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ORIGINAL RESEARCHES

ORIGINAL RESEARCH

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The Effectiveness of the İzmir March Rhythm Compared to the International Musical Metronome ("Stayin' Alive") in Cardiopulmonary Resuscitation (CPR) Training for Military Personnel: A Randomized Controlled Crossover Pilot Study

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Abstract

Objective: Maintaining the correct chest compression rate is a critical challenge in cardiopulmonary resuscitation (CPR). Although musical metronomes such as "Stayin' Alive" are widely used, their effectiveness may vary across cultural contexts. This pilot study evaluated whether a culturally relevant Turkish military march, The İzmir March, could serve as an alternative pacing aid for compression-only CPR training in military personnel and described within-cohort retention of the compression rate at 6 weeks.

Materials and Methods: We conducted a randomized controlled crossover pilot study involving 20 male military personnel without prior healthcare training. Participants were randomized to receive initial training paced by either the Izmir March (Group M, n=10) or "Stayin' Alive" (Group S, n=10). CPR performance was recorded using a QCPR manikin at baseline, during music-paced sessions (trained and untrained after a 1-day washout crossover), and at a 6-week music-free follow-up. Paired t-tests and Wilcoxon signed-rank tests with Bonferroni correction were performed.

Results: At 6 weeks, 70% of participants (14/20) maintained a compression rate within the target range of 100–120/min. The Izmir March group achieved a higher mean compression rate than the Stayin' Alive group (114.8±5.3 vs. 105.5±6.1 compressions/min; p<0.001). However, the Stayin' Alive group achieved a higher proportion of compressions within the optimal 100–120/min range (adequate rate: 86.3% vs. 79.3%). No carryover effects were observed between conditions.

Conclusion: In this military cohort, within-cohort compression rates moved closer to the recommended target range of 100–120/min at 6 weeks compared with baseline. The Izmir March (115 BPM) yielded a higher mean compression rate than "Stayin' Alive" (103 BPM), although this between-song difference is heavily confounded by beat frequency. The findings should be interpreted as differences between two music-based pacing strategies rather than as evidence that music-assisted training improves retention compared with standard training. Further trials with non-music controls are needed to evaluate the Izmir March as a culturally familiar pacing aid.

Keywords: Cardiopulmonary resuscitation; compression rate; crossover design; military personnel; music; skill retention.

Introduction

Sudden cardiac arrest remains a major cause of mortality worldwide, and survival is critically dependent on the immediate delivery of high-quality cardiopulmonary resuscitation (CPR). A cornerstone of effective CPR is maintaining chest compressions at a rate of 100–120 per minute and at an adequate depth [1]. However, rescuers, particularly novices, often find it difficult to sustain this target rate, leading to a gradual deviation from the target over time, a phenomenon known as "rate drift" [3].

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To mitigate this challenge, auditory metronomes and feedback devices have been integrated into CPR training [4]. The Bee Gees' song "Stayin' Alive," with a tempo of approximately 103 beats per minute (BPM), has gained international recognition as a musical metronome for CPR, and its utility has been documented in simulation studies [2,5]. Several studies suggest that music-assisted training can enhance CPR pacing and skill retention compared with no-music or metronome-only conditions [6–8].

This study focused on CPR training and skill retention in a military context. Military personnel are uniquely conditioned to synchronize their movements with rhythmic marches during training and official duties, which may enhance their performance in physically demanding tasks [9]. Furthermore, cultural and native-language familiarity with music has been associated with stronger motor synchronization compared with unfamiliar music in a randomized crossover trial of culture-specific popular songs for CPR pacing [10]. The Izmir March, a well-known and integral part of the Turkish military tradition, was identified as a candidate that could leverage this principle. Its national and military significance may enhance soldiers' motivation and rhythmic synchronization.

Although culture-specific popular music has been examined as a CPR pacing aid in civilian populations [10], its application in military personnel using a national military march has not, to our knowledge, been previously studied. This pilot study evaluated the Izmir March, a Turkish military anthem, as a musical metronome during compression-only CPR training in military personnel. The primary aim was to assess within-cohort retention of the compression rate within the 100–120/min target range at 6 weeks. The secondary aim was to compare CPR quality metrics between the Izmir March and "Stayin' Alive" on Day 0. We acknowledge a priori that the Izmir March (approximately 115 BPM) and "Stayin' Alive" (approximately 103 BPM) differ in beat frequency and that observed differences in compression rate will partly reflect this tempo difference rather than cultural or motivational factors alone.

Our primary hypothesis was that, within this military cohort, post-training compression rates at 6 weeks would lie within the target range in at least 70% of participants. Our secondary hypothesis was that the Izmir March would not be inferior to "Stayin' Alive" in achieving compression rates within the 100–120/min target range. Because no non-music control group was included, the present study cannot establish that music-assisted training is superior to standard CPR training without music; it can only compare two music-based pacing strategies and describe post-training retention within this cohort.

Materials and Methods

Study Design and Participants

This was a randomized, controlled, single-center, crossover pilot study. The study population consisted of 20 male volunteer military personnel aged 18–45 years who had not received CPR training within the previous 5 years and had no physical limitations that would impede their ability to perform CPR. Individuals with prior healthcare training were excluded. Of 22 individuals assessed for eligibility, 2 were excluded prior to randomization (1 declined participation; 1 did not meet the inclusion criteria), leaving 20 participants for randomization. The study protocol was approved by the Van Training and Research Hospital Ethics Committee (Decision No. GOKAEK/2025-08-04; Date: 24.10.2025), and all participants provided written informed consent prior to enrollment. The flow of participants through the study is shown in Figure 1.

Randomization and Allocation

Sequentially numbered participants were allocated 1:1 to Group M (Izmir March, n=10) or Group S ("Stayin' Alive," n=10) using a web-based random number generator (Research Randomizer; https://www.randomizer.org/) operated by the principal investigator. Formal allocation concealment using sealed, opaque envelopes prepared by an independent third party was not implemented; this is acknowledged as a limitation. Given the nature of the intervention, blinding of participants was not feasible; however, all CPR performance data were captured automatically by the QCPR software, eliminating subjectivity from the primary outcome measurement. All participants first received standardized compression-only CPR instruction consistent with the 2025 AHA Guidelines for CPR and ECC [1], after which each group practiced using their assigned music.

Music Selection

The military march selected for this study was based on CPR suitability criteria, including a steady tempo (minimal tempo variation), clear beats, and a tempo within the AHA-recommended range of 100–120 beats/min (BPM). Various marches that met these criteria, such as the Harbiye March (118 BPM), Ceddin Deden (108–112 BPM), and the Izmir March (115–120 BPM), were evaluated, and a 115 BPM version of the Izmir March was selected for the study.

The specific Izmir March recording used in this study was a vocal version with original Turkish lyrics, with the tempo confirmed at 115 BPM (source recording publicly available at https://www.youtube.com/watch?v=khabhCrXHvU). For "Stayin' Alive," the original 1977 Bee Gees vocal recording (approximately 103 BPM)

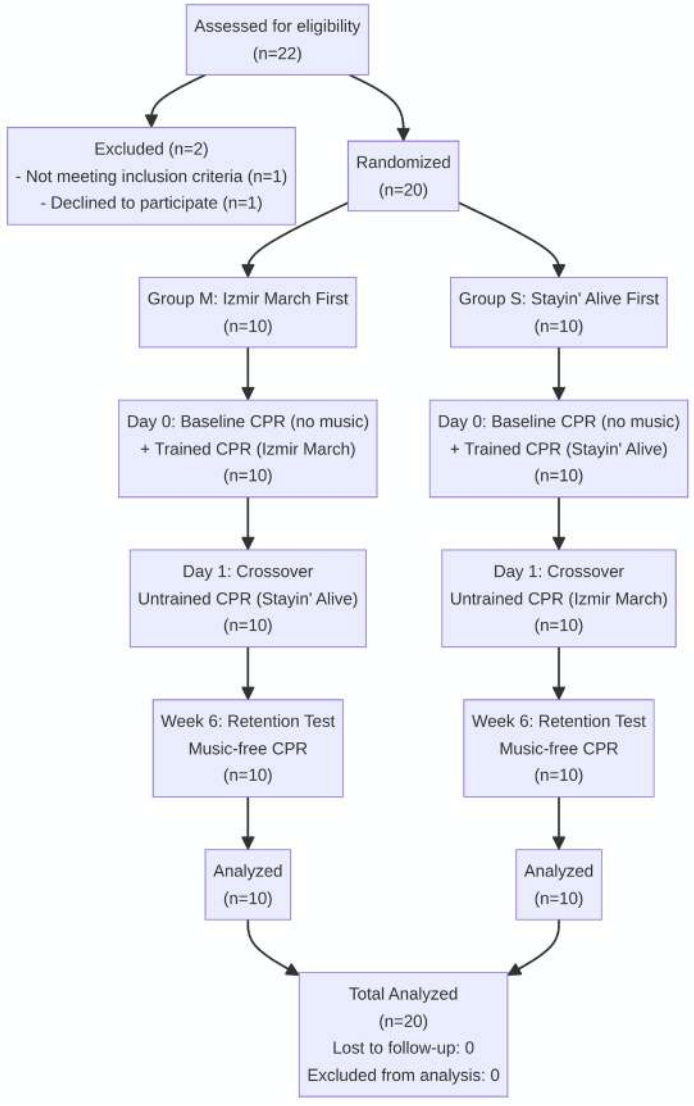

Figure 1. CONSORT flow diagram of the study. Group M: Izmir March group; Group S: Stayin' Alive group.

was used. A 2-minute clip from each recording was prepared and used uniformly across all training and testing sessions. The exact audio clips used in this study are archived and available from the corresponding author upon reasonable request.

CPR Format and Test Environment

All CPR sessions were performed as continuous compression-only CPR, without rescue breaths, in accordance with compression-only protocols suitable for non-healthcare lay rescuers. The Laerdal Little Anne QCPR manikin was placed on a flat, firm floor surface in a quiet training room. Music was delivered via a standard stereo speaker at a fixed volume (approximately 70 dB at the participant's position) rather than through personal headphones, replicating realistic group training conditions. Participants were instructed to begin chest compressions synchronously with the first audible beat of the assigned music clip and to maintain the music's rhythm throughout the 2-minute session. The same operator timed all sessions and ensured uniform clip onset.

Measurement Protocol

The data collection process was conducted in three stages:

Day 0 (Training and Initial Measurement): Participants first performed 2 min of compression-only CPR without music (baseline). Following this, they performed 2 min of CPR under the "trained" condition with their assigned music.

Day 1 (Crossover): After a 1-day washout period, participants performed 2 min of CPR under the "untrained" condition using the alternate music selection. A 1-day washout was deemed sufficient to minimize potential carryover effects from the previous day's music, consistent with similar crossover studies [10].

Week 6 (Skill Retention): To assess skill retention, participants performed 2 min of compression-only CPR without musical guidance 6 weeks after the initial training.

All CPR performance data were recorded using a Laerdal Little Anne QCPR manikin (Little Anne Mk1 platform) and the associated Laerdal QCPR application (Laerdal Medical, Stavanger, Norway). The manikin was calibrated to the standard AHA settings, with a target compression depth of 50–60 mm. Before and after each CPR session, participants' pulse and peripheral oxygen saturation (SpO_2) were measured. After each session, perceived exertion was assessed using the Borg Rating of Perceived Exertion (RPE) scale (6–20), and muscle fatigue was rated using a visual analog scale (VAS) (0–10). Additionally, satisfaction with the training, perceived ease of maintaining the compression rate, and overall confidence in performing CPR were evaluated using a 5-point Likert scale.

Endpoints

Primary Endpoint: The primary endpoint was the successful maintenance of a mean compression rate within the 100–120/min target range during the music-free CPR assessment at 6 weeks post-training. Success was defined a priori as at least 70% of participants achieving the target, representing a pragmatic feasibility benchmark in which the majority of trainees retained target-range performance after a single training session. Higher thresholds (e.g., 80–90%) would likely require booster or repeated training sessions, which were beyond the scope of this pilot study.

Secondary endpoints included comparisons of CPR quality metrics (e.g., rate, depth, and overall score) between the Izmir March and "Stayin' Alive" conditions on Day 0, performance differences

between the trained and untrained conditions, and changes in subjective scores (Borg RPE and VAS) and physiological measures (pulse and SpO_2) across all conditions.

Sample Size Rationale

As an external pilot feasibility study, this trial was not powered for definitive between-group inference. The sample size of n=20 (10 per group) follows established pilot study recommendations. These recommendations suggest that 10–15 participants per arm are adequate for estimating key parameters, such as standard deviations, recruitment feasibility, and retention rates, to inform a future definitive trial powered for a small-to-medium standardized effect [11,12]. The chosen sample size was also constrained by the availability of an eligible military cohort and the practical feasibility of completing the 6-week retention assessment within a single training cycle. Reporting follows the CONSORT 2010 extension for randomized pilot and feasibility trials [16].

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics software (version 26.0; IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was used to assess the normality of data distributions. For normally distributed data, paired-samples t-tests were used, whereas the nonparametric equivalent, the Wilcoxon signed-rank test, was applied to non-normally distributed data. To control for Type I errors arising from multiple comparisons, a Bonferroni correction was applied across the eight primary comparisons, setting the threshold for statistical significance at $p<0.0063$. Effect sizes were calculated using Cohen's d. Ninety-five percent confidence intervals (CIs) are reported for primary outcome comparisons.

Results

All 20 participants enrolled in the study completed every stage of the study (Fig. 1). The demographic characteristics and baseline CPR performance were comparable between the two groups, with no statistically significant differences observed in age, anthropometric measurements, or initial CPR metrics ($p>0.05$ for all; Tables 1 and 2).

Primary Endpoint: Skill Retention

During the music-free evaluation at 6 weeks, 70% (14/20) of participants successfully maintained a compression rate within the 100–120/min target range. The mean compression rate at 6 weeks (111.0±9.5 comp/min) was significantly lower than the baseline rate (121.6±14.1 comp/min), moving closer to the recommended range (mean difference: 10.7 comp/min; 95% CI [4.0, 17.3]; $p=0.003$; Cohen's $d=0.89$). The proportion of compressions delivered within the target range also increased from 43.5% at baseline to 66.8% at 6 weeks, although this change did not reach statistical significance after Bonferroni correction ($p=0.015$). The results are presented in Table 5.

Secondary Endpoints

Comparison of Music Types: On Day 0, the mean compression rate achieved with the Izmir March (114.8±5.3 comp/min) was significantly higher than that achieved with "Stayin' Alive" (105.5±6.1 comp/min), with a mean difference of 9.3 comp/min (95% CI [6.1, 12.5]; $p<0.001$; Cohen's $d=1.63$). No significant difference in compression depth was observed between the two types of music ($p>0.05$). Although the Izmir March produced a higher mean compression rate that remained within the target range, the "Stayin' Alive" group achieved a higher proportion of compressions within the optimal 100–120/min range (adequate rate: 86.3% vs. 79.3%; $p<0.001$; Cohen's $d=0.25$), as well as nonsignificantly higher percentages of correct chest release and overall quality scores. This pattern suggests that lower-tempo music may provide a wider "safety margin" against rate drift toward the upper limit, whereas higher-tempo music produces faster but more variable rates. The findings are presented in Table 4.

Crossover and Subjective Effects: No significant carryover effect was detected, as CPR performance metrics did not differ between the trained and untrained music conditions ($p>0.05$; Table 3). Participants' subjective ratings of exertion (Borg RPE) and

Table 1. Demographic characteristics of participants

Characteristic	Group M (n=10)	Group S (n=10)	Total (n=20)	p
Age (years), mean±SD	21.5±1.5	21.2±1.3	21.4±1.4	0.62
Height (cm), mean±SD	175.4±5.2	176.1±4.8	175.8±4.9	0.75
Weight (kg), mean±SD	72.1±8.5	73.5±7.9	72.8±8.1	0.68
Arm Circumference (cm), mean±SD	30.5±2.1	30.8±2.3	30.7±2.2	0.79
Regular Exercise, n (%)	5 (50%)	4 (40%)	9 (45%)	0.69
Smoking, n (%)	6 (60%)	5 (50%)	11 (55%)	0.69

Group M: Izmir March group; Group S: Stayin' Alive group; SD: Standard deviation

Table 2. Baseline CPR performance

Metric	Group M (n=10)	Group S (n=10)	Total (n=20)	p
Compression Rate (comp/min) mean±SD	122.1±15.2	121.1±13.5	121.6±14.1	0.85
Adequate Rate (%) mean±SD	45.2±35.1	41.8±38.2	43.5±36.0	0.84
Compression Depth (mm) mean±SD	75.1±6.2	76.5±5.8	75.8±5.9	0.59
Correct Release (%) mean±SD	75.2±30.1	72.8±32.5	74.0±30.8	0.86
Total Score	65.2±10.1	66.8±9.5	66.0±9.7	0.68

CPR: Cardiopulmonary Resuscitation; comp/min: Compressions per minute; SD: Standard deviation

Table 3. Crossover effect (trained vs. untrained)

Metric	Trained (n=20)	Untrained (n=20)	p
Compression Rate (comp/min) mean±SD	109.3±8.3	111.0±5.9	0.52
Compression Depth (mm) mean±SD	77.5±5.1	77.3±5.3	0.89
Total Score	70.5±8.1	70.0±8.5	0.78

Trained: CPR performed with the music type the participant was initially trained with; Untrained: CPR performed with the other music type

fatigue (VAS) were also similar across all conditions (Table 6), as were physiological responses (Table 7). Participants reported high levels of satisfaction with the training and confidence in their ability to perform CPR, with no significant differences between the music groups (Table 8).

Table 4. Comparison of music types (Day 0)

Metric	Izmir March (n=10)	Stayin' Alive (n=10)	p
Compression Rate (comp/min) mean±SD	114.8±5.3	105.5±6.1	<0.001*
Compression Depth (mm) mean±SD	77.0±5.5	77.8±4.8	0.68
Adequate Rate (%) mean±SD	79.3±31.1	86.3±24.9	<0.001*
Correct Release (%) mean±SD	68.0±41.1	89.2±24.7	0.15
Total Score	68.7±9.5	71.8±7.6	0.23

*Statistically significant after Bonferroni correction (p<0.0063). Effect sizes: Compression Rate (Izmir March vs. Stayin' Alive), Cohen's d=1.63, mean difference 9.3 comp/min, 95% CI [6.1, 12.5]; Adequate Rate, Cohen's d=0.25. comp/min: Compressions per minute; SD: Standard deviation; CI: Confidence interval

Table 5. Skill retention (6-week follow-up)

Metric	Baseline (n=20)	6-Week (n=20)	p
Compression Rate (comp/min) mean±SD	121.6±14.1	111.0±9.5	0.003*
Adequate Rate (%) mean±SD	43.5±36.0	66.8±35.1	0.015
Compression Depth (mm) mean±SD	75.8±5.9	76.5±5.5	0.59
Total Score	66.0±9.7	68.5±8.9	0.18

*Statistically significant after Bonferroni correction (p<0.0063). Effect size for the primary outcome (Compression Rate, baseline vs. 6-week): Cohen's d=0.89, mean difference 10.7 comp/min, 95% CI [4.0, 17.3]. comp/min: compressions per minute; SD: Standard deviation; CI: Confidence interval

Table 6. Subjective measurements (VAS and Borg RPE)

Measurement	Baseline	March	Stayin' Alive	6-Week
VAS (0–10), mean±SD	6.7±0.7	5.8±0.8	6.5±0.5	6.5±0.6
Borg RPE (6–20), mean±SD	11.7±1.3	10.9±0.8	11.2±1.0	11.3±1.0

VAS: Visual Analogue Scale; RPE: Rating of Perceived Exertion; SD: Standard Deviation

Table 7. Physiological responses (pulse and saturation)

Measurement	Baseline	March	Stayin' Alive	6-Week
Pulse Change (bpm), mean±SD	38.5±9.5	37.0±10.1	40.0±7.8	38.2±9.1
SpO_2 Change (%), mean±SD	-0.5±0.8	-0.4±0.7	-0.6±0.9	-0.5±0.8

bpm: Beats per minute; SpO_2: Peripheral oxygen saturation; SD: Standard deviation

Table 8. Training satisfaction and self-confidence			
Measurement	**Mean±SD**	**5-Point (%)**	**4-Point (%)**
Training Satisfaction	4.75±0.43	75%	25%
Ease of Rate Maintenance	4.80±0.40	80%	20%
Overall CPR Confidence	4.85±0.36	85%	15%
Likert scale (1–5): 1=Not at all satisfied/Very difficult/Not at all confident, 5=Very satisfied/Very easy/Very confident			

Discussion

This randomized controlled crossover pilot study describes post-training compression-rate retention in a military cohort and compares two music-based pacing strategies. Participants paced with the Izmir March (115 BPM) achieved higher mean compression rates than those paced with "Stayin' Alive" (103 BPM). Because we did not include a non-music control group, we cannot conclude whether music-assisted training outperforms standard training. We therefore report these findings as a comparison of two pacing strategies rather than as evidence of a music-versus-no-music effect on retention.

In this cohort, both music conditions maintained mean compression rates within the AHA-recommended target range of 100–120/min. The Izmir March, a culturally significant Turkish military anthem, produced rates closer to the upper end of this range, whereas "Stayin' Alive" produced rates closer to the lower end. The faster compression rate observed with the Izmir March (114.8 comp/min) is largely explained by its inherent tempo (115 BPM). However, subjective effort ratings (VAS) were slightly lower with the Izmir March despite its faster tempo, suggesting a possible additional contribution from cultural or motivational factors that the present design cannot disentangle from beat frequency. These mechanisms are discussed below.

Tempo Confound and Mechanism Disambiguation

The most important threat to internal validity in this study is that the two musical pieces inherently differ in beat frequency (Izmir March ~115 BPM vs. "Stayin' Alive" ~103 BPM). A substantial portion of the observed between-song difference in compression rate likely reflects this tempo difference rather than cultural familiarity or motivational arousal alone. The current design cannot disentangle three plausible mechanisms:

(1) Beat-frequency entrainment, in which participants synchronize compressions with the audible beat regardless of music identity;

(2) Cultural familiarity and native-language semantic activation, whereby the Izmir March is a familiar Turkish anthem with culturally meaningful lyrics that may enhance rhythmic adherence through long-term sensorimotor associations [9,10];

(3) Motivational arousal and military identity, as the Izmir March, a national military anthem, may evoke heightened arousal, collective identity, and motivation distinct from generic cultural familiarity [9,15].

Although beat frequency is the dominant explanation for the differences in compression rate, two observations are consistent with an additional contribution from familiarity and/or arousal. First, subjective ratings of effort (VAS) were modestly lower for the Izmir March (5.8±0.8) than for "Stayin' Alive" (6.5±0.5; Table 6), despite the faster tempo of the former, which would ordinarily be expected to increase perceived exertion. Second, participants performed compressions within their native cultural and military context, in which the Izmir March holds symbolic significance not present for "Stayin' Alive." These observations are exploratory; future trials should disentangle these mechanisms using factorial designs (e.g., culturally familiar vs. unfamiliar music at matched BPM; instrumental vs. vocal versions of the same piece; tempo-matched military marches from a different cultural context).

Trade-off Between Rate and Quality

An important nuance is the potential trade-off between rate and quality. Although the Izmir March yielded a higher mean rate, the "Stayin' Alive" condition produced a higher adequate-rate proportion (within-target compressions) and slightly higher correct-release and total-score metrics, although the latter two did not reach statistical significance. This pattern is consistent with the hypothesis that tempos closer to the lower end of the target range may allow a wider tolerance for rate drift and better preservation of compression quality [13]. Future research should explore whether an optimal tempo near 105–110 BPM balances rate accuracy and quality and whether supplemental training (e.g., real-time feedback devices [14]) can mitigate quality decrements at higher tempos.

Study Limitations

This study had several limitations. As a pilot study, the sample size (n=20) was small and intended for preliminary parameter estimation [11,12], which limits the generalizability of our findings to other populations and may not have been sufficient to detect smaller effect sizes. Consequently, a formal power analysis was not performed. The homogeneous nature of the participant group (young male soldiers), the unblinded design, and the use of manikin-based measurements [17] further

indicate that these results should be interpreted as foundational rather than definitive.

Additionally, the two musical pieces differ in beat frequency, which is the most likely dominant explanation for the differences in compression rate and limits causal attribution to cultural or motivational mechanisms. Allocation concealment using sealed, opaque envelopes was not implemented; randomization was performed by the principal investigator using a web-based generator, which may have introduced selection bias, although baseline characteristics were comparable across groups (Tables 1 and 2). Musical preference, prior exposure, and emotional attachment to the Izmir March were not measured before randomization and may represent unmeasured confounders.

Notably, the study did not include a non-music control group; therefore, we cannot conclude that music-assisted training improves long-term retention compared with standard CPR training alone. The retention observed at 6 weeks is reported as a within-cohort exploratory observation rather than as a comparative claim against a non-music condition. However, these findings provide a foundation for larger, adequately controlled trials.

Conclusion

In this pilot study, compression-only CPR paced by the Izmir March (115 BPM) produced higher mean compression rates than pacing with "Stayin' Alive" (103 BPM), although this between-song difference is largely attributable to differences in beat frequency. Within the cohort, post-training compression rates moved closer to the 100–120/min target range at 6 weeks. Both music conditions maintained mean compression rates within the target range; "Stayin' Alive" resulted in a higher proportion of within-target compressions, whereas the Izmir March produced a higher absolute mean rate. Further studies should evaluate the Izmir March in larger trials with non-music control groups and designs that distinguish the effects of beat frequency, cultural familiarity, and motivational arousal.

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Ethics Committee Approval: This study was approved by the Van Training and Research Hospital Ethics Committee (Decision No: GO-KAEK/2025-08-04, Date: 24.10.2025).

Informed Consent: Written informed consent was obtained from all participants included in this study.

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ORIGINAL RESEARCH

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Institution-level Emergency Department Care Processes and Flow Metrics from Hospital Information Systems: A Retrospective Descriptive Study

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Abstract

Objective: Full-year, reproducible operational profiles derived from hospital information systems are rarely reported. This study aimed to describe a 2025 institution-level emergency department operational profile derived from a hospital information management system.

Materials and Methods: We performed a retrospective, descriptive, single-center analysis of aggregated, de-identified outputs for all presentations to adult/general, pediatric, and obstetric/gynecology emergency units between January 1 and December 31, 2025. Indicators included visit volume and triage category; laboratory testing, imaging, and consultation activity; mean triage-to-first-physician waiting time by shift; observation unit length-of-stay categories; quarterly 24-hour revisits with the same diagnosis; and the 50 most frequently assigned International Classification of Diseases, 10th Revision diagnosis codes, grouped by chapter.

Results: There were 1,421,126 presentations; the triage distribution was 68.9% green, 28.3% yellow, 2.8% red, and 0.006% black. Resource use increased with acuity (laboratory testing: 9.7%, 21.5%, and 58.0%; any imaging: 13.7%, 39.0%, and 78.3% for green, yellow, and red triage, respectively). The mean triage-to-first-physician waiting time was 12.0 minutes overall and 5.5 minutes overnight (00:00–08:00). Observation stays totaled 268,847, of which 89.8% lasted 0–2 hours. The 24-hour revisit rate was 1.44%, increasing from 1.09% (January–March) to 1.62% (October–December).

Conclusion: Aggregated hospital system outputs can support a reproducible operational dashboard describing demand, acuity-stratified care processes, flow, early returns, and diagnostic mix for monitoring and benchmarking.

Keywords: Crowding, emergency service, health services research, hospital information systems, triage

Introduction

Emergency departments (EDs) sit at the fault line between community demand and hospital capacity and therefore function as a sensitive barometer of health-system performance. Beyond crowding alone, ED operational performance is increasingly evaluated through indicator sets that capture demand, acuity, resource use, and patient flow across the care pathway [1]. ED crowding, prolonged waiting, and delays in downstream flow are widely recognized threats to timely assessment and safe care [1]. Contemporary studies consistently link prolonged ED exposure to clinically meaningful harms, particularly in older or medically vulnerable populations. For example, waiting overnight in the ED prior to ward admission has been associated with increased in-hospital mortality and morbidity among older adults [2]. Similar concerns extend to system-level flow and access: crowding metrics based on occupancy and workload have been investigated as predictors of short-term mortality, with findings varying by setting and measurement approach [3,4]. Waiting time to first physician assessment remains a core operational metric because it reflects both access and triage effectiveness, and large registry-based analyses show that waiting time can also differ systematically across patient subgroups even after accounting for acuity and ED context [5]. In parallel, observation care has expanded as a strategy to manage uncertainty and reduce unnecessary admissions, and recent studies have evaluated both traditional and novel observation models for their effects on ED length of stay and return visits [6,7].

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Despite this growing evidence base, important gaps limit translation into actionable, locally relevant quality improvement. First, the observed associations between crowding-related measures and mortality are not uniform across studies, underscoring context sensitivity and heterogeneity in operational definitions [3,4]. Second, much of the published literature focuses on single outcomes or narrowly defined cohorts rather than on a consolidated indicator set that simultaneously describes case mix (e.g., triage distribution), diagnostic intensity (laboratory and imaging use), patient flow (waiting time and observation unit length of stay), and post-discharge quality signals (early return visits) [1,8,9]. Third, ED dashboards and performance indicator frameworks based on routinely collected data have been described, but their implementation characteristics, indicator selection, and reproducible reporting logic are inconsistently reported across settings [10,11]. Fourth, routine hospital information management systems, when used to generate aggregated and reproducible institutional dashboards, remain underdescribed in the peer-reviewed literature, particularly across multiple ED streams such as adult/general, pediatric, and obstetric/gynecology emergency services within the same institution. These limitations impede benchmarking, obscure where delays accumulate along the ED pathway, and reduce the transparency needed for other centers to replicate indicator-based monitoring.

In Türkiye, high ED utilization and the predominance of lower-acuity presentations are frequently discussed in clinical and policy contexts, but full-year empirical profiles that integrate triage distribution, diagnostic resource use, waiting time, observation unit flow, early revisits, and diagnostic mix within the same institutional framework remain limited. Routine HIMS data can help address this gap when indicator definitions, denominators, and system-related constraints are reported transparently. Therefore, the contribution of this study is not to provide patient-level causal or prognostic inference but to demonstrate a reproducible institution-level operational profiling framework for ED monitoring and benchmarking.

Accordingly, the aim of this study was to describe a full-year, institution-level profile of ED service delivery indicators derived from routine Hospital Information Management System (HIMS) outputs from January 1, 2025, to December 31, 2025. To support monitoring and benchmarking, we summarized key operational domains, including demand and acuity distribution, care processes and resource use, patient flow metrics, observation unit utilization, early return visits, and diagnostic mix, within a reproducible, aggregated reporting framework. We reported ED volume and triage distribution, key process indicators (laboratory testing, imaging and modality components, prescriptions, consultations, observation unit use, hospital admission, and interhospital transfer), mean triage-to-physician waiting time by shift, observation unit length-of-stay categories, quarterly 24-hour return-visit rates, and the most frequent ICD-10 code assignments aggregated by ICD-10 chapter.

Materials and Methods

Study Design and Setting

We performed a retrospective, descriptive, single-center analysis of institutional ED service indicators generated by the HIMS at a large tertiary training and research hospital in eastern Türkiye. The study hospital functions as an A1-role regional referral institution with 1,500 registered beds and serves both the province of Van and the wider second health service region, including Van, Hakkari, Muş, Bitlis, and selected districts of Ağrı. Emergency care is organized through three operationally distinct service lines: adult/general emergency, pediatric emergency, and obstetric/gynecology emergency. These service lines are recorded separately in the HIMS reporting structure but function within the same institutional emergency care framework. Therefore, the annual ED volume reported in this study reflects the combined emergency workload of these three service streams rather than the volume of a single adult-only emergency department.

We set the observation window from January 1, 2025, through December 31, 2025, and included aggregated outputs from these three ED service lines. We treated the ED encounter as the unit of analysis, as represented in HIMS reporting outputs, rather than an identifiable individual. We analyzed only aggregated, de-identified institutional indicators produced as routine operational reports and did not access, extract, or link any individual-level patient records. All analyses were conducted at the institutional indicator level; therefore, the findings are interpreted as service profiling rather than patient-level inference.

Ethics Statement

This study was approved by the Non-Interventional Clinical Research Ethics Committee of SBU Van Education and Research Hospital on February 6, 2026 (approval number: GOKAEK/2026-02-24). We conducted the study in accordance with applicable national regulations and the principles of the Declaration of Helsinki.

Participants/Subjects

We included all ED presentations recorded in the HIMS within the predefined time window for the adult/general, pediatric, and obstetric/gynecology emergency units. We applied no patient-level inclusion or exclusion criteria because the HIMS extracts

were limited to aggregated institutional indicators and did not contain individual identifiers or person-level covariates. We did not characterize the population by age, sex, comorbidities, or other individual clinical variables because such data were not available in the aggregated exports. For triage-based analyses, we used the national triage categories recorded in the HIMS (green, yellow, red, and black). We retained black-triage encounters for overall volume reporting but considered them not applicable to analyses in which the underlying construct required waiting for evaluation or downstream care processes (e.g., waiting time), consistent with routine ED workflow definitions. Black triage was operationally treated as "not applicable" for pathway-dependent indicators rather than excluded from overall volume counts.

