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Early Intravenous Iron Sucrose Supplementation for Absolute Iron Deficiency in Acute Heart Failure in the Emergency Department: A Single-Center Randomized Pilot Study

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Abstract

Introduction: Iron deficiency is common in heart failure and is associated with impaired functional capacity and adverse outcomes independently of anemia. Evidence remains limited for intravenous iron initiated directly from the emergency department (ED), particularly iron sucrose. This pilot study evaluated the feasibility, safety, and short-term outcomes of a single early dose of intravenous iron sucrose added to oral iron in stabilized ED patients with acute heart failure and absolute iron deficiency.

Methods: We conducted a prospective, randomized, open-label, pilot study in the Tunisia ED from August 2017 to June 2018. After stabilization, adults with acute heart failure and absolute iron deficiency (ferritin <100 µg/L) were randomized to intravenous iron sucrose plus three months of oral iron or oral iron alone. Primary outcomes were three-month changes in 6MWT distance and iron-deficiency correction; secondary outcomes included functional status, fatigue, healthcare use, length of stay, and exploratory mortality.

Results: Among 510 screened patients, 114 were included (60 IV-plus-oral; 54 oral-only). Mean age was 66 ± 7 years and sex ratio was 1.33. No in-hospital death, shock, cardiac arrest, invasive mechanical ventilation, infusion-related allergic reaction, or anaphylaxis was documented. At three months, mean 6MWT distance increased more in the IV-plus-oral group than in the oral-only group (+43 m vs +11 m; p=0.010). Any increase from baseline occurred in 46/57 (80.7%) versus 17/45 (37.8%), respectively (OR 6.89, 95% CI 2.82–16.81; p<0.001). Correction of absolute iron deficiency occurred in 37/57 (64.9%) versus 23/45 (51.1%; p=0.160). NYHA class, ED revisits, and rehospitalization did not differ significantly. Three-month mortality was 3/60 (5.0%) versus 9/54 (16.7%); this exploratory difference was not statistically significant (OR 0.26, 95% CI 0.07–1.03; p=0.065).

Conclusion: This pilot study suggests that administering a single 200 mg dose of intravenous iron sucrose after clinical stabilization and before ED discharge is feasible, with no documented serious infusion-related hypersensitivity reactions. The observed difference in 6MWT improvement should be interpreted cautiously given the small sample, open-label design, and absence of significant differences in iron-deficiency correction or clinical outcomes. These findings are hypothesis-generating and warrant confirmation in larger, methodologically robust trials

Keywords: Acute Heart Failure; Iron Deficiency; Intravenous Iron; Emergency Department; Six-Minute Walk Test.

INTRODUCTION

Heart failure is a clinical syndrome caused by a structural or functional cardiac abnormality and remains a major cause of ED visits, hospitalization, impaired quality of life, and mortality (1). Iron deficiency is frequent in heart failure and is associated with reduced exercise capacity and poorer outcomes independently of anemia (2).

Randomized evidence has focused mainly on ferric carboxymaltose or ferric derisomaltose. FAIR-HF demonstrated symptomatic and functional improvement with ferric carboxymaltose (3), whereas FERRIC-HF is directly relevant because it evaluated iron sucrose (4). AFFIRM-AHF subsequently assessed ferric carboxymaltose after acute heart failure hospitalization (5). Current ESC guidance supports ferric carboxymaltose or ferric derisomaltose in selected symptomatic patients with HFrEF or HFmrEF and iron deficiency (6).

Evidence remains limited for iron-deficiency screening and intravenous treatment initiated directly within an ED pathway, which requires rapid eligibility assessment, confirmation of stability, monitored infusion, and an actionable transition plan. Conducted in 2017–2018, before contemporary guidance, this study the feasibility, safety, and short-term outcomes of administering a single intravenous dose after stabilization in ED patients with acute heart failure and absolute iron deficiency.

METHODS

Study design and setting

This prospective, randomized, open-label, single-center pilot study was conducted in a university-affiliated ED from August 2017 to June 2018. The manuscript was prepared several years later from the original thesis and archived dataset, limiting the recovery of some methodological details.

Study population and eligibility criteria

Eligible participants had to meet all of the following criteria: age >18 years; de novo left-sided or global acute heart failure or acute decompensation of chronic heart failure; clinical stabilization after initial ED treatment; absolute iron deficiency defined as ferritin <100 µg/L measured before discharge; ability to complete a baseline 6MWT; and written informed consent. Eligibility was irrespective of anemia or left ventricular ejection fraction (LVEF). Acute heart failure diagnosis followed the 2016 ESC guidance applicable during enrollment and required acute or worsening compatible symptoms or signs supported by radiographic and/or echocardiographic evidence of pulmonary or systemic congestion. BNP and NT-proBNP were not systematically measured. Patients were excluded if they had gastrointestinal bleeding, known malabsorption, iron supplementation or blood transfusion within the preceding four weeks, active infection, hepatic or hematological disease, acute COPD exacerbation, acute coronary syndrome, shock, known iron sucrose allergy, persistent clinical instability, or inability to complete the baseline 6MWT.

