.206	**<0.001**	1.331	1.046-1.695	**0.020**

OR: Odds ratio, CI: Confidence interval, WBC: White blood cell, TRP: Troponin, CRP: C-reactive protein, LV: Lung volume IV: Involvement volume IP: Involvement percentage

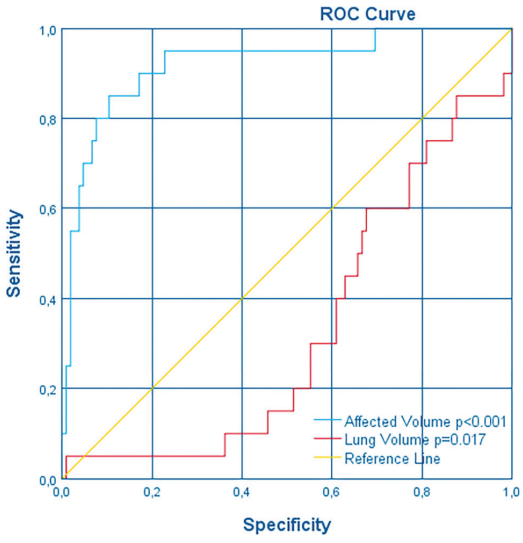

Figure 2. ROC curves showing the diagnostic performance of infiltration volume and involvement percentage for predicting mortality

Ground glass opacities are the predominant CT finding in cases of COVID-19 pneumonia. Research has documented their characteristic profiles: bilateral, peripheral, multilobar, and posterior localization (13). Ground glass opacities may be observed either independently or in conjunction with consolidation, thickening of the interlobular septum, and dilatation of blood vessels (14). Consolidations often have multifocal, segmental patchy patterns primarily observed in the lower lobe and peripheral areas, and may also include air bronchograms (15). It has been documented that they are more commonly seen in individuals of advanced age, in patients who have seen disease progression, or in the later stages of the illness (15). The experiments conducted by Pan et al. (10) revealed that consolidation is infrequent during the initial phases, but it undergoes expansion and diffusion in subsequent stages.

If we look at the main factors of age and gender, Ozdemir et al. (16) have shown in compatible studies that clinical severity increases significantly with increasing age. Regarding gender, Jin et al. (17) reported that male patients showed a worse prognosis in their study on gender factors. Similarly, in our study, we observed that both the volume involved and mortality increased significantly with increasing age. However, in our study, there was no association between gender and mortality. Unlike other studies, we did not include cases with additional diseases in our study. With this result, we can state that gender has no relationship with prognosis, even if we exclude additional diseases.

Inflammatory markers have been shown to be associated with disease severity and prognosis in COVID-19 (18,19). It is known that blood CRP and WBC elevation are associated with oxygen demand and disease severity (18,19). Many studies in the literature have reported different results regarding blood cell counts associated with the immune response. In one study, increased CRP and CRE were found to be associated with a high mortality rate. A strong relationship between increased CRP and acute lung injury in COVID-19 cases was previously shown in a study (20). Another analysis showed that CRP was higher in the group with higher severity (21). In the study by Majure et al. (22) including 6247 COVID-19 patients, TRP was a predictor of death, and significantly increased mortality rates were observed in the group of patients with high TRP levels compared to patients with normal TRP levels. Du et al. (23) studies have shown that advanced age (≥65), pre-existing concurrent cardiovascular or cerebrovascular diseases, and especially high cTnI levels of 0.05 ng/mL and above are important biomarkers for mortality in COVID-19 pneumonia patients. In our study, the relationship between some laboratory parameters and the increase in IV and mortality was evaluated. The increase in WBC, CRP, and TRP values was related to both IV and mortality, similar to findings of other studies. However, we found that CRE values were not related to these variables. This may be because we did not include chronic renal failure patients in our study, which evaluated spontaneous CRE values in cases without additional diseases.

A study by Saeed et al. (24) revealed a significant correlation between CT score and both lymphopenia and elevated levels of serum CRP, D-dimer, and ferritin. Furthermore, Zhang et al. (25) observed a positive correlation between chest CT score and CRP, erythrocyte sedimentation rate, WBC count, procalcitonin, and impaired coagulation function, and a negative correlation with lymphocyte count.

The typical findings in COVID-19 pneumonia and the changes in findings over time in the course of the disease, as well as rare and atypical findings, have been described in many studies (26). However, it should not be forgotten that similar findings can be seen in many diseases such as viral pneumonia, especially influenza, organized pneumonia, or drug toxicity. Typical CT findings and changes in findings over time have been described in the diagnosis and triage of COVID-19 pneumonia. With thoracic CT, areas with increased density, number of segments of pneumonia, and the extent to which each segment is involved can be scored using various software or visually, and the rate of lung involvement and severity of inflammation can be predicted (27). Determining severity can help predict which patients need hospitalization and mechanical ventilation. It has been reported that not only the area covered by lesions but also some findings is effective in predicting severity.

Li et al. (28) reported that a decline in the total lung capacity suggested a poor prognosis. The study conducted by Lanza et al. (29) revealed that patients with COVID-19 who required intubation had reduced total LV. Carvalho et al. (30) showed that the degradation of lung capacity directly correlated with the escalation of disease severity. In contrast to the majority of research, Ippolito et al. (31) did not demonstrate a correlation between the reduction in LV and a negative prognosis. Varying technical specifications may exist in the three-dimensional applications and devices employed in these investigations carried out at different centers. In addition, Uzun et al. (32) reported in their study that mortality increased with decreasing LV values in both sexes. In our study, consistent with previous research, both the severity and percentage of pulmonary involvement and the mortality rate were higher in patients with lower total LV. This finding can be physiologically explained by the fact that a reduction in vital capacity increases the work of breathing, leading to impaired ventilation efficiency and a higher proportional involvement of the remaining functional lung tissue.

The primary observation of COVID-19 pneumonia on thorax CT was the extensive involvement of peripheral and particularly posterior regions, as well as consolidation areas. Our findings were consistent with those documented in existing literature (33,34). Timely and precise medical evaluation of patients and proper treatment of their illnesses before they deteriorate are crucial (35). Several chest CT scoring systems were created to establish a uniform criterion for evaluating the extent of radiological lung involvement (36,37). Analysis of chest CT severity grading systems was conducted to assess interobserver agreement, revealing a high level of agreement. Nevertheless, other research is necessary to validate the findings due to the limited number of severe and critically ill patients included in both reviews. Although we created groups classifying severity as mild, moderate, and severe in the study, we think that calculating the involvement volume as a numerical percentage directly makes the results more realistic. Most studies have been conducted on the CT severity score (38), and although they show similar results to our study, our specific numerical IP calculation makes the result more valuable. As reported by Li et al. (9), the current chest CT score demonstrated a sensitivity of 80% and specificity of 82.8%, with a threshold value of 7. A semi-quantitative CT-SS devised by Pan et al. (10) was used by Francone et al. (33) to determine that a CT score of ≥18 was linked to a higher risk of mortality.

As mentioned above, previous studies have investigated the relationship between the extent of pulmonary involvement on CT and both clinical severity and mortality. In the present study, we similarly demonstrated that reduced total LV, a higher percentage of pulmonary involvement, and the overall severity of infiltration were all directly associated with increased mortality. Unlike several earlier studies that categorized disease severity using semi-quantitative CT scores, our analysis directly calculated the IP, which provided a more objective and reproducible indicator of disease burden. As the percentage of lung involvement increased, both mortality rates and ICU admissions rose proportionally. Consistent with this radiologic progression, inflammatory biomarkers such as CRP, WBC, and TRP levels also showed a significant positive correlation with the degree of parenchymal involvement.

The strongest discrimination for mortality prediction was achieved with an IP cutoff value of approximately 45% evidenced by the ROC curve analysis, which gave an AUC of 0.92. In the clinical setting, this threshold may function as an early radiological marker to identify patients who are at risk of accelerated deterioration. Patients who presented with a parenchymal involvement of ≥45% on their initial chest CT were more likely to require admission to the intensive care unit and had a significantly higher mortality rate. This observation implies that the quantitative CT assessment of lung involvement may facilitate early risk stratification and triage decisions in the emergency department. Previous imaging-based investigations have disclosed comparable results. For example, Colombi et al. (39) found that patients with more than 40-50% lung involvement on admission CT had significantly higher rates of ICU admission and mortality than those with moderate disease. Other studies have verified that quantitative CT metrics are significantly correlated with the severity of hypoxemia, inflammatory markers, and short-term outcomes in viral pneumonias, such as COVID-19 (33,40). Consequently, a clinically meaningful and reproducible cut-off of approximately 45% for IP may be used to identify patients at high risk, offering both radiologic and prognostic insight during the initial evaluation. Integrating quantitative CT assessment into emergency department workflows may help physicians identify high-risk patients earlier, guide timely escalation of care, and improve the allocation of critical care resources during surges of viral pneumonia cases.

Study Limitations

This research contains several limitations that necessitate acknowledgment. Initially, the research was conducted in a single-center, retrospective design, which may inherently restrict the generalizability of the findings and introduce selection bias. Nevertheless, a representative sample was guaranteed by the consecutive inclusion of all eligible patients in accordance with predefined criteria, thereby mitigating potential bias. Secondly, the internal validity of the results was improved by the implementation of stringent inclusion and exclusion

criteria, which in turn resulted in a more homogeneous study population, despite the fact that the sample size (n=125) was modest in comparison to the total number of screened cases. Third, only the initial chest CT scans that were obtained at the time of presentation were analyzed. As a result, the temporal evolution of lung involvement could not be assessed, and alterations in CT findings during the clinical course remain unexplored. Further longitudinal investigations that incorporate serial CT examinations are necessary to resolve this limitation. Fourth, to mitigate confounding effects, patients with substantial chronic comorbidities were excluded. Although this method restricts the external generalizability of the results to broader COVID-19 populations, it facilitated a more precise evaluation of the isolated impact of acute viral pneumonia on outcomes. Ultimately, two seasoned radiologists, each with over a decade of experience in thoracic imaging, conducted quantitative CT analyses independently. Despite the absence of formal quantification of inter-observer agreement, both readers adhered to standardized segmentation protocols and cross-validated a subset of cases to guarantee consistency. This dual-reader design significantly reduces subjective bias and improves the reliability of volumetric measurements. The present study provides a unique, quantitative, and reproducible perspective on the relationship between patient outcomes and CT-derived lung involvement, despite these limitations. The results may be a valuable reference for future multicenter prospective investigations that involve a more diverse and extensive patient population.

Conclusion

This study revealed that both quantitative increases in infiltration, and decreases in total LV on chest CT are strongly associated with adverse outcomes in viral pneumonia. A greater volume of infiltration and percentage of involvement were significantly associated with disease severity, intensive care unit hospitalization, and mortality, whereas a reduced total LV indicated advanced parenchymal damage and compromised breathing capacity. As pulmonary involvement intensified, markers of inflammation (CRP, WBC) and heart damage (TRP) increased correspondingly, highlighting a strong correlation between radiologic burden and systemic response. Among all quantitative CT characteristics, IP exhibited the most reliable predictive capability, serving as an independent indicator of worse prognosis. The findings indicate that quantitative CT assessment, encompassing both infiltration and volume analysis, might offer objective early risk classification and may inform clinical decision-making and resource allocation in emergency care.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and with the consent of the Institutional Ethics Committee (protocol code: 129, date: 15.03.2021) prior to its commencement.

Informed Consent: This is a retrospective study.

Footnotes

Author Contributions

Surgical and Medical Practices: B.D., Concept: B.D., Design: B.D., E.F., Data Collection or Processing: B.D., E.F., A.C., S.G., Analysis or Interpretation: B.D., E.F., A.C., S.G., Literature Search: B.D., E.F., A.C., S.G., Writing: B.D., E.F.

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Predictive Value of Electrocardiogram for Intracranial Hemorrhage After Thrombolysis in Acute Ischemic Stroke Patients: Retrospective Single-center Cohort Study

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Abstract

Aim: Intravenous thrombolytic therapy (IVT) is an effective treatment modality for acute ischemic stroke (AIS). However, post-treatment intracranial hemorrhage (ICH), particularly symptomatic ICH (sICH), is associated with significant morbidity and mortality. This study aims to investigate the relationship between electrocardiogram (ECG)-detected left ventricular hypertrophy (LVH) and the risk of hemorrhage following IVT.

Materials and Methods: Patients who received IVT for AIS between 2022 and 2025 in a tertiary care center were retrospectively analyzed. LVH was assessed using the Gubner, Cornell, and Sokolow-Lyon ECG criteria. The primary endpoint was the development of sICH after IVT. The predictive power of ECG voltage criteria for LVH was evaluated using ROC curve analysis, and both univariable and multivariable logistic regression analyses were conducted.

Results: A total of 135 patients were included. The incidence of sICH was 11%. Increased voltage (R I + S III) according to the Gubner criterion and elevated systolic blood pressure were identified as independent risk factors for sICH ($p<0.01$). The area under the curve values for the Gubner and Cornell criteria in predicting sICH were 0.764 and 0.751, respectively. The Gubner criterion exhibited a sensitivity of 60% and a specificity of 80.8%, whereas the Cornell criterion demonstrated higher sensitivity (66.7%) but comparatively lower specificity (65.0%). The Sokolow-Lyon criterion was not statistically significant ($p=0.237$).

Conclusion: ECG-LVH may serve as a simple adjunct marker to identify patients at higher risk of sICH after IVT, but further validation is required.

Keywords: Stroke, intracranial hemorrhage, electrocardiography

Introduction

Intravenous thrombolytic therapy (IVT) with recombinant tissue plasminogen activator (rtPA) remains the cornerstone of treatment for acute ischemic stroke (AIS), particularly when administered within the therapeutic window. Despite its effectiveness in restoring cerebral perfusion, one of the most feared complications of rtPA is symptomatic intracranial hemorrhage (sICH) (1). This condition adversely affects post-treatment prognosis and constitutes a major limitation to the broader use of thrombolytic therapy. Numerous studies in the literature have investigated the predictors of post-thrombolytic hemorrhage, with cerebral microbleeds (CMB) being particularly associated with increased risk (2,3). CMB is small, round hemosiderin deposits resulting from chronic small vessel leakage, and they are detectable by magnetic resonance imaging (MRI) (4). However, due to the

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need for urgent decision-making in acute stroke management, imaging is often limited to non-contrast computed tomography (CT), which restricts the evaluation of CMB.

Given the time-sensitive nature of stroke management, it is crucial that emergency physicians, neurologists, and intensive care specialists possess adequate knowledge of thrombolytic therapy and its potential complications (5). Previous studies have highlighted variability in physicians' knowledge regarding thrombolytic treatment and emphasized the importance of continuous training and protocol optimization in acute stroke care (6,7).

Although the association between CMB and increased hemorrhagic risk is well established, the inability to assess these lesions in the emergency department (ED) creates a significant diagnostic gap. Therefore, in situations requiring rapid decision-making under ED conditions, there is a need for easily accessible and applicable alternatives to advanced imaging techniques. Since chronic hypertension is the most common underlying cause of CMB, its indirect assessment through organ-based manifestations gains clinical importance in this context (8). Electrocardiography (ECG) could be a pragmatic, accessible tool, especially where MRI is not feasible. ECG-detected left ventricular hypertrophy (LVH) is the most prominent cardiac manifestation of chronic hypertension and may reflect chronic microvascular involvement. However, the association between this form of electrical remodeling and the development of ICH following IVT has not been adequately investigated in the literature.

In this retrospective cohort study, we aimed to investigate the relationship between ECG findings of LVH and the risk of both sICH and overall ICH in patients receiving IVT for AIS. If an increased risk of sICH is demonstrated among patients with LVH on ECG, this may represent a clinically valuable marker to support patient selection and ensure safer administration of IVT.

Materials and Methods

Patients and Study Design

This was a single-center retrospective cohort study conducted in a tertiary ED between 2022 and 2025, including patients diagnosed with AIS who received IVT. The study was approved by the University of Health Sciences Türkiye, Ankara Etlik City Hospital Ethics Committee (decision no: AEŞH-BADEK-2025-0230; date: 26.02.2025). It was conducted in accordance with the Declaration of Helsinki, and all patient data collected by the researchers were kept confidential.

Patients with a pre-stroke Modified Rankin scale (mRS) score greater than 2, patients with Alzheimer's disease, Parkinson's disease, or other neurodegenerative disorders, and those without available ECG data were excluded, as these conditions may cause cognitive impairment or confounding neurological deficits that could bias functional outcome assessment. In addition, patients with a history of major brain surgery, those on anticoagulant therapy, and those with inadequate brain imaging were excluded based on the predefined criteria.

Data Collection and Handling of Missing Data

Data were obtained using the hospital's electronic medical record system. Sociodemographic characteristics such as age and sex, vital signs (blood pressure, heart rate, respiratory rate, and oxygen saturation), laboratory parameters (hemoglobin, platelet count, urea, creatinine, and lactate), and patients' current medications were recorded on a standardized data collection form. mRS scores, assessed at the time of hospital admission, were also recorded (9). The etiology of ischemic stroke was classified according to the Trial of Org 10172 in acute stroke treatment criteria (10). The Alberta Stroke Program Early CT Score (ASPECTS) was calculated for the patients included in the study group (11). Additionally, three-month mortality and mRS scores at the end of the third month were obtained from the patients' electronic records.

Missing data were carefully assessed; variables with excessive missingness were excluded from the final analyses. In particular, onset-to-treatment time (OTT) was missing in the majority of patients and therefore was not included in the statistical models.

Calculation of MARS and Fazekas Scale

The Microbleed Anatomical Rating scale (MARS) was independently applied by a radiologist with 17 years of experience in neuroimaging, who was blinded to the clinical data of the patients (12). The evaluation was conducted in three stages. In the first stage, each microbleed lesion was classified as either "definite" or "possible." "Definite" lesions were defined as round, well-demarcated, hypointense foci ranging in diameter from 2 to 10 mm. "Possible" lesions were those with less distinct borders and uncertain differentiation. For lesions located in the basal ganglia, corresponding regions were carefully examined on T2-weighted and FLAIR sequences to rule out infarcts or calcifications. Vascular structures that could mimic microbleeds, imaging artifacts, air–bone interfaces, non-microbleed small hemorrhages, and mineralization foci were also meticulously evaluated.

In the second stage, microbleeds were anatomically categorized into three regions: deep, lobar, and infratentorial. Deep microbleeds included lesions located in the basal ganglia, thalamus, the internal and external capsules, corpus callosum,

and deep or periventricular white matter. Lobar microbleeds were defined as those localized to cortical or subcortical areas. Infratentorial microbleeds encompassed those identified in the brainstem and cerebellum. In the final stage, the total MARS score was calculated by summing the number of microbleeds observed in the aforementioned regions.

Leukoaraiosis (white matter lesions) was evaluated using the Fazekas scale on FLAIR MRI sequences. The Fazekas score was assigned separately for periventricular and deep white matter hyperintensities, each rated from 0 to 3. Periventricular signal abnormalities were assessed based on the presence of caps, rims, or extensive lesions, while deep white matter lesions were scored according to the number, size, and degree of confluence. The sum of both subscores constituted the total Fazekas score.

Evaluation of Electrocardiographic and Echocardiographic Left Ventricular Hypertrophy

For the assessment of LVH on ECG, three commonly used criteria were adopted: the Cornell voltage criterion (13), the Gubner criterion (14), and the Sokolow-Lyon criterion (15), each representing unipolar limb, bipolar limb, and chest leads. All ECGs were independently evaluated by three emergency medicine specialists blinded to the hemorrhagic outcomes. For each ECG, the average of the voltage measurements was calculated, and it was subsequently reviewed and confirmed by the cardiologist who was also blinded to clinical outcomes. The values approved by the cardiologist were used for statistical analysis. Although blinding was ensured, inter-rater reliability among the emergency specialists was not measured, which represents a limitation of the ECG interpretation process.

The definitions for the three voltage criteria were as follows:

Cornell voltage criterion: Male: RaVL + SV3 >28 mm (=2.8 mV), Female: RaVL + SV3 > 20 mm (=2.0 mV)

Gubner voltage criterion: RI + SIII ≥ 25 mm (=2.5 mV)

Sokolow-Lyon criterion: SV3 + RV5 or V6 > 35 mm (=3.5 mV)

In our hospital, echocardiographic (ECHO) evaluation is routinely performed within one week of hospitalization in patients diagnosed with AIS. ECHO reports and archived imaging were reviewed by a cardiologist experienced in echocardiography. LVH was recorded in the data form if the left ventricular wall thickness exceeded 11 mm in men or 10 mm in women.

Intracranial Hemorrhage Outcome

Any ICH detected by CT within 24 hours after rtPA administration was defined as post-thrombolytic ICH. In clinical practice, post-thrombolytic ICH includes both sICH and asymptomatic ICH. Symptomatic hemorrhages were classified according to the Heidelberg Bleeding Classification, which involves a structured seven-step process for categorizing hemorrhagic events (16). In this study, the Heidelberg classification was performed by more than one reviewer; however, inter-rater reliability was not assessed, which represents a limitation of the outcome definition. However, due to the inherent limitations of retrospective data review, hemorrhages were defined in this study as events associated with any of the following: ≥4-point worsening in the total National Institutes of Health Stroke scale (NIHSS) score compared to the most recent pre-deterioration assessment (not baseline); ≥2-point worsening in any individual NIHSS category (to detect new hemorrhages causing new symptoms); or the need for intubation, hemicraniectomy, external ventricular drainage, or other major medical/surgical interventions.

The anatomical classification of ICH was conducted according to the predefined criteria summarized in Table 1.

Sample Size

Based on previous studies that reported a 30% incidence of ICH in patients who received thrombolytic therapy for AIS (17), and assuming a clinically meaningful difference in the prevalence of LVH between those with and without ICH (18), it was estimated that a minimum of 24 patients with ICH would be sufficient to achieve 85% statistical power with a two-sided alpha of 0.05. The post-hoc power was computed in G* Power (Exact test; one-sample proportion, two-tailed, α=0.05) using the expected ICH incidence under H0 of 30% and the observed incidence of 17.8% with n=135. The achieved power was approximately 66%.

Table 1. Anatomical classification of intracranial hemorrhage according to the Heidelberg bleeding classification

Class	Type	Description
1		Hemorrhagic transformation of infarcted brain tissue
	HI[1]	Scattered small petechiae, no mass effect
	HI[2]	Confluent petechiae, no mass effect
	PH[1]	Hematoma within infarcted tissue, occupying <30%, no substantive mass effect
2	PH[2]	Hematoma occupying ≥30% of infarcted tissue, with significant mass effect
3		Intracerebral hemorrhage outside infarcted tissue or extracerebral bleeding
	3[a]	Parenchymal hematoma remote from infarcted tissue
	3[b]	Intraventricular hemorrhage
	3[c]	Subarachnoid hemorrhage
	3[d]	Subdural hemorrhage

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as medians and interquartile ranges (IQRs), while categorical variables were expressed as frequencies and percentages. Between-group comparisons were performed using the Mann-Whitney U test for continuous variables and the Chi-square or Fisher's exact test for categorical variables, as appropriate.

To evaluate the predictive performance of ECG LVH criteria for sICH, ROC curve, analysis was conducted, and area under the curve (AUC), optimal cut off values, sensitivity, and specificity were reported. Univariable and multivariable logistic regression analyses were used to identify independent predictors of sICH. Variables with a p value <0.20 in univariable analysis were included in the multivariable model. A two-sided p value of <0.05 was considered statistically significant.

Results

A total of 135 patients diagnosed with AIS and treated with IVT were included in the final analysis. Figure 1 presents the patient selection process and flowchart. The mean age of the cohort was 67.2±14.8 years, and 60.7% (n=82) were male. The median systolic and diastolic blood pressures at presentation were 150.5 mmHg and 89 mmHg (IQR: 80-95), respectively. Table 2 summarizes the baseline demographic and clinical characteristics of the study population.

When stratified by the presence of sICH, no significant differences were observed in age or sex. However, systolic and diastolic blood pressures were significantly higher in the sICH group (p=0.002 and p=0.004, respectively). While ASPECTS and MARS scores did not differ significantly between groups, the 3-month mRS score was lower in the sICH group (p=0.005), likely reflecting the significantly higher mortality observed in this group (40% vs. 8%, p<0.001). There was no statistically significant difference in the rate of bridging therapy between patients with and without ICH, and between those with and without sICH. These findings are presented in Table 3. Detailed data are provided in Supplementary Table 1.

For predicting ICH, the Cornell voltage criterion demonstrated the highest [AUC: 0.641, 95% confidence interval (CI): 0.510-0.773, p=0.030], with 83.3% sensitivity and 27% specificity. The Gubner criterion also reached statistical significance (AUC: 0.628, 95% CI: 0.491–0.766, p=0.049), whereas the Sokolow-Lyon criterion did not show a significant discriminative ability (p=0.398) (Figure 2).

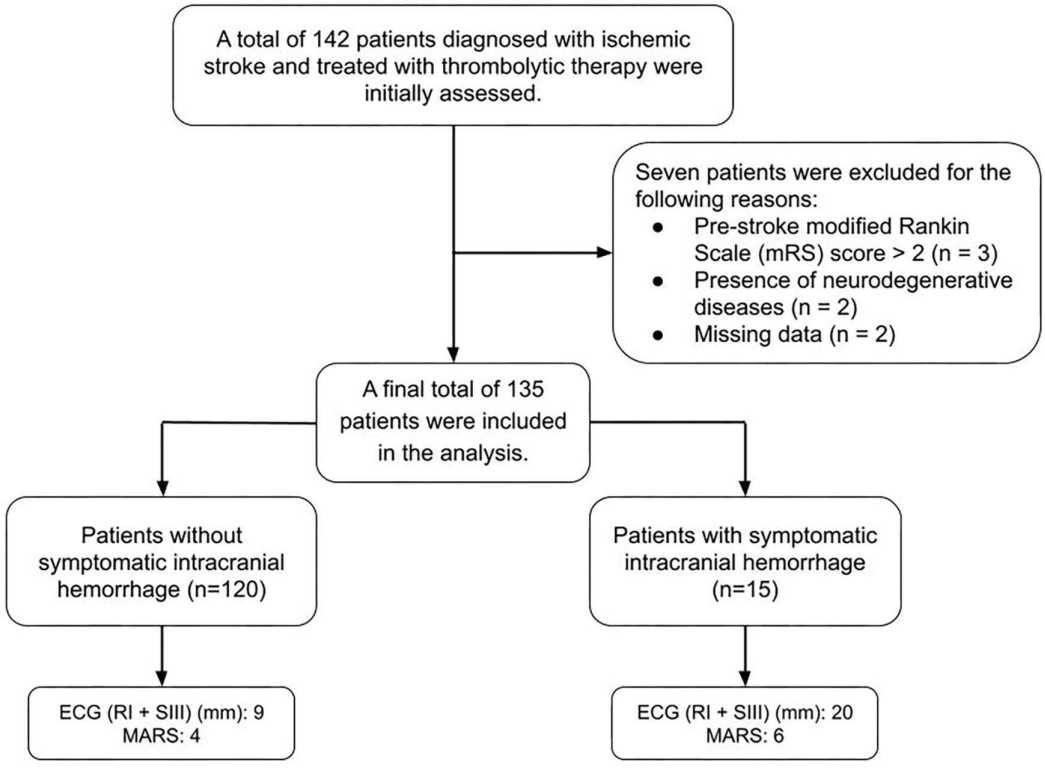

Figure 1. Flowchart of patient selection and group stratification
ECG: Electrocardiogram, MARS: Microbleed Anatomical Rating scale

Table 2. General characteristics of the study population	
Variables (n=135)	
Sex	
Female	53 (39.3%)
Male	82 (60.7%)
Age	67.19±14.78
Vital parameters	
Systolic blood pressure (mmHg)	150.5±21.96
Diastolic blood pressure (mmHg)	89 (IQR: 80-95)
Pulse (beat/minute)	76 (IQR: 69-87)
Respiratory rate (per minute)	20 (IQR: 18-20)
Oxygen saturation (%)	95 (IQR: 92-97)
Pharmacological therapies administered	
Antiplatelet therapy	59 (43.7%)
Anticoagulant therapy	10 (7.4%)
Statin therapy	15 (11.1%)
Antihypertensive therapy	84 (62.2%)
Laboratory parameters	
Hemoglobin (g/dL)	13.9±2.09
Platelet count (.103/L)	242.8±75.8
Urea level (mg/dL)	36.9 (IQR: 28-48.5)
Creatinine level (mg/ dL)	0.9 (IQR: 0.78-1.09)
Lactate level (mmol/L)	1.81 (IQR: 1.38-2.28)
Trial of Org 10172 for acute stroke treatment classification	
Large-artery atherosclerosis	85 (63%)
Cardioembolic stroke	23 (17%)
Small-vessel disease/penetrating artery disease	12 (8.9%)
Stroke of other determined cause	8 (5.9%)
Stroke of undetermined cause (cryptogenic stroke)	7 (5.2%)
Alberta stroke program early CT score	9 (IQR: 7-10)
Microbleed Anatomical Rating scale	4 (IQR: 2-6)
Fazekas scale score (n=87)	
Periventricular white matter	2 (IQR: 1-2)
0 =no lesion	11 (12.6%)
1 =“caps” or pencil-thin lining	32 (36.8%)
2 =smooth “halo”	41 (47.1%)
3 =irregular periventricular signal extending into the deep white matter	3 (3.4%)
Deep white matter	1 (IQR: 1-2)
0 =no lesion	16 (18.4%)
1 =punctate lesions	37 (42.5%)
2 =beginning confluence	31 (35.6%)
3 =extensive confluent areas	3 (3.4%)
Modified Rankin scale at administration	3 (IQR: 3-4)
Post- thrombolytic bleeding	
Yes	24 (17.8%)
Heidelberg bleeding classification (n=24)	1
Class 1: hemorrhagic transformation of infarcted brain tissue	2
1^a: HI1: scattered small petechiae, no mass effect	6
1^b: HI2: confluent petechiae, no mass effect	
1^c: PH1: hematoma within infarcted tissue, occupying <30%, no substantive mass effect	
Class 2: intracerebral hemorrhage within and beyond infarcted brain tissue	4
PH^2: hematoma occupying ≥30% of the infarcted tissue, with obvious mass effect (PH^2)	
Class 3: intracerebral hemorrhage outside the infarcted brain tissue or intracranial-extracerebral hemorrhage	
3^a: parenchymal hematoma remote from infarcted brain tissue	1
3^b: intraventricular hemorrhage	2
3^c: subarachnoid hemorrhage	7
3^d: subdural hemorrhage	1

Table 2. Continued	
Variables (n=135)	
Electrocardiographic criteria of left ventricular hypertrophy The Gubner criteria (voltage) Hypertrophic (R I + S III >25 mm) **The Sokolow-Lyon criteria (voltage)** Hypertrophic (S V3 + R V5-6 >35 mm) The Cornell Voltage Criteria (voltage) Hypertrophic (R aVL + S V3 >35 mm for men, >25 mm for women) Hypertrophic findings at echocardiography (*n=115)	 9 (IQR: 6-15) mm 11 (8.1%) 16.5 (IQR: 12-22) mm 5 (3.7 %) 14 (IQR: 9-18) mm 6 (4.4%) 38 (33%)
Length of hospital stay (days)	8 (IQR: 5-13)
Modified Rankin scale at 3rd month	3 (IQR: 1-3)
Bridging therapy (mechanical thrombectomy)	32 (24 %)
Symptomatic intracranial hemorrhage	15 (11 %)
Survey Alive Died	 119 (88.1%) 16 (11.9%)
*Number of patients that performed echocardiography. All data are presented as counts and percentages for categorical variables, and as either mean ± standard deviation or median and interquartile range (IQR: 25th-75th percentiles), depending on the distribution of the data, and adherence to normality assumptions CT: Computed tomography, IQR: Interquartile range	

Table 3. Comparison of clinical, radiological, and electrocardiographic characteristics according to the presence of intracranial hemorrhage and symptomatic intracranial hemorrhage

Variables **Outcome 1: intracranial hemorrhage**	**Yes (n=24)**	**No (n=111)**	**p value**
Sex Female Male	 12 (50%) 12 (50%)	 41 (36.9%) 70 (63.1%)	 0.235
Age	72.08±11.86	66.13±15.17	0.073
Vital parameters Systolic blood pressure (mmHg) Diastolic blood pressure (mmHg)	 164.5 (IQR: 142.5-177.5) 92.5 (IQR: 87-100)	 145 (IQR: 135159) 88 (IQR: 80-93)	 **0.004** 0.066
Microbleed Anatomical Rating scale	5 (IQR: 3-6.75)	4 (IQR: 2-6)	0.205
Survey Died	 10 (42%)	 6 (5%)	 **<0.001**
Electrocardiographic criteria of left ventricular hypertrophy The Gubner criteria (voltage) Hypertrophic (R I + S III >25 mm) The Sokolow-Lyon criteria (voltage) Hypertrophic (S V3 + R V5-6 >35 mm) The Cornell Voltage Criteria (voltage) Hypertrophic (R aVL + S V3 >35 mm for men, >25 mm for women)	 9 (IQR: 6-13) mm 6 (25%) 16 (IQR: 13-23) mm 2 (8.3%) 15 (IQR: 13-22) mm 3 (12.5%)	 6 (IQR: 12-26) mm 5 (4.5%) 17 (IQR: 12-22) mm 3 (2.7%) 13 (IQR: 9-17) mm 3 (2.7%)	 0.083 **<0.001** 0.380 0.185 0.054 **0.035**
Hypertrophic findings at echocardiography (*n=115) Hypertrophic	n=16 9 (56.3%)	n=99 29 (29.3%)	**0.033**
Variables Outcome 2: symptomatic intracranial hemorrhage	**Yes (n=15)**	**No (n=120)**	**p value**
Sex Female Male	 7 (47%) 8 (53%)	 46 (38%) 74 (62%)	 0.582
Age	71.1±11.4	66.7±15.1	0.300
Vital parameters Systolic blood pressure (mmHg) Diastolic blood pressure (mmHg)	 166 (IQR: 155-180) 100 (IQR: 89-109)	 147 (IQR: 135-160) 88 (IQR: 80-94)	 **0.002** **0.004**

Table 3. Continued			
Variables **Outcome 1: intracranial hemorrhage**	**Yes (n=24)**	**No (n=111)**	**p value**
Survey Died	 6 (40 %)	 10 (8%)	 **<0.001**
Electrocardiographic criteria of left ventricular hypertrophy The Gubner criteria (voltage) Hypertrophic (R I + S III >25 mm) The Sokolow -Lyon criteria (voltage) Hypertrophic (S V3 + R V5-6 >35 mm) The Cornell Voltage Criteria (voltage) Hypertrophic (R aVL + S V3 >35 mm for men, >25 mm for women)	 20 (IQR: 12-28) mm 5 (33%) 18 (IQR: 11-21) mm 1 (7%) 20 (IQR: 14-26) mm 3 (20%)	 9 (IQR: 5-13) mm 6 (5%) 16 (IQR: 12-24) mm 4 (3%) 13 (IQR: 9-17) mm 3 (3%)	 **0.001** **<0.001** 0.236 0.521 **0.002** **0.002**
Hypertrophic findings at echocardiography (*n=115) Hypertrophic	n=10 6 (40%)	n=105 32 (27%)	 0.281
*: Patients who underwent echocardiography (number of patients provided), CT: Computed tomography, IQR: Interquartile range			

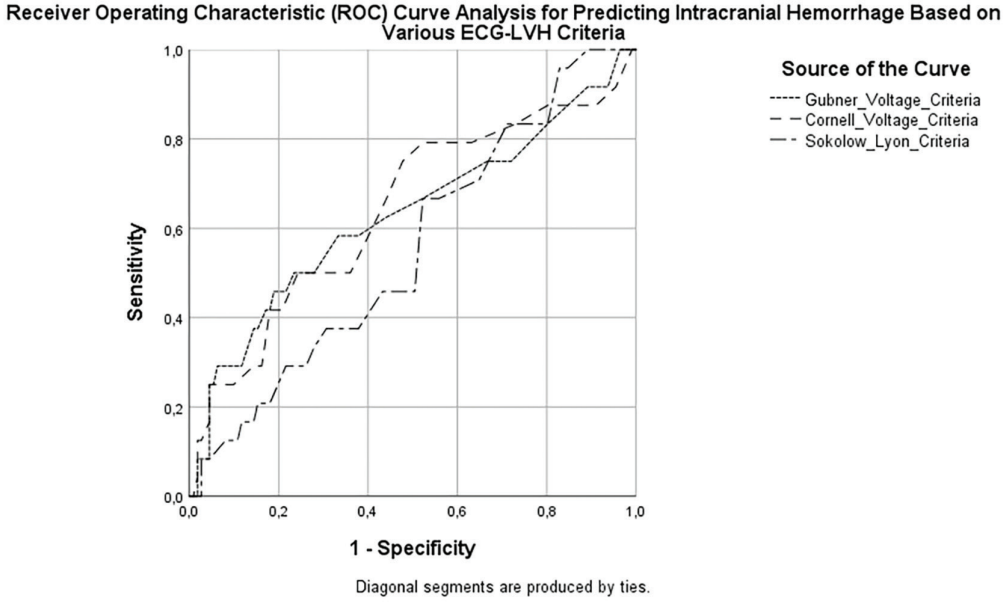

Figure 2. ROC curve analysis of ECG-LVH criteria for predicting any intracranial hemorrhage
ECG-LVH: Electrocardiogram- left ventricular hypertrophy

In predicting sICH, both the Gubner and Cornell Voltage Criteria demonstrated statistically significant performance (AUC: 0.764 and 0.751, respectively; both p<0.01) (Figure 3). These AUC values indicate moderate, rather than high, discriminative power. The Gubner criterion achieved 60% sensitivity and 80.8% specificity, while the Cornell criterion demonstrated slightly lower specificity (65.0%) but higher sensitivity (66.7%). The Sokolow-Lyon criterion again yielded nonsignificant results (AUC: 0.594, p=0.237) (Table 4).

Univariable and multivariable logistic regression analyses were conducted to identify independent predictors of sICH. In the univariable analysis, Gubner voltage [odds ratio (OR): 1.120, 95% CI: 1.045-1.201, p=0.001] and systolic blood pressure (OR: 1.039, 95% CI: 1.012-1.066, p=0.004) were significantly associated with sICH, while age was not (p=0.166).

In the multivariable model, which included Gubner voltage and systolic blood pressure, both remained independent predictors of sICH. Gubner voltage (OR: 1.126, 95% CI: 1.049-1.210, p=0.001) and systolic blood pressure (OR: 1.038, 95% CI: 1.011-1.066, p=0.006) were both independently associated with an increased risk of sICH (Table 5).

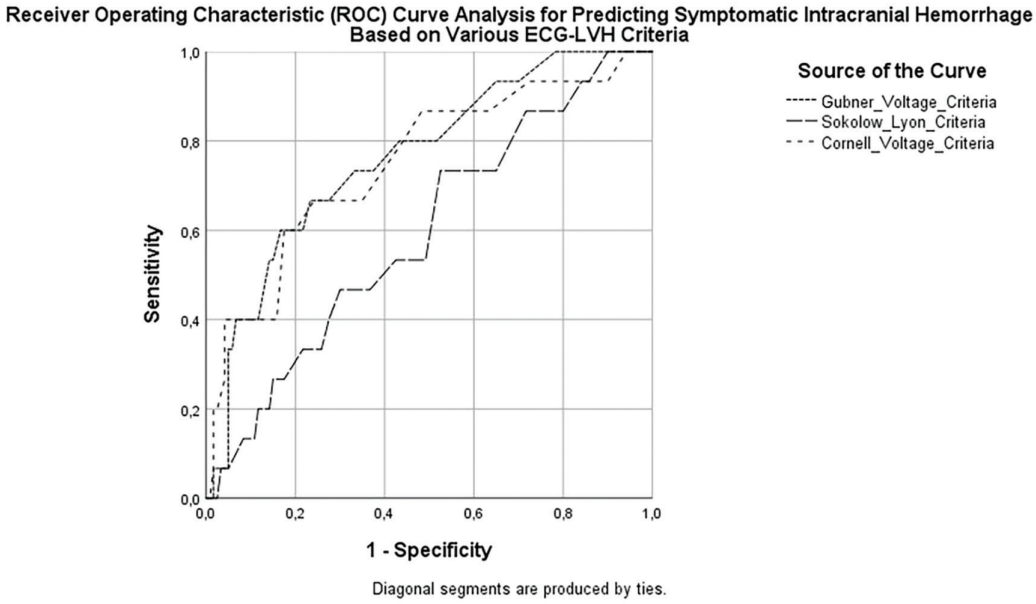

Figure 3. ROC curve analysis of ECG-LVH criteria for predicting symptomatic intracranial hemorrhage
ECG-LVH: Electrocardiogram- left ventricular hypertrophy

Tablo 4. Predictive performance of electrocardiographic left ventricular hypertrophy criteria for intracranial hemorrhage and symptomatic intracranial hemorrhage

Outcome 1: Diagnostic performance of ECG criteria for predicting intracranial hemorrhage								
LVH criteria	AUC	95% CI	p value	Best cut off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
The Gubner criteria	0.628	0.491 -0.766	**0.049**	10.5	66.7	47.7	73.3	62.5
Cornell voltage criteria	0.641	0.510 -0.773	**0.030**	14.5	83.3	27	66.7	55.9
Sokolo-Lyon criteria	0.555	0.434- 0.676	0.398	13.5	83.3	19.8	70.8	35.1
Outcome 2: Diagnostic performance of ECG criteria for predicting symptomatic intracranial hemorrhage								
The Gubner criteria	0.764	0.640- 0.888	**0.001**	15.5	60.0	80.8	32.0	93.8
Cornell voltage criteria	0.751	0.611- 0.891	**0.002**	15.5	66.7	65.0	28.0	94.5
Sokolow-Lyon criteria	0.594	0.448- 0.740	0.237	16.5	53.3	50.8	25.0	90.0

ECG: Electrocardiography, AUC: Area under the curve, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

Table 5. Univariable and multivariable logistic regression analysis of factors associated with symptomatic intracranial hemorrhage

Variable	**Univariable OR (95% CI)**	**p value**	**Multivariable OR (95% CI)**	**p value**
Gubner voltage	1.120 (1.045-1.201)	**0.001**	1.126 (1.049-1.210)	**0.001**
Systolic blood pressure	1.039 (1.012-1.066)	**0.004**	1.038 (1.011-1.066)	**0.006**
Age	1.034 (0.986-1.085)	0.166		

OR: Odds ratio, CI: Confidence interval

Discussion

In this study evaluating ECG left ventricular voltage criteria as predictors of ICH and sICH following thrombolytic therapy, in patients with AIS, the Gubner and Cornell Voltage Criteria demonstrated moderate discriminatory power (AUC values around 0.75). Moreover, the RI + SIII (Gubner voltage criterion) was identified as an independent predictor of symptomatic hemorrhage. These findings suggest that ECG-detected LVH showed moderate predictive value and may complement, rather than replace, established predictors.