Materials and Equipment

We used the institution's HIMS reporting module to generate aggregated indicators within the specified date range and service lines and exported these outputs as Microsoft Excel files using built-in institutional reporting functions. We processed, checked, and analyzed the exported datasets using Microsoft Excel and Python (version 3.13; Python Software Foundation, Wilmington, DE, USA). We generated tables and figures using Python with standard scientific libraries (e.g., pandas, NumPy, SciPy, and Matplotlib) and performed spreadsheet-based verification in Excel. No medical devices, drugs, or laboratory instruments were used for research purposes because the study relied exclusively on routinely produced institutional indicators. Figures were created as editable vector outputs (e.g., PDF) to comply with journal requirements for modifiable figure files.

Study Procedures

We prespecified the indicator set, time window, and stratification scheme before extraction. We first generated annual totals for ED volume and triage distribution by service line (adult/general, pediatric, and obstetric/gynecology). We then extracted triage-stratified process indicators generated by the HIMS as aggregated operational counts. For each triage category, the denominator was the number of ED presentations in that category. Laboratory testing was interpreted as a presentation-associated indicator representing ED presentations for which at least one laboratory request was recorded in the HIMS. Any imaging was interpreted as a presentation-associated indicator representing ED presentations with at least one imaging request, whereas modality-specific imaging components, including radiography, ultrasonography, computed tomography, and magnetic resonance imaging, were interpreted as HIMS-derived imaging request indicators summarized by triage category. Because the exported data were aggregated operational reports rather than patient-level linked records, these indicators should not be interpreted as unique patient-level utilization measures, and repeated or multiple requests within the same encounter could not be separately evaluated. We also extracted aggregated counts of presentations with a prescription issued and presentations with at least one specialty consultation requested, as defined by the HIMS operational reporting logic.

We extracted aggregated counts for hospital admission and interhospital transfer as generated by the HIMS. Because institutional HIMS workflow rules system-disabled admission and transfer transactions for green-triage encounters, green-triage values for these endpoints were treated as structural zeros driven by system rules rather than as clinically observed absences of admissions or transfers. To avoid misinterpretation in reporting, green-triage values for admission and transfer were presented as NA (structural zero) rather than 0%.

We defined waiting time as the mean time, in minutes, from triage registration to first physician assessment, as recorded in the HIMS. We extracted HIMS-reported mean waiting times separately for three shifts (08:00–16:00, 16:00–00:00, and 00:00–08:00) and obtained, for each shift and triage category, the number of visits contributing to the reported mean. We did not attempt to reconstruct waiting-time distributions because the HIMS outputs provided aggregated means without dispersion measures. Accordingly, waiting-time comparisons were restricted to descriptive contrasts of the reported means.

We defined ED observation unit length of stay as the elapsed time between admission to an ED observation bed and discharge from the observation unit or conversion to hospital admission, based on routine HIMS timestamps. We used the HIMS quality-monitoring categorization of observation length of stay into four bins (0–2 hours, 3–8 hours, 9–24 hours, and ≥24 hours) and extracted both annual totals and month-by-month distributions for these categories. We additionally defined "prolonged observation" as a length of stay ≥9 hours (9–24 hours plus ≥24 hours) for summary reporting.

We evaluated early return visits using the institution's HIMS-linked quality indicator for return ED presentations within 24 hours with the same diagnosis. This indicator was generated by the HIMS quality-monitoring module according to the institutional diagnosis-matching rule and predefined eligibility-denominator framework. Same-diagnosis matching was based on the diagnosis information recorded in the HIMS for the index and return ED presentations, as operationalized by the institutional quality indicator specification. The 24-hour interval was calculated from the registration time of the index ED presentation to the registration time of the return

ED presentation. We extracted quarterly and annual numerator and denominator values for 2025, with quarters prespecified as January–March, April–June, July–September, and October–December. Because the indicator used a denominator defined by institutional reporting rules and exclusions for quality monitoring, we treated its denominator as indicator-specific and did not assume equivalence to overall ED visit counts derived from other HIMS extracts. Accordingly, the return-visit indicator was interpreted within its own eligibility-denominator framework rather than as a crude proportion of total ED presentations. We also reported a Q4-versus-Q1 contrast (risk ratio and absolute difference) as an interpretable summary of temporal change.

For diagnostic profiling, we extracted aggregated counts of ICD-10 diagnosis code assignments and identified the 50 most frequently assigned codes within the study period. Because aggregated ICD-10 outputs represented code assignments rather than unique patients, and because encounters could receive more than one ICD-10 code, we interpreted these data as assignment frequencies. We grouped the top 50 codes into ICD-10 chapters and summarized the distribution at the chapter level for descriptive reporting. To summarize diagnostic-mix concentration and diversity, we computed the Herfindahl–Hirschman Index and Shannon entropy from the chapter-level distribution and derived the effective number of chapters as exp(entropy).

Data Processing and Quality Assurance

We cross-checked HIMS exports with the hospital quality management unit to ensure internal consistency with routine institutional reporting. We verified concordance between overall annual totals and the sums across triage categories and service lines when both were available and assessed the completeness and plausibility of monthly and quarterly subtotals (observation unit length-of-stay distributions and the 24-hour return-visit indicator). We maintained a fixed extraction schema (variable names, stratification levels, and time windows) across datasets to support traceability and reproducibility of the aggregated workflow. We additionally screened exported tables for formatting anomalies (e.g., truncated or locale-formatted numeric strings) and flagged such fields for source-level verification prior to final submission. All derived measures (risk ratios, absolute differences, and indices) were computed reproducibly from the exported aggregates using scripted analysis.

Statistical Analysis

We summarized aggregated indicators using counts and percentages for categorical measures and HIMS-reported means for waiting time. For key proportions, we reported binomial Wilson 95% confidence intervals using the extracted n/N pairs. Between-triage contrasts for process indicators were expressed as absolute percentage-point differences (RD, percentage points) and relative risks (RRs), with 95% confidence intervals computed on the log scale from aggregated counts. Given the very large denominators, we prioritized effect sizes and confidence intervals over p values to reduce overinterpretation of statistical significance driven by sample size.

As an additional operational analysis, we calculated the contribution of each triage category to the aggregate diagnostic and process workload. For each selected indicator, the number of HIMS-derived indicator events in each triage category was divided by the total number of corresponding indicator events across triage categories. This analysis was intended to distinguish within-category utilization rates from each triage category's contribution to the total institutional workload.

For the 24-hour return-visit quality indicator, we computed quarterly and annual rates with Wilson 95% confidence intervals. We evaluated temporal change across quarters using binomial logistic regression with a logit link, with quarter entered as a linear term, and reported an odds ratio (OR) per quarter with a 95% confidence interval and a two-sided p value. This model used only the aggregated numerator/denominator pairs and was interpreted as a trend analysis under the institutional indicator definition. In addition, we reported an absolute quarterly contrast (Q4–Q1) and a relative contrast (Q4 vs. Q1) derived from the quarterly aggregates.

We evaluated differences in mean waiting times across shifts and triage categories descriptively without formal hypothesis testing because the HIMS provided aggregated means without accompanying measures of dispersion, precluding standard inferential comparisons of means. We did not perform an a priori sample size or power calculation because the study used a census of all eligible aggregated ED encounters and institutional indicators within a fixed annual time window, and the analytic sample size was determined by the operational volume captured in the HIMS exports. We conducted statistical analyses using Python 3.13 and produced tabular and graphical outputs using Python and Microsoft Excel.

Reporting Guideline

We prepared the manuscript in accordance with the STROBE principles for observational research, with adaptations appropriate to an aggregated, institution-level indicator design without access to individual-level variables. Given the use of routinely collected institutional indicators, we also applied RECORD-aligned principles where applicable, including data provenance, indicator definitions, and traceability of aggregated denominators.

Results

Study Population and Data Inclusion

A total of 1,421,126 emergency department presentations were recorded across adult/general, pediatric, and obstetric/gynecology service lines during the study period (Table 1). Green-triage encounters accounted for 978,848 presentations (68.9%), followed by yellow-triage encounters with 402,859 presentations (28.3%) and red-triage encounters with 39,328 presentations (2.8%). Black-triage encounters were rare, with 91 presentations (0.006%). Black-triage encounters were retained for overall volume reporting but excluded from analyses in which waiting time or downstream care pathways were not applicable (Table 1). Uncertainty for key proportions was summarized using 95% confidence intervals (Tables 2 and 3).

ED Workload by Service Line and Triage Acuity

Case mix differed by service line. Pediatric ED presentations were predominantly green triage, with 331,846 of 400,349 presentations (82.9%) categorized as green. Obstetric/gynecology ED presentations were predominantly yellow triage, with 25,127 of 30,419 presentations (82.6%) categorized as yellow. The adult/general ED accounted for the largest overall workload and the majority of higher-acuity encounters, including 37,585 of 39,328 red-triage presentations (95.6%) (Table 1).

Care Processes by Triage Category

Care intensity increased stepwise with triage acuity across laboratory testing and imaging. Laboratory testing was recorded in 95,343 green-triage presentations (9.7%), 86,560 yellow-triage presentations (21.5%), and 22,799 red-triage presentations (58.0%). Any imaging was recorded in 134,038 green-triage presentations (13.7%), 157,282 yellow-triage presentations (39.0%), and 30,773 red-triage presentations (78.3%). CT use increased from 10,543 green-triage presentations (1.1%) to 33,076 yellow-triage presentations (8.2%) and 9,534 red-triage presentations (24.2%) (Table 2).

Although green-triage presentations had the lowest within-category rates of laboratory testing and imaging, their high volume meant that they contributed substantially to the aggregate diagnostic and process workload. Based on the counts shown in Table 2, green-triage presentations accounted for approximately 46.6% of all laboratory-testing indicators and 41.6% of all imaging indicators. They also accounted for approximately 73.1% of prescription-associated presentations. In contrast, consultation workload was concentrated mainly in the yellow- and red-triage categories, with green-triage presentations accounting for only approximately 1.1% of consultation indicators.

Consultation and admission indicators demonstrated the largest acuity gradients. Specialty consultation was recorded in 0.03% of green-triage presentations, 4.47% of yellow-triage presentations, and 22.01% of red-triage presentations. Hospital admission was recorded in 24,405 yellow-triage presentations (6.06%) and 7,136 red-triage presentations (18.14%). Admission and interhospital transfer workflows were system-disabled for green-triage encounters and were therefore reported as structural zeros rather than as an observed clinical absence of admission or transfer (Table 2). Prescribing showed the opposite pattern, decreasing from 40.65% in green-triage presentations to 34.22% in yellow-triage presentations and 21.36% in red-triage presentations (Table 2).

Time-to-Physician Assessment (Waiting Time)

The mean triage-to-first-physician waiting time was 12.0 minutes overall. The overnight shift had the shortest overall mean waiting time, at 5.5 minutes, compared with 12.8 minutes during 08:00–16:00 and 12.5 minutes during 16:00–00:00. Waiting time also decreased with increasing triage acuity. The overall mean waiting time was 13.9 minutes for green-triage presentations, 8.1 minutes for yellow-triage presentations, and 4.0 minutes for red-triage presentations (Table 4).

Observation Unit Length of Stay

Observation unit stays were predominantly short. Of 268,847 observation stays, 241,323 (89.8%) lasted 0–2 hours, and 27,257 (10.1%) lasted 3–8 hours. Prolonged observation, defined as an observation unit length of stay of ≥9 hours, was rare and occurred

Table 1. Emergency department presentations and triage distribution by service line (2025)

Service line	Total	Green	Yellow	Red	Black
Pediatric ED	400349	331846 (82.9)	66791 (16.7)	1709 (0.43)	3 (0.001)
Obstetrics/Gynecology ED	30419	5257 (17.3)	25127 (82.6)	34 (0.11)	1 (0.003)
Adult/General ED	990358	641745 (64.8)	310941 (31.4)	37585 (3.8)	87 (0.009)
Overall	1421126	978848 (68.9)	402859 (28.3)	39328 (2.8)	91 (0.006)

Values are n (%). Percentages are row-wise within each service line and may not sum to 100 due to rounding. Black indicates deceased on arrival/exit (Ex). ED: Emergency department.

Table 2. Care processes by triage category and effect measures (2025)

Indicator	Green (n=978,848)	Yellow (n=402,859)	Red (n=39,328)	Yellow vs Green RR (95% CI)	Yellow vs Green RD, pp (95% CI)	Red vs Yellow RR (95% CI)	Red vs Yellow RD, pp (95% CI)
≥1 laboratory test	95,343 (9.74; 9.68–9.80)	86,560 (21.49; 21.36–21.61)	22,799 (57.97; 57.48–58.46)	2.206 (2.187–2.225)	+11.746 (+11.606 to +11.886)	2.698 (2.670–2.726)	+36.485 (+35.981 to +36.989)
Any imaging	134,038 (13.69; 13.63–13.76)	157,282 (39.04; 38.89–39.19)	30,773 (78.25; 77.84–78.65)	2.851 (2.833–2.869)	+25.348 (+25.183 to +25.513)	2.004 (1.991–2.017)	+39.206 (+38.771 to +39.640)
Radiography	116,334 (11.88; 11.82–11.95)	110,463 (27.42; 27.28–27.56)	18,118 (46.07; 45.58–46.56)	2.307 (2.290–2.324)	+15.535 (+15.383 to +15.687)	1.680 (1.660–1.700)	+18.649 (+18.138 to +19.161)
CT	10,543 (1.08; 1.06–1.10)	33,076 (8.21; 8.13–8.30)	9,534 (24.24; 23.82–24.67)	7.623 (7.460–7.789)	+7.133 (+7.046 to +7.220)	2.953 (2.893–3.013)	+16.032 (+15.600 to +16.464)
Ultrasound	6,203 (0.63; 0.62–0.65)	11,586 (2.88; 2.82–2.93)	934 (2.37; 2.23–2.53)	4.538 (4.401–4.679)	+2.242 (+2.188 to +2.296)	0.826 (0.773–0.882)	−0.501 (−0.660 to −0.342)
MRI	958 (0.10; 0.09–0.10)	2,157 (0.54; 0.51–0.56)	2,187 (5.56; 5.34–5.79)	5.471 (5.070–5.903)	+0.438 (+0.414 to +0.461)	10.386 (9.795–11.013)	+5.026 (+4.798 to +5.253)
Prescription	397,868 (40.65; 40.55–40.74)	137,845 (34.22; 34.07–34.36)	8,401 (21.36; 20.96–21.77)	0.842 (0.838–0.846)	−6.430 (−6.606 to −6.254)	0.624 (0.612–0.637)	−12.855 (−13.286 to −12.425)
Consultation	306 (0.03; 0.03–0.03)	18,001 (4.47; 4.40–4.53)	8,658 (22.01; 21.61–22.43)	142.935 (127.671–160.024)	+4.437 (+4.373 to +4.501)	4.927 (4.813–5.044)	+17.547 (+17.132 to +17.961)
Hospital admission*	NA (structural zero)	24,405 (6.06; 5.98–6.13)	7,136 (18.14; 17.77–18.53)	NA	NA	2.995 (2.923–3.069)	+12.087 (+11.699 to +12.475)
Inter-hospital transfer*	NA (structural zero)	176 (0.04; 0.04–0.05)	84 (0.21; 0.17–0.26)	NA	NA	4.889 (3.771–6.339)	+0.170 (+0.124 to +0.216)

Values are n (%), with percentages calculated within triage category unless otherwise stated. Confidence intervals for proportions are Wilson 95% confidence intervals. Laboratory testing and any imaging represent presentation-associated HIMS indicators, whereas modality-specific imaging variables represent HIMS-derived request indicators summarized by triage category. Because the exported data were aggregated operational reports rather than patient-level linked records, repeated or multiple requests within the same encounter could not be separately evaluated. RR indicates risk ratio; RD indicates absolute risk difference in percentage points (pp); CI indicates confidence interval; NA indicates not applicable due to structural zero. Effect measures are presented for the comparisons shown in the column headers (yellow vs green; red vs yellow). Hospital admission and inter-hospital transfer workflows were system-disabled for green-triage encounters (structural zeros) and are therefore reported as NA.

in 267 stays (0.10%; Wilson 95% CI, 0.09–0.11). Only 61 stays (0.02%) lasted ≥24 hours (Table 5).

Return Visits Within 24 Hours With the Same Diagnosis

The annual 24-hour same-diagnosis revisit rate was 1.44% (20,457/1,421,126). The quarterly rate increased from 1.09% in January–March to 1.44% in April–June, 1.59% in July–September, and 1.62% in October–December. The binomial logit trend estimate showed an increase across quarters (OR per quarter=1.130, 95% CI, 1.116–1.144; p<0.001). The Q4-versus-Q1 contrast corresponded to a risk ratio of 1.488 (95% CI, 1.429–1.551) and an absolute difference of +0.533 percentage points (95% CI, +0.479 to +0.587) (Table 3).

Table 3. 24-hour revisits with the same diagnosis (quality indicator), by quarter (2025)

Period (2025)	Numerator/ Denominator	Rate (%)	95% CI (Wilson)
January–March	3,666 / 335,919	1.091	1.057–1.127
April–June	5,397 / 375,677	1.437	1.399–1.475
July–September	5,555 / 350,063	1.587	1.546–1.629
October–December	5,839 / 359,467	1.624	1.584–1.666
Overall	**20,457 / 1,421,126**	**1.439**	**1.420–1.459**
Trend (binomial logit; per quarter)	—	OR = 1.130	95% CI 1.116–1.144; p < 0.001
Additional contrast: Q4 vs Q1	—	RR = 1.488	95% CI 1.429–1.551
Additional contrast: Q4 – Q1	—	RD = +0.533 pp	95% CI +0.479 to +0.587

OR: Odds ratio; RR: Risk ratio; RD: absolute risk difference (percentage points, pp); CI: Confidence interval; Q1: January–March; Q4: October–December.

Diagnostic Profile (ICD-10 Chapter Aggregation of Top 50 Codes)

The top 50 ICD-10 diagnosis code assignments showed a diagnostic profile dominated by respiratory diseases and symptom-based

Table 4. Mean triage-to-first-physician waiting time (minutes) by triage category and shift (2025)

Triage	08:00–16:00 mean (n)	16:00–00:00 mean (n)	00:00–08:00 mean (n)	Overall mean (n)
Red	4.13 (13471)	4.56 (14638)	3.09 (11219)	3.99 (39328)
Yellow	8.77 (185147)	8.07 (185064)	4.37 (32648)	8.09 (402859)
Green	14.69 (438859)	14.56 (454697)	6.21 (85292)	13.89 (978848)
Overall	12.75 (637477)	12.50 (654399)	5.48 (129159)	11.97 (1421035)

Table 5. Observation unit length-of-stay categories (2025)

Length of stay category	n	%
0–2 hours	241,323	89.76
3–8 hours	27,257	10.14
9–24 hours	206	0.08
≥24 hours	61	0.02
Prolonged observation (≥9 hours)	267	0.10 (Wilson 95% CI 0.09–0.11)
Total	268,847	100

Prolonged observation was defined as length of stay ≥9 hours; the percentage is reported with a Wilson 95% confidence interval.

presentations. Respiratory diseases accounted for 585,142 code assignments (41.7%) among the top 50 diagnoses, followed by symptoms and signs with 260,469 assignments (18.5%) and musculoskeletal disorders with 142,790 assignments (10.2%). The diagnostic-mix indices indicated moderate concentration, with a Herfindahl–Hirschman Index of 0.232, Shannon entropy of 1.844, and an effective number of chapters of 6.33 (Table 6).

Discussion

This retrospective, aggregated indicator study described a full-year institutional profile of emergency department service delivery across adult/general, pediatric, and obstetric/gynecology emergency streams. This study adds to the emergency care literature by showing how routinely generated HIMS indicators can be assembled into a full-year operational profile of a high-volume ED system. Rather than examining a single outcome, the analysis brings together demand, triage acuity, diagnostic workload, waiting time, observation unit flow, early revisit signals, and diagnostic mix within the same institutional year. In a setting where high ED utilization and lower-acuity demand are frequently discussed but comprehensive full-year empirical profiles remain limited, this reporting approach provides a data-based baseline for local monitoring and future benchmarking. Overall, the ED workload was dominated by lower-acuity presentations, accompanied by an internally coherent "acuity gradient" in diagnostic intensity and escalation pathways, shift-dependent variation in time to first physician assessment, predominantly short observation unit stays, a low but nonzero early return-visit signal that varied by quarter, and a diagnostic profile dominated

Table 6. Distribution of top 50 ICD-10 code assignments by ICD-10 chapter

ICD-10 chapter	n*	% of code assignments among top-50 diagnoses
Respiratory diseases (J00–J99)	585,142	41.7
Symptoms and signs (R00–R99)	260,469	18.5
Musculoskeletal disorders (M00–M99)	142,790	10.2
Factors influencing health status / encounters (Z00–Z99)	98,986	7
Infectious and parasitic diseases (A00–B99)	74,396	5.3
External causes of morbidity and mortality (V01–Y98)	62,429	4.4
Digestive diseases (K00–K93)	61,974	4.4
Genitourinary diseases (N00–N99)	48,711	3.5
Eye and ear diseases (H00–H95)	31,788	2.3
Injury, poisoning and other consequences of external causes (S00–T98)	26,208	1.9
Skin and subcutaneous tissue diseases (L00–L99)	11,539	0.8
Diagnostic-mix indices (chapter distribution)		
Herfindahl–Hirschman Index (HHI)	—	0.232
Shannon entropy	—	1.844
Effective number of chapters (exp[entropy])	—	6.33

Values represent counts of ICD-10 code assignments among the 50 most frequently assigned diagnosis codes; percentages are calculated as the proportion of all top 50 code assignments. n indicates the number of code assignments (not unique patients or visits). Diagnostic-mix indices (Herfindahl–Hirschman Index and Shannon entropy) were calculated from the chapter-level distribution of top 50 code assignments shown in this table; the effective number of chapters was computed as exp(entropy).

by respiratory and symptom-based codes in our institutional data [9]. Framed against evidence-based quality measurement frameworks, these findings provide a reproducible baseline for local benchmarking and for prioritizing operational domains for iterative monitoring rather than implying causal effects or patient-level outcomes [12]. In particular, the explicit specification of indicator definitions and system rules strengthens interpretability and supports cross-time comparability.

A central operational implication of the observed case mix is that high-volume, low-acuity demand can still generate substantial resource use and throughput pressure [1]. Prior multisite analyses show that "nonurgent" ED visits often require laboratory and imaging resources and therefore cannot be assumed to be operationally trivial. In our institution-level profile, green-triage presentations had the lowest within-category rates of laboratory testing and imaging, but they accounted for approximately 46.6% of all laboratory-testing indicators, 41.6% of all imaging indicators, and 73.1% of prescription-associated presentations because of their large volume. Therefore, interpreting ED workload only through triage-specific percentages would underestimate the contribution of high-volume, lower-acuity care. In practical terms, workload is shaped not only by acuity but also by how frequently each group uses diagnostic and prescribing resources. Accordingly, demand management and streaming strategies should consider both the clinical acuity of presentations and their aggregate contribution to diagnostic, prescribing, and staffing workload. This also helps contextualize the service-line differences, including the predominance of green-triage presentations in the pediatric ED and yellow-triage presentations in the obstetric/gynecology ED, which likely reflect stream-specific triage rules and referral patterns rather than simple differences in illness severity [13,14].

Across triage strata, process indicators demonstrated a stepwise increase in laboratory testing, imaging, consultation, observation use, and admission among higher-acuity encounters, consistent with the intended function of triage as a prioritization and resource-allocation instrument. External validation studies of widely used triage systems support the association of higher-acuity categories with greater resource utilization and downstream care needs, aligning with the internal face validity of the patterns observed here. At the same time, the interpretation of some downstream indicators in our dataset required attention to the "data-generating process": because admissions and transfers were system-disabled for green-triage encounters, those cells represent structural zeros rather than an observed clinical absence. This is not a minor technicality; it directly affects between-triage comparisons and reinforces the need for explicit indicator metadata, including definitions, system rules, and denominators, as part of institutional dashboards to ensure comparability over time and across centers [12,13]. Without such metadata, apparent between-triage or between-center differences may reflect reporting rules rather than true clinical or operational variation.

The waiting-time profile suggests two complementary operational signals. First, shorter times to first physician assessment among higher-acuity encounters are consistent with effective prioritization. Second, the observed shift-level variation indicates that access to timely assessment is not uniform throughout the day, plausibly reflecting the interaction among arrival patterns, staffing, and competing workflow constraints (e.g., diagnostics and disposition during peak hours). Large population-based studies have reported associations between longer ED waiting times and adverse downstream outcomes, including short-term mortality and hospital admission, underscoring why time to provider remains a core access and safety proxy even when patient-level outcomes are not directly measured in a given dataset [15]. In parallel, patient-reported experience has been shown to worsen as waiting times increase in both admitted and discharged cohorts, supporting the relevance of this metric for quality governance beyond clinical endpoints alone [16]. These findings support the use of waiting time as a practical monitoring metric for staffing alignment and surge-response planning, while recognizing that aggregate means cannot identify the longest waits [15,16].

Observation unit utilization in this profile was characterized by predominantly short stays, with a very small proportion of prolonged observation periods. This pattern is broadly consistent with the conceptual role of ED observation care as a time-limited diagnostic and treatment strategy to manage uncertainty, reduce unnecessary inpatient admissions, and maintain flow when protocolized pathways are available. In our institution, the predominance of 0–2-hour observation stays may suggest that the observation unit functioned primarily as a short-term reassessment, treatment, and disposition-decision area rather than as a prolonged boarding space. Possible systemic explanations include rapid discharge after short-term treatment or reassessment, early conversion to inpatient admission when needed, and local workflow rules for opening and closing observation records. The available aggregate data did not include patient-level observation indications, diagnoses linked to observation stays, treatment details, or disposition after observation; therefore, these explanations remain interpretive rather than causal. Although we did not evaluate condition-specific observation pathways, the short-stay distribution observed here is consistent with a time-limited observation model at the institutional level. In our data, the rarity of prolonged observation stays may indicate effective

conversion to admission or discharge decisions within expected time windows, but it may also mask clinically relevant congestion episodes if prolonged stays cluster within short periods. Therefore, future monitoring may benefit from complementing categorical LOS bins with time-series dashboards, such as weekly or shift-level monitoring, to detect episodic access block [17–19].

The ICD-10 chapter distribution provides an additional operational perspective on ED demand. The predominance of respiratory diseases among the top 50 diagnosis code assignments suggests a substantial burden of acute respiratory and seasonal infectious presentations within the institutional ED workload. The high proportion of symptom- and sign-based codes is also clinically plausible in the emergency care context, where initial assessment often focuses on syndromic presentation, rule-out evaluation, and short-term management before a definitive outpatient or inpatient diagnosis is established. Musculoskeletal disorders, digestive diseases, genitourinary diseases, and external-cause-related codes further indicate that the ED case mix extends beyond high-acuity resuscitation and includes a broad range of ambulatory, diagnostic, and injury-related presentations. From an operational perspective, this diagnostic profile can inform staffing, fast-track design, respiratory-season preparedness, imaging and laboratory planning, and coding-quality monitoring. However, because these data represent ICD-10 code assignments among the top 50 diagnoses rather than unique patients or adjudicated final diagnoses, they should be interpreted as an operational diagnostic profile rather than as epidemiological disease incidence.

The early return-visit indicator (return within 24 hours with the same diagnosis under institutional rules) provides a quality signal that warrants cautious interpretation. Prior national and single-center studies emphasize that short-interval returns are heterogeneous, driven by disease progression, discharge decisions under uncertainty, access to follow-up care, and patient behavior, and may not function as a specific safety indicator when used in isolation [8]. However, because definitions and time windows differ across studies (e.g., 24 hours vs. longer intervals), comparisons should focus on the concept of short-interval return rather than assume equivalence of indicator specifications. Moreover, return visits resulting in admission have been proposed as a potentially more "actionable" subset, but even these remain an imperfect proxy for preventable harm without clinical review and risk adjustment. In this context, the quarter-to-quarter variation observed in our institutional indicator can reasonably be treated as a trigger for targeted audit (e.g., condition-specific review, shift-level clustering, and linkage to observation/discharge pathways) rather than as a standalone performance judgment [20–22]. For this reason, the 24-hour same-diagnosis revisit rate is best viewed as a routine quality-monitoring signal rather than as evidence of preventable return visits, diagnostic error, or unsafe discharge at the patient level.

This study has several strengths relevant to institutional benchmarking. It used a full-year census of ED presentations across three service lines, applied a prespecified indicator set aligned with evidence-based measurement priorities, and used a reproducible extraction-and-cross-check workflow with the quality management unit, supporting internal traceability [12]. Although the absolute indicator values are institution-specific, the indicator framework and reporting logic are transferable to other centers using routinely collected information-system outputs.

Study Limitations

However, several limitations are intrinsic to the aggregated design. First, the absence of patient-level variables precluded case-mix adjustment and subgroup analyses, including age, sex, comorbidity, arrival mode, and clinical severity, thereby limiting causal interpretation and comparisons with outcome-focused literature. Because the dataset consisted of aggregated institutional HIMS-derived indicators rather than patient-level linked records, patient-level correlational or regression analyses were not methodologically appropriate. Therefore, associations between individual patient characteristics, clinical outcomes, resource use, waiting time, observation duration, and revisit risk could not be evaluated. Second, several indicators were constrained by information-system rules, notably structural zeros for green-triage admission and transfer, which can bias acuity comparisons if not explicitly handled as "not applicable" rather than "none." Third, waiting time was available only as aggregated means without measures of dispersion, preventing inference regarding high-risk distribution tails and formal statistical comparisons between shifts. Fourth, the 24-hour same-diagnosis revisit indicator was generated according to institutional HIMS quality-monitoring rules and was not adjudicated through chart review; therefore, it should not be interpreted as a patient-level preventable revisit outcome. Finally, ICD-10 outputs represented code assignments rather than unique patients and may vary according to coding practices; therefore, chapter-level distributions should be interpreted as an operational diagnostic profile rather than as epidemiological incidence.

Conclusion

This study provided a reproducible, full-year, institution-level profile of emergency department service indicators derived from routine HIMS outputs across adult/general, pediatric, and obstetric/gynecology emergency streams. The findings

supported internally coherent acuity gradients in diagnostic and escalation processes and identified shift-dependent access patterns and a predominantly short observation unit length-of-stay distribution, thereby enabling actionable operational benchmarking. This framework is important because transparent, standardized indicator reporting is a prerequisite for comparing performance across time and institutions. Future work should, where feasible, link these dashboards to patient-level outcomes through governance-approved data linkage to enable risk-adjusted benchmarking and targeted pathway audits.

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Informed Consent: Not applicable. The study used only aggregated, de-identified institutional indicators and did not involve access to individual-level patient records

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ORIGINAL RESEARCH

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The Association Between the HALP Score and Disease Severity in Patients with Diabetic Foot Disease Presenting to the Emergency Department: A Prospective Observational Study

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Abstract

Objective: Rapid assessment of disease severity in diabetic foot disease is essential in the emergency department. While the Wagner classification reflects local wound severity, the HALP score reflects systemic inflammatory and nutritional status. This study evaluated the association between the HALP score and Wagner stage and assessed its ability to identify advanced disease.

Materials and Methods: This prospective, single-center observational study included 130 patients with diabetic foot disease. The primary outcome was the association between the HALP score and Wagner stage. Secondary outcomes included amputation, in-hospital mortality, and 28-day mortality. Group comparisons, ROC analysis, DeLong's test, and multivariable logistic regression were performed.

Results: The median age was 66 years, and 65.4% of the patients were male. Amputation was performed in 48.5% of patients, and the median Wagner stage was 4 (3–5). HALP scores did not differ according to amputation status (p=0.212) but were significantly lower in Wagner grade 5 than in grades 1–2, 3, and 4 (all adjusted p≤0.026). HALP demonstrated good discrimination for Wagner grade 5 disease (AUC=0.790, 95% CI, 0.712–0.868), outperforming hemoglobin, lymphocyte count, and platelet count while performing similarly to albumin. Lower HALP scores remained independently associated with Wagner grade 5 disease (adjusted OR=0.857, 95% CI, 0.794–0.925; p<0.001).

Conclusion: Lower HALP scores were independently associated with advanced diabetic foot disease. Rather than replacing the Wagner classification, the HALP score may serve as a complementary biomarker during the initial emergency department assessment.

Keywords: Amputation, Diabetic Foot, Emergency Medicine, HALP Score

Introduction

Diabetic foot disease is one of the most common and serious complications of diabetes mellitus (DM) and a significant cause of emergency department presentations. It is associated with high morbidity, mortality, and impaired quality of life. Diabetic foot ulcers affect millions of people worldwide and represent a leading cause of diabetes-related hospitalizations [1]. Approximately 80% of nontraumatic lower extremity amputations are attributable to diabetic foot disease, and the lifetime risk of limb loss is markedly higher in patients with DM than in the nondiabetic population [2].

Accurate assessment of disease severity in patients presenting to the emergency department is essential for clinical decision-making and prognostic evaluation. The Wagner classification, based on ulcer depth and the presence of infection and gangrene, remains one of the most widely used systems because of its simplicity and prognostic utility [3]. Higher Wagner stages are associated with more severe infection, increased need for surgical intervention, and poorer clinical outcomes, including amputation [4].