Sample size and allocation

No formal sample-size calculation was performed because this was a pilot study, and the sample size was determined by recruitment feasibility during the study period. According to the archived study materials, treatment allocation was performed after clinical stabilization and written consent using a die-based procedure described as block allocation, with each die face corresponding to a prespecified allocation block. However, the block structure, sequence implementation, and allocation-concealment procedures could not be fully reconstructed.

Analysis population and missing data

Follow-up analyses were based on participants with available outcome data. The archived

records did not allow the timing of all exclusions relative to allocation or their treatment-group distribution to be reconstructed; therefore, a strict intention-to-treat analysis could not be performed. All follow-up analyses were consequently considered complete-case and exploratory, with potential selection and attrition bias.

Eligibility sequence, interventions, and blinding

Operational screening proceeded sequentially from confirmation and initial treatment of acute heart failure to clinical stabilization, ferritin measurement before discharge, baseline 6MWT, written consent, and randomization. Ferritin was measured by chemiluminescent microparticle immunoassay using an ARCHITECT ci8200 Abbott analyzer. Transferrin saturation was unavailable. Anemia was defined as hemoglobin <13 g/dL in men and <12 g/dL in non-pregnant women (7).

The IV-plus-oral group received a single 200 mg dose of intravenous iron sucrose (two Venofer ampoules diluted in 250 mL of 5% glucose and infused over 20 minutes through a peripheral line), followed by oral elemental iron 100 mg/day for three months. The oral-only group received oral elemental iron 100 mg/day for three months without intravenous loading.

The fixed dose was a pragmatic early-loading strategy based on the locally available formulation and ED workflow; it was not intended to replace individualized correction of the total iron deficit. Both groups received oral iron because it represented the locally used maintenance strategy at the time, so the comparison estimates the incremental effect of early intravenous loading. No placebo infusion was used; participants and treating staff were not blinded, although staff administering the infusion did not assess outcomes.

Follow-up and outcomes

The baseline 6MWT was performed after clinical stabilization and before discharge. At three months, it was repeated by the same

physician under the same local protocol. Corridor length, encouragement wording, stopping criteria, and test–retest reproducibility were not retained. Oral-iron adherence was assessed by interview without a validated scale or pill count. Infusion allergy and anaphylaxis were recorded clinically, but a standardized adverse-event grading system, observation duration, and complete capture of minor events could not be recovered.

The co-primary outcomes at three months were change in 6MWT distance and ferritin-defined correction of absolute iron deficiency (ferritin ≥ 100 $\mu\text{g/L}$). A post hoc sensitivity analysis defined a 6MWT responder as a participant with an improvement ≥ 30 m.

Secondary outcomes included changes in Self-Assigned NYHA class and fatigue category, ED revisits for acute heart failure, rehospitalization, and length of stay. Improvement, stability, and worsening denoted a lower, unchanged, or higher follow-up category, respectively. The original fatigue instrument and its category anchors were not recoverable. Ferritin and hemoglobin changes were summarized continuously. Mortality and the post hoc composite of all-cause death or heart failure rehospitalization were exploratory.

Statistical analysis

Between-group comparisons used Welch's t test for continuous variables and Pearson's chi-square or two-sided Fisher's exact test for categorical variables, as appropriate. Odds ratios with 95% confidence intervals were calculated using the log-Wald method. Results are presented as mean $\pm$ SD, median, or n (%). Analyses were based on available cases, all tests were two-sided, and $p < 0.05$ was considered significant.

The ≥ 30 m responder and death-or-rehospitalization analyses were post hoc and unadjusted for multiplicity. No multivariable analysis was performed because of the small pilot sample and limited event counts; residual

confounding from baseline imbalances therefore cannot be excluded.

Ethical considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants and documented using a consent form. Participant data were anonymized, and medical confidentiality was maintained.

RESULTS

Study population

Of 510 patients screened, 194 initially met the eligibility criteria. Of these, 80 were not retained in the final analytic cohort: 14 did not attend the three-month follow-up, 18 did not adhere to the prescribed treatment, and 48 had protocol violations. The final analytic cohort therefore comprised 114 participants: 60 in the IV-plus-oral group and 54 in the oral-only group (Figure 1).