Both hemorrhagic transformation (HT) and remote ICH following IVT are known to independently increase the risk of poor outcomes (19). Therefore, predicting the occurrence of any type of ICH after IVT is of clinical importance. While some risk factors are shared, distinct predictors have been identified for HT, parenchymal hematoma (PH), and remote ICH. Male sex, a history of prior stroke, OTT, and infarct size have been found to be independent risk factors for HT (20,21). On the other hand, congestive heart failure, advanced age, elevated systolic blood pressure, and atrial fibrillation are known risk factors for PH (22). Pathophysiological mechanisms underlying some of these factors have also been described. For instance, prior research has demonstrated that blood–brain barrier (BBB) permeability increases with age (23). Hypertension may impair vascular elasticity, leading to hyperperfusion injury. Markers of small vessel disease such as cerebral amyloid angiopathy, white matter hyperintensities, and CMB may predict remote ICH through endothelial dysfunction and disruption of the BBB (24,25).

In this context, MARS has been proposed as a potential tool to evaluate the functional consequences of CMBs in AIS patients treated with IVT (26). Since CMBs are often regarded as a consequence of chronic hypertension, their presence may confer predictive value for hemorrhagic complications following IVT. This could explain why mean ECG voltages were found to be significantly higher in patients who experienced post-thrombolytic hemorrhage—whether symptomatic or not—compared to those who did not.

In the current study, no significant difference in LVH was observed between sICH and non-sICH patients based on ECHO findings. However, both the proportion of patients meeting LVH criteria and the mean voltages were significantly higher in the sICH group when assessed using the Gubner and Cornell criteria. While ECHO-LVH reflects anatomical changes in left ventricular wall thickness, ECG-LVH encompasses both anatomical and electrical remodeling (27). Both ECHO-LVH and ECG-LVH have been shown to possess independent prognostic value (28). In our study, the discrepancy between ECG and ECHO-based findings should be cautiously interpreted and requires further validation, rather than being solely attributed to electrical versus anatomical remodeling.

Assessing LVH using ECG voltage criteria may help improve acute care quality in emergency settings by enabling early prediction of sICH after IVT. Although current guidelines clearly define indications for IVT in AIS patients (29), predicting post-thrombolytic hemorrhage remains a challenge. An increased risk of hemorrhage in patients with CMB has been well documented (30). However, detecting CMBs in the ED MRI, and calculating MARS scores requires radiological expertise, both of which increase time and cost. In contrast, evaluating LVH on ECG is simple, widely accessible, and does not require additional testing. Nevertheless, ECG findings should not be used in isolation for treatment decisions but may be integrated into multiparametric risk models that also include established predictors such as NIHSS, blood pressure, and imaging findings.

In the present study, the Gubner and Cornell Voltage Criteria demonstrated sufficient predictive power for sICH, whereas the Sokolow-Lyon criterion did not perform adequately. Previous research has also shown the superiority of the Cornell and Gubner criteria over the Sokolow-Lyon criterion in predicting sudden cardiac death and detecting anatomical LVH (31,32). Notably, an RI + SIII voltage sum exceeding 15.5 mm was associated with approximately 80% specificity for sICH, suggesting that even patients not formally meeting LVH criteria (e.g., RI + SIII >25 mm) based on Gubner may still carry elevated hemorrhagic risk.

The association between cardiac and cerebral injury appears to stem from the systemic effects of arterial hypertension. Both organs are recognized target of hypertension, as previously demonstrated (33). Consistent with prior studies establishing the prognostic value of LVH in cerebrovascular events (34), our findings indicate that RI + SIII on ECG serves as an independent risk factor for sICH following IVT in AIS patients.

Study Limitations

This study has several limitations. First, its retrospective design, may have introduced potential bias in data collection and, by nature, is more susceptible to confounding factors. Second, the study was conducted at a single center. However, the center where the study was performed is the largest hospital in the country and serves as a major referral center for AIS patients.

Third, although the Heidelberg Bleeding Classification was used to define hemorrhagic outcomes, comparison with findings in the existing literature may be limited, as some previous studies have utilized different classification systems, such as the European Cooperative Acute Stroke Study (ECASS) II or ECASS

III. Nevertheless, the Heidelberg classification offers a more comprehensive framework than ECASS III, and it has been shown to have good interobserver agreement (35,36).

Fourth, although ECG evaluations were independently performed by three emergency medicine specialists, inter-rater reliability was not assessed, which may limit the robustness of ECG interpretation. Fifth, the relatively small number of sICH cases (n=15) reduces statistical power and limits the generalizability of the findings.

Sixth, although the impact of OTT on post-IVT ICH is well established in AIS, it could not be analyzed in this study due to a lack of data for the majority of patients. Nonetheless, in our hospital, current guideline-based indications for IVT are strictly followed, suggesting that OTT may have had minimal influence on treatment-related complications in our cohort.

Finally, MARS scoring could not be performed in all included patients, which may have influenced the findings related to CMB. However, it is important to note that MRI prior to IVT is not mandatory in the acute stroke setting. Even so, we acknowledge this as a methodological limitation.

Conclusion

ECG-detected LVH, particularly by the Gubner and Cornell criteria, was associated with sICH after IVT. These findings are hypothesis-generating and suggest that ECG may serve as an adjunct risk marker, but larger, prospective multicenter studies are needed for validation.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Türkiye, Ankara Etlik City Hospital Ethics Committee (decision no: AEŞH-BADEK-2025-0230; date: 26.02.2025). It was conducted in accordance with the Declaration of Helsinki, and all patient data collected by the researchers were kept confidential.

Informed Consent: This was a single-center retrospective study.

Generative AI Usage Statement

Generative AI and AI-assisted technologies were NOT used in the preparation of this work.

Footnotes

Surgical and Medical Practices: İ.Ş., Concept: İ.Ş., R.P.K., E.S., Design: İ.Ş., T.S.M., G.Ç.I., N.V.V., M.Y.A., Data Collection or Processing: İ.Ş., R.P.K., E.S., Analysis or Interpretation: İ.Ş., G.Ç.I., Literature Search: İ.Ş., G.Ç.I., Writing: İ.Ş., R.P.K., E.S., T.S.M., G.Ç.I., R.P.K., E.S.

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

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Supplementary Table 1. Comparison of baseline characteristics, pharmacological therapies, imaging findings, and clinical outcomes between patients who developed intracranial hemorrhage or symptomatic intracranial hemorrhage and those who did not

Variables **Outcome 1: Intracranial hemorrhage**	**Yes (n=24)**	**No (n=111)**	**p value**
Pharmacological therapies administered Antiplatelet therapy Anticoagulant therapy Antihypertensive therapy	 11 (45.8%) 4 (16.7%) 19 (79.2%)	 48 (43.2%) 6 (5.4%) 65 (58.6%)	 0.817 0.056 0.059
Alberta stroke program early CT score	8 (IQR: 7.75-10)	8 (IQR: 7-10)	0.178
Modified rankin scale at administration	4 (IQR: 3- 4)	3 (IQR: 3-4)	**0.027**
Length of hospital stay (days)	12.5 (IQR: 6.5-23)	7 (IQR: 5-12)	**0.012**
Modified rankin scale at 3rd month	4 (IQR: 3-6)	2.5 (IQR: 1-3)	**<0.001**
Bridging therapy (mechanical thrombectomy)	5 (21 %)	26 (23%)	0.784
Variables Outcome 2: symptomatic intracranial hemorrhage	**Yes (n=15)**	**No (n=120)**	**p value**
Alberta stroke program early CT score	8.5 (IQR: 7-10)	8 (IQR: 6.5-9.5)	0.558
Microbleed anatomical rating scale	6 (IQR:1.5-7.5)	4 (IQR: 2-6)	0.255
Modified rankin scale at administration	4 (IQR: 3.5-4.5)	3 (IQR: 2.5-3.5)	0.305
Length of hospital stay (days)	17.5 (IQR: 4.5-30.5)	8 (IQR: 4-12)	0.075
Modified rankin scale at 3rd month	2.5 (IQR: 1-4)	3 (IQR: 2-4)	**0.005**
Bridging therapy (mechanical thrombectomy)	4 (27%)	11 (9%)	0,747

CT: Computed tomography, IQR: Interquartile range

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Case-Based Radiology Education In Interns: Comparing Learning And Retention Across Modalities

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Abstract

Aim: This study aimed to evaluate intern physicians' ability to interpret basic radiological imaging methods and to investigate the effect of a case-based training program on knowledge acquisition and retention.

Materials and Methods: In this prospective study, participants underwent a pre-test before training, a post-test after training, and a retention test four weeks later. Assessments were performed using direct radiography, ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) modalities. The data were statistically analyzed, and performance changes between modalities were examined.

Results: This study included 50 intern physicians enrolled in medical school. Of the participants, 40% (n=20) were male and 60% (n=30) were female. The median age was 24 years (interquartile range: 24-24). A statistically significant increase was found in all imaging modalities in the post-test results compared to the pre-test (direct radiography, US, CT: $p<0.001$; MRI: $p=0.019$). In the retention test, a statistically significant increase was observed in all modalities compared to the pre-test ($p=0.001$). However, when the post-test was compared with the retention test, no statistically significant difference was observed in direct radiography and US ($p=0.381$; $p=0.059$), while a statistically significant decrease was observed in CT and MRI ($p=0.006$; $p=0.001$).

Conclusion: Case-based training significantly improves interns' ability to interpret basic radiologic imaging modalities. While permanent learning was achieved primarily in direct radiography and basic US applications, loss of knowledge was observed in more complex modalities such as CT and MRI. Structuring training programs taking into account these differences may contribute to the development of clinical decision-making skills.

Keywords: Intern physician, radiology education, case-based learning, ultrasound, retention

Introduction

Radiologic imaging modalities are an indispensable part of the diagnosis and treatment process in the emergency department. Direct radiography, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US) especially facilitate rapid decision-making in emergency patient management. However, many studies have shown that intern physicians feel inadequate in the interpretation and application of these imaging modalities. In a study by Glenn-Cox et al. (1), a large proportion of intern physicians reported that they did not receive adequate radiology training in the medical school curriculum and therefore experienced deficiencies in clinical practice. Similarly, Harthoorn et al. (2) emphasized that radiology education should be integrated more effectively into the curriculum, and restructuring teaching methods and content could increase students' acquisition of clinical skills. In addition, other studies in the field of radiology have demonstrated the positive relationship between students' attitudes, skills, and clinical competencies, indicating the need for more effective planning of educational processes (3).

In recent years, online or case-based learning methods have come to the forefront alongside traditional methods in clinical education (4). Case-based learning enables students to acquire

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knowledge through real clinical scenarios and to develop problem-solving and decision-making skills. Fromke emphasized that case-based learning is an effective and efficient teaching model, especially for new generation students (Gen Z and Millennial generation) (5). Sugi et al. (6) showed that the use of interactive case materials in radiology education enriches the learning process by increasing student participation. In addition, the new case-based and competency-oriented teaching format developed by Masthoff et al. (7) increased student motivation and supported skill acquisition. this study aimed to evaluate the effectiveness of a case-based theoretical and practical training program designed to improve the radiological interpretation and application skills of intern physicians. It also aimed to investigate its impact on short-term learning and long-term knowledge retention.

Materials and Methods

Study Design and Setting

This prospective study was conducted in a medical school within the scope of the Scientific and Technological Research Council of Türkiye (TÜBİTAK) 2209-A University Students Research Projects Support Program. Within the scope of the study, a case-based theoretical and practical training program on radiological imaging frequently encountered in the emergency department was implemented. The results of the pre-test, post-test, and retention test conducted after the training constituted the research data. This study was approved by the institutional review board and ethics committee of Recep Tayyip Erdoğan University in Türkiye (decision no: 2025/357, date: 31.07. 2025).

Participant Selection and Data Collection

A total of 62 intern physicians studying in a medical school, who were in the internship period, did not have a shift or outpatient clinic/service shift at the hospital on the dates of the study, and were able to participate in all sessions uninterruptedly during the training were invited to the study. Four of the intern physicians missed their theoretical training, two missed their practical training, two missed the pre-test, one missed the post-test, and three missed the retention test. As a result, out of the intern physicians were excluded, and 50 who completed all training and evaluation processes were included in the study.

Prior to the training, a questionnaire including demographic information, subjective perceptions of skills and attitudes towards radiology, and a 10-question case-based multiple-choice pre-test was administered to the participants. After the completion of the training, the 10-question post-test and questionnaire were reapplied which were prepared at equivalent content and difficulty level. To evaluate the retention of learning, a retention test consisting of 28 questions was conducted 1 month after the training. All data were recorded using a standard data coding template and converted into a format suitable for analysis.

Training Program and Content

The training program was planned for two days. On the first day, case-based theoretical training were held. In this context, lectures titled "The Importance of Direct Radiography", "Commonly Missed Direct Radiography Examples", "Computed Tomography with All Sections", "Common Pathological Computed Tomography Cases", "US, the Shining Star of Recent Years", "Common Ultrasound Case Examples" and "Magnetic Resonance imaging Reading Principles and Case Examples" were presented. In the theoretical sessions, each topic was explained through case examples of common pathologies encountered in the emergency department.

On the second day, hands-on practical training were held to improve the participants' skills in the use of US. Four stations were created in this context: "Trauma US — the Focused Assessment with Sonography in Trauma (FAST) and the extended FAST (eFAST)", "hepatobiliary US", "Doppler US", and "US-Guided Interventional Procedures (vascular access, venipuncture, central venous catheter placement)". At each station, the training sessions were supported by visual materials, video recordings, and live model applications. The training program was conducted in an integrated structure, aiming to provide both theoretical knowledge and practical skills.

All theoretical and practical training sessions were conducted by emergency medicine specialists who had completed at least five years of professional experience. For the US practice sessions, two instructors were selected, who had both attended and successfully completed a basic US course approved by professional emergency medicine associations. Both had at least five years of experience in point-of-care ultrasound (PoCUS), with an average of 250 US examinations per year.

Data Collection Tools and Measurements

The data collection process in the study consisted of three main components: a demographic and subjective assessment questionnaire, case-based knowledge tests (pre-test and post-test), and a retention test.

Questionnaires: In the questionnaires administered before and after the training, participants' gender, age, grade level, the specialty they planned to choose in the future, their subjective evaluation of the type, duration, and adequacy of their previous radiology education, their self-initiated learning activities, and their perception of their skills in interpreting imaging methods were questioned. In the questionnaires administered after the training, additional questions were included regarding the scientific adequacy of the program, its appropriateness in terms

of duration, the level of experience gained, and the imaging technique in which improvement was achieved. Likert-type scales were also used to assess the effect of the training program on the participants' ability to interpret or apply different imaging modalities. Accordingly, the participants were asked to respond on a five-point scale before and after the training program for direct radiography, CT, and MRI, by selecting "definitely can interpret, can interpret, undecided, cannot interpret, definitely cannot interpret" and for US by selecting definitely can apply, can apply, undecided, cannot apply, definitely cannot apply. Thus, an attempt was made to measure whether there was a change in individual perceptions resulting from the training.

Pre-test and post-test: Both tests consisted of 10 questions and were prepared at a similar level of difficulty. The questions were organized in a case-based multiple-choice format based on four direct radiographs, 3 CT, 2 US, and 1 MRI image. The pre-test was administered just before the start of the training, and the post-test was administered after the completion of the training. In tests, the number of correct answers was evaluated based on both total score and modality (direct radiography, CT, US, MRI).

Retention test: It was administered 1 month after the completion of the training and consisted of 28 questions. The questions were prepared in a case-based multiple-choice format including eight direct radiographs, nine CT, seven US, and four MR images. With this test, the long-term retention of the information obtained from the training was evaluated.

All test questions were developed collaboratively by three emergency medicine specialists with at least five years of clinical experience and active involvement in undergraduate radiology and US education. The content validity of the questions was ensured through consensus among the educators, focusing on common emergency radiology scenarios. To guarantee equivalence of difficulty and scope between the pre-test and post-test, the questions were constructed using identical learning objectives, similar case complexity, and parallel distributions of imaging modalities. The retention test questions were independently reviewed and validated by two external emergency medicine educators, to confirm that they assessed the same level of knowledge and comprehension without reproducing identical cases.

Statistical Analysis

All analyses were performed in Jamovi version 1.6 statistical software (The Jamovi Project, 2021, Computer Software, version 1.6, Sydney, Australia). Continuous variables were expressed as mean ± standard deviation or median interquartile range (IQR). Categorical variables were expressed as number (percentage, %). In modality-based learning outcome and retention assessments, the percentage of correct answers for the relevant modality was calculated. Pre-tests, and post-tests retention tests were compared using paired Student's t-test when parametric assumptions were met, and Wilcoxon signed-rank test, when parametric assumptions were not met. In all statistical analyses, p values <0.05 were considered significant.

Results

A total of 50 intern physicians were included in the study. Of the participants, 40% (n=20) were male, and 60% (n=30) were female. The median age was 24 years (IQR: 24-24), and the age distribution of the participants was relatively homogeneous. Urology (12%, n=6), emergency medicine (10%, n=5), cardiology (8%, n=4), and psychiatry (8%, n=4) were the most frequently considered specialties in career choices. Of the participants, 46% (n=23) reported previous didactic radiology training, 30% (n=15) had case-based training experience, and 92% (n=46) had attempted self-learning. The median values for didactic training time and case-based training time were 0 hours (IQR: 0-10) and 0 hours (IQR: 0-2), respectively. Basic demographic information is shown in Table 1.

Figure 1 shows the pre- and post-training self-assessment results of the intern physicians. While 50% of the participants stated that they could interpret direct radiographs before the training, this rate increased to 98% after the training. In US: while 74% of the participants answered "I cannot" or "I am undecided" before the training, 64% stated that they could perform the application after the training. In CT, while only 28% thought that they could interpret before the training, 80% stated that they could interpret after the training. In magnetic resonance interpretation, while 50% of the participants were undecided before the training, 52% stated that they could interpret, after the training. In general evaluation, most of the participants reported that the training made a significant contribution, especially in the fields of direct radiography and US (Figure 1).

The pre-test and post-test performances of the intern physicians participating in the study are presented in Table 2. According to the post-test results, a significant increase was found in all imaging modalities: direct radiography ($p<0.001$), US ($p<0.001$), CT ($p<0.001$), and MRI ($p = 0.019$). Similarly, in Table 3, where the results of the pre-test and retention test were compared, a significant improvement was observed in all modalities ($p=0.001$ for all). In Table 4, where post-test and retention test performances were evaluated, no significant difference was found between the direct radiography and US results ($p=0.381$, $p=0.059$, respectively). In contrast, a significant difference was found in CT and MRI ($p=0.006$, $p=0.001$, respectively). These data revealed that case-based training provided more permanent learning, especially in direct radiography and US applications.

Table 1. The volunteers' demographic data and baseline characteristics	
Characteristics	**All volunteers (n=50)**
Gender	
Male, n (%)	20 (40.0)
Female, n (%)	30 (60.0)
Age (years), median (IQR)	24 (IQR: 24-24)
Specialties considered in career preference	
Emergency medicine, n (%)	5 (10.0)
Family medicine, n (%)	2 (4.0)
Internal medicine, n (%)	2 (4.0)
Infectious diseases, n (%)	3 (6.0)
General surgery, n (%)	1 (2.0)
Eye diseases, n (%)	3 (6.0)
Thoracic surgery, n (%)	2 (4.0)
Public health, n (%)	1 (2.0)
Obstetrics and gynecology, n (%)	1 (2.0)
Cardiology, n (%)	4 (8.0)
Neurosurgery, n (%)	1 (2.0)
Orthopedics, n (%)	2 (4.0)
Pediatrics, n (%)	1 (2.0)
Psychiatry, n (%)	4 (8.0)
Medical genetics, n (%)	1 (2.0)
Anesthesia, n (%)	1 (2.0)
Dermatology, n (%)	3 (6.0)
Pulmonologist, n (%)	1 (2.0)
Plastic surgery, n (%)	1 (2.0)
Urology, n (%)	6 (12.0)
Child psychiatry, n (%)	1 (2.0)
Unknown, n (%)	4 (8.0)
Didactic education, n (%)	23 (46.0)
Didactic education (time), median (IQR)	0 (IQR: 0-10)
Case-based education, n (%)	15 (30.0)
Case-based education (time), median (IQR)	0 (IQR: 0-2)
Self-directed learning, n (%)	46 (92.0)
IQR: Interquartile Range (25p, 75p)	

Discussion

This study showed that after case-based theoretical training enriched with emergency cases and structured US practice, short-term cognitive acquisition increased significantly in all modalities for intern physicians. One month later, the data showed that the increase in direct radiography and US performance was maintained, while there was a partial decline in CT and MRI. The findings reveal that case-based learning strengthens basic interpretation and application skills by focusing on the clinical context and decision-making steps. This aligns with the approaches supported by case discussions, small group studies, and competency-based modules in the literature, especially in radiology education (5-7).

The significant and permanent gain in the US component may be associated with the enrichment of the training with visual materials as well as early and intensive practices, working in small groups, and using peer-supported or peer-educator models. In particular, abundant visual content, scenarios supported by videos, and applications on live mannequins make the learning process more concrete and permanent. Comprehensive reviews in recent years show that peer educators can achieve a level of proficiency close to that of the instructor in teaching activities. Appropriate preparation, audiovisual materials, and live applications contribute significantly to skill development, and short-session practices with frequent feedback significantly increase learning (8,9).

The modality-specific segregation seen in the retention window is also consistent with the trend in the literature: POCUS/basic US image acquisition and interpretation skills are significantly maintained at mid-term (6-8 weeks), whereas performance in more complex image acquisition/interpretation processes (e.g., cardiac windows, multistep slice analysis) fades more rapidly (10,11). These findings support the higher persistence observed for US and direct radiography in our study. Some studies have demonstrated that superficial vascular structures can be easily visualized via US by all physicians (12). Our training was designed at the basic US/POCUS level, and the evaluation questions were prepared within this framework, which may explain the retention success in US training. However, a similar retention may not be achieved in a training program targeting more advanced imaging windows or complex analyses.

Another implication is that learning should be distributed and reinforced over time. Systematic reviews focused on radiology education show that spaced learning, retrieval practice, and interleaving strategies can provide significant advantages in both short-term and long-term examinations, and that spaced digital education contributes to knowledge growth and behavioral change in health professions (13-15). Future studies should examine learning curves for CT/MRI with longitudinal designs involving intermittent reinforcement and repeated presentation of rare pathologies. To ensure long-term retention in CT and MRI imaging, incorporating periodic reinforcement and simulation-based case discussions is recommended. Integrating CT/MRI interpretation into longitudinal curricula, supported by spaced digital learning and structured feedback, may help sustain diagnostic accuracy and cognitive retention over time.

In this study, 50 intern physicians participated, representing diverse specialty interests including emergency medicine, internal medicine, surgery, and psychiatry. Although participants reported a wide range of specialty preferences, no statistically significant difference was found between these preferences and the learning outcomes in radiology education. However, students planning to specialize in clinically dynamic disciplines such as emergency medicine or internal medicine may have higher

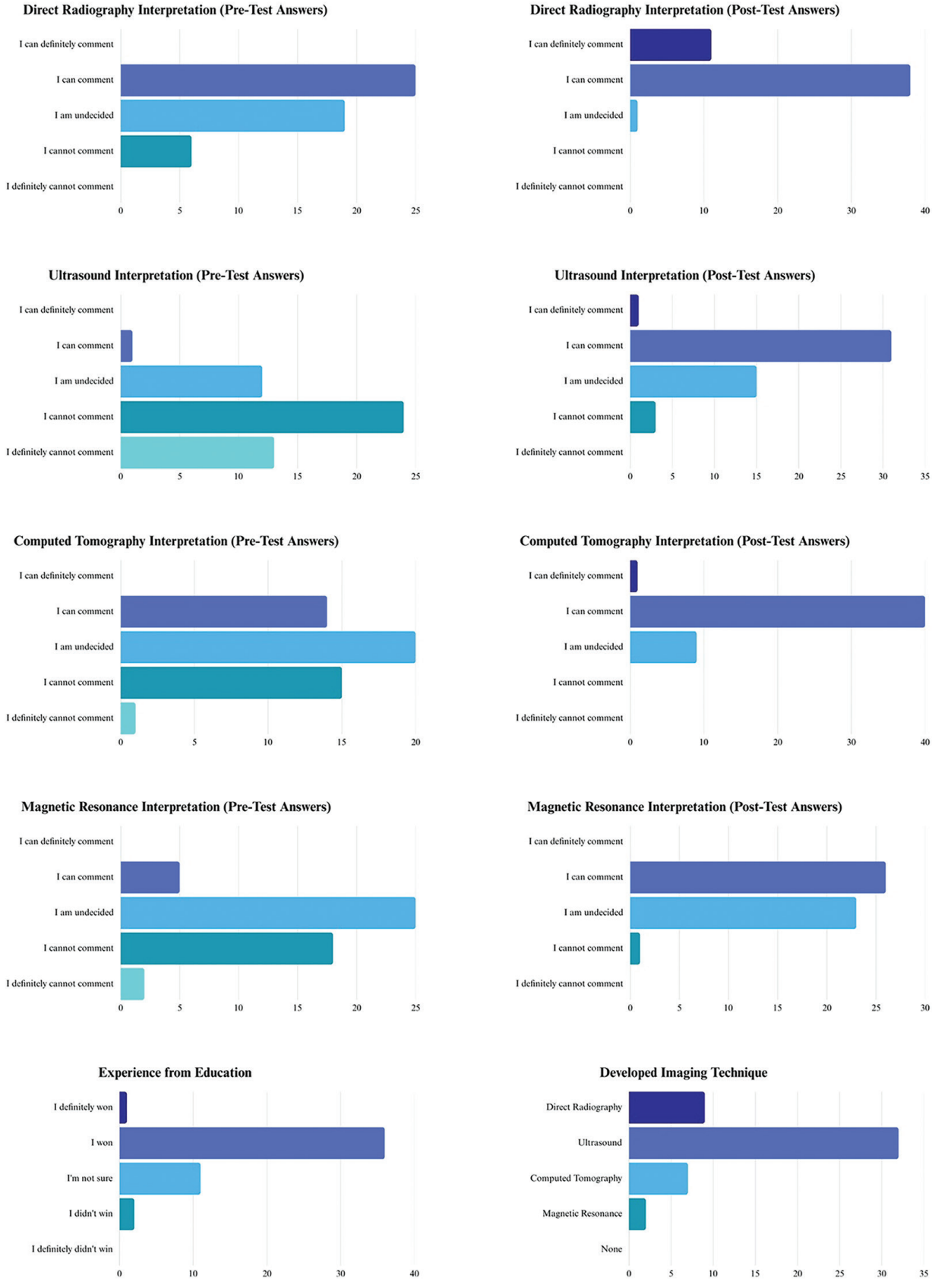

Figure 1. Graphical visualization volunteers' responses

Table 2. Pre- and post-test average score statistics			
Radiological method	**Pre-test**	**Post-test***	**p-value**
Direct radiography (%), median (IQR)	25 (IQR: 25-50)	75 (IQR: 50-75)	**0.001**
Ultrasound (%), median (IQR)	0 (IQR: 0-0)	100 (IQR: 100-100)	**0.001**
Computed tomography (%), median (IQR)	33.3 (IQR: 33.7-66.7)	100 (IQR: 66.7-100)	**0.001**
Magnetic resonance (%), median (IQR)	(IQR: 0-100)	100 (IQR: 0-100)	**0.019**
*: Correct answer percentage, IQR: Interquartile range (25p, 75p)			

Table 3. Pre- and persistence test average score statistics			
Radiological method	**Pre-test**	**Persistence test***	**p-value**
Direct radiography (%), median (IQR)	25 (IQR: 25-50)	75 (IQR: 50-75)	**0.001**
Ultrasound (%), median (IQR)	0 (IQR: 0-0)	85.7 (IQR: 71.4-96.4)	**0.001**
Computed tomography (%), median (IQR)	33.3 (IQR: 33.7-66.7)	77.8 (IQR: 66.7-77.8)	**0.001**
Magnetic resonance (%), median (IQR)	0 (IQR: 0-100)	100 (IQR: 75-100)	**0.001**
*: Correct answer percentage, IQR: Interquartile range (25p, 75p)			

Table 4. Post- and persistence test average score statistics			
Radiological method	**Post-test***	**Persistence test***	**p-value**
Direct radiography (%), median (IQR)	75 (IQR: 50-75)	75 (IQR: 50-75)	0.381
Ultrasound (%), median (IQR)	100 (IQR: 100-100)	85.7 (IQR: 71.4-96.4)	0.059
Computed tomography (%), median (IQR)	100 (IQR: 66.7-100)	77.8 (IQR: 66.7-77.8)	**0.006**
Magnetic resonance (%), median (IQR)	100 (IQR: 0-100)	100 (IQR: 75-100)	**0.001**
*: Correct answer percentage, IQR: Interquartile range (25p, 75p)			

intrinsic motivation and engagement during case-based imaging training, as radiologic interpretation directly contributes to their future clinical decision-making processes.

In the assessment dimension, it is emphasized that standardized and comparable assessment tools are still limited in US education; multiple-choice knowledge tests and self-assessment forms are frequently used. Objective structured clinical exams directed objective procedural skills/objective structured assessment of ultrasound skills (OSAUS) like frameworks that measure practical competence objectively and observationally need more systematic integration (8). In this context, the pre-, post-, and retention-knowledge exams used in our study are effective. It is recommended to add performance-based measures with structured practice stations (e.g., FAST/eFAST OSAUS checklists) at a later stage.

Study Limitations

The main limitations of the study are the single-center design, sample size, and the presence of a subjective perception component in the questionnaire items. In addition, the retention assessment was conducted only one month after the training, which does not allow for definitive conclusions about long-term knowledge retention. Given the partial decline observed in CT and MRI performance, it is possible that this decrease will further progress over longer follow-up periods (e.g., 6 months or 1 year).

Conclusion

The data obtained show that the case-based and practice-oriented mixed curriculum, in the emergency department context, significantly enhances short-term learning and provides high retention in direct radiography and US in one month.

Ethics

Ethics Committee Approval: This study was approved by the institutional review board and ethics committee of Recep Tayyip Erdoğan University in Türkiye (decision no: 2025/357, date: 31.07. 2025).

Informed Consent: Patients' consent was obtained from the patients before starting the study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: İ.A., Ö.B., Concept: İ.A., D.H., O.K., Design: M.M.Y., A.B.Ş., H.A., Data Collection or Processing: İ.A., E.G., Analysis or Interpretation: İ.A., Literature Search: İ.A., Writing: İ.A., Ö.B.

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Ultrasound Assessment of Quadriceps Muscle Layer Thickness as a Predictor of Outcome in Critically ill Patients

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Abstract

Aim: Muscle weakness in critically ill patients is associated with complications, but its accurate quantification at the bedside remains challenging. Our aim was to assess whether loss of quadriceps muscle layer thickness (QMLT) predicts mortality, and to examine its correlation with duration of mechanical ventilation and other severity indices.

Materials and Methods: A total of 100 intensive care unit (ICU) patients were prospectively assessed with QMLT measurements on the dominant side on days 1, 3, and 7 of the ICU stay, or on the day of discharge, whichever occurred earlier.

Results: Percentage decline in QMLT on days 3 and 7 (or discharge) was a significant predictor of mortality [for day 3: hazard ratio (HR): 1.06, 95% confidence interval (CI): 1.03-1.1, p=0.001; for day 7 or discharge: HR: 1.05, 95% CI: 1.02-1.07, p=0.0002]. The decline in QMLT correlated well with mortality (p=0.50, p<0.001 at day 3, and p=0.77, p<0.001 at day 7 or on the day of discharge). A decline in QMLT correlated with duration of mechanical ventilation on day 7 (p=0.46, p<0.001) and with mNUTRIC score on day 3 and on day 7 of ICU stay or on the day of discharge (p=0.36, p <0.001 at day 3; p=0.44, p<0.001 at day 7 or on the day of discharge). The decline in QMLT did not correlate with the duration of ICU stay. A >25.97% decline in QMLT on day 7 of ICU stay was associated with a high area under the curve (AUC) (AUC 0.96; p<0.0001).

Conclusion: Continuous monitoring of QMLT decline by ultrasound independently predicts mortality.

Keywords: ICU patients, ICU outcome, quadriceps muscle, ultrasound

Introduction

Muscle weakness in critically ill patients is linked to a wide range of health challenges (1,2). The causes are multifactorial and include deranged glycaemia, inflammatory stress responses, immobilization, nutrient deficiencies, and various medications—all of which contribute to intensive care unit (ICU)–associated muscle weakness (1,3). Early identification of muscle weakness in critically ill patients is essential (4). Muscle wasting can progress at a rate of up to 2% per day, with the greatest losses observed in patients with multiorgan dysfunction syndrome during the first 10 days of illness (3,5). Such muscle loss can delay recovery and is associated with longer hospital stays, higher mortality, and increased healthcare costs (6).

Accurate bedside quantification of muscle wasting remains a challenge (7,8). Conventional anthropometric measurements are often unreliable in the ICU, while advanced imaging techniques such as computed tomography are impractical for routine use (7,9,10). Ultrasonography (USG) has therefore emerged as a valuable bedside tool—non-invasive, cost-effective, and widely accessible (4,10-13).

Loss of quadriceps muscle-layer thickness (QMLT) has been shown to correlate with in-hospital survival, duration of mechanical ventilation, and other indicators of severity in the ICU (3,7,14). However, data on this topic remain limited in Asian populations (15). Therefore, we designed this study to assess QMLT, measured by USG, as a predictor of mortality in critically ill patients. The secondary objectives were to examine the relationships between

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QMLT and the duration of mechanical ventilation, the length of ICU stay, and the modified Nutrition Risk in the Critically Ill (mNUTRIC) score among patients admitted to our ICU.

Materials and Methods

This prospective observational study involved 100 patients admitted to the ICU of our institute and was conducted after obtaining this study received approval the Vardhman Mahavir Medical College and Safdarjung Hospital Institutional Ethics Committee (desicion number: IEC/VMMC/SJH/Thesis/06/2022/CC-47, date: 11.07.2022). Toledo et al. (7) reported hazard ratios (HRs) of 2.1 for requiring mechanical ventilation, 3.7 for probability of ICU survival, and 4.5 for probability of hospital survival, based on thigh muscle thickness. Using these values as references, the minimum required sample size to achieve 80% study power at a 5% significance level was calculated as 97.13 patients. To reduce the margin of error, 100 patients were recruited.

All adults aged 18 years and above who were expected to require mechanical ventilation for at least 48 hours were included after obtaining written informed consent. Patients were excluded if they had documented neuromuscular disease (e.g., myopathy, neuropathy), cerebrovascular accident, lower limb amputation or orthopedic surgery, pregnancy, requirement for prone positioning, transfer from another hospital after an ICU stay of more than 48 hours, extubation within 48 hours, or a hospital stay of less than 72 hours due to death or discharge.

During the first 24 hours after ICU admission, demographic, biochemical, and clinical data were collected. Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, Sequential Organ Failure Assessment (SOFA) scores, and mNUTRIC scores were recorded at admission. Quadriceps muscle thickness was measured using a portable B-mode Sonosite M-Turbo (Digi 600 A Pro) ultrasound device with a 6-12 MHz linear array probe. The assessor was trained through 20 supervised scans to ensure standardization. All measurements were taken in a semi-recumbent position (30°-45°), with the knees extended and the toes pointing upward.

A line was drawn between the anterior superior iliac spine and the upper pole of the patella. The point at the junction between the upper two-thirds and the lower one-third of this line was marked, and ultrasound gel was applied. The transducer was held perpendicular to the line, and the depth was adjusted to visualize the femur. Once an optimal image was obtained, it was frozen. QMLT was measured as the distance between the upper surface of the femoral bone and the lower border of the superficial fascia of the rectus femoris, thereby including both the rectus femoris and vastus intermedius muscles. Each measurement was taken twice on the dominant leg (defined by the hand used for eating), and the average value was recorded. QMLT measurements were obtained on days 1, 3, and 7 of the ICU stay, or earlier if the patient was discharged.

All patients were monitored for biochemical parameters, treatments received, duration of mechanical ventilation, length of ICU stay, total hospital stay, and 28-day mortality. Caloric and protein intakes (calorie/protein debt) from days 1 to 7 were also recorded, using baseline requirements of 25 kcal/kg/day and 1.2 g/kg/day of protein. Intake was documented on days 1, 3, and 7.

Statistical Analysis

Data entry was performed using Microsoft Excel, and statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS), version 25.0 (IBM, Chicago, USA). Quantitative data with a normal distribution were expressed as mean ± SD, whereas non-normally distributed data were expressed as median (interquartile range). Normality was assessed using the Shapiro-Wilk test. Non-normal data were analyzed using the Mann-Whitney U test, and normally distributed data were analyzed using the independent t-test.

ROC curves were used to determine the cut off point, sensitivity, specificity, positive predictive value, and negative predictive value for predicting mortality based on the percentage decrease in QMLT. Kaplan-Meier survival curves with log-rank testing were used to assess overall survival. Univariate and multivariate Cox proportional hazards regression analyses were performed to identify significant risk factors for mortality. Spearman's rank correlation coefficient was used to evaluate the relationships between the percentage change in QMLT and duration of mechanical ventilation (days), ICU stay (days), and mNUTRIC score. A point-biserial correlation was used to assess the association between the percentage change in QMLT and mortality.

Results

The demographic characteristics of the study population are presented in Table 1. The mean age of participants was 38.1±18 years; 67% were male and 33% were female. The mean body mass index (BMI) was 22.36±3.21 kg/m^2. A majority of the patients (73%) had no comorbidities. Among the remaining 27%, diabetes mellitus was the most common condition (14%), followed by chronic obstructive pulmonary disease (11%). The median APACHE II, SOFA, and mNUTRIC scores at admission were 14, 7, and 2, respectively. Based on a standard daily requirement of 25 kcal/kg and 1.2 g/kg of protein, the median calorie intake increased from 47.6% on day 1 to 77.4% on day 7; the median protein intake increased from 15.9% on day 1 to 49.2% on day 7. All patients required mechanical ventilation; the median

duration was 5 days, and the mean length of ICU stay was 6 days. The overall mortality in the cohort was 51%.

Table 1. Demographic data and patient parameters

Variables	Mean (±SD), median (IQR), n (%)
Age (years)*	38.1 (±18)
Gender#	
Male	67 (67)
Female	33 (33)
Height (cm) #	171.50 (9.56)
Weight (kg) #	66.02 (11.9)
BMI (kg/m^2) #	22.36 (3.21)
Comorbidity#	
Diabetes mellitus	14 (14)
COPD	11 (11)
Hypertension	9 (9)
Renal	3 (3)
Cardiac	2 (2)
Absent	73 (73)
APACHE II**	14 (10.2-17)
SOFA score**	7 (4-9)
mNUTRIC score**	2 (1-3)
Serum glucose (mg/dL)*	141.8 (70.4)
Creatinine (mg/dL) *	2.1 (2.8)
Urea (mg/dL)*	75.7 (70)
Sodium (mEq/L)*	138.8 (8.3)
Potassium (mEq/L)*	4.5 (1)
Calcium (mg/dL)*	7.6 (1.1)
Magnesium (mg/dL)*	2.2 (0.5)
Phosphate (mg/dL)*	4.1 (2)
Procalcitonin (ng/mL) *	22 (20.1)
Lactate (mmol/L)*	2.5 (2.3)
Bicarbonate (mmol/L)*	22.7 (6.9)
pH*	7.355 (0.1)
Percentage of expected calorie intake#	
Day 1	47.6 (29.7)
Day 3	74.4 (27.6)
Day 7	77.4 (36.1)
Percentage of expected protein intake#	
Day 1	15.9 (21)
Day 3	44.55 (32.4)
Day 7	49.25 (36.6)
Mechanical ventilation#	100 (100)
Duration of mechanical ventilation (days)**	5 (4-7)
Length of ICU stay (days)**	6 (5-7)
Mortality#	51 (51)

*: Mean (±SD), **: Median (IQR), #: n (%), APACHE II: Acute Physiology and Chronic Health Evaluation 2, SOFA: Sequential Organ Failure Assessment, mNUTRIC: Modified Nutritional Risk in Critically Ill, ICU: Intensive care unit, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation, IQR: Interquartile range

There were no significant differences in age or BMI between survivors and non-survivors. However, non-survivors had significantly higher APACHE II, SOFA, and mNUTRIC scores at admission compared with survivors [APACHE II: confidence interval (CI): 0.63-5.1, p=0.013; SOFA: CI: 1.42-3.81, p<0.0001; mNUTRIC: Z=3.9, p<0.0001]. Median urea and creatinine levels were also significantly higher in non-survivors (Z=3.61, p=0.0003; Z=3.85, p=0.0001, respectively). Non-survivors were more acidotic, with significantly lower mean pH (CI: -0.25 to 5.2; p=0.009). The median duration of mechanical ventilation was significantly lower in survivors (Z=3.29; p=0.001), although the length of ICU stay was comparable between groups.

Median calorie and protein intake on day 1 did not differ significantly between survivors and non-survivors. However, non-survivors demonstrated significantly lower calorie intake (day 3: Z=3.42, p=0.0006; day 7: Z=3.10, p=0.002) and protein intake (day 3: Z=3.12, p = 0.002; day 7: Z=2.81, p=0.005). A significant reduction in QMLT in the dominant leg was observed on ICU days 3 and 7 (Z=4.85, p < 0.0001; Z=7.86, p<0.0001, respectively). These results are summarized in Table 2.

The percentage decline in QMLT was evaluated on days 3 and 7 to determine its predictive value for mortality. ROC curve analysis identified cut-offs of a 14.5% decline on day 3 and a 25.97% decline on day 7 (Table 3, Figure 1). A decline exceeding these thresholds had a specificity of 85.7% and a sensitivity of 62.8% for predicting mortality on day 3. By day 7, sensitivity and specificity increased to 86.3% and 93.9%, respectively. The positive predictive value improved from 82.1% on day 3 to 93.6% on day 7, and the negative predictive value increased from 68.9% to 86.8%. The diagnostic accuracy increased from 72% on day 3 to 90% on day 7. The area under the curve was significantly higher for the day-7 cut off (0.96) compared with the day-3 cut-off (0.75) (p<0.0001).

Cox regression analyses were performed using age, BMI, APACHE II, SOFA, and mNUTRIC scores, along with percentage decline in QMLT, in two models: day 3 (model A) and day 7 (model B) (Table 4). The Percentage decline in QMLT on days 3 and 7 remained the only significant predictor of mortality: HR: 1.06 (95% CI: 1.03-1.10), p=0.001 for day 3; HR: 1.05 (95% CI: 1.02-1.07), p=0.0002 for day 7 This suggests that each percentage decline in QMLT is associated with an approximately 5-6% increase in mortality risk during the ICU stay.