Peripheral neuropathy, vascular insufficiency, chronic inflammation, and malnutrition play interconnected roles in the pathophysiology of diabetic foot disease. Neuropathy increases susceptibility to trauma, while hyperglycemia-related metabolic dysfunction impairs wound healing and immune responses. Systemic

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inflammation and poor nutritional status further reduce tissue repair capacity [5,6]. Therefore, while the Wagner classification remains the cornerstone of local disease severity assessment, additional biomarkers reflecting systemic inflammatory and nutritional status may provide complementary information regarding the overall disease burden.

The HALP score, consisting of hemoglobin, albumin, lymphocyte, and platelet parameters, reflects nutritional status, systemic inflammation, and immune response and was initially described as a prognostic marker in oncology [7]. Its prognostic value has also been demonstrated in nonmalignant conditions, including cardiovascular and inflammatory diseases [8,9]. Given the central roles of systemic inflammation, immune dysfunction, and malnutrition in diabetic foot disease, the HALP score may provide complementary information beyond local wound assessment by reflecting the patient's overall physiological status.

The primary aim of this prospective study was to investigate the association between the HALP score and diabetic foot disease severity according to the Wagner classification in patients presenting to the emergency department. We further evaluated whether the HALP score could provide complementary information beyond the Wagner classification by examining its discriminative performance for identifying advanced disease, comparing its performance with that of its individual laboratory components, and assessing its independent association with Wagner grade 5 disease after adjustment for clinically relevant covariates.

Materials and Methods

Study Design and Setting

This study was designed as a single-center, prospective, observational study conducted in the Emergency Medicine Department of a tertiary care center. Patient recruitment began on August 15, 2024, and continued for approximately one year until the predetermined sample size was reached. Adult patients aged ≥18 years who presented to the emergency department with clinical findings suggestive of diabetic foot disease were enrolled. This study was conducted after obtaining approval from the local ethics committee and in accordance with the Declaration of Helsinki. Written informed consent, including the patient's name, surname, and signature, was obtained from all patients or their legally authorized representatives.

Participant Selection

A total of 158 patients presenting to the emergency department with clinical findings suggestive of diabetic foot disease were assessed for eligibility. Based on the inclusion and exclusion criteria, 28 patients were excluded, and 130 patients constituted the final analysis cohort. The numbers of included and excluded patients, reasons for exclusion, and the patient selection process are presented in Figure 1.

The diagnosis of diabetic foot disease was established based on the presence of previously diagnosed type 2 diabetes mellitus together with pathological clinical findings in the foot, such as ulceration, infection, gangrene, or deformity, and confirmation that these findings were associated with peripheral neuropathy

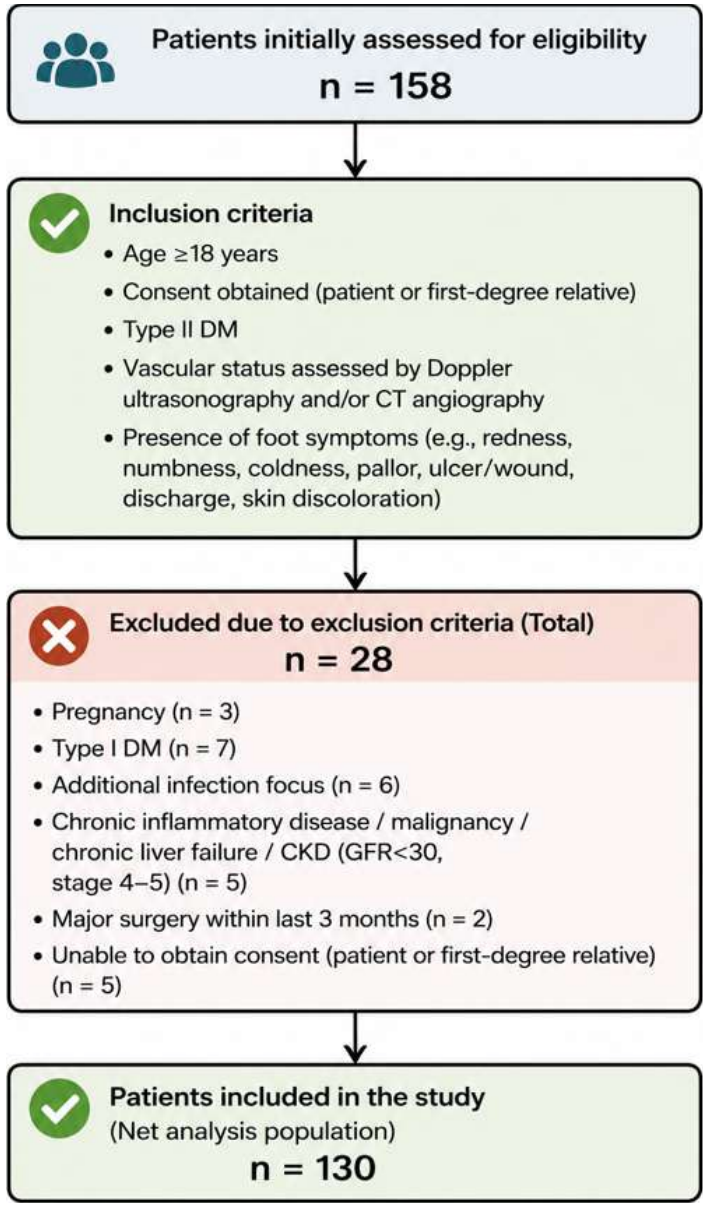

Figure 1. Flowchart of the patient selection. Of 158 patients assessed for eligibility, 28 were excluded based on predefined exclusion criteria, and 130 patients were ultimately included in the final analysis.

and/or peripheral vascular insufficiency. Peripheral neuropathy was assessed based on the presence of sensory loss and/or loss of reflexes on clinical examination. Peripheral vascular insufficiency was evaluated based on palpation of peripheral pulses and ischemic findings such as coldness of the foot and color changes. Patients who met the inclusion criteria were enrolled in the study, as shown in the study flowchart (Fig. 1).

Data Collection

The parameters evaluated in the study included patients' sociodemographic characteristics (age, sex, and comorbidities), vital signs (systolic and diastolic blood pressure, body temperature, heart rate, respiratory rate, and fingertip oxygen saturation [SpO_2]), Glasgow Coma Scale (GCS) score, complete blood count and biochemical parameters, as well as radiological imaging findings, including plain radiography, Doppler ultrasonography, and/or computed tomography angiography. Data on clinical outcome variables, including the need for amputation, in-hospital mortality, and 28-day mortality, were obtained from the hospital's electronic medical record system.

Definitions

The HALP score was calculated using hemoglobin (g/dL), albumin (g/dL), lymphocyte count (/mm^3), and platelet count (/mm^3) values according to the following formula: HALP=(hemoglobin×albumin×lymphocyte count)/platelet count [7]. Patients were classified according to the Wagner Diabetic Foot Classification as follows: Stage 0 (high-risk foot without an open ulcer), Stage 1 (superficial ulcer confined to the skin), Stage 2 (deep ulcer extending to the tendon, capsule, or bone), Stage 3 (deep ulcer accompanied by abscess, osteomyelitis, or severe infection), Stage 4 (localized gangrene involving part of the foot), and Stage 5 (extensive gangrene involving the entire foot) [3].

For ROC curve and multivariable logistic regression analyses, Wagner stage 5 was defined as advanced diabetic foot disease and compared with Wagner stages 1–4. Owing to the small number of patients in Wagner stages 1 and 2, these categories were combined for nonparametric comparisons across Wagner stages.

Sample Size

An a priori sample size calculation was performed in accordance with the planned statistical analyses. Assuming an effect size of 0.5, a two-sided alpha level of 0.05, and a statistical power of 80%, a minimum of 128 patients was calculated to be sufficient to meet the study objectives. The sample size calculation was performed using G*Power software (version 3.1).

Outcomes

The primary outcome of the study was the association between the HALP score and diabetic foot disease severity according to the Wagner classification. Secondary outcomes included the need for amputation, the level of amputation, in-hospital mortality, and 28-day mortality.

Statistical Analysis

All statistical analyses were performed using Jamovi software (The Jamovi Project, version 2.7.31.0). Data distribution was assessed using visual methods (histograms and Q–Q plots) and the Shapiro–Wilk test. Continuous variables were expressed as medians and interquartile ranges (IQRs), and categorical variables as numbers and percentages.

Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Continuous variables between two independent groups were compared using the Mann–Whitney U test, with rank-biserial correlation (r_rb) reported as the effect size when applicable. Differences in HALP scores across Wagner stages were analyzed using the Kruskal–Wallis test, and the effect size was reported as epsilon-squared (ε^2). When significant, pairwise comparisons were performed using Dunn's post hoc test with Bonferroni correction.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the ability of the HALP score and its individual components to discriminate Wagner grade 5 disease. The optimal cutoff value was determined using Youden's index. Areas under the ROC curves (AUCs) were compared using DeLong's test. To evaluate the independent association between the HALP score and Wagner grade 5 disease, multivariable binary logistic regression analysis was performed, including clinically relevant covariates. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. All tests were two-sided, and $p<0.05$ was considered statistically significant.

Results

The median age of the 130 patients included in the study was 66 years (59–72), and 65.4% were male. The most common comorbidities were hypertension (67.7%), coronary artery disease (41.5%), and heart failure (30.8%). Vital signs at emergency department presentation were generally stable, and the median Glasgow Coma Scale (GCS) score was 15 in all patients. Laboratory evaluations revealed marked hyperglycemia, elevated inflammatory markers, and low albumin levels. On radiological assessment, vascular pathology was detected on Doppler ultrasonography in 77.7% of patients, while findings consistent

with osteomyelitis were present on plain radiography in 75.4%. During follow-up, 48.5% of the patients underwent amputation; the rates of intensive care unit admission, in-hospital mortality, and 28-day mortality were 10.0%, 7.7%, and 6.9%, respectively. According to the Wagner classification, the median stage was 4 (3–5). The demographic, clinical, and laboratory characteristics of the study population are summarized in Table 1.

Table 1. Baseline demographic, clinical, laboratory, and imaging characteristics of the study population (n=130)

Age, years	66.0 (59.0–72.0)
Male sex, n (%)	85 (65.4)
Co-morbidities	
Hypertension, n (%)	88 (67.7)
Coronary artery disease, n (%)	54 (41.5)
Heart failure, n (%)	40 (30.8)
Chronic kidney disease, n (%)	28 (21.5)
Cerebrovascular disease, n (%)	12 (9.2)
Other comorbidities, n (%)	92 (70.8)
Vital signs	
Body temperature, °C	36.7 (36.5–37.1)
Heart rate, /min	85.0 (74.3–95.0)
Respiratory rate, /min	20.0 (20.0–22.0)
SpO_2, %	95.0 (93.0–96.0)
Systolic BP, mmHg	129 (116–142)
Diastolic BP, mmHg	73.5 (65.0–81.0)
GCS score	15 (15–15)
Laboratory parameters	
Glucose, mg/dL	220 (148–349)
Creatinine, mg/dL	1.21 (0.85–1.83)
eGFR, mL/min/1.73 m^2	62.5 (37.3–84.0)
Urea, mg/dL	55.1 (37.4–91.0)
C-reactive protein, mg/L	157 (54.0–256)
Procalcitonin, ng/mL	0.29 (0.08–1.14)
Albumin, g/L	32.9 (27.8–36.4)
WBC, $\times10^3$/µL	14.8 (9.66–18.5)
Hemoglobin, g/dL	11.3 (9.72–12.4)
Platelet count, $\times10^3$/µL	336 (234–418)
Neutrophil count, $\times10^3$/µL	12.0 (7.07–15.7)
Lymphocyte count, $\times10^3$/µL	1.32 (0.96–1.95)
Monocyte count, $\times10^3$/µL	0.89 (0.63–1.13)
Radiologic assessment	
Doppler ultrasound pathology present, n (%)	101 (77.7)
CT angiography performed, n (%)	21 (16.2)
Osteomyelitis on plain radiography, n (%)	98 (75.4)
Outcome	
Amputation during follow-up, n (%)	63 (48.5)
ICU admission, n (%)	13 (10.0)
In-hospital mortality, n (%)	10 (7.7)
28-day mortality, n (%)	9 (6.9)
Wagner classification	4 (3–5)

Continuous variables are presented as median (interquartile range), and categorical variables as number (%). Laboratory and vital signs correspond to measurements obtained at emergency department presentation. Radiologic variables indicate whether the examination was performed and/or pathology was detected, regardless of specific anatomical distribution. ICU admission refers to admission during the index hospitalization. GCS: Glasgow Coma Scale; CT: Computed tomography

According to Doppler ultrasonography findings, no vascular pathology was detected in 22.3% of patients, whereas the most frequently observed flow pattern was monophasic flow (51.5%); arterial occlusion was present in 13.8% of patients. The most commonly affected vessels on Doppler ultrasonography were the posterior tibial artery (23.8%) and the anterior tibial artery (16.9%). Computed tomography angiography was performed in 16.2% of patients, and arterial occlusion was detected in 18 patients (13.8% of the overall cohort). On CT angiography, occlusion was most frequently observed in the superficial femoral artery and anterior tibial artery segments. On plain radiographic examination, findings consistent with osteomyelitis were present in 75.4% of patients. Detailed radiological findings are presented in Table 2.

Wagner stage was significantly higher in patients who underwent amputation. The median Wagner stage was 4 (4–5) in the amputation group, compared with 3 (3–4) in patients without amputation ($p<0.001$). When the distribution across Wagner stages was examined, most patients who underwent amputation were classified as stages 4 and 5, whereas patients who did not undergo amputation were predominantly clustered in stage 3. No statistically significant difference was found in HALP scores between patients with and without amputation ($p=0.212$) (Table 3A).

Due to the very small number of patients in Wagner stage 1 (n=2) and the limited number in stage 2 (n=8), these two stages were combined into a single group (grades 1–2) for statistical comparisons. Overall, HALP scores differed significantly across Wagner groups (Kruskal–Wallis $H=27.9$, $df=3$, $p<0.001$), with a moderate effect

Table 2. Radiologic findings of diabetic foot patients (n=130)

Doppler ultrasound findings	
No vascular pathology	29 (22.3)
Monophasic flow	67 (51.5)
Biphasic flow	9 (6.9)
Triphasic flow	7 (5.4)
Arterial occlusion	18 (13.8)
Arterial segments involved on Doppler ultrasound*	
No arterial segment involvement	35 (26.9)
Common femoral artery	10 (7.7)
Superficial femoral artery	12 (9.2)
Deep femoral artery	1 (0.8)
Popliteal artery	7 (5.4)
Posterior tibial artery	31 (23.8)
Anterior tibial artery	22 (16.9)
Dorsalis pedis artery	12 (9.2)
CT angiography findings	
CT angiography performed	21 (16.2)
Arterial occlusion detected	18 (13.8)
Affected vessels on CT angiography*	
Superficial femoral artery	5 (3.8)
Popliteal artery	2 (1.5)
Anterior tibial artery	6 (4.6)
Posterior tibial artery	4 (3.1)
Dorsalis pedis artery	1 (0.8)
No arterial segment involvement	3 (2.3)
Plain radiography findings	
Osteomyelitis present	98 (75.4)

Values are presented as number (%). Percentages are calculated based on the total study population (N = 130). Percentages may exceed 100% as multiple vascular segments could be involved in the same patient. CT: Computed tomography.

Table 3. Distribution of Wagner classification by amputation status and post-hoc pairwise comparisons of HALP scores across Wagner grades

A) Wagner classification according to amputation status (n=130)

Wagner grade	No amputation (n=67)	Amputation (n=63)	Total n (%)
Grade 1	2 (3.0%)	0 (0.0%)	2 (1.5%)
Grade 2	8 (11.9%)	0 (0.0%)	8 (6.2%)
Grade 3	28 (41.8%)	7 (11.1%)	35 (26.9%)
Grade 4	21 (31.3%)	28 (44.4%)	49 (37.7%)
Grade 5	8 (11.9%)	28 (44.4%)	36 (27.7%)
Wagner classification, median (IQR)	3 (3–4)	4 (4–5)	<0.001

B) Dunn post-hoc pairwise comparisons of HALP scores across Wagner groups*

Wagner group comparison	z	Adjusted p (Bonferroni)
Grade 1–2 vs Grade 3	0.546	1.000
Grade 1–2 vs Grade 4	−0.305	1.000
Grade 1–2 vs Grade 5	2.848	0.026
Grade 3 vs Grade 4	−1.363	1.000
Grade 3 vs Grade 5	3.464	0.003
Grade 4 vs Grade 5	5.120	< 0.001

Values are presented as n (%) unless otherwise stated. Percentages in the "No amputation" and "Amputation" columns are calculated within each amputation group, whereas total percentages are calculated based on the overall study population (n=130). Wagner classification is presented as median (IQR) and compared between amputation groups using the Mann–Whitney U test. *Pairwise comparisons were performed using Dunn's test with Bonferroni correction following a significant Kruskal–Wallis test for HALP scores across Wagner grades. Wagner grades 1 (n=2) and 2 (n=8) were combined due to small sample sizes. Kruskal–Wallis H=27.9, df=3, p<0.001, ε^2=0.216

size (ε^2=0.216). Bonferroni-corrected Dunn post hoc analysis demonstrated that HALP scores in patients with Wagner grade 5 disease were significantly lower than those in patients with grades 1–2, 3, and 4 (adjusted p=0.026, p=0.003, and p<0.001, respectively). No statistically significant differences in HALP scores were observed among grades 1–2, 3, and 4 (Table 3B).

To further evaluate the discriminatory performance of the HALP score, receiver operating characteristic (ROC) curve analyses were performed to identify Wagner grade 5 disease. The HALP score demonstrated the highest discriminative performance among the evaluated laboratory markers, with an AUC of 0.790 (95% CI, 0.712–0.868; p<0.001). Albumin also showed good discriminative ability (AUC=0.757, 95% CI, 0.664–0.850; p<0.001), whereas platelet count, lymphocyte count, and hemoglobin demonstrated lower AUC values (Table 4, Figure 2). The optimal HALP cutoff value was 15.09, corresponding to a sensitivity of 88.9% and a specificity of 61.7%.

Pairwise comparisons of ROC curves using DeLong's test demonstrated that the HALP score had significantly greater discriminatory performance than hemoglobin (ΔAUC=0.182, p<0.001), lymphocyte count (ΔAUC=0.177, p<0.001), and platelet count (ΔAUC=0.153, p=0.016), whereas no statistically significant difference was observed between the HALP score and

Table 4. Receiver operating characteristic (ROC) analysis of the HALP score and its individual components for identifying Wagner grade 5 diabetic foot disease

Marker	AUC	95% CI	p
HALP	0.790	0.712–0.868	<0.001
Albumin	0.757	0.664–0.850	<0.001
Platelet	0.637	0.529–0.746	0.013
Lymphocyte	0.613	0.501–0.725	0.048
Hemoglobin	0.607	0.499–0.715	0.051

AUC: Area under the receiver operating characteristic (ROC) curve; CI: Confidence interval. ROC analyses were performed to evaluate the discriminatory performance of the HALP score and its individual components for identifying Wagner grade 5 disease. P values indicate the statistical significance of each AUC compared with the null hypothesis (AUC=0.50).

albumin (ΔAUC=0.033, p=0.447) (Table 5). Among the individual components, albumin demonstrated the highest discriminatory performance, whereas the composite HALP score showed the greatest overall discriminative performance.

To account for potential confounding factors, a multivariable logistic regression analysis was performed including the HALP score, age, chronic kidney disease, and C-reactive protein. The overall model was statistically significant (Omnibus χ^2=37.7, p<0.001; Nagelkerke R^2=0.364). After adjustment for these clinically relevant covariates, lower HALP scores remained independently associated with Wagner grade 5 disease (adjusted OR=0.857, 95% CI, 0.794–0.925; p<0.001). Chronic kidney disease was also independently associated with Wagner grade 5 disease (adjusted OR=0.245, 95% CI, 0.074–0.813; p=0.022), whereas age and C-reactive protein were not significantly associated with the outcome (Table 6).

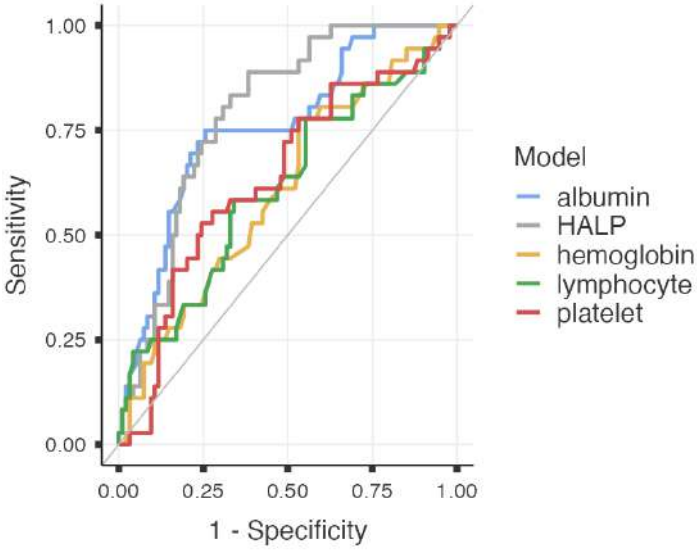

Figure 2. Receiver operating characteristic (ROC) curves of the HALP score and its individual components for identifying Wagner grade 5 diabetic foot disease.

Table 5. Pairwise comparison of the ROC curves of the HALP score and its individual components using DeLong's test

Comparison	ΔAUC	95% CI	z	p
HALP vs Hemoglobin	0.182	0.077 to 0.288	3.401	<0.001
HALP vs Albumin	0.033	–0.052 to 0.118	0.761	0.447
HALP vs Lymphocyte	0.177	0.076 to 0.277	3.449	<0.001
HALP vs Platelet	0.153	0.028 to 0.277	2.404	0.016

ΔAUC indicates the difference in area under the receiver operating characteristic (ROC) curve between the HALP score and each individual component. Pairwise comparisons were performed using DeLong's test. Positive ΔAUC values indicate superior discriminatory performance of the HALP score.

Table 6. Multivariable logistic regression analysis for factors independently associated with Wagner grade 5 diabetic foot disease

Variable	Adjusted OR	95% CI	p
HALP	**0.857**	**0.794–0.925**	**<0.001**
Age	1.004	0.958–1.052	0.867
Chronic kidney disease	0.245	0.074–0.813	0.022
C-reactive protein	1.002	0.998–1.006	0.319

OR: Odds ratio; CI: Confidence interval; AIC: Akaike information criterion. Variables entered into the multivariable logistic regression model were HALP, age, chronic kidney disease, and C-reactive protein. The overall model was statistically significant (Omnibus χ^2=37.7, df=4, p<0.001), with a Nagelkerke R^2 of 0.364 (AIC=126; n=130).

Additional analyses were performed to explore the association between the HALP score and mortality outcomes. Median HALP scores were lower among patients who died during hospitalization or within 28 days than among survivors; however, these differences did not reach statistical significance (Mann–Whitney U=452, p=0.197 and Mann–Whitney U=363, p=0.097, respectively).

Discussion

When evaluating patients with diabetic foot disease in the emergency department, rapid assessment of disease severity is essential for appropriate risk stratification and timely clinical decision-making. In the present study, lower HALP scores were significantly associated with increasing diabetic foot disease severity, with the most pronounced decline observed in patients with Wagner grade 5 disease. ROC analysis further demonstrated that the HALP score showed good discriminative performance for identifying Wagner grade 5 disease and outperformed most of its individual components, while multivariable logistic regression

confirmed that this association remained significant after adjustment for clinically relevant covariates. Rather than serving as a substitute for the Wagner classification, which primarily reflects local tissue involvement, the HALP score may provide complementary information by reflecting the patient's systemic inflammatory and nutritional status.

In this study, a substantial proportion of patients exhibited elevated inflammatory markers, low albumin levels, and radiological evidence of significant vascular pathology and osteomyelitis. These findings are consistent with previous studies reporting that advanced diabetic foot disease is frequently accompanied by systemic inflammation and malnutrition [2,10]. Likewise, high rates of osteomyelitis and peripheral arterial disease have been reported in patients managed at tertiary referral centers, and our radiological findings are consistent with these observations [11,12]. Nearly half of the patients underwent amputation, and the median Wagner stage was 4, indicating that our cohort predominantly consisted of patients with advanced diabetic foot disease. This likely reflects the tertiary referral nature of our institution, where patients are commonly referred after unsuccessful treatment elsewhere or because of severe disease requiring specialized care. Previous studies have consistently demonstrated that higher Wagner stages are associated with increased rates of amputation and mortality, particularly in patients with Wagner grades 4 and 5 [4,13]. In contrast, substantially lower amputation rates have been reported in centers with well-established multidisciplinary diabetic foot programs [14]. Therefore, our findings should primarily be interpreted within the context of patients with advanced diabetic foot disease managed in tertiary care settings, where rapid risk stratification and early multidisciplinary intervention remain particularly important.

The key components of the HALP score—hemoglobin, albumin, lymphocytes, and platelets—play critical roles in the pathophysiology of diabetic foot disease. Hemoglobin is a fundamental parameter that determines the oxygen-carrying capacity of the blood; anemia may impair adequate oxygen delivery to tissues, leading to local hypoxia, which can trigger an inflammatory response and thereby exacerbate disease severity. In a meta-analysis, a significant association was demonstrated between anemia and diabetic foot ulcers, and a one-unit decrease in hemoglobin level was reported to markedly increase the risk of diabetic foot ulceration [15]. Albumin is one of the most important indicators of nutritional status and plays a critical role in protein synthesis required for wound healing, immune function, and tissue repair [16]. Moreover, one study demonstrated that an albumin level of ≤28 g/L in patients with pneumonia was associated with a more severe and potentially fatal course of infection [17]. Malnutrition has been reported in 15–62% of patients with diabetic foot ulcers, and by delaying wound healing, it increases the risk of amputation by approximately threefold [18]. Lymphocytes are key components of the adaptive immune response and play a critical role in host defense against infections. A reduction in lymphocyte count may weaken the immune response to infection and thereby contribute to accelerated disease progression in diabetic foot disease, particularly in clinical presentations complicated by infection [19]. Platelets play a central role in hemostasis and endothelial function and help prevent infection by initiating blood coagulation during the early phase of wound healing. In patients with diabetic foot disease, a decrease in platelet count may adversely affect the wound-healing process and contribute to weakened defense against infection. In the study by Yang et al. [20], a linear relationship was demonstrated between platelet count and wound-healing outcomes, and a low platelet count was reported to predict poorer wound-healing outcomes. In addition, platelets regulate the inflammatory response and support tissue repair by secreting proinflammatory cytokines and growth factors. By integrating these parameters into a single composite index, the HALP score provides a more comprehensive reflection of nutritional status, systemic inflammation, immune competence, and hemostatic function than any individual component alone.

Within this framework, we further evaluated the relationship between the HALP score and Wagner stage. Post hoc analyses demonstrated that HALP scores remained comparable across Wagner grades 1–4 but declined significantly in patients with Wagner grade 5 disease. These findings suggest that the HALP score is more useful for identifying end-stage diabetic foot disease than for discriminating incremental differences across intermediate Wagner stages. Consistent with this observation, ROC analysis demonstrated good discriminative performance of the HALP score for identifying Wagner grade 5 disease. Furthermore, comparison with its individual components showed that the HALP score outperformed hemoglobin, lymphocyte count, and platelet count while demonstrating discriminative performance comparable to that of albumin alone. These findings support the concept that combining multiple laboratory parameters into a composite index may better reflect the complex systemic alterations accompanying advanced diabetic foot disease than most individual biomarkers. Previous studies have similarly reported that lower HALP scores are associated with more advanced Wagner stages and worse clinical outcomes in diabetic foot disease [21–23].

In agreement with previous reports, a strong association was observed between the Wagner classification and the need for amputation in our cohort, reinforcing its established role

in reflecting local tissue destruction and guiding surgical management [13,24]. The significantly higher Wagner stages among patients who underwent amputation further support the clinical utility of the Wagner classification in identifying patients requiring surgical intervention. In contrast, HALP scores did not differ significantly between patients with and without amputation, suggesting that the HALP score should not be interpreted as a direct predictor of surgical intervention. Likewise, no significant association was observed between the HALP score and short-term mortality, although median HALP values tended to be lower among nonsurvivors. Nevertheless, our stage-based analyses demonstrated that HALP scores declined markedly in patients with Wagner grade 5 disease, and multivariable logistic regression further confirmed that this association remained significant after adjustment for clinically relevant covariates. Taken together, these findings suggest that the HALP score primarily reflects the systemic disease burden accompanying advanced diabetic foot disease rather than individual clinical outcomes such as amputation or short-term mortality. From a practical perspective, the HALP score can be readily calculated from routine laboratory parameters obtained during the initial emergency department evaluation and therefore requires no additional testing, cost, or equipment. Accordingly, it may provide complementary information regarding the patient's systemic inflammatory burden and nutritional status when interpreted alongside the Wagner classification. Therefore, rather than replacing the Wagner classification, the HALP score may serve as a complementary biomarker for identifying patients with advanced diabetic foot disease when interpreted alongside established clinical assessment tools.

Study Limitations

This study has several limitations. First, the HALP score was calculated using laboratory parameters obtained only at emergency department presentation and therefore does not reflect dynamic changes during the course of the disease. Second, although multivariable analyses were performed to adjust for selected clinically relevant covariates, several important factors known to influence diabetic foot disease severity, including diabetes duration, glycemic control (e.g., HbA1c), smoking status, peripheral neuropathy, previous diabetic foot disease, and prior amputation history, were unavailable and could not be incorporated into the analyses. Therefore, residual confounding cannot be excluded. In addition, the study population predominantly consisted of patients with advanced diabetic foot disease treated at a tertiary referral center, while Wagner grades 1 and 2 were underrepresented, which may limit the generalizability of our findings to patients with less severe disease. Future multicenter studies including primary care, secondary care, and outpatient diabetic foot clinics are warranted to evaluate the clinical utility of the HALP score across the full spectrum of diabetic foot disease. Finally, the decision to perform amputation was influenced by multiple clinical factors, including local wound characteristics, vascular status, and multidisciplinary clinical judgment, which could not be fully standardized. Nevertheless, the prospective study design and inclusion of consecutive patients presenting to the emergency department provide valuable insight into the potential role of the HALP score as a complementary biomarker in the initial assessment of diabetic foot disease.

Conclusion

In this prospective study, lower HALP scores were associated with advanced diabetic foot disease, with the most pronounced decline observed in patients with Wagner grade 5 disease. Although the HALP score was not associated with amputation or short-term mortality, it remained independently associated with Wagner grade 5 disease after adjustment for clinically relevant covariates. Rather than replacing the Wagner classification, the HALP score may serve as a complementary biomarker reflecting systemic inflammatory burden, nutritional status, and physiological reserve. Given that it can be readily calculated from routine laboratory parameters, the HALP score may assist in the initial assessment of patients presenting to the emergency department with diabetic foot disease. Further multicenter studies with larger and more diverse patient populations are warranted to validate these findings and better define the clinical role of the HALP score in diabetic foot disease.

Ethics Committee Approval: This study was approved by The Ankara Etlik City Hospital Clinical Research Ethics Committee (Approval no: 2024-696 – 31.07.2024)

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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ORIGINAL RESEARCH

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Clinical Characteristics and Outcomes of Patients Admitted to the Ophthalmology Department Through the Emergency Department: A Tertiary Hospital Experience

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Abstract

Objective: To analyze the clinical characteristics, indications for hospitalization, surgical requirements, and visual outcomes of patients admitted from the emergency department to the ophthalmology department of a tertiary hospital, with a particular focus on ocular trauma and hospitalization patterns.

Materials and Methods: This retrospective study included 105 patients admitted from the emergency department to the ophthalmology department between April 2022 and April 2025. Demographic and clinical characteristics, admission diagnoses, ocular examination findings at admission and discharge, length of hospital stay, surgical interventions, and systemic steroid use were recorded. Patients were categorized according to trauma status (trauma vs. non-trauma), trauma type (blunt, penetrating, or chemical), and length of hospital stay.

Results: The mean age was 50.4±22.9 years, and 66% of patients were male. The median hospital stay was 3 days, with 46.6% of patients hospitalized for >3 days. Ocular trauma accounted for 53.4% of admissions, with blunt trauma (54.5%) being the most common injury type, followed by penetrating trauma (38.2%). The leading admission diagnoses were retinal detachment, penetrating ocular trauma, and eyelid laceration. Trauma patients were significantly younger and more likely to have left-eye involvement than non-trauma patients. Surgical intervention was required in 69.9% of all cases. Visual acuity improved in both the trauma and non-trauma groups, with greater improvement observed in blunt trauma than in penetrating trauma. Longer hospitalization was associated with poorer baseline visual acuity.

Conclusion: Ocular trauma was the leading cause of hospitalization from the emergency department, with blunt trauma representing the most common injury type. Retinal detachment was the most frequent non-traumatic indication for hospitalization, and nearly 70% of patients required surgical intervention.

Keywords: Emergency department, hospitalization, ocular trauma, retinal detachment, visual acuity

Introduction

Ophthalmic emergencies are a group of diseases that can cause permanent vision loss and affect quality of life if not diagnosed and treated early [1]. Retinal detachment, endophthalmitis, and traumatic ocular injuries are among such diseases. For these patients, immediate referral from the emergency department to an ophthalmologist is important [2,3]. Timely diagnosis and appropriate management are essential to optimize visual outcomes [4,5].