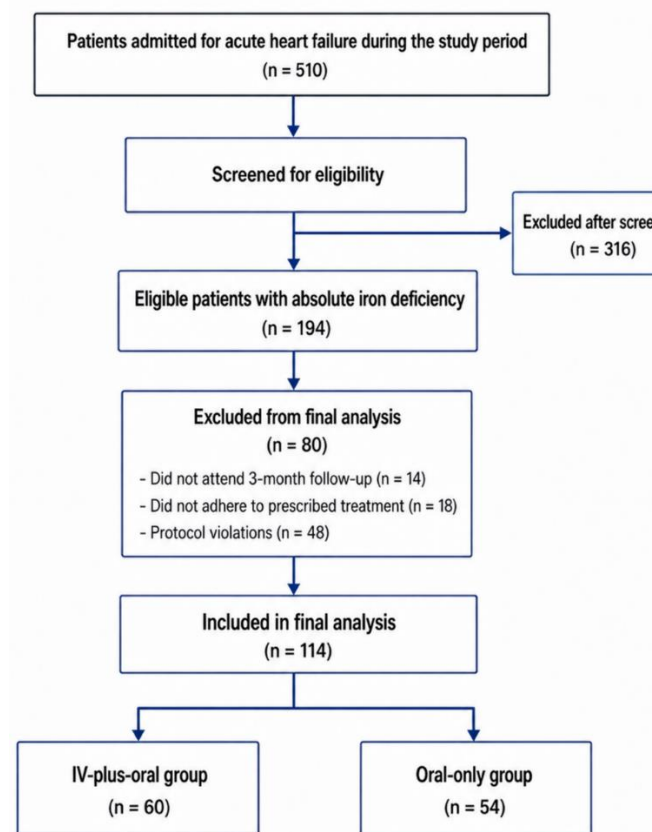


Figure 1. Study flow diagram

At three months, paired functional and biological measurements were available for 102 participants (57 IV-plus-oral and 45 oral-only). Mortality, ED revisits, heart failure rehospitalization, and the death-or-rehospitalization composite were analyzed using the full analytic-cohort denominators of 60 and 54 participants. Functional, biological, NYHA, and fatigue outcomes were analyzed as complete cases using the 57 and 45 participants with available follow-up measurements.

Baseline characteristics and clinical course

Mean age was 66 ± 7 years, and sex ratio was 1.33. Hypertension and coronary artery disease were more frequent in the IV-plus-oral group, whereas atrial fibrillation and COPD were more frequent in the oral-only group (Table 1).

During the index episode, orthopnea was more frequent in the IV-plus-oral group (42/60 (70.0%) vs 27/54 (50.0%); $p=0.029$). Respiratory distress occurred in 12/60 (20.0%) versus 6/54 (11.1%; $p=0.194$), room-air oxygen saturation $<90\%$ in 15/60 (25.0%) versus 5/54 (9.3%; $p=0.027$), and non-invasive ventilation in 23/60 (38.3%) versus 14/54 (25.9%; $p=0.158$). No participant had systolic blood pressure <90 mmHg or required invasive mechanical ventilation; vasopressor exposure was not recorded separately.

Mean ED/hospital stay was 42.1 ± 16 versus 41 ± 22 hours. No in-hospital death, shock, cardiac arrest, documented infusion-related allergic reaction, or anaphylaxis occurred; minor adverse events were not systematically captured. Selected discharge treatments were broadly similar: beta-blocker 53/60 (88.3%) versus 41/54 (75.9%), loop diuretic 60/60 (100%) versus 52/54 (96.3%), angiotensin-converting enzyme inhibitor 52/60 (86.7%) versus 47/54 (87.0%), spironolactone 14/60 (23.3%) versus 12/54 (22.2%), and statin 57/60 (95.0%) versus 52/54 (96.3%). Doses and subsequent treatment changes were unavailable.

Table 1. Baseline characteristics by treatment group

Characteristic	IV-plus-oral group (n=60)	Oral-only group (n=54)	p value
Age, years	65 ± 7	67 ± 8	0.208
Male sex	34 (56.7)	31 (57.4)	0.936
Previously known heart failure	31 (51.7)	28 (51.9)	0.984
Hypertension	47 (78.3)	31 (57.4)	0.016
Diabetes mellitus	29 (48.3)	20 (37.0)	0.224
Coronary artery disease	21 (35.0)	10 (18.5)	0.048
Atrial fibrillation	8 (13.3)	20 (37.0)	0.003
COPD	3 (5.0)	15 (27.8)	0.001
Anemia	40 (66.7)	39 (72.2)	0.521
Hemoglobin, g/dL	11.4 ± 1.8	11.6 ± 1.8	0.569
Serum ferritin, µg/L	52.0 ± 25.0	51.5 ± 23.7	0.914
Creatinine clearance <60 mL/min	18 (30.0)	15 (27.8)	0.794
LVEF, %*	50.2 ± 11.5	47.6 ± 12.0	0.460

Values are mean ± SD or n (%), as appropriate. *LVEF was available for 47 participants: 25 in the IV-plus-oral group and 22 in the oral-only group.

Abbreviations: COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; SD, standard deviation.

Co-primary outcomes

Among participants with paired measurements, mean 6MWT distance increased from 298.6 to 342.4 m in the IV-plus-oral group and from 320.2 to 332.0 m in the oral-only group (Figure 2). Mean change was +43.8 versus +11.8 m, giving an unadjusted between-group mean difference of 32.0 m (95% CI 8.2–55.8; $p=0.009$). Any increase occurred in 46/57 (80.7%) versus 17/45 (37.8%; OR 6.89, 95% CI 2.82–16.81; $p<0.001$).

Ferritin-defined correction occurred in 37/57 (64.9%) versus 23/45 (51.1%; OR 1.77, 95% CI 0.80–3.93; $p=0.160$). Mean ferritin and hemoglobin changes are reported in Table 2, where the biological co-primary outcome is repeated for completeness.