Kaplan-Meier difference in survival curves showed a significant between patients with QMLT declines below versus above the identified thresholds on day 3 and on day 7 or on the day of discharge (log-rank test p=0.001 and p<0.0001, respectively). Patients with smaller declines demonstrated consistently better survival (Figure 2).

Table 2. Comparison of patient parameters between survivors and non-survivors

Parameters	Survivors	Non survivors	Z/mean diff (CI)/χ^2 value	p-value
Age (years)	35.35±17.25	40.57±20.13	5.22 (2.23-12.67)	0.17*
Body mass index (kg/m²)	22.47±3.11	22.25±3.33	0.22 (-1.06-1.5)	0.74*
APACHE II score	12.69±4.62	15.55±6.43	2.86 (0.63-5.1)	**0.013***
SOFA score	5.57±2.38	8.19±3.51	2.62 (1.42-3.81)	**<0.0001***
mNUTRIC score	1 (1-2)	3 (1.5-4)	3.9	<0.0001†
Creatinine (mg %)	0.8 (0.5-1.2)	1.5 (0.85-3.25)	3.85	0.0001†
Urea (mg/dL)	37 (21-57)	71 (35.5-137)	3.61	0.0003†
Procalcitonin (ng/mL)	12.3 (2.5-40.9)	15.7 (3.65-50)	0.36	0.72†
Lactate (mmol/L)	1.4(1-2.6)	1.9 (1.15-3.9)	1.81	0.07†
Bicarbonate (mmol/L)	23.98±7.38	21.5±6.33	2.48 (-0.25-5.2)	0.08*
pH	7.38±0.09	7.33±0.12	0.06 (0.01-0.1)	**0.009***
Duration of mechanical ventilation (days)	5 (3-6)	6 (5-7)	3.29	0.001†
Length of ICU stay (days)	6 (5-7)	6 (5-7.5)	0.47	0.64†
% calorie intake day 1	59.21 (16.05-75.32)	43.8 (17.93-66.58)	1.06	0.29†
% calorie intake day 3	84 (72.91-97.05)	67 (49.44-81.922)	3.42	**0.0006†**
% calorie intake day 7	95.88 (91.865-113.75)	67.5 (34.77-90)	3.1	**0.002†**
% protein intake day 1	0 (0-35.71)	0 (0-33.69)	1	0.32†
% protein intake day 3	60.48 (28.48-75.94)	34 (13.815-52.12)	3.12	**0.002†**
% protein intake day 7	81.65 (36.88-87.575)	29.49 (19.9-56.96)	2.81	**0.005†**
% decline in QMLT day 3	9.5 (4.808-12.632)	16.73 (11.655-25.516)	4.85	**<0.0001†**
% decline in QMLT day 7 or discharge	12.38 (8.466-15.819)	34.45 (28.954-40.017)	7.96	**<0.0001†**

*: Independent t test, †: Mann-Whitney test
QMLT: Quadriceps muscle layer thickness, APACHE II: Acute Physiology and Chronic Health Evaluation 2, SOFA: Sequential Organ Failure Assessment, mNUTRIC: Modified Nutritional Risk in Critically Ill, COPD: Chronic obstructive pulmonary disease, CI: Confidence interval

Table 3. Sensitivity, specificity, positive predictive value and negative predictive value of percentage decrease in QMLT for predicting mortality

Variables	Percentage decline in QMLT dominant leg day 3	Percentage decline in QMLT dominant leg day 7 or discharge
Area under the ROC curve (AUC)	0.78	0.96
Standard error	0.047	0.016
95% confidence interval	0.69-0.86	0.9-0.99
p-value	<0.0001	<0.0001
Cut off	>14.48	>25.97
Sensitivity	62.8	86.3
Specificity	85.7	93.9
PPV	82.1	93.6
NPV	68.9	86.8
Diagnostic accuracy	72	89

QMLT: Quadriceps muscle layer thickness, PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the curve

A significant correlation was found between a decline in QMLT and duration of mechanical ventilation on day 7 (p=0.46, p<0.001), and between a decline in QMLT and mNUTRIC scores on days 3 and 7 (p=0.36, p<0.001 and p=0.44, p < 0.001, respectively). A decline in QMLT did not correlate significantly with ICU length of stay (Table 5), suggesting limited reliability for predicting ICU length of stay. The decline in QMLT correlated strongly with mortality (p=0.50, p<0.001 on day 3; p=0.77, p<0.001 on day 7).

Discussion

This study reflects the characteristic demographics of the Asian subcontinent, with all patients in our cohort requiring mechanical ventilation. The high median SOFA scores highlight the severity of illness and explain the elevated mortality rate. This makes our cohort well suited to draw meaningful conclusions regarding QMLT decline as assessed by ultrasound. Although several ultrasound protocols for monitoring muscle mass exist in the literature, we chose to measure quadriceps muscle thickness

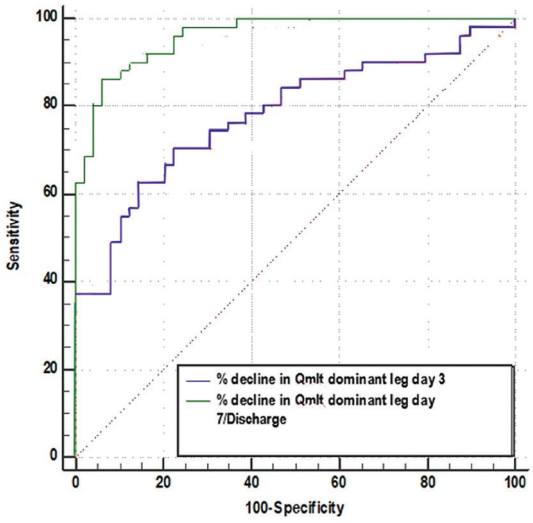

Figure 1. Receiver operating characteristic curve of percentage decrease in QMLT for predicting mortality

QMLT: Quadriceps muscle layer thickness

without compression rather than assessing cross-sectional area (CSA), owing to its simplicity. Previous research has demonstrated comparable results between measurements taken with and without compression, supporting the reliability of this method (4,5,7,10). However, a standardized ultrasound protocol for QMLT assessment has yet to be established (11).

We found that a 24% decrease in QMLT from baseline—measured on day 7 of the ICU stay or on the day of discharge—is a significant risk factor for mortality. A decline in QMLT was also correlated with higher mNUTRIC scores on days 3 and 7 and with prolonged mechanical ventilation by day 7. The association between QMLT decline and mortality is consistent with findings from other studies, which emphasize that serial decline, rather than single-time-point QMLT values, is more clinically meaningful (7).

Furthermore, patients who exhibited a greater loss of QMLT had a lower probability of survival, as demonstrated by Kaplan-Meier analysis. Cox regression analysis identified QMLT decline as an independent risk factor for mortality. Our findings suggest that each percentage-point decline in QMLT corresponds to a 5-6% increase in mortality risk at both time points evaluated. We analyzed decline in QMLT on days 3 and 7 using separate Cox models to avoid confounding between the two time points. Prior studies employing similar statistical methods have shown comparable trends (7,16-18). To the best of our knowledge, however, no previous study has demonstrated QMLT decline as an independent predictor of mortality using Cox proportional hazards analysis. Studies using CT imaging to assess muscle loss in critically ill patients have similarly reported an association between muscle loss and increased mortality (19).

A few studies in the literature, however, report findings that differ from ours (10,20,21). The VALIDUM study, a prospective multicenter trial, concluded that QMLT and CSA assessments were insufficient to identify patients with low muscle mass; patients with a poor prognosis who were unlikely to survive were excluded, and this exclusion may have influenced the results (10). Palakshappa et al. (20) reported a moderate correlation between the decline in rectus femoris CSA and muscle strength, but their study included only 29 predominantly septic patients. A systematic review by Bunnell et al. (21) questioned the utility of neuromuscular ultrasound in assessing critical illness neuromyopathy due to methodological inconsistencies, variable tissue water content, interobserver variability, differences in probe angle, and variation in transducer frequency.

The American Society for Parenteral and Enteral Nutrition recommends screening tools such as the mNUTRIC score for assessing nutritional risk (22). Özdemir et al. (18) argued that mNUTRIC scores may not fully reflect nutritional status because

Table 4. Univariate and multivariate cox proportional hazard regression for significant risk factors of mortality

Variables	Univariate hazards ratio (95% CI)	p-value	Multivariate hazards ratio (95% CI)	p-value
Age (years) A, B	1.01 (0.99-1.03)	0.06	...	...
Body mass index (kg/m²) A, B	0.96 (0.87-1.05)	0.38	...	...
APACHE II score A,B	1.04 (0.99-1.09)	0.15	...	...
SOFA score A, B	1.1 (1.01-1.2)	0.03	...	...
mNUTRIC score A, B	1.28 (1.07-1.53)	0.006	...	...
Percentage decline in QMLT dominant leg day 3 A, B	1.07 (1.04-1.11)	<0.0001	1.06 (1.03-1.1)	**0.001**
Percentage decline in QMLT dominant leg day 7 or discharge A, B	1.051 (1.03-1.07)	<0.0001	1.05 (1.02-1.07)	**0.0002**

Model A: Age, BMI, APACHE II, SOFA, mNUTRIC, QMLT decline percent day 3 dominant side
Model B: Age, BMI, APACHE II, SOFA, mNUTRIC, QMLT decline percent day 7 dominant side
QMLT: Quadriceps muscle layer thickness, APACHE II: Acute Physiology and Chronic Health Evaluation 2, SOFA: Sequential Organ Failure Assessment, mNUTRIC: Modified Nutritional Risk in Critically Ill, COPD- Chronic Obstructive Pulmonary Disease, CI: Confidence interval

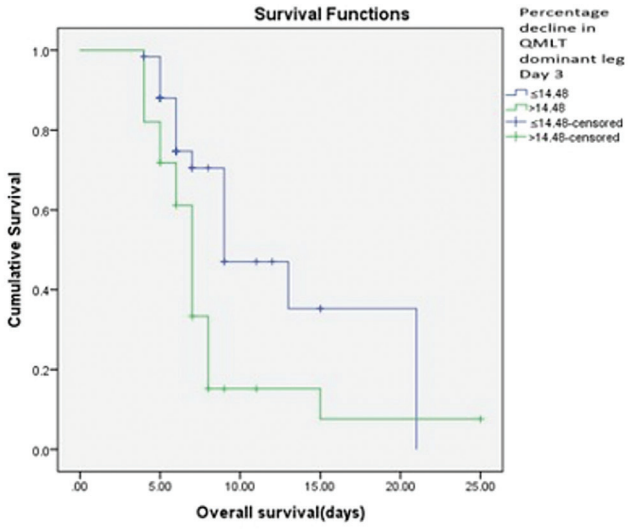

Figure 2.1. Kaplan Meier survival analysis curve to compare overall survival between percentage decline in QMLT in dominant leg on day 3 (log rank test, p=0.001)

QMLT: Quadriceps muscle layer thickness

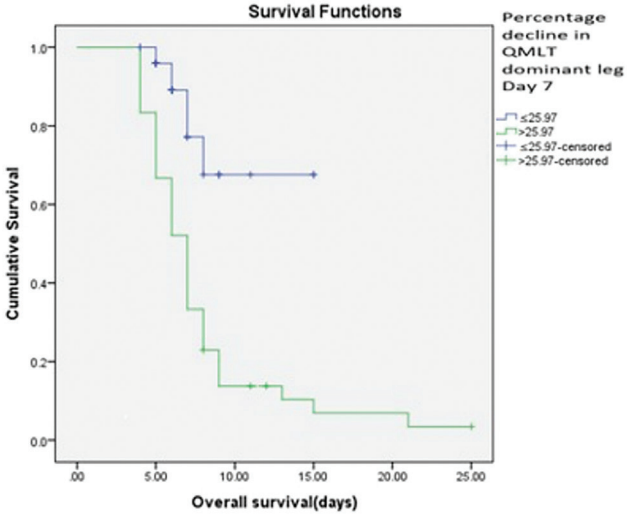

Figure 2.2. Kaplan Meier survival analysis curve to compare overall survival between percentage decline in QMLT in dominant leg on day 7 or discharge (log rank test, p<0.0001)

QMLT: Quadriceps muscle layer thickness

they lack anthropometric components. This highlights the need for improved nutritional risk assessment tools for ICU patients. The moderate correlation between QMLT decline and mNUTRIC scores on days 3 and 7 in our study suggests that QMLT may serve as a useful adjunctive tool for nutritional assessment. Previous research indicates that muscle loss is greatest during the first week of mechanical ventilation (5,7). Our study also demonstrated a moderate correlation between QMLT decline and duration of mechanical ventilation, although no correlation was observed with ICU length of stay. These findings support the potential role of QMLT decline as a prognostic marker.

Non-survivors in our cohort consistently failed to meet the recommended calorie and protein targets from day 2 onward, compared with survivors. Some studies have shown that achieving individualized caloric and protein targets in critically ill patients may reduce mortality by up to 50% (23). However, another study found that this benefit was limited to female patients, likely due to their lower baseline muscle mass (24). Such mixed evidence underscores the need for more robust and objective parameters—such as USG-based QMLT—provided they can be standardized. These may ultimately outperform traditional nutritional targets and risk scores.

Nutritional status plays a crucial role in preserving skeletal muscle mass, and inadequate calorie–protein intake accelerates muscle catabolism in critically ill patients. Studies have shown that ICU patients can lose up to 2% of muscle mass per day during the first week, and undernutrition amplifies this decline. Poor nutritional intake reduces amino acid availability for muscle protein synthesis, leading to a measurable decrease in QMLT. Research demonstrates that greater early muscle loss, including QMLT reduction, is strongly associated with prolonged mechanical ventilation and higher mortality rates. Undernutrition heightens the inflammatory and stress responses, further driving catabolism and worsening muscle wasting.

Study Limitations

Our study has certain limitations. Sepsis- and trauma-related fluid shifts may have been because intramuscular fluid accumulation could have affected QMLT measurements. Muscle edema can mask true muscle atrophy, resulting in measurements that appear deceptively stable or even elevated. This complicates

Table 5. Correlation of QMLT with various parameters

Percentage change in QMLT	Duration of mechanical ventilation (days)	Duration of ICU stay (days)	mNUTRIC score	Mortality
Dominant leg day 3	p* 0.18, p=0.08	p* -0.04, p 0.8	p* 0.36, **p<0.001**	p** 0.50, **p<0.001**
Dominant leg day 7	p* 0.46, **p<0.001**	p* 0.17, p 0.09	p* 0.44, **p<0.001**	p** 0.77, **p<0.001**

*: Spearman's rank correlation,**: Point-biserial correlation, mNUTRIC: Modified Nutritional Risk in Critically Ill, ICU: Intensive care unit, QMLT: Quadriceps muscle layer thickness

the interpretation of our measurements. Second, this single-center observational study may therefore serve primarily as a hypothesis-generating investigation. Additionally, assessing quadriceps dimensions in a single plane may not accurately represent muscle loss throughout the body. This may explain why we observed only a moderate correlation with the duration of mechanical ventilation and no correlation with the ICU length of stay. The quadriceps muscle contains both type I and type II fibers—type II fibers serving as power generators and type I fibers as stabilizers (4). Our measurement technique did not allow differentiation between fiber types, which may also influence the interpretation of muscle loss patterns.

Conclusion

Continuous monitoring of QMLT by USG shows that loss of muscle mass during ICU stay is an independent predictor of mortality and correlates with mNUTRIC score and increased days of mechanical ventilation by day 7. This tool is applicable at the bedside, noninvasive, and cost-effective. Intensivists should thus prioritize the routine evaluation of QMLT and adjust nutritional support accordingly. These findings underscore the importance of integrating QMLT assessment into clinical practice to improve patient care in intensive care settings.

Highlights

Continuous monitoring of quadriceps muscle layer thickness using ultrasound is a cost-effective, safe, and valuable tool for intensivists. It can be used to monitor recovery as well as to predict mortality.

Ethics

Ethics Committee Approval: this study received approval the Vardhman Mahavir Medical College and Safdarjung Hospital Institutional Ethics Committee (desicion number: IEC/VMMC/SJH/Thesis/06/2022/CC-47, date: 11.07.2022).

Informed Consent: All adults aged 18 years and above who were expected to require mechanical ventilation for at least 48 hours were included after obtaining written informed consent.

Footnotes

Authorship Contributions

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

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

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First Aid Knowledge and Attitudes of Restaurant Employees in Foreign Body Aspiration Accidents: A District-Based Study in İstanbul

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Abstract

Aim: The aim of this study is to examine the level of first aid knowledge and attitudes of the personnel working in restaurant establishments in a selected district of İstanbul province.

Materials and Methods: The sample of the study consists of 44 restaurant/restaurant employees. SPSS 22 Package Program was used to analyze the data.

Results: Among participants, 31.8% had first aid knowledge-skills, 15.3% had encountered a tracheal foreign body incident, and 6.9% had intervened. Knowledge-skills specific to tracheal foreign body were present in 28.4%, and 19.3% held a first aid certificate; 59.6% were willing to receive training. Knowledge scores differed significantly by first aid knowledge-skills and by encountering or intervening in such cases. Attitude scores differed significantly by age, workplace position, years of employment, first aid knowledge-skills, prior intervention, and certification status.

Conclusion: The rates of having first aid knowledge, skills, and prior intervention experience among restaurant employees were low despite their frontline role in settings where choking incidents are likely to occur. The strong association between higher knowledge and attitude scores and having first aid training or experience indicates that structured education can effectively improve preparedness. Given that most participants were willing to receive training, incorporating regular first aid and basic life support programs into workplace safety policies for the food service sector could strengthen bystander response and reduce preventable deaths from foreign body airway obstruction.

Keywords: Airway obstruction, first aid, foreign body aspiration, respiratory aspiration, restaurants

Introduction

Foreign body aspiration (FBA) is a time-critical medical emergency in which delays in recognition or intervention may rapidly lead to hypoxia and death (1). Survival often depends on the ability of bystanders to deliver effective first aid, most notably abdominal thrusts (the heimlich maneuver), which remain the primary method for relieving airway obstruction in conscious individuals (2). Although national data on choking events in restaurant environments in Türkiye are lacking, foreign body airway obstruction (FBAO) carries an adult fatality rate exceeding 3% globally (3), and is accurately identified in fewer than 10% of cases requiring assistance (4).

Choking episodes frequently occur during meals, making public dining environments a high-risk setting. Recent epidemiological evidence from Türkiye, based on 192 media-reported cases, indicates that 21.4% of FBA incidents took place in restaurants, with food items predominating as aspirated materials (5). This pattern highlights the need to assess and strengthen the preparedness of restaurant personnel, who are often the only individuals present during the critical early moments of airway obstruction.

Consistently, international studies report food as the leading cause of FBA across all age groups (6,7), yet the readiness of non-medical frontline workers in dining settings remains insufficiently

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studied. Despite their pivotal role in recognizing and responding to choking, restaurant workers are not included in mandatory first aid certification frameworks in Türkiye. This gap underscores the need for evidence to guide workplace safety regulations and community-based emergency response strategies.

This study therefore aims to evaluate the first aid knowledge and attitudes of restaurant workers in a district of İstanbul, providing baseline data to inform targeted training programs and support policy development to enhance emergency response capacity in restaurant settings.

Materials and Methods

Study Design

This study was designed as a cross-sectional study. The research hypotheses are as follows:

H1-1: The sociodemographic characteristics of restaurant staff substantially affect their knowledge of first aid for FBA.

H1-0: The sociodemographic characteristics of restaurant staff do not substantially affect their knowledge of first aid for FBA.

H2-1: The first aid training and experience of restaurant staff significantly affect their knowledge of first aid for FBA.

H2-0: The first aid training and experience of restaurant staff do not significantly affect their knowledge of first aid for FBA.

H3-1: Restaurant staff who have received first aid training and have experience in FBA incidents have significantly more positive attitudes toward first aid interventions.

H3-0: There is no significant relationship between first aid training, experience, and attitudes toward first aid interventions.

Study Population and Sample

The study population comprises employees from 260 restaurants situated in the Üsküdar area. The number and locations of these restaurants were acquired from the Licensing Department of the Üsküdar Municipality.

The district consists of 33 neighborhoods, with the distribution of restaurants as follows: Twenty-two neighborhoods contain between 1 and 10 restaurants, five neighborhoods contain between 11 and 20, four neighborhoods contain 21 or more, and two neighborhoods have no restaurants at all. A total of 44 restaurants were included in the sample. One restaurant was selected from each of the 22 neighborhoods with 1-10 restaurants, two restaurants from each of the five neighborhoods with 11-20 restaurants, and three restaurants from each of the four neighborhoods with 21 or more restaurants.

A simple random sampling technique was used for sample selection. Restaurants were sorted according to their license numbers and neighborhoods, and 44 establishments were randomly chosen. Furthermore, 44 other restaurants were randomized as contingency possibilities should a selected restaurant refuse participation.

The study was conducted between March 8 and March 20, 2023.

Every member of staff present during the in-person visits to the selected restaurants were invited to participate in the study. Participation was optional, and no staff members dropped out. The sample comprises all on-site staff who provided consent to participate during the data collecting period. A flow diagram titled “Participant Recruitment and Inclusion Process” has been inserted in the Methods section (Figure 1).

Sample Size and Power Analysis

A priori power analysis was performed with G*Power (version 3.1.9.4) to ascertain the minimal sample size necessary for the investigation. With a medium effect size (Cohen’s d=0.5), a significance threshold of α=0.05, and a target power of 0.80 for a two-tailed independent samples t-test, the necessary total sample size was determined to be 128 individuals.

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Data Collection Tools

In this study, staff from restaurants were instructed to independently complete a three-part questionnaire under observation. The questionnaire comprised:

Section 1: 12 questions assessing basic demographic and professional information.

Section 2: 26 questions measuring knowledge levels regarding FBA accidents.

Section 3: 13 questions evaluating attitudes towards FBA accidents.

The researchers constructed the questionnaire items based on the content of the Turkish Ministry of Health First Aid Handbook. Prior to the preparation of the original draft, the questionnaire underwent evaluation by a panel including a public health professor, a public health expert, an emergency medicine

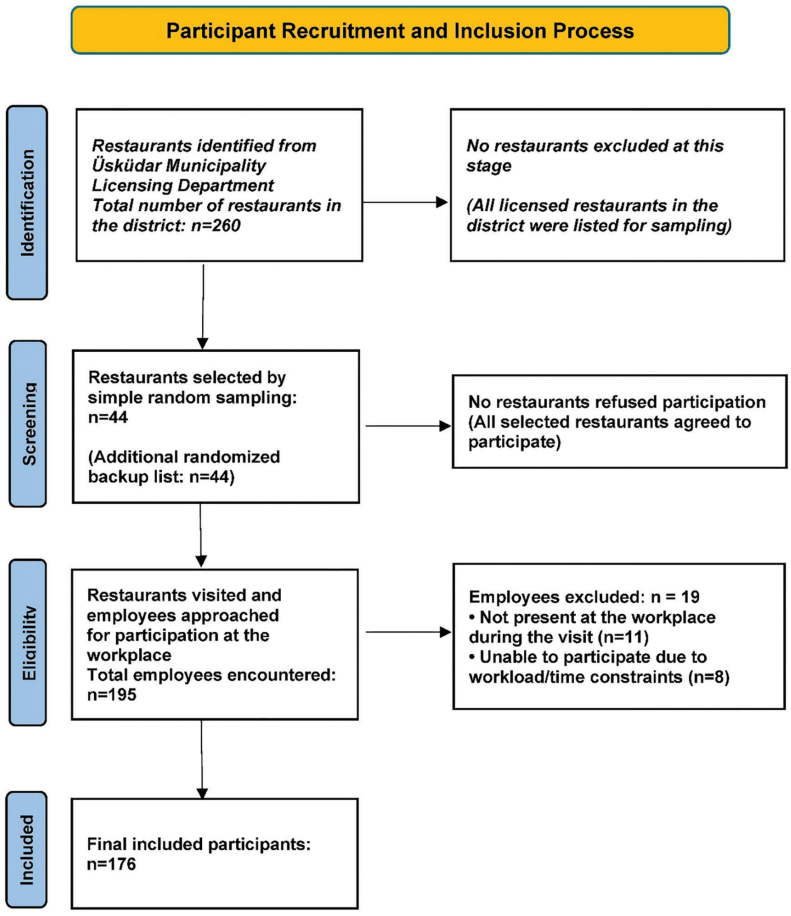

Figure 1. Flow diagram of the participant recruitment and inclusion process

professor, and a psychiatric counselor. Modifications were implemented in response to their suggestions to enhance clarity, content validity, and relevance. A pilot test was administered to evaluate comprehensibility with a cohort of 10 volunteer restaurant staff. Their feedback was utilized to make final modifications prior to deployment. The pilot group data were exclusively utilized for questionnaire refinement and excluded from the final analysis.

The researchers formulated the questions utilizing the Turkish Ministry of Health First Aid Handbook (8). In the knowledge evaluation survey, replies were evaluated as follows: accurate answers earned 1 point, but erroneous answers or "I don't know" responses received 0 points. The total potential scores varied from a minimum of 0 to a maximum of 26.

Knowledge levels were categorized as follows:

Inadequate knowledge level: 0-7 points (<25% correct answers)

Moderate knowledge level: 8-13 points (25-50% correct answers)

Adequate knowledge level: 14-26 points (>50% correct answers)

For the attitude survey, responses were rated on a five-point likert scale: "Strongly agree," "Agree," "Neutral," "Disagree," and "Strongly disagree." The questionnaire included 24 statements, each scored between 1 and 5 points, with a total possible score ranging from a minimum of 13 to a maximum of 65.

The internal consistency of the questionnaire was evaluated using Cronbach's alpha. The reliability analysis demonstrated satisfactory internal consistency for both sections of the instrument, with α=0.789 for the 26-item knowledge section and α=0.777 for the 13-item attitude section.

Ethical Considerations

Before the initiation of the investigation, formal consent was obtained from the University of Health Sciences Hamidiye Scientific Research Ethics Committee (decision no.: 2023/3, date: 10.02.2023). The principles of the Declaration of Helsinki were rigorously followed throughout the study.

Participant Consent

Informed consent was obtained from all participants prior to their inclusion in the study.

Statistical Analysis

The data acquired in this study were analyzed utilizing SPSS version 23. Descriptive statistics were reported as mean ± standard deviation, median (1st quartile-3rd quartile), frequency, and percentage. The normality of continuous variables was evaluated using Shapiro-Wilk tests. Both the knowledge and attitude score distributions deviated from normality; therefore, non-parametric tests were used in the analyses. Consequently, non-parametric tests were utilized. The Mann-Whitney U test was used for pairwise comparisons of non-normally distributed continuous variables, whilst the Kruskal-Wallis test was applied for comparisons involving more than two independent groups. Upon discovering significant differences, post hoc pairwise comparisons were performed with the Dunn-Bonferroni test. A p value of less than 0.05 was deemed statistically significant.

Results

Of the participants, 79% were male, and 42% belonged to the 17-30 age demographic. Regarding educational attainment, 55.7% were high school graduates. Concerning employment positions, 39.8% were employed as waiters. The distribution of work experience indicated that 50.6% had been working for 0 to 8 years. Furthermore, 36.9% of participants were employed in firms with 1 to 14 employees. 31.8% of participants reported possessing knowledge and abilities in first aid procedures. The incidence of those who had previously experienced a FBA event was 15.3%, but the percentage of those who had intervened in such cases at least once was 6.9%. 28.4% of participants have knowledge and abilities in first aid interventions for FBA. Furthermore, 19.3% of participants possessed a first aid certification, although 59.6% indicated a readiness to undergo first aid training. The participants' average knowledge score was 11.68±4.32, signifying a moderate degree of knowledge level (Table 1). The distribution of participants across knowledge-level categories was as follows: 17.04% were classified as inadequate, 46.02% as moderate, and 36.94% as adequate (Figure 2).

The analysis of the correlation between participants' knowledge level scores and their socio-demographic features, as well as their knowledge and practices about first aid, reveals no statistically significant difference in the median scores among parents. Upon analysis by age groups, the median score for the 31-44 age cohort was elevated, with no statistically significant differences identified. The analysis revealed that the median score of secondary school graduates was elevated, while that of elementary school graduates was reduced, with no statistically significant difference identified. The analysis revealed that the median scores of waiters and managers were elevated and not statistically significant. No statistically significant difference exists between the median scores based on years of employment at the workplace. No statistically significant variation was seen in the median ratings based on the number of employees at the workplace. The median score of those possessing a first aid certificate is elevated, and there exists no statistically significant disparity. The median score of individuals inclined to obtain a first aid certificate is elevated in the response "I am undecided," and it lacks statistical significance. Significant differences were observed in knowledge level scores related to the possession of knowledge and skills in first aid practices ($p=0.001$, $r=0.26$), prior experience with a FBA incident ($p=0.036$, $r=0.16$), intervention in such incidents ($p=0.040$, $r=0.15$), and possession of knowledge and skills in first aid interventions for FBA ($p<0.001$, $r=0.34$) (Table 2).

The findings indicate that there is no statistically significant difference in the median attitude scores of participants when compared to their socio-demographic characteristics, knowledge, and practices related to first aid. The analysis indicated that the median score for high school graduates was elevated, while the median score for literate individuals was lower, with no statistically significant difference observed. No statistically significant difference was observed in the median scores based on the number of employees in the workplace. The median score of individuals who intervened in FBA incidents was higher, though this difference was not statistically significant. The median score of individuals willing to obtain a first aid certificate was higher for the statement "I don't want to," although this difference was not statistically significant. Significant differences in attitude scores were observed based on age group ($p=0.012$, $\eta^2=0.04$), job position ($p=0.022$, $\eta^2=0.03$), and years of employment ($p=0.018$, $\eta^2=0.03$). No statistically significant difference was observed when comparing the attitude scores of participants regarding FBA incidents and their willingness to receive first aid training. Significant differences in attitude scores were observed based on knowledge and skills in first aid practices ($p<0.001$, $\eta^2=0.07$), intervention during a FBA incident ($p=0.002$, $\eta^2=0.05$), knowledge and skills in first aid interventions for FBA ($p<0.001$, $\eta^2=0.08$), and possession of a first aid certification ($p=0.040$, $\eta^2=0.02$) (Table 3).

Participants exhibited a low percentage of correct responses to specific key statements in the knowledge assessment survey. A notable proportion of respondents failed to correctly identify the key signs of complete airway obstruction, including inability to breathe, clutching the neck, inability to speak, and cyanosis. Among the items with the lowest correct response rates, only 2.3% of participants correctly identified the proper positioning of an infant during a choking intervention.

Table 1. Distribution of data about the socio-demographic characteristics of participants and their knowledge and habits related to first aid		
Age, years (median, minimum-maximum)		34 (17-70)
Years of employment (median, minimum-maximum)		8 (0-40)
Number of employees in the workplace (median, minimum-maximum)		25 (1-343)
Knowledge level score (mean ± SD)		11.68±4.32
Attitude score (mean ± SD)		50.06±7.26
		n (%)
Gender	Male	139 (79.0)
	Female	37 (21.0)
Age group	17-30 years	74 (42.0)
	31-44 years	72 (41.0)
	45-70 years	30 (17.0)
Educational status	Literate	6 (3.4)
	Primary school	16 (9.1)
	Secondary school	30 (17.0)
	High school	98 (55.7)
	University	26 (14.8)
Job position	Waiter	70 (39.8)
	Kitchen staff	30 (17.0)
	Busboy	14 (8.0)
	Business owner	12 (6.8)
	Cashier	10 (5.7)
	Other	19 (10.8)
	Manager/supervisor	21 (11.9)
Years of employment	0-8 years	89 (50.6)
	9-20 years	58 (33.0)
	21-40 years	29 (16.5)
Number of employees in the workplace	1-14 employees	65 (36.9)
	15-40 employees	51 (29.0)
	41-343 employees	60 (34.1)
Possession of knowledge and skills in first aid practices	No	36 (20.5)
	Partially	84 (47.7)
	Yes	56 (31.8)
Encountering a foreign body aspiration incident	No	149 (84.7)
	Yes	27 (15.3)
Number of interventions for foreign body aspiration incidents	Never intervened	164 (93.1)
	Once	7 (4.0)
	Twice	4 (2.3)
	Three times	1 (0.6)
Possession of first aid knowledge and skills related to foreign body aspiration incidents	No	41 (23.3)
	Partially	85 (48.3)
	Yes	50 (28.4)
Possession of a first aid certification	No	142 (80.7)
	Yes	34 (19.3)
Willingness to receive first aid training	Do not want	33 (18.8)
	Undecided	38 (21.6)
	Want	105 (59.6)

SD: Standard deviation

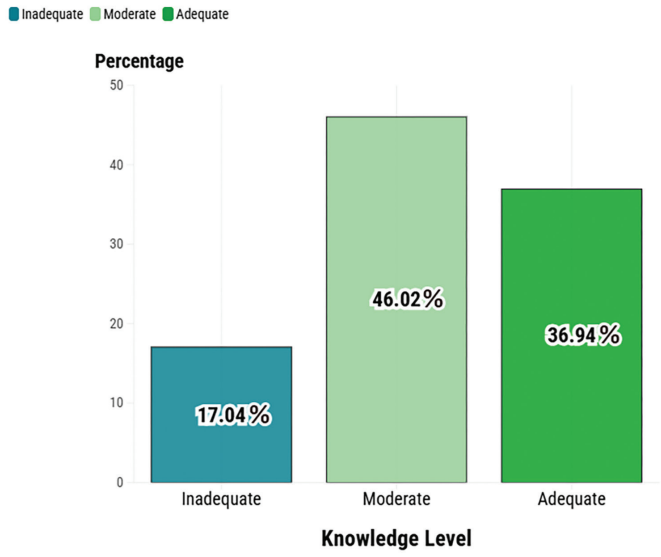

Figure 2. Distribution of participants by knowledge level scores

Table 2. Analysis of participants' knowledge level scores in relation to their socio-demographic factors and conclusions of their knowledge and behaviors regarding first aid

		Median (Q_1-Q_3)	p
Gender	Male	12 (9-15)	0.364
	Female	12 (7-14.5)	
Age group	17-30 years	12 (8-15)	0.067
	31-44 years	13 (11-15)	
	45-70 years	11 (8.5-14)	
Educational status	Literate	11 (4.75-17.5)	0.107
	Primary school	9 (7-13.25)	
	Secondary school	13 (8.75-14.25)	
	High school	12.5 (10.75-15)	
	University	11.5 (8.75-15)	
Job position	Waiter	13 (10-16)	0.159
	Kitchen staff	12 (9-15)	
	Busboy	9 (4.25-13)	
	Business owner	11.5 (7.5-14)	
	Cashier	11.5 (6.75-15.25)	
	Other	11 (7-14)	
	Manager/supervisor	13 (10-15)	
Years of employment	0-8 years	12 (8-15)	0.637
	9-20 years	12 (9-15)	
	21-40 years	12 (11-15)	
Number of employees in the workplace	1-14 employees	12 (8.5-15.5)	0.696
	15-40 employees	12 (9-15)	
	41-343 employees	11.5 (10-14)	
Possession of knowledge and skills in first aid practices	No[1]	10.5 (6-13.75)	**0.001****
	Partially[2]	12 (9-14.75)	
	Yes[3]	13 (11-16)	1<3

Table 2. Continued

		Median (Q_1-Q_3)	p
Encountering a foreign body aspiration incident	No	12 (9-15)	**0.036***
	Yes	14 (11-16)	
Number of interventions in foreign body aspiration incidents	Never intervened	12 (9-15)	**0.040***
	Intervened (includes 1, 2 and 3 times)	14.5 (12.25-15.75)	
Possession of first aid knowledge and skills in foreign body aspiration incidents	No[1]	10 (6-13)	**<0.001*****
	Partially[2]	12 (9-15)	1<2
	Yes[3]	14.5 (11.75-16)	1<3 2<3
Possession of a first aid certification	No	12 (9-15)	0.147
	Yes	13 (11-15)	
Willingness to receive first aid training	Do not want	13 (9-15)	0.201
	Undecided	13.5 (9.5-16)	
	Want	12 (9-14)	

Q_1: 25th percentile, Q_3: 75th percentile, *p<0.05, **p<0.01, ***p<0.001
Superscripts ([1]–[7]): Subgroup numbering for post-hoc comparisons. "1<2" indicates a significantly lower median in subgroup 1 than in subgroup 2

Table 3. Analysis of participants' attitude ratings in relation to their socio-demographic factors and findings of their knowledge and behaviors on first aid

		Median (Q_1-Q_3)	p
Gender	Male	50 (47-55)	0.607
	Female	51 (46.5-56)	
Age group	17-30 years[1]	49 (44.75-53)	**0.012***
	31-44 years[2]	52 (48-56)	
	45-70 years[3]	52 (47-57.25)	1<2
Educational status	Literate	48 (32-51.25)	0.479
	Primary school	50.5 (39.75-54)	
	Secondary school	50.5 (44.75-57)	
	High school	51 (47-55.25)	
	University	50 (48-54.5)	
Job position	Waiter[1]	51 (47-56)	**0.022***
	Kitchen staff[2]	51 (49-56)	3<1
	Busboy[3]	46.5 (39-50.75)	3<7
	Business owner[4]	53.5 (49.25-58.5)	3<2
	Cashier[5]	50 (44-54)	3<4
	Other[6]	49 (42-52)	6<2
	Manager/supervisor[7]	52 (48-56.5)	6<4
Years of employment	0-8 years[1]	47 (40.25-50.75)	**0.018***
	9-20 years[2]	50 (45.5-53)	
	21-40 years[3]	46 (38-54)	1<3
Number of employees in the workplace	1-14 employees	51 (48-56)	0.487
	15-40 employees	50 (46-55)	
	41-343 employees	50.5 (47-55)	

Table 3. Continued

		Median (Q_1-Q_3)	p
Possession of knowledge and skills in first aid practices	No[1]	47 (40.25-51.75)	**<0.001*****
	Partially[2]	51 (48-54)	1<2
	Yes[3]	52 (48-57)	1<3
Encountering a foreign body aspiration incident	No	50 (47-55)	0.316
	Yes	52 (45-58)	
Number of interventions in foreign body aspiration incidents	Never intervened	57 (46-60)	0.002**
	Intervened (includes 1, 2 and 3 times)	62 (55.75-64.5)	
Possession of first aid knowledge and skills in foreign body aspiration incidents	No[1]	47 (42-51.5)	**<0.001*****
	Partially[2]	51 (47.5-55)	1<2
	Yes[3]	52 (49-58.25)	1<3
Possession of a first aid certification	No	50 (46-55)	**0.040***
	Yes	52 (49-59)	
Willingness to receive first aid training	Do not want	51 (47-57)	0.405
	Undecided	50.5 (47-56)	
	Want	50 (47-54)	

Q_1: 25th percentile, Q_3: 75th percentile, *p<0.05, **p<0.01, ***p<0.001
Superscripts ([1]–[7]): Subgroup numbering for post-hoc comparisons. "1<2" indicates a significantly lower median in subgroup 1 than in subgroup 2

Additionally, just 4.0% recognized that FBA can cause fatal airway obstruction in all age groups. Furthermore, only 6.2% of participants accurately recognized that the abdominal thrust maneuver necessitates firm backward and upward pressure exerted with the hands. Additionally, prevalent misconceptions were noted concerning the age group most commonly affected, the significance of children maintaining concentration during meals, and the risks associated with walking or running while eating. Significant misconceptions were identified in first aid practices, particularly regarding the appropriate order of back blows and chest compressions. The findings underscore the necessity for specialized first aid training, with an emphasis on identifying symptoms of airway obstruction and executing suitable first aid techniques (Table 4).

The table below shows the response rates for the attitude survey, classified into the categories of "Strongly agree," "Agree," "Neutral," "Disagree," and "Strongly disagree" (Table 5).

Discussion

This study provides essential insights into an often neglected aspect of public health preparedness: the ability of frontline restaurant personnel to respond effectively to life-threatening choking incidents. Only 6.9% of participants reported having intervened in high-risk food service emergencies, and fewer than one-third indicated possessing the requisite first aid skills. The low prevalence of first aid certification, combined with a significant willingness to undergo training (59.6%), highlights the unmet demand and untapped potential for community-based interventions. These findings highlight the potential value of integrating context-specific, scenario-based first aid training into workplace safety programs, particularly in settings where FBA may occur.

Participants with both knowledge and practical skills in first aid exhibited significantly higher knowledge scores than those lacking such training. Furthermore, individuals possessing full or partial knowledge and skills exhibited more favorable attitudes towards first aid practices compared to those without any training. The findings indicate that theoretical understanding and practical experience are significant factors in emergency preparedness. Previous studies have reported similar associations, indicating that first aid training is correlated with enhanced knowledge and attitudes regarding emergency response (9,10). In the current study, only 28.4% of respondents reported possessing adequate first aid knowledge and skills, highlighting a significant deficiency in public preparedness. The disparity was notably pronounced among individuals with lower educational attainment, underscoring the necessity for enhanced access to first aid education, particularly via community-based initiatives.

Experiencing a real-life choking episode correlated with elevated knowledge scores among participants, although this experience seemingly did not affect their attitudes towards emergency response. This conclusion aligns with other studies indicating that direct exposure to emergencies may improve information retention but does not necessarily influence confidence or the propensity to act (11,12).