Ocular trauma is one of the leading causes of monocular blindness worldwide [6,7]. Ocular injuries account for 10–15% of all ophthalmic diseases and represent an important preventable cause of visual impairment. Ocular trauma includes blunt, penetrating, chemical, and thermal injuries and is particularly common in young males following work-related, traffic, and sports accidents [8]. Visual prognosis after ocular trauma is associated with the type and severity of injury, as well as the timing of treatment, with both blunt and penetrating trauma carrying a substantial risk of permanent visual loss [9]. Furthermore, ocular trauma results not

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only in individual disability but also in significant socioeconomic losses.

Ophthalmic emergency services may be influenced by global health crises such as the COVID-19 pandemic. During the pandemic, changes in healthcare utilization and restrictions on access to medical services altered the epidemiology of ophthalmic emergency presentations [10–12]. To minimize the influence of these temporary changes and better reflect routine clinical practice, the present study included only patients admitted after this period. The aim of this study was to evaluate the reasons for admission from the emergency department to the ophthalmology department of a tertiary hospital, as well as trauma characteristics, visual outcomes, surgical requirements, and the impact of trauma presence and type on clinical outcomes.

Materials and Methods

This retrospective, single-center, hospital-based observational study was approved by the Ethics Committee of Göztepe Prof. Dr. Süleyman Yalçın City Hospital (approval no. 20205/0014). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The study included 105 patients aged 1–80 years who presented to the emergency department of a tertiary hospital and were subsequently hospitalized in the ophthalmology department between April 2022 and April 2025. Patient information was obtained from the hospital automation system. Patients with incomplete medical records and those requiring hospitalization after previous ocular surgery were excluded from the study. In cases of multiple hospital admissions, only the first admission was included.

Patients presenting to the emergency department with ocular complaints were initially evaluated by an emergency physician and subsequently referred for ophthalmology consultation. The patients were examined by an ophthalmology resident using the Snellen chart to determine best-corrected visual acuity (BCVA) and underwent intraocular pressure (IOP) measurement, slit-lamp biomicroscopy, and a detailed dilated fundus examination. Following evaluation by an ophthalmologist, patients requiring surgery or those unsuitable for outpatient follow-up were admitted to the ophthalmology department. Demographic characteristics, trauma types, ocular diagnoses, and data regarding surgical treatment and systemic steroid therapy were retrieved from the hospital database. Patients were categorized according to trauma status, trauma type (blunt, penetrating, or chemical), and length of hospital stay (≤3 days or >3 days).

Statistical Analysis

Research data were analyzed using SPSS version 26.0 (Statistical Package for the Social Sciences, Chicago, IL, USA). The normality of the data was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Continuous variables were compared using the independent-samples t test or Mann–Whitney U test, categorical variables using the chi-square or Fisher's exact test, and admission and discharge values using the paired t test or Wilcoxon signed-rank test, as appropriate. A p value of <0.05 was considered statistically significant.

Results

A total of 105 patients were included, with a mean age of 50.4±22.9 years, and 66% were male. The median hospital stay was 3 days, and 46.6% of patients were hospitalized for >3 days. Ocular trauma accounted for 53.4% of admissions, with blunt trauma representing the most common injury type. The leading

Table 1. Demographic and clinical characteristics of hospitalized ophthalmology patients

Age (years) (mean±SD)	50.4±22.9
Male gender (n, %)	68 (66%)
Duration of hospitalisation, days, median (range)	3 (1-80)
Duration of hospitalisation >3 days (n, %)	48 (46.6%)
Left eye (n, %)	61 (59.2%)
Surgical intervention (n, %)	72 (69.9%)
Systemic steroid therapy (n, %)	10 (9.7%)
Ocular trauma (n, %)	55 (53.4%)
Blunt trauma	30 (54.5%)
Penetrating trauma	21 (38.2%)
Chemical trauma	4 (7.3%)
Admission diagnoses (n, %)	
Retinal detachment	20 (19.4%)
Perforation	18 (17.5%)
Eyelid laceration	15 (14.6%)
Rupture	11 (10.7%)
Keratitis/Corneal abscess	10 (9.7%)
Endophthalmitis	6 (5.8%)
Corneal oedema	4 (3.9%)
Uveitis	4 (3.9%)
Non-arteritic ischaemic optic neuropathy	4 (3.9%)
Preseptal/orbital cellulitis	3 (2.9%)
Intraocular foreign body	2 (1.9%)
Retinitis	2 (1.9%)
Hyphaema	2 (1.9%)
Orbital myositis	1 (1%)
Orbital inflammatory syndrome	1 (1%)
Retinal artery occlusion	1 (1%)
Orbital compartment syndrome	1 (1%)

SD: Standard deviation.

Table 2. Comparison of demographic and clinical features between patients with and without ocular trauma

Variables	Ocular Trauma (+) (n=55)	Ocular Trauma (-) (n=48)	p
Age (years) (mean±SD)	45.6±23.6	55.8±21.1	**0.024**
Male gender (n, %)	39 (70.9%)	29 (60.4%)	0.262
Hospitalisation duration, days, median (range)	3 (1-58)	3.5 (1-80)	0.114
Hospitalisation period >3 days (n, %)	24 (43.6%)	24 (50%)	0.518
Left eye (n, %)	39 (70.9%)	22 (45.8%)	**0.010**
Surgical intervention (n, %)	48 (87.3%)	24 (50%)	**<0.001**
Systemic steroid therapy (n, %)	3 (5.5%)	7 (14.6%)	0.119
BCVA (logMAR) (mean±SD) At admission At discharge Change Within-group p value	 1.5±1.13 1.3±1.11 -0.2±0.58 **0.019**	 1.7±1.02 1.45±1.08 -0.24±0.92 **0.049**	 0.556 0.456 0.831
IOP (mmHg) (mean±SD) At admission At discharge Change Within-group p value	 14.1±6.1 14.0±2.4 -0.02±5.62 0.681	 18.1±8.2 16±4.3 -2.02±7.63 0.105	 **0.001** **0.031** 0.293

Values are presented as mean±SD, median (range), or n (%). Between-group comparisons were performed using the independent-samples t-test, Mann–Whitney U test, chi-square test or Fisher's exact test, as appropriate. Within-group comparisons of BCVA and IOP were performed using the Wilcoxon signed-rank test. BCVA: best-corrected visual acuity; IOP: intraocular pressure; SD: standard deviation.

admission diagnoses were retinal detachment, penetrating ocular trauma, and eyelid laceration. Overall, 69.9% of patients required surgical intervention (Table 1).

Compared with non-trauma patients, trauma patients were significantly younger (p=0.024), more frequently had left-eye involvement (p=0.010), and underwent surgical intervention more often (p<0.001). Visual acuity improved significantly in both

Table 3. Comparison of demographic and clinical parameters between blunt and penetrating ocular trauma

Variables	Blunt trauma (n=30)	Penetrating trauma (n=21)	p
Age (years) (mean±SD)	50.1±25.1	41.3±21.9	0.202
Male gender (n, %)	18 (60)	18 (85.7)	0.047
Hospitalisation duration, days, median (range)	3 (1-16)	2 (1-23)	0.923
Hospitalisation period >3 days (n, %)	14 (46.7)	8 (38.1)	0.543
Left eye (n, %)	22 (73.3)	14 (66.7)	0.607
Surgical intervention (n,%)	26 (86.7)	21 (100)	0.134
Systemic steroid therapy (n, %)	1 (3.3)	2 (9.5)	0.561
BCVA (logMAR) (mean±SD) At admission At discharge Change Within-group p value	 1.43±1.22 1.27±1.14 -0.16±0.4 0.012	 1.60±1.07 1.52±1.09 -0.09±0.65 0.645	 0.685 0.434 0.582
IOP (mmHg) (mean±SD) At admission At discharge Change Within-group p value	 15.3±6.9 14±2.7 -1.33±6.29 0.080	 12±4.9 14.1±2.2 2.10±4.36 0.039	 0.036 0.930 0.026

Values are presented as mean±SD, median (range), or n (%). Between-group comparisons were performed using the independent-samples t-test, Mann–Whitney U test, chi-square test, or Fisher's exact test, as appropriate. Within-group comparisons of BCVA and IOP were performed using the Wilcoxon signed-rank test. BCVA: best-corrected visual acuity; IOP: intraocular pressure; SD: standard deviation.

Table 4. Comparison of visual acuity and intraocular pressure according to length of hospital stay

Variables	Hospitalisation period ≤ 3 days (n=55)	Hospitalisation period >3 days (n=48)	p
BCVA (logMAR) (mean±SD)			
At admission	1.34±1.05	1.88±1.05	0.006
At discharge	1.30±1.10	1.45±1.09	0.169
Change	-0.04±0.72	-0.42±0.74	0.057
Within-group p value	0.523	<0.001	
IOP (mmHg) (mean±SD)			
At admission	16.1±6.8	15.8±8.1	0.142
At discharge	15.6±3.4	14.3±3.7	0.045
Change	-0.47±6.77	-1.5±6.58	0.326
Within-group p value	0.911	0.260	

Values are presented as mean±SD. Between-group comparisons were performed using the Mann–Whitney U test. Within-group comparisons were performed using the Wilcoxon signed-rank test. BCVA: best-corrected visual acuity; IOP: intraocular pressure; SD: standard deviation.

groups, whereas intraocular pressure was lower in trauma patients at both admission and discharge. The comparison between trauma and non-trauma patients is presented in Table 2.

Among trauma patients, visual acuity improved significantly in the blunt trauma group (p=0.012), whereas no significant improvement was observed in the penetrating trauma group (p=0.645). Penetrating trauma was more common in males (p=0.047) and was associated with a statistically significant increase in intraocular pressure from admission to discharge (p=0.039). The demographic and clinical characteristics of patients with blunt and penetrating trauma are summarized in Table 3.

Patients hospitalized for >3 days had poorer baseline visual acuity (p=0.006) and showed significant visual improvement by discharge (p<0.001). No significant changes in intraocular pressure were observed during hospitalization in either group (p=0.911 and p=0.260, respectively). The comparison according to length of hospital stay is shown in Table 4.

Discussion

In this study, we evaluated the epidemiological and clinical characteristics of patients admitted to the ophthalmology department from the emergency department of a tertiary hospital. Ocular trauma was the leading cause of hospitalization, with blunt trauma representing the most common injury type. Retinal detachment was the most frequent non-traumatic indication for admission, and approximately 70% of patients required surgical intervention. These findings highlight the broad spectrum of ophthalmic emergencies requiring inpatient management and emphasize the substantial burden of trauma-related conditions on ophthalmic emergency services.

The predominance of ocular trauma, particularly among young males, is consistent with previous studies. Agrawal et al. [13] and Omotoye et al. [5] similarly reported a higher risk of ocular trauma in males. Likewise, Krishnaiah et al. [14] demonstrated that ocular trauma occurs more frequently in males and represents an important cause of visual impairment. Pandemic-related studies have shown that, although healthcare utilization and emergency attendance patterns changed substantially during the COVID-19 pandemic, ocular trauma remained one of the leading reasons for emergency ophthalmic care [10–12]. Similar to these reports, ocular trauma was the leading cause of hospitalization in our post-pandemic cohort. However, unlike the pandemic-era study by Şahin Vural et al. [10], which reported pandemic-related changes in injury mechanisms and shorter hospital stays without significant differences in clinical characteristics or surgical outcomes, our study reflects routine post-pandemic emergency practice and demonstrates that ocular trauma continues to constitute the major indication for ophthalmic hospitalization. The higher risk observed in males is likely related to greater occupational exposure and participation in outdoor activities. In addition, the more frequent involvement of the left eye in our cohort may reflect the tendency of individuals to protect their dominant eye, as suggested in previous studies [8,15].

Blunt trauma was the most common trauma subtype, accounting for 54.5% of all ocular trauma cases. This proportion was comparable to the 54% reported by Maurya et al. [8] but higher than the 28% reported by Rahman et al. [16]. Consistent with the generally more favorable prognosis of blunt trauma, significant visual improvement was observed after treatment in this group, whereas improvement was limited in patients with penetrating trauma. The poorer visual recovery associated with penetrating trauma is likely attributable to more extensive damage to intraocular structures at presentation. Chemical injuries accounted for only 7.3% of trauma cases in our cohort, indicating that they represented a relatively uncommon cause of hospitalization.

Approximately 70% of patients in our cohort required surgical intervention. This rate is comparable to the 77% reported by May et al. [17] in a cohort of 8,952 trauma patients in the United States but higher than the 43% reported by Sahu et al. [9] in a prospective study involving 180 patients. The high proportion of patients requiring surgery underscores the severity of ophthalmic conditions necessitating hospitalization and highlights the importance of timely surgical management, particularly in vision-threatening conditions such as retinal detachment and penetrating ocular trauma. Likewise, the timing of presentation and treatment is an important determinant of visual outcomes in ophthalmic emergencies, and previous studies have shown that earlier intervention is associated with a better visual prognosis [5,18]. However, owing to the retrospective design of our study, we were unable to determine the interval between symptom onset and treatment or the duration of patients' stay in the emergency department before ophthalmology evaluation. This should be considered when interpreting our findings.

Non-traumatic conditions also represented an important indication for hospitalization, with retinal detachment being the most common non-traumatic diagnosis in our cohort. Previous studies have similarly identified retinal detachment, ocular infections, and uveitis as the leading non-traumatic causes requiring emergency ophthalmic admission [19,20]. These findings emphasize that, in addition to ocular trauma, non-traumatic ophthalmic emergencies constitute a substantial proportion of inpatient admissions and require timely recognition and management. Patients hospitalized for more than 3 days had poorer baseline visual acuity but demonstrated significant visual improvement during follow-up. This finding is consistent with previous studies reporting that initial visual acuity is an important prognostic factor for visual outcomes [5,18,21,22]. Similarly, Kang et al. [23] reported that visual acuity may predict the need for hospitalization among patients presenting to the emergency department.

Study Limitations

The main limitations of this study include its retrospective design, single-center setting, relatively small sample size, and variability in hospitalization indications and duration according to clinician judgment. In addition, only patients requiring hospitalization were included; therefore, our findings may not be generalizable to all ophthalmic emergency presentations. As a tertiary referral center, the distribution of diagnoses may also have been influenced by referral patterns. Despite these limitations, our study provides real-world data on the epidemiological and clinical characteristics of patients requiring hospitalization from the emergency department to an ophthalmology service and contributes contemporary evidence to the existing literature.

Conclusion

In conclusion, ocular trauma was the leading cause of hospitalization, predominantly affecting young males, with blunt trauma representing the most common injury type. Retinal detachment was the most frequent non-traumatic indication for admission, and a high proportion of patients required surgical intervention, reflecting the severity of conditions requiring inpatient ophthalmic care. These findings provide contemporary data on patients requiring hospitalization for ophthalmic emergencies and may help guide emergency ophthalmic care.

Main Points

- Ocular trauma was the leading cause of hospitalization from the emergency department, with blunt trauma representing the most common injury type.
- Retinal detachment was the most frequent non-traumatic indication for hospitalization and, together with ocular trauma, accounted for most emergency admissions.
- Approximately 70% of hospitalized patients required surgical intervention, highlighting the severity of ophthalmic emergencies requiring inpatient care.
- Poor baseline visual acuity was associated with longer hospitalization, suggesting its potential value as a marker of clinical severity.

Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Göztepe Prof. Dr. Süleyman Yalçın City Hospital (decision date: 29 May 2025; approval no. 20205/0014).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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ORIGINAL RESEARCH

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Prevalence of Potentially Inappropriate Medication Use and Polypharmacy Among Older Adults Presenting to the Emergency Department

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Abstract

Objective: To determine the prevalence of polypharmacy and potentially inappropriate medication use (IMU) among older adults presenting to the emergency department (ED), identify demographic and clinical factors associated with IMU, and compare the performance of three validated screening tools in this setting.

Materials and Methods: This prospective, single-center observational study was conducted in the ED of a tertiary training and research hospital over a three-month period beginning on March 1, 2022. Consecutive patients aged 65 years and older who were triaged as green or yellow, used at least one systemic medication, and had a complete, verifiable medication history were enrolled. Each medication list was independently screened using the 2019 American Geriatrics Society Beers Criteria, the STOPP version 2 criteria, and the Turkish TIME-to-STOP/TIME-to-START criteria. Agreement between the tools was quantified using Cohen's kappa. Associations with IMU and hospitalization were examined using the chi-square or Fisher's exact test, the independent-samples t-test or Mann–Whitney U test, and multivariable logistic regression.

Results: A total of 203 patients were included (mean age, 76.5±7.4 years). Polypharmacy, defined as the use of five or more medications, was present in 94.1% of patients, with a mean of seven medications per patient. At least one potentially inappropriate medication was identified in 100 patients (49.3%) by at least one tool. The STOPP criteria identified the highest proportion (69/203, 34.0%), followed by the Beers Criteria (54/203, 26.6%) and the TIME criteria (31/203, 15.3%); only one patient (0.5%) was identified by all three tools. Agreement was low to moderate between Beers and STOPP (κ=0.316) and poor between Beers and TIME (κ=−0.182) and between STOPP and TIME (κ=−0.039). Proton pump inhibitors, antipsychotics, and non-steroidal anti-inflammatory drugs were the medication classes most frequently flagged. Coronary artery disease was associated with IMU in the unadjusted analysis (p=0.03). The frequency of IMU did not differ between hospitalized and discharged patients (53.5% versus 58.0%; p=0.544), and IMU positivity by any tool was not independently associated with hospitalization after multivariable adjustment.

Conclusion: Polypharmacy and potentially inappropriate medication use are highly prevalent among older adults presenting to the ED, but the three screening tools identified substantially different patient groups. The tools should be regarded as complementary rather than interchangeable, and structured medication review remains necessary alongside any single instrument.

Keywords: Aged, Deprescribing, Emergency service, Hospital, Inappropriate prescribing, Polypharmacy, Potentially inappropriate medication list

Introduction

The global population is aging rapidly, including in Türkiye. As of 1 July 2025, the population aged 65 years and older in Türkiye reached approximately 9,583,059 individuals, corresponding to 11.1% of the total population according to estimates and demographic data from the Turkish Statistical Institute. Population projections produced by TurkStat indicate that, if current demographic trends persist, the share of the population aged 65 years and older is expected to rise further in the coming decades. Specifically, projections suggest that this share will reach approximately 13.5% by 2030, 17.9% by 2040, 27.0% by 2060, and 33.4% by 2080 [1]. These projected increases reflect the ongoing process

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of population aging in Türkiye and have important implications for social policy, economic planning, and healthcare systems. This demographic transition increases healthcare utilization and leads to a growing number of geriatric presentations to emergency departments (EDs).

A key feature of the geriatric population is multimorbidity, which often necessitates the concurrent use of multiple medications [2]. Polypharmacy, commonly defined as the use of five or more medications, has been associated with adverse drug reactions, drug–drug interactions, falls, cognitive impairment, and poor adherence [3,4]. Studies indicate that, in developed countries, approximately 30% of adults aged 65 years and older use at least five medications [5]. Age-related pharmacokinetic and pharmacodynamic changes further increase vulnerability to drug-related problems, contributing to higher rates of hospitalization and mortality [6].

To mitigate these risks, several evidence-based tools have been developed to identify potentially inappropriate medication use in older adults. The most widely used tools include the American Geriatrics Society Beers Criteria and the European STOPP/START criteria [7]. In Türkiye, the TIME (Turkish Inappropriate Medication Use in the Elderly) criteria provide population-specific guidance for optimizing prescribing in older adults [8]. These instruments support clinicians in designing safer and more rational pharmacotherapy regimens.

The concurrent application of three potentially inappropriate medication use (IMU) screening tools enables a more comprehensive assessment of inappropriate prescribing among older adults in emergency department settings. Given the rising number of older adults presenting to the emergency department and their increasing clinical complexity, this strategy may help optimize medication use and enhance patient safety by facilitating the identification of individuals at risk for adverse drug events.

This study aimed to determine the prevalence of polypharmacy and IMU among geriatric ED patients, examine demographic and clinical factors associated with IMU, and assess the frequency of potential drug–drug and drug–disease interactions in this population.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted in the Emergency Department of Erzurum Training and Research Hospital. The study was initiated following approval from the Erzurum Regional Training and Research Hospital Ethics Committee, with decision number KAEK 2020/07-76 and reference number 37732058-514.10. Patient recruitment started on 1 March 2022 and included all eligible older adults who presented during a three-month period. All procedures were integrated into routine clinical care, and no additional interventions were performed. The primary objective was to determine the prevalence of polypharmacy and potentially inappropriate medication use (IMU) among older adults presenting to the emergency department and to identify demographic and clinical factors associated with inappropriate medication use.

The study was conducted in a tertiary emergency department with approximately 1,500–2,000 patient visits per day. Only patients aged ≥65 years who fulfilled all eligibility criteria and had a complete, verifiable medication history were included to ensure reliable assessment using the three IMU screening tools, resulting in a limited number of eligible participants.

Study Population

The study population comprised patients aged 65 years and older who presented to the Emergency Department of Erzurum Training and Research Hospital during the study period. The study sample included patients triaged as green or yellow according to the emergency triage system who provided informed consent to participate. Patients with life-threatening conditions (red triage), those requiring intensive care, and individuals unable to provide informed consent were excluded. All eligible patients meeting the inclusion criteria were consecutively enrolled.

Inclusion Criteria

Participants were eligible if they met all of the following criteria:

- Age ≥65 years
- Presentation to the Emergency Department during the study period
- Triage category classified as green or yellow
- Use of at least one systemic medication
- Ability to provide informed consent directly or via a legally authorized caregiver

Exclusion Criteria

Patients were excluded if they met any of the following criteria:

- Red triage (life-threatening condition requiring immediate resuscitation)
- Requirement for intensive care unit admission at presentation
- Terminal-stage malignancy under end-of-life care
- Severe cognitive impairment without reliable caregiver

support
- Incomplete or unverifiable medication records
- Repeated ED visits during the study period (only the first visit was included)

Data Collection

Data were collected using a structured data collection form developed by the researchers based on the relevant literature. Information was obtained through face-to-face interviews with patients or their caregivers and by reviewing electronic medical records. The data collection form included demographic characteristics, presenting complaints, comorbid conditions, and complete medication histories, including prescription drugs, over-the-counter medications, and herbal products.

Assessment of Potentially Inappropriate Medication Use

Each patient was independently evaluated using three validated screening tools:

- 2019 American Geriatrics Society Beers Criteria
- STOPP version 2 criteria
- Turkish TIME-to-STOP/TIME-to-START criteria

Overlapping potentially inappropriate medications identified by more than one tool were recorded separately for analytical comparison.

Statistical Analysis

Statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed variables are presented as mean±standard deviation (SD), whereas non-normally distributed variables are expressed as median (interquartile range [IQR]). Categorical variables are presented as frequencies and percentages. Comparisons between groups were performed using the independent-samples t-test or the Mann–Whitney U test for continuous variables, as appropriate according to the data distribution, and the chi-square test or Fisher's exact test for categorical variables. Factors associated with potentially inappropriate medication use were evaluated by calculating odds ratios (ORs) with 95% confidence intervals (CIs). A two-sided p value <0.05 was considered statistically significant.

Agreement between the three screening tools was quantified using Cohen's kappa coefficient for each pairwise comparison. Factors associated with hospitalization were examined using multivariable logistic regression; complete-case analysis was used, and the number of observations included in each model is reported with the corresponding results.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Erzurum Training and Research Hospital prior to the initiation of the study. Written informed consent was obtained from all participants or their legally authorized representatives.

Results

A total of 203 patients were included in the study. The mean age was 76.5±7.4 years. There was no statistically significant difference in mean age between patients with IMU and those receiving appropriate medications (p>0.05). Similarly, sex distribution did not differ significantly between the groups.

The most common presenting complaint among geriatric patients was dyspnea, observed in 35 patients (17.2%), representing the leading reason for emergency department admission. Gastrointestinal complaints, particularly abdominal pain, were reported in 11 patients (5.4%). Similarly, deterioration in general condition was identified in 11 patients (5.4%), reflecting the nonspecific but clinically significant presentations frequently encountered in older adults.

Cardiovascular-related symptoms were also prominent. Chest pain was documented in 5 patients (2.5%), while combinations of chest pain and dyspnea were observed in several additional cases. Neurological complaints, including headache and dizziness, were each reported in 4 patients (2.0%).

When categorized by system involvement, respiratory complaints constituted the largest proportion of admissions, followed by gastrointestinal and cardiovascular symptoms. These findings indicate a predominance of cardiopulmonary and systemic presentations in the geriatric emergency population.

Polypharmacy, defined as the use of ≥5 medications, was present in 94.1% of patients. In our cohort, patients used a mean of 7 medications; this reflects a significant medication burden in the older population in Türkiye [9]. Overall, 49.3% of the study population had at least one potentially inappropriate medication according to the Beers, STOPP, or TIME criteria [7,8]. The proportion of patients at risk of clinically significant drug–drug interactions was 2.46%.

The most common classes of potentially inappropriate medications were proton pump inhibitors (PPIs), antipsychotics, and nonsteroidal anti-inflammatory drugs (NSAIDs). Examples of condition-specific problematic medications included:

- Pantoprazole: risk in osteoporosis and chronic kidney disease
- Etodolac: gastrointestinal bleeding and impaired renal function
- Quetiapine and olanzapine: increased risk in dementia and falls and increased cardiovascular risk
- Donepezil: bradycardia and syncope
- Metformin: contraindicated in severe renal impairment (eGFR<30 mL/min/1.73 m^2)
- Diltiazem: not recommended in NYHA class III–IV heart failure
- Insulin: risk of hypoglycemia in frail older adults

Drugs identified as potentially inappropriate by all three screening tools included proton pump inhibitors when used long-term, antipsychotics in patients with dementia, benzodiazepines, and chronic NSAID therapy in high-risk patients.

Hypertension, diabetes mellitus, and coronary artery disease were the most prevalent chronic conditions. Table 1 presents the distribution of chronic diseases according to IMU status, along with the statistical associations between each chronic disease and IMU.

Drug–disease interaction risk was identified in 11 patients (5.4%), reflecting known contraindications between specific medications and underlying chronic conditions.

Chi-square analysis demonstrated a statistically significant association between coronary artery disease and IMU (p=0.03). Patients with coronary artery disease had higher odds of receiving potentially inappropriate medications than those without coronary artery disease. No statistically significant associations were observed for hypertension, diabetes mellitus, chronic obstructive pulmonary disease, heart failure, stroke, chronic kidney disease, atrial fibrillation, hyperlipidemia, or Alzheimer's disease (Table 1).

Table 1. Association between chronic diseases and potentially inappropriate medication use

Chronic disease	IMU (n)	No-IMU group (n)	p
Hypertension (HT)	70	84	0.48
Diabetes mellitus (DM)	45	57	0.84
Coronary artery disease	65	38	**0.03**
COPD	29	34	0.67
Heart failure	18	40	0.08
Stroke	6	13	0.45
Chronic kidney disease	6	12	0.56
Atrial fibrillation	4	11	0.31
Hyperlipidemia	4	10	0.42
Alzheimer's disease	5	8	0.98

Values are presented as number of patients (n). Comparisons between groups were performed using the chi-square test or Fisher's exact test, as appropriate. Bold indicates a statistically significant difference (p<0.05). IMU: inappropriate medication use, HT: hypertension, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease.

Key laboratory parameters and demographic characteristics of patients with and without IMU are summarized in Table 2. No significant differences were found between the groups regarding age, hemoglobin, renal function markers, liver enzymes, or coagulation parameters (p>0.05 for all comparisons).

Among the total study population (n=203), 56.2% required hospitalization, 43.3% were discharged from the emergency department, and 0.5% died during follow-up. When patients discharged from the ED were compared with those requiring hospitalization, several clinical and laboratory parameters differed significantly. Hospitalized patients had higher blood urea nitrogen and creatinine levels, indicating more advanced renal impairment (p<0.05). D-dimer levels were also significantly higher among hospitalized patients (p<0.05), consistent with a greater thromboembolic or inflammatory burden (Table 3).

Presenting complaints differed between the groups: patients admitted to inpatient wards more frequently presented with deterioration in general condition, respiratory distress, and infectious symptoms. Age did not differ significantly between discharged and hospitalized patients (p>0.05).

Regarding the comparative performance of the IMU screening tools, the STOPP criteria identified the highest proportion of patients with potentially inappropriate medication use (69/203, 34.0%), followed by the Beers criteria (54/203, 26.6%) and the TIME criteria (31/203, 15.3%). Only one patient (0.5%) was identified by all three tools. Pairwise agreement was low to moderate between Beers and STOPP (κ=0.316) and poor between Beers and TIME (κ=−0.182) and between STOPP and TIME (κ=−0.039), indicating substantial variability in patient identification across the screening tools (Table 4).

The frequency of potentially inappropriate medication use did not differ significantly between hospitalized and discharged patients (53/99, 53.5% versus 51/88, 58.0%; p=0.544) (Table 3), and IMU was not independently associated with hospitalization after multivariable adjustment. Hospitalized patients more frequently presented with systemic complaints, elevated markers of infection and inflammation, impaired renal function, and abnormal vital signs, although not all differences reached statistical significance.

Table 2. Key laboratory data and demographics by IMU status

Variable	IMU, mean±SD	No-IMU group, mean±SD	p
Age (years)	76.79±7.74	76.23±7.05	0.700
HGB (g/dL)	13.27±2.70	13.76±1.75	0.251
HCT (%)	41.90±8.52	42.87±5.84	0.418
MCV (fL)	85.94±6.99	87.93±5.85	0.161
PLT (×10^9/L)	247.99±84.77	249.79±87.93	0.701
NEUT (%)	64.77±26.60	72.33±15.68	0.401
LYMPH (%)	15.26±12.15	16.49±10.91	0.466
BUN (mg/dL)	37.04±24.87	36.36±29.29	0.433
Creatinine (mg/dL)	1.34±0.81	1.30±0.77	0.635
GFR (mL/min/1.73 m^2)	61.94±28.12	63.59±32.75	0.874
Sodium (mmol/L)	138.67±6.62	138.20±4.09	0.944
Potassium (mmol/L)	4.46±0.66	4.34±0.72	0.605
Calcium (mg/dL)	9.02±0.81	8.78±0.89	0.216
Magnesium (mg/dL)	1.88±0.34	1.79±0.45	0.390
CK (U/L)	95.11±91.29	116.16±154.03	0.747
Direct bilirubin (mg/dL)	0.36±0.39	0.40±0.36	0.458
Total bilirubin (mg/dL)	0.87±0.61	1.10±0.87	0.114
ALT (U/L)	28.02±35.60	31.71±56.51	0.231
AST (U/L)	38.86±39.73	43.01±85.66	0.704
Albumin (g/L)	40.10±4.86	39.20±6.17	0.330
Chloride (mmol/L)	105.77±6.58	103.18±15.67	0.763
APTT (s)	32.40±10.54	29.95±6.15	0.440
INR	1.67±1.68	1.36±0.60	0.491
Fibrinogen (mg/dL)	461.65±154.08	435.12±158.44	0.920
PT (s)	21.14±19.58	18.14±7.80	0.607

Values are presented as mean ± standard deviation (SD) and were compared using the independent-samples t-test or the Mann–Whitney U test, as appropriate. No comparison reached statistical significance (p>0.05 for all). IMU: inappropriate medication use, HGB: hemoglobin, HCT: hematocrit; MCV: mean corpuscular volume, PLT: platelet count, NEUT: neutrophils, LYMPH: lymphocytes, BUN: blood urea nitrogen, GFR: glomerular filtration rate, CK: creatine kinase, ALT: alanine aminotransferase, AST: aspartate aminotransferase, APTT: activated partial thromboplastin time, INR: international normalized ratio, PT: prothrombin time, SD: standard deviation.

In a multivariable logistic regression model adjusted for age, sex, medication count, vital signs, comorbidities, and IMU positivity according to each tool (n=144), IMU positivity according to the Beers, STOPP, or TIME criteria was not independently associated with hospitalization. In a secondary complete-case model including laboratory variables (n=62), higher BUN levels were independently associated with hospitalization (aOR 1.067 per mg/dL, 95% CI 1.007–1.130; p=0.028).

Discussion

This study demonstrates that polypharmacy and potentially inappropriate medication use are highly prevalent among geriatric ED patients. The observed polypharmacy rate of 94.1% is higher than that reported in many previous studies. We believe that this finding may be attributable to the advanced age and high burden of multimorbidity in the study population, the use of a polypharmacy definition based on five or more medications, and the inclusion of medications intended for short-term use when they were being used at the time of assessment [2,5].

Across the three screening tools, proton pump inhibitors, antipsychotics, and nonsteroidal anti-inflammatory drugs were the medication classes most frequently identified as potentially inappropriate. Their recurrent identification reflects clinically relevant concerns in older adults, including prolonged treatment without a clear indication, increased risks of falls and cognitive adverse effects, gastrointestinal bleeding, and impaired renal function. These findings emphasize the importance of interpreting IMU classifications in relation to treatment duration, comorbidities, and individual clinical risk rather than considering screening results in isolation.

In our study, nearly half of the participants (49.3%) were exposed to at least one potentially inappropriate medication. Similar findings have been reported in previous studies. Wong et al. [10] demonstrated that approximately 65% of older patients with frequent emergency department visits were prescribed at least one potentially inappropriate medication. Likewise, studies conducted in Türkiye have revealed a high prevalence of inappropriate medication use among older adults [11,12].