In the post hoc sensitivity analysis, a ≥ 30 m improvement occurred in 35/57 (61.4%) versus

13/45 (28.9%; OR 3.92, 95% CI 1.70–9.04; $p=0.001$).

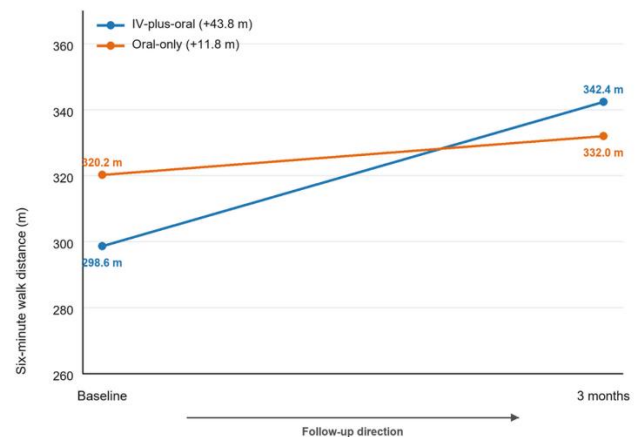


Figure 2. Progression of mean six-minute walk test distance from baseline to three months.

Mean distance increased from 298.6 to 342.4 m and from 320.2 to 332.0 m, respectively; mean changes were +43.8 and +11.8 m (Welch $p=0.009$). Lines show group means, not individual trajectories.

Secondary and exploratory outcomes

NYHA class, fatigue improvement, ED revisits, and rehospitalization did not differ significantly. Fatigue worsening was less frequent in the IV-plus-oral group (14.0% vs 33.3%; $p=0.021$), but this isolated secondary comparison was not adjusted for multiplicity. Three-month mortality was 3/60 (5.0%) versus 9/54 (16.7%; OR 0.26, 95% CI 0.07–1.03; $p=0.065$). The post hoc death-or-heart-failure-rehospitalization composite occurred in 13/60 (21.7%) versus 19/54 (35.2%; OR 0.51, 95% CI 0.22–1.17; $p=0.109$). Remaining outcomes are summarized in Table 2.

DISCUSSION

The strengths of this study include its prospective randomized design, pragmatic ED-based pathway, and assessment of functional, biological, and clinical outcomes. The main finding was a greater improvement in 6MWT distance with IV-plus-oral therapy (+43.8 m vs

+11.8 m), consistent with the functional signal previously reported with iron sucrose in FERRIC-HF (4). Similar functional benefits have been reported with ferric carboxymaltose in FAIR-HF (3) and CONFIRM-HF (8). However, these trials predominantly included stable patients with reduced LVEF and used substantially higher cumulative iron doses, limiting direct comparison with our acute heart failure population and single 200 mg iron sucrose dose.

The post hoc ≥ 30 m responder analysis supported the continuous 6MWT result but remains exploratory. Clinically important thresholds range from approximately 14–15 m in iron-deficient HFrEF to approximately 36 m in stable chronic heart failure (9,10). Recovery from acute decompensation, the open-label design, participant motivation, baseline imbalances, and absence of adjusted analysis may also have influenced this effort-dependent outcome.

Iron-deficiency correction was not significantly different between groups, and ferritin and hemoglobin increased in both groups without a clear incremental effect. Oral iron in both groups may have attenuated the treatment contrast, although IRONOUT-HF found limited repletion and no improvement in exercise capacity with oral iron in HFrEF (11). The fixed intravenous dose may also have been insufficient for complete repletion. Furthermore, ferritin is influenced by inflammation, and the absence of transferrin saturation limits interpretation (12).

No significant overall difference was observed in NYHA class, fatigue evolution, ED revisits, rehospitalization, or the post hoc death-or-rehospitalization composite. Although fatigue worsening was less frequent with IV-plus-oral therapy, this was one of several secondary comparisons, the fatigue instrument was incompletely documented, and no multiplicity adjustment was applied. AFFIRM-AHF

reported fewer heart failure hospitalizations after ferric carboxymaltose following acute heart failure (5), while IRONMAN showed a favorable numerical effect with ferric derisomaltose, although its primary analysis did not reach statistical significance (13). HEART-FID did not demonstrate a significant benefit for its hierarchical primary outcome (14), and FAIR-HF2 did not meet its multiplicity-adjusted criteria for its primary outcomes (15).

A 2025 meta-analysis nevertheless suggested that intravenous iron reduces recurrent heart failure hospitalizations, while its independent effect on mortality remains uncertain (16).

Accordingly, the numerically lower mortality observed in our IV-plus-oral group cannot be interpreted as evidence of efficacy.

evidence. EFFECT-HF suggested preservation of exercise capacity with ferric carboxymaltose,

although its open-label design and handling of deaths complicate interpretation (17). FAIR-HFpEF subsequently reported improvement in 6MWT distance, but recruitment stopped after only 39 participants, making this finding hypothesis-generating (18). These results cannot be directly extrapolated to a fixed 200 mg iron sucrose regimen.

The timing of iron assessment may also be relevant during acute heart failure. Iron indices can change between admission, clinical stabilization, and follow-up, with functional iron deficiency sometimes resolving spontaneously whereas absolute deficiency is more likely to persist (19).