Table 4. Responses of participants to the knowledge assessment survey

	Incorrect	Don't know	Correct
	n (%)	n (%)	n (%)
Coughing and grasping the neck may indicate foreign body aspiration into the airways.	16 (9.1)	23 (13.1)	137 (77.8)
In cases of partial airway obstruction, where the individual is attempting to remove the foreign object by coughing, back blows should be administered to facilitate its clearance.	30 (17.1)	21 (11.9)	125 (71.0)
If the individual is attempting to remove the foreign object by coughing, they should be urged to persist in coughing.	34 (19.3)	36 (20.5)	106 (60.2)
Dyspnea, neck gripping in distress, aphonia, and cyanosis are indicators of total airway obstruction.	148 (84.1)	21 (11.9)	7 (4.0)
Intrusion of foreign items, including food particles, plastic, and metal, into the airways can result in life-threatening blockage across all age groups.	153 (86.9)	16 (9.1)	7 (4.0)
Foreign body aspiration in the airway is predominantly reported in adults across all age demographics.	77 (43.8)	37 (21.0)	62 (35.2)
Children should not be interrupted during meals to ensure adequate chewing, swallowing, and focus.	147 (83.6)	21 (11.9)	8 (4.5)
There is no harm in walking or running while eating.	140 (79.6)	18 (10.2)	18 (10.2)
Interruption of oxygen flow to the brain for over five minutes during foreign body aspiration episodes can result in brain damage and mortality.	149 (84.6)	20 (11.4)	7 (4.0)
Rescue interventions for infants and young children are the same as for adults.	25 (14.2)	35 (19.9)	116 (65.9)
The initial step should be to have the individual consume water.	42 (23.9)	25 (14.2)	109 (61.9)
The head should be tilted backward.	84 (47.7)	38 (21.6)	54 (30.7)
A maximum of three back blows should be administered in a sweeping motion.	28 (15.9)	35 (19.9)	113 (64.2)
To initiate the intervention, the rescuer should position themselves behind the individual and secure their torso.	6 (3.4)	20 (11.4)	150 (85.2)
One hand should be clenched into a fist and positioned just below the sternum, while the other hand provides support.	6 (3.4)	31 (17.6)	139 (79.0)
The hands must be forced forcefully backward and upward, with the thumb exerting pressure on the abdomen.	133 (75.6)	32 (18.2)	11 (6.2)
The abdominal thrust procedure must be performed repeatedly until the item is dislodged or the individual becomes unconscious.	21 (12.0)	52 (29.5)	103 (58.5)
When interfering with a newborn, the baby should be positioned face down on the arm, with the head supported and inclined forward.	134 (76.1)	38 (21.6)	4 (2.3)
A maximum of three rapid and vigorous back punches should be delivered between the infant's shoulder blades in a sweeping manner.	30 (17.0)	38 (21.6)	108 (61.4)
Following the administration of back blows, it is imperative to ascertain whether the airway is unobstructed.	7 (4.0)	30 (17.0)	139 (79.0)
If the item does not dislodge following back strikes, the child should be positioned supine with head support.	42 (23.9)	68 (38.6)	66 (37.5)
Position two fingers directly behind the sternum and provide five compressions.	14 (7.9)	70 (39.8)	92 (52.3)
The compression maneuver must be sustained until the foreign object is evacuated or the child becomes unconscious.	24 (13.7)	71 (40.3)	81 (46.0)
An individual may execute the move independently.	49 (27.9)	37 (21.0)	90 (51.1)
They should form a fist and position it behind the sternum.	29 (16.4)	55 (31.3)	92 (52.3)
They should apply pressure to the abdomen by pressing their fist against a solid surface, such as the back of a chair.	14 (8.0)	50 (28.4)	112 (63.6)

Table 5. Responses of participants to the attitude survey

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
	n (%)	n (%)	n (%)	n (%)	n (%)
I anticipate that I could witness an individual choking as a result of foreign body aspiration in everyday situations.	67 (38.1)	59 (33.5)	34 (19.3)	5 (2.8)	11 (6.3)
It is my belief that all individuals should possess the capability to execute first aid interventions.	83 (47.2)	41 (23.3)	15 (8.5)	18 (10.2)	19 (10.8)
I argue that restaurant personnel ought to undergo first aid training.	99 (56.3)	51 (29.0)	11 (6.3)	4 (2.3)	11 (6.3)
Consuming meals with bones or fishbones without meticulous removal poses no risk.	96 (54.5)	54 (30.7)	26 (14.8)	0 (0.0)	0 (0.0)
I am certain that I possess the information to intervene.	22 (12.5)	40 (22.7)	76 (43.2)	20 (11.4)	18 (10.2)
I am capable of intervening in such a case.	25 (14.2)	50 (28.4)	69 (39.2)	17 (9.7)	15 (8.5)
I might be unable to intervene out of panic.	42 (23.9)	69 (39.2)	65 (36.9)	0 (0.0)	0 (0.0)
I may assess if an individual's airway is partially or fully clogged by observation.	21 (11.9)	42 (23.9)	84 (47.7)	15 (8.5)	14 (8.0)
I believe that I should call 112 immediately.	67 (38.1)	53 (30.1)	20 (11.4)	22 (12.5)	14 (8.0)
I should not intervene until 112 arrives.	78 (44.3)	59 (33.5)	39 (22.2)	0 (0.0)	0 (0.0)
I believe that the person should be assisted immediately.	76 (43.2)	54 (30.7)	26 (14.8)	8 (4.5)	12 (6.8)
I believe that the abdominal thrust maneuver is life-saving.	77 (43.8)	50 (28.4)	28 (15.9)	5 (2.8)	16 (9.1)
I think that striking the person's chest may be beneficial.	68 (38.6)	56 (31.8)	52 (29.5)	0 (0.0)	0 (0.0)

Participants who intervened in FBA incidents demonstrated significantly greater knowledge and attitude scores than those who did not intervene. This finding indicates that participation in real-life emergencies may improve cognitive comprehension and attitudinal preparedness for first aid. The findings align with prior research, highlighting the reinforcing impact of direct involvement on emergency preparedness (13). Only 6.9% of participants in our study reported intervening in such situations, reflecting a low level of active bystander participation.

The scores for knowledge and attitude were positively correlated with the level of proficiency in first aid. Participants possessing comprehensive first aid knowledge and skills achieved the highest scores, followed by those with partial knowledge, and finally those lacking any training. This sequential pattern reinforces the hypothesis that perceived self-efficacy in first aid is associated with increased knowledge and more positive attitudes. Our findings align with existing literature that similarly associates self-reported competence with enhanced preparedness for emergency situations (14,15). Only 31.8% of participants reported having first aid knowledge and skills. This suggests that both training and opportunities for practical reinforcement —such as scenario-based exercises— may help strengthen preparedness.

No statistically significant differences in knowledge or attitude scores were found between genders, consistent with previous research indicating that gender does not substantially influence first aid knowledge or attitudes (16). Approximately 80% of participants were male, which may have limited the ability to detect potential gender-related differences. Future studies with more balanced samples could help clarify whether gender plays a meaningful role in first aid preparedness.

No statistically significant differences were observed in knowledge scores across age groups. In contrast, attitude scores were significantly higher among participants aged 31-44 compared with those aged 17-30. This pattern is consistent with previous literature indicating that age does not necessarily enhance factual first aid knowledge, yet may be associated with more positive attitudes toward emergency response behaviors (17,18). The age distribution in our sample was relatively balanced—42.0% aged 17-30 and 41.0% aged 31-44—suggesting that the observed difference is unlikely to be attributable to unequal group sizes. The more favorable attitudes in the older cohort may reflect accumulated life experience, including greater exposure to emergencies or caregiving roles, which could enhance perceived responsibility or willingness to intervene in FBA events.

No significant differences in either knowledge or attitude scores were identified across educational levels. This finding is aligned with previous studies reporting that formal educational attainment alone does not reliably predict first aid competence or readiness to intervene (12,19). In our sample, more than half of participants (55.7%) had completed only secondary education, and no significant differences in knowledge or attitude scores were identified across educational levels. These findings suggest that first aid readiness may be independent of formal educational attainment. Accordingly, first aid training programs should be designed to remain accessible and applicable to individuals with varied educational backgrounds.

No significant differences in knowledge levels were seen among occupational occupations; however, attitude ratings exhibited considerable variation. Waiters, managers/directors, culinary workers, and business owners exhibited markedly superior attitude scores compared to bellboys. Furthermore, kitchen personnel and proprietors had elevated attitude ratings relative to other occupational groups. The findings correspond with previous studies indicating that employment status may influence individuals' attitudes about first aid, possibly owing to differences in duties, perceived accountability, and direct engagement in high-risk situations (15). Considering that roughly fifty percent of our sample comprised waiters, this subgroup constitutes a pivotal target for intervention. The variation in attitude scores across occupational groups suggests that training needs may differ among staff roles. Therefore, first aid programs in food service settings should be implemented in a way that ensures all personnel receive consistent and role-appropriate instruction.

No significant differences in knowledge scores were seen according to years of work. Participants with 21-40 years of work experience had markedly superior attitude ratings in comparison to those with 0-8 years of experience. These findings align with other research suggesting that professional tenure may not directly impact theoretical understanding, although might positively alter attitudes toward emergency response (20). Differences in attitude scores across experience groups suggest that longer employment may be associated with greater comfort or willingness to intervene, although this study was not designed to determine causality. The absence of variation in knowledge scores across experience levels indicates that work tenure alone may not influence factual first aid knowledge.

Participants exhibited a moderate level of first aid knowledge. This aligns with findings from other sectors. Previous studies have indicated intermediate levels of first aid knowledge among cab drivers (21). Although many studies indicate that persons with previous first aid training often have superior knowledge ratings, they may nevertheless see themselves as unprepared or inefficient in real emergency situations (22). In a separate research, 27.1% of participants characterized their first aid knowledge as moderate (23), reinforcing the idea that both the quality of training and knowledge retention are essential for effective emergency response.

Although holding of a first aid certification did not correlate with significantly elevated knowledge scores, certified individuals had more favorable opinions regarding first aid procedures. In our survey, around 20% of participants possessed a valid first aid certification. This implies that although certification by itself may not ensure superior information retention, it may enhance confidence and preparedness to take action. The limited overall perceptions identified in the study highlight the need to improve the accessibility and structure of first aid education. No significant differences in knowledge or attitude ratings were detected about participants' readiness to undergo first aid instruction. Nonetheless, over half (59.6%) indicated a desire to participate in such training. This corresponds with previous research, wherein participants indicated unhappiness with earlier first aid training and stated a want for re-education (24). These observations present a significant potential for public health initiatives to leverage community motivation by enhancing the accessibility and attractiveness of first aid programs. This interpretation is consistent with international evidence: a quasi-experimental study from Indonesia demonstrated that community-based choking first aid education resulted in substantial improvements in laypersons' knowledge, skills, and intervention confidence, underscoring the transformative effect of structured, scenario-based training models in diverse populations (25).

This study enhances the Turkish public health literature by concentrating on the preparation of restaurant staff for FBA events, a subject usually examined in pediatric or clinical contexts. This research examines a high-risk, frequently neglected occupational category that routinely engages with the public in environments where choking incidents are probable, contrasting with other studies that focused on legally obliged professions such as educators or healthcare workers. This study contributes to the limited evidence on the preparedness of non-medical frontline workers to respond to choking incidents by examining their first aid knowledge and attitudes. To our knowledge, it is the first district-based study in Türkiye focusing on restaurant staff in this context. The findings provide baseline data that may inform future workplace training strategies and community-oriented public health initiatives.

Study Limitations

This study has several limitations. First, it was conducted in a single district of Istanbul, which restricts the external validity of the findings and limits their applicability to other regions or restaurant settings. Second, data collection occurred during a single visit to each establishment, and only employees who were present at that moment were included. This may have introduced selection bias, as individuals with different shifts, levels of experience, or varying preparedness may not have been represented. Third, all responses were based on self-report, which is susceptible to social desirability and recall bias, potentially leading participants to overestimate their knowledge or confidence. Additionally, the knowledge assessment instrument—although developed using national guidelines and expert opinion—has not undergone formal psychometric validation, as no standardized tool exists for measuring FBA first aid knowledge. Finally, the study did not incorporate direct observation or practical skill assessment; therefore, the results reflect perceived rather than demonstrated first aid competence.

Conclusion

This study underscores a significant deficiency in first aid readiness among restaurant personnel in addressing FBAO occurrences. Despite operating in high-risk settings where prompt intervention is critical, only a little percentage of participants possessed genuine first aid certification, and an even smaller fraction had previously intervened in choking incidents. Despite over half stating a readiness to undergo training, this has not resulted in sufficient preparedness, highlighting a disparity between intention and actual readiness.

Considering that restaurant staff frequently serve as the initial and only responders in crises, it is essential to incorporate mandatory, scenario-based first aid and basic life support training into occupational safety regulations. Broadening access to this training outside the food service industry—via community-oriented public health initiatives—could also elevate bystander intervention rates and increase survival outcomes in FBAO incidents.

First aid education must be rendered more accessible, consistently updated, and tailored to the requirements of non-healthcare professionals. As rules and norms develop, continuous refresher training for all occupational groups is essential to sustain competency and avert skill deterioration over time.

These findings highlight the necessity of including systematic, ongoing, and pragmatic first aid training within workplace safety rules and comprehensive health education initiatives. Legal certification requirements, bolstered by simulation-based learning, may improve information retention and the confidence necessary for successful action in real-life situations.

This study effectively fills a significant gap in the literature by examining the preparation of restaurant personnel in FBAO circumstances. Future study should investigate obstacles to training access—such as cost, time, and availability—and assess the long-term effects of tailored interventions in both professional and community contexts. Addressing these concerns can enhance the capacity of laypersons as effective first responders, hence improving emergency outcomes and fostering community resilience.

Ethics

Ethics Committee Approval: Prior to the commencement of the study, written approval was obtained from the University of Health Sciences Türkiye Hamidiye Scientific Research Ethics Committee (decision no.: 2023/3, date: 10.02.2023). Throughout the study, the principles of the Declaration of Helsinki were strictly adhered to.

Informed Consent: Informed consent was obtained from all participants prior to their inclusion in the study.

*This study was presented as an oral presentation at the Third National Congress on Holistic Approach to Medicine on October 7-8, 2020 (pages: 268-272).

Footnotes

Authorship Contributions

Concept: M.T.U., F.Y., G.A., H.K., M.N.Ü., G.B., Design: M.T.U., F.Y., G.A., H.K., M.N.Ü., G.B., Data Collection or Processing: M.T.U., F.Y., E.Ç., G.A., H.K., M.N.Ü., Analysis or Interpretation: M.T.U., E.Ç., Literature Search: M.T.U., F.Y., E.Ç., G.A., H.K., M.N.Ü., G.B., Writing: M.T.U., F.Y., E.Ç., G.A., H.K., M.N.Ü., G.B.

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Assessment of the Educational Value and Technical Competence of Surgical Incision Repair Videos Shared on YouTube

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Abstract

Aim: This study aimed to evaluate the educational quality, reliability, and technical accuracy of surgical incision repair videos on YouTube and to investigate the influence of video source, country of origin, and content characteristics on overall quality scores.

Materials and Methods: All videos were independently assessed by two researchers using four validated scoring systems: the Journal of the American Medical Association (JAMA) criteria, modified DISCERN, Global Quality score (GQS), and objective structured assessment of technical skills (OSATS). Video popularity was calculated using the video power index. Statistical analyses were conducted using the Mann-Whitney U test, Spearman's correlation analysis, and ROC curve evaluation, with statistical significance set at $p<0.05$.

Results: According to the DISCERN classification, 48.5% of videos were of very poor quality, while 12.1% were categorized as good quality. Institutional videos achieved significantly higher scores across all evaluation systems compared with individual uploads ($p<0.05$). Videos with spoken narration received higher scores for educational and technical quality than silent videos. Content originating from the United States had significantly higher JAMA, GQS, and DISCERN scores than content from other countries ($p<0.05$). Positive correlations were identified between OSATS scores and JAMA ($r=0.315$), GQS ($r=0.782$), and DISCERN ($r=0.702$) scores.

Conclusion: The overall educational quality of YouTube videos on surgical incision repair was moderate. Institutional and narrated videos yielded significantly higher quality scores, underscoring the importance of academic oversight and structured content development. Although YouTube represents a valuable supplementary tool for surgical education, standardization and scientific regulation are essential to ensure educational reliability.

Keywords: Surgical incision repair, educational quality, JAMA, modified DISCERN, Global Quality score, OSATS, video power index

Introduction

Surgical incision repair is a fundamental skill that directly influences wound healing, infection risk, and aesthetic outcomes. Optimal repair requires adherence to basic surgical principles, including appropriate suture selection, balanced tissue tension, elimination of dead space, and minimization of tissue trauma (1,2). Consequently, acquiring proper incision repair technique constitutes an essential component of surgical education for medical students and residents.

The rapid digital transformation in medical education has increased the use of online video platforms as supplementary learning tools. YouTube, being freely accessible and visually rich, has become one of the most frequently used platforms for observing surgical techniques. However, the uncontrolled nature of user-generated content raises concerns regarding the accuracy, reliability, and educational adequacy of such videos (3-5).

To objectively evaluate online surgical content, several validated scoring systems have been introduced. The Journal of the American Medical Association (JAMA) criteria, the Global Quality score (GQS), and the modified DISCERN instrument assess the reliability and completeness of medical information (6,7). Furthermore, the objective structured assessment of technical skills (OSATS) has been utilized to evaluate the technical quality of surgical performance in video format (8). Prior studies have consistently demonstrated that videos produced by academic or institutional sources receive higher quality scores, whereas individually uploaded content

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often lacks accuracy and completeness (9-11). These findings emphasize the need for standardized and structured evaluation of surgical educational videos.

The urgency of wound care underscores the critical role of both emergency departments and general surgery services in the timely management of acute injuries. Emergency physicians are often the first clinicians to assess traumatic or surgical wounds, and their initial decisions regarding incision, exploration, and early repair have direct consequences for infection control, functional recovery, and cosmetic outcomes. General surgeons subsequently provide definitive management and ensure that repair techniques adhere to established surgical principles.

The present study aims to assess the educational quality, reliability, and technical accuracy of videos of surgical incision repair available on YouTube. Additionally, the effects of video source (institutional vs. individual), country of origin, and presentation style on video quality scores were examined. The findings are intended to contribute to the growing body of literature on digital surgical education and highlight the need for scientifically supervised, high-quality online instructional content.

Materials and Methods

Video Selection

A comprehensive video search was conducted on the YouTube platform on September 10, 2025. To ensure methodological reproducibility, each keyword was searched separately, and the first 50 results for each keyword were recorded. In total, 250 videos (5 keywords × 50 results each) were initially screened. The keyword set-"surgical incision," "scalpel handling," "tissue dissection," "surgical cutting techniques," and "safe cutting in surgery" was deliberately selected to encompass the entire spectrum of surgical steps that directly precede or accompany incision repair. Although the study primarily focused on incision repair, videos demonstrating incision techniques were generally uploaded under broader surgical skill categories such as instrument use, tissue dissection, or general surgical cutting.

Duplicate and Irrelevant Video Elimination

All 250 initial videos were exported into a screening spreadsheet. Duplicates were identified by matching identical uniform resource locators, identical uploader names with repeated titles, and algorithmically overlapping videos across different keyword searches.

Irrelevant videos were excluded based on their title, description, and the first 60 seconds of content. Videos were removed if they did not include any live, cadaveric, or simulated incision or dissection step; consisted solely of animations without procedural depiction; focused exclusively on postoperative wound care or complications; or included advertisements, promotional content, or non-instructional material. After this multistep elimination, 66 videos met the predefined criteria and were included in the final analysis.

Inclusion and Exclusion Criteria

Inclusion Criteria Were:

1. Videos demonstrating step-by-step surgical incision or related dissection techniques, (justification added: Incision repair cannot be evaluated independently of the preceding incision technique; poor incision may influence subsequent repair quality).

2. Visual resolution ≥480p to ensure evaluable technical detail,

3. Real surgery, cadaveric, animal model, or validated simulation footage,

4. Availability of English narration or subtitles for accurate interpretation of procedural intent and terminology.

Exclusion Criteria Were

1. Promotional, humorous, or entertainment-oriented content,

2. Videos dedicated solely to postoperative care or complication management,

3. Videos with insufficient audio/visual quality preventing technical assessment,

4. Repetitive uploads from the same uploader to prevent content duplication bias.

Data Collection

For each video, the following parameters were recorded:

- Title, duration, upload date, number of views and likes,
- Video source: institutional (university, hospital, surgical society) or individual (surgeon, student, general user),
- Country of origin (United States, Türkiye, others),
- Type of presentation (spoken narration, silent, or subtitled).

The country of origin for each video was determined using a multi-step verification protocol. First, the uploader's profile information was examined, including self-declared institutional affiliation, professional designation, and geographic details. Channel metadata, such as language, institutional logos, and linked websites, was also reviewed. When this information was unclear, cross-verification was performed using publicly available data regarding the affiliated institution or surgeon featured in the video, official web pages linked to the YouTube channel, and

professional registry records, when applicable. If none of these sources provided reliable information, the video was classified as "others/not identifiable" to avoid misclassification bias.

All videos were independently assessed by two reviewers. In cases of scoring discrepancies, reviewers discussed the differences and reached agreement; because consensus-based final scores were used for statistical analyses, formal inter-rater reliability metrics could not be calculated. Each video was examined for the appropriateness of the surgical incision technique, including incision line planning, scalpel handling, tissue tension management, hemostasis, and tissue preservation.

Video Quality Assessment Systems

Each video was evaluated using four validated scoring systems:

1. JAMA Criteria:

Comprising four parameters-authorship, attribution, disclosure, and currency-each assigned one point, with a maximum possible score of 4.

2. Modified DISCERN:

A five-question instrument assessing information reliability and content integrity. Each "Yes" response was assigned 1 point, and each "no" response was assigned 0 points, yielding a maximum score of 5.

3. GQS:

A five-point scale evaluating overall flow, informativeness, and educational value, where 1 indicates poor and 5 indicates excellent quality.

4. OSATS:

Used to evaluate technical performance across five criteria:

- Scalpel handling,
- Tissue manipulation,
- Field of vision control,
- Hemostasis management,
- Safety and surgical planning.

Each item was rated from 1 to 5, with a maximum possible score of 25.

For technical evaluation, we used a video-adapted version of the OSATS. The selected OSATS domains—scalpel handling, tissue manipulation, field-of-vision control, hemostasis, and safety/surgical planning—represent components that can be objectively assessed from recorded videos rather than by real-time observation. Both reviewers were trained general surgeons with experience in surgical skills education. These surgeons independently assigned OSATS scores before reaching a consensus.

The mean total score obtained from these four systems was recorded as the overall video quality indicator.

Popularity Analysis

The duration, title, number of views, time elapsed since upload, viewing rate (views/day), number of comments, number of likes and number of dislikes, and like ratio [likes × 100 / (likes + dislikes)] were recorded for each video. Video popularity was assessed using the video power index (VPI), a standardized indicator of user engagement and visibility on the platform. The VPI was calculated using the formula: (like ratio × viewing rate) / 100, which incorporates the number of views, likes, and comments.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as median and interquartile range (IQR), while categorical variables were presented as percentages (%). Comparisons between two groups (e.g., institutional vs. individual videos) were performed using the Mann-Whitney U test. Correlations between video quality metrics were analyzed using the Spearman's correlation test. A p value <0.05 was considered statistically significant.

Results

Quantitative data for YouTube videos are presented in Table 1 as median and IQR. YouTube Global score [2069.5 (1509.2-2069.5)], subscribers [(5670 (196.7-70575)], likes [(222.5 (23.2-2500)], views [33001.1 (1618.7-239.682)], video duration [5.1 (2-8.7)], JAMA [1 (1-2)], GQS [3 (2.7-4)], DISCERN [2 (1-3)], OSAST [3 (2.7-3)], viewing rate [6.9 (1.2-48.2)], like ratio [0.07 (0.01-0.4)].

According to the DISCERN classification, 48.5% (32) of the videos were of very poor quality, 21.2% (14) were of poor quality, 18.2% (12) were of medium quality, and 12.1% (8) were of good quality. No videos of excellent quality met the validation criteria for this classification. According to the OSATS classification, 10.6% (7) of the videos were rated as low technical quality, 13.6% (9) as medium quality, 53% (35) as good quality, and 22.7% (15) as excellent quality.

When videos were categorised as corporate or individual, the numbers of subscribers and likes, and the JAMA, GQS, DISCERN, and Osast scores were statistically significantly higher for corporate videos. ($p=0.006$, $p=0.007$, $p=0.016$, $p=0.002$, $p=0.004$, $p=0.001$)

The videos were divided into two groups based on whether they contained spoken narration. The group containing spoken narration had statistically significantly higher values for subscriber count, like count, view count, video duration, and JAMA, GQS, DISCERN, and OSATS scores compared to the other group. (p=0.012, p=0.005, p=0.019, p=0.004, p=0.014, p=0.001, p=0.001, p=0.001)

The JAMA, GQS, and DISCERN scores for trending videos in the USA were significantly higher (p=0.032, p=0.001, and p=0.02).

When correlation analysis was performed using the OSATS Monitoring index and the JAMA, GQS, and DISCERN classifications, all indices showed a positive correlation with OSATS. The correlation analyses are presented in Table 2. When ROC analysis was performed with corporate and individual loaders using the JAMA, GQS, DISCERN, and OSATS scoring indices, the highest sensitivity (84.1%) was observed in corporate loaders with OSATS, followed by DISCERN (72.7%), GQS (61.4%), and JAMA (47.7). (Table 3, Figure 1)

Table 1. Quantitative data for YouTube videos: median and interquartile range

	Median	IQR	
		25%	75%
NDRA	2069.5	1509.2	2069.5
Subscriber	5670	196.7	70575
Likes	222.5	23.2	2500
View	33001.1	1618.7	239.682
Video duration	5.1	2	8.7
JAMA	1	1	2
GQS	3	2.7	4
DISCERN	2	1	3
OSAST	3	2.7	3
Viewing rate	6.9	1.2	48.2
Like ratio	0.07	0.01	0.4

NDRA: Number of days it remained on air, JAMA: Journal of American Medical Association, GQS: Global Quality score, OSAST: Objective structured assessment of technical skills

Table 2. Correlation analysis between the OSATS Monitoring index and the JAMA, GQS, DISCERN classifications

		r	p value
JAMA	OSATS	0.315*	0.01
GQS		0.782**	0.001
DISCERN		0.702**	0.001

*: Low, **: High, JAMA: Journal of American Medical Association, GQS: Global Quality score, OSAST: Objective structured assessment of technical skills

Discussion

In this study, we evaluated the educational quality, reliability, and technical accuracy of surgical incision repair videos on the YouTube platform. Overall, the moderate JAMA, modified DISCERN, GQS, and OSATS scores indicate that, although many videos provide basic instructional content, they often lack the depth, structure, and standardization expected in formal surgical education.

Consistent with prior research, institutional videos demonstrated significantly higher quality scores than individual uploads. Similar findings have been reported in studies assessing sleeve gastrectomy, laparoscopic prostatectomy, and resuscitation-related videos, where academic or professionally produced content consistently received higher scores on established quality indicators (7,9,12). These results underscore the continued influence of content source reliability on educational accuracy and completeness.

Our findings also showed that videos originating in the United States had higher overall quality and viewership metrics than those from other countries, which aligns with previous literature suggesting that North American and European institutions tend to produce more structured, professionally edited surgical videos (13). Nevertheless, the influence of geographic origin should be interpreted cautiously, as cross-country comparisons remain relatively limited in the current literature.

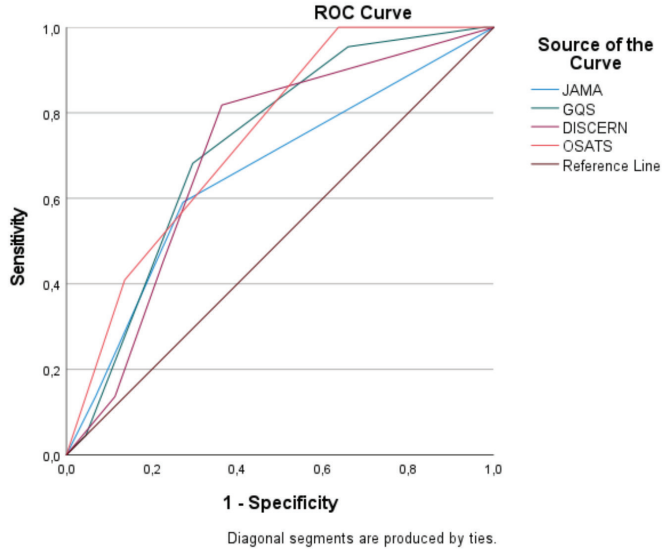

Figure 1. ROC graph according to JAMA, GQS, DISCERN, and OSATS scoring indices with corporate and individual loaders

JAMA: Journal of American Medical Association, GQS: Global Quality score, OSAST: Objective structured assessment of technical skills

Table 3. ROC analysis according to JAMA, GQS, DISCERN, and OSATS scoring indices for institutional and individual uploaders						
	AUC	p value	Cutoff	Sensitivite	Spesifite	Youden index
JAMA	0.66	0.035	1.5	47.7	81.8	0.295
GQS	0.803	0.001	3.5	61.4	95.5	0.568
DISCERN	0.839	0.001	1.5	72.7	90.9	0.636
OSATS	0.735	0.002	2.5	84.1	40.9	0.25
JAMA: Journal of American Medical Association, GQS: Global Quality score, OSAST: Objective structured assessment of technical skills, AUC: Area under the curve						

The moderate OSATS scores further highlight gaps in the technical accuracy of many videos. Suboptimal demonstrations of incision execution, scalpel handling, tissue manipulation, and hemostasis management may mislead inexperienced trainees and reinforce improper techniques. Although the LAP-VEGaS guidelines provide a structured framework for high-quality surgical video reporting (8), adherence appears limited among publicly available videos. Similar observations have been made in studies examining suturing, knot-tying, and instrument-handling videos, in which a substantial proportion of the content was found to be technically inadequate (12,14).

Another noteworthy finding was the lack of a strong correlation between popularity metrics, such as the VPI, and educational or technical quality. Videos with lower quality scores often received high view counts, reflecting a discrepancy between viewer engagement and scientific accuracy. Previous studies have similarly reported that popularity on YouTube does not necessarily reflect educational value (4,15).

Overall, the results of this study support the growing consensus that YouTube can serve as a complementary tool for surgical training; however, its lack of peer review, standardization, and quality control continues to limit its reliability as a stand-alone educational resource. Further efforts by academic institutions to develop and disseminate high-quality, peer-reviewed educational videos are essential for improving the pedagogical value of online surgical content (16,17).

Study Limitations

This study has several limitations. First, although searches were performed in incognito mode to minimize bias, YouTube's search algorithm is dynamic and personalized, and variations in displayed content cannot be fully eliminated. Second, restricting the analysis to English-language videos may have excluded potentially valuable content in other languages and may have limited the generalizability of the findings. Third, although a video-adapted OSATS approach was used, OSATS was originally developed for real-time observation, and certain nuances of technical performance may not be fully captured in recorded footage. Fourth, despite independent evaluations by two reviewers, subjective bias cannot be entirely excluded; because consensus scoring was applied, formal inter-rater reliability calculations could not be performed. Fifth, YouTube metadata such as likes, views, and comments are user-generated, non-standardized, and susceptible to external influences, which may limit the interpretability of these popularity metrics.

Conclusion

Finally, the rapidly evolving nature of YouTube content means that video availability and engagement statistics may change over time.

Ethics

Ethics Committee Approval: This study included only YouTube videos and did not involve any patient data or interventional procedures; therefore, ethical committee approval was not required.

Informed Consent: The study did not involve direct patient participation or the use of identifiable patient data; therefore, informed consent was not obtained.

Footnotes

Financial Disclosure: The author declared that this study received no financial support.

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Large Language Models in Emergency Medicine: A Critical Appraisal of Validity, Reproducibility, and Clinical Utility (2020-2025)

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Abstract

Recent studies on large language models (LLMs) in emergency medicine (EM)-have expanded rapidly, yet core threats to validity and reproducibility remain under-addressed. We critically synthesized the methods, reporting quality, and clinical relevance of LLM-focused work in emergency care published between January 2020 and April 2025. We conducted a PubMed search and verified journal indexing in the Web of Science (WoS) to restrict screening to EM-relevant studies published in journals indexed under the WoS 'EM' category, excluding editorials that lacked primary or secondary analysis. Two reviewers independently coded protocol availability; prompt transparency; data realism; reference standards; calibration and decision-curve reporting; external validation; and expert benchmarking, resolving discrepancies by consensus. Ninety-one studies met the inclusion criteria; sixty were original investigations. Prompt disclosure was complete in roughly one-third of studies, and real-world clinical data were used less often than synthetic or examination-style vignettes. Calibration, decision-curve analysis, and demonstrations of incremental value over parsimonious clinical baselines were infrequently reported. Expert benchmarking appeared inconsistently across journal strata, and "near-expert" claims often relied on proxy tasks with limited ecological validity. External validation was uncommon, and model/version identifiers were frequently incomplete, undermining reproducibility. Overall, the current LLM literature within this core EM journal corpus is method-lean and report-light: high-level accuracy claims rarely translate into decision-useful evidence. A minimum reporting set—transparent prompts, code, and versioning; calibration; decision-curve analysis; and expert benchmarking on real data—is needed; absent these elements, deployment in time-critical emergency care remains premature.

Keywords: Large language models, emergency informatics, decision support, methodological evaluation, artificial intelligence

Introduction

Large language models (LLMs), such as OpenAI's GPT and Google's Gemini, have rapidly entered clinical discourse not through careful, protocolized integration but largely propelled by enthusiasm and marketing narratives about their capacity to parse unstructured data, aid diagnostics, and streamline documentation across specialties, including emergency medicine (EM) (1,2). Yet the pace of adoption has outstripped the maturation of evaluation science, creating a widening gap between performance claims and decision-useful, reproducible evidence (3).

Unlike traditional clinical tools, LLMs are non-stationary systems. Their behavior evolves due to silent backend updates, architectural shifts, and access-path changes; the same prompt can yield materially different outputs over time—a form of version drift that undermines reproducibility and weakens causal attribution of observed effects (4). Compounding this instability is prompt sensitivity: minor phrasing changes can produce large, unpredictable swings in outputs, challenging any assumption of determinism or reliability in time-critical EM settings (5).

Despite these well-described failure modes, published LLM evaluations in medicine, including those appearing in core EM journals, frequently omit core methodological details. Model/version identifiers, release dates, full prompt templates, and data provenance are inconsistently reported; synthetic prompts, exam-

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style questions, or proxy tasks often substitute for authentic clinical inputs and adjudicated reference standards (3,6). Consequently, reported accuracies are rarely accompanied by calibration, decision-curve analysis (net benefit), or incremental value over parsimonious clinical baselines—elements required to judge whether a tool improves triage, resource allocation, or patient-relevant outcomes under real EM constraints (7).

This review systematically evaluates peer-reviewed LLM studies pertinent to EM, as represented by studies published in journals indexed under the Web of Science (WoS) "emergency medicine" category (SCI-E/ESCI), focusing on methodological transparency, empirical rigor, and clinical grounding. Using a structured framework centered on input fidelity, evaluation strategy, and functional use case, we (1) characterize the evidentiary landscape within this core EM journal corpus, (2) identify recurrent threats to validity and reproducibility, and (3) outline priorities for future research that make EM deployment transparent, calibrated, externally validated, and resilient to technological volatility (3,6,7).

Review Scope and Approach

Scope and Conceptual Approach

We conducted a retrospective, descriptive review of the peer-reviewed literature to evaluate how LLMs [including ChatGPT/Generative Pre-trained Transformer (GPT)-4 and Gemini] have been applied, evaluated, and reported methodologically in EM. The review emphasized three core dimensions aligned with EM workflows: (1) transparency in model use (versioning, access modality, prompt disclosure), (2) empirical rigor (real-world data, expert benchmarking, calibration, and decision-curve analysis), and (3) clinical applicability (task-workflow fit). A structured, three-axis framework—input fidelity, evaluation strategy, and functional use case—guided classification and subsequent comparisons.

Literature Identification and Study Selection

Information Sources and Search Strategy

A structured PubMed search was performed in May 2025 directly via the PubMed web search interface using the Boolean string below to capture EM-relevant LLM studies between 01/01/2020 and 04/30/2025: "ChatGPT" or "(GPT)-3" or "GPT-3.5" or "GPT-4" or "GPT-4.5" or "large language model" or "LLM" or "generative AI" or "generative artificial intelligence" or "transformer-based model" or "foundation model" or "instruction-tuned model" or "GPT" and [2020.01.01 (date-publication): "2025.04.30" (date-publication)]. The search returned 12.125 records prior to de-duplication and journal-scope filtering.

Journal Corpus Definition (WoS Emergency Medicine Category)

To define a core corpus of EM journals and to ensure comparability of scope across included venues, we retained only articles published in journals indexed in WoS under SCI-E or ESCI. WoS was used solely to verify the SCI-E/ESCI indexing status of journals; no literature search was conducted within WoS. A curated list of 57 EM-category journal titles was used for this index-verification filter.

Screening and Eligibility Assessment

Two independent reviewers screened titles and abstracts, and subsequently full texts, against pre-specified criteria. Reasons for exclusion included: (1) passing mention of LLMs without evaluative content, (2) general AI discussion lacking LLM-specific evaluation, and (3) abstract-only or unavailable full text. Disagreements were resolved by consensus after discussion. Following screening, 91 studies were retained for full-text analysis. Operational definitions, decision rules, and study-level coding outputs are provided in Supplementary Table S1.

Data Abstraction and Methodological Appraisal

All 91 studies were assessed using a structured codebook covering five methodological indicators: model identification (model name, release/version, and access pathway), prompt disclosure (full, partial, absent, or ambiguous), use of real clinical data (authentic EM inputs vs. synthetic/proxy tasks), human expert benchmarking (comparison with domain experts where clinical judgment is implicated), and methodological consistency (alignment between stated aims and data/evaluation choices). Articles were independently coded by two reviewers; disagreements were adjudicated by consensus. Because our primary aim was appraisal of transparency and reporting rather than effect estimation, we did not perform a formal risk-of-bias assessment. The full codebook (variable definitions and decision rules) and the per-study coding matrix are provided in Supplementary Table S1.

High-Rigor Subset (Predefined Methodological Benchmark)

Among the 60 studies classified as original research, we applied a secondary filter to identify a high-rigor subset that met all of the following criteria: (1) real-world clinical data, (2) expert-based benchmarking, and (3) no reliance on standardized multiple-choice exams as surrogate evaluations (to mitigate data leakage and poor ecological validity). Seventeen studies met these criteria.

Three-Axis Classification Framework

To map methodological diversity across original investigations, we applied a three-axis schema: input fidelity (real-world EM

data vs. simulated/synthetic content), evaluation strategy (e.g., expert benchmarking, external validation, calibration/decision-curve reporting vs. internal metrics alone), and functional use case (clinical decision support, documentation/communication, education/training, or other EM-relevant tasks). Operational definitions and coding rules appear in Supplementary Table S1. For visualization, the evaluation strategy and the use case were collapsed into broader themes; these groupings were visualized in the alluvial (Sankey) plot (Figure 1).

Positioning Relative to Reporting Guidance

We compared our classification outputs with healthcare MInimum reporting items for CLear Evaluation of Accuracy Reports (MI-CLEAR)-LLM reporting frameworks MI-CLEAR-LLM and Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD)-LLM. While these guidelines prioritize documentation of model metadata and evaluation design, our schema extends them by explicitly encoding functional role and data realism, enabling granular, metric-specific appraisal. A side-by-side summary is presented in Supplementary Table S2.

Journal-Tier Summaries

Original research articles were grouped according to indexing in SCI-E or ESCI. For each stratum, we calculated the proportions reporting full prompt disclosure, use of real clinical data, and human expert benchmarking. Results are summarized in Table 1 with risk differences (SCI-E-ESCI) and 95% confidence intervals (CI) (Newcombe method). Given the small denominators, particularly in ESCI, findings were interpreted cautiously and treated as descriptive. Because several tier-stratified 2×2 tables involved small expected cell counts (<5), large-sample z- or χ^2-approximations were not used for inference.

Exploratory Cross-tabulations

Exploratory Fisher's exact tests were prespecified for the interaction between journal tier and reporting items (full prompt, real clinical data, expert benchmarking), and for the interaction between prompt disclosure (full vs. not-full) and high-rigor status. Two-sided Fisher's exact tests were used, and the corresponding 2×2 tables and p-values are provided in Table 2. Fisher's exact test was selected because it remains valid when expected cell counts are small, unlike χ^2- and z-based procedures that rely on large-sample assumptions. Other planned tests (e.g., real data × expert benchmarking, use case × prompt) required joint counts not available from the final abstraction set and were not performed.

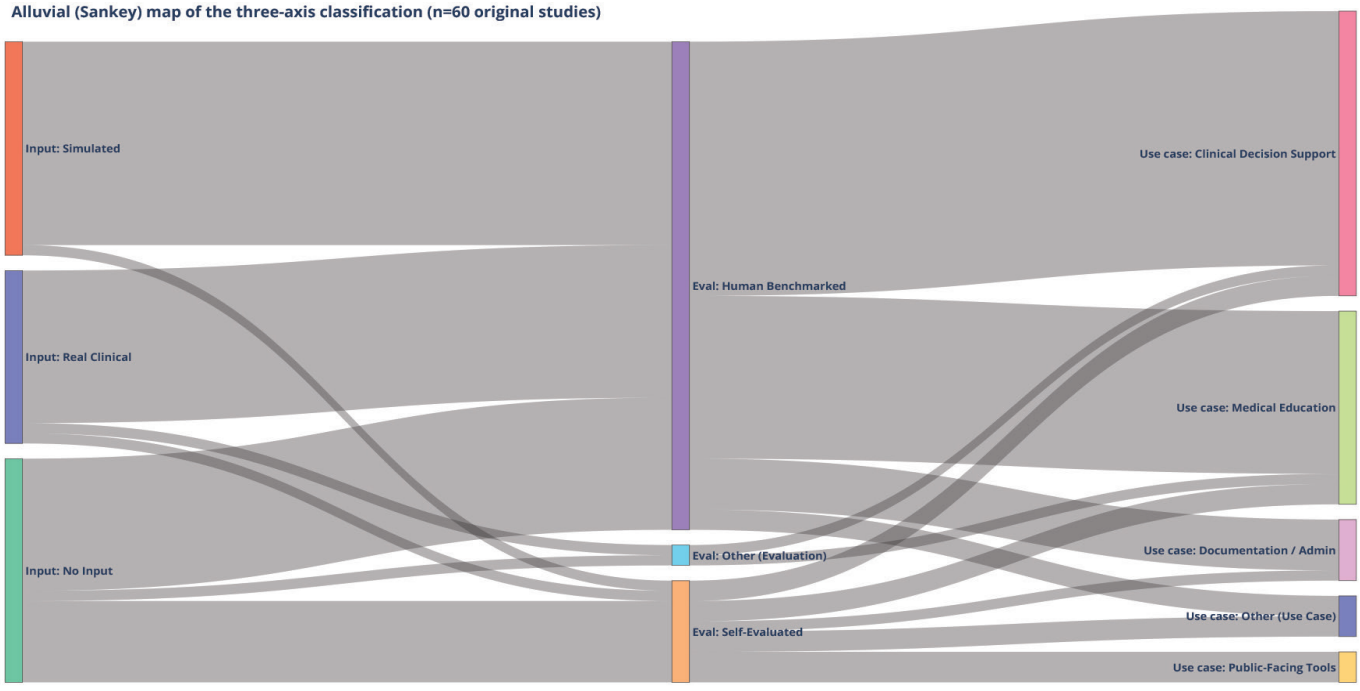

Figure 1. Alluvial (Sankey) map of the three-axis classification of original investigations (n=60)

Nodes represent input fidelity (real clinical / simulated/no input), evaluation strategy (human benchmarked/self-evaluated/other), and functional use cases (clinical decision support/medical education/documentation/admin/public-facing tools/other). Link widths are proportional to the number of studies in each pathway

Evidence Synthesis

Publication Trends and Study Types

Ninety-one peer-reviewed articles met the inclusion criteria, of which sixty were classified as original research. Publications were concentrated between 2023 and 2025, peaking in 2024. Across all included articles, most were published in SCI-E-indexed journals (SCI-E: 80/91; ESCI: 11/91). Among original research articles, 53 appeared in SCI-E-indexed journals and 7 in ESCI-indexed journals. The distribution of publication types by year and journal tier is summarized in Table 3.