Among geriatric patients presenting to the emergency department, polypharmacy has been reported in up to 55.6% of cases, and at least one potentially inappropriate medication has been identified in 63.0% of patients. In our cohort, the mean number of medications used was 7. In comparison, Wong et al. [10] reported a higher medication burden, with a mean of 9 regularly prescribed medications. Recent international studies further support these findings and highlight the impact of potentially inappropriate medication use on emergency department utilization and admission outcomes [13,14].

An important finding of this study is the significant association between coronary artery disease and IMU. Patients with coronary artery disease typically receive complex pharmacological regimens, including antiplatelet agents, beta-blockers, statins, and renin–angiotensin system blockers, often in combination with drugs prescribed for other comorbidities [15]. This complexity increases

Table 3. Comparison of clinical and laboratory characteristics between hospitalized and discharged patients

Variable	Hospitalized (n=99)	Discharged (n=88)	p
Age, years	76.00 (71.50–82.00)	75.00 (70.50–80.00)	0.256
Male sex	51 (51.5)	35 (39.8)	0.108
Any IMU	53 (53.5)	51 (58.0)	0.544
General deterioration/weakness	20 (20.2)	5 (5.7)	**0.004**
Respiratory complaint	33 (33.3)	43 (48.9)	**0.031**
Infectious symptom	8 (8.1)	6 (6.8)	0.743
Heart rate, beats/min	91.00 (84.00–104.00)	92.50 (77.75–105.25)	0.609
Respiratory rate, breaths/min	24.00 (20.00–27.00)	23.00 (20.00–25.00)	0.096
Oxygen saturation, %	90.00 (83.25–93.00)	91.00 (85.00–94.00)	0.294
Temperature, °C	36.40 (36.20–36.60)	36.40 (36.00–36.55)	0.104
WBC ($\times 10^9$/L)	9.44 (7.88–12.59)	8.62 (6.92–10.63)	0.142
BUN (mg/dL)	36.00 (23.00–57.00)	23.50 (18.00–34.00)	**<0.001**
Creatinine (mg/dL)	1.23 (0.82–1.73)	1.04 (0.84–1.39)	0.211
D-dimer (ng/mL)	1614.50 (1076.25–2873.00)	1040.00 (609.00–2744.00)	**0.013**
Lactate (mmol/L)	2.15 (1.48–3.00)	2.10 (1.80–2.80)	0.644

Values are presented as n (%) or median (interquartile range), as appropriate. Normality was assessed using the Shapiro–Wilk test. Continuous variables were compared using Welch's independent-samples t-test or the Mann–Whitney U test; categorical variables were compared using Pearson's chi-square or Fisher's exact test, as appropriate. Bold indicates a statistically significant difference (p<0.05). Outcome analysis included 99 documented hospitalizations and 88 documented discharges. One death and 15 records with missing or uncertain disposition were excluded. Presenting-complaint categories were derived from prespecified keyword coding and were not mutually exclusive. IMU: Inappropriate medication use, WBC: white blood cell count, BUN: blood urea nitrogen, IQR: interquartile range.

Table 4. Prevalence of potentially inappropriate medication use according to each screening tool (n=203)

Screening tool	n	%
Beers criteria	54	26.6
STOPP criteria	69	34.0
TIME criteria	31	15.3
Identified by all three tools	1	0.5
≥1 IMU by any tool	100	49.3

Percentages are calculated over the total study population (n=203). Categories are not mutually exclusive. IMU: Inappropriate medication use.

the risk of drug–drug interactions, therapeutic duplication, and deviation from guideline-recommended therapy [16]. Regular medication reconciliation and periodic comprehensive medication review are therefore particularly important in older patients with cardiovascular disease [17].

The association between coronary artery disease and IMU observed in the unadjusted analysis suggests that patients with cardiovascular multimorbidity may be particularly vulnerable to inappropriate prescribing; however, this relationship was not evaluated in a multivariable model due to statistical limitations.

Neither the presence of potentially inappropriate medication use (OR 0.91, 95% CI 0.50–1.66; p=0.76) nor increasing IMU burden per unit increase (OR 1.03, 95% CI 0.89–1.19; p=0.68) was significantly associated with hospitalization.

STOPP identified the largest proportion of patients with potentially inappropriate medication use, whereas TIME identified the smallest proportion. However, the higher detection rate of STOPP should not be interpreted as evidence of superior accuracy because no independent gold standard was available. The limited agreement among the three tools suggests that they capture different aspects of inappropriate prescribing. Differences in medication lists, clinical conditions, health system context, and the populations for which the criteria were developed may contribute to this variability. Accordingly, the tools may be more appropriately considered complementary rather than interchangeable.

Unlike previous Turkish studies conducted primarily in outpatient or community settings, this study evaluates potentially inappropriate medication use in an emergency department population using three validated screening tools simultaneously. The findings demonstrate a significant association between coronary artery disease and IMU, highlighting cardiovascular

multimorbidity as a high-risk context for inappropriate prescribing in acute care settings.

In contrast, potentially inappropriate medication use was not associated with hospitalization in this cohort, either in the unadjusted comparison (53.5% of hospitalized versus 58.0% of discharged patients; p=0.544) or after multivariable adjustment. This suggests that emergency admission decisions in older adults are driven primarily by acute physiological derangement and presenting severity rather than by the appropriateness of the chronic medication regimen. Inappropriate prescribing should therefore be regarded as an important target for medication safety in its own right rather than as a proxy marker of short-term admission risk.

Study Limitations

This study has several limitations. First, it was conducted in a single tertiary emergency department, which limits external validity. Second, medication histories were obtained through patient or caregiver interviews supplemented by electronic records and are therefore subject to recall and reporting bias. Third, the cross-sectional design precludes causal inference regarding the relationship between inappropriate prescribing and clinical outcomes. Fourth, laboratory and disposition data were incomplete for a proportion of the cohort; the multivariable models were therefore restricted to complete cases (n=144 for the clinical model and n=62 for the model including laboratory variables), which reduced statistical power and may have introduced selection bias. Fifth, associations between individual chronic diseases and IMU were tested without adjustment for multiple comparisons and should therefore be regarded as exploratory and hypothesis-generating. Finally, no long-term follow-up data were available, so the effects of inappropriate prescribing on mortality, rehospitalization, and functional status could not be assessed.

Conclusion

Polypharmacy and potentially inappropriate medication use are highly prevalent among older adults presenting to the emergency department. Nearly all patients in this cohort used five or more medications, and approximately half were exposed to at least one potentially inappropriate medication according to at least one screening tool.

Coronary artery disease was significantly associated with IMU in unadjusted analyses, suggesting that older adults with cardiovascular multimorbidity may represent a particularly vulnerable subgroup. However, this association was not evaluated in a multivariable model due to statistical limitations and should therefore be interpreted cautiously.

The frequency of potentially inappropriate medication use did not differ between hospitalized and discharged patients, and IMU was not independently associated with hospitalization after multivariable adjustment. These findings suggest that acute clinical severity, rather than inappropriate prescribing, primarily drives emergency admission decisions in this population.

The low agreement observed among the Beers, STOPP, and TIME criteria highlights substantial variability in patient identification depending on the screening instrument used. This variability underscores the importance of contextual clinical judgment and supports the complementary use of multiple validated tools in geriatric emergency care.

Routine implementation of structured medication reconciliation processes and the integration of clinical pharmacists into emergency department teams may enhance medication safety in older adults. Future multicenter longitudinal studies are warranted to evaluate the long-term impact of inappropriate prescribing on mortality, rehospitalization, and functional outcomes.

Ethics

Ethics Committee Approval: This study was approved by the Erzurum Training and Research Hospital (decision number KAEK 2020/07-76; reference number 37732058-514.10, date: 06.04.2020).

Informed Consent: Written informed consent was obtained from all participants or from their legally authorized representatives before enrolment.

Conflict of Interest: None declared.

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ORIGINAL RESEARCH

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Inflammatory Indices and Clinical Indication for Hospitalization in Patients Presenting with Acute Psychosis

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Abstract

Objective: Growing evidence suggests that inflammatory mechanisms may contribute to psychotic disorders, and hematologic indices derived from routine complete blood count parameters may offer practical biomarkers in emergency settings. This retrospective, single-center, observational study evaluated the relationship of the systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV) with clinical outcomes in adults presenting to the emergency department with acute psychosis.

Materials and Methods: Adult patients presenting between January 1, 2021, and December 31, 2023, were included. The primary outcome was the clinical indication for hospitalization after emergency department assessment, defined as either completed admission or refusal of a recommended admission. Patients discharged without a recommendation for admission constituted the no-indication group. Secondary outcomes were inpatient length of stay, emergency department length of stay, and 12-month revisits.

Results: A total of 260 patients were analyzed (mean age, 36.89±12.29 years; 43.1% female). A clinical indication for hospitalization was documented in 201 patients (77.3%): 176 were admitted, and 25 declined the recommended admission. SII was higher in the indication group in the unadjusted analysis (1084.57±828.79 vs 884.53±590.99; p=0.045), but this association was not retained after multivariable adjustment. SIRI and PIV were not associated with the clinical indication for hospitalization. ROC analysis showed limited discriminative performance for SII (AUC, 0.586; 95% CI, 0.523–0.646; p=0.041). No significant associations were found between the inflammatory indices and inpatient length of stay or revisit frequency.

Conclusion: Although SII showed a modest unadjusted association with the clinical indication for hospitalization, its limited discrimination and lack of an independent association after adjustment do not support its clinical use. These exploratory findings do not support SII, SIRI, or PIV as triage biomarkers in acute psychosis at present.

Keywords: Acute psychosis, biomarkers, clinical indication for hospitalization, disposition, emergency department, inflammatory indices

Introduction

Acute psychosis is a psychiatric condition characterized by marked disturbances in thought content, perception, behavior, and reality testing, often requiring urgent evaluation and intervention [1]. Patients commonly present to emergency departments with agitation, disorganized behavior, risk of harm to self or others, impaired insight, and an inability to maintain self-care [2]. Emergency assessment is primarily aimed at excluding underlying medical causes, ensuring safety, determining clinical severity, and making appropriate disposition decisions regarding hospitalization or discharge. However, the heterogeneous presentation of acute psychosis and the frequent lack of reliable collateral history may complicate early risk stratification.

In recent years, increasing evidence has suggested that psychotic disorders may involve not only neurochemical abnormalities but also immune and inflammatory mechanisms [3,4]. Alterations in peripheral inflammatory markers, elevated cytokine levels, and dysregulated immune responses have been reported during psychotic episodes in schizophrenia spectrum disorders and mood disorders with psychotic features [5–7]. These findings raise the possibility that systemic inflammation may accompany acute psychiatric exacerbations.

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Composite inflammatory indices derived from routine complete blood count parameters, including neutrophils, lymphocytes, monocytes, and platelets, have attracted growing interest as practical biomarkers [8–10]. Among these, the systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV) may provide a more integrated reflection of the inflammatory burden than single laboratory parameters alone. Their low cost, rapid availability, and ease of calculation make them potentially attractive for investigation in emergency settings, where timely decision-making is essential [11,12].

Nevertheless, the potential investigational relevance of these indices in patients presenting with acute psychosis remains uncertain. Previous studies have largely focused on specific diagnostic categories, involved relatively small samples, or provided limited data regarding emergency department outcomes [13–15]. In particular, the relationship between inflammatory indices and disposition-related endpoints, such as the clinical indication for hospitalization, length of stay, and revisit rates, has not been sufficiently clarified [16].

The aim of this study was to evaluate SII, SIRI, and PIV in patients presenting to the emergency department with acute psychosis and to examine their associations with emergency department disposition, particularly the clinical indication for hospitalization. We also investigated whether these indices were related to inpatient length of stay and subsequent revisits.

Methods

Study Design and Setting

This retrospective, single-center, observational study was conducted in the emergency department of İzmir Katip Çelebi University Ataturk Research and Training Hospital Training and Research Hospital. Adult patients presenting with acute psychosis between January 1, 2021, and December 31, 2023, were eligible for inclusion.

Data Collection

Potential cases were identified through the hospital information system using ICD-10 diagnostic codes F20, F23, F25, F28, F30, and F32. Diagnoses were verified through a review of electronic medical records, emergency physician notes, and available psychiatric consultation records.

Demographic variables included age and sex. Clinical variables comprised emergency department length of stay, the documented clinical recommendation regarding hospitalization, actual disposition, inpatient length of stay among admitted patients, and post-discharge revisits. Admission recommendations were made jointly by the emergency medicine and psychiatry teams according to routine clinical assessment. The documented clinical recommendation was abstracted separately from actual disposition so that patients who declined a recommended admission could be classified according to the clinical indication.

Laboratory analyses were based on the first complete blood count obtained at presentation. SII was calculated as platelet count×neutrophil count/lymphocyte count, SIRI as neutrophil count×monocyte count/lymphocyte count, and PIV as platelet count×neutrophil count×monocyte count/lymphocyte count. Cell counts were entered as $\times 10^9$/L. Because these are calculated composite indices without standardized clinical units, SII, SIRI, and PIV are reported as arbitrary units (AU).

Study Population

Patients younger than 18 years; those with suspected alcohol- or substance-induced psychosis, psychosis secondary to an organic medical condition, active infection, or pregnancy; those with incomplete clinical or laboratory data; and those transferred to another institution with unavailable outcome data were excluded. During the study period, 663 records were screened; after application of the exclusion criteria, 260 patients were included in the final analysis. Analyses were conducted on complete cases, and no missing-value imputation was performed.

Outcome Measures

The primary outcome was the presence or absence of a clinical indication for hospitalization after emergency department assessment. The indication-present group included patients who were admitted and patients who declined a documented recommendation for admission. The no-indication group comprised patients discharged from the emergency department without a recommendation for hospitalization. Actual disposition (hospitalized, discharged, or refused recommended hospitalization) was reported separately. This pragmatic endpoint reflected real-world clinical decision-making but was not considered a validated measure of psychosis severity. Secondary outcomes were inpatient length of stay among admitted patients, emergency department length of stay, and revisits within 12 months.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Distributional assumptions for continuous variables were assessed using the Shapiro–Wilk test together with visual inspection of histograms and Q–Q plots. Continuous variables are presented as mean±standard deviation for consistent descriptive reporting. Group comparisons were performed using the independent-samples t test when parametric assumptions were met and the Mann–Whitney U or

Kruskal–Wallis test when they were not. No logarithmic or other transformation was applied to SII, SIRI, or PIV. Categorical variables were compared using the chi-square test. Associations between continuous variables were examined using Spearman correlation analysis. Multivariable logistic regression was used to evaluate factors associated with the clinical indication for hospitalization; SII was entered on its original scale and reported per 100-AU increase. Receiver operating characteristic (ROC) curve analysis was used to assess discrimination. Missing data were handled by complete-case analysis without imputation. A two-sided p value of <0.05 was considered statistically significant.

Results

A total of 260 patients were included in the study. Of these, 112 (43.1%) were female and 148 (56.9%) were male. The mean age was 36.89±12.29 years. Diagnostic categories were manic episode in 50 patients (19.2%), depressive episode in 42 (16.2%), schizophrenic episode in 74 (28.5%), and nonorganic psychotic disorder in 94 (36.1%). Mean neutrophil, lymphocyte, platelet, and monocyte counts were 6.71±2.78×10^9/L, 2.15±0.80×10^9/L, 283.38±77.75×10^9/L, and 0.71±0.27×10^9/L, respectively. Mean SII, SIRI, and PIV values were 1039.18±784.66 AU, 2.74±2.49 AU, and 784.35±771.92 AU, respectively (Table 1).

Table 1. Baseline characteristics of the study population

Variable	Total (n=260)
Age, years	36.89±12.29
Female sex, n (%)	112 (43.1)
Male sex, n (%)	148 (56.9)
Manic episode, n (%)	50 (19.2)
Depressive episode, n (%)	42 (16.2)
Schizophrenic episode, n (%)	74 (28.5)
Nonorganic psychotic disorder, n (%)	94 (36.1)
Neutrophil, ×10^9/L	6.71±2.78
Lymphocyte, ×10^9/L	2.15±0.80
Platelet, ×10^9/L	283.38±77.75
Monocyte, ×10^9/L	0.71±0.27
SII, AU	1039.18±784.66
SIRI, AU	2.74±2.49
PIV, AU	784.35±771.92
Emergency department stay, days	1.40±1.85
Hospital stay, days*	32.29±19.14

*Among hospitalized patients. AU: arbitrary units; PIV: pan-immune-inflammation value; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index.

A clinical indication for hospitalization was documented in 201 patients (77.3%). Of these, 176 (67.7% of the total cohort) were hospitalized, and 25 (9.6%) declined the recommended admission. The remaining 59 patients (22.7%) had no indication for hospitalization and were discharged from the emergency department. Among hospitalized patients, the mean inpatient length of stay was 32.29±19.14 days, whereas the mean emergency department length of stay in the total cohort was 1.40±1.85 days. During the 12-month follow-up period, 66 patients (25.4%) had at least one revisit (Table 2).

In sex-based comparisons, only SIRI was significantly higher in male patients than in female patients (2.98±2.78 vs 2.42±2.01 AU; p=0.017). No significant sex-related differences were observed for SII or PIV (p=0.724 and p=0.298, respectively).

No significant differences in SII, SIRI, or PIV were identified across diagnostic subgroups (all p>0.05). When patients were compared according to actual disposition status (hospitalized, discharged, or refused recommended admission), none of the inflammatory indices differed significantly among the three groups (SII, p=0.090; SIRI, p=0.245; PIV, p=0.161).

In the prespecified binary analysis based on the clinical indication for hospitalization, SII was higher in the indication-present group than in the no-indication group (1084.57±828.79 vs 884.53±590.99 AU; p=0.045). Neither SIRI nor PIV showed a significant between-group difference (p=0.107 and p=0.071, respectively) (Table 3).

In multivariable logistic regression analysis adjusting for age, sex, and diagnostic category, SII was not independently associated with the clinical indication for hospitalization (adjusted OR, 1.03 per 100-AU increase; 95% CI, 1.00–1.07; p=0.076) (Table 4). No other covariates were significantly associated with the outcome.

The discriminatory performance of SII for identifying a clinical indication for hospitalization was assessed using ROC analysis. The area under the curve was 0.586 (95% CI, 0.523–0.646; p=0.041), indicating limited

Table 2. Clinical outcomes and dispositions

Variable	n (%)
Clinical indication for hospitalization present	201 (77.3)
Hospitalized	176 (67.7)
Refused recommended hospitalization	25 (9.6)
No clinical indication; discharged from ED	59 (22.7)
No revisit within 12 months	194 (74.6)
≥ 1 revisit within 12 months	66 (25.4)

ED: emergency department. Patients who refused recommended hospitalization were included in the indication-present group for the primary analysis.

Table 3. Inflammatory indices according to clinical indication for hospitalization

Variable	Indication present (n=201)	No indication (n=59)	p
SII, AU	1084.57±828.79	884.53±590.99	0.045
SIRI, AU	2.84±2.60	2.41±2.03	0.107
PIV, AU	817.17±806.11	672.52±635.34	0.071

AU: arbitrary units; PIV: pan-immune-inflammation value; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index.

Table 4. Multivariable logistic regression analysis for clinical indication for hospitalization

Variable	Adjusted OR (95% CI)	p
Age (per 1-year increase)	1.00 (0.98–1.02)	0.910
Male sex	0.91 (0.53–1.56)	0.740
Manic episode	1.19 (0.46–3.04)	0.720
Schizophrenic episode	0.89 (0.41–1.96)	0.780
Nonorganic psychotic disorder	0.86 (0.39–1.88)	0.700
SII (per 100-AU increase)	1.03 (1.00–1.07)	0.076

AU: arbitrary units; CI: confidence interval; OR: odds ratio; SII: systemic immune-inflammation index. The outcome was the documented clinical indication for hospitalization (present vs absent).

Table 5. Correlation of inflammatory indices with outcomes

Variable	Hospital stay, rho / p	12-month revisit count, rho / p
SII	–0.060 / 0.501	–0.049 / 0.433
SIRI	–0.102 / 0.256	–0.084 / 0.174
PIV	–0.126 / 0.159	–0.060 / 0.336

PIV: pan-immune-inflammation value; SII: systemic immune-inflammation index; SIRI: systemic inflammation response index.

discrimination. The optimal cutoff value was >668.42 AU, yielding a sensitivity of 69.15% and a specificity of 47.6% (Fig. 1).

Correlation analysis showed no significant association between the inflammatory indices and inpatient length of stay: SII (rho=–0.060, p=0.501), SIRI (rho=–0.102, p=0.256), and PIV (rho=–0.126, p=0.159). Similarly, no significant correlations were found between these indices and total revisit count: SII (rho=–0.049, p=0.433), SIRI (rho=–0.084, p=0.174), and PIV (rho=–0.060, p=0.336) (Table 5).

Discussion

Interest in inflammatory mechanisms in psychotic disorders has increased substantially in recent years [14,15]. In this cohort, SII

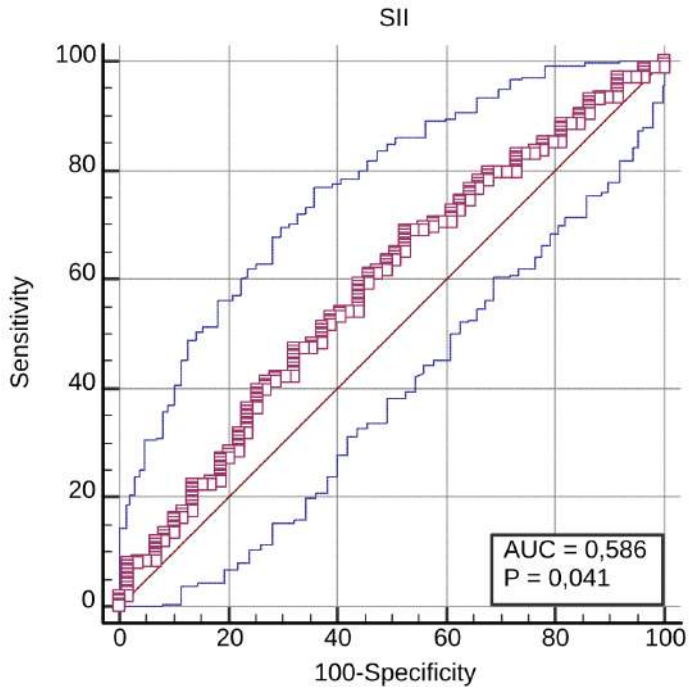

Figure 1. ROC Curve of SII for identifying a clinical indication for hospitalization

was the only composite index to show a nominal unadjusted difference according to the clinical indication for hospitalization. However, this association was not independent after adjustment, and none of the examined indices demonstrated clinically useful discrimination. The observed unadjusted SII difference may reflect the combined contribution of neutrophils, lymphocytes, and platelets to systemic stress and inflammatory responses [11,17], but the present study cannot establish a causal or clinically actionable relationship.

Inflammatory indices did not differ across diagnostic subgroups. In the emergency setting, acute agitation, behavioral dyscontrol, insomnia, autonomic arousal, and psychological stress may overlap across schizophrenia spectrum disorders, mood episodes with psychotic features, and brief psychotic presentations. Any biological signal captured by these indices may therefore relate to nonspecific acute decompensation rather than to formal diagnostic categories. This interpretation remains exploratory.

The clinical indication for hospitalization was used as a pragmatic disposition-associated endpoint. To avoid conflating the clinical recommendation with the disposition ultimately completed, the 25 patients who declined the recommended admission were included in the indication-present group, whereas actual disposition was reported separately. Although the endpoint reflects factors commonly considered in routine care—such as prominent psychotic symptoms, risk to self or others, impaired judgment, inability to meet basic needs, or poor treatment

adherence [18]—it is not a substitute for a standardized psychosis severity scale and may also be influenced by clinician judgment and contextual factors.

The predictive performance of SII was clearly limited. An AUC of 0.586, low specificity at the identified cutoff, and loss of significance after multivariable adjustment do not support SII as either an independent or supplementary triage biomarker. SIRI and PIV also showed no clinically meaningful associations. Accordingly, these findings should be viewed as exploratory and hypothesis-generating rather than as evidence for clinical implementation.

We did not observe associations between the inflammatory indices and either inpatient length of stay or revisit frequency. These outcomes are shaped by many determinants beyond the initial biological state, including treatment response, medication adherence, substance use, family support, housing stability, outpatient follow-up, and healthcare access [19]. Such factors may outweigh any contribution from baseline inflammatory activity.

Although CBC-derived indices are inexpensive and readily available, accessibility alone does not establish clinical value. The present results do not show that SII, SIRI, or PIV adds useful information beyond routine clinical assessment. At present, these indices should remain investigational and should not be used to determine psychiatric admission or discharge decisions.

Study Limitations

Several limitations should be acknowledged. The retrospective, single-center design limits causal inference and external validity. Standardized psychosis severity scales were not consistently available, necessitating the use of a clinician-determined disposition endpoint. Admission recommendations were made by different emergency medicine and psychiatry clinicians in routine practice; therefore, interclinician variability and the absence of a standardized admission algorithm or interrater reliability assessment may have affected classification. Although suspected substance-induced psychosis was excluded, substance exposure was based mainly on clinical documentation and was not systematically confirmed by toxicology testing. Data on smoking, body mass index or obesity, and psychotropic or anti-inflammatory medication exposure were not consistently available, leaving potential residual confounding. The inclusion of patients who refused recommended admission in the indication-present group preserves the documented clinical recommendation but does not equate refusal with completed hospitalization. The multivariable model may have been underpowered to detect small independent effects. Only the first blood sample was analyzed, temporal changes in inflammatory markers were not assessed, and the interval between symptom onset and emergency department presentation was unavailable.

Conclusion

In this exploratory study, SII showed a modest unadjusted association with the clinical indication for hospitalization, but the association was not independent after adjustment, and discrimination was limited. SIRI and PIV were not associated with the primary or secondary outcomes. These findings do not support the clinical use of SII, SIRI, or PIV as triage biomarkers in acute psychosis. Prospective, multicenter studies using standardized severity and disposition criteria would be required before any clinical role could be considered.

Ethics

Ethics Committee Approval: This study was approved by The Izmir Katip Celebi University Health Research Ethics Committee on 16 January 2025 (Approval No: 0038)

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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ORIGINAL RESEARCH

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Botulism in the Emergency Department: Clinical Characteristics, Diagnostic Challenges, and Patient Outcomes

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Abstract

Objective: Botulism is a rare but potentially life-threatening neuroparalytic disease. In recent years, the increasing use of botulinum toxin for cosmetic and therapeutic purposes has led to a rise in iatrogenic cases. This study aimed to evaluate the clinical characteristics, diagnostic process, management strategies, and outcomes of patients diagnosed with botulism in the emergency department.

Materials and Methods: This retrospective, observational, single-center study included adult patients diagnosed with botulism in the emergency department of a tertiary-care referral hospital between January 1, 2022, and January 1, 2026. The diagnosis was established on clinical grounds based on compatible neurological findings together with a documented history of botulinum toxin exposure and was confirmed by neurological consultation in all patients. Demographic characteristics, exposure history, clinical findings, laboratory parameters, treatment approaches, and outcomes were analyzed.

Results: A total of 16 patients were included, with a median age of 34 years (IQR: 32–44), and 81.2% were female. The median time from symptom onset to hospital admission was 7 days (IQR: 5–8). The majority of cases (93.7%) were associated with iatrogenic botulinum toxin exposure, with intragastric (37.5%) and cosmetic facial or cervical (37.5%) injections being equally frequent sources. The most common presenting features were neurological symptoms without impaired consciousness, particularly cranial nerve involvement such as diplopia, dysphagia, dysarthria, and ptosis (81.3%). Laboratory findings were generally within normal limits. Management consisted of pyridostigmine in seven patients (43.8%), botulinum antitoxin in three (18.8%), and observation with supportive care alone in six (37.5%). All three patients treated with antitoxin had bulbar or respiratory symptoms, and in two of them, treatment had been initiated at the referring institution. No patient required mechanical ventilation, and no mortality was observed. Most patients were discharged with clinical recovery.

Conclusion: Iatrogenic botulism represents an emerging clinical entity in emergency practice. The presence of cranial nerve dysfunction with preserved consciousness should raise suspicion for botulism, particularly in patients with recent botulinum toxin exposure. Early recognition and timely management are essential to prevent disease progression and ensure favorable outcomes. The uniformly favorable outcomes observed here should be interpreted in the context of a cohort that presented late and had predominantly mild disease and do not exclude a clinically relevant risk of respiratory failure in iatrogenic botulism.

Keywords: Botulism, botulinum toxin, emergency department, iatrogenic botulism, neuromuscular junction disease

Introduction

Botulism is a rare but potentially life-threatening disease caused by botulinum neurotoxins produced by *Clostridium botulinum* and related species [1]. These toxins inhibit acetylcholine release at presynaptic nerve terminals, leading to flaccid paralysis characterized by blurred vision, dry mouth, dysphagia, diplopia, dysarthria, dyspnea, and progressive muscle weakness[1,2]. Early symptoms may include fatigue, weakness, and dizziness, followed by gastrointestinal manifestations such as vomiting, diarrhea, constipation, and abdominal distension [3]. Although mild alterations in mental status may occasionally be observed, loss of consciousness and fever are typically not expected [1]. Due to its rarity and the nonspecific nature of its clinical presentation,

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diagnosis is often delayed, which may increase mortality in untreated cases.

Botulism presents in five main clinical forms: foodborne, wound, iatrogenic, infant, and adult intestinal toxemia [4–7]. Among these, foodborne botulism is the most common and typically results from the ingestion of improperly stored or home-canned foods in which bacterial spores have proliferated and produced toxins [8,9]. Wound botulism develops following contamination of traumatic wounds with bacterial spores [10]. In recent years, the increasing use of botulinum toxin for both cosmetic and therapeutic purposes has been accompanied by a rise in reported cases of iatrogenic botulism [11]. These cases, often associated with high doses or nonstandard preparations, highlight the changing epidemiology of the disease [12].

Symptoms usually appear within 12–36 hours after exposure to botulinum toxin, although the incubation period may range from 4 hours to 8 days [2]. Clinically, newly developed cranial nerve involvement (diplopia, ptosis, dysphagia, dysarthria), accompanied by progressive, typically descending neuromuscular weakness, is characteristic of botulism [13]. In patients presenting to the emergency department, obtaining a history of potential toxin exposure, such as the consumption of home-canned foods, the presence of wounds, or recent botulinum toxin injections, is critical for diagnosis [2,3]. Early recognition of these clinical and anamnestic clues is essential for considering botulism in the differential diagnosis and preventing diagnostic delays. However, the fact that laboratory findings are often within normal limits at initial presentation further complicates the diagnostic process [12]. As a result, botulism may be misdiagnosed as other neurological emergencies, such as myasthenia gravis, Guillain–Barré syndrome, or stroke [14].

The indications for botulinum toxin use have expanded considerably in recent years [15]. It is widely used across a broad spectrum of conditions, ranging from neurological disorders and hyperhidrosis to migraine treatment and aesthetic procedures. Although generally considered safe, inappropriate dosing, the use of unlicensed preparations, or uncontrolled administration may result in systemic toxicity [16]. This has led to an increase in cases of iatrogenic botulism, particularly with the growing popularity of cosmetic and intragastric ("gastric Botox") procedures [15–18]. These trends suggest that botulism should be considered not only as a rare disease but also as an important clinical entity in the differential diagnosis of emergency department presentations.

The rise in iatrogenic botulism has become more evident with outbreaks associated with cosmetic botulinum toxin applications [17,18]. For example, a 2025 outbreak in the United Kingdom involving 25 cases linked to cosmetic botulinum toxin injections demonstrated that all patients presented to emergency departments and that a substantial proportion required antitoxin treatment [19]. The same study identified the use of unlicensed preparations and exposure to specific practitioners as major risk factors for disease development [19]. These findings indicate that iatrogenic botulism may occur not only as isolated complications but also as clusters and outbreaks with public health implications.

Despite this, data on the clinical presentation, follow-up, and management of botulism in the emergency setting remain limited. Most of the available evidence originates either from outbreak investigations and public health reports, which are designed for epidemiological case finding rather than for describing bedside decision-making, or from isolated case reports [11,15,19]. In particular, the emergency department course of iatrogenic botulism related to intragastric botulinum toxin injection performed for weight reduction, a procedure that has expanded rapidly in Türkiye and has already generated internationally reported clusters, has rarely been described in a consecutive clinical series [15,18]. The present study addresses this gap by presenting a consecutive, single-center, four-year emergency department series of botulism cases, with a particular focus on iatrogenic exposures. We describe the diagnostic pathways followed in these patients and the treatment approaches applied in practice, including botulinum antitoxin, pyridostigmine, and observation. In this study, we aimed to evaluate the clinical characteristics, diagnostic and treatment processes, and outcomes of patients with botulism presenting to the emergency department.

Materials and Methods

Study Design and Setting

This retrospective, observational, single-center study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board of Başakşehir Çam and Sakura City Hospital, Istanbul, Türkiye (Date: 29.04.2026 – Decision: 187/2026). The study cohort comprised all patients diagnosed with botulism who were admitted to the emergency department of this tertiary-care referral hospital between January 1, 2022, and January 1, 2026.

Adult patients aged 18 years and older who were diagnosed with botulism and managed in the emergency department during the study period were included. A total of 16 patients met the inclusion criteria and were included in the final analysis. Of these, 15 cases were classified as iatrogenic botulism, whereas one case was attributed to a non-iatrogenic cause. Patients were excluded if they were under 18 years of age, had incomplete or missing

clinical data, or did not have a confirmed diagnosis of botulism based on clinical findings and specialist evaluation.