Additional studies provide supportive functional Measuring ferritin after stabilization therefore supports the biological rationale of our eligibility pathway, although the absence of transferrin saturation prevented more precise characterization of iron status. Consistently, an individual-patient-data meta-analysis associated ferric carboxymaltose with fewer recurrent cardiovascular and heart failure hospitalizations

Table 2. Three-month co-primary biological, secondary, and exploratory outcomes excluding the six-minute walk test

Outcome	IV-plus-oral group	Oral-only group	p value	Effect estimate [95% CI]
Co-primary biological outcome				
Correction of absolute iron deficiency	37/57 (64.9%)	23/45 (51.1%)	0.160	OR 1.77 [0.80–3.93]
Continuous biological changes				
Change in serum ferritin, µg/L	+73.8 ± 49.3	+61.9 ± 50.5	0.234	MD +11.9 [–7.8 to +31.7]
Change in hemoglobin, g/dL	+0.57 ± 0.49	+0.41 ± 0.62	0.156	MD +0.16 [–0.06 to +0.39]
Self-Assigned NYHA class				
Improvement	8/57 (14.0%)	8/45 (17.8%)	0.606	OR 0.76 [0.26–2.20]
Stability	43/57 (75.4%)	32/45 (71.1%)	0.623	OR 1.25 [0.52–3.02]
Worsening	6/57 (10.5%)	5/45 (11.1%)	1.000	OR 0.94 [0.27–3.31]
Fatigue score				
Improvement	32/57 (56.1%)	21/45 (46.7%)	0.342	OR 1.46 [0.67–3.21]
Stability	17/57 (29.8%)	9/45 (20.0%)	0.258	OR 1.70 [0.67–4.29]
Worsening	8/57 (14.0%)	15/45 (33.3%)	0.021	OR 0.33 [0.12–0.86]
Clinical events				
ED revisit for acute heart failure*	38/60 (63.3%)	34/54 (63.0%)	0.967	OR 1.02 [0.47–2.18]
Rehospitalization for acute heart failure*	12/60 (20.0%)	14/54 (25.9%)	0.451	OR 0.71 [0.30–1.72]
Three-month mortality*	3/60 (5.0%)	9/54 (16.7%)	0.065	OR 0.26 [0.07–1.03]
Death or heart failure rehospitalization*,†	13/60 (21.7%)	19/54 (35.2%)	0.109	OR 0.51 [0.22–1.17]

Values are n/N (%) or mean change ± SD. Continuous comparisons use Welch's t test. Categorical comparisons use Pearson's chi-square test, except sparse tables, for which two-sided Fisher's exact p-values are reported. Effect estimates are unadjusted ORs for categorical outcomes and unadjusted MDs (IV-plus-oral minus oral-only) for continuous outcomes; 95% CIs for ORs use the log-Wald method. For NYHA and fatigue, each OR compares the displayed category with the other categories combined. *Analyzed using the 60 and 54 analytic-cohort denominators; other outcomes use available cases. †Post hoc composite. **Abbreviations:** CI, confidence interval; ED, emergency department; MD, mean difference; NYHA, New York Heart Association; OR, odds ratio; SD, standard deviation.

but no apparent mortality benefit, with greater benefit suggested at lower baseline transferrin saturation (20).

No serious infusion-related hypersensitivity event was documented, supporting the operational feasibility of ED-based screening and infusion. However, the small sample and incomplete adverse-event grading preclude definitive safety conclusions. As this study was

conducted in 2017–2018, its fixed iron sucrose strategy predates current ESC guidance supporting individualized ferric carboxymaltose or ferric derisomaltose in selected patients with HFrEF or HFmrEF (6) and should be considered a pragmatic historical strategy rather than current standard care.

Principal limitations include the single-center pilot design, small sample, three-month follow-

up, open-label treatment, lack of prospective registration, incompletely documented allocation concealment, baseline imbalances, fixed low intravenous dose, and oral iron in both groups. Overall, the study supports the feasibility of an ED-initiated strategy and generates a functional hypothesis but does not establish efficacy, safety, or survival benefit.

CONCLUSION

This randomized pilot study shows that a single 200 mg iron sucrose infusion can be integrated into the ED pathway after stabilization, with no serious infusion-related reaction documented. The greater three-month 6MWT improvement with IV-plus-oral therapy is an encouraging functional signal, although biological and clinical outcomes were not significantly different. These findings support further evaluation of ED-initiated intravenous iron strategies in adequately powered, prospectively registered multicenter trials using contemporary diagnostic criteria, individualized dosing, concealed allocation, and blinded outcome assessment.

DECLARATIONS

Use of generative artificial intelligence

Generative artificial intelligence was used solely for English-language editing and stylistic improvement of the manuscript. The authors reviewed and approved all revisions and remain fully responsible for the accuracy, integrity, and scientific content.

Competing interests

The authors declare no competing interests.

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Authors' contributions

All authors contributed to study conception, data collection, analysis, interpretation of results, and

manuscript preparation. All authors read and approved the final manuscript.