Methodological Rigor Subset

Original research articles were evaluated against three a priori criteria: use of real-world clinical data, inclusion of human expert benchmarking, and avoidance of standardized multiple-choice examinations as surrogate tasks. Seventeen studies satisfied all three criteria and were designated as methodologically robust. The remaining forty-three studies did not meet these criteria due to methodological incompleteness or ambiguity (n=32), reliance on simulated data and/or the absence of expert comparison (n=6), or use of examination-style proxies (n=5). Non-robust studies were assigned a primary reason using a mutually exclusive hierarchy, as reflected in the study-level coding (Supplementary Table S1). Counts and definitions are presented in Table 3, with study-level coding in Supplementary Table S1.

Prompt Transparency and Implications for Reproducibility

Prompt reporting was inconsistent across the original research corpus. Only 20 studies (33.3%) disclosed complete prompt text, 36 (60.0%) provided partial or paraphrased examples, 3 (5.0%) did not report prompts, and 1 (1.7%) used ambiguous formatting. Even among the methodologically robust subset, full prompt disclosure was observed in six of the seventeen studies. This limited transparency constrains reproducibility for tasks in which model behavior is highly sensitive to input design, including diagnostic reasoning, triage, and clinical documentation. Tier-stratified prompt disclosure is summarized in Table 1, and the exploratory 2×2 comparison of full prompt disclosure versus high-rigor status is reported in Table 2; study-level prompt coding is provided in Supplementary Table S1.

Journal-tier Summary

Descriptive comparisons between SCI-E and ESCI strata are shown in Table 1. Full prompt disclosure was reported in 18 of 53 SCI-E studies (34.0%) and in 2 of 7 ESCI studies (28.6%), yielding a risk difference of +5.4 percentage points (95% CI: -41.4 to +39.2; Newcombe method). The use of real clinical data was nearly identical across tiers—15/53 (28.3%) in SCI-E and 2/7 (28.6%) in ESCI—corresponding to a risk difference of −0.3 percentage points (95% CI: -46.1 to +33.3 percentage points). Human-expert benchmarking was reported in 17 of 53 SCI-E studies (32.1%) and 3 of 7 ESCI studies (42.9%), yielding a risk difference of -10.8

Table 1. Reporting metrics by journal tier (SCIE vs. ESCI): proportions and risk differences (95% CI)

Metric	SCIE (x/n)	SCIE (%)	ESCI (x/n)	ESCI (%)	Risk difference (SCIE-ESCI), %	95% CI (%, Newcombe)
Full prompt disclosure	18/53	34	2/7	28.6	5.4	(-41.4, 39.2)
Use of real clinical data	15/53	28.3	2/7	28.6	-0.3	(-46.1, 33.3)
Human expert benchmarking	17/53	32.1	3/7	42.9	-10.8	(-53.9, 29.7)

Values are presented as x/n (%) for SCIE and ESCI original research; the risk difference (SCIE-ESCI) and 95% CI (Newcombe method) are also reported. Positive RD favors SCIE; negative RD favors ESCI. Interpret with caution due to the small ESCI denominator. SCIE: Science Citation Index-Expanded, ESCI: Emerging Sources Citation index, CI: Confidence interval

Table 2. Exploratory Fisher's exact tests

Comparison	Group 1 (row 1)	a	b	Group 2 (row 2)	c	d	Odds ratio (Fisher's exact tests)	p (two-sided)
Journal tier × Full prompt disclosure	SCIE (full, not full)	18	35	ESCI (full, not full)	2	5	1.286	1.000
Journal tier × Real clinical data	SCIE (real, not real)	15	38	ESCI (real, not real)	2	5	0.987	1.000
Journal tier × Human expert benchmarking	SCIE (Yes, No)	17	36	ESCI (Yes, No)	3	4	0.630	0.676
Prompt (full vs not-full) × High-rigor (Yes, No)	High-rigor = Yes (full, not full)	6	14	High-rigor = No (full, not full)	11	29	1.130	1.000

Cells follow the 2×2 convention: [(a, b), (c, d)]. For journal-tier comparisons, row 1 =SCIE and row 2 =ESCI; columns indicate feature presence and absence. For the prompt × high-rigor comparison, row 1= High-rigor= Yes, row 2= High-rigor= No; columns are (full, not full). Two-sided Fisher's exact tests p-values are reported, SCIE: Science Citation Index-Expanded, ESCI: Emerging Sources Citation index

percentage points (95% CI: -53.9 to +29.7 percentage points). Overall, CIs were wide and included the null, limiting inference about tier-level differences and highlighting the imprecision resulting from the small ESCI denominator. Accordingly, tier comparisons are interpreted descriptively, and inferential testing relies on Fisher's exact test given the small expected cell counts.

Exploratory Cross-tabulations

Pre-specified exploratory 2×2 tests are reported in Table 2. Two-sided Fisher's exact tests did not identify statistically significant associations between journal tier and full prompt disclosure (odds ratio: 1.286, p=1.000), real clinical data (odds ratio: 0.987, p=1.000), or human expert benchmarking (odds ratio: 0.630, p=0.676). Likewise, the association between full prompt disclosure and inclusion in the high-rigor subset was not significant (odds ratio: 1.130, p=1.000). Planned analyses for real data × expert benchmarking, and use case × prompt transparency could not be conducted because joint counts were not available in the final abstraction; these omissions are noted in Methods 2.8. All contingency tables and p-values are presented in Table 2.

Methodological Structure Across Studies

Using the three-axis framework (input fidelity, evaluation strategy, functional use case), we characterized methodological patterns across the sixty original research articles. Real clinical data were used in 28.3% of studies (17/60), and human expert benchmarking was reported in 33.3% (20/60). Clinical decision support was the most frequent use case, followed by educational and administrative applications (Supplementary Table S1). Overall, the corpus exhibits rapid growth alongside substantial heterogeneity in reporting and design, with a small but identifiable subset meeting more stringent criteria for empirical and clinical rigor. The distribution of studies across the three axes and their interrelationships are visualized in the alluvial (Sankey) plot (Figure 1).

Discussion

Fragile Foundations Amid Rapid Growth

The present synthesis reveals a corpus expanding faster than its evidentiary substrate. Following the release of contemporary LLMs (e.g., GPT-4), publication volume rose sharply; however, reporting quality and clinical grounding have not kept pace within the core EM journal set examined. Much of the literature remains anchored in capability demonstrations rather than decision-useful evidence, a gap reflected in incomplete description of model provenance, insufficient transparency around inputs, and limited assessment of clinical impact. These findings align with prior critiques of methodological shortfalls and checklist non-adherence in medical LLM research. (1-3,6,7).

Version Instability and Prompt Sensitivity as Threats to Reproducibility

LLMs are non-stationary: silent model updates, undocumented architectural changes, and evolving access pathways introduce version drift, whereby identical prompts can yield divergent outputs across time (4,5). Together with prompt sensitivity, defined as large output variability induced by minor input changes, this dynamic undermines reproducibility and complicates

Table 3. Tier totals

Journal tier	Commentary (n)	Original research (n)	Review (n)	Total (n)
ESCI	1	7	3	11
SCIE	27	53	0	80
All	28	60	3	91

Counts are numbers of articles by publication year and Web of Science Emergency Medicine journal tier. "Original research" denotes empiric investigations; "commentary" includes editorials, viewpoints, and letters; "review" comprises narrative or systematic reviews. SCIE: Science Citation-Index Expanded, ESCI: Emerging Sources Citation index. Row totals equal the sum of commentary, original research, and review for each year-tier combination; tier totals and the grand total (SCIE: 80, ESCI: 11, overall n=91) are reported beneath the main table. Figures reflect the curated Emergency Medicine journal set used for study selection and may not generalize beyond this corpus

Table 3. Distribution of studies by year, journal tier, and publication type (2023-2025)

Year	Journal tier	Commentary (n)	Original research (n)	Review (n)	Total (n)
2023	ESCI	1	2	1	4
2023	SCIE	13	10	0	23
2024	ESCI	0	4	2	6
2024	SCIE	10	27	0	37
2025	ESCI	0	1	0	1
2025	SCIE	4	16	0	20

SCIE: Science Citation Index-Expanded, ESCI: Emerging Sources Citation index

longitudinal interpretation. Reproducibility challenges are not unique to LLMs; variability across runs and pipelines has also been documented in other medical AI domains such as deep learning–based image segmentation (8). Studies that omit model/version identifiers, release timing, or access modality produce findings that are difficult to replicate or reconcile with subsequent evaluations in this corpus (3-5).

Transparency Deficits and Their Implications

Prompt disclosure was inconsistent in the included EM-journal corpus: complete prompts were reported in only one-third of original studies and even less frequently in the methodologically robust subset. Absence or partial reporting of prompts constrains replication, especially for tasks in which outputs are highly sensitive to input design (diagnostic reasoning, triage, documentation). These observations are consistent with emerging guidance that positions transparent prompts, versioning, and code availability as prerequisites for credible evaluation (3,6,7).

Methodological Weaknesses in Study Design

A recurrent limitation was the reliance on standardized multiple-choice or examination-style instruments as proxy measures. Such tasks are vulnerable to training-data contamination and fail to capture EMs complexity, thereby risking optimistic but clinically uninformative estimates (6). By contrast, the high-rigor subset combined real clinical inputs with expert benchmarking and avoided using exam proxies, illustrating that empirically grounded LLM evaluation in EM is feasible when the study design is aligned with clinical workflow, as demonstrated in studies published in core EM journals.

Journal-tier Comparisons Interpreted with Caution

Tier-stratified summaries suggested a slightly higher prompt disclosure in SCI-E, no meaningful difference in the use of real clinical data, and no consistent advantage in human expert benchmarking (the ESCI proportion was numerically higher); CIs were wide across all metrics. However, these tier-stratified comparisons are constrained by the small ESCI subgroup (n=7) relative to SCI-E (n=53), which limits precision and precludes robust inference. These patterns argue against tier-level generalizations and should be interpreted as descriptive patterns within the WoS "EM" journal category rather than as field-wide differences. Accordingly, tier patterns are not used to support the study's primary conclusions.

Beyond Checklists: A Structural Lens on Study Quality

Reporting frameworks such as MI-CLEAR-LLM and TRIPOD-LLM have improved transparency, but cannot, by themselves, remedy deeper design deficits (3,7). Our three-axis schema—input fidelity, evaluation strategy, and functional use case—provides a complementary structural framework, highlighting the persistence of synthetic tasks, the infrequency of calibration and decision-curve analyses, and the variability of expert benchmarking, even among studies presented as rigorous within the examined EM-journal corpus. The framework's relationship to existing guidance is detailed in Supplementary Table S2.

Structural Barriers to External Validation

Opaque model internals, undisclosed training data, and proprietary constraints impede error analysis and durable external validation (9-11). Absent auditable versioning and accessible artifacts (prompts/code), even well-designed evaluations risk becoming brittle as platforms evolve. A version-aware, documentation-first approach is therefore integral to any clinically credible assessment strategy for EM-facing use cases, including those evaluated in core EM journals.

Toward a More Reliable Evaluation Paradigm

The field should pivot from leaderboard-style claims of accuracy to process-oriented evaluation that prioritizes version tracking, prompt transparency, calibration, decision-curve analysis, external validation, and expert benchmarking using authentic EM data (1,3,6,7,9). Studies exemplifying these elements already exist, demonstrating the feasibility and value of methodologically disciplined LLM research in EM, as reflected by a subset of rigorously designed studies identified in this journal corpus (12,13). Consolidating such practices will be essential to move from exploratory promise to defensible deployment.

Methodological Considerations

This review was restricted to journals indexed in the WoS "EM" category (SCI-E and ESCI); therefore, our findings should be interpreted as describing the LLM evidence base within this core EM journal corpus, rather than the entire EM literature. Relevant EM-facing LLM studies published in general medicine, critical care, resuscitation, trauma, prehospital/EMS, radiology, and medical informatics venues may have been overlooked. This venue restriction may introduce publication-location (venue) bias, potentially affecting the observed distribution of use cases, evaluation designs, and reporting practices. For example, clinically grounded or implementation-focused studies may be more likely to appear outside EM-category journals, whereas capability demonstrations may cluster differently across venues.

Study-level coding was performed systematically, yet some classifications, particularly along the evaluation-strategy and use-case axes, required interpretive judgment due to inconsistent reporting in source articles. To enable visual synthesis, we collapsed several categories in the alluvial mapping, a simplification that may obscure finer methodological distinctions. We did not

perform a sensitivity analysis using an expanded journal set beyond the WoS EM category; future work should assess the robustness of these patterns by broadening sampling frames (e.g., predefined acute-care-relevant journal lists and/or topic-based retrieval with EM-relevance adjudication). Tier-stratified summaries should also be interpreted cautiously because the ESCI subgroup was small (n=7) relative to SCI-E (n=53), limiting precision and precluding robust inference about tier differences. In addition, some tier-stratified 2×2 tables had expected cell counts below conventional thresholds (e.g., <5), which preclude reliable χ^2- or z-based inference and z-score calculations. We therefore relied on Fisher's exact tests; this reliance contributes to wide CIs and low power to detect differences between tiers. Consequently, these tier-stratified estimates have limited clinical usability and generalizability, and should not be used to draw tier-level inferences. Finally, we did not undertake a longitudinal analysis of temporal drift in model behavior or prompt practices; given ongoing platform evolution, future meta-research should explicitly incorporate time-stamped versioning and repeated-measures designs.

Recommendations and Conclusion

Report the Model-Precisely and Time-Stamped

Responsible evaluation begins with unambiguous model metadata. Every study should document the model's canonical name, release or build identifier, access pathway (e.g., API versus web interface), and the exact date and time of use. Absent these anchors, results are not reproducible in a non-stationary ecosystem and cannot be meaningfully compared across replications or versions. Contemporary guidance (MI-CLEAR-LLM, TRIPOD-LLM) already positions version transparency as a first-order requirement; clinical LLM research must normalize it as standard practice (3,7).

Treat Prompts as Experimental Conditions

Prompts and associated parameters shape outputs as deterministically as any intervention in a clinical experiment. Studies should provide complete prompt text (including system instructions), retry logic, and sampling parameters. Summaries or partial exemplars are insufficient for replication and hinder meta-research on prompt sensitivity. This expectation is both methodologically necessary and aligned with emerging recommendations on reproducible LLM evaluation (3,5,7).

Replace Exam Proxies with Clinical Reality

Standardized multiple-choice items are convenient but of low ecological validity and vulnerable to training-data contamination. Evaluations should be grounded in authentic clinical artifacts — electronic health records, clinician notes, and imaging reports — and should mirror real emergency workflows and constraints. Synthetic benchmarks frequently overstate performance and obscure operational failure modes; they should be used only for preliminary exploration and not presented as evidence of clinical readiness (3,6,12).

Benchmark Against Human Experts

For high-stakes tasks (diagnosis, triage, disposition), human expert comparators and adjudicated reference standards are indispensable. Model-to-model comparisons are insufficient for clinical inference and pose a risk of circular validation. The clinical literature and reporting guidance converge on this point: expert benchmarking is a prerequisite for decision-useful claims (3,7,12,13).

Shift the Emphasis from Point Accuracy to Process Understanding

Leaderboard accuracy is an inadequate proxy for safety or usefulness. Future studies should interrogate reasoning pathways and failure modes, incorporating calibration, decision-curve analysis, error taxonomies, and qualitative audits. Robustness, not isolated point estimates, must become the currency of clinical evaluation (9,10).

Anticipate—and Measure—Drift

Because LLMs evolve over time, validation should include repeated assessments across versions and time points, with explicit cross-version comparisons and time-stamped artifacts. Version drift is no longer hypothetical; it is a documented source of variance that threatens longitudinal interpretability if not prospectively measured (4,7,9,10).

Enforce Minimum Reporting at Publication

Editorial policies should require, as a condition of acceptance, complete model metadata, full prompt disclosure, and clinically grounded evaluation design. Manuscripts lacking these elements are methodologically incomplete regardless of novelty or apparent performance. Reproducibility and transparency —not speed to publication— should define publication worthiness (1,3,7,9).

Conclusion

LLMs hold clear promise for EM, particularly in decision support, documentation, and clinical education. Realizing that promise, however, demands a decisive shift in scientific practice: version-aware reporting, full prompt transparency, expert-anchored evaluation on real clinical data, and routine use of calibration and decision-curve analysis. Within the body of LLM studies published in core EM journals (WoS "EM" category), our synthesis

shows that the current evidence base remains fragmented, with critical gaps in documentation and external validity that limit clinical translation. The path forward is not to celebrate higher scores on synthetic tasks but to establish rigorous, reproducible, and clinically coherent methods. If EM embraces this standard—prioritizing process over performance and accountability over expediency—LLM integration can proceed with the trust and durability required for high-stakes care.

Ethics

Footnotes

Authorship Contributions

Concept: A.A., Design: A.A., Data Collection or Processing: A.A., C.Y., E.G., Analysis or Interpretation: A.A., C.Y., E.G., Literature Search: A.A., Writing: A.A., C.Y., E.G.

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Supplementary Table S1 - Table S2: https://d2v96fxpocvxx.cloudfront.net/580eb5e7-1480-44a6-9404-b8b7446acbcb/content-images/bde585b6-1102-437f-bfa1-2f70f12a1d2b.pdf

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Quality of Three Chest Compression Techniques During Two-Rescuer Infant CPR: A Randomised Crossover Manikin Study

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Abstract

Aim: To evaluate the quality and ergonomic impact of three infant chest compression techniques the two-thumb encircling technique (TTHT), the cross-thumb technique (CTT), and the one-hand open-palm technique (OHT) during two-rescuer infant cardiopulmonary resuscitation (CPR) utilizing a 15:2 compression-to-ventilation ratio.

Materials and Methods: This prospective, randomized, crossover simulation study included 50 registered nurses who performed three 2-minute CPR sequences on an infant manikin, each using one of the three techniques. The primary outcomes were the depth of the compression, the percentage of target-range compressions, and the chest compression fraction (CCF). Secondary outcomes encompassed compression rate, recoil, hand position accuracy, excessive compressions, fatigue, pain, perceived difficulty, and hand slippage. We used repeated-measures statistical models to look at the data.

Results: Both thumb-based methods (TTHT and CTT) yielded significantly deeper compressions, elevated proportions of target-range compressions, increased CCF, and enhanced accuracy in hand positioning in comparison to OHT (all $p<0.01$). TTHT and CTT exhibited similar mechanical performance in all primary outcomes. However, CTT had much less fatigue, hand pain, and perceived difficulty than TTHT (all $p<0.01$). OHT caused shallower compressions, the lowest CCF, more over-depth compressions, and the highest rate of hand slippage.

Conclusion: During two-rescuer infant resuscitation, TTHT and CTT are better than OHT at biomechanical CPR quality. CTT has the same compression quality as TTHT but is more comfortable to use, making it a good choice when thumb-based techniques are feasible. OHT should only be used when it is not possible to wrap the chest. More clinical studies are needed to support these simulation results.

Keywords: Infant cardiopulmonary resuscitation, chest compression techniques, cardiopulmonary resuscitation, simulation study, compression quality, pediatric basic life support

Introduction

Infant cardiopulmonary resuscitation (CPR) is vital in emergency pediatric care and closely linked to survival and neurological outcomes. In infants, cardiac arrest usually results from respiratory failure or asphyxia, not heart disease. Thus, both proper chest compressions and effective ventilation are necessary (1-3). The American Heart Association (AHA) and American Academy of Pediatrics (AAP) recommend a 15:2 compression-to-ventilation ratio when two healthcare providers perform CPR on infants or children. This delivers more rescue breaths and aligns with the asphyxial nature of most pediatric arrests (2-4).

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Several steps must be taken to ensure high-quality CPR in infants. The correct compression depth is about one-third of the anterior–posterior chest diameter. Hands need to be placed in the correct position, on the lower third of the sternum, and kept away from the xiphoid process (5-7). The chest must fully recoil after each compression. Interruptions in compressions should be kept to a minimum. The compression rate should be 100-120·min^{-1}. Experimental and clinical evidence indicate that incomplete chest recoil, characterized by frequent and prolonged pauses, reduces coronary perfusion pressure. These factors are associated with poorer resuscitation outcomes (8,9). Therefore, any change in technique that affects depth, rate, or recoil could significantly change how well CPR works.

It is crucial to select the right method for chest compressions. The AHA and AAP now recommend the two-thumb encircling technique (TTHT) as the most effective for two-person infant CPR. This method results in deeper compressions, higher coronary perfusion pressures, and less rescuer fatigue compared to the two-finger technique. Despite this, several alternative methods have been proposed and tested in simulations and observational studies over the past decade. However, concerns remain about compression depth, hand stability, and the risk of over-compression.

Although many manikin studies and registry data show infant CPR is effective, few head-to-head comparisons of these three methods exist in realistic two-rescuer, 15:2 basic life support (BLS) scenarios (10-15). Current research suggests the one-hand technique may, under certain conditions, achieve greater depth than thumb-based methods. However, its effects on chest recoil, hand positioning, and rescuer fatigue remain unclear, especially during extended team efforts (4). Studies also show that ergonomic changes such as using a step stool, the “elbow-lock” position, or rotating compressors, can affect compression quality and reduce fatigue. However, these adjustments have not been widely tested with different infant compression techniques (4).

Due to these gaps, we needed a thorough, well-designed comparison of current infant compression techniques under conditions that reflect recommended practice. We compared the two-thumb encircling, cross-thumb, and one-hand open-palm techniques (OHT) during two-rescuer infant CPR using a 15:2 ratio.

Materials and Methods

Study Design and Oversight

We conducted a prospective, randomized, three-arm crossover study. It compared the quality of infant chest compressions given with three techniques: (1) two-thumb encircling, (2) cross-thumb, and (3) one-hand (open-palm). An infant manikin was used in a high-fidelity pediatric simulation setting for all scenarios. Following modern pediatric resuscitation guidelines, each sequence involved two rescuers giving BLS for two minutes with a 15:2 compression-to-ventilation ratio. Participants were randomly assigned to the order in which they performed the three techniques, using a computer-generated allocation sequence.

The Institutional Review Board of the Polish Society of Disaster Medicine reviewed and approved the protocol (approval no: 14/02/2024, date: 14.02.2024). All study procedures adhered to the Declaration of Helsinki and relevant national regulations governing research with human subjects. Volunteers received written and verbal information and provided written consent before participating. The study followed EQUATOR-aligned standards for simulation research. This included specifying prospective endpoints, detailing the simulation model and parameters, and documenting the data structure and analysis workflow.

Participants and Sample Size

The study population included 50 registered nurses. All participants were enrolled in scheduled BLS training courses, taught by AHA–certified instructors. Each participant was actively working in clinical practice and regularly cared for pediatric or neonatal patients. Eligibility required current employment as a nurse, prior completion of at least one BLS course, and willingness to participate in simulation research. Nurses who reported musculoskeletal conditions that made chest compressions unsafe were excluded. Participation was voluntary with no financial incentives. Every participant was assigned a unique ID number. All nurses performed each of the three compression techniques, using a within-subject, randomized three-period crossover design. This resulted in 150 resuscitation attempts (50 participants × 3 techniques).

Simulation Protocol

For each study condition, participants performed a standard infant BLS scenario using a dummy. Each 120-second sequence required nurses to administer chest compressions and ventilations continuously. According to the latest pediatric BLS guidelines, the compression–ventilation ratio was 15:2. Each participant delivered 15 compressions, followed by two ventilations, and repeated this cycle for the full 2 minutes.

The order of the three compression techniques was randomized in a crossover manner. ResearchRandomizer (Randomizer.org; Figure 1) was used to create a unique sequence of techniques for each participant. Allocations were made before enrollment.

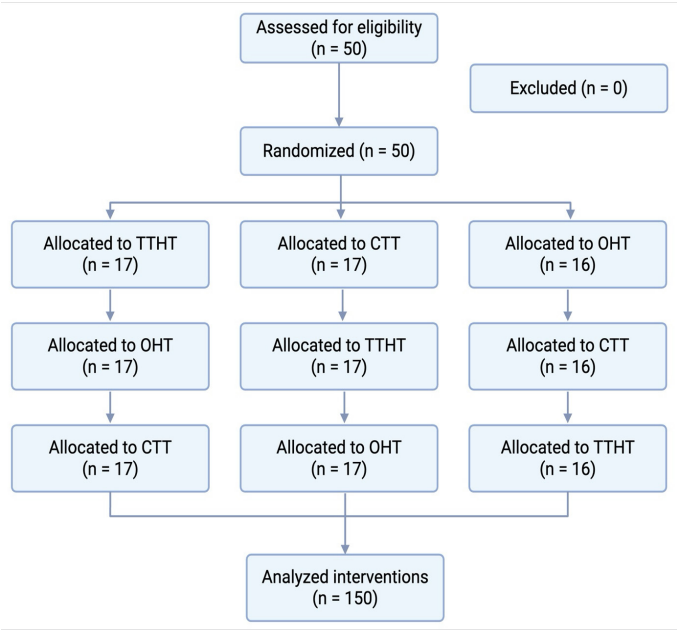

Figure 1. Randomization flow chart
TTHT: Two-thumb encircling technique, CTT: Cross-thumb technique, OHT: Open-palm technique

Participants were assigned to the following available sequence by numerical order. Each nurse performed all three techniques in a different order. This helped reduce learning fatigue and the effects of menstrual periods.

Before the event began, instructors asked participants to keep a compression rate between 100 and 120 per minute. They did not use a metronome. Instead, participants were told to "compress fast and regularly" to allow for natural variation. A second rescuer, also trained in BLS, performed bag-mask ventilation. This person gave two chest-rise breaths after each set of 15 compressions. This is similar to real-life resuscitations, where short breaks occur between compressions.

To prevent fatigue and minimize the mixing of techniques, participants rested for at least 30 minutes between sequences. They took breaks in the simulation room. However, they did not practice compressions or receive extra coaching. This approach ensured that subsequent attempts were based on random technique allocation, not ongoing instruction or warm-up. Before data collection, an AHA-certified instructor demonstrated each technique to all participants. There was a brief practice session. Instructors did not give corrective feedback during recorded attempts.

Three chest compression techniques were used during the study:

- **TTHT:** The rescuer stood at the baby's feet. Both thumbs pointed up, side by side, on the lower third of the sternum. The fingers wrapped around the thorax to support the back. To compress, both thumbs pressed straight down while the hands encircled the chest. This allowed for full chest recoil after each compression.
- **Cross-thumb technique (CTT):** The rescuer stood beside the manikin. Both thumbs were on the lower half of the sternum, with one crossing over the other at the midline. The fingers of both hands wrapped around the thorax for stability. The overlapping thumbs applied vertical pressure. The focus was on vertical compression, full release between compressions, and no lateral movement.
- **One-hand (open-palm) technique:** The rescuer stood next to the mannequin. The heel of one hand was on the lower sternum. Fingers were held up to avoid the ribs and abdomen. The second hand could rest on the forearm or chest for support, but added no force. Compressions were given using the heel of the hand, pressing straight down to about one-third of the chest depth. The hand fully recoiled after each compression (Figure 2).

Figure 2. Chest compression techniques used during two-rescuer infant cardiopulmonary resuscitation (CPR) with a 15:2 compression-to-ventilation ratio: (A) two-thumb encircling technique (TTHT), (B) cross-thumb technique (CTT), and (C) one-hand open-palm technique (OHT)

For all techniques, participants were instructed to minimize interruptions, avoid leaning between compressions, and maintain their focus on maintaining the correct rate, depth, and 15:2 sequence. During the experimental phase, a different neonatal simulator (Laerdal Medical SimBaby, Laerdal Medical, Stavanger, Norway) was used to ensure standardization of resuscitation.

Outcomes

All outcomes were predetermined and based on objective measurements obtained from the manikin, supplemented by concise post-scenario self-reports from participants. To clarify the outcomes, they were divided into two groups: primary measures of the quality of chest compressions and secondary measures of the mechanics of compressions, hemodynamic surrogates, ergonomics, and technical performance.

Primary Outcomes

The average compression depth, measured in millimeters, was the most critical sign of compression quality. The manikin recorded the depth of each compression for every 2-minute sequence. The average value for that sequence was used in the analysis. Since guidelines recommend that compressions should be at least one-third of the anterior-posterior chest diameter in babies, we also counted how many were within the target range of 40-50 mm. This percentage indicates the frequency with which a rescuer achieved a clinically acceptable depth, not just the average. The chest compression fraction (CCF) was the third primary outcome. It shows how much of the 2 minutes was spent giving compressions. Lower values indicate more time spent in pauses, for example, during ventilations or repositioning.

Secondary Outcomes

We initially looked at the compression rate — the number of compressions per minute averaged over two minutes—to understand how chest compression's function. Additional variables assessed compression technique performance. Full chest recoil was the proportion of compressions where the chest returned to neutral without tilting. According to pediatric BLS standards, the correct hand posture was the proportion of compressions with the thumbs or heel centered on the bottom half of the sternum. We tracked the percentage of "over-depth compressions," or compressions deeper than 50 mm, to assess if the force was excessive. Participants rated their fatigue and hand pain on a 0-10 visual analogue scale immediately after each sequence and the perceived difficulty of the technique on a 5-point Likert scale (1 =very easy to 5 =very difficult) to assess the ergonomic burden of each technique. The nurses' subjective judgments were used to estimate each method's physical and technical demands. Finally, we included measures of safety and technical strength. The hand slippage count revealed how often the compressing hand or thumbs left the sternum during a sequence. This variable had a Poisson-like count distribution.

Sample Size

Based on randomized crossover trials of baby chest compression techniques on manikins (10,16), the sample size was chosen. These investigations showed mean compression depth variations of 2-3 mm and within-subject standard deviations (SDs) of 2.5 mm between approaches, indicating a medium effect magnitude. The primary endpoint for sample size calculation was compression depth (mm).

For a one-way repeated-measures ANOVA with three levels (TTHT, CTT, OHT), $\alpha = 0.05$, 80% power, and $f = 0.25$, G* Power 3.1 suggests 40 participants are sufficient. We planned to enroll 44 individuals to cover dropouts and missing data. Fifty participants completed all three approaches once recruitment exceeded this minimum aim to increase estimate accuracy and secondary outcome power. This final sample size has at least 80% power to detect clinically relevant differences in compression depth and sufficient power to detect secondary outcomes (compression rate and rescuer fatigue).

Statistical Analysis

Statistics were based on each participant's three resuscitation attempts (one for each procedure). Intra-subject variables included technique (TTHT, CTT, OHT). The primary analyses used one-way repeated-measures models with technique as a fixed effect and a random intercept for individuals, similar to repeated-measures ANOVA for this balanced design. The overall impact of the strategy on each outcome was tested using F-tests. Pairwise comparisons between approaches were performed using estimated marginal means, with Holm-Bonferroni adjustment for multiple testing when the omnibus test was significant.

Residual plots, Shapiro-Wilk, and Levene's tests were used to assess normality and homogeneity of variance. Greenhouse-Geisser corrected p-values were reported when Mauchly's test indicated non-sphericity. For non-normal or ordinal outcomes such as fatigue, pain, perceived difficulty, and hand slippage frequency, we used nonparametric Friedman tests and Wilcoxon signed-rank tests with Benjamini–Hochberg correction as sensitivity analyses. These yielded the same statistical significance as the primary models and are not discussed. For symmetric continuous data, the mean ± SD is used, whereas skewed variables are summarized as the median interquartile

range. Effect sizes are reported using partial eta-squared (η^2p) for omnibus testing and Cohen's d for significant pairwise contrasts. All tests were two-sided and had a significance level of $\alpha=0.05$.

All statistical analyses were performed using Python 3.11 (Python Software Foundation, Wilmington, DE, USA) with Pandas, NumPy, and SciPy/statsmodels libraries for data management and modeling, and Matplotlib for figure creation.

Results

Participants and Dataset

Fifty registered nurses working in acute care settings participated in the study, and all of them adhered to the protocol. Each participant executed three resuscitation sequences, one utilizing each chest compression technique, yielding 150 analyzable sequences (50 per technique). There were no missing or excluded observations, and no participant withdrew or deviated from the protocol. This means that all recorded sequences were kept for the final analyses. At the time of the study, all the nurses were undergoing a BLS training session certified by the AHA. They had all already taken at least one accredited BLS course. The research component was optional and separate from the course assessment, and it did not affect completion of the course or certification status.

Chest Compression Quality

Table 1 presents descriptive statistics for all compression variables. There was a big difference in the compression rate between the two methods ($F=3.70$, $p=0.027$). TTHT and CTT had almost the same rates, but OHT had a slightly lower rate. In pairwise tests, TTHT and CTT were different from OHT ($p=0.019$ and $p=0.040$, respectively), but TTHT and CTT were not ($p=0.661$; Figure 3).

The CCF was high in all groups, but it varied depending on the method ($F=9.34$, $p<0.001$). CTT produced the highest CCF, TTHT produced an intermediate value, and OHT produced the lowest. There was no difference in CCF between the two thumb-based techniques ($p=0.085$), but both were better than OHT (TTHT vs OHT $p=0.008$; CTT vs OHT $p<0.001$).

Table 1. Chest compression outcomes

Outcome	TTHT	CTT	OHT	TTHT vs. CTT	TTHT vs. OHT	CTT vs. OHT	ANOVA
Compression rate	112 (110-113)	111.0 (110-113.5)	109 (107-110)	0.661	0.019	0.040	F (2.147)=3.70; p=0.027
	112 (5.0)	111.6 (4.54)	109.4 (6.1)				
Chest compression fraction	0.712 (0.706-0.720)	0.720 (0.715-0.728)	0.702 (0.691-0.708)	0.085	0.008	<0.001	F (2.147)=9.34; p<0.001
	0.712 (0.021)	0.720 (0.025)	0.701 (0.023)				
Compression depth	42.64 (41.86-43.27)	41,18 (40.38-42.22)	39.49 (37.52- 40.68)	0.074	<0.001	0.005	F (2.147)=10.97; p=0,000036
	42.23 (2.42)	31.38 (2.33)	39.42 (4.15)				
Percentage of compression with target depth range 40-50 mm	52.3 (44.-56.6) %	43.1 (36.3-47.4)%	35.0 (35-35) %	0.051	<0.001	<0.001	F (2.147)=21.59; p<0.001
	53.2 (15.2) %	47.4 (14.0)%	37.1 (5.7) %				
Percentage of compressions with full chest recoil	96.6 (96.2-97.2)	97 (96.8-97.2)	95 (94.45-95.30)	0.232	<0.001	<0.001	F (2.147)=40.16; p<0.001
	96.69 (1.29)%	96.98 (1.14)%	94.75 (1.59)%				
Correct hand placement	99.0 (98.9-99.3)	98.9 (98.7-99.1)	97.2 (96.5-97.4)	0.192	<0.001	<0.001	F (2.147)=88.62; p<0.001
	99.1 (0.60)%	98.9 (0.54)%	97.2 (1.10) %				
Percentage to deep over 50mm	2.4 (1.6-2.8)	2.2 (1.5-2.5)	3.35 (3.0-3.9)	0.454	<0.001	<0.001	F (2.147)=13.18; p<0.001
	2.24 (1.39)%	2.05 (1.19)%	3.39 (1.64) %				
Rescuer fatigue	4.3 (4.0-4.7)	3.25 (2.8-3.5)	4.6 (4.2-5.05)	<0.001	0.034	<0.001	F (2.147)=31.86; p<0.001
	4.25 (0.93)	3.19 (0.82)	4.70 (1.13)				
Rescuer hand pain	3.5 (3.3- 3.75)	3.1 (2.8-3.4)	4.3 (3.95-4.6)	0.002	<0.001	<0.001	F (2.147)=33.75; p<0.001
	3.54 (0.67)	3.06 (0.83)	4.31 (0.80)				
Technique difficulty	2.5 (2.25-2.70)	2.2 (2.0-2.35)	2.9 (2.6-3.25)	0.017	<0.001	<0.001	F (2.147)=18.26; p<0.001
	2.48 (0.55)	2.20 (0.61)	2.97 (0.78)				
Hand slippage count	0 (0-1)	0 (0-1)	1 (1-1)	0.863	<0.001	<0.001	F (2.147)=10.30; p<0.001
	0.50 (0.58)	0.52 (0.58)	1.02 (0.77)				

TTHT: Techniques the two-thumb encircling technique, CTT: Cross-thumb technique, OHT: One-hand open-palm technique

Compression depth varied by technique (F =10.97, p<0.001). TTHT and CTT produced deeper compressions than OHT (TTHT vs OHT p<0.001; CTT vs OHT p=0.005); TTHT and CTT did not differ significantly (p=0.074).

There was a significant difference between the techniques in the percentage of compressions within the target depth range (40-50 mm) (F =21.59, p<0.001). Both thumb-based methods achieved a higher percentage of target-depth compressions than OHT (all p<0.001). The only difference between TTHT and CTT was very small (p=0.051). The proportion of excessive compressions (>50 mm) was minimal but markedly greater with OHT compared to TTHT or CTT (F =13.18, p<0.001; both comparisons vs OHT p<0.001); TTHT and CTT exhibited no significant difference (p=0.454).

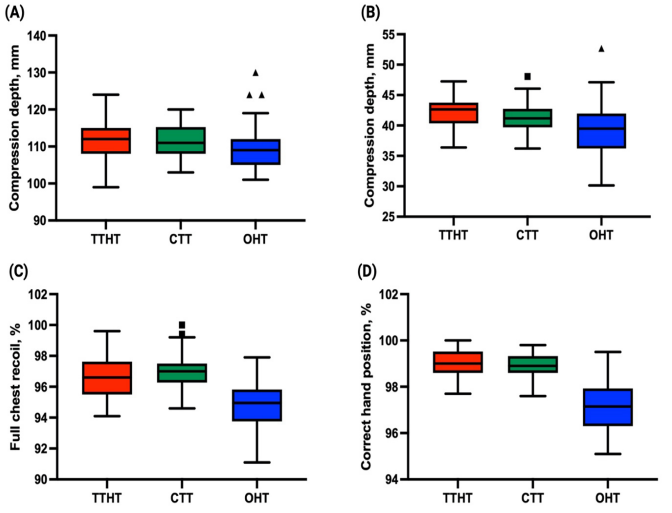

Figure 3. Comparison of chest compression quality parameters between the three infant chest compression techniques: two-thumb encircling technique (TTHT), cross-thumb technique (CTT), and one-hand open-palm technique (OHT). Data are presented as box-and-whisker plots showing median, interquartile range, and minimum/maximum values

Table 1 shows that all techniques achieved nearly full chest recoil, but OHT had slightly less. The technique had a strong effect (F =40.16, p<0.001): TTHT and CTT were similar (p=0.232), both of which were higher than OHT (both p<0.001).

All groups did a great job of placing their hands correctly on the lower half of the sternum; however, the thumb-based methods were more effective (F =88.62, p<0.001). TTHT and CTT were not significantly different from each other (p=0.192), but both were more accurate than OHT (both p<0.001).

Ergonomic Outcomes and Hand Stability

Self-reported fatigue differed by technique (F =31.86, p<0.001; Table 1). CTT had the lowest scores, TTHT was intermediate, and OHT had the highest. CTT caused less fatigue than TTHT and OHT (both p<0.001), and TTHT less than OHT (p=0.034; Figure 4).

Hand pain exhibited a comparable trend (F =33.75, p<0.001): CTT < TTHT < OHT. Pairwise comparisons revealed reduced pain with CTT compared to TTHT (p=0.002) and OHT (p<0.001), as well as diminished pain with TTHT relative to OHT (p<0.001).

The perceived difficulty, rated on a 1-5 scale, also differed by technique (F =18.26, p<0.001). CTT was the easiest, TTHT was a little harder, and OHT was the hardest. The ratings for CTT were lower than those for TTHT and OHT (p=0.017 and p<0.001, respectively), and the ratings for TTHT were lower than those for OHT (p<0.001).

Lastly, the number of times a hand slipped per attempt was low, but technique had a significant effect on it (F =10.30, p<0.001). The number of slippages was similar for TTHT and CTT (p=0.863) but higher for OHT. Both thumb-based techniques had significantly fewer slippages than OHT (both p<0.001).

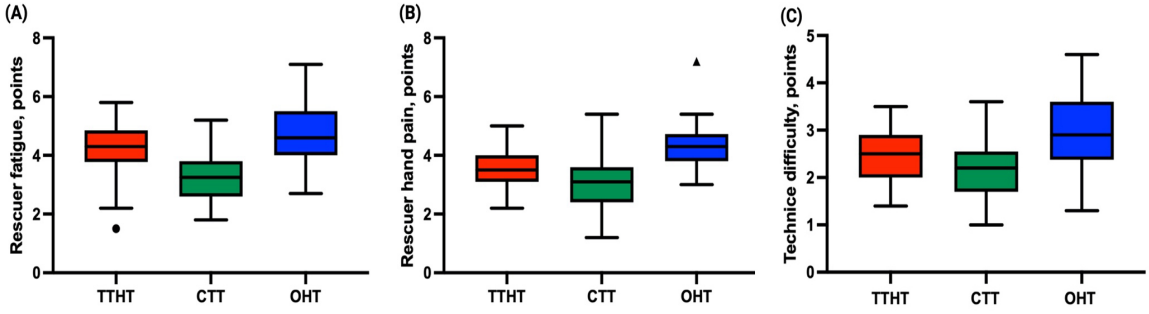

Figure 4. Comparison of ergonomic and subjective outcomes associated with the three infant chest compression techniques: two-thumb encircling technique (TTHT), cross-thumb technique (CTT), and one-hand open-palm technique (OHT). Data are presented as box-and-whisker plots showing median, interquartile range, and minimum/maximum values

Discussion

This randomized crossover simulation study evaluated three infant chest compression techniques –two-thumb encircling hands, cross-thumb, and one-hand open-palm chest– administered by nurses during 2-minute, two-rescuer CPR with a 15:2 ratio. In all core biomechanical outcomes, both thumb-based techniques produced better compressions than OHT. CTT, on the other hand, had similar mechanical performance but much better ergonomic profiles.