Case Definition and Diagnostic Process

Because laboratory confirmation of botulinum neurotoxin is not routinely available in our setting, the diagnosis was established clinically, in line with current clinical guidelines [20]. A case was defined as the acute onset of compatible neurological findings, namely cranial nerve involvement (diplopia, ptosis, blurred vision, dysarthria, or dysphagia), with or without symmetrical descending muscle weakness, occurring in an afebrile patient without impairment of consciousness and in association with documented exposure to botulinum toxin (cosmetic, therapeutic, or intragastric administration) or, in the single non-iatrogenic case, ingestion of a suspected food source. All patients were first assessed by an emergency physician and subsequently evaluated by a neurologist during the index emergency department visit, and the final diagnosis was reached by consensus between the emergency physician and the consulting neurologist. Alternative causes of acute neuromuscular weakness were excluded by neurological examination, routine laboratory testing, and cranial imaging; further investigations, such as cranial magnetic resonance imaging or cerebrospinal fluid examination, were performed at the discretion of the consulting neurologist when the presentation was considered atypical. Neither electrodiagnostic testing nor laboratory toxin detection was routinely applied as a diagnostic criterion, and this is addressed in the Study Limitations section. Patients in whom the diagnosis remained unconfirmed after specialist evaluation were not included.

Management Strategy

No standardized institutional treatment protocol for botulism was in place during the study period. Management decisions were made jointly by the treating emergency physician and the consulting neurologist and, in the case of botulinum antitoxin, in coordination with the infectious diseases department and the public health authority responsible for antitoxin supply in Türkiye. Decisions were therefore based on clinical severity and the interval since symptom onset. In general, botulinum antitoxin was considered for patients with bulbar or respiratory involvement, such as dysphagia, dyspnea, or orthopnea, or with objective or progressive limb weakness, that is, features indicating a risk of further deterioration, provided that these patients presented sufficiently early in the disease course for antitoxin to be expected to limit further toxin binding. Pyridostigmine was administered empirically to selected patients with persistent but nonprogressive symptoms, predominantly those presenting late, when antitoxin was no longer considered likely to alter the disease course. Patients with mild, stable, and nonprogressive findings were managed with observation and supportive care alone. It should be noted that a proportion of our patients were referred from other institutions with an established suspicion of botulinum intoxication, and in these patients, the decision to administer antitoxin had already been made and treatment initiated at the referring center; in such cases, treatment was continued at our hospital. Irrespective of the treatment group, all patients underwent serial neurological examinations and monitoring of respiratory status, with immediate availability of intensive care in the event of deterioration.

Data Collection

Patient data were retrospectively obtained from the hospital information management system. Iatrogenic botulism was defined as the presence of compatible clinical findings following recent botulinum toxin administration for therapeutic or cosmetic purposes. The collected variables included demographic characteristics (age, sex, and comorbidities), etiological exposure (categorized as iatrogenic, foodborne, or other), presenting symptoms (neurological, gastrointestinal, respiratory, and cardiac), and relevant time intervals (time from symptom onset to emergency department admission and from admission to diagnosis). Additional data included initial diagnoses, including misdiagnoses, neurological examination findings, vital signs at presentation, laboratory parameters (hematological, biochemical, coagulation, and blood gas values), and imaging findings. Treatment-related variables, such as antitoxin administration and its timing, were also recorded, along with the need for intensive care unit admission, requirement for mechanical ventilation, length of hospital stay, and clinical outcomes, including discharge, treatment refusal, and mortality.

Statistical Analyses

Statistical analyses were performed using SPSS software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as medians and interquartile ranges, whereas categorical variables were presented as frequencies and percentages. The normality of continuous variables was assessed using the Shapiro–Wilk test. Given the small sample size and the nonnormal distribution of several variables, nonparametric tests were used for comparative analyses. Continuous variables were compared using the Mann–Whitney U test, and categorical variables were analyzed using Fisher's exact test. Associations between continuous variables were examined using Spearman's rank correlation coefficient (rho). Because of the exploratory nature of these analyses and the limited sample size, no adjustment for multiple comparisons was performed, and the results of subgroup and correlation analyses

were regarded as hypothesis-generating. A p value of <0.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics

A total of 16 patients diagnosed with botulism were included in the study (Table 1). The median age was 34 years (interquartile range [IQR]: 32–44; range: 24–67). Thirteen patients (81.2%) were female, and three (18.8%) were male. The median time from symptom onset to hospital admission was 7 days (IQR: 5–8; range: 0–9).

Table 1. Demographic, clinical, and laboratory characteristics of patients with botulism (n=16)

Variable	n=16
Demographics	
Age, years — median (IQR)	34 (32–44)
Age, years — min–max	24–67
Female, n (%)	13 (81.2)
Male, n (%)	3 (18.8)
Time from exposure to admission, days — median (IQR)*	7 (5–8)
Time from exposure to admission, days — min–max*	0–9
Etiology (source of exposure)	
Gastric botulinum toxin, n (%)	6 (37.5)
Cosmetic botulinum toxin (face/neck), n (%)	6 (37.5)
Axillary (hyperhidrosis) botulinum toxin, n (%)	2 (12.5)
Canned mushrooms, n (%)	1 (6.3)
Masseter botulinum toxin, n (%)	1 (6.3)
Mechanism of intoxication	
Accidental, n (%)	1 (6.3)
Iatrogenic, n (%)	15 (93.7)
Clinical symptoms	
Altered consciousness, n (%)	3 (18.8)
Gastrointestinal symptoms, n (%)	5 (31.3)
Cardiac symptoms, n (%)	1 (6.3)
Respiratory symptoms, n (%)	3 (18.8)
Neurological symptoms (excluding consciousness), n (%)	13 (81.3)
Comorbidities	
Diabetes mellitus, n (%)	1 (6.3)
Hypertension, n (%)	0 (0.0)
Asthma/COPD, n (%)	1 (6.3)

Table 1. Continue

Variable	n=16
Vital parameters at presentation	
GCS — median (IQR)	15 (15–15)
Systolic BP, mmHg — median (IQR)	122 (109–127)
Diastolic BP, mmHg — median (IQR)	67 (61–74)
MAP, mmHg — median (IQR)	80 (74–88)
Temperature, °C — median (IQR)	36.5 (36.1–36.5)
Heart rate, /min — median (IQR)	81 (73–90)
SpO_2, % — median (IQR)	98 (98–99)
Respiratory rate, /min — median (IQR)	16 (15–17)
Laboratory findings	
Leukocytes, /mm^3 — median (IQR)	6,540 (6,140–8,220)
Hemoglobin, g/dL — median (IQR)	12.7 (11.5–14.4)
Hematocrit, % — median (IQR)	38.5 (35.3–43.2)
MCV, fL — median (IQR)	85.1 (81.7–87.8)
Platelets, /mm^3 — median (IQR)	261,500 (217,750–304,750)
CRP, mg/dL — median (IQR)	0.8 (0.4–5.2)
Glucose, mg/dL — median (IQR)	92 (88–96)
Urea, mg/dL — median (IQR)	23.6 (18.4–27.9)
Creatinine, mg/dL — median (IQR)	0.71 (0.67–0.77)
Sodium, mEq/L — median (IQR)	140 (139–141)
Potassium, mEq/L — median (IQR)	4.2 (4.0–4.5)
Chloride, mEq/L — median (IQR)	105 (104–106)
Calcium, mg/dL — median (IQR)	9.0 (8.6–9.6)
ALT, U/L — median (IQR)	17 (12–21)
AST, U/L — median (IQR)	19 (15–32)
aPTT, s — median (IQR)	28.5 (25.8–30.8)
INR — median (IQR)	1.1 (1.0–1.1)
pH — median (IQR)	7.39 (7.37–7.42)
HCO_3 , mEq/L — median (IQR)	25.8 (24.3–27.8)
Lactate, mmol/L — median (IQR)	1.1 (0.9–1.2)
Emergency department / inpatient treatment	
Botulinum antitoxin, n (%)	3 (18.8)
Pyridostigmine, n (%)	7 (43.8)
Observation, n (%)	6 (37.5)
Outcomes	
Endotracheal intubation, n (%)	0 (0.0)
Length of hospital stay, days — median (IQR)	2.5 (2–3)
Length of hospital stay, days — min–max	1–5
APACHE-II — median (IQR)	5 (2–10)

Table 1. Continue

Variable	n=16
Outcomes	
Discharged, n (%)	14 (87.5)
Treatment refusal, n (%)	2 (12.5)
In-hospital mortality, n (%)	0 (0.0)

Data are presented as median (interquartile range, IQR), min–max, or n (%). GCS: Glasgow Coma Scale; BP: blood pressure; MAP: mean arterial pressure; SpO_2: peripheral oxygen saturation; MCV: mean corpuscular volume; CRP: C-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; aPTT: activated partial thromboplastin time; INR: international normalized ratio; HCO_3 : bicarbonate; COPD: chronic obstructive pulmonary disease; APACHE-II: Acute Physiology and Chronic Health Evaluation II. **Time from exposure to admission was available for 13 of 16 patients (missing in 3).*

Etiology

According to the source of exposure, the most common etiologies were gastric botulinum toxin injections (n=6; 37.5%) and cosmetic botulinum toxin applications involving the face and neck (n=6; 37.5%). These were followed by hyperhidrosis treatment (n=2; 12.5%), foodborne botulism related to canned mushrooms (n=1; 6.3%), and masseter botulinum toxin injection (n=1; 6.3%). Overall, 15 patients (93.7%) had iatrogenic exposure, whereas one patient (6.3%) had foodborne botulism (Table 1). No concurrent medication use, alcohol consumption, substance use, or pregnancy was identified in any patient.

Diagnostic Process

All 16 patients were evaluated by a neurologist during the index emergency department visit, and in every case, the diagnosis was established clinically based on compatible neurological findings and a documented exposure history. No patient had laboratory confirmation of botulinum neurotoxin. Cranial imaging and routine laboratory testing, performed to exclude alternative causes of acute neuromuscular weakness, did not reveal findings that accounted for the clinical picture in any patient. Electrodiagnostic testing was not used as a diagnostic criterion; when it was obtained at the discretion of the consulting neurologist, the findings were normal and did not alter the clinical diagnosis.

Clinical Presentation

The most common presenting features were neurological symptoms without impaired consciousness, including diplopia, dysphagia, dysarthria, ptosis, and motor weakness (n=13; 81.3%). Gastrointestinal symptoms (nausea, vomiting, and diarrhea) were observed in 5 patients (31.3%), altered consciousness in 3 patients (18.8%), respiratory symptoms in 3 patients (18.8%), and cardiac symptoms in 1 patient (6.3%).

Comorbidities

Most patients had no significant comorbidities. Diabetes mellitus and asthma/chronic obstructive pulmonary disease were each present in one patient (6.3%). Additionally, one patient had a history of cervical disc herniation, and another had osteoporosis.

Vital Signs

At presentation, the median Glasgow Coma Scale score was 15 (IQR: 15–15). The median systolic blood pressure was 122 mmHg (IQR: 109–127), diastolic blood pressure was 67 mmHg (IQR: 61–74), and mean arterial pressure was 80 mmHg (IQR: 74–88). The median body temperature was 36.5°C (IQR: 36.1–36.5), heart rate was 81 beats/min (IQR: 73–90), peripheral oxygen saturation was 98% (IQR: 98–99), and respiratory rate was 16 breaths/min (IQR: 15–17).

Laboratory Findings

Hematological analysis showed a median leukocyte count of 6,540/mm^3 (IQR: 6,140–8,220), hemoglobin level of 12.7 g/dL (IQR: 11.5–14.4), hematocrit of 38.5% (IQR: 35.3–43.2), mean corpuscular volume of 85.1 fL (IQR: 81.7–87.8), and platelet count of 261,500/mm^3 (IQR: 217,750–304,750).

Biochemical analysis revealed a median C-reactive protein level of 0.8 mg/dL (IQR: 0.4–5.2), glucose level of 92 mg/dL (IQR: 88–96), urea level of 23.6 mg/dL (IQR: 18.4–27.9), and creatinine level of 0.71 mg/dL (IQR: 0.67–0.77). Median electrolyte levels were as follows: sodium, 140 mEq/L (IQR: 139–141); potassium, 4.2 mEq/L (IQR: 4.0–4.5); chloride, 105 mEq/L (IQR: 104–106); and calcium, 9.0 mg/dL (IQR: 8.6–9.6). The median alanine aminotransferase level was 17 U/L (IQR: 12–21), and the median aspartate aminotransferase level was 19 U/L (IQR: 15–32).

Coagulation parameters showed a median activated partial thromboplastin time (aPTT) of 28.5 seconds (IQR: 25.8–30.8) and an international normalized ratio (INR) of 1.1 (IQR: 1.0–1.1). Blood gas analysis demonstrated a median pH of 7.39 (IQR: 7.37–7.42), bicarbonate level of 25.8 mEq/L (IQR: 24.3–27.8), and lactate level of 1.1 mmol/L (IQR: 0.9–1.2).

According to the Shapiro–Wilk test, several variables deviated from a normal distribution; therefore, nonparametric tests were used for comparative analyses.

Treatment and Outcomes

Regarding management, 7 patients (43.8%) received pyridostigmine, 3 patients (18.8%) received botulinum antitoxin, and 6 patients (37.5%) were managed with observation (Table 1). All three patients who received botulinum antitoxin had bulbar or

respiratory symptoms at presentation: dysphagia was reported by two patients, and dyspnea or orthopnea by two; one of them, who had been exposed to approximately three vials of a botulinum toxin type A preparation at multiple injection sites, additionally had nasal speech and objective proximal limb weakness (upper extremity muscle strength, 3/5). In two of these three patients, antitoxin had been initiated at the referring institution before transfer and was continued at our hospital, whereas in the third, it was initiated on the day of admission, within three days of symptom onset; in this patient, limb muscle strength improved to 4/5 within 24 hours. No patient required endotracheal intubation. The median length of hospital stay was 2.5 days (IQR: 2–3; range: 1–5). The median APACHE II score was 5 (IQR: 2–10). Fourteen patients (87.5%) were discharged, whereas two patients (12.5%) refused treatment. No mortality was observed during the study period.

Comparative Analyses

Treatment vs. Observation Groups

Patients were categorized into two groups: those receiving treatment (antitoxin or pyridostigmine; n=10) and those managed with observation (n=6) (Table 2).

There was no significant difference in age (median: 33.5 [IQR: 28.5–41.2] vs. 41.5 [IQR: 34.0–49.8]; p=0.102), APACHE II score (p=0.114), or length of hospital stay (p=0.382) between the groups.

Etiological distribution differed significantly between the groups (p=0.035), with cosmetic botulinum toxin exposure predominating in the treatment group (50.0%), whereas gastric botulinum toxin exposure was more common in the observation group (83.3%).

Patients in the treatment group had significantly lower systolic blood pressure (p=0.039), diastolic blood pressure (p=0.045), and mean arterial pressure (p=0.011) than those in the observation group. Blood gas analysis revealed a significantly higher pH in the treatment group (p=0.009). As treatment was allocated on clinical grounds rather than randomly, these differences are interpreted with caution in the Discussion.

Glucose and urea levels showed borderline differences between the groups, whereas no significant differences were observed in other hematological, biochemical, or coagulation parameters.

Neurological Symptom-Based Comparison

Patients were divided into those with neurological symptoms (n=13) and those without neurological symptoms (n=3) (Table 3). No significant differences were observed between the groups in terms of age, APACHE II score, or length of hospital stay.

Among laboratory parameters, only serum chloride levels were significantly lower in patients with neurological symptoms (p=0.044). No other significant differences were identified.

Correlation Analysis

Using Spearman's rank correlation analysis, platelet count was positively correlated with length of hospital stay (rho=0.508, p=0.045). Similarly, aPTT showed a significant positive correlation with length of hospital stay (rho=0.538, p=0.031) (Table 4).

A moderate positive correlation was observed between calcium levels and length of hospital stay (rho=0.449; p=0.081), whereas a moderate negative correlation was found between INR and length of hospital stay (rho=-0.456; p=0.076), both at a trend level. No significant correlations were observed for other variables.

Discussion

In this study, we evaluated the etiological characteristics, clinical findings at emergency department presentation, neurological involvement, and the follow-up and treatment processes of patients who developed botulism following exposure to botulinum toxin for various reasons. In this retrospective study, the vast majority of cases were found to be attributable to iatrogenic botulism. To our knowledge, this is one of the few consecutive emergency department series in which iatrogenic botulism, rather than foodborne disease, accounted for almost all cases and in which intragastric botulinum toxin injection performed for weight reduction was as frequent a source as cosmetic facial injection. Its contribution is therefore primarily practical: it describes how these patients present at the front door of the hospital, which alternative diagnoses are considered, how treatment is selected in the absence of a standardized protocol, and what the corresponding outcomes are.

Botulinum toxin injections have become widely used in clinical practice, with proven efficacy in cosmetic procedures, hyperhidrosis treatment, chronic migraine, urological conditions such as overactive bladder, obesity-related interventions, and the management of neurological disorders, including spasticity and dystonia [21–23]. Following administration, systemic dissemination of the toxin, particularly if it enters the circulation, may lead to peripheral neuromuscular blockade and result in a clinical picture consistent with botulism [23]. However, the expanding range of indications and challenges in individual dose adjustment have contributed to an increasing number of iatrogenic botulism cases worldwide [18,19,24]. In addition, exposure to unlicensed or nonstandard botulinum toxin preparations represents an important risk factor for the development of such cases [19].

Table 2. Comparison of patients managed with treatment versus observation

Variable	Treatment (n=10)	Observation (n=6)	Test statistic	p
Demographic and clinical				
Age, years	33.5 (28.5–41.2)	41.5 (34.0–49.8)	U=14.5	0.102
APACHE-II	8.5 (4.2–11.8)	2.0 (1.2–4.2)	U=45.0	0.114
Length of stay, days	3 (2–3)	2.0 (2.0–2.8)	U=38.0	0.382
Time from exposure, days†	7.0 (6.0–7.5)	7.0 (4.8–7.8)	U=22.0	0.941
Vital parameters				
Systolic BP, mmHg	119.0 (104.2–122.5)	128.0 (124.0–133.5)	U=10.5	0.039 *
Diastolic BP, mmHg	61.5 (59.2–69.5)	72.0 (69.2–77.0)	U=11.0	0.045 *
MAP, mmHg	74.5 (72.0–80.0)	89.0 (87.2–90.8)	U=6.0	0.011 *
Temperature, °C	36.5 (36.0–36.7)	36.2 (36.1–36.5)	U=34.5	0.660
Heart rate, /min	77.0 (66.2–86.5)	87.0 (78.2–91.2)	U=16.5	0.158
Respiratory rate, /min	16 (14–16)	17.0 (15.5–18.5)	U=16.0	0.136
Laboratory findings				
Leukocytes, /mm^3	6,990 (6,300–8,400)	6,375 (5,995–6,522)	U=36.5	0.515
Hemoglobin, g/dL	12.3 (11.7–13.7)	13.8 (11.4–15.0)	U=26.0	0.704
Hematocrit, %	38.0 (35.5–41.2)	42.0 (34.6–45.8)	U=24.0	0.551
MCV, fL	85.1 (82.0–87.1)	85.3 (81.8–88.2)	U=28.0	0.871
Platelets, /mm^3	276,500 (230,250–314,000)	236,000 (214,000–292,500)	U=39.0	0.356
Neutrophils, /mm^3	4,020 (3,292–4,667)	4,030 (3,530–6,480)	U=27.0	0.792
Lymphocytes, /mm^3	2,725 (1,947–3,027)	1,765 (1,530–1,955)	U=39.0	0.368
CRP, mg/dL	0.6 (0.1–2.8)	2.9 (0.7–5.8)	U=18.0	0.211
Glucose, mg/dL	89.5 (82.0–93.5)	97.5 (92.5–104.0)	U=11.5	0.050 ‡
Urea, mg/dL	19.7 (17.7–24.2)	26.7 (24.9–29.9)	U=14.0	0.093 ‡
Creatinine, mg/dL	0.71 (0.68–0.76)	0.73 (0.67–0.77)	U=30.0	1.000
Sodium, mEq/L	139.5 (138.2–140.8)	140.5 (139.2–141.8)	U=23.0	0.476
Potassium, mEq/L	4.1 (4.0–4.4)	4.3 (3.9–4.4)	U=28.0	0.875
Chloride, mEq/L	104 (104–105)	106.0 (103.5–107.8)	U=20.5	0.322
Calcium, mg/dL	9.1 (8.9–9.5)	8.8 (8.6–9.5)	U=36.5	0.515
Magnesium, mg/dL	2.02 (1.94–2.25)	2.02 (1.91–2.10)	U=33.0	0.786
Albumin, g/L	42 (41–45)	41 (38–45)	U=34.0	0.702
CK, U/L	91.0 (73.5–113.8)	75.5 (50.2–121.8)	U=37.0	0.492
ALT, U/L	16.0 (12.2–20.5)	17.0 (12.8–33.2)	U=26.5	0.744
AST, U/L	19.0 (15.8–27.8)	18.0 (13.8–33.5)	U=29.5	1.000
aPTT, s	28.5 (26.9–30.1)	27.4 (25.4–31.5)	U=30.5	1.000
INR	1.00 (1.00–1.10)	1.10 (1.02–1.18)	U=20.0	0.277
pH	7.420 (7.397–7.437)	7.364 (7.344–7.381)	U=54.5	0.009 **
HCO_3 , mEq/L	24.8 (24.2–26.4)	27.4 (26.4–27.8)	U=19.0	0.254
Lactate, mmol/L	1.00 (0.80–1.20)	1.20 (0.97–1.27)	U=19.0	0.249
Ionized Ca^2 , mmol/L	1.19 (1.18–1.22)	1.17 (1.07–1.23)	U=35.5	0.584
Base excess, mEq/L	0.0 (–0.3–1.2)	2.0 (1.2–2.6)	U=21.0	0.356

*Data are presented as median (interquartile range, IQR). Comparisons were performed using the Mann–Whitney U test. The treatment group received botulinum antitoxin and/or pyridostigmine; the observation group received supportive care only. * $p < 0.05$; ** $p < 0.01$; ‡ borderline ($0.05 \leq p < 0.10$). †Time from exposure to admission was available for 7 patients in the treatment group and 6 in the observation group (3 patients with missing data).*

Table 3. Comparison of patients with versus without neurological symptoms

Variable	Neurological (+) (n=13)	Neurological (–) (n=3)	Test statistic	p
Demographic and clinical				
Age, years	34.0 (29.0–44.5)	42.0 (34.0–67.0)	U=10.0	0.201
APACHE-II	5.0 (1.5–10.5)	5.0 (0.0–12.0)	U=20.5	0.893
Length of stay, days	2.0 (2.0–3.0)	3.0 (2.0–4.0)	U=13.5	0.420
Time from exposure, days†	7.0 (7.0–7.8)	5.0 (2.5–6.5)	U=20.5	0.383
Vital parameters				
Systolic BP, mmHg	123 (108–129)	118 (104–132)	U=22.5	0.687
Diastolic BP, mmHg	69 (61–76)	62 (56–70)	U=26.5	0.346
MAP, mmHg	80 (73–89)	80 (72–90)	U=19.5	1.000
Temperature, °C	36.2 (36.0–36.5)	36.5 (36.5–37.2)	U=8.0	0.122
Heart rate, /min	80 (70–89)	92 (70–92)	U=14.0	0.459
Respiratory rate, /min	16 (14–18)	16 (15–18)	U=17.5	0.788
Laboratory findings				
Leukocytes, /mm^3	6,570 (6,060–9,395)	6,280 (4,920–6,540)	U=29.5	0.179
Hemoglobin, g/dL	13.2 (11.1–14.9)	12.5 (12.2–12.8)	U=21.0	0.840
Hematocrit, %	40.5 (34.6–44.5)	37.9 (35.3–38.8)	U=24.5	0.501
MCV, fL	84.9 (80.8–86.8)	91.0 (82.0–91.9)	U=9.5	0.179
Platelets, /mm^3	237,000 (214,000–305,500)	288,000 (258,000–322,000)	U=13.0	0.382
Neutrophils, /mm^3	4,070 (3,580–5,555)	3,020 (2,950–42,500)	U=24.0	0.545
Lymphocytes, /mm^3	2,180 (1,470–3,345)	1,870 (1,620–2,850)	U=23.0	0.638
CRP, mg/dL	1.0 (0.6–10.2)	2.6 (0.2–4.9)	U=15.0	0.584
Glucose, mg/dL	91 (83–97)	96 (92–106)	U=9.5	0.179
Urea, mg/dL	20.8 (17.8–28.9)	24.4 (22.9–37.3)	U=13.0	0.382
Creatinine, mg/dL	0.73 (0.67–0.87)	0.71 (0.64–0.72)	U=25.5	0.420
Sodium, mEq/L	139 (138–142)	141 (140–142)	U=11.0	0.253
Potassium, mEq/L	4.20 (3.81–4.46)	4.14 (4.10–4.47)	U=17.0	0.737
Chloride, mEq/L	104 (103–105)	107 (106–108)	U=4.5	0.044 *
Calcium, mg/dL	9.00 (8.75–9.68)	8.64 (8.60–9.76)	U=23.5	0.590
Magnesium, mg/dL	2.00 (1.87–2.28)	2.10 (1.93–2.16)	U=17.0	0.737
Albumin, g/L	43 (39–48)	41 (37–46)	U=24.0	0.545
CK, U/L	81 (69–135)	95 (60–136)	U=19.0	0.946
ALT, U/L	15 (12–22)	19 (10–62)	U=17.5	0.788
AST, U/L	18 (14–26)	37 (14–38)	U=11.5	0.282
aPTT, s	28.3 (25.5–31.4)	28.8 (27.2–31.5)	U=15.0	0.545
INR	1.1 (1.0–1.2)	1.0 (1.0–1.0)	U=30.0	0.158
pH	7.390 (7.349–7.434)	7.420 (7.386–7.420)	U=16.5	0.687
HCO_3 , mEq/L	26.2 (23.9–27.9)	25.3 (24.4–27.8)	U=19.0	0.946
Lactate, mmol/L	1.1 (0.9–1.4)	1.2 (0.8–1.2)	U=20.5	0.893
Ionized Ca^2 , mmol/L	1.18 (1.10–1.23)	1.21 (1.15–1.24)	U=16.0	0.638
Base excess, mEq/L	0.9 (–0.8–3.7)	2.0 (1.3–2.8)	U=8.0	0.466

*Data are presented as median (interquartile range, IQR). Comparisons were performed using the Mann–Whitney U test. Neurological symptoms refer to cranial nerve or motor involvement excluding altered consciousness. * p<0.05. †Time from exposure to admission was available for 10 patients in the Neurological(+) group and 3 in the Neurological(–) group (3 patients with missing data).*

Table 4. Correlations between clinical/laboratory variables and length of hospital stay.

Variable	n	r_s	p	Interpretation
Demographic				
Age	16	0.000	1.000	No correlation
Time from exposure, days	8	0.140	0.741	Weak positive
Vital parameters				
Systolic BP	16	–0.196	0.466	Weak negative
Diastolic BP	16	0.172	0.523	Weak positive
MAP	16	0.034	0.900	No correlation
Temperature	16	–0.101	0.710	Weak negative
Heart rate	16	0.002	0.995	No correlation
Laboratory findings				
Leukocytes	16	0.365	0.164	Moderate positive
Hemoglobin	16	–0.058	0.832	No correlation
Hematocrit	16	–0.121	0.655	Weak negative
MCV	16	0.238	0.375	Weak positive
Platelets	16	0.508	0.045	Strong positive *
Neutrophils	16	0.218	0.417	Weak positive
Lymphocytes	16	0.063	0.816	No correlation
CRP	14	0.389	0.170	Moderate positive
Glucose	16	0.082	0.762	No correlation
Urea	16	–0.338	0.200	Moderate negative
Creatinine	16	–0.313	0.237	Moderate negative
Sodium	16	0.263	0.326	Weak positive
Potassium	16	0.368	0.161	Moderate positive
Chloride	16	–0.072	0.791	No correlation
Calcium	16	0.449	0.081	Moderate positive ‡
Magnesium	16	0.149	0.581	Weak positive
Albumin	16	0.212	0.432	Weak positive
CK	16	0.137	0.612	Weak positive
ALT	16	0.344	0.192	Moderate positive
AST	16	0.257	0.336	Weak positive
aPTT	16	0.538	0.031	Strong positive *
INR	16	–0.456	0.076	Moderate negative ‡
pH	16	0.110	0.684	Weak positive
HCO_3^-	16	–0.055	0.839	No correlation
Lactate	16	–0.090	0.740	No correlation
Ionized Ca^2	16	–0.076	0.780	No correlation
Base excess	14	0.186	0.525	Weak positive

*r_s, Spearman rank correlation coefficient. Dependent variable: length of hospital stay (days). * $p<0.05$; ‡ borderline ($0.05 \leq p<0.10$). Oxygen saturation (SpO_2) was excluded from the analysis due to insufficient data (n=7) and one suspected data entry error.*

The etiological distribution observed in our cohort differs substantially from that reported in classical botulism series. In large reviews of foodborne and wound botulism, improperly preserved home-canned foods and injection drug use account for the overwhelming majority of cases, and affected patients are, on average, older and have a more balanced sex distribution [5,6,8–10]. In our cohort, by contrast, 15 of 16 patients (93.7%) had iatrogenic exposure, 81.2% were women, and the median age was 34 years, a profile that mirrors the demographic characteristics of the population undergoing aesthetic and weight-reduction procedures. Comparable patterns have been reported recently: the multinational outbreak that followed intragastric botulinum neurotoxin injections performed in Türkiye in 2023 predominantly affected young women [15]; in the 2025 outbreak in England linked to cosmetic injections of unlicensed products, all 25 identified cases presented to emergency departments [19]; and Eser et al. [18] described iatrogenic botulism after gastric and axillary administration in a Turkish cohort with similar characteristics. The equal contribution of intragastric (37.5%) and cosmetic facial or cervical (37.5%) injections in the present series suggests that, in settings where intragastric botulinum toxin is widely offered, this indication has become as important a source of iatrogenic botulism as aesthetic facial use, a shift that has not yet been reflected in most emergency medicine literature.

Previous studies have consistently reported that botulism typically presents with cranial nerve involvement and preserved consciousness, with symptoms such as diplopia, ptosis, dysarthria, and dysphagia being the most common initial findings [1,3]. In line with the existing literature, the majority of patients in our cohort presented with prominent neurological symptoms without impaired consciousness, predominantly involving cranial nerve dysfunction. Gastrointestinal symptoms were observed in a subset of patients, whereas altered consciousness and respiratory symptoms were relatively uncommon, supporting the classical clinical spectrum of botulism [3]. The absence of fever and the relative preservation of mental status in most patients may help differentiate botulism from other acute neurological conditions, particularly in emergency settings, where misdiagnosis can delay appropriate management. The frequency of cranial nerve involvement in our series (81.3%) is comparable to that reported in systematic reviews of foodborne and wound botulism, in which such findings are present in the great majority of patients [6]. The interval between symptom onset and presentation, however, differed markedly: the median of 7 days observed here is substantially longer than the 12–36-hour incubation period usually cited [2] and longer than that observed in outbreak settings, where active public health case finding accelerates presentation [15,19]. A plausible explanation is that patients with iatrogenic exposure initially attribute their symptoms to the procedure itself and seek care only when the symptoms fail to resolve.

In addition to the characteristic neurological presentation, laboratory findings in botulism are generally expected to remain within normal limits, reflecting the primarily neurotoxic rather than inflammatory or myopathic nature of the disease [25]. In our cohort, most laboratory parameters were within normal ranges, supporting this observation. Although gastrointestinal symptoms such as nausea, vomiting, or diarrhea may occur and can occasionally be associated with mild metabolic disturbances, marked biochemical abnormalities are typically not expected [2,3].

This pattern is particularly helpful in differentiating botulism from other neuromuscular and neurological conditions. Unlike disorders such as hypokalemic periodic paralysis, which is characterized by episodic weakness associated with low serum potassium levels, or inflammatory myopathies, botulism is not associated with significant laboratory abnormalities or elevated creatine kinase levels [25,26]. Furthermore, whereas Guillain–Barré syndrome typically presents with ascending weakness, botulism is characterized by a descending pattern of paralysis [27]. In contrast to variants such as Miller Fisher syndrome, in which cranial nerve involvement is accompanied by sensory deficits, deep sensation is generally preserved in botulism [28]. These distinctions are particularly important in emergency settings, where episodic or acute neuromuscular weakness may initially suggest alternative diagnoses and contribute to delayed recognition of botulism.

The diagnostic process in this cohort illustrates these difficulties in practice. Because the initial complaints, such as blurred vision, diplopia, ptosis, dysphagia, generalized weakness, and, in some patients, nausea and vomiting, are nonspecific, and because routine laboratory tests and cranial imaging are typically unremarkable, botulism tends to be considered only after alternative diagnoses have been entertained. Conditions commonly considered first in such patients include myasthenia gravis, Guillain–Barré syndrome and its Miller Fisher variant, brainstem ischemia, ophthalmological disease, electrolyte disturbances, and functional neurological disorders [14,25,26]. Electrodiagnostic testing is of limited help in this situation: in our cohort, the studies that were performed were normal and did not modify the clinical diagnosis, which is consistent with the recognized insensitivity of routine nerve conduction studies and needle electromyography in mild botulism, particularly when high-frequency repetitive nerve stimulation is not performed [20,25]. In our setting, the decisive diagnostic step was therefore not a laboratory or electrophysiological test but the exposure history combined with specialist neurological assessment. This has a direct

practical implication: in a patient with acute, afebrile, symmetrical cranial nerve dysfunction and preserved consciousness, explicit questioning about botulinum toxin administration is essential, including intragastric procedures, which patients may not spontaneously report as medical interventions, and cosmetic injections performed outside licensed medical settings.