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Prognostic Value of the ACTION ICU Score Compared to GRACE and TIMI Scores in Non-ST-Segment Elevation Acute Coronary Syndromes

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Abstract

Background: Non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) represent the primary manifestation of acute coronary syndromes, accounting for 60% to 70% of hospital admissions. Effective emergency department (ED) management relies on accurate risk stratification to guide triage. While established scores like GRACE and TIMI are widely used for long-term prognosis, they are not specifically validated to predict immediate in-hospital complications in the acute ED phase. This study evaluated the prognostic value of the ACTION ICU score compared to the performance of the GRACE and TIMI scores for short-term ED complications and 6-month major adverse cardiovascular events (MACE).

Methods: We conducted a retrospective observational analysis of a prospective registry at a regional hospital in Tunisia, over nine years (2014–2022). Inclusion of patients admitted for NSTEMI-ACS in the ED. Diagnostic performance was evaluated using Receiver Operating Characteristic (ROC) curves to identify optimal cut-off values for acute in-hospital complications (acute pulmonary edema, arrhythmias, death) and 6-month MACE.

Results: The cohort had a mean age of 60 ± 12 years with 59.3% males. In-hospital complications occurred in 6.3% of patients. For predicting these acute events, the ACTION ICU score significantly outperformed other models with an Area Under the Curve (AUC) of 0.88 (95% CI: 0.836–0.941), compared to 0.77 for GRACE and 0.59 for TIMI. An ACTION ICU cut-off value of >5.5 provided 80% sensitivity, 77.39% specificity, and a negative predictive value of 98.29%. Conversely, the GRACE score was the most accurate for 6-month MACE (AUC 0.707).

Conclusion The ACTION ICU score is an effective tool for immediate ED triage, providing high accuracy in predicting short-term complications. Its systematic implementation could optimize intensive care unit resource allocation in constrained healthcare settings without compromising patient safety.

Key-words: Score, Prognosis, Emergency Department, Acute Coronary Syndrome, NSTEMI, Mortality.

INTRODUCTION

Cardiovascular diseases are the leading cause of morbidity and mortality worldwide, with an increasing incidence in developing countries. Acute coronary syndromes (ACS) are the most

frequent cardiovascular manifestation of these diseases. Among them, non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) represent the primary manifestation, causing 60% to 70% of hospital admissions with a mortality rate of approximately 3.4% (1,2).

For frontline physicians, managing these patients is a daily challenge. While the management of ST-segment elevation myocardial infarction is well codified and relies on immediate coronary reperfusion, the emergency management of NSTEMI-ACS depends entirely on the risk stratification of cardiovascular complications and death.

To guide this risk stratification, medical societies have validated several scoring systems. The TIMI (Thrombolysis In Myocardial Infarction) score is a simple tool designed to stratify the medium-term risk of complications (3). The GRACE (Global Registry of Acute Coronary Events) score predicts both in-hospital and six-month mortality, and its use is currently recommended by the European Society of Cardiology to guide therapeutic decisions (4).

However, no specific score is used to predict the risk of in-hospital complications directly in the emergency department for NSTEMI-ACS patients.

To address this issue, the ACTION

ICU (Acute Coronary Treatment and Intervention Outcomes Network) score was first proposed in 2018 to predict the development of complications requiring intensive care unit admission during the initial phase of care (5).

Very few studies in international and national literature have focused on evaluating the ACTION ICU score. The aim of this study was to evaluate the short-term prognostic value of the ACTION ICU score by comparing it against the traditional GRACE and TIMI scores in the emergency department.

METHODS

Study Design and Setting

We conducted a retrospective observational analysis of a prospective monocentric registry of patients presenting with non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) during a nine-year period, from January 2014 to December 2022. Data were collected at

the Emergency Department of a regional hospital in Tunisia.

Patient Selection

We included adult patients of both sexes, who presented to the emergency department with clinical, electrocardiographic, and biological findings consistent with NSTEMI-ACS. We defined the diagnosis of NSTEMI-ACS using standard diagnostic criteria: symptoms suggestive of acute myocardial ischemia (chest pain, dyspnea, or epigastric discomfort), associated with electrocardiographic normal findings or ischemic changes (such as ST-segment depression, T-wave inversion or non-specific ST-T abnormalities), and the dynamic change of high-sensitivity cardiac troponin to distinguish between NSTEMI (rise or fall of troponin) and unstable angina (normal value).

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

Presentation with complications requiring immediate intensive care upon admission (cardiac arrest, cardiogenic shock, severe arrhythmias).

Presence of persistent ST-segment elevation on the initial ECG (STEMI).

Final diagnosis unrelated to NSTEMI-ACS (coronary angiography showing no significant lesions).

Missing contact information, leaving against medical advice, or being lost to follow-up.

Unavailable coronary angiography data.

The final diagnosis of ACS was confirmed either by ischemia tests conducted in outpatient cardiology clinics or by coronary angiography demonstrating a stenosis of more than 50% in a major coronary artery.

Data Collection and Definitions

For each included patient, data were retrospectively extracted from the registry using standardized medical records completed by the emergency physicians. We collected demographic characteristics, cardiovascular risk factors, and previous medical history.