Chest Compression Performance and Alignment with Current Guidelines

Our findings support existing resuscitation guidelines, which favor TTHT for baby compression, especially with two rescuers. In our study, TTHT and CTT yielded comparable compression rates and CCF, both considerably higher than OHT. The average TTHT and CTT compression depth was 41-42 mm. OHT made shallower compressions and had the lowest target range compression rate of 40–50 mm (13,14).

These findings confirm earlier manikin and animal studies that TTHT provides greater depth, more consistent compressions, and higher coronary perfusion pressures than the two-finger technique (4,15). Recently, Solecki et al. (16) completed a meta-analysis and narrative review. Due to its better depth accuracy than lateral or two-finger approaches, TTHT is still the best way to perform CPR on babies and neonates. We also found that TTHT beats OHT in a 2-rescuer, 15:2 scenario that follows AHA/AAP baby CPR standards.

The percentage of over-deep compressions (>50 mm) was low across all procedures, except OHT. This shows that providers may overshoot when trying to compensate for one-handed depth. OHT also has the lowest target range compressions, thus it does not offer the best depth or safety. These findings imply that OHT should not be routinely employed when TTHT or CTT are practicable, even though the most recent pediatric BLS recommendations recommend the one-hand technique when the chest cannot be ringed (17).

Cross-thumb Technique Versus Two-Thumb Encircling

A significant contribution of this study is the direct comparison between TTHT and the more recent CTT in a two-rescuer context. We discovered that CTT attained compression rates, CCF, depths, target-depth proportions, and over-depth rates that were statistically indistinguishable from those of TTHT. These results are very similar to those found by Joyner et al. (9) in their randomized manikin study. They found that CTT and TTHT had similar depth and guideline-compliant compression rates, both of which were much better than the two-finger technique (4). Recent comparative data also demonstrate that CTT provides comparable or marginally enhanced mechanical performance while enabling the rescuer to maintain a lateral position, which could be beneficial in confined spaces.

Our findings reveal a significant distinction: despite the mechanical equivalence of TTHT and CTT, CTT was consistently associated with reduced fatigue, diminished hand pain, lower perceived difficulty, and no increase in hand slippage. This ergonomic advantage is clinically significant, as rescuer fatigue is known to degrade CPR quality over time and may be especially detrimental during extended pediatric resuscitation. CTT may be a good alternative to TTHT because it offers both high-quality compressions and reduced physical strain. This is especially true when the compressor must remain next to the patient (for example, in transport incubators, crowded ED bays, or limited workspace around an infant bed).

Nonetheless, it is crucial to underscore that the current evidence for CTT, including our own, is limited to simulation studies. There are no clinical outcome data available to show that CTT is better than or even as satisfactory as TTHT in real cases of infant cardiac arrest. Until such evidence surfaces, TTHT should remain the standard technique endorsed by guidelines, while CTT should be regarded as a promising adjunct or alternative in particular circumstances.

One-hand Technique in the Context of Emerging Evidence

Recent research has rekindled interest in one-handed techniques for infant CPR. Smereka et al.(18) found that the one-hand open-palm technique (OPT) on an infant manikin produced greater depth and was rated as easier than standard two-finger or two-thumb methods. However, the absolute depths still did not consistently meet AHA targets. In a two-rescuer 15:2 scenario, however, our results show that OHT is inferior to TTHT and CTT in several ways: it has shallower compressions, a lower CCF, a significantly lower percentage of target-depth compressions, and a higher percentage of over-deep compressions.

This apparent discrepancy likely stems from differences in how the studies were designed and what they examined. The OPT studies focused on single-rescuer CPR and primarily compared OHT with the two-finger technique, which is commonly acknowledged as inadequate due to its limitations in depth and fatigue. In that context, OHT might be a better option. In our study, OHT was compared to two highly effective thumb-based methods in a two-rescuer scenario, revealing its relative deficiencies. These results support the cautious stance of recent guideline updates, which position the one-hand technique as an option when the provider cannot adequately encircle the chest, rather than as a first-line approach.

Ergonomics and Technical Stability

The ergonomic outcomes in our study provide further insight into the practical trade-offs among techniques. CTT had the lowest scores for fatigue and pain, as well as the lowest perceived difficulty. TTHT was in the middle, and OHT always scored the worst on these measures (13,19).

These results are similar to earlier data, which showed that two-thumb techniques require less rigorous work than two-finger compressions, both in terms of subjective ratings and physiological measures (20). There weren't many instances when hands slipped, but there were significantly more with OHT than with either of the thumb-based methods.

This could be due to the smaller contact area and less stable leverage of the heel of one hand on a small chest. From a patient-safety standpoint, heightened slippage may result in more frequent off-target compressions, especially on compliant infant ribs or in the presence of fluids or gel, although this remains conjectural in the absence of clinical evidence. Our results suggest that OHT may be less forgiving in terms of technical stability, especially for providers with limited pediatric experience, because there are more over-deep compressions.

Clinical and Educational Implications

Our data collectively substantiate multiple pragmatic conclusions for clinical practice and education. First, they support the guidelines that state TTHT should be the standard method for infant CPR when two rescuers are available. Second, they suggest that CTT can be safely regarded as a distinct thumb-based technique that functions mechanically just as well but is more comfortable to use. For teams that frequently revive babies in settings where the compressor must remain near the patient, it may be beneficial to incorporate CTT into local training programs, provided that students also learn TTHT and are aware that it remains the standard (11,21). Third, our results suggest that OHT should not be used when high-quality thumb-based compressions are possible. OHT is useful when the chest can't be encircled, such as with larger babies, unusual body types, or certain situations where the baby can't move. However, our data show that for normal-sized babies and in controlled settings, OHT leads to shallower compressions, less time spent in compression, more technical errors, and increased workload for the rescuer. This nuance may be especially significant as recent consensus documents broaden the application of one-hand techniques in pediatric BLS (22). From an educational standpoint, the substantial influence of technique on both objective quality metrics and subjective workload underscores the imperative of deliberate practice coupled with feedback (1). Training that utilizes simulations to teach students various techniques, focusing on depth, recoil, and minimizing pauses, may help them adjust to different patient sizes, environments, and team compositions without compromising the quality of their care.

Study Limitations

Strengths and Limitations

This study has several strengths. The randomized crossover design, wherein each participant acts as their control, diminishes inter-subject variability and facilitates significant comparison of techniques under uniform conditions. We used a two-rescuer, 15:2 scenario that followed current pediatric guidelines. We also used a group of nurses who had recently completed BLS training and were fairly similar, which makes the results more reliable. There was no missing data in any of the sequences, so the dataset was complete for analysis.

However, significant limitations must be recognized. First, this was a simulation study conducted on an infant manikin; the degree to which observed differences correlate with clinically significant outcomes (return of spontaneous circulation, survival, neurological status) in actual infants remains uncertain. Second, our participants were practicing nurses from a single institution, which may not encompass the full spectrum of pediatric resuscitation experience. Third, we looked at 2-minute bouts of CPR. Rescuer fatigue and technique degradation may differ over longer periods or during more complex resuscitations that involve multiple tasks. Fourth, we examined a single configuration for each technique; alternative configurations, including over-the-head TTHT or adjusted hand positions for CTT, were not investigated. Finally, making multiple comparisons across various endpoints increases the likelihood of committing a Type I error. However, the consistency and magnitude of the effects we observed—especially for OHT versus thumb-based techniques—make it unlikely that our main conclusions are merely random.

Future Directions

Subsequent research must extend beyond the use of manikins to assess these techniques in authentic environments, preferably through multicenter observational registries or pragmatic trials that measure CPR quality metrics during actual infant resuscitations. The incorporation of high-fidelity manikins that can estimate hemodynamic surrogates alongside real-time feedback devices may elucidate whether the ergonomic benefits of CTT result in enduring quality during prolonged resuscitations. Moreover, research contrasting these methodologies in solo-rescuer contexts, during transit, and in restricted settings would enhance the precision of their ideal applications. Finally, cost-effectiveness and learning-curve analyses could help determine

the most effective way to incorporate CTT and OHT into pediatric life support courses without compromising important skills in TTHT.

Conclusion

In this randomized crossover simulation of two-rescuer infant CPR, both TTHT and CTT yielded superior chest compression quality compared to the one-hand OHT, demonstrating increased depth, enhanced target-range compressions, and improved recoil and hand positioning. CTT had similar mechanical performance to TTHT, but it caused less fatigue and pain in the hands and was perceived as easier, suggesting that it could be a practical and more comfortable alternative when thumb-based methods are possible. OHT should still be an option when the chest can't be encircled. Further clinical studies are needed to determine whether the benefits of simulations translate into improved patient outcomes.

Ethics

Ethics Committee Approval: The Institutional Review Board of the Polish Society of Disaster Medicine reviewed and approved the protocol (approval no. 14/02/2024, date: 14.02.2024). All study procedures adhered to the Declaration of Helsinki and relevant national regulations governing research with human subjects. Volunteers

Informed Consent: Volunteers received written and verbal information and provided written consent before participating.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.S., Concept: M.S., Design: M.S., Data Collection or Processing: M.S., H.K., L.S., B.M., W.W., Analysis or Interpretation: M.K., M.S., L.S., B.M., W.W., Literature Search: M.K., M.S., H.K., L.S., B.C., B.M., A.C., W.W., Writing: M.K., M.S., H.K., L.S., B.C., B.M., A.C., W.W.

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Diagnostic Value of Serum Asymmetric Dimethyl Arginine and Arginine Derivatives Levels in Distinguishing Potentially Life-Threatening Causes in Patients Presenting with Chest Pain to the Emergency Department

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Abstract

Aim: Chest pain a common complaint in the emergency department, often associated with serious cardiovascular conditions such as ischemic heart disease, pulmonary embolism, and aortic aneurysm. Rapid and accurate diagnosis is crucial. Asymmetric dimethylarginine (ADMA), an inhibitor of nitric oxide synthase, contributes to the pathogenesis of cardiovascular disease. Measuring serum ADMA and arginine levels may aid in distinguishing life-threatening conditions and in improving clinical decision-making. This study explores the diagnostic value of ADMA and arginine derivatives in patients presenting with chest pain, aiming to enhance early and effective medical intervention

Materials and Methods: Blood samples were collected from each participant and analyzed for serum ADMA and arginine levels using liquid chromatography-mass spectrometry. Patients were classified based on potentially life-threatening versus benign causes of chest pain. Serum ADMA and arginine levels were compared between the patient and control groups.

Results: A total of 219 participants were included in the study. For biochemical measurements, no significant differences were observed in levels of ADMA, symmetric dimethyl arginine, and NG-monomethyl-l-arginine, whereas arginine and the ratios differed significantly between groups.

Conclusion: The findings offer new approaches to improve early diagnosis and treatment processes. It is anticipated that the results will determine whether the levels of ADMA and arginine can serve as clinically useful adjuncts in the management of chest pain. This could enable the rapid and accurate differentiation of potentially fatal causes, ultimately improving patient management and outcomes.

Keywords: Arginine, ADMA, cardiovascular disease, biomarkers, chest pain

Introduction

Chest pain is one of the most common complaints encountered in emergency departments. It can be a sign of potentially life-threatening conditions, such as myocardial infarction, aortic aneurysm, and pulmonary embolism (PE). Consequently, the rapid and accurate assessment of patients presenting with chest pain is lifesaving. However, a diverse range of potential causes complicates the diagnostic process. In recent years, biomarkers have made significant contributions to clinical practice, particularly the serum markers asymmetric dimethylarginine (ADMA) and arginine. ADMA is an endogenous inhibitor of nitric oxide synthase, and elevated ADMA levels are associated with vascular dysfunction and atherosclerosis (1). Arginine plays a pivotal role in nitric oxide production and supports vascular function. Both molecules may possess substantial diagnostic

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value in distinguishing cardiovascular events. High levels of ADMA may aid the early diagnosis of cardiovascular diseases, while examining arginine levels can provide insights into vascular function by reflecting nitric oxide levels (2).

This study aims to evaluate the diagnostic value of serum ADMA and arginine levels for differentiating potentially life-threatening causes of chest pain in patients presenting to the emergency department. Studies indicate that ADMA and arginine levels are vital for the diagnosis and management of cardiovascular events. For instance, the work of Zhou et al. (1) highlights the relationship between ADMA and coronary artery disease, demonstrating that elevated ADMA levels are associated with an increased risk of myocardial infarction (1). Numerous studies underscore the diagnostic significance of ADMA and arginine in identifying cardiovascular diseases (3,4).

In this context, evaluating serum ADMA and arginine levels alongside traditional biomarkers may improve the accuracy and effectiveness of diagnostic processes in the emergency department. The findings of this study are intended to contribute significantly to clinical diagnostic algorithms and decision-making processes for emergency medical interventions.

Materials and Methods

This prospective study was conducted between June and November 2016 with approval from the Selçuk University Faculty of Medicine Ethics Committee (decision number: 2016/147 date: 18.05.2016). The study included patients aged 18 years and older who presented with chest pain. Informed consent forms were obtained from all participants. Healthy volunteers without complaints who agreed to participate in the study and showed no pathological findings on physical examination were included as the control group. Patients who met one or more of the following exclusion criteria: chest pain lasting longer than 48 hours; pregnancy or breastfeeding; malignancy; trauma; chronic diseases; or thoracic or esophageal pathologies were excluded from the study. Demographic data, complaints, vital signs, and physical examination findings were recorded. Blood samples were collected from each participant and analyzed for serum ADMA and arginine levels using liquid chromatography-mass spectrometry (LC-MS). Patients were classified according to whether the cause of chest pain was potentially life-threatening (e.g., acute coronary syndrome (ACS), PE, aortic dissection) or benign. Serum ADMA and arginine levels were compared between the patient and control groups. Additionally, medication use, family history, electrocardiogram (ECG) findings, emergency department outcomes, and patients' final status were evaluated.

Quantitative Measurement of ADMA and Other Arginine Derivatives

The normal range for ADMA in adults is accepted to be 0.5-1.2 µmol/L. Serum samples were collected in gel tubes, centrifuged, and stored at -80°C. Plasma samples for measurement of ADMA, symmetric dimethyl arginine (SDMA), NG-monomethyl-l-arginine (L-NMMA), arginine, and citrulline were analyzed at the Selçuk University Faculty of Medicine Biochemistry Laboratory using the AB SCIEX API 3200 LC-MS/MS system. The analysis was conducted in positive-ion mode using Turbo Ion Spray electrospray ionization source on a Phenomenex Luna 50 × 4.6 mm, 5 µm C18 HPLC column. A gradient was established using two mobile phases: water containing 0.1% formic acid (pump A) and methanol containing 0.1% formic acid (pump B). Butanol containing 5% acetyl chloride was used for derivatization. Each sample was processed using prepared reagents, and internal standards were used as necessary (5).

Statistical Analysis

Data analysis was conducted using the SPSS 20.0 statistical software (IBM Inc., Chicago, IL) on the dataset compiled in Microsoft Excel. Descriptive statistics for all variables were calculated. The normality of the data was evaluated using the Kolmogorov-Smirnov test; most of the data did not conform to a normal distribution. Therefore, the Mann-Whitney U test was used to assess differences between two independent groups, and the Kruskal-Wallis test was used for comparisons among multiple groups. Pairwise comparisons were analyzed using the Wilcoxon signed-rank test.

Results

Of the 219 participants included in the study, 47.5% were in the patient group presenting with chest pain and 52.5% were in the control group. Of the participants, 58.4% were male. The cases were classified as ACS, non-specific chest pain (NSGA), PE, and other diagnoses, with NSGA (42.3%) and ACS (35.6%) being the most frequent. The demographic analysis showed similar average ages; the control group had a greater average height, whereas the case group's body mass index (BMI) was 2 kg/m² higher than that of the control group.

Regarding biochemical measurements, no significant differences were found among the levels of ADMA, SDMA, and L-NMMA, whereas arginine ($p<0.001$) and the ratios (arginine/ADMA, $p<0.001$; arginine/total methyl arginine, $p=0.001$) showed significant differences between the groups. The arginine concentration in the patient group was approximately 111 µmol/L, whereas in the control group it was 131 µmol/L. The arginine/ADMA ratio was 403 and 131 µmol/L in the patient

and control groups, respectively (Table 1). All participants in the control group presented in autumn, whereas participants in the patient group presented similarly in summer and autumn. No significant differences were found in the levels of ADMA, SDMA, and L-NMMA. The rates of non-ST elevation myocardial infarction (NSTEMI) and STEMI were notable, and the similarity in pain presentation was 34%.

Cardiovascular risk factors were examined in the patient group: a history of angiography and smoking were present in 40.4%, hypertension in 42.3%, and a family history in 39.4%. Among the patients, 42.2% were discharged after examination, whereas angiography was performed in 33.7%. Among the ECG findings, ST depression was the most commonly observed (15.5%). Presentations occurred during daytime hours in 47.1% of cases. In the initial diagnosis grouping, NSGA (42.3%) and ACS (35.6%) rates were notable, while the PE rate was 8.7%. Troponin and creatine kinase-MB (CK-MB) levels were higher in the NSGA group than in the PE group. Among the arginine derivatives, ADMA levels were lowest in PE and highest in ACS. No mortality was observed in the emergency department; however, three patients died during hospitalization.

In patients with PE, L-NMMA levels were elevated (p=0.013). Simultaneously, SDMA and total methyl arginine increased in cases of cardiomegaly, whereas arginine and the arginine-to-total methyl arginine ratio decreased in cases of atelectasis. In fatal cases, D-dimer, ADMA, SDMA, and L-NMMA levels were elevated; aspartate aminotransferase was elevated in NSGA. D-dimer was significantly elevated in patients with STEMI. Troponin levels did not differ significantly among the groups, with measurements of 100 ng/mL in STEMI, 120 ng/mL in NSTEMI, and 165 ng/mL in unstable angina pectoris (USAP). Four hours later, decreases were observed in STEMI and USAP, while increases were noted in NSTEMI and other groups. CK-MB levels were elevated in NSTEMI and other groups. D-dimer levels were significantly elevated in patients with STEMI. The arginine/ADMA (p=0.017) and arginine/total methyl arginine (p=0.037) ratios showed significant differences among the STEMI, NSTEMI, and USAP groups. Arginine/ADMA was 642 µmol/L in STEMI, 318 µmol/L in NSTEMI, and 176 µmol/L in USAP. Arginine/total methyl arginine was 313 µmol/L in STEMI, 187 µmol/L in NSTEMI, and 104 µmol/L in USAP. ADMA levels were elevated in NSTEMI and USAP but reduced in STEMI. SDMA concentrations were 314 µmol/L in NSTEMI and 172 µmol/L in STEMI. L-NMMA was elevated in USAP to 0.045 µmol/L. Citrulline concentration peaked at 23.78 µmol/L in USAP. Total methylarginine values were similar in NSTEMI and USAP (both 0.700 µmol/L) (Table 2).

In patients with a history of angiography, levels of troponin, CK-MB, and D-dimer were lower, whereas levels of ADMA and total methyl arginine were higher. In patients with typical pain, CK-MB levels were significantly higher. SDMA levels were substantially higher in those with a history of heart failure (p=0.040). Smokers had lower citrulline levels (p=0.038), whereas physically active individuals had lower SDMA and total methylarginine levels (p=0.045 and p=0.009, respectively). In those with a history of hypertension, troponin and citrulline levels were elevated (p=0.006 and p=0.009, respectively). As the duration of the stay in the intensive care unit increased, SDMA levels rose while arginine levels decreased. A positive correlation was found between ADMA and total methyl arginine, whereas an inverse correlation was observed between ADMA and the arginine/ADMA ratio. The ROC analysis of the arginine-to-ADMA ratio demonstrated high diagnostic accuracy (area under the curve: 0.867) with a cutoff value of 218.15 µmol/L. Alcohol use was more common in the group with fatal cardiovascular disease (p=0.019). Most of the fatal cases were male and presented during daytime hours (Table 3, Figure 1).

Table 1. Arginine derivatives values in patients

Parameter	Patients (n=104)	Control (n=115)	p value
ADMA (µmol/L)	0.315±0.133	0.327±0.136	0.515
SDMA (µmol/L)	0.229±0.182	0.189±0.080	0.184
L-NMMA (µmol/L)	0.038±0.034	0.034±0.014	0.567
Arginine (µmol/L)	111.34±63.33	131.52±44.90	<0.001*
Citrulline (µmol/L)	18.76±15.37	19.44±11.33	0.103
Total methyl arginine (µmol/L)	0.583±0.261	0.551±0.182	0.556
Arginine/ADMA	403.19±318.09	131.75±44.91	<0.001*
Arginine/total methyl arginine	218.36±160.09	151.0±48.3	0.001*

*: p<0.001, ADMA: Asymmetric dimethylarginine, SDMA: Symmetric dimethyl arginine, L-NMMA: NG-monomethyl-l-arginine

Table 2. Biochemical findings of cardiac markers according to detailed diagnostic categories					
Parameter	**STEMI (n=11)**	**NSTEMI (n=22)**	**USAP (n=4)**	**Other (n=67)**	**p value**
Troponin (ng/L)	98.38±250.5	121.32±298	164.9±186.2	130.4±330	0.703
CK-MB (ng/mL)	3.44±2.56	5.60±12.5	3.05±1.8	9.74±26.3	0.886
D-dimer (ng/mL)	2520±353	1963±2439	-	-	0.946
INR	1.31	1.27	-	-	0.984
ADMA (µmol/L)	0.254±0.12	0.328±0.14	0.381±0.12	0.315±0.13	0.384
SDMA (µmol/L)	0.172±0.04	0.314±0.36	0.273±0.11	0.208±0.10	0.150
L-NMMA (µmol/L)	0.034±0.01	0.041±0.02	0.045±0.01	0.038±0.04	0.942
Arginine (µmol/L)	139.6±104.7	102.5±65.7	68.17±40.8	112.5±54.8	0.151
Citrulline (µmol/L)	19.63±11.4	18.96±23.1	23.78±24.3	18.27±13.9	0.941
Total methyl arginine (µmol/L)	0.460±0.16	0.692±0.20	0.700±0.02	0.562±0.21	0.122
Arginine/ADMA	642.0±508.7[a,b]	318.7±135.3[b]	176.8±107.6[a]	407.1±308.4	0.017*
Arginine/total methyl arginine	313.3±210.3[a,b]	187.8±88.9[b]	104.1±75.3[a]	227.1±163.9	0.037*

Significant differences marked with asterisks. "a" and "b" represent groups with significant differences (comparison indicated in the table
CK-MB: Creatine kinase-MB INR: International normalized ratio, ADMA: Asymmetric dimethylarginine, SDMA: Symmetric dimethyl arginine, L-NMMA: NG-monomethyl-l-arginine, NSTEM: non-ST elevation myocardial infarction, STEM: ST elevation myocardial infarction

Table 3. Differential diagnostic information determined for the arginine/ADMA ratio			
Arginin/ADMA	**Patients**	**Control**	**Total**
>218.16	78	5	83
<218.15	26	110	136
Total	104	115	219
Sensitivity	75.0%	False negative	25.0%
Specificity	95.65%	False positive	4.34%
Positive predictive value	93.97%	Positive probability	1725%
Negative predictive value	80.88%	Negative probability	26.13%
Accuracy	85.84%		
ADMA: Asymmetric dimethylarginine			

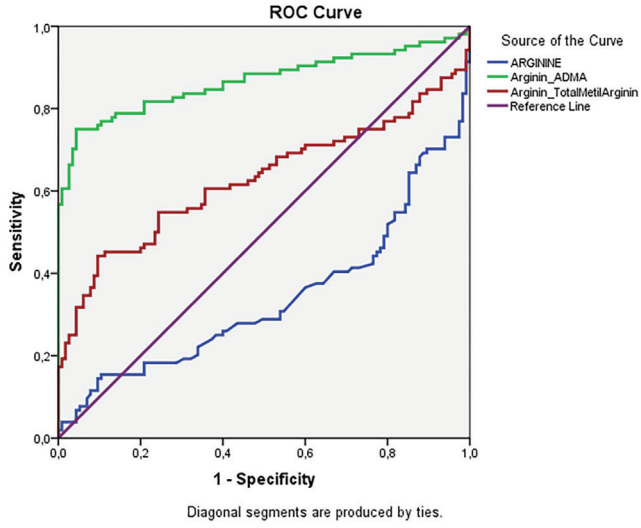

Figure 1. Results of ROC analysis for arginine and its ratios
ADMA: Asymmetric dimethylarginine

Discussion

This study investigated the relationship between arginine derivatives (ADMA, SDMA, L-NMMA) and cardiovascular diseases. Elevated plasma ADMA levels are an important risk factor for atherosclerosis and cardiovascular events. The finding of lower citrulline levels in smokers highlights the effects of smoking on metabolism. A positive correlation has been observed between age and ADMA levels, indicating that ADMA levels increase with age. The study by Cavusoglu et al. (6) indicates that high levels of ADMA and SDMA can serve as cardiovascular risk factors and are associated with potentially fatal cardiovascular events. These findings are consistent with previous studies (7,8).

Previous research has examined the effects of arginine derivatives on cardiovascular disease. Borgeraas et al. (9) found that ADMA levels were higher in the low BMI group, indicating that arginine derivatives are associated with increased cardiovascular risk. In another study conducted by Borgeraas et al. (9), male gender and age were associated with ADMA levels in patients grouped by trans fatty acids. These findings align with the results of this study and strengthen the relationship between arginine and ADMA levels and cardiovascular diseases.

Previous studies have shown that ADMA and SDMA could serve as cardiovascular risk factors (10). Souza-Costa et al. (11) examined the effects of L-NMMA on pulmonary hypertension and provided evidence of a relationship between arginine derivatives and cardiovascular conditions. Böger et al. (3) emphasized the significance of the relationship between ADMA and cardiovascular diseases. In our study, elevated levels of ADMA were observed in patients with chest pain admitted to the emergency department. Cavusoglu et al. (6) also examined the relationship between ADMA and BMI, and found a significant association between obesity and elevated ADMA levels. Our study similarly demonstrates that ADMA is associated with BMI, hypertension, and other cardiovascular risk factors, consistent with previous studies.

Das et al. (12) examined the effects of hypertension and diabetes on ADMA levels and observed significantly elevated levels in patients with hypertension. Our study also found increases in arginine and SDMA levels in patients with a history of hypertension. Zoccali et al. (13) pointed out that inflammation increases ADMA levels; our study also demonstrated an association between inflammatory conditions and ADMA. Kumar et al. (14) examined the relationship between pulmonary hypertension and L-NMMA, indicating that L-NMMA could be used for clinical diagnosis. Lippi et al. (15) investigated the diagnostic value of arginine derivatives in ACS and noted the elevation of the arginine/ADMA ratio. These findings suggest that arginine derivatives may be important in clinical diagnosis.

A major limitation of this study is the small sample size in certain diagnostic subgroups, particularly the USAP group (n=4). This small subgroup size reduces the statistical power and limits the reliability of subgroup comparisons. Therefore, the findings related to USAP should be interpreted with caution and considered hypothesis-generating rather than definitive.

Study Limitations

The study's generalizability is limited by the small sample size and heterogeneous group composition. Larger population-based, long-term studies are needed to understand the value of arginine derivatives better. To reduce confounding, patients with conditions known to elevate ADMA independently of cardiovascular disease—such as renal failure, infection/sepsis, systemic inflammatory or autoimmune disorders, malignancy, and chronic liver disease—were excluded. This ensured that observed changes in ADMA and arginine metabolism primarily reflected cardiovascular pathology.

Conclusion

Elevated ADMA levels and an increased arginine/ADMA ratio have been identified as important biomarkers in the differential diagnosis of cardiovascular events and fatal conditions. Findings emphasize the connection between ADMA and factors such as inflammation, hypertension, and obesity, suggesting potential contributions to early diagnosis and treatment. The use of the arginine/ADMA ratio in diagnostic processes is recommended. This study highlights that these biomarkers could be critical tools in emergency management and lays the groundwork for future research.

Ethics

Ethics Committee Approval: The study was conducted between June and November 2016 and was approved by the Selçuk University Faculty of Medicine Ethics Committee (decision no: 2016/147, date: 18.05.2016).

Informed Consent: Informed consent forms were obtained from all participants.

Footnotes

Authorship Contributions

Concept: HSY., Design: HSY, AB., Data Collection or Processing: HSY, AB, AU., Analysis or Interpretation: HSY, AB, FA., Literature Search: HSY, AB, AU, MA, BT., Writing: HSY.

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

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Clinical Characteristics of Pulmonary Contusion in Trauma Patients and Determinants of Mortality: A Retrospective Analysis

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Abstract

Aim: Pulmonary contusion is a leading cause of morbidity and mortality in trauma patients. This study retrospectively evaluated the clinical characteristics of patients with pulmonary contusion who presented to the emergency department, as well as the factors associated with mortality.

Materials and Methods: This retrospective, cross-sectional study included patients aged 18 years and older who were diagnosed with pulmonary contusion by computed tomography and who presented to the emergency department of a tertiary university hospital between 2019 and 2024. The analysis included demographic characteristics, trauma mechanism, associated injuries, including by body region, laboratory parameters, complications, treatment approaches, and clinical outcomes.

Results: A total of 350 patients were evaluated; mean age was 47.8±18.6 years, and 79.4% were male. The most common trauma mechanism was blunt trauma. Pulmonary contusion was most frequently observed in the lower lobes. The most prevalent associated injuries were rib fractures, pneumothorax, and hemothorax. The 30-day total mortality rate was 8%. Among non-survivors, the following were significantly higher: age, chest trauma scores, complication rates, lactate levels, and pCO_2 levels.

Conclusion: In trauma patients, pulmonary contusion most frequently occurs in the lower lobes and commonly accompanies chest wall and pleural injuries. Advanced age, a higher chest trauma score, the development of complications, and elevated lactate and pCO_2 levels are risk factors for mortality. Early evaluation of these parameters may facilitate prompt identification of high-risk cases.

Keywords: Pulmonary contusion, trauma, thoracic injury, mortality, emergency department

Introduction

Trauma is a significant cause of morbidity and mortality among young and working-age individuals (1). Blunt thoracic trauma, in particular, accounts for a significant number of emergency department visits and hospital admissions. It can lead to severe intrathoracic injuries, including pulmonary contusion, pneumothorax, hemothorax, and rib fractures (2,3). The most common parenchymal injury in thoracic trauma is pulmonary contusion, which leads to respiratory failure through pathophysiological processes such as alveolar hemorrhage, edema, ventilation–perfusion mismatch, and intrapulmonary shunting. This condition not only causes local complications but may also trigger a systemic inflammatory response, thereby adversely affecting patient prognosis (4).

Pulmonary contusions are reported in 17-75% of blunt chest trauma cases and are considered an independent risk factor for mortality (5,6). Pathologies accompanying pulmonary contusion, such as rib fractures, pneumothorax, and hemothorax, increase morbidity and the need for invasive interventions (4). Additionally, the development of complications such as pneumonia and acute respiratory distress syndrome (ARDS) is one of the main factors that worsen the clinical course and increase mortality (7). Nevertheless, the clinical course of pulmonary contusion

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is unpredictable, and varying outcomes are observed among patients (8).

Therefore, clarifying the clinical characteristics of pulmonary contusion and the factors influencing prognosis is important for enabling early risk stratification. This study aimed to retrospectively evaluate the demographic characteristics, trauma mechanisms, associated injuries, laboratory parameters, treatment approaches, and clinical outcomes of patients with pulmonary contusion presenting to the emergency department, and to identify determinants associated with mortality.

Materials and Methods

Study Design

This study was designed as a retrospective, cross-sectional analysis. Patients who presented to the emergency department of a tertiary university hospital between January 1, 2019, and December 31, 2024, and who were referred to the thoracic surgery clinic from the emergency department were included if pulmonary contusion was diagnosed by computed tomography (CT) (i.e., CT reports confirming pulmonary contusion). The study group consisted of all cases recorded within the specified time frame that met the inclusion criteria. For the analysis, only patients aged 18 years and older with complete and verifiable medical records were included. Cases with incomplete or unverifiable records, patients younger than 18 years, and patients referred to another healthcare facility for whom follow-up data were unavailable were excluded from the study.

The Institutional Review Board of Karadeniz University, Faculty of Medicine, approved the study (decision number: 2025/125, date: 14.05.2025). The study had a retrospective design, and patient data were obtained solely from medical records. Patient names and identifying information were not used; all data were anonymized before analysis. The study was conducted in accordance with the principles of the Declaration of Helsinki, and patient confidentiality was maintained.

As this was a retrospective study, informed consent was waived. Patient records were anonymized, and no personal identifiers were used.

Data Collection Process

Eligible patients were identified through the hospital's information management system and Picture Archiving and Communication System. Patient lists were generated using the ICD-10 code S20.2 (Thorax Contusion). Additionally, patients referred from the emergency department to the thoracic surgery clinic were included in the study group. The collected variables included:

- Demographic data: age and sex.
- Trauma characteristics: mechanism of trauma (blunt, penetrating, fall from height, other).
- Associated injuries: rib fracture, sternal fracture, clavicle fracture, pneumothorax, hemothorax, contusion, subcutaneous emphysema, pneumomediastinum, diaphragmatic injury, pulmonary laceration, and cardiac contusion.
- Laboratory parameters included blood gases (pO_2, pCO_2), hemoglobin, lactate, and troponin.
- Treatment process: conservative management, tube thoracostomy, thoracotomy, and need for surgical intervention.
- Clinical outcomes include discharge, ward admission, intensive care admission, hospital length of stay, development of complications, and mortality.
- Chest injury score: Chest trauma score (CTS)(9).
- Contusion localization: right upper, right lower, right middle, left upper, and left lower lung zones.

All data were recorded in an electronic spreadsheet, verified using a double-check method, and prepared for analysis.

Statistical Analysis

Data analysis was performed using Jamovi software (version 2.6.24.0). The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Continuous variables with a normal distribution were expressed as the mean ± standard deviation, while those without a normal distribution were expressed as the median (minimum-maximum). Categorical variables were presented as numbers and percentages.

For comparisons between groups, the Independent Samples t-test was used for continuous variables with normal distribution, while the Mann-Whitney U test was applied for those without normal distribution. The chi-square test or Fisher's exact test, as appropriate, was used to analyze categorical variables. A p value <0.05 was considered statistically significant in all analyses.

Results

A total of 350 patients were included in the study. The mean age was 47.8±18.6 years, and 79.4% of the patients were male. The majority of patients sustained blunt trauma (96.3%, n=337), followed by penetrating trauma (3.7%, n=13). The most common associated injuries were rib fractures (68.9%), pneumothorax (44.3%), and hemothorax (28.6%). Severe intrathoracic injuries, such as diaphragmatic rupture or esophageal injury, were infrequent (less than 1%). The most frequently injured sites

were the right lower lobe (57.7%) and the left lower lobe (54.3%). The overall 30-day mortality rate was 8% (n=28). A subgroup analysis revealed that mortality was exclusively observed in the polytrauma group (10.4%, n=28), whereas no deaths occurred in the isolated pulmonary contusion group (0%, n=0). Among the 350 patients with pulmonary contusion, the majority had associated extra-thoracic injuries. The most frequently affected body regions were the extremities (39.1%, n=137) and the spine (34.0%, n=119). Other associated injuries included traumatic brain injuries n=(23.4%, n =82), maxillofacial injuries (18.9%, n=66), abdominal injuries (16.0%, n=56), and pelvic fractures (10.9%, n=38). Less common injuries were vascular injuries (1.4%, n=5) and cardiac injuries (0.6%, n=2). The demographic and clinical characteristics of the patients are presented in Table 1.

The mean age of deceased patients was significantly higher than that of survivors: 57±19.3 years versus 47±18.2 years (p=0.006). There was no significant difference in sex distribution between the groups (p=0.712). The proportion of patients with a CTS

Table 1. Demographic ınformation and clinical characteristics

	Age (mean ± SD)	n (%)
Gender		
Male	45.7±18	278 (79.4%)
Female	55.7±18.7	72 (20.6%)
Trauma characteristics		**n (%)**
Blunt trauma		337 (96.3%)
Penetrating trauma		13 (3.7%)
Patient group		
Isolated thorax trauma		80 (22.9%)
Polytrauma		270 (77.1%)
Associated injuries		
Rib fracture		241 (68.9%)
Pneumothorax		155 (44.3%)
Hemothorax		100 (28.6%)
Subcutaneous emphysema		57 (16.3%)
Clavicle fracture		30 (8.6%)
Pneumomediastinum		18 (5.1%)
Pulmonary laceration		18 (5.1%)
Sternal fracture		17 (4.9%)
Diaphragmatic injury		1 (0.3%)
Contusion location		
Right lower lobe		202 (57.7%)
Left lower lobe		190 (54.3%)
Right upper lobe		113 (32.3%)
Left upper lobe		113 (32.3%)
Right middle lobe		77 (22.0%)
Associated ınjuries by body region		
Extremity		137 (39.1%)
Spinal		119 (34.0%)
Brain		82 (23.4%)
Maxillofacial		66 (18.9%)
Abdominal		56 (16.0%)
Pelvis		38 (10.9%)
Vascular		5 (1.4%)
Cardiac		2 (0.6%)

Table 1. Continued

	n (%)
Complications	
Total number of patients with complications	98 (28.0%)
Pneumonia	22 (6.3%)
Pneumothorax	15 (4.3%)
Hemothorax	16 (4.6%)
Atelectasis	5 (1.4%)
ARDS	4 (1.1%)
Hemoptysis	1 (0.3%)
Other	58 (16.6%)
Treatment methods	
Observation/follow-up	268 (76.8%)
Tube thoracostomy	77 (22.1%)
Surgery	4 (1.1%)
Hospitalization and outcomes	
Number of hospitalized patients	288 (82.3%)
Discharged from ED	54 (15.4%)
Ward admission	170 (48.6%)
ICU admission	116 (33.1%)
Death in ED	10 (2.9%)
30-day mortality	
Isolated thorax trauma	0 (0%)
Total polytrauma	28 (8.0%)
	Median (minimum-maximum)
Average length of stay (days)	5 (0-67)

ED: Emergency department, ICU: Intensive care unit, SD: Standard deviation, ARDS: Acute respiratory distress syndrome

greater than five was 92.9% in the mortality group and 56.2% among survivors, a statistically significant difference (p<0.001). Complications during clinical follow-up also occurred more frequently in the mortality group (89.3%) than in the survivor group (22.7%), with a statistically significant difference (p<0.001).

We then compared the patients who survived (n=322) with those who died (n=28) to identify factors associated with mortality. When examining treatment methods, tube thoracostomy was required significantly more often in the mortality group than among survivors (p=0.002). Regarding laboratory parameters, the median lactate level was 28 mg/dL in patients who died, compared with 15 mg/dL in survivors (p=0.001). Similarly, pCO_2 levels were higher in the mortality group (p<0.001). In contrast, troponin, pO_2, and hemoglobin values were not significantly associated with mortality (p>0.05). A comparison of variables associated with mortality is summarized in Table 2.

Discussion

This study retrospectively evaluated the clinical characteristics of patients with pulmonary contusion who presented to the emergency department and the factors associated with mortality. Our findings suggest that advanced age, CTS, and the development of complications are key determinants of mortality. These results demonstrate both similarities and differences relative to previous studies of factors influencing the prognosis of pulmonary contusion.

In this study, which evaluated 350 patients, the majority of patients were male, with a mean age of 47.8 years. Similarly, in a 10-year retrospective study conducted by Demirhan et al., the proportion of male patients was 85%, and the mean age was 36.2 years (10). This finding is consistent with the literature reporting that trauma occurs among young and middle-aged males (3,11).

Examination of trauma mechanisms showed that nearly all cases were caused by blunt-force trauma or falls, whereas penetrating injuries occurred at very low rates. Previous studies have reported that most thoracic injuries result from blunt force, with traffic accidents and falls from heights being the most common causes (2,11-13). In our study, falls also emerged as the most significant mechanism associated with blunt trauma.

Pulmonary contusions were most frequently localized in the lower lobes: the right lower lobe (57.7%) and the left lower lobe (54.3%). This may be explained by the larger anatomical volume of the lower lobes and their greater exposure to trauma (14). The literature also reports that the lower lobes are more susceptible to contusion (13,15).

The most common associated injuries were rib fractures, pneumothorax, and hemothorax. These findings demonstrate that pulmonary contusion is frequently accompanied by chest wall and pleural pathologies. According to Tyburski et al. (16), rib fractures were the most frequent associated injury, occurring in 67% of pulmonary contusion cases. In a study by Dumanlı evaluating pulmonary contusions, pneumothorax was detected in 51.9% of cases and hemothorax was detected in 45.4% (2). Our findings are consistent with previous research.

When complications were evaluated, 28% of cases exhibited complications; the most prominent were respiratory problems, including pneumonia (6.3%), pneumothorax (4.3%), hemothorax (4.6%), and ARDS (1.1). Pulmonary contusion has also been reported in the literature as an important risk factor, particularly for the development of pneumonia and ARDS (5,7,11,17). In the study by Lee et al. (18), 38% of patients with contusions developed pneumonia, while 6.8% developed ARDS. Our study, observed lower rates, possibly owing to effective patient monitoring, early diagnosis and intervention, and the widespread use of

Table 2. Comparison of clinical and laboratory findings according to mortality status

Variable	Mortality (-) (n = 322)	Mortality (+) (n = 28)	p-value
Age (years, mean ± SD)	47.0±18.2	57.1±19.3	0.006
Gender (M/F)	256/66	22/6	0.712
Complication (%)	22.7	89.3	<0.001
CTS score >5 (%)	56.2	92.9	<0.001
Treatment: tube thoracostomy (%)	19.6	53.6	0.002
Troponin (ng/L, median)	19.3 (3.1-4761.0)	18.8 (3.5-216.1)	0.632
pCO_2 (mmHg, mean ± SD)	41.0±9.5	47.0±11.2	<0.001
pO_2 (mmHg, mean ± SD)	69.2±58.0	65.8±63.4	0.253
HGB (g/dL, mean ± SD)	13.7±2.0	13.3±2.1	0.053
Lactate (mg/dL, median)	14.0 (0.7-219.0)	28.5 (0.9-81.0)	0.001

SD: Standard deviation, M/F: Male/female, CTS: Chest trauma score, HGB: Hemoglobin

conservative treatment approaches. However, the development of respiratory complications remains an important factor in determining the clinical course. Close monitoring and effective management of these complications are critical to the success of treatment in such patients.