In our cohort, different management strategies were observed, including supportive care alone, pyridostigmine administration, and botulinum antitoxin treatment. Notably, patients who received antitoxin presented earlier in the disease course and exhibited symptoms suggestive of potential clinical progression, such as dysphagia and dyspnea. In contrast, patients managed with supportive care or pyridostigmine typically presented later, often several days after symptom onset, and had relatively milder clinical manifestations. Two features of the antitoxin group deserve comment. First, the indication in practice was symptom-based rather than dose-based: bulbar or respiratory symptoms and, in the most severely affected patient, objective proximal weakness, rather than the reported number of units injected, determined the decision. Second, in two of the three patients, the decision had already been made at the referring institution, so our role was to continue treatment and monitor for deterioration. This is a common situation for tertiary referral centers and means that treatment allocation in such cohorts is only partly under the control of the receiving hospital, a point that also limits any comparison between treated and untreated patients.

These findings likely reflect real-world clinical decision-making rather than treatment efficacy, as antitoxin administration is generally prioritized in patients at risk of progression, particularly when respiratory or bulbar involvement is suspected [20]. Early administration of botulinum antitoxin, ideally within the first 24–48 hours after symptom onset, is recommended to limit disease progression and improve clinical outcomes [20]. Conversely, delayed presentation and milder symptoms may lead clinicians to adopt a more conservative approach. Although pyridostigmine has been used as a symptomatic treatment in selected cases, its role in botulism remains unclear and controversial and is not supported by current clinical guidelines, given the presynaptic mechanism of the disease and the limited and inconsistent clinical evidence [20,29].

The comparisons between the treatment and observation groups must therefore be interpreted with considerable caution. Patients were not allocated at random; allocation was determined by clinical severity, symptom progression, and the interval since exposure. The differences observed between the two groups, namely lower systolic, diastolic, and mean arterial pressures and higher pH in the treated group, are more plausibly markers of the clinical profile that prompted treatment or chance findings arising from multiple comparisons in a small sample than consequences of treatment itself. The same reasoning applies to the significant difference in etiological distribution between the groups, which reflects the observation that patients with intragastric exposure presented later and with milder findings. Consequently, no inference regarding the comparative effectiveness of antitoxin, pyridostigmine, or observation can be drawn from these data, and the present study should not be used to support or discourage any of these strategies.

Early recognition of botulism and timely initiation of appropriate management are critical determinants of clinical outcomes. Previous studies have demonstrated that early administration of botulinum antitoxin is associated with reduced mortality and improved clinical outcomes [20]. In addition, advances in supportive care, particularly respiratory management, have significantly decreased mortality rates in recent decades [1,3,20]. In our cohort, no mortality was observed, and all patients who received appropriate management were discharged with clinical recovery.

The absence of both endotracheal intubation and mortality is among the most notable findings of this study, and several explanations should be considered before this is interpreted as evidence of effective management. First, and probably most importantly, the cohort was shaped by its own natural history: the median interval from symptom onset to admission was 7 days, and patients who were still ambulatory and self-presenting a week after the onset of neuroparalytic symptoms necessarily represented the milder end of the disease spectrum, since respiratory compromise in botulism typically develops within the first days after exposure [3,20]. Second, the toxin burden after localized intramuscular or intragastric injection is generally lower than that associated with foodborne disease, in which large amounts of preformed toxin are ingested; accordingly, foodborne series report frequent mechanical ventilation, whereas most published iatrogenic cases recover without ventilatory support [6,11,17]. Third, our patients were young (median age, 34 years), predominantly female, and largely free of cardiopulmonary comorbidities, with a median APACHE II score of 5, indicating limited physiological derangement at presentation. Fourth, awareness of iatrogenic botulism has increased considerably in Türkiye since the widely reported 2023 intragastric botulinum toxin cluster [15,18], which is likely to have shortened the time from admission to recognition and ensured that patients were monitored for respiratory deterioration from the outset. Fifth, the three patients with bulbar or respiratory involvement, that is, the group genuinely at risk of progression, all received antitoxin, in two cases already at the referring institution,

and all patients were observed at a tertiary center with immediate access to intensive care.

The statistical interpretation of a zero-event rate also deserves emphasis. With 16 patients and no observed intubations or deaths, the upper limit of the 95% confidence interval for these outcomes is approximately 19% [30]. The present data are therefore fully compatible with a clinically important risk of respiratory failure in iatrogenic botulism and should not be interpreted as evidence that the condition is benign. Similarly, the correlations between length of hospital stay and platelet count or aPTT should be regarded as hypothesis-generating only: all of these values were within the reference range, no biologically plausible mechanism links them to the duration of a neuroparalytic illness, and with 16 patients and multiple correlations tested without adjustment, findings at the $p<0.05$ level are expected to occur by chance. The same caution applies to the isolated difference in serum chloride between patients with and without neurological symptoms.

Study Limitations

This study has several limitations. First, the sample size was small and derived from a single tertiary center, which limits both statistical power and external validity; the subgroup and correlation analyses, in particular, should be regarded as exploratory. Second, the diagnosis was established on clinical grounds and by specialist consensus, without laboratory confirmation of botulinum neurotoxin or routine electrodiagnostic testing, so misclassification of mimicking conditions cannot be excluded with certainty. Third, the retrospective design carries the risk of information bias and incomplete documentation, particularly regarding the exact dose, preparation, and licensing status of the injected botulinum toxin, which were rarely recorded. Fourth, treatment was not randomized, and the treatment and observation groups differed in clinical severity and timing of presentation, precluding any conclusion regarding comparative effectiveness; moreover, in some patients, antitoxin had already been started at the referring institution, so the indication and timing of the first dose were not determined by a uniform protocol. Fifth, patients were not followed systematically after discharge, so the time to complete symptom resolution and possible long-term sequelae are unknown. Finally, patients with milder disease who did not seek emergency care and those who presented to other institutions were not captured, which may have biased the cohort toward a particular severity profile.

Conclusion

In conclusion, botulism should be considered in patients presenting with acute cranial nerve dysfunction and preserved consciousness, particularly in the context of recent botulinum toxin exposure. The predominance of iatrogenic cases and the equal contribution of intragastric and cosmetic injections highlight the growing clinical relevance of this condition in modern emergency practice. Early recognition and timely administration of antitoxin are critical to preventing disease progression and ensuring favorable outcomes. Increased awareness among clinicians, especially in emergency settings, may help reduce diagnostic delays and improve patient management. The favorable outcomes observed in this cohort, however, were achieved in patients who presented late and had predominantly mild disease, and they should not be generalized to patients presenting early after high-dose exposure, in whom close respiratory monitoring remains essential.

Ethics

Ethics Committee Approval: This study was approved by The Local Ethics Committee of Çam and Sakura City Hospital (Date: 29.04.2026 – Decision: 187/2026).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

Conflict of Interest: The authors declare that there is no conflict of interest.

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Authorship Contributions:

Concept: R.S., S.T.; Design: R.S., R.K.B., S.T.; Supervision: –; Resource: –; Materials: –; Data Collection and/or Processing: R.K.B., S.T.; Analysis and/or Interpretation: R.K.B.; Literature Search: –; Writing: R.S., R.K.B., S.T.; Critical Reviews: R.S., R.K.B., S.T.

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ORIGINAL RESEARCH

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Evaluation of the Relationship Between the Change in Base Excess and Clinical Conditions in Patients with Diabetic Ketoacidosis

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Abstract

Objective: The aim of this study was to evaluate the post-treatment change in base excess (ΔBE) in diabetic ketoacidosis (DKA) and to assess how both the magnitude of correction and the resulting acid–base status relate to presenting severity and routine laboratory parameters.

Materials and Methods: We retrospectively analyzed 202 adults presenting with DKA to a tertiary emergency department between 2020 and 2025 who underwent blood gas analysis at presentation and after treatment. ΔBE was defined as post-treatment minus baseline base excess. Comparisons were performed using the Mann–Whitney U and Kruskal–Wallis tests, and associations were assessed using Spearman's rho.

Results: The median age was 39 years, and 59.9% were male. At presentation, the median pH was 7.08 and HCO_3 was 7.7 mmol/L, indicating marked acidemia. Following treatment, the median ΔBE was 11.9 mmol/L. The magnitude of correction increased with the depth of presenting acidosis (Spearman's rho=−0.75) and was greater in patients with higher baseline white blood cell counts, glucose, urea, creatinine, and C-reactive protein levels and in those admitted to the intensive care unit versus the ward (16.1 vs 7.8 mmol/L, p<0.001). Although ΔBE differed according to presenting severity (p=0.026), post-treatment base excess was statistically similar across severity strata (p=0.374), indicating that treatment brought patients to a comparable acid–base endpoint regardless of the severity at presentation.

Conclusion: In DKA, the change in base excess following treatment (ΔBE) is a parameter that can be easily derived from laboratory data and is associated with patients' clinical status.

Keywords: Acidosis, base excess, blood gas analysis, critical care, diabetic ketoacidosis

Introduction

Diabetic ketoacidosis (DKA) is more than a simple complication; it is a life-threatening diabetic emergency. Developing against a background of insulin deficiency and increased levels of counter-regulatory hormones, it is characterized by hyperglycemia, ketosis, and anion-gap metabolic acidosis and requires rapid diagnosis and treatment [1,2]. Although classically associated with type 1 diabetes, DKA can also occur in the context of type 2 diabetes [2]. Most patients with DKA first present to the emergency department, where diagnosis, severity assessment, and risk stratification are largely performed. Despite advances in diagnostic and treatment options, DKA remains a significant cause of morbidity, mortality, and healthcare expenditure among patients with diabetes, and its diagnosis and management continue to be actively debated [3]. This highlights the importance of both early diagnosis and objective monitoring of treatment response.

The latest international consensus report on the diagnosis and treatment of DKA, published in 2024, has redefined the criteria for diagnosis and resolution. In this report, the anion gap has been removed from the diagnostic criteria; beta-hydroxybutyrate measurement has been placed at the center of diagnosis, severity assessment, and monitoring of resolution; the treatment regimen has been simplified to focus on the fluid–insulin–potassium axis; and, in the assessment of acid–base status, arterial blood gas

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sampling has been deemed unnecessary, with venous sampling considered sufficient [1,3]. These changes have increased interest in integrated acid–base parameters, which can be readily obtained from venous blood gas analysis, during the process of suppressing ketone production and correcting metabolic acidosis, the primary treatment objectives [1,4].

Various blood gas parameters are used to assess the severity and course of acidosis. Base excess is a measure that reflects the degree of metabolic acid–base disturbance as a single numerical value and is automatically reported in every blood gas analysis [5]. In DKA, baseline base excess has been shown to be more useful than the anion gap in predicting disease severity and the duration of acidosis resolution and to be unaffected by short-term changes in carbon dioxide pressure [6]. Furthermore, although base excess is not included in current severity classifications, it may contribute to risk stratification [7].

The extent to which acidosis resolves in a critically ill patient may be as informative as the initial severity. In patients with sepsis and those in intensive care, the rate at which lactate is cleared over a specific period (lactate clearance) is a widely used indicator [8]; similarly, base excess has been reported to be superior to pH in assessing the resolution of acidosis following traumatic shock [9] and to have prognostic value in intensive care [10,11]. In DKA, high lactate levels have also been associated with adverse outcomes [12]. However, while lactate is not routinely measured in every center or by every blood gas analyzer, base excess is universally available.

It has been reported that the median resolution time for DKA is approximately 18 hours, although this may vary among patients from 2 to 32 hours [6]; such interpatient variation points to determinants of treatment response that remain poorly understood. Nevertheless, existing studies have primarily focused on the predictive value of base excess at presentation; the magnitude of the change in base excess following treatment and the clinical determinants of this change have not been specifically investigated. In this study, we aimed to characterize the change in base excess (ΔBE) following treatment in patients with DKA and to evaluate its relationship with patients' clinical and laboratory status.

Materials and Methods

Study Design and Patient Selection

This single-center, retrospective, observational cohort study included adult patients (aged ≥18 years) who presented to the emergency department of a tertiary teaching and research hospital with diabetic ketoacidosis between March 1, 2020, and March 1, 2025. The diagnosis of DKA was made in accordance with current guidelines [1], based on the combination of hyperglycemia (blood glucose >250 mg/dL), metabolic acidosis (pH <7.30, HCO_3 <18 mmol/L), and ketosis (documented by urine or blood ketone positivity). Because the study period spanned the 2024 revision of the diagnostic criteria, the diagnosis rested primarily on the combination of metabolic acidosis and ketosis; the blood glucose value of 250 mg/dL was applied as a supporting threshold rather than a strict cutoff, and lower-glucose or euglycemic ketoacidosis presentations that met the acidosis and ketosis criteria were not excluded. A total of 245 adults presenting with DKA during the study period were evaluated. Forty-three patients were excluded: those under 18 years of age, those who died within the first 24 hours, and those with incomplete data. To enable calculation of the change in base excess, each patient was required to have at least two blood gas measurements, one at presentation and one following treatment. The 202 cases meeting these criteria were analyzed (Fig. 1). The study was reported in accordance with the STROBE guideline for observational studies.

Data Collection and Definitions

Demographic data, type of diabetes, admission laboratory values, serial blood gas measurements, admission unit (intensive care unit/ward), length of stay, and in-hospital mortality were obtained from the hospital's electronic records system. The severity of presentation was classified as mild, moderate, or severe according to the American Diabetes Association criteria, based on the pH value at presentation [1]. Diabetes type was recorded as type 1, type 2, or other/unspecified from the diagnostic records in the

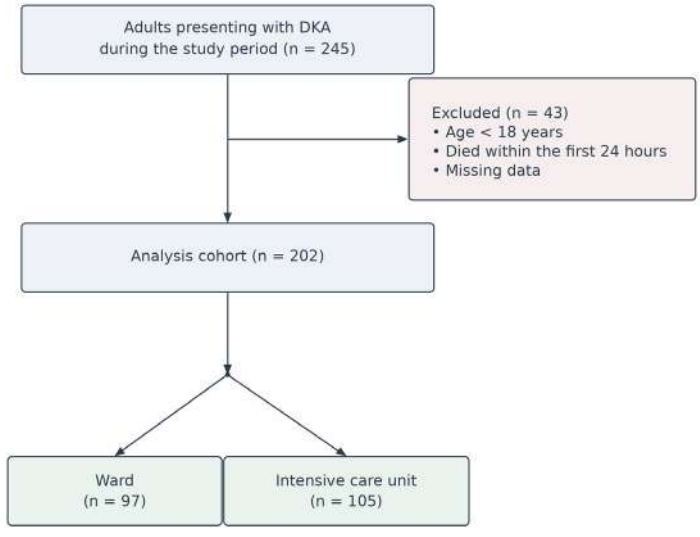

Figure 1. Study flow chart. Of the 245 adults who presented with diabetic ketoacidosis during the study period, 43 were excluded (those under 18 years of age, those who died within the first 24 hours, and those with incomplete data), leaving 202 cases for analysis; of these, 97 were managed on the ward and 105 in the intensive care unit.

hospital's electronic records system. Base excess is a parameter calculated from blood gas analysis that reflects metabolic acid–base status [13,14]; in this study, base excess and other blood gas values were obtained from venous or arterial blood gas analysis. Although venous and arterial blood gas measurements have been reported to agree closely for bicarbonate and overall acid–base parameters [15,16], this agreement has not been demonstrated specifically for base excess. For each patient, blood gas base excess values at presentation (presentation BE) and after treatment (post-treatment BE) were recorded; post-treatment base excess was defined as the last blood gas measurement obtained during the treatment course following admission. The change in base excess, ΔBE, was defined as post-treatment BE−presentation BE; percentage improvement was calculated as ΔBE/|presentation BE|×100. In cases where post-treatment base excess reached positive values, this percentage could exceed 100%.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA). The normality of distributions was assessed using the Shapiro–Wilk test. Continuous variables that did not follow a normal distribution were summarized as medians with 25th and 75th percentiles, and two groups were compared using the Mann–Whitney U test. The Kruskal–Wallis test was used to compare three independent groups, such as the presentation severity strata. Categorical variables were presented as counts (percentages), and groups were compared using the chi-square or Fisher's exact test. Relationships between continuous variables were examined using Spearman's rank correlation coefficient (rho). A p value of <0.05 was considered statistically significant.

Ethics

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the local ethics committee (approval no. E-62190176-663.05-269193889, dated August 7, 2024). Owing to the retrospective design, the requirement for informed consent was waived.

Results

Cohort Characteristics

Following the exclusion of 43 of the 245 patients who presented during the study period, 202 cases of DKA were analyzed (Fig. 1); of these, 97 (48.0%) were managed on the ward and 105 (52.0%) in the intensive care unit. The median age of the patients was 39 (26–52) years, and 59.9% were male. Regarding diabetes type, 26.2% of cases were recorded as type 1 and 7.4% as type 2; the remaining 66.3% were coded as other or unspecified. On admission, the median pH was 7.08 (6.90–7.19), and HCO_3 was 7.7 (4.0–11.0) mmol/L. Baseline characteristics by admission unit are presented in Table 1. Intensive care unit patients were older than ward patients and, at admission, had more severe acidosis and higher white blood cell counts and glucose, urea, creatinine, and C-reactive protein (CRP) levels.

Change in Base Excess from Presentation to Post-Treatment

While the median base excess (BE) at presentation was −15.9 (−21.9, −11.9) mmol/L, it increased to −3.4 (−7.3, 0.6) mmol/L after treatment. The corresponding median change in base excess (ΔBE) was 11.9 (7.0–17.7) mmol/L, indicating a median improvement of 77% in baseline base excess.

Variables Associated with the Change in Base Excess

Spearman's rho values between ΔBE and admission and clinical variables are summarized in Table 2. ΔBE showed the strongest association with the severity of acidosis at presentation: there was a strong negative correlation between baseline base excess and ΔBE (rho=−0.75, p<0.001); the more severe the acidosis at presentation, the greater the improvement (Fig. 2). Similarly, ΔBE was negatively correlated with baseline HCO_3 (rho=−0.47, p<0.001) and baseline pH (rho=−0.19, p=0.007). ΔBE was also positively correlated with admission white blood cell count (rho=+0.38), glucose (rho=+0.30), urea (rho=+0.20), creatinine (rho=+0.18), and CRP (rho=+0.15) (all p<0.05). No significant relationship was found with age, sodium, potassium, or length of stay.

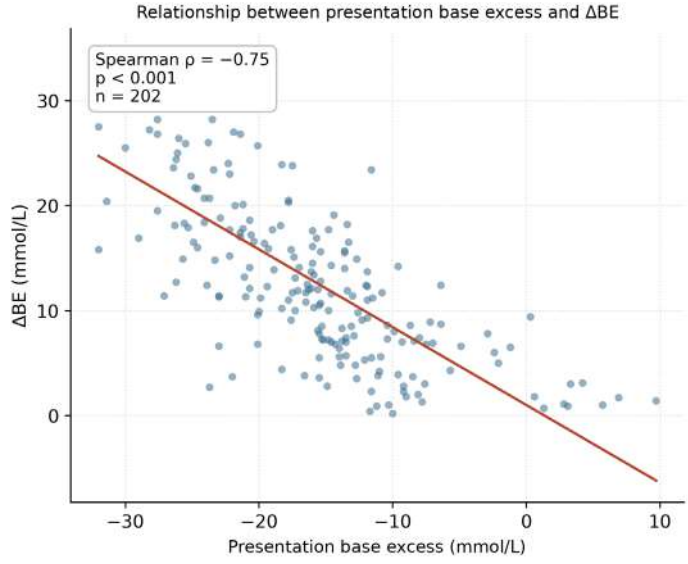

Figure 2. Relationship between presentation base excess and the change in base excess (ΔBE). Each point represents a patient. As acidosis at presentation deepens, ΔBE increases (Spearman's rho = −0.75, p < 0.001; n = 202). The solid line indicates the linear trend.

Table 1. Characteristics of the overall cohort and subgroups by admission unit

Variable	Overall (n=202)	Ward (n=97)	ICU (n=105)	p
Age, years	39 (26–52)	33 (25–48)	45 (28–57)	0.004
Male, n (%)	121 (59.9)	64 (66.0)	57 (54.3)	0.121
DM type, n (%)				0.008
Type 1	53 (26.2)	34 (35.1)	19 (18.1)	
Type 2	15 (7.4)	9 (9.3)	6 (5.7)	
Other/unspecified	134 (66.3)	54 (55.7)	80 (76.2)	
Severity at presentation				
Presentation pH	7.08 (6.90–7.19)	7.10 (7.00–7.20)	7.00 (6.90–7.18)	0.022
Presentation HCO_3, mmol/L	7.7 (4.0–11.0)	9.7 (5.3–12.6)	7.1 (3.9–9.7)	<0.001
Severe / Moderate / Mild, n	68 / 117 / 17	22 / 66 / 9	46 / 51 / 8	
Base excess				
Presentation BE, mmol/L	−15.9 (−21.9, −11.9)	−13.4 (−16.0, −9.3)	−20.4 (−24.1, −15.5)	<0.001
Post-treatment BE, mmol/L	−3.4 (−7.3, 0.6)	−4.2 (−7.6, −0.1)	−2.9 (−6.8, 1.7)	0.125
ΔBE, mmol/L	11.9 (7.0–17.7)	7.8 (4.8–11.9)	16.1 (11.3–23.0)	<0.001
Improvement, %	77 (51–100)	68 (42–92)	83 (64–103)	0.005
Admission laboratory				
White blood cells, 10^3/μL	13.3 (9.7–18.0)	10.4 (7.2–14.4)	16.0 (12.2–21.4)	<0.001
Glucose, mg/dL	255 (187–319)	208 (156–273)	287 (210–367)	<0.001
Urea, mg/dL	28 (18–50)	21 (15–30)	42 (26–60)	<0.001
Creatinine, mg/dL	0.85 (0.67–1.09)	0.75 (0.62–0.96)	1.00 (0.77–1.32)	<0.001
Sodium, mmol/L	135 (133–138)	135 (133–137)	135 (132–141)	0.533
Potassium, mmol/L	4.08 (3.61–4.58)	4.08 (3.64–4.43)	4.14 (3.60–4.92)	0.359
CRP, mg/L	14.2 (4.9–73.8)	10.9 (3.3–24.0)	25.0 (6.9–124.7)	<0.001
Clinical course				
Length of stay, days	3.0 (2.0–4.0)	3.0 (2.0–5.0)	2.0 (2.0–4.0)	0.263
In-hospital mortality, n (%)	8 (4.0)	1 (1.0)	7 (6.7)	0.067

BE: base excess; ΔBE: post-treatment BE − presentation BE; CRP: C-reactive protein; ICU: intensive care unit. Continuous variables are presented as median (25th–75th percentile) and categorical variables as count (%). p-values were obtained from the Mann-Whitney U or chi-square/Fisher test.

Change in Base Excess According to Severity at Presentation

The base excess variables according to severity at presentation are presented in Table 3. Base excess at presentation differed significantly between the severity groups (Kruskal–Wallis p=0.011), with the most severe acidosis observed in the severe group. In parallel, ΔBE also differed between the groups (p=0.026), with the greatest improvement observed in the severe group. In contrast, post-treatment base excess (p=0.374) and percentage improvement (p=0.429) were similar across the severity groups.

Change in Base Excess by Admission Unit

The change in base excess was significantly higher in intensive care cases than in ward cases: the median ΔBE was 7.8 (4.8–11.9) mmol/L on the ward, whereas it was 16.1 (11.3–23.0) mmol/L in the intensive care unit (p<0.001) (Fig. 3). Similarly, the percentage improvement was higher in the intensive care unit (83% vs. 68%; p=0.005). This difference was consistent with intensive care patients presenting with more severe acidosis (a more negative baseline BE) on admission (Table 1).

Discussion

In this retrospective cohort, we demonstrated that treatment produced a median improvement of 77% in baseline base excess in patients admitted with DKA. The magnitude of the change in base excess (ΔBE) was largely determined by the severity of acidosis at presentation, was associated with laboratory markers at presentation, and showed marked differences according to the admission unit. These findings suggest that ΔBE is an easily obtainable indicator in DKA that reflects patients' clinical condition.

The relationship between ΔBE and severity at presentation was as expected: the lower the baseline base excess, bicarbonate, and pH at presentation, the greater the improvement achieved with treatment. A substantial part of this relationship is conceptual because, by definition, the amount of base excess to be corrected is greater in patients presenting with more severe acidosis. The positive correlation between ΔBE and admission markers such as white blood cell count, CRP, glucose, urea, and creatinine is also consistent with this framework: in patients with more severe illness and more pronounced metabolic disturbances, these markers are elevated and the amount of base excess corrected is greater. ΔBE therefore tracks the overall disease burden and is not an independent marker in its own right.

Table 2. Spearman's rho values between ΔBE and the admission and clinical variables (n=202)

Variable	rho	p
Presentation HCO_3	−0.47	<0.001
White blood cells	+0.38	<0.001
Glucose	+0.30	<0.001
Urea	+0.20	0.010
Presentation pH	−0.19	0.007
Creatinine	+0.18	0.018
CRP	+0.15	0.036
Potassium	+0.13	0.074
Length of stay	+0.09	0.187
Age	+0.06	0.421
Sodium	−0.05	0.539

rho: Spearman's rank correlation coefficient. Positive values indicate an association with a greater ΔBE. ΔBE: post-treatment BE − presentation BE. The baseline base excess is not included in the table, as it is associated with ΔBE by definition.

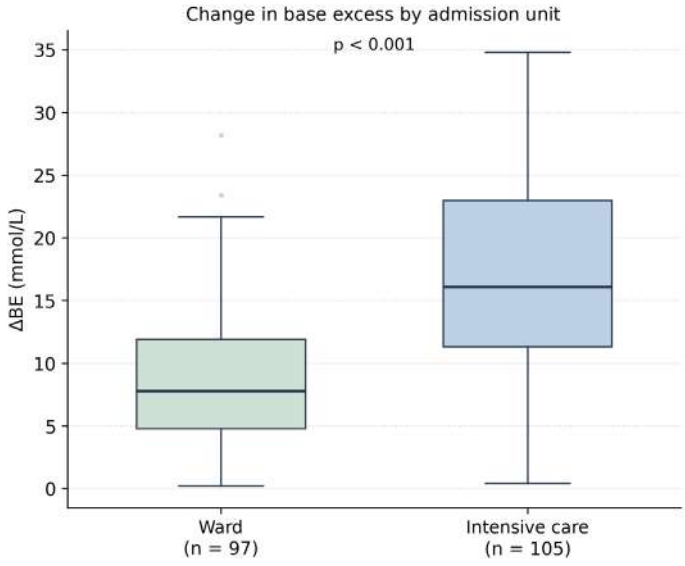

Figure 3. Change in base excess (ΔBE) by admission unit. Boxes show the median and interquartile range, and whiskers show the extremes of the distribution. ΔBE is higher in intensive care cases than in ward cases (Mann-Whitney U, p < 0.001).

Our findings are complementary to previous studies examining base excess in DKA. Jasso-Avila et al. [6] reported that, in a cohort of 79 adult patients, baseline pH, bicarbonate, and base excess predicted the duration of DKA resolution; that a lower baseline base excess was associated with a longer resolution time; and that base excess was superior to the anion gap for this purpose. Güzel et al. [7] correlated base excess with the American Diabetes Association severity strata using serial venous blood gas measurements and demonstrated that base excess contributes to risk stratification. While these studies focused on the predictive value of baseline base excess, we addressed a complementary question: we quantified the change in base excess (ΔBE) in response to treatment, as well as its clinical determinants, in a

Table 3. Base excess variables according to severity strata at presentation.

Variable	Severe (n=68)	Moderate (n=117)	Mild (n=17)	p
Presentation BE, mmol/L	−19.3 (−24.1, −13.6)	−15.5 (−21.0, −11.5)	−14.6 (−15.9, −12.0)	0.011
Post-treatment BE, mmol/L	−3.2 (−7.4, 2.1)	−3.2 (−7.2, 0.0)	−4.6 (−7.6, −2.1)	0.374
ΔBE, mmol/L	15.2 (8.6, 20.5)	11.4 (6.5, 16.6)	8.5 (7.1, 12.5)	0.026
Improvement, %	80 (53, 106)	78 (49, 99)	65 (51, 85)	0.429

BE: base excess; ΔBE: post-treatment BE − presentation BE. Severity was classified according to American Diabetes Association criteria based on presentation pH (severe: pH < 7.0; moderate: 7.0–7.24; mild: 7.25–7.30). Values are median (25th–75th percentile). p-values were obtained from the Kruskal-Wallis test.

relatively large cohort. The fact that the severity of acidosis on admission determines ΔBE (rho=−0.75 for baseline base excess) links these two observations: the lower the baseline base excess on admission, the longer resolution may take and the greater the correction required.

The mechanism underlying the improvement in base excess with treatment can be explained by the pathophysiology of DKA. In DKA, the fundamental problem is lipolysis triggered by insulin deficiency and an increase in counter-regulatory hormones; beta-oxidation of free fatty acids in the liver produces acetoacetate and beta-hydroxybutyrate, both strong acids, and the hydrogen ions released during their breakdown deplete the bicarbonate buffer, leading to anion-gap metabolic acidosis [1–4]. Insulin therapy halts ketogenesis; bicarbonate is regenerated through the metabolism of accumulated keto-anions, and the improvement in tissue perfusion following fluid therapy reduces the lactate load. The combined effect of these processes is observed as a substantial improvement in base excess, shifting from the deeply negative values seen on admission to near-normal levels following treatment.

However, in most cases, base excess did not return to normal following treatment (median −3.4 mmol/L). One reason for this is that chloride-rich fluids, commonly used in the treatment of DKA, can cause iatrogenic hyperchloremic metabolic acidosis, thereby partially masking the expected resolution of acidosis [17]. Indeed, this is one of the reasons why the 2024 consensus removed the anion gap from the diagnostic criteria: hyperchloremic acidosis and mixed acid–base disorders developing during treatment with isotonic fluids can confound the anion gap and, indirectly, base excess, thereby complicating the assessment of resolution [1]. For this reason, post-treatment base excess should be interpreted as a composite measure reflecting not only residual ketoacidosis but also the effect of the administered fluid therapy on acid–base balance.

The severity-stratified analysis is consistent with this: while the absolute improvement (ΔBE) was greatest in patients with the most severe acidosis at presentation, the level of base excess achieved post-treatment and the percentage improvement were similar across the strata (Table 3). This pattern can be interpreted as treatment steering patients of varying severity toward a common acid–base target; indeed, current guidelines define the resolution of DKA as the suppression of ketonemia and the normalization of acid–base parameters [1]. Consequently, while the difference in severity at presentation is reflected in the magnitude of the absolute improvement, the level achieved post-treatment more closely reflects the common treatment target.

The fact that ΔBE is approximately twice as high in intensive care cases as in ward cases can be explained by two factors. First, patients admitted to intensive care presented with more severe acidosis; consequently, the correction required was greater. Second, the more intensive treatment administered in intensive care (insulin infusion and strict fluid and electrolyte monitoring) may have contributed to faster and near-complete correction of the acidosis. It is known that the use of intensive care in DKA varies between centers and is generally required in more severe cases [18–20]. For this reason, ΔBE should be interpreted here not as a prognostic tool but as an indicator of disease severity and intensity of care; concluding that ΔBE predicts the need for intensive care would be misleading, as patients are admitted to intensive care precisely because they are already in a severe condition.

Assessing the rate of acidosis resolution is an approach that has long been used in sepsis and trauma through lactate clearance [8] and base excess [9–11]; our study applies this concept of resolution to base excess in DKA. Although high lactate levels in DKA have been shown to be associated with adverse outcomes [12], lactate is not always measured; the availability of base excess in every blood gas analysis makes ΔBE an accessible monitoring parameter, particularly in settings where lactate is not routinely measured.

Approximately one-quarter of our cases were registered as having type 1 diabetes. As adult diabetic ketoacidosis can occur in the context of both type 1 and type 2 diabetes [21,22], whether the change in base excess differs according to diabetes type is a question that requires further investigation.

From a clinical perspective, ΔBE is a measure that can be obtained from every blood gas analysis already performed, without requiring any additional cost or intervention, and can support monitoring as a practical indicator summarizing the severity of the patient's presentation and the intensity of care. The fact that the 2024 consensus renders arterial sampling unnecessary for acid–base assessment makes base excess derived from venous blood gas analysis even more useful in clinical monitoring [1]. However, the management of DKA, including fluid selection and insulin administration, remains an area of active research [23], and the treatment protocol employed may directly influence acid–base correction. For now, then, ΔBE is best regarded as a supporting marker of severity and treatment response; it has not been validated as an independent prognostic tool.