Clinical presentation details included the characteristics of chest pain, time from symptom onset to first medical contact (FMC), vital signs (systolic and diastolic blood pressure, heart rate, respiratory rate, and oxygen saturation), Killip classification, and pain intensity using a visual analog scale.

A standard 17-lead ECG was performed within 10 minutes of FMC. Biological data obtained at admission included blood glucose, renal function, ionogram, complete blood count, and troponin levels. From 2016 onwards, high-sensitivity troponin assays were utilized following the 0/3h rule-out algorithm recommended by ESC guidelines (6).

Prognostic Risk Scores and Outcomes

Three prognostic risk scores were systematically calculated for each patient at admission based on clinical, biological, and electrical data:

TIMI Score (Thrombolysis In Myocardial Infarction).

GRACE Score (Global Registry of Acute Coronary Events).

ACTION ICU Score (Acute Coronary Treatment and Intervention Outcomes Network).

The primary short-term outcome was the occurrence of in-hospital complications during the emergency department stay. Complications were defined as acute pulmonary edema, cardiogenic shock, severe arrhythmias, conduction disorders, or death.

The long-term prognostic outcome was evaluated through telephonic follow-up at 6 months. We assessed the occurrence of Major Adverse Cardiovascular Events (MACE), defined as death, non-fatal myocardial infarction, recurrent angina, stroke, or the need for coronary artery bypass grafting (7).

Statistical Analysis

We performed data entry and statistical analyses were performed using SPSS software (version 23.0). Continuous variables were expressed as means $\pm$ standard deviations (SD) and compared using the Student's t-test or Analysis of Variance

(ANOVA). Categorical variables were expressed as frequencies and percentages and compared using Pearson's chi-squared test or Fisher's exact test when appropriate. A p-value of <0.05 was considered statistically significant.

To evaluate the predictive accuracy of the GRACE, TIMI, and ACTION ICU scores for short-term complications and 6-month MACE, we generated Receiver Operating Characteristic (ROC) curves. The Area Under the Curve (AUC) with 95% confidence intervals were calculated for each score. Optimal cut-off values were determined based on the highest combined sensitivity and specificity. Finally, AUCs were formally compared to establish statistical superiority among the models.

RESULTS

During the study period, out of the overall emergency department, 793 patients met the inclusion criteria and were managed for non-ST-segment elevation acute coronary syndromes. Figure 1 represents the inclusion flowchart.

The mean age was 60 ± 12 years. Men represented most of the cohort, accounting for 59.3% (n=470) of the patients.

The most prevalent cardiovascular risk factors were hypertension, present in 57.1% (n=453) of the cohort, followed by diabetes mellitus in 42.4% (n=336), active smoking in 30.1% (n=239), and dyslipidemia in 29.3% (n=232). A known history of coronary artery disease before admission

was present in 27.9% (n=221) of patients.

Clinically, chest pain was the cardinal symptom, motivating the emergency consultation in 92.4% (n=733) of cases. The median delay from symptom onset to first medical contact was 19.5 hours. Upon initial electrocardiographic (ECG) assessment, 48%

(n=381) of patients demonstrated ST-segment depression, 17.3% (n=137) showed isolated negative T waves, and 32.2% (n=256) had a normal initial ECG.

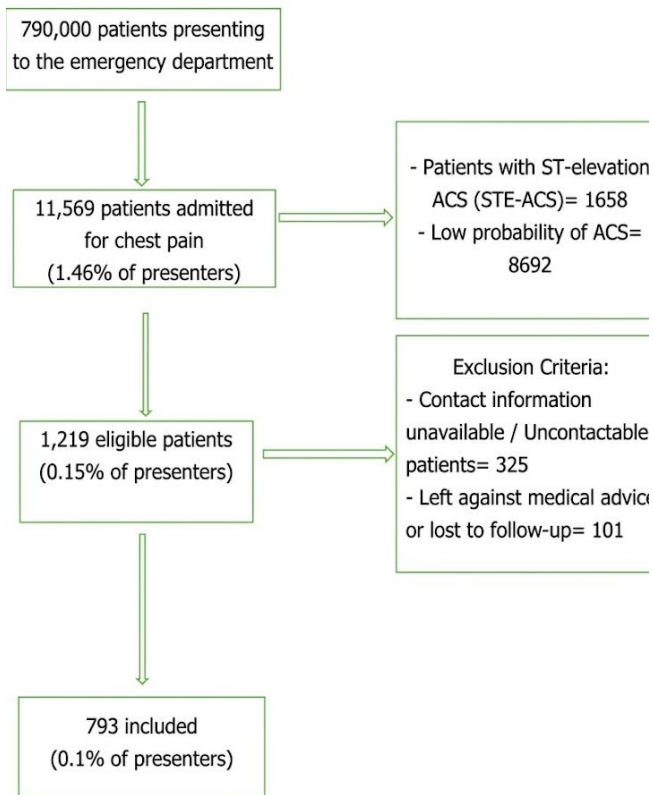


Figure 1: Patient inclusion flowchart in the study

The occurrence of complications during the emergency department stay was observed in 6.3% of patients (n=50). The most frequent complication was acute pulmonary edema (3.5%, n=28), followed by arrhythmias (1.9%, n=15) and conduction disorders (0.9%, n=7). In-hospital mortality occurred in 3 cases (0.37%). Table 1 highlights the significant clinical and biological differences between the stable group and the group that developed acute complications during their emergency department stay.