Examination of laboratory findings revealed that lactate levels were significantly higher in the mortality group. However, troponin and hemoglobin values were not associated with mortality. Previous studies have also emphasized the importance of lactate levels as prognostic biomarkers (19-21). The higher pCO_2 values observed in the mortality group demonstrate the impact of ventilatory impairment on prognosis (22). These results show that respiratory failure is a critical factor in determining mortality in patients with pulmonary contusion. Elevated lactate levels, an indicator of tissue hypoperfusion and oxygen deficiency, stand out among laboratory parameters as strong biomarkers of mortality (19). Elevated pCO_2 values reflect impaired alveolar ventilation and demonstrate the impact of respiratory failure on mortality. In contrast, troponin, hemoglobin, and pO_2 levels were not significantly associated with mortality. These results suggest that cardiac biomarkers and oxygenation parameters may play only a secondary role in contusion-related mortality (23). These findings are consistent with those of earlier studies that identified similar parameters as risk factors for mortality (24).

In our study, when treatment approaches were evaluated, the majority of cases were managed conservatively. However, the rate of tube thoracostomy was significantly higher among patients who died. This finding suggests that pleural complications negatively affect prognosis and increase the need for invasive interventions. Most patients with thoracic trauma recover clinically within 5-7 days with conservative management; however, a subset may require invasive treatment (5). In particular, tube thoracostomy is the first-line intervention for managing complications of pulmonary contusion. At the same time, the need for surgical intervention arises in a limited number of cases (5,8). Accordingly, the low rate of surgical treatment in our study is consistent with existing literature. However, a greater frequency of invasive interventions in cases of high CTS with complications underscores the importance of early risk assessment in treatment strategies.

Our study found a mortality rate of 8%, which is notably lower than the 14-40% reported in the literature for pulmonary contusion (5,12,16). Reasons for this difference may include the centre's advanced intensive care facilities, early diagnosis and effective resuscitation strategies, a predominance of younger patients, and a relatively low incidence of major concomitant trauma. Examination factors affecting mortality identified advanced age, the development of complications, higher CTS, and elevated lactate and pCO_2 levels as the strongest determinants of mortality. Reduced physiological reserves, increased prevalence of comorbidities, and diminished recovery capacity can explain the impact of advanced age on mortality (5). Similarly, the presence of complications, particularly pneumonia and ARDS, prolongs the hospital stay, worsens the clinical course, and increases mortality (8). The correlation between a high CTS and mortality underscores the pivotal role of trauma severity and associated injuries in informing prognosis (25). Therefore, early evaluation of age, trauma score, lactate, and pCO_2 levels in patients with pulmonary contusion may facilitate the rapid identification of high-risk cases and contribute to the implementation of treatment strategies aimed at improving prognosis.

Study Limitations

This study has several limitations. First, because of its retrospective design, data were obtained from existing medical records; therefore, the possibility of missing or incomplete information cannot be excluded. Second, since the study was conducted at a single center, the results may not be generalizable to other patient populations. Third, while we utilized the CTS to assess thoracic injury severity, global trauma scores such as the injury severity score or TRISS were not calculated. The impact of multi-trauma was instead evaluated through the analysis of specific associated injuries. Additionally, the clinical effects of trauma severity and associated injuries may not have been evaluated uniformly.

Conclusion

Pulmonary contusion most commonly occurs after blunt trauma or falls and is frequently accompanied by rib fractures, pneumothorax, and hemothorax. In our study, the mortality rate was 8%; advanced age, development of complications, higher CTS, elevated pCO_2, and increased lactate levels were identified as risk factors. These results highlight the critical importance of early clinical and laboratory assessments in the emergency department for identifying high-risk patients and planning appropriate treatment strategies.

Ethics

Ethics Committee Approval: The Institutional Review Board of Karadeniz University, Faculty of Medicine, approved the study (decision number: 2025/125, date: 14.05.2025). The study had a retrospective design, and patient data were obtained solely from medical records. Patient names and identifying information were not used; all data were anonymized before analysis. The study was conducted in accordance with the principles of the Declaration of Helsinki, and patient confidentiality was maintained.

Informed Consent: As this was a retrospective study, informed consent was waived. Patient records were anonymized, and no personal identifiers were used.

Footnotes

Authorship Contributions

Concept: A.S.S., B.K.A., İ.D., Design: A.S.S., E.D., İ.D., S.P., Data Collection or Processing: S.Ö., B.K.A., İ.D., S.P., Analysis or Interpretation: A.S.S., E.D., B.K.A., İ.D., Literature Search: S.Ö., S.P., Writing: A.S.S., S.Ö., E.D., S.P.

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SCAMPER-based First Aid Training: Effect on Students' Knowledge and Innovation-Oriented Attitudes

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Abstract

Aim: This study aimed to evaluate the impact of the SCAMPER technique in first aid training on students' first aid awareness, development of safe-behavioral practices, and innovative product design thinking.

Materials and Methods: The study was conducted at Konya BİLSEM with 122 systematically sampled students, divided into two groups: one receiving traditional first aid training and the other instructed using the interactive SCAMPER technique. Pre- and post-training questionnaires assessed knowledge levels, anxiety about intervention, and attitudes toward equipment design. The traditional group was trained via classical presentations, while the SCAMPER group received training through interactive, creative exercises.

Results: Both groups showed a significant increase in first aid knowledge, adoption of safe-behavioral practices, and willingness to design first aid equipment after the training ($p<0.001$). The inclination to design innovative equipment was significantly higher in the SCAMPER group compared to the traditional group ($p<0.001$). Additionally, the majority of students expressed a desire for further first aid education (62.3%). SCAMPER-based training was associated with stronger innovation-oriented attitudes toward equipment design and interactive participation.

Conclusion: First aid education utilizing the SCAMPER technique is as effective as traditional methods in enhancing knowledge and fostering safe-behavioral practices, while offering additional benefits in stimulating innovative thinking regarding equipment design. Early first aid education incorporating SCAMPER is recommended to improve public health awareness and expand the reach of first aid practices within the community.

Keywords: Emergency medicine, first aid, education, educational models, innovativeness, early intervention, child behavior, experimental study

Introduction

First aid refers to the immediate care provided until medical staff arrive in unexpected events, accidents, acute health problems, or when encountering a life-threatening situation. The primary purpose of first aid is to eliminate danger, prevent the person's health from deteriorating further, and facilitate recovery. The most important distinction between first aid, emergency treatment, or emergency care and professional or emergency medical services is that "although first aid can often be delivered with minimal or improvised resources, the availability and appropriate use of basic first aid equipment may enhance safety and effectiveness in bleeding control." The timely and proficient administration of first aid using the correct techniques significantly contributes to the reduction of death and morbidity. Competent individuals are required for this. (1,2). Well-structured training programs are also necessary for individuals who are proficient in first aid practices.

There are different procedures for first aid training in various countries (3). Providing first aid training from an early age should be considered a strategic step for public health, not only for societal response within the emergency response system and the inclusion of the youngest individuals in this response, but also for the purpose of establishing safe-related behaviors behavioral. Therefore, including first aid lessons in the curriculum from elementary school onward, and repeating them in high school and university years, is beneficial in many ways (4). Because first aid is a need that can arise for every individual, initially in life-threatening situations, and sometimes in situations posing a smaller health risk. In addition, first aid application may be

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needed by anyone in the community, at any time, starting with the person themselves or their loved ones. Additionally, school is an environment where incidents requiring first aid are frequent, and these trainings can also raise awareness about accident prevention. Additionally, it will be easier to periodically repeat first aid training in formal education (5,6). In addition to this, although first aid doesn't require medical equipment, recognizing first aid materials is also an added benefit of these trainings. The creation of personal first aid kits in areas such as homes and vehicles, and the availability of first aid bags or cabinets in public spaces, are encouraged. Sometimes, however, this is a legal requirement (7-10). The advantage this brings is an increase in safe, hygienic, fast, accurate, and effective intervention. The basic principle regarding first aid supplies is that they should be easy to apply and readily available. However, these principles also highlight the need for ergonomic first aid supplies. This situation should not be overlooked in first aid training, and information about first aid equipment should also be provided (11,12).

In addition to traditional training methods, many new methods are being continuously tested and the results discussed regarding how first aid training will be delivered and the techniques to be used, utilizing the possibilities offered by technology. While the advancement of technology provides different opportunities for teaching and learning information, it also increases accessibility to knowledge (13). In addition to the goal of ensuring an adequate level of effectiveness in first aid training, it is expected to create the safe-behavioral practices, reduce avoidance of intervention during an event, and decrease nervousness or hesitant behavior. Another important topic that is perhaps overlooked in first aid training is the importance of training methods that also increase awareness of the introduction and use of first aid kits. This will increase the importance these individuals place on first aid kits, and will increase the attention given to having personal first aid kits or first aid supplies in public areas such as workplaces and schools. It will also facilitate the development of ergonomic, effective, and easy-to-use kits. In such an educational method, the components of brainstorming and interactive participation still maintain their importance, although certain limittaions have been reported (14-16). When examining educational methods, the SCAMPER technique, first proposed by Alex Osborn and developed by Robert F. Eberle, is one of the techniques used to facilitate creative thinking. This technique is named after the acronym of the steps: Substitute, Combine, Adapt, Modify/magnify/minify, Put to other uses, Eliminate, Reverse or rearrange. The advantage of the SCAMPER technique is that it provides an interactive learning environment by conducting brainstorming through specific steps, and prevents the topic from reaching a deadlock or from always revolving around the same ideas (17).

Within this context, the importance of first aid lessons in formal education for the development of first aid awareness, effective practices, and a safe-behavioral practices becomes evident. This topic is of particular interest from a medical perspective, including school health (18,19). In addition to this, another goal of the first aid training should be to develop ideas for the design of innovative products that can be used in the field of first aid and healthcare, which also relate to the field of medical engineering. This study aims to investigate the change in first aid awareness, s safe-behavioral practices, and innovative product design opinions regarding first aid areas and kits after training using the SCAMPER technique.

Materials and Methods

Study Design

The study was planned as an educational intervention study and examined how first aid awareness, safe-behavioral practices for bleeding, and innovative product design thinking in the field of first aid changed among groups when first aid training was delivered to two groups using the traditional method and the SCAMPER technique. The study was carried out at a Konya BİLSEM. In Türkiye, BİLSEM's are state-affiliated institutions where gifted students receive additional lessons in their areas of talent, alongside their formal education. This setting was selected due to the potential of students to engage in creative and innovation-oriented learning activities and this research could be more valuable in this regard for selected groups. According to the sample size calculation performed with the G* Power program for the research (test: Student's t test, effect size= 0.5 and $p<0.05$ and 85% power), it was found that a total of 118 people were needed for the two groups. The aim was to recruit 120 cases, with 60 for Group 1 and 60 for Group 2.

Permission was obtained from the KTO Karatay University Ethics Committee for Non-Pharmaceutical and Medical Device Research (desicion number 2024/015, date: 31.10.2024) for the research. Administrative leave was obtained from the institutions. Students' parents were informed with the help of the school administration and consent was obtained from the families. The trainings were held between 01.11.2024 and 30.11.2024.

Systematic Sampling and Student Selection

The systematic sampling method was used for sample selection. The complete list of BİLSEM students has been received. From this list, high school seniors and first and second-grade students were removed due to test anxiety and the intensity of their

programs, with the aim of preventing potential disagreements in reading and comprehension and reducing group heterogeneity. Then, planning was done to ensure an equal number of students were taken from each class. After registered students were ranked using student numbers for systematic sampling, at least 60 people were selected based on a random number table. Later, new students were selected in the same way to replace those who could not obtain permission from their parents or did not wish to participate. Group heterogeneity emerged during the election due to the internal dynamics of the center where the study was conducted. For students admitted to the center, there was a different number of students each year. Additionally, the lack of mandatory attendance at this center led to some students not participating and being unable to obtain permission from their families. To reduce group heterogeneity, students who scored high on the pre-test, those who received first aid training as part of the program, and students with a first-degree relative who is a healthcare worker were excluded from the study. Considering that the sample size calculated based on the two students' strong desire to participate in the education exceeded 5% of the total, both groups were increased to 61 people.

Education and Evaluation

Before the training, participants were asked questions such as, "Would you like to be a first responder?" and "Would you be worried if you encountered a person with bleeding who needed first aid?", and "Would you consider designing first aid equipment that could be used for bleeding patients?" In addition to this, a 15-question survey was administered, including a socio-demographic data. The questionnaire was developed by the authors through a literature review and reviewed for content validity by three experts in the field. However, no further psychometric testing (e.g., construct validity, reliability analysis) was conducted. The expected answer in the survey was coded as "1" point, while other answers were coded as "0" points. First aid awareness training was provided to the first group in groups of 20-20-21 people, using the classic presentation technique (first aid awareness training through PowerPoint and projector, equipment introduction, and practical applications), lasting 45 minutes. The training included an introduction to first aid equipment that can be used with the safe first aid behavior model in case of bleeding. The second group was taught using the SCAMPER technique in groups of 20-20-21 people each (first aid awareness training content, equipment introduction, and practical applications via PowerPoint and projector) (Figure 1). In both methods, the trainers covered the same topics in the same amount of time and by the same instructor. After the training, the 15-question survey was administered again, and the question "Would you like to receive more first aid training?" was also asked.

Statistical Analysis

The data obtained from the study results were analyzed using the Statistical Packages for the Social Sciences (SPSS) 18.0 Windows software package (SPSS Inc., Chicago, IL, US). When presenting the data, descriptive analyzes provided frequency data as numbers and percentages, while continuous numerical data were presented as mean ± standard deviation or median values. The normal distribution of the data was examined using the Shapiro-Wilk and Kolmogorov-Smirnov tests. The chi-square test

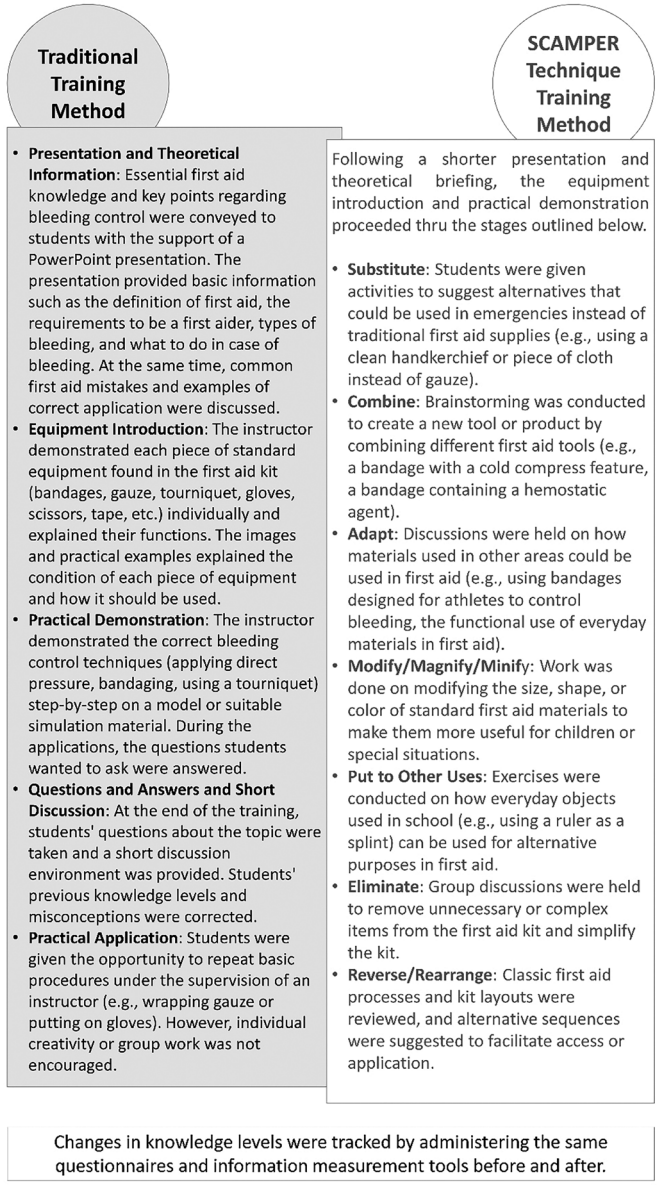

Figure 1. Implementation phases and illustrative examples of the traditional training method and the SCAMPER technique training method in first aid education

was used for comparing categorical data, the Wilcoxon test for comparing numerical data, and the Mann-Whitney U test. The Bonferroni correction was used to identify significant groups in the chi-square test with multiple eyes. Jamovi (version 2.6.26) software was used to determine effect sizes and CIs.

The level of statistical significance for all tests was considered to be $p<0.05$.

Results

The participants had a median age of 14 years, with a minimum age of 10 and a maximum age of 16. Of the participants, 62 (50.8%) were in primary and middle school, whereas 60 (49.2%) were in high school. The gender distribution consisted of 56% males (n=68) and 44% females (n=54). Of the participants, 73.8% (n=90) reported that they had not previously received first aid training. In response to the question, "Do you have sufficient knowledge about intervening in bleeding?" 82% of participants (n=100) indicated a lack of knowledge. Table 1 presents the changes in first aid knowledge levels following training, concerns regarding the application of first aid, and considerations for the design of first aid equipment and innovative products. The analysis revealed statistically significant differences in responses to the question "Do you have knowledge about first aid products/equipment that can be used in bleeding patients?" before and after the training ($p<0.001$, $X^2=133.954$). The observed difference originated from the group that responded affirmatively, the group that responded partially, and the group that responded negatively. The responses to the inquiry, "Would you consider designing first aid equipment for use on bleeding patients?" exhibited statistically significant differences pre- and post-training ($p<0.001$, $X^2=66.705$). A notable distinction emerged among the group that affirmed, the group that expressed uncertainty, and the group that denied.

The pre-training score of participants in the group trained with general first aid techniques was 6.13±1.88, while the post-training score was determined to be 10.07±1.67. It was found that the score for Safe Behavior and First Aid Awareness after the training was statistically significantly higher than before the training ($p<0.001$, effect size= 1.00). The data for the pre- and post-training comparison results are presented in Table 2.

It was found that the average of the scores participants received from the questionnaire administered before and after the training given using the SCAMPER technique was 6.16±2.07 before the training and 10.89±1.69 after the training. It was found that the score for Safe Behavior and First Aid Awareness after the training was statistically significantly higher than before the training ($p<0.001$, effect size= 1.00). The data for the pre- and post-training comparison results are presented in Table 3.

In the subgroup analyses for primary and secondary school students and high school students, the pre-training survey score was 5.85±2.14 for the primary and secondary school group, but the score for the high school group was 6.21±2.01. The mean

Table 1. Changes in Safe-Behavioral Practices and First Aid Awareness in Bleeding Before and After Training with Traditional First Aid Techniques (n=61)

		Pre-training		Pre-training		p
		n	%	n	%	
Would you like to be a first responder?	Yes	60	49.2	78	63.9	**p=0.02** $X^2=5.404$
	No	62	50.8	44	36.1	
Do you know how to get a first aid certificate?	Yes	8	6.6	118	96.7	**p<0.001** $X^2=198.504$
	No	114	93.4	4	3.3	
Do you know the conditions for being a first aider or who is called a first aider?	Yes	6	4.9	118	96.7	**p<0.001** $X^2=205.695$
	No	116	95.1	4	3.3	
Would you be concerned if you encountered someone who was bleeding and needed first aid?	Never	12	9.8	18	14.8	p=0.108 $X^2=6.076$
	Rarely	46	37.7	56	45.9	
	Often	50	41.0	42	34.4	
	Always	14	11.5	6	4.9	
Do you have any information about first aid products/equipment that can be used for bleeding patients?	Yes	16	13.0	106	86.9	**p<0.001** $X^2=133.954$
	Partially	72	59.0	14	11.5	
	No	34	27.9	2	1.6	
Would you consider designing first aid equipment that could be used on bleeding patients?	Yes	16	13.1	78	63.9	**p<0.001** $X^2=66.705$
	No idea	38	31.2	14	11.5	
	No	68	55.7	30	24.6	

post-training survey score rose to 9.72±2.98 for primary and secondary school pupils trained using the traditional technique, and to 10.88±1.68 for those trained with the SCAMPER technique. The average post-training survey score for high school students rose to 10.55±2.98 for those trained using the traditional method, and to 10.88±1.69 for those trained with the SCAMPER technique. No statistically significant difference was observed among the post-test scores of the primary, secondary, and high school groups following training using the SCAMPER approach (p=0.44, U=1709.0).

After the training, it was determined that 62.3% (n=76) of the participants answered "Yes" to the question "Would you like to take more first aid lessons or training?" A statistically significant difference was found between the idea of designing equipment and the increased demand for first aid training. Those considering designing new first aid equipment had a significantly higher demand for first aid lessons compared to other groups. Training provided using the SCAMPER technique (mean= 4.72±1.47) was statistically significantly associated with a greater inclination toward new equipment design compared to training provided using the traditional technique (mean= 3.93±1.58) [p<0.001, U=3178, mean difference= 1, 95% confidence interval (CI)= 1.00-1.50, effect size= 0.552]. Descriptive plots showing the changes in pre- and post-training survey scores with the training technique and the comparison of the two training techniques on these changes are presented in Figure 2.

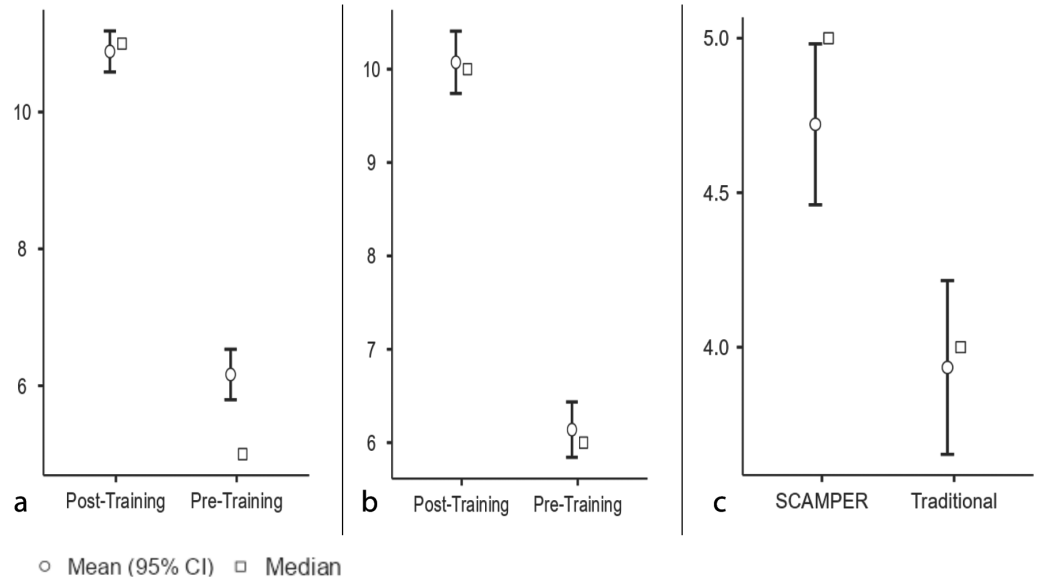

Figure 2. Descriptive plots. (a) Pre-test and post-test comparison of the SCAMPER technique. (b) Pre-test and post-test comparison of the traditional technique. (c) Comparison of the impact of SCAMPER and Traditional techniques on the idea of developing new first aid equipment, CI: Confidence interval

Table 2. Change in Safe Behaviors and First Aid Awareness in Bleeding Before and After Training with Traditional First Aid Techniques (n=61)

	Questionnaire score			p	Mean difference	95% CI	Effect size
	Mean ± SD	Median	Q^1-Q^3			Lower-upper	
Pre-training	6.13±1.88	5	5-7	**p<0.001** W=7381	4.00	3.50-4.50	1.00
Post-training	10.07±1.67	10	8-11				

CI: Confident interval, SD: Standard deviation, Q: Quartile, W: Wilcoxon test, SE difference= 0.143

Table 3. Pre- and Post-Training Changes in Safe Behaviors and First Aid Awareness in Bleeding Using the SCAMPER Technique (n=61)

	Questionnaire score			p	Mean difference	95% CI	Effect size
	Mean ± SD	Median	Q^1-Q^3			Lower-Upper	
Pre-training	6.16±2.07	5	5-8	**p<0.001** W=7503	4.50	4.50-5.00	1.00
Post-training	10.89±1.69	11	9-12				

CI: Confident interval, SD: Standard deviation, Q: Quartile, W: Wilcoxon test, SE difference= 0.133

Figure 3 present's several participants' concepts on the development and innovation of first aid products, generated throughout the training utilising the SCAMPER technique.

Discussion

According to the findings of this study, the training provided using traditional and SCAMPER techniques had a positive impact on increasing students' first aid awareness and ensuring safe behavior in bleeding situations. In the development of the idea of designing new equipment, the SCAMPER technique was found to be more effective.

Figure 3. Summary of ideas generated by participants during training using the SCAMPER technique, organized by stage

Studies on first aid knowledge levels emphasize the importance of starting first aid training at the primary school level, and even at the kindergarten level. It is reported that starting education at an early age also increases the expected benefits of first aid training repeated in later years (20,21). According to the results obtained in this study, 73.8% of primary-middle school and high school students stated that they had not received first aid training before, and 82.0% answered "no" to the question "Do you have sufficient knowledge about intervening in bleeding?" This situation not only highlights the lack of first aid training at an early age but also reveals the need for efforts in this area. Studies conducted in other countries regarding the pre-graduation first aid knowledge level also report being below the desired level, highlighting the need to work on this issue and provide training on first aid practices during education. It is known that in some countries, these trainings are offered with certification (22-24). Regarding first aid, there is an age limit in Türkiye. It is conceivable that similar practices may exist in other countries for legal reasons. Encouraging students to develop a positive attitude toward first aid and practice may be more important than the certificate program. However, a registration and tracking system can be established to ensure that all students receive similar training in this regard. It is also a fact that these awareness, understanding, and knowledge-raising practices for students will not provide the desired benefit to society without the participation of teachers and family support.

In this study, it was found that the level of knowledge about first aid and the conditions for being a first aider significantly increased after the training provided. One of the most striking points is the positive change in the desire to be a first responder. This output not only demonstrates that first aid training should be part of community-based awareness-raising efforts, but also supports studies (2,4,6,20,21,25) that emphasize the importance of providing first aid training at an early age. There is also a continued need for developments in the most accurate first aid training methods for this age group. Because general first aid training and community-based practices are mostly single-session, non-repetitive training. However, research is increasing that suggests user experiences and interaction-focused training methods will be more beneficial for learners in first aid training. Virtual reality, game-based or mobile applications, and many different methods focused on personalization and gamification are still being tested and positive results are being reported (25-27). In this study, an intensive method was used in terms of interaction and interactive communication, and findings were reached that support these results. However, the fact that there was no significant change in the responses to the question of whether they would hesitate to intervene in a bleeding patient after the training indicates that practitioners still have some

hesitation about taking action. In many publications, it is seen that this is a general problem affecting other age groups as well (28-30). Although it is thought that this problem can be somewhat reduced by increasing practical training, and the results indicate the need for new studies on the causes of this situation.

Before training, 13% of students stated they had sufficient knowledge of the equipment that could be used on a bleeding patient and most people thought they didn't have enough knowledge on this topic. This result is also related to the topic discussed in the first paragraph, as it could be an indicator of the lack of early first aid training. Additionally, this could be due to insufficient introduction of the kits during first aid training, or an overemphasis on the "without the need for any materials" aspect of first aid's definition. This is actually a situation that highlights the distinction between first aid and emergency care. However, using a kit or equipment for first aid is beneficial in many ways and is encouraged in many countries. This point should be carefully emphasized during training (10,31,32). It was observed that the group who said they had knowledge about the equipment that could be used on a bleeding patient after the training was statistically significantly larger.

The evaluation of response scores from the 15-question survey presented to participants revealed that both the standard method and the SCAMPER technique resulted in a statistically significant enhancement in students' awareness of first aid and their attitudes towards the safe behaviour model for wounds. This is significant as it demonstrates that the SCAMPER technique is equally effective as traditional methods in first aid awareness training. This serves as evidence that the SCAMPER technique is applicable in first aid training. The absence of a statistically significant difference in the post-training test survey results between the elementary and secondary school age groups and the high school age group indicates that the SCAMPER technique exhibits comparable effectiveness throughout these subgroups.

According to the research results, there was also a significant increase in the participants' thinking about designing new equipment compared to before the training. Regarding increasing students' awareness of designing first aid equipment, the SCAMPER technique was more effective than the traditional method. While research on new equipment in the field of first aid is ongoing, children's first aid practices will likely require more equipment usage than adults. For example, the basic first aid intervention for bleeding is direct pressure (33). It could be difficult for him to apply and maintain this pressure during the period when there is no other savior beside the children, or until the request for help is met. This equipment differentiation will undoubtedly be even more pronounced in critical applications such as basic life support. The accessibility of first aid kits, the clarity and applicability of instructions during use, are also important issues (34,35). While recommendations for the composition of materials used for children in first aid kits are still ongoing (10), designing equipment for a child first responder might be premature at this point and this could be the subject of another research project. However, first aid training will undoubtedly be very important for raising awareness of accidents and for developing safe behaviors in emergency situations. Also, the idea of designing equipment is undoubtedly an idea that will be used in the future. Therefore, as in this study, using the SCAMPER technique in first aid training for students who could be in the target group in terms of equipment design, and who are considering fields such as engineering or medical engineering, could be beneficial. In addition, using the SCAMPER technique in first aid training can have a positive impact on first aid kit innovation, as it can generate ideas for using everyday materials as first aid tools in other groups as well.

When examining publications that emphasize the importance of disseminating first aid knowledge within society and reiterate this need, it is evident that research on how to approach this issue is still ongoing. It would not be the correct approach to consider the educational method's subject matter, instructor, environment, and materials independently of the target group. This situation leads us to believe that the expectation of a single and most correct educational method does not reflect reality. The correct training method will also differ depending on the variables. Current discussions and research focus on the impact of technology use and the increasing online methods it will create. In addition, the lack of structured tests that can fully measure the results of first aid training poses a significant problem for researchers in determining the correct training methods for first aid (16,26). The focus of this study is that different first aid methods can yield different results in designing innovative first aid products. In this regard, the SCAMPER technique stands out as an attention-grabbing educational method. Publications related to the development of first aid equipment and kits are not common in the literature. This could be related to the economic and commercial aspects of this issue. The importance of health interventions performed until emergency medical assistance arrives has been highlighted many times. Although these applications focus more on basic life support, there is a need to attract researchers' interest in the topics of first aid and equipment. It is extremely important for school children to acquire the concept of first aid with this awareness for their future perspective. The fact that participants in the study expressed a greater demand for first aid training also indicates that there is a willing party for this, suggesting that this opportunity should not be missed. However, instilling this idea should not be limited to school age. In addition to the idea of facilitating access to

equipment for rescuers from the public, necessary steps should be taken to make basic first aid tools ergonomic and easy to use.

Study Limitations

This study was conducted with a relatively small number of students. Although studies with similar or even smaller sample sizes can be found in the literature, the fact that the study was conducted at only one center requires careful interpretation of the results in terms of generalizability. The study focused on the use of the SCAMPER technique in first aid training. Additionally, since the center where the study was conducted is a school that accepts talented students selected from many different schools, and the class and age distribution were not balanced, more detailed analyzes could not be performed for subgroups (especially by age level). Other reasons for the wide age range of participating students were that groups did not have to come to the center (attendance was optional) and that students came to the center on different days and at different times. This limitation was partially addressed through subgroup analysis, which showed that students in primary, middle, and high school benefited similarly from the SCAMPER technique. In addition, heterogeneity and limited sample size have led to limitations in the interpretation of the findings. However, the pre-test found generally similar levels of first aid knowledge for both groups. In some students, a higher level of awareness was observed, influenced by their families, personal interests, and education. To minimize comment errors, factors such as outliers during sampling and the presence of a healthcare worker in the family were considered exclusion criteria. We believe this can be considered a factor in reducing heterogeneity and contributing to the accurate interpretation of findings.

Another important limitation is that the 15-item questionnaire used in this study was developed by the authors. Although reviewed by field experts, no formal validity or reliability (psychometric) analysis was conducted on the survey. Therefore, the psychometric properties of the survey instrument have not been definitively established, which could affect the generalizability and robustness of the findings. In future studies, it is recommended to use measurement tools with proven validity and reliability and to conduct psychometric evaluations.

Conclusion

This study emphasizes the need of early first aid training with the SCAMPER technique for innovative equipment design and creative thinking. This age group has a poor level of first aid knowledge and awareness, and there is a need to improve this condition in order to strengthen the effectiveness of the emergency response system in their future lives as well as promote public health awareness and levels. However, the readiness of participating students to receive more first aid classes suggests that this group is receptive to a prospective early first aid training campaign, waiting for a chance, and eager to fill gaps in first aid knowledge. In this study, it was discovered that the SCAMPER technique is as effective as the traditional way in boosting first aid awareness and knowledge levels, as well as in developing a safe behavior model in emergency scenarios. This shows that incorporating this strategy into first aid training is appropriate. Furthermore, the SCAMPER technique, which is well-known for its benefits in brainstorming and interactive learning, can be applied in first aid training and equipment introduction to increase awareness of first aid kits. Furthermore, encouraging students to design first aid equipment and create creative goods in this field can emphasize the benefits of this training method, particularly in certain groups.

Ethics

Ethics Committee Approval: Permission was obtained from the KTO Karatay University Ethics Committee for Non-Pharmaceutical and Medical Device Research (desicion number 2024/015, date: 31.10.2024) for the research.

Informed Consent: Students' parents were informed with the help of the school administration and consent was obtained from the families.

Footnotes

Authorship Contributions

Concept: F.C.T., B.Y., Design: F.C.T., B.Y., Data Collection or Processing: F.C.T., B.Y., Analysis or Interpretation: F.C.T., Literature Search: F.C.T., Writing: F.C.T., B.Y.

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

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Artificial Intelligence Applications in Oral and Maxillofacial Surgery: A Bibliometric and Science Mapping Analysis of Global Research Trends (2000-2025)

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Abstract

Aim: To map the scientific landscape of artificial intelligence (AI) applications in oral and maxillofacial surgery (OMFS) over the last 25 years using bibliometric and science-mapping methods.

Materials and Methods: Publications related to AI and OMFS were retrieved from the Web of Science Core Collection. A comprehensive search was performed, and the complete set of 2153 records was exported. After restricting the timespan to 2000-2025 and limiting the document type to articles and reviews, 1955 documents were included. Bibliometric indicators were calculated, and science maps were generated in VOSviewer for co-authorship, co-occurrence, citation, and co-citation analyses.

Results: The annual number of publications increased markedly after 2015, with a steep rise from 2020 onwards and a peak of 275 publications in 2025. Overall, 1678 articles (87.8%) and 232 reviews (12.2%) were identified, totaling 38648 citations (mean 20.2 citations per document). The most productive journals were the Journal of Craniofacial Surgery, the Journal of Cranio-Maxillofacial Surgery, and the International Journal of Oral and Maxillofacial Surgery. Keyword co-occurrence analysis revealed major thematic clusters related to orthognathic surgery, mandibular reconstruction, computer-assisted surgery, virtual surgical planning, 3D printing, and deep learning.

Conclusion: AI research at the interface of OMFS has expanded rapidly between 2000 and 2025, particularly in AI-assisted surgical planning, anatomical segmentation for operative workflows, and computer-assisted surgery. These findings highlight how AI-supported technologies are increasingly being investigated for integration into contemporary clinical workflows in OMFS and provide guidance for clinicians regarding future implementation and validation priorities. In addition to clinical insights, these findings provide an overview of the AI research landscape in OMFS, offering guidance for future algorithm development, validation strategies, and interdisciplinary research directions.

Keywords: Artificial intelligence, bibliometric analysis, oral and maxillofacial surgery, science mapping, surgical planning

Introduction

Over the past 10 years, advances in machine learning and deep learning, along with the increased availability of digital surgical data, have driven growing interest in artificial intelligence (AI) in oral and maxillofacial surgery (OMFS). The growing importance of AI in OMFS has been highlighted by recent narrative and systematic studies, particularly in surgical planning, anatomical analysis, and clinical decision-making. (1-4).

Among the various clinical applications, orthognathic surgery has emerged as a key area for integrating digital and AI-assisted technologies. Virtual surgical planning, simulation, and patient-specific surgical guides have been widely investigated as tools to

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improve surgical accuracy and predictability (5-9). In parallel, deep learning–based methods have been introduced to automate tasks such as mandibular segmentation and identification of critical anatomical structures, which are essential components of contemporary OMFS workflows (10-14).

These methods enhance surgical planning and operative decision-making rather than relying solely on stand-alone radiological evaluations, even though they often rely on imaging-derived data. This differentiation highlights the essentially surgical focus of AI applications in OMFS and distinguishes them from studies in diagnostic imaging.

Several authors have discussed the broader implications of AI in dentistry and healthcare, in addition to procedure-specific studies. These contributions offer crucial conceptual and methodological frameworks for comprehending the creation, verification, and constraints of AI-based systems in clinical practice (16-18). More recently, OMFS-specific systematic reviews have synthesised evidence on AI applications across surgical subspecialties, highlighting the field's existing methodological shortcomings and potential advantages (19).

Despite the growing volume of literature, existing reviews primarily offer qualitative or application-focused perspectives and provide limited insight into publication trends, collaborative research structures, and the thematic evolution of AI-related OMFS research over time. Bibliometric and science mapping approaches are well-suited to address these gaps by quantitatively assessing research output, identifying influential contributors, and visualising emerging research themes.

Beyond its clinical relevance, systematically mapping the structure, evolution, and thematic focus of AI research in OMFS is essential to guide future algorithm development, foster interdisciplinary collaboration, and identify methodological gaps within the AI research landscape (16-18).

Therefore, the present study aimed to conduct a comprehensive bibliometric and science-mapping analysis of AI applications in OMFS published between 2000 and 2025.

Materials and Methods

Study Design

This study followed a bibliometric and science-mapping design and was conducted in accordance with reporting recommendations for bibliometric analyses. Because only published literature was analysed and no individual patient data were used, ethical approval was not required.

Data Source and Search Strategy

The Web of Science (WoS) Core Collection was chosen as the data source for its strict indexing guidelines and suitability for citation-based analysis. A thorough search was conducted to find articles on AI applications in OMFS. OMFS and dental imaging terms were merged with free-text terms pertaining to deep learning and AI in the search approach. Excluded were studies with a primary focus on dentomaxillofacial radiography that had no direct bearing on surgical planning, intervention, or results in OMFS. A representative Boolean query was:

Topic search= [("AI " or "deep learning" or "machine learning" or "neural network*" or "radiomics")] and ("oral and maxillofacial" or "maxillofacial surgery" or "orthognathic" or "mandibular reconstruction" or "dentofacial deformit*" or "dental implant*" or "cone-beam computed tomography" or " CBCT" or "panoramic radiograph*").

The initial search of the WoS Core Collection retrieved 2153 records with no restrictions. All records were exported in plain-text format with complete records and cited references.

Study Selection and Data Cleaning

In a first screening step, the timespan was restricted to publications from 1 January 2000 to 31 December 2025. Publication counts for 2025 reflect partial-year data, as records were retrieved on 9, 2025, before the calendar year ended. Only items indexed as "article" or "review" were retained; conference proceedings, editorial materials, letters, and corrections were excluded by using WoS document-type filters. After this restriction and the exclusion of records, 1955 documents remained and were included in the quantitative analyses.

To prepare the data for science-mapping analyses, author names, institutional affiliations, and keywords were cleaned and normalised. Variants of the same term (e.g., "computer-aided surgery" and "computer-assisted surgery") were merged, spelling errors were corrected, and singular and plural forms were unified where appropriate. Author keywords (DE field) and Keywords Plus (ID field) were combined to generate a unified keyword list. Data cleaning was performed using spreadsheet tools and custom scripts before importing the dataset into VOSviewer. Conceptually overlapping terms such as computer-aided surgery, computer-assisted surgery, and computer-aided design (CAD)/computer-aided manufacturing (CAM) were merged under unified keyword categories prior to frequency analysis. Imaging-related terms were included to ensure comprehensive retrieval of AI studies supporting surgical planning and workflows, while studies focusing solely on diagnostic radiology without surgical relevance were excluded during data cleaning. Following data

cleaning procedures and the application of predefined inclusion criteria, 1.955 publications were retained for bibliometric and science mapping analyses.

Bibliometric Indicators

Descriptive bibliometric indicators were calculated for the overall dataset, including the annual number of publications, document types, total and average citations per document, and productivity rankings for countries, institutions, authors, and journals. Citations were counted as of the WoS export date.

Statistical Analysis

Science-Mapping Analysis

Science maps were generated using VOSviewer (version 1.6.20; Centre for Science and Technology Studies, Leiden University, The Netherlands). Co-authorship analyses were performed at the author, institution, and country levels using complete counting. Co-occurrence analyses were conducted for author keywords; only keywords with a minimum of five occurrences in the dataset were included in the maps. Citation and co-citation analyses were carried out for journals and individual documents. Normalisation of similarities was based on the association strength method, and clusters were identified using VOSviewer's default clustering algorithm. Overlay visualisation was used to explore temporal trends, with node colour representing the average publication year of items.

Results

Descriptive Overview of the Dataset

A total of 1955 WoS-indexed documents on AI applications in OMFS were published between 2000 and 2025. Of these, 1720 (87.9%) were original research articles and 235 (12.1%) were review papers. The cumulative number of publications increased modestly in the early 2000s and then accelerated from approximately 2015 onwards, with a marked rise after 2020, peaking at 275 in 2025. (Figure 1) The total number of citations received by the included documents was 38648, corresponding to an average of 20.2 citations per document. Most publications were written in English (97.4%), with only a limited number published in other languages.

The country collaboration network is visualised in Figure 2, revealing dense collaborative clusters among high-output countries and indicating that international co-authorship plays a substantial role in advancing research on AI in OMFS.

Most Highly Cited Publications

Table 1 lists the 20 most highly cited documents in the dataset. These publications predominantly address 3D printing, computer-assisted and image-guided surgery, virtual surgical planning, and mandibular reconstruction, which together form the historical core of digital OMFS.

Most Productive Journals

The most productive journals in this field were Journal of Craniofacial Surgery (n=145), Journal of Cranio-Maxillofacial Surgery (n=138), International Journal of OMFS (n=123), and Journal of Oral and Maxillofacial Surgery (n=108). Several multidisciplinary and engineering journals, such as Applied Sciences and Scientific Reports, also contributed substantially to the literature, reflecting the interdisciplinary nature of AI research in OMFS. The 10 most productive journals publishing AI-related OMFS research are summarised in Table 2. The dominance of core OMFS journals highlights that AI-related research is being increasingly disseminated within speciality-specific surgical outlets rather than general radiology or engineering journals.

Keyword Co-occurrence

Author keywords and Keywords Plus were combined for co-occurrence analysis. Table 3 presents the 20 most frequent keywords in the dataset. Orthognathic surgery, computer-assisted surgery, AI and mandibular reconstruction were among the most common terms, together with virtual surgical planning and CAD/CAM. Imaging-related keywords such as CBCT appeared predominantly in the context of surgical planning, navigation, and outcome assessment in OMFS, rather than as stand-alone radiological applications. "Accuracy" was among the most frequently occurring keywords, particularly with respect to surgical outcome prediction and anatomical segmentation tasks in OMFS. The keyword co-occurrence network is presented in Figure 2, demonstrating several well-defined thematic clusters centred on AI applications in OMFS, including surgical planning, deep learning-based segmentation, and computer-assisted surgical workflows.