Study Limitations

This study has several limitations. Its single-center, retrospective design limits its generalizability. As diabetes type was not

specified in the records for approximately two-thirds of the cases, a type-specific analysis could not be performed. Because time data were recorded at the daily level, the hourly rate of improvement could not be calculated, and the timing of the post-treatment measurement could not be standardized; consequently, ΔBE reflects the course of care rather than a single time point. Furthermore, the more frequent collection of blood gas samples in intensive care cases may have introduced differences in measurement frequency between the groups. In addition, because base excess values were obtained from either venous or arterial blood gas samples, the mixture of sample types, which are not strictly equivalent and were not standardized in terms of type or timing, may be a further source of variability. As patients who died within the first 24 hours were excluded, the earliest and most severe fatal cases fell outside the ΔBE cohort, introducing selection bias whereby the analyzed sample underrepresents the most fulminant presentations. As the number of events was small, the association with mortality was not analyzed, and mortality is presented descriptively only. Finally, as ΔBE is mathematically dependent on baseline base excess at presentation, a model including baseline base excess as a predictor would be tautological; therefore, ΔBE was not modeled as a prognostic outcome but was addressed at a descriptive and correlational level.

Conclusion

In diabetic ketoacidosis, the change in base excess (ΔBE) following treatment is a parameter that can be easily obtained from laboratory data and is associated with patients' clinical status. Whether ΔBE has independent prognostic value should be investigated in future studies involving serial measurements with precisely recorded measurement times and outcome data.

Ethics

Ethics Committee Approval: This study was approved by The Ethics committe of University of Health Sciences, Taksim Training and Research Hospital (approval no. E-62190176-663.05-269193889, dated 7 August 2024).

Informed Consent: Owing to the retrospective design of the study, the requirement for written informed consent was waived by the ethics committee.

Conflict of Interest: The authors declare that there is no conflict of interest.

Use of AI for Writing Assistance: The authors declared that artificial intelligence was not used in the study.

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ORIGINAL RESEARCH

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Predictors of ED Outcomes and 30-Day Mortality in Oldest Olds Presenting with Trauma

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Abstract

Objective: Trauma-related emergency department (ED) admissions among older adults are increasing with population aging. The oldest-old, defined as patients aged ≥85 years, are particularly vulnerable, as even low-energy mechanisms may result in clinically important morbidity and mortality. This study aimed to evaluate the epidemiological, clinical, and prognostic features of trauma presentations among the oldest-old and to identify factors associated with ED outcomes and 30-day mortality.

Materials and Methods: This single-center retrospective observational study included trauma patients aged ≥85 years who presented to the ED between May 1, 2020, and August 1, 2023. Demographic characteristics, mechanisms of injury, frailty levels, clinical and laboratory parameters, injury severity scores, ED outcomes, and 30-day mortality were recorded. Frailty was assessed using the Clinical Frailty Scale. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of 30-day mortality.

Results: A total of 467 patients were included. The median age was 88 years, and 70.2% were female. Falls were the predominant mechanism of injury (91.9%). Overall, 47.8% were discharged, 48.8% were admitted to hospital wards, 2.8% required ICU admission, and 0.6% died in the ED. The 30-day mortality rate was 8.1%. In multivariate logistic regression analysis, the shock index, Geriatric Trauma Outcome Score, and frailty level were identified as independent predictors of 30-day mortality.

Conclusion: Trauma among the oldest-old was predominantly related to low-energy mechanisms, particularly falls, yet was associated with clinically important morbidity and mortality. Injury severity scoring, early physiological assessment, and frailty evaluation may improve ED risk stratification. Further prospective studies are required to validate these findings.

Keywords: Emergency; frailty; geriatrics; oldest old; trauma.

Introduction

Trauma-related emergency department (ED) admissions among older adults have increased in recent years, largely reflecting population aging, improved health services, longer life expectancy, increased mobility, and the growing vulnerability of geriatric patients to injury [1-3]. Even low-energy mechanisms may lead to clinically significant morbidity in this population because of age-related physiological changes, reduced functional reserve, osteoporosis, comorbidities, and the frequent use of antithrombotic medications [4,5]. Therefore, trauma in older adults represents an important challenge for emergency physicians, not only because of injury management itself but also because adverse outcomes may occur despite apparently minor mechanisms of trauma.

The oldest-old population, generally defined as individuals aged 85 years and older, warrants particular attention, as this rapidly growing demographic group is expected to double in size by 2050 [6,7]. Ground-level falls are the predominant mechanism of injury in this age group, and these low-energy events may result in serious injury patterns, including hip fractures, intracranial hemorrhage, and rib fractures [8]. However, the literature focusing specifically on trauma presentations among patients aged ≥85 years remains limited, and reported admission rates, mechanisms of trauma, and clinical outcomes vary substantially across countries, healthcare systems, and hospital settings.

Early identification of oldest-old trauma patients at high risk for poor outcomes is essential for appropriate triage, resource

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allocation, and clinical decision-making in the emergency department. Traditional injury severity metrics, such as the Injury Severity Score (ISS) and Geriatric Trauma Outcome Score (GTOS), have been widely used to estimate trauma severity and mortality risk in older adults [9,10]. In addition, physiological markers such as the Glasgow Coma Scale, shock index, renal function, albumin level, and inflammatory parameters, including the neutrophil-to-lymphocyte ratio, may provide important information regarding acute physiological derangement. Nevertheless, the predictive value of these parameters in the oldest-old trauma population remains incompletely defined, particularly in cohorts with predominantly low-energy mechanisms and low injury severity.

Frailty has increasingly been recognized as a clinically meaningful predictor of adverse outcomes in geriatric trauma, independent of chronological age and injury severity [11]. Because frailty reflects reduced physiological reserve and vulnerability to stressors, its assessment may improve risk stratification beyond conventional trauma scoring systems. Therefore, this study aimed to characterize the epidemiological, clinical, and prognostic features of trauma presentations among patients aged ≥85 years and to identify factors associated with ED outcomes and 30-day mortality. In particular, we sought to evaluate the prognostic contributions of injury severity metrics, physiological parameters, laboratory markers, and frailty level in this oldest-old trauma cohort.

Materials and Methods

Study Setting and Population

This single-center retrospective observational study was conducted at one of the largest tertiary care centers in the country, with more than 900,000 annual ED visits and a total hospital capacity of 2,682 beds. Trauma patients aged ≥85 years who presented to the ED during the 3-year and 3-month study period between May 1, 2020, and August 1, 2023, were included in the study.

Patients who were directly transferred to hospital wards or the intensive care unit (ICU) without ED evaluation; experienced trauma secondary to underlying medical conditions such as cerebrovascular events, cardiac syncope, pulmonary embolism, or sepsis; had pathological fractures; voluntarily discontinued treatment; or had missing or incomplete study data were excluded.

Data Collection

The study was approved by the Ethics Committee of Basaksehir Cam and Sakura City Hospital on November 6, 2023, with protocol number KAEK/25.10.2023.520. Following approval by the institutional review board, eligible patients were identified through the hospital information system by screening trauma-related ICD-10 diagnostic codes (S00-S99 and T00-T14), codes related to traffic accidents (V00-V99), burns (T20-T32), and falls (W00-W19).

All study variables were recorded using a standardized data collection form by the investigating physicians. Collected variables included age, sex, type of admission (walk-in or ambulance), time of admission, chief complaint, chronic medical conditions, antithrombotic medications, mechanism of injury, injury-to-ED time, frailty level, GCS, and vital parameters on admission. In addition, the shock index (SI), Abbreviated Injury Scale (AIS), Injury Severity Score (ISS), and Geriatric Trauma Outcome Score (GTOS) were calculated and recorded on the form.

Frailty status was retrospectively assessed using the Clinical Frailty Scale (CFS), a 9-point clinical tool used to grade frailty based on baseline functional status, independence in daily activities, comorbidity burden, mobility, and need for assistance. Frailty status was retrospectively assigned based on information available in the electronic medical records, including pre-injury functional status, mobility, dependency in activities of daily living, comorbidities, cognitive impairment, and nursing and physician notes at admission.

SI was calculated as the ratio of heart rate to systolic blood pressure. The AIS was determined by assigning each injury to an anatomical region and grading its severity on a 6-point ordinal scale ranging from minor (1) to unsurvivable (6). The ISS was calculated as the sum of the squares of the highest AIS scores from the three most severely injured body regions. The GTOS was calculated using the following formula: GTOS=Age+(2.5×ISS)+22 (if RBC transfusion was administered).

Laboratory parameters were recorded at the initial ED presentation and included hemoglobin, hematocrit, platelet count, red cell distribution width (RDW-CV), international normalized ratio (INR), activated partial thromboplastin time (aPTT), neutrophil-to-lymphocyte ratio (NLR), C-reactive protein (CRP), creatinine, GFR, and albumin. NLR was defined as the neutrophil count (10^9/L) divided by the lymphocyte count (10^9/L).

The study was conducted in accordance with the principles of the Declaration of Helsinki. The ethics committee waived the requirement for individual patient consent because of the retrospective observational nature of the study and the use of anonymized data.

Definition of Outcomes

The primary clinical outcome of the study was 30-day mortality,

defined as death from any cause within 30 days after the index ED admission for trauma. Secondary outcomes included ED disposition (discharge, ward admission, ICU admission, or death in the ED). Outcomes were assessed based on in-hospital medical records, electronic hospital information system data, and the e-Nabız system.

Data Analysis

Statistical analyses were performed using IBM SPSS Statistics (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as frequencies and percentages, whereas continuous variables were expressed as medians and interquartile ranges (IQRs) because the data were non-normally distributed. Normality was assessed using the Shapiro–Wilk test. Comparisons between categorical variables were performed using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared using the Mann–Whitney U test for two-group analyses and the Kruskal–Wallis test for comparisons involving more than two groups.

Univariate logistic regression analyses were initially performed to evaluate the associations between clinical variables and 30-day mortality. Variables with $p<0.10$ in the univariate analyses were included in the multivariable logistic regression model to identify independent predictors of 30-day mortality. Odds ratios (ORs) with 95% confidence intervals (95% CIs) were reported. Receiver operating characteristic (ROC) curve analyses were performed to evaluate the predictive performance of the ISS and GTOS for 30-day mortality. A two-tailed $p<0.05$ was considered statistically significant.

Results

A total of 15,150 patients aged ≥85 years were admitted to the ED during the 3-year and 3-month study period. Among them, 672 patients primarily presented with trauma. After meticulous evaluation, 205 patients were excluded for the following reasons: direct transfer to hospital wards without proper ED evaluation (n=20), pathological fractures (n=3), missing data (n=87), discontinuation of treatment (n=30), and trauma secondary to syncope/presyncope caused by cardiac conditions (n=21), cerebrovascular events (n=33), pulmonary embolism (n=2), or sepsis (n=9). Ultimately, 467 patients were included in the final analysis.

Trauma admissions most commonly occurred during the afternoon hours (12:00–17:59) (37.3%), in the summer months (28.9%), and on weekdays (74.4%). The majority of patients arrived by ambulance rather than as walk-in admissions (66.4% vs. 33.6%). Blunt trauma accounted for the vast majority of cases (n=457, 97.9%), whereas penetrating trauma was uncommon (n=10, 2.1%). Falls were the predominant mechanism of injury (n=429, 91.9%), followed by simple hitting/bumping injuries (n=14, 2.9%), traffic accidents (n=10, 2.1%), and burns (n=7, 1.5%). Among fall-related injuries, same-level falls were the most common mechanism (n=374, 87.2%), followed by falls from bed (n=36, 8.4%), falls down stairs (n=12, 2.8%), and falls from a toilet seat or chair (n=7, 1.6%). The most common chief complaints were hip pain (n=215, 46.0%), headache (n=56, 12.0%), and back pain (n=49, 10.5%). The most frequently affected anatomical regions were the lower extremities (n=266, 57.0%), followed by the head and face region (n=62, 13.3%) and the upper extremities (n=58, 12.4%). Hip fractures were detected in 200 patients.

The study cohort comprised 139 males (29.8%) and 328 females (70.2%). Patient age ranged from 85 to 108 years, with a median age of 88 years (IQR, 86–91). Most patients (n=411, 88%) had at least one chronic medical condition. The most common comorbidity was hypertension (n=334, 71.5%), followed by diabetes mellitus (n=95, 20.3%), Alzheimer's disease (n=81, 17.3%), and coronary artery disease (n=66, 14.1%). Patient demographics are presented in detail in Table 1.

Median time from injury to ED admission was 6 hours (IQR, 3–24). There was a moderate positive correlation between frailty level and time to ED admission (Spearman's $\rho=0.34$, $p<0.001$). Additionally, a significant association was observed between frailty status and mode of admission, with frail patients more frequently arriving by ambulance than non-frail patients ($p<0.001$).

Among the 467 patients, 223 (47.8%) were discharged directly from the ED, 228 (48.8%) were admitted to hospital wards, 13 (2.8%) required ICU admission, and 3 (0.6%) died in the ED. During hospitalization, 195 patients (41.8%) underwent surgical intervention for their injuries. The 24-hour mortality rate was 1.2% (n=6/467), whereas the 30-day mortality rate was 8.1% (n=38/467).

The Kruskal–Wallis analysis for ED outcomes is shown in Table 2. In addition, frailty level was significantly associated with severe ED outcomes ($\chi^2=33.3$, $p<0.001$); the proportion of frail patients increased progressively from the discharged group to the deceased group.

In univariate logistic regression analysis, age, GCS, shock index, ISS, GTOS, NLR, CRP, GFR, albumin, and frailty level were identified as significant predictors of 30-day mortality. In contrast, INR, aPTT, RDW-CV, creatinine, male sex, and antithrombotic medication use were not associated with 30-day mortality.

Among the individual predictors, GTOS demonstrated the highest discriminative ability (AUC=0.831), followed by ISS (AUC=0.789),

Table 1. Baseline demographic and clinical characteristics of patients aged ≥85 years with trauma

Variable	N	Min- Max	Median (IQR) or n (%)
Continuous Variables			
Age, years	467	85-108	88 (86-91)
SBP (mmHg)	467	60-200	140 (130-160)
DBP (mmHg)	467	37-140	80 (72-90)
HR (bpm)	467	47-155	88 (78-98)
RR (/min)	467	12-40	19 (18-22)
GCS	467	6-15	15 (15-15)
Shock Index	467	0.31-2.58	0.61 (0.55-0.68)
ISS	467	0-34	9 (3-9)
GTOS	467	87-175	107.5 (96-112)
HGB (g/dL)	371	4.4-17	11.20 (10.30 - 12.80)
HCT (%)	371	12.1-55	34.90 (31.00-38.70)
PLT (10^9/L)	371	1.50-875	226 (176-287)
RDW-CV	371	11.7-23.6	14.20 (13.30-15.20)
NLR	371	0.5-50.7	5.15 (2.99-8.73)
INR	363	0.80-6.56	1.05 (1.00-1.10)
APTT (seconds)	363	14-58	28 (24.20-32.00)
CRP (mg/L)	363	0.10-289	20 (4.90-51.45)
Creatinine (mg/dL)	363	0.46-75	1.02 (0.81-1.28)
GFR (mL/min/1.73m^2)	363	6-92	52.50 (39-70)
Albumin (g/L)	336	23-46	35 (33-38)
Categorical Variables			
Sex	467	Male:139 (29.8%) | Female:328 (70.2%)	
Comorbidities	467	None:56 (12%) | One:163 (34.9%) | 2 or more:248 (53.1%)	
Antithrombotic Use	467	None:286 (61.2%) | Single:157 (33.6%) | Dual:24 (5.1%)	
Frailty	467	Non-Frail:83(17.8%) | Pre-frail:232(49.7%) | Frail:152(32.5%)	
Injury to ED admission	467	Immediate (≤1 hour):12 (2.6%) | Early (1-6 hours):307 (65.7%) | Delayed (6-24 hours): 84 (18%) |Very delayed (>24 hours):64 (13.7%)	
Severity of Injury (ISS)	467	No injury (0): 4 (0.9%) | Minor (1-8): 227 (48.6%)| Moderate (9-15): 217 (46.5%) | severe (16-24): 15 (3.2%) | Very severe (>25): 4 (0.9%)	

APTT: Activated partial thromboplastin time; CRP: C-reactive protein; DBP: Diastolic blood pressure. ED: Emergency department; GCS: Glasgow Coma Scale; GFR: Glomerular filtration rate; GTOS: Geriatric Trauma Outcome Score; HCT: Hematocrit; HGB: Hemoglobin; HR: Heart rate; INR: International normalized ratio; IQR: Interquartile range; ISS: Injury Severity Score; NLR: Neutrophil-to-lymphocyte ratio; PLT: Platelet count; RBC: Red blood cell; RDW-C: Red cell distribution width–coefficient of variation; RR: Respiratory rate; SBP: Systolic blood pressure.

shock index (AUC=0.738), and frailty (AUC=0.738) (Figure 1). Optimal cutoff values determined by the Youden index were GTOS>112.50 (sensitivity, 71.1%; specificity, 79.5%), ISS>8.00 (sensitivity, 97.4%; specificity, 53.1%), shock index>0.71 (sensitivity, 55.3%; specificity, 86.5%), and frailty=3 (sensitivity, 71.1%; specificity, 70.9%).

Prior to multivariate modeling, collinearity was assessed among candidate variables. ISS and GTOS demonstrated severe collinearity (r=0.941); accordingly, ISS was excluded from the multivariate model, and GTOS was retained given its superior discriminative ability in univariate analysis (AUC=0.831 vs. 0.789). Complete-case analysis was also performed, yielding a final analytic sample of n=333 patients (36 events; event rate, 10.8%).

Table 2. Kruskal-Wallis Analysis —emergency department outcome

Variable	Discharged (n=223) Median [IQR]	Ward (n=228) Median [IQR]	ICU (n=13) Median [IQR]	Deceased (n=3) Median [IQR]	p
Age (years)	88.00 [86.00-91.00]	89.00 [86.75-91.00]	89.00 [87.00-90.00]	90.00 [88.00-91.00]	0.5964
GCS	15.00 [15.00-15.00]	15.00 [15.00-15.00]	13.00 [12.00-14.00]	13.00 [12.50-14.00]	**<0.001**
Shock Index	0.59 [0.55-0.65]	0.62 [0.55-0.70]	0.64 [0.55-0.82]	1.18 [1.06-1.22]	**0.0007**
ISS	2.00 [1.00-4.00]	9.00 [9.00-9.00]	10.00 [9.00-18.00]	27.00 [18.50-30.50]	**<0.001**
GTOS	96.00 [91.00-100.00]	111.50 [108.5-114.5]	115.50 [112.0-133.0]	153.50 [135.25-164.25]	**<0.001**
NLR	3.83 [2.51-7.01]	5.79 [3.55-9.22]	5.98 [4.49-20.16]	11.86 [6.90-13.27]	**<0.001**
INR	1.06 [1.00-1.10]	1.03 [0.99-1.10]	1.10 [1.00-1.20]	1.20 [1.10-1.34]	0.3952
APTT (sec)	28.25 [25.57-32.00]	27.50 [24.00-32.00]	30.00 [25.90-39.00]	29.80 [26.55-30.40]	0.5285
RDW-CV	13.90 [13.30-14.70]	14.40 [13.30-15.53]	14.40 [13.40-14.80]	16.90 [14.80-17.45]	0.0616
CRP (mg/L)	20.00 [4.75-27.05]	20.00 [5.03-57.60]	51.50 [3.40-157.00]	45.70 [24.00-82.85]	0.1157
Creatinine (mg/dL)	0.99 [0.81-1.22]	1.01 [0.81-1.29]	1.72 [1.04-2.34]	1.36 [1.19-1.87]	**0.0036**
GFR (mL/min/1.73m^2)	54.00 [42.00-69.50]	53.00 [39.00-72.00]	35.00 [23.00-47.00]	45.00 [31.00-47.50]	**0.0072**
Albumin (g/L)	35.50 [35.00-39.00]	35.00 [32.00-38.00]	32.00 [29.00-35.00]	31.50 [29.75-33.25]	**0.0017**

APTT: Activated partial thromboplastin time; CRP: C-reactive protein; GCS: Glasgow Coma Scale; GFR: Glomerular filtration rate; GTOS: Geriatric Trauma Outcome Score; ICU: Intensive care unit; INR: International normalized ratio; IQR: Interquartile range; ISS: Injury Severity Score; NLR: Neutrophil-to-lymphocyte ratio; RDW-C: Red cell distribution width–coefficient of variation

Multivariate logistic regression analysis is shown in Table 3. Our multivariate model demonstrated excellent discriminative ability, with an AUC (C-statistic) of 0.879 (95% CI, approximately 0.82–0.94).

Discussion

In this study, we characterized the epidemiological, clinical, and prognostic features of trauma presentations among patients aged ≥85 years and identified independent predictors of 30-day mortality. Frailty emerged as a clinically meaningful variable across multiple dimensions; frail patients experienced longer delays to ED presentation, were more likely to arrive by ambulance, and were associated with worse ED outcomes. Patients who experienced more serious ED outcomes demonstrated significantly higher ISS, GTOS, shock index, NLR, and creatinine values, whereas GCS, GFR, and albumin levels were significantly lower than those of patients discharged from the ED or admitted to the ward. In multivariate logistic regression analysis, SI, GTOS, and frailty level were identified as independent predictors of 30-day mortality (model AUC=0.879). Our findings underscore the importance of incorporating injury severity metrics and frailty assessment into the risk stratification of oldest-old patients presenting with trauma.

Trauma-related emergency admissions among geriatric patients have increased in recent years [12–14]. Previous studies have reported that trauma accounts for 18–36.7% of emergency department presentations among patients aged ≥65 years [12,15,16]. However, the literature on the oldest-old population (aged ≥85 years) remains limited and inconsistent. A study from the United Kingdom reported that injuries and falls constituted approximately 31% of all emergency admissions among patients

Table 3. Multivariate logistic regression- independent predictors of 30-day mortality (n=333, events=36)

Variable	Adjusted OR	95% CI Lower	95% CI Upper	p	Model AUC	95% CI of AUC
Age (years)	1.059	0.950	1.181	0.297	0.879	0.82-0.94
GCS	1.060	0.626	1.794	0.830	0.879	0.82-0.94
Shock Index	**1.656**	**1.265**	**2.167**	**<0.001**	0.879	0.82-0.94
GTOS	**1.048**	**1.002**	**1.096**	**0.039**	0.879	0.82-0.94
NLR	1.022	0.964	1.084	0.465	0.879	0.82-0.94
CRP (mg//L)	1.052	0.978	1.130	0.172	0.879	0.82-0.94
GFR (mL/min/1.73m^2)	1.002	1.000	1.004	0.057	0.879	0.82-0.94
Albumin	1.061	0.954	1.179	0.273	0.879	0.82-0.94
Frailty	**2.780**	**1.263**	**6.122**	**0.011**	0.879	0.82-0.94

Data are presented as adjusted odds ratios with 95% confidence intervals. The model AUC represents the discriminative performance of the multivariable logistic regression model for predicting 30-day mortality. Abbreviations: AUC: Area under the receiver operating characteristic curve; CI: Confidence interval; CRP: C-reactive protein; GCS: Glasgow Coma Scale; GFR: Glomerular filtration rate; GTOS: Geriatric Trauma Outcome Score; NLR: Neutrophil-to-lymphocyte ratio; OR: Odds ratio.

aged ≥85 years (3,991/12,883) [17]. In contrast, a Turkish study reported a trauma-related admission rate of 1.7% among patients aged ≥80 years (361/21,850), while another study reported that soft tissue injuries, traffic accidents, and falls together accounted for 18% (142/780) of presentations among patients aged ≥85 years [18,19]. Similarly, a study from India reported that trauma accounted for only 6% of all emergency department admissions among patients aged >80 years (53/8,563) [20]. In the present study, trauma-related admissions accounted for 4.4% of all emergency admissions among patients aged ≥85 years (672/15,150). These variations may be attributed to differences in healthcare systems, health policies, hospital settings, patient populations, and cultural factors.

Trauma may result in more serious outcomes in geriatric patients because of diminished physiological reserve, characteristic injury patterns, pre-existing comorbidities, and medications such as anticoagulants [21-23]. Early recognition of factors associated with worse outcomes is therefore essential. ISS and GTOS are among the most widely studied scoring systems for trauma severity and outcome prediction in this population, and both have been validated as strong predictors of mortality in geriatric trauma patients [24-26,9]. However, the predictive adequacy of ISS alone has been questioned; Kim et al. [27] argued that ISS may be insufficient for the comprehensive assessment of geriatric trauma because it does not incorporate physiological parameters or patient-specific factors such as age and transfusion requirements. Indeed, several studies have reported superior predictive performance of GTOS compared with ISS for mortality in this population [24-26,9]. Consistent with these findings, in our oldest-old cohort, GTOS demonstrated a higher AUC than ISS (0.831 vs. 0.789), and in multivariate analysis, GTOS emerged as one of the strongest independent predictors of 30-day mortality.

Physiological instability at presentation, as reflected by GCS and shock index in our cohort, is well supported by the existing literature. Moradi et al. [28] demonstrated that elderly trauma

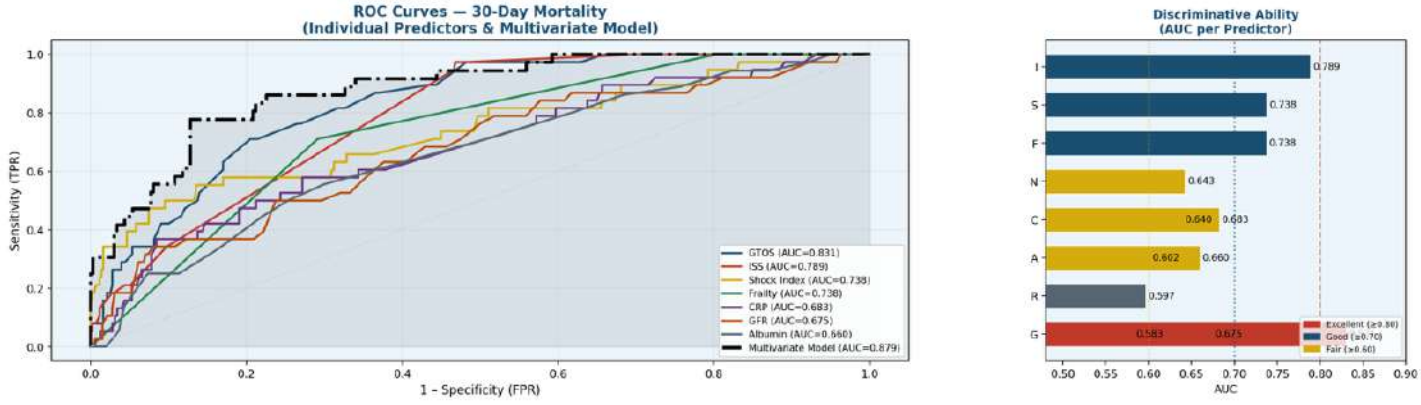

Figure 1. ROC curves-30-Day Mortality (Individual Predictors and Multivariate Model)

patients who died during hospitalization presented with significantly lower GCS scores and systolic blood pressure than survivors, consistent with our findings. The predictive value of the shock index in geriatric trauma, however, remains a subject of debate. Physiological aging and the widespread use of antihypertensive medications may alter baseline vital signs, potentially obscuring traditional hemodynamic markers of shock. Autonomic dysfunction has been shown to blunt the expected tachycardic response to physiological stress in elderly patients, meaning that SI values may appear falsely reassuring despite significant underlying hemodynamic instability [29-31]. Consistent with this, Vandrajabpour et al. [32] reported SI to be an unreliable predictor of mortality in an elderly cohort, with a sensitivity of only 48.48% and an AUC of 0.339 at a cutoff of 0.9. Nevertheless, several studies have demonstrated the utility of SI in predicting adverse outcomes in geriatric trauma patients [33,34], and our findings align with this evidence; shock index was associated with both ICU admission and in-ED death and emerged as an independent predictor of 30-day mortality in multivariate analysis. The variability in reported predictive performance across studies likely reflects differences in threshold selection, patient populations, and injury profiles, reinforcing the need for age-specific validation of SI cutoff values in geriatric trauma.

Elevated NLR, reflecting systemic inflammation, was also associated with ICU admission and in-ED death in our oldest-old cohort. Although immune responses may be attenuated in older adults because of immunosenescence, aging is paradoxically characterized by chronic low-grade inflammation and impaired regulation of the inflammatory response, a phenomenon often referred to as "inflammaging" [35]. This underlying dysregulation may partly explain why higher NLR at presentation was associated with ICU admission and in-ED death in our cohort. However, NLR did not emerge as an independent predictor of 30-day mortality in multivariate analysis. This may suggest that although NLR captures the overall inflammatory and physiological stress burden following trauma, its prognostic signal is not independent; rather, it is likely mediated or confounded by closely related factors such as injury severity, hemodynamic instability, renal dysfunction, frailty, or nutritional compromise [36]. In this context, NLR may be better understood as a marker of overall physiological derangement than as a standalone predictor of mortality in this population.

Notably, age and coagulation parameters were not associated with ICU admission, in-ED death, or 30-day mortality in our cohort. The lack of an association with age is consistent with the broader literature, which suggests that ICU admission decisions are primarily driven by injury severity, physiological instability, and pre-existing medical conditions rather than chronological age alone [37]. Regarding coagulation parameters, although trauma-induced coagulopathy is well recognized as a contributor to adverse outcomes, its prognostic impact may be more pronounced in higher-acuity trauma populations; the predominantly low-severity injury profile of our cohort may have limited its discriminatory value. These findings should nonetheless be interpreted with caution. The majority of our patients sustained low-severity injuries (ISS 1–2), and the cohort included only 13 ICU admissions and 3 in-ED deaths, resulting in limited statistical power to detect associations with less common outcomes. Larger prospective studies with more balanced severity distributions are needed to draw more definitive conclusions regarding the prognostic role of age and coagulation parameters in oldest-old trauma patients.

Frailty has been shown to predict in-hospital complications, longer hospital and ICU lengths of stay, and mortality in geriatric trauma patients, independent of injury severity [38]. In our multivariate analysis, frailty emerged as an independent predictor of 30-day mortality, reinforcing its prognostic value beyond traditional trauma scoring systems. These findings highlight the importance of routine frailty assessment at the time of ED presentation, as early identification of frail patients may guide triage decisions, inform goals-of-care discussions, and facilitate the timely mobilization of geriatric-specific resources.

The clinical implications of our multivariate analysis are particularly relevant to emergency department triage and early risk stratification. Current triage systems, such as the Emergency Severity Index and the Canadian Triage and Acuity Scale, rely primarily on presenting acuity, vital sign thresholds, and anticipated resource needs, without formally incorporating frailty or trauma-specific severity indices. This may result in miscalibrated triage decisions in oldest-old trauma patients, whose physiological reserve and injury tolerance may differ substantially from those of younger patients. In light of our findings, a combined approach integrating acute hemodynamic status (shock index), age-adjusted injury severity (GTOS), and baseline vulnerability (frailty level) may provide a more comprehensive framework for risk stratification, resource allocation, and goals-of-care discussions than any single score in isolation.

This study has several limitations. First, it was conducted retrospectively at a single tertiary ED, which may limit the generalizability of the findings to other healthcare systems, hospital settings, and trauma populations. Second, although the overall sample size was acceptable, the number of severe outcomes was limited, particularly ICU admissions, in-ED deaths, and 30-day mortality events. This may have reduced the statistical

power for some comparisons and increased the risk of model instability or overfitting in the multivariate analysis. Third, the study population predominantly consisted of patients with low-energy trauma and relatively low injury severity; therefore, the prognostic performance of the identified predictors may differ in cohorts with higher-acuity trauma or more balanced injury severity distributions. Finally, this study evaluated 30-day mortality but did not assess longer-term outcomes such as functional decline, institutionalization, quality of life, or delayed complications. Prospective multicenter studies with standardized frailty assessment and longer follow-up are needed to validate these findings and clarify their role in clinical decision-making.

Conclusion

Trauma in the oldest-old population was predominantly related to low-energy mechanisms, particularly falls. However, even these low-energy injuries may be associated with clinically important morbidity and mortality. Among the evaluated clinical, physiological, and prognostic variables, shock index, GTOS, and frailty level were identified as independent predictors of 30-day mortality. Further prospective studies are required to validate these findings and clarify their applicability across different emergency care settings.

Abbreviations

AIS: Abbreviated Injury Scale
aPTT/APTT: Activated Partial Thromboplastin Time
AUC: Area Under the Curve
CFS: Clinical Frailty Scale
CI: Confidence Interval
CRP: C-Reactive Protein
DBP: Diastolic Blood Pressure
ED: Emergency Department
GCS: Glasgow Coma Scale
GFR: Glomerular Filtration Rate
GTOS: Geriatric Trauma Outcome Score
HCT: Hematocrit
HGB: Hemoglobin
HR: Heart Rate
ICD-10: International Classification of Diseases, 10th Revision
ICU: Intensive Care Unit
INR: International Normalized Ratio
IQR: Interquartile Range
ISS: Injury Severity Score
NLR: Neutrophil-to-Lymphocyte Ratio
OR: Odds Ratio
PLT: Platelet Count
RBC: Red Blood Cell
RDW-CV: Red Cell Distribution Width–Coefficient of Variation
ROC: Receiver Operating Characteristic
RR: Respiratory Rate
SBP: Systolic Blood Pressure
SI: Shock Index
SPSS: Statistical Package for the Social Sciences

Ethics Committee Approval: This study was approved by The Basaksehir Cam and Sakura City Hospital on 06.11.2023 with protocol number of KAEK/25.10.2023.520.

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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