Receiver Operating Characteristic (ROC) curve analysis for short-term complications revealed that the ACTION ICU score demonstrated significant superiority over both the GRACE and TIMI scores (Fig 2). The ACTION ICU score yielded an Area Under the Curve (AUC) of 0.88 (95% CI: 0.836–0.941; $p < 0.01$). A cut-off value of 5.5 provided the best balance, with a sensitivity of 80% and a specificity of 77.39%. The GRACE score had an AUC of 0.777 (IC95%

(0,710-0,844)) with a cut-off of 110; sensitivity 76%, and specificity 57.32%, and the TIMI score an AUC of 0.599 (95% CI: 0.520–0.678) with a cut-off of 2.5; sensitivity 62% and specificity 52.32%.

Table 1: Comparative Analysis of Patients with and without In-Hospital Complications

Factor	Complications + (n=50)	Complications - (n=743)	p-value
Mean Age (years)	69.4 ± 12.6	60.1 ± 12.0	<0.001
Age > 65 years, n (%)	33 (66.0)	252 (33.9)	<0.001
Hypertension, n (%)	39 (78.0)	414 (55.7)	0.002
Diabetes, n (%)	30 (60.0)	306 (41.2)	0.009
Heart Rate (bpm)	102.4 ± 31.0	81.6 ± 15.5	<0.001
Respiratory Rate (c/min)	21.4 ± 7.3	16.6 ± 2.7	<0.001
Blood Glucose (mmol/l)	10.3 ± 5.0	8.4 ± 4.4	0.005
Creatinine (μmol/l)	119.2 ± 94.0	87.4 ± 69.0	0.002
ACTION ICU Score (mean)	9.0 ± 3.3	4.2 ± 1.9	<0.001
GRACE Score (mean)	141.2 ± 36.9	102.7 ± 35.0	<0.001
TIMI Score (mean)	3.0 ± 2.5	2.5 ± 1.4	0.016

At the six-month follow-up, 16% of the overall cohort (n=127) had experienced at least one Major Adverse Cardiovascular Event (MACE). Table 2 illustrates the variables that significantly influenced the occurrence of major adverse cardiovascular events at the six-month follow-up.

ROC curve analysis for predicting 6-month MACE showed that while all scores had

statistically significant predictive value, their overall accuracy was moderate compared to short-term predictions (Fig 3).

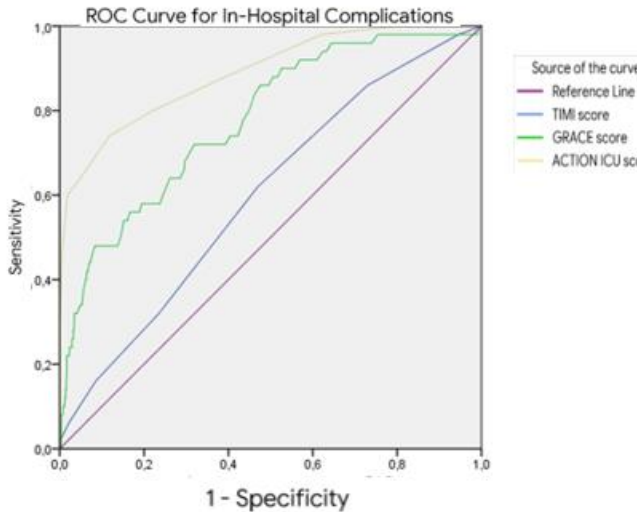


Figure 2: ROC Curves comparing the predictive accuracy of ACTION ICU, GRACE, and TIMI scores for in-hospital complications

The GRACE score performed slightly better for this long-term endpoint with an AUC of 0.707 (IC95% [0,659-0,756]) with a cut-off 114.5; sensitivity 62.7%, specificity 64.91%. The ACTION ICU score showed an AUC of 0.643 (IC95% [0,591-0,695]) with a cut-off 4.5 a sensitivity of 59.8%, and a specificity of 60.2%, and the TIMI score had an AUC of 0.624 (IC95% [0,576-0,672]). With a cut-off of 2.5, the sensitivity was 62%, and the specificity was 52.3%.

DISCUSSION

The aim of our study was to evaluate the prognostic value of the ACTION ICU score by comparing it against established baselines (GRACE and TIMI) in predicting ED complications and 6-month Major Adverse Cardiovascular Events (MACE) among patients presenting with non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS).

Table 2: Comparative analysis of factors associated with 6-month MACE

Factor	MACE +	MACE -	p-value
	(n=127)	(n=666)	
Mean Age (years)	64.6 ± 10.8	60.6 ± 11.7	<0.001
Male Gender, n (%)	88 (69.3)	201 (30)	<0.001
Heart Rate (bpm)	89.7 ± 24.1	81.7 ± 15