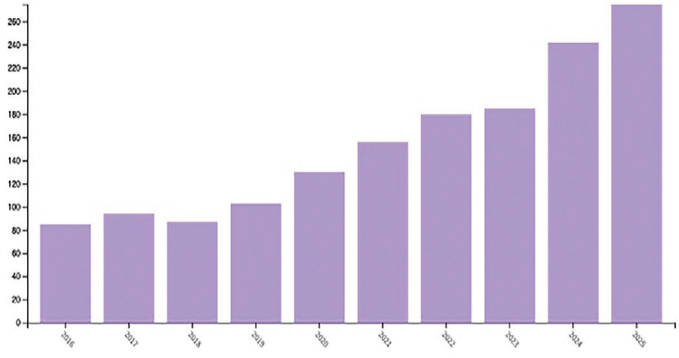

Figure 1. Annual publication trend (2000-2025) Data for the year 2025 represent a partial dataset collected up to December 9, 2025, and therefore do not reflect a complete calendar year

The overlay visualisation shown in Figure 3 illustrates the temporal evolution of research topics, indicating a shift from early computer-assisted surgical approaches toward a more recent emphasis on deep learning, virtual surgical planning, and data-driven decision-support systems in OMFS.

Geographical Distribution of Publications

The geographical distribution of publications revealed that research on AI in OMFS was dominated by a limited number of countries (Table 4). The People's Republic of China and the United States were the most productive countries, followed by Germany, Italy, and South Korea. Other major contributors included Japan, France, and the Netherlands, indicating strong research activity across East Asia and Western Europe. The country collaboration network is visualised in Figure 4, revealing dense collaborative clusters among high-output countries and indicating that international co-authorship plays a substantial role in advancing research on AI in OMFS.

Institutional Productivity

Institutional analysis demonstrated that a small number of academic and clinical centres accounted for a substantial proportion of the published literature (Table 5). Shanghai Jiao Tong University and Peking University emerged as the most productive institutions, followed by several major universities and university hospitals from East Asia, Europe, and North America. This distribution reflects the concentration of AI-related OMFS research within high-volume tertiary care and research-orientated institutions.

Author Productivity

Analysis of author productivity showed that a limited group of researchers contributed disproportionately to the literature (Table 6). Gellrich NC, Lo LJ, and Marchetti C were among the most productive authors, each contributing more than 20 publications. The remaining highly productive authors demonstrated comparable publication outputs, suggesting the

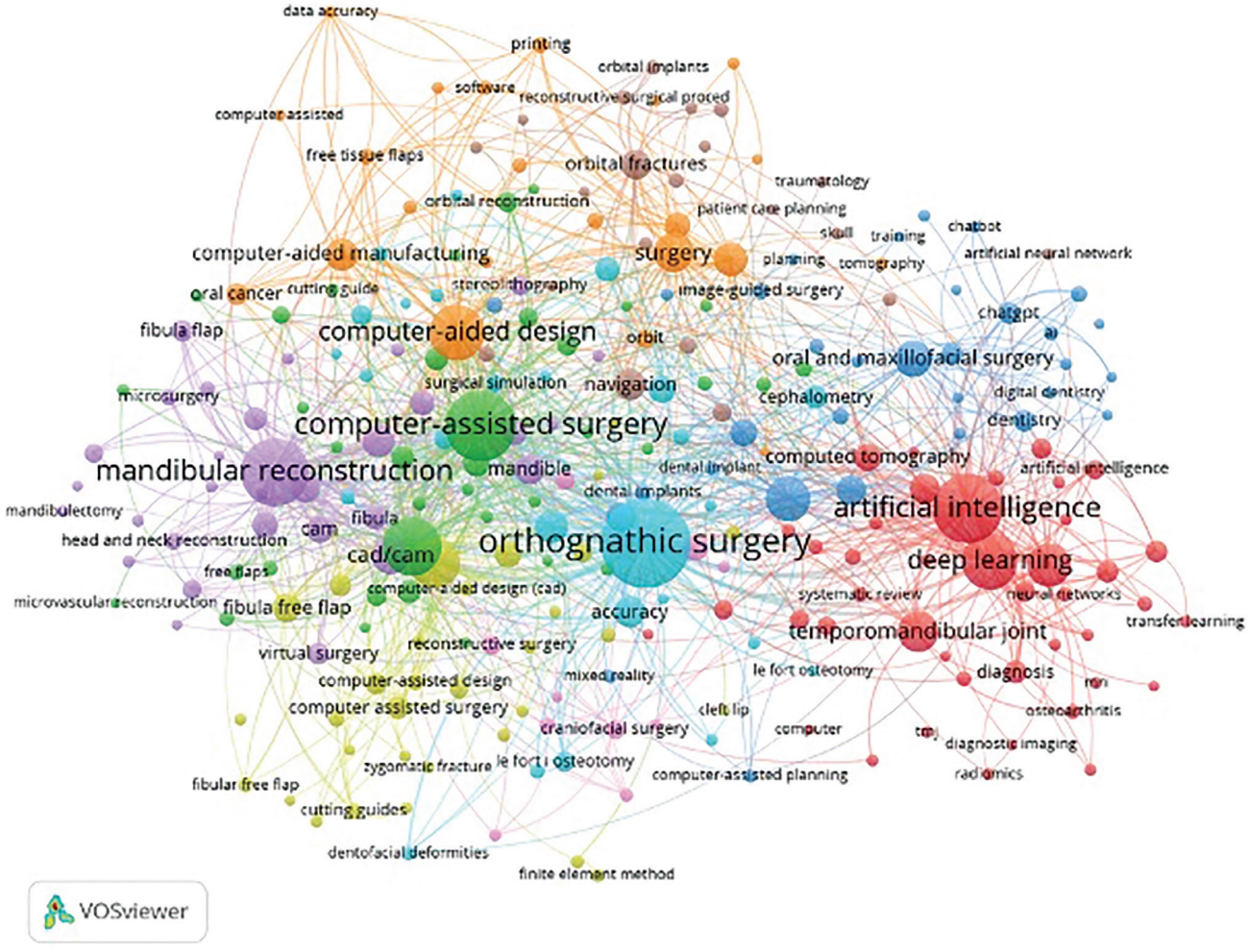

Figure 2. Keyword co-occurrence network generated using VOSviewer. Colours represent thematic clusters, and node size indicates the relative frequency of each keyword in the dataset

Table 1. The 20 most highly cited publications on artificial intelligence applications in oral and maxillofacial surgery (2025-2000)

Rank	First author	Year	Title	Journal	Document type	Citations
1	Tack, Philip	2016	3D-printing techniques in a medical setting: a systematic literature review	Biomedical Engineering Online	Review	738
2	Warnke, PH	2004	Growth and transplantation of a custom vascularised bone graft in a man	Lancet	Article	537
3	Martelli, Nicolas	2016	Advantages and disadvantages of 3-dimensional printing in surgery: a systematic review	Surgery	Review	460
4	Hsu, Sam Sheng-Pin	2013	Accuracy of a computer-aided surgical simulation protocol for orthognathic surgery: a prospective multicenter study	Journal of Oral and Maxillofacial Surgery	Article	321
5	Cohen, Adir	2009	Mandibular reconstruction using stereolithographic 3-dimensional printing modelling technology	Oral Surgery Oral Medicine Oral Pathology Oral Radiology and Endodontology	Article	281
6	Tian, Yueyi	2021	A review of 3D printing in dentistry: technologies, affecting factors, and applications	Scanning	Review	275
7	Hirsch, David L.	2009	Use of computer-aided design and computer-aided manufacturing to produce orthognathically ideal surgical outcomes: a paradigm shift in head and neck reconstruction	Journal of Oral and Maxillofacial Surgery	Article	267
8	Chae, Michael P.	2015	Emerging applications of bedside 3D printing in plastic surgery	Frontiers in Surgery	Review	257
9	Malik, Hammad H.	2015	Three-dimensional printing in surgery: a review of current surgical applications	Journal of Surgical Research	Review	250
10	Plooij, Joanneke M.	2011	Digital three-dimensional image fusion processes for planning and evaluating orthodontics and orthognathic surgery. A systematic review	International Journal of Oral and Maxillofacial Surgery	Review	221
11	Hoang, Don	2016	Surgical applications of three-dimensional printing: a review of the current literature & how to get started	Annals of Translational Medicine	Review	217
12	Hanasono, Matthew M.	2013	Computer-assisted design and rapid prototype modelling in microvascular mandible reconstruction	Laryngoscope	Article	215
13	Widmann, G	2006	Accuracy in computer-aided implant surgery - a review	International Journal of Oral & Maxillofacial Implants	Review	206
14	Block, Michael S.	2017	Implant placement accuracy using dynamic navigation	International Journal of Oral & Maxillofacial Implants	Article	206
15	Hassfeld, S	2001	Computer-assisted oral and maxillofacial surgery - a review and an assessment of technology	International Journal of Oral and Maxillofacial Surgery	Review	203
16	Ewers, R	2005	Basic research and 12 years of clinical experience in computer-assisted navigation technology: a review	International Journal of Oral and Maxillofacial Surgery	Review	201
17	Eggers, G.	2006	Image-to-patient registration techniques in head surgery	International Journal of Oral and Maxillofacial Surgery	Review	189
18	Stokbro, K.	2014	Virtual planning in orthognathic surgery	International Journal of Oral and Maxillofacial Surgery	Article	187
19	Plooij, J. M.	2009	Evaluation of reproducibility and reliability of 3D soft tissue analysis using 3D stereophotogrammetry	International Journal of Oral and Maxillofacial Surgery	Article	183
20	Antony, Anuja K.	2011	Use of virtual surgery and stereolithography-guided osteotomy for mandibular reconstruction with the free fibula	Plastic and Reconstructive Surgery	Article; Proceedings Paper	182

presence of several active research groups rather than a single dominant author.

Discussion

This bibliometric and science-mapping analysis demonstrates a steep and accelerating increase in AI-related publications in OMFS over the last 25 years. The surge in output after 2015 parallels the broader diffusion of deep learning frameworks and accessible GPU computing in medicine (1,3,15). Recent narrative reviews similarly emphasise that AI has transitioned from experimental proof-of-concept work to an integral component of digital OMFS workflows (1-4).

Geographical Distribution and International Collaboration

Analysis of publication output demonstrated that research activity related to AI in OMFS is concentrated in a limited number of countries. China emerged as the most prolific contributor, followed by several European countries, including Germany and Italy. Similar geographical patterns have been described

Table 2. The most productive journals publishing AI-related OMFS research (2025-2000)

Rank	Journal	Number of Documents
1	Journal of Craniofacial Surgery	145
2	Journal of Cranio-Maxillofacial Surgery	138
3	International Journal of Oral and Maxillofacial Surgery	123
4	Journal of Oral and Maxillofacial Surgery	108
5	Journal of Stomatology Oral and Maxillofacial Surgery	44
6	Journal of Clinical Medicine	43
7	British Journal of Oral & Maxillofacial Surgery	43
8	Applied Sciences-Basel	38
9	Scientific Reports	34
10	Plastic and Reconstructive Surgery	34

AI: Artificial intelligence, OMFS: Oral and maxillofacial surgery

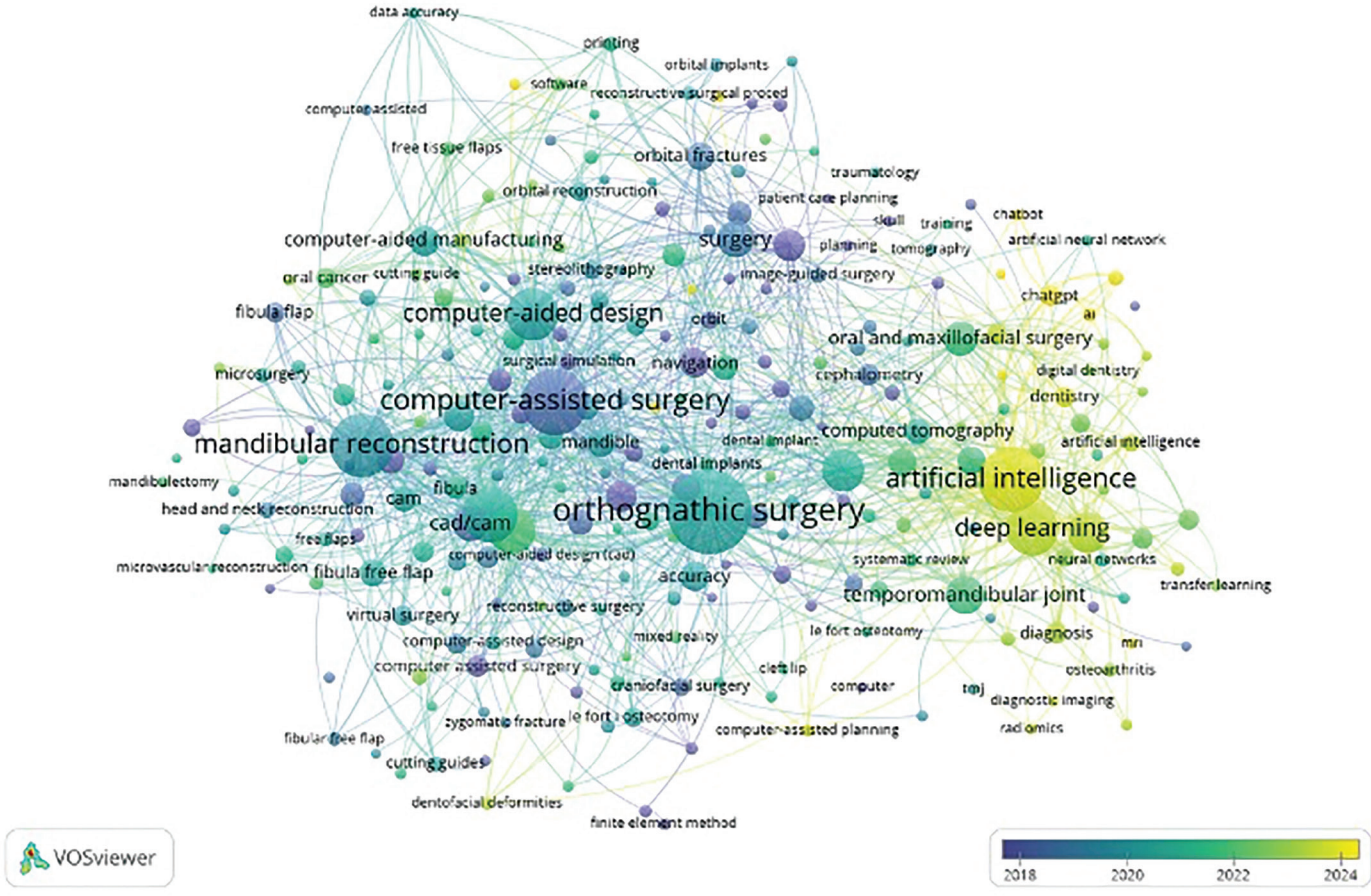

Figure 3. Overlay visualisation of keyword co-occurrence network. Colours indicate the average publication year of studies associated with each keyword, highlighting the shift toward deep learning and virtual surgical planning in recent years

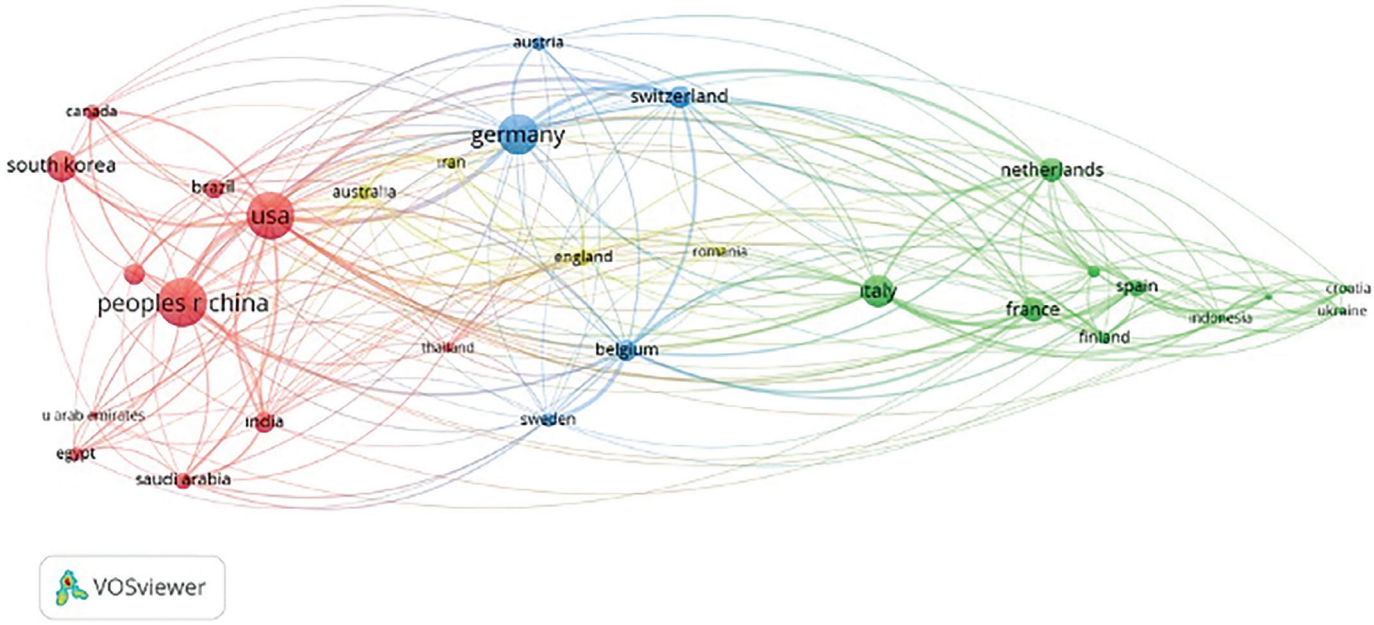

Figure 4. International collaboration network among countries, visualised using VOSviewer. Node size represents publication volume, and link strength reflects the intensity of international co-authorship connections

Table 3. Most frequent keywords related to artificial intelligence applications in oral and maxillofacial surgery

Rank	Keyword	Occurrences
1	Orthognathic surgery	318
2	Computer-assisted surgery	244
3	Computer-aided design/CAD/CAM	224
4	Artificial intelligence	186
5	Mandibular reconstruction	179
6	Virtual surgical planning	172
7	3D printing	126
8	Deep learning	124
9	Maxillofacial surgery	81
10	Surgical navigation	77
11	Machine learning	76
12	Temporomandibular joint	65
13	Accuracy	41
14	Cone-beam computed tomography	37
15	Mandible	36
16	Orbital fractures	36
17	Patient-specific implants	29
18	Facial asymmetry	29
19	Cephalometry	22
20	ChatGPT	20

CAD/CAM: Computer-aided design/computer-aided manufacturing

in previous reviews of AI applications in dentistry and surgical disciplines, where research productivity has been linked to early technological adoption, availability of large digital datasets, and targeted national research funding strategies (1,2,16). The country collaboration network further revealed dense collaborative clusters among high-output countries, suggesting that international co-authorship plays an important role in advancing AI-related OMFS research.

Institutional Productivity and Research Concentration

At the institutional level, AI-related OMFS research was primarily conducted within large academic centres and university-affiliated hospitals. This finding is consistent with observations in the broader healthcare AI literature, where access to advanced computational infrastructure, annotated datasets, and interdisciplinary expertise is often required to develop and validate AI-based systems (18). Systematic reviews focusing on OMFS have similarly noted that methodological innovation and clinical translation are frequently driven by specialised tertiary centres, which may limit the immediate applicability of AI tools in smaller clinical settings (19).

Author Productivity and Collaborative Research Groups

Author productivity analysis indicated that a relatively small group of researchers contributed a substantial proportion of publications in this field. Such authorship patterns are common in emerging research areas and typically reflect the presence of established research groups that function as focal points for

Table 4. The 10 most productive countries in AI-related OMFS publications (2025-2000).

Country	Number of publications	Percentage (%)
People's Republic of China	355	18.16
USA	344	17.60
Germany	252	12.89
Italy	157	8.03
South Korea	144	7.37
Japan	98	5.01
France	92	4.71
Switzerland	85	4.35
Netherlands	82	4.19
Belgium	70	3.58

AI: Artificial intelligence, OMFS: Oral and maxillofacial surgery

Table 5. Leading Institutions in AI-related OMFS Publications (2000-2025)

Rank	Institution	Publications	% of Total records
1	Shanghai Jiao Tong University	87	4.450%
2	Peking University	59	3.018%
3	Sichuan University	50	2.558%
4	Chang Gung Memorial Hospital	49	2.506%
5	Chang Gung University	44	2.251%
6	KU Leuven	40	2.046%
7	Seoul National University	38	1.944%
8	University of Hong Kong	37	1.893%
9	Harvard University	35	1.790%
10	University Hospital Leuven	35	1.790%

AI: Artificial intelligence, OMFS: Oral and maxillofacial surgery

Table 6. Most productive authors in AI-related OMFS publications (2000-2025)

Rank	Author	Publications	% of Total records
1	Gellrich NC	25	1.279%
2	Lo LJ	24	1.228%
3	Marchetti C	24	1.228%
4	Hölzle F	23	1.176%
5	Luo E	23	1.176%
6	Politis C	23	1.176%
7	Modabber A	22	1.125%
8	Schramm A	21	1.074%
9	Sun Y	21	1.074%
10	Lin HH	20	1.023%

AI: Artificial intelligence, OMFS: Oral and maxillofacial surgery

innovation and collaboration (19). Following manual author name disambiguation, no single author was found to dominate the literature overwhelmingly, suggesting that research on AI in OMFS is distributed across multiple active groups rather than centred around a single leading contributor. This distribution may facilitate methodological diversity and promote balanced scientific development within the field.

Thematic Evolution and Emerging Research Trends

Keyword co-occurrence and overlay analyses demonstrated a clear temporal shift in research focus over the study period. Early publications predominantly addressed computer-assisted surgery and basic image-processing techniques, whereas more recent studies increasingly emphasise deep learning, virtual surgical planning, and data-driven decision-support systems. Although not all 3D printing technologies are inherently AI-driven, their frequent integration within AI-supported digital surgical workflows justifies their inclusion in the present analysis. Comparable thematic transitions have been reported in reviews examining AI applications in implant dentistry and related digital workflows (20). Although several studies employed imaging-based data, these approaches were primarily integrated into surgical workflows rather than used as stand-alone radiological analyses, reinforcing the operative orientation of AI research in OMFS. The appearance of generative AI-related keywords, such as ChatGPT, reflects emerging interest in large language models (LLMs) for education, documentation, and decision-support tasks within OMFS. From a bibliometric perspective, the relatively low frequency of generative AI-related keywords compared with established surgical AI themes suggests that LLM-based applications remain an emerging and underrepresented research area within the OMFS literature. While AI has been extensively discussed in dentistry and broader clinical research with respect to its opportunities, limitations, and ethical challenges, the reflection of LLM-focused applications in OMFS publications remains limited. This discrepancy highlights a thematic gap between rapidly evolving AI methodologies and their current representation in OMFS-focused scientific literature, suggesting a potential direction for future research (16). From the perspective of AI research, current bibliometric analysis highlights several key trends and shortcomings. While deep learning-based approaches dominate recent literature, methodological heterogeneity, limited external validation, and reliance on retrospective single-center datasets remain prevalent. Mapping these patterns is essential to guide future AI model development efforts toward standardized evaluation frameworks, transparent reporting, and clinically robust validation strategies. Furthermore, the concentration of research activity in a limited number of

institutions underscores the need for broader interdisciplinary and multicenter collaboration to improve the generalizability of AI-based systems in OMFS (18,21).

Clinical Implications and Future Directions

From a clinical perspective, the observed trends suggest that AI is becoming increasingly embedded in routine OMFS workflows, particularly in orthognathic surgery, mandibular reconstruction, trauma management, and computer-assisted surgical planning. Despite this progress, existing literature remains dominated by retrospective designs and single-centre datasets, which may constrain external validity and real-world implementation (19). Future research efforts should therefore prioritise multicentre collaboration, standardised evaluation protocols, and prospective validation studies to support the safe and effective integration of AI technologies into everyday OMFS practice. From a clinical medicine perspective, the rapid growth of AI-supported OMFS research underscores the increasing integration of digital technologies into surgical decision-making, planning accuracy, and intraoperative guidance. Understanding these trends is essential for clinicians to critically evaluate emerging AI tools and support evidence-based adoption in daily practice.

AI applications supporting imaging-based components of OMFS workflows are dominated by deep learning-based segmentation and classification tasks. Layered convolutional networks have achieved expert-level performance for 3D segmentation of the mandible and other craniofacial structures on CBCT (10,11), and several comparative studies report clinically acceptable accuracy for mandibular canal or defect segmentation, with substantial reductions in manual workload (11,12,14,22).

Taken together, the existing literature suggests that AI has substantial potential to enhance diagnosis, planning precision, and intraoperative guidance in OMFS, but translation into routine clinical practice will depend on rigorous validation, standardisation of workflows, and careful consideration of ethical issues such as data privacy and algorithmic bias (1-4,15,21).

Study Limitations

A limitation of this study is that the bibliometric analysis was based solely on the WoS Core Collection, which may not capture all relevant publications indexed in other databases such as Scopus or PubMed. However, WoS was chosen for its standardized indexing criteria and widespread use in citation-based and science-mapping analyses.

Conclusion

Over the last 25 years, research at the interface of AI and OMFS has expanded rapidly, shifting from early work on stereolithography and navigation to deep learning-based image analysis and fully digital surgical workflows. The present bibliometric analysis shows that orthognathic surgery, mandibular reconstruction, virtual surgical planning, and computer-assisted surgery constitute the main thematic hubs, with deep learning and 3D printing emerging as key enabling technologies.

Although the existing literature demonstrates that AI has considerable potential to enhance diagnostic accuracy, planning precision, and workflow efficiency in OMFS, the evidence base remains dominated by retrospective, single-centre studies. To translate AI tools into routine clinical practice, future research should focus on multicentre prospective validation, rigorous reporting standards, and careful evaluation of clinical and patient-reported outcomes. The science-mapping results presented here can help researchers and clinicians identify influential contributions, recognise gaps in current knowledge, and prioritise high-impact avenues for future investigation.

Notably, the limited representation of ethics-related keywords in the bibliometric findings stands in contrast to the growing ethical complexity of AI applications in OMFS, including data confidentiality, algorithmic bias, and clinical accountability. This mismatch highlights a critical research gap and underscores the need for more explicit and systematic ethical discourse in future OMFS-focused AI research.

Ethics

Ethics Committee Approval: This study followed a bibliometric and science-mapping design and was conducted in accordance with reporting recommendations for bibliometric analyses.

Informed Consent: Only published literature was analysed and no individual patient data were used, ethical approval was not required.

Footnotes

Authorship Contributions

Concept: CG.T., M.K.H., M.Ü., N.A.G., O.Y., Ö.O.G., Design: CG.T., M.K.H., Data Collection or Processing: CG.T., M.K.H., N.A.G., O.Y., Ö.O.G., Analysis or Interpretation: CG.T., M.Ü., N.A.G., O.Y., Ö.O.G., Literature Search: CG.T., M.K.H., N.A.G., O.Y., Ö.O.G., Writing: CG.T., M.K.H., M.Ü.

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

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Pseudoephedrine and Acute Coronary Events: A Real-World Assessment in Acute Myocardial Infarction Patients

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Abstract

Aim: The decongestants are frequently prescribed for symptomatic relief to reduce mucosal congestion. However, even in the absence of overt cardiovascular symptoms, patients may subsequently present with serious acute cardiac events. The present study aims to assess the potential association between recent pseudoephedrine exposure and the occurrence of coronary vasospasm in patients presenting with acute myocardial infarction (AMI) to the emergency department, who reported the use of pseudoephedrine-containing products within the preceding week.

Materials and Methods: The study population included patients who presented with chest pain and were diagnosed with AMI [either ST-elevation myocardial infarction (STEMI) or non-STEMI]. The primary objective was to evaluate the history of pseudoephedrine use within the week preceding symptom onset.

Results: Among patients with a history of pseudoephedrine use, the 1-month incidence of major adverse cardiac events (MACE) was 13% (n=3), compared to 12.7% (n=21) in those without such a history. When comparing age, diagnosis, and MACE rates between patients with and without pseudoephedrine use, no statistically significant differences were observed. Regarding MACE subtypes, the most frequent event was death, occurring in 7.4% (n=14) of all patients. Heart failure was identified in 2.6% (n=5), while recurrent myocardial infarction was observed in 2.1% (n=4) patients.

Conclusion: Our findings suggest a clinically relevant association between recent pseudoephedrine use and acute cardiac events in vulnerable patients. This calls for increased awareness among clinicians, pharmacists, and the general public regarding the possible adverse outcomes associated with pseudoephedrine, even when used short-term or at therapeutic doses.

Keywords: Pseudoephedrine, major adverse cardiac events, acute myocardial infarction, percutaneous coronary intervention, emergency

Introduction

Over-the-counter (OTC) decongestants are commonly used worldwide for the symptomatic relief of upper respiratory tract infections, particularly to reduce mucosal congestion. These agents exert their effects through direct or indirect sympathomimetic activity, acting as agonists at both α- and β-adrenergic receptors. When administered orally (e.g., pseudoephedrine, phenylephrine) or intranasally (e.g., oxymetazoline, naphazoline, phenylephrine, ephedrine), they induce vasoconstriction of the nasal mucosa and reduce mucosal edema (1). However, their pharmacologic actions are not confined to the respiratory tract; systemic cardiovascular effects may also occur.

Cardiovascular adverse events, such as hypertension, tachyarrhythmias, and coronary vasospasms, have been documented, particularly in individuals with underlying ischemic heart disease, prompting regulatory restrictions on their use in several countries (2). Among these agents, pseudoephedrine has been particularly associated with serious complications, including

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coronary vasospasm and cerebrovascular events, such as stroke (3-5). These effects are pharmacodynamically consistent with the sympathomimetic profile of the drug. Nevertheless, no clear consensus has not been established, and such adverse outcomes have been reported regardless of patient age, dosage, or vascular health status (4-7). It is also important to consider that pre-existing endothelial dysfunction may serve as a predisposing factor for these events.

In routine clinical practice, especially in outpatient settings, these decongestants are frequently prescribed for symptomatic relief. However, even in the absence of overt cardiovascular symptoms, patients may subsequently present with serious acute cardiac events. Given these risks, it is imperative to re-evaluate the safety profile of pseudoephedrine-containing decongestants, particularly in patients with potential cardiovascular vulnerability.

The present study aims to explore the relationship between pseudoephedrine exposure and reversible coronary artery constriction that may contribute to myocardial ischemia in patients presenting to the emergency department (ED) with acute myocardial infarction (AMI) who reported using pseudoephedrine-containing products within the preceding week.

Materials and Methods

Study Design and Ethical Approval

This observational study was conducted from January 1 to June 30, 2024, in the ED of a tertiary-care hospital. The study population included patients who presented with chest pain and were diagnosed with AMI [either ST-elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI)]. The primary objective was to evaluate the history of pseudoephedrine use within the week preceding symptom onset. Approval was obtained from Manisa Celal Bayar University Ethics Committee prior to study initiation (approval number: E-20478486-050.04-756900, date: 03.04.2024). The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Study Population and Variables

During the study period, patients presenting to the ED with chest pain were triaged, monitored, and evaluated by electrocardiography (ECG). Necessary diagnostic tests and initial treatments were administered, and patients with suspected acute coronary syndrome were referred to the cardiology department. Among these, 189 patients were diagnosed with STEMI or NSTEMI and subsequently evaluated for a self-reported history of pseudoephedrine use within the previous seven days. Only patients aged 18 years or older who were conscious, cooperative, oriented, and willing to provide informed consent were included. Patients with myocardial injury secondary to conditions such as hemorrhagic shock or sepsis were excluded from the study.

Demographic data (age, sex, comorbidities), presenting complaints, ECG findings, vital signs at admission, history of pseudoephedrine use, emergency outcomes, cardiology department interventions, and the occurrence of major adverse cardiac events (MACE) within one month among pseudoephedrine-exposed individuals were systematically recorded using a standardized data collection form. MACE was defined as recurrent myocardial infarction, heart failure, ischemic stroke, or death.

Statistical Analysis

All statistical analyses were conducted using the Statistical Package for the Social Sciences, version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were employed to summarize the data, including frequencies and percentages for categorical variables and the mean, standard deviation (SD), median, and range (minimum-maximum) for continuous variables. The Kolmogorov-Smirnov test was used to assess the normality of continuous variables. For univariate analysis, normally distributed continuous variables were expressed as mean $\pm$ SD and compared using the independent samples t-test. Categorical variables were analyzed using the Pearson's chi-square test. A p value of less than 0.05 was considered indicative of statistical significance.

Results

A total of 189 patients diagnosed with AMI who presented to the ED with chest pain between January and June 2024 were included in the data analysis. The demographic characteristics, comorbidities, clinical presentations, and outcomes of all patients are summarized in Table 1.

The mean age of the study population was 60.88$\pm$13.82 years; the majority of participants were male (n=143, 75.7%). Among these patients, 57.1% (n=108) were diagnosed with NSTEMI. When patients' comorbidities were evaluated, the most common comorbidity was hypertension (53.4%), followed by ischemic heart disease (38.1%) and diabetes mellitus (34.9%). On admission, non-specific ECG changes were the most frequent finding, observed in 45% of cases. Of the 189 patients, 23 (12.2%) reported a history of pseudoephedrine use within the week preceding the onset of AMI symptoms. Among these 23 patients, 8 (34.8%) had a history of ischemic heart disease, 7 (30.4%) hypertension, and 7 (30.4%) diabetes mellitus (7).

Regarding ED outcomes, 87.8% of patients were admitted to the coronary intensive care unit for further monitoring and treatment. One patient died in the ED, while two patients refused further treatment and were discharged against medical advice.

Table 1. Demographic and clinical data of the patients

Age, years, mean ± SD	60.88±13.82	
Gender	Male Female	143 (75.7) 46 (24.3)
Comorbidities	Hypertension Ischemic heart disease Diabetes mellitus Heart failure COPD CKF Stroke Obesity	101 (53.4) 72 (38.1) 66 (34.9) 20 (10.6) 14 (7.4) 11 (5.8) 3 (1.6) 45 (23.8)
Major complaint	Chest pain Shortness of breath Epigastric pain Nausea-vomiting Palpitations Sweating Back pain Numbness in arms Weakness-malaise Syncope	147 (77.8) 15 (7.9) 10 (5.3) 5 (2.6) 3 (1.6) 3 (1.6) 2 (1.1) 2 (1.1) 1 (0.5) 1 (0.5)
Diagnosis	STEMI NSTEMI	81 (42.9) 108 (57.1)
Electrocardiography findings	ST segment elevation ST segment depression T wave inversion Non-specific	80 (42.3) 14 (7.4) 10 (5.3) 85 (45)
History of pseudoephedrine use	Yes No	23 (12.2) 166 (87.8)
Percutaneous coronary intervention	Yes No	171 (90.5) 17 (9)
Intervention type	Balloon-stent Medical follow-up By-pass	110 (58.2) 37 (19.6) 24 (12.7)
One-month MACE	Yes No	24 (12.7) 165 (87.3)

COPD: Chronic obstructive pulmonary disease, CKF: Chronic kidney disease, STEMI: ST-segment elevation myocardial ınfarction, NSTEMI: Non-ST-segment elevation myocardial ınfarction, MACE: Major adverse cardiovascular events, Data were presented as n (%) except age

Following diagnosis, 90.5% of patients (n=171) underwent percutaneous coronary intervention, and 58.2% (n=110) received balloon angioplasty and/or stent placement.

Among patients with a history of pseudoephedrine use, the one-month incidence of MACE was 13% (n=3), compared with 12.7% (n=21) among those without such a history. No statistically significant differences in age, diagnoses, and MACE rates were observed between patients with and without pseudoephedrine use (Table 2).

Regarding MACE subtypes, the most frequent event was death, occurring in 7.4% (n=14) of all patients. Heart failure was identified in 2.6% (n=5) of patients, while recurrent myocardial infarction was observed in 2.1% (n=4) of patients.

Discussion

This study provides valuable insights into the potential cardiovascular risks of pseudoephedrine use, especially in populations with underlying vulnerabilities. Pseudoephedrine, a sympathomimetic agent commonly included in OTC cold and allergy medications, is frequently perceived as benign due to its widespread availability and symptomatic efficacy. However, our findings highlight that a non-negligible proportion (12.2%) of patients presenting with AMI had used pseudoephedrine within the preceding week, underscoring the importance of reevaluating the cardiovascular safety of pseudoephedrine in susceptible individuals.

Although no statistically significant association was identified between pseudoephedrine use and the incidence of coronary vasospasm in AMI patients, this observation must be interpreted with caution due to the limited sample size. Importantly, a considerable proportion of patients exposed to pseudoephedrine had pre-existing cardiovascular comorbidities: 34.8% had ischemic heart disease, 30.4% had hypertension, and 30.4% had diabetes mellitus. These conditions are well-known contributors to endothelial dysfunction, which plays a critical role in the pathogenesis of vasospasm and thrombosis, particularly in the presence of vasoconstrictive agents such as pseudoephedrine (8,9). Although definitive causality cannot be determined from

Table 2. Comparison of patients with and without a history of pseudoephedrine use

History of pseudoephedrine use	**Yes (n=23)**	**No (n=166)**	**p value**
Age, years, mean ± SD	58.52±18.04	61.20±13.17	0.384
Diagnosis (n, %) STEMI NSTEMI	 8 (34.8) 15 (65.2)	 73 (44) 93 (56)	0.404
1-month MACE, n (%) Pozitive Negative	 3 (13) 20 (87)	 21 (12.7%) 145 (87.3%)	0.958

SD: Standard deviation STEMI: ST-segment elevation myocardial ınfarction, NSTEMI: Non-ST-segment elevation myocardial ınfarction, MACE: Major adverse cardiovascular events

our cross-sectional design, the data suggest that pseudoephedrine may precipitate ischemic events in predisposed individuals.

One of the most compelling aspects of our findings is the continued use of pseudoephedrine despite advanced age and significant cardiovascular comorbidities patient profiles for which regulatory bodies such as the Food and Drug Administration and European Medicines Agency have issued cautionary guidelines (10). This points to a concerning gap in clinical awareness and risk stratification regarding the systemic effects of pseudoephedrine, particularly in emergency and primary care settings where comprehensive medication histories may not always be obtained. Easy access to pseudoephedrine-containing products exacerbates this risk, particularly among individuals who self-medicate without consulting healthcare professionals.

While establishing a causal link between pseudoephedrine use and AMI through long-term prospective studies is methodologically complex, the real-world data presented here provide a compelling signal. In particular, our findings align with prior literature and case reports suggesting that pseudoephedrine can induce coronary vasospasm, arrhythmias, and cerebrovascular events via sympathomimetic mechanisms (11,12). In our study, pseudoephedrine users frequently exhibited non-specific electrocardiographic changes, such as ST-segment alterations, which may reflect transient myocardial ischemia or vasospastic phenomena. Although we did not evaluate QT intervals or utilize ambulatory electrocardiographic monitoring, this absence underscores a broader gap in the assessment of the cardiovascular effects of OTC medications in clinical practice and highlights the need for more comprehensive monitoring in future studies.

Furthermore, the 1-month rate of MACE was comparable between pseudoephedrine users (13%) and non-users (12.7%). However, the presence of serious outcomes including death among recently exposed individuals is clinically significant and warrants attention. These findings support the hypothesis that pseudoephedrine may not act as a direct etiological factor but rather as a physiological stressor capable of triggering cardiovascular events in patients with preexisting endothelial vulnerability or atherosclerotic disease.

In addition to cardiovascular concerns, pseudoephedrine's potential neurotoxicity must be considered. Although our study primarily focused on cardiac outcomes, it is worth noting that the mean age of the cohort was 60 years. Elderly individuals are particularly vulnerable to the systemic effects of sympathomimetics. Pseudoephedrine has been associated with central nervous system depression, seizures, and even fatal outcomes, especially in patients with pre-existing neurological conditions (7,13). A notable case report describes an 83-year-old woman who developed prolonged seizures after ingesting 120 mg of pseudoephedrine; her symptoms persisted for three months (14). These findings underscore the need for heightened vigilance when prescribing or recommending OTC medications in geriatric populations.

Study Limitations

Our study has several limitations, most notably its single-center design and relatively small sample size, which may limit generalizability. In addition, the absence of data on patients' baseline vital signs, vascular health, renal and hepatic function, as well as detailed information on pseudoephedrine dosage, frequency, and route of administration introduces further uncertainty. Furthermore, the relatively small number of patients reporting pseudoephedrine use and the absence of detailed dosage information limit the strength of the conclusions. Additionally, given the lack of statistically significant differences, the findings should be interpreted with caution and not be considered evidence of a causal relationship.

Conclusion

Pseudoephedrine remains a widely used agent for symptomatic relief in conditions such as the common cold and allergic rhinitis. However, its systemic sympathomimetic effects particularly in elderly individuals and those with cardiovascular or neurological comorbidities carry potential risks that are frequently underrecognized. Although not statistically significant, our findings suggest a clinically relevant association between recent pseudoephedrine use and acute cardiac events among vulnerable patients. This calls for increased awareness among clinicians, pharmacists, and the general public of the possible adverse outcomes associated with pseudoephedrine, even when used in the short term or at therapeutic doses. Patient education, enhanced pharmacovigilance, and more stringent regulatory oversight may be warranted to mitigate these risks. Particularly in high-risk populations, medication histories should be carefully evaluated before initiating even seemingly benign symptomatic therapies.

Ethics

Ethics Committee Approval: Approval was obtained from Manisa Celal Bayar University Ethics Committee prior to study initiation (approval number: E-20478486-050.04-756900, date: 03.04.2024). The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Informed Consent: Only patients aged 18 years or older who were conscious, cooperative, oriented, and willing to provide informed consent were included.

Footnotes

Authorship Contributions

Surgical and Medical Practices: C.Y., M.İ.Ş., Concept: C.Y., M.İ.Ş., A.A., Design: M.İ.Ş., M.U., Data Collection or Processing: C.Y., Analysis or Interpretation: C.Y., M.İ.Ş., Ö.B., A.A., Literature Search: C.Y., Ö.B., A.A., Writing: C.Y., M.İ.Ş., M.U.

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Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request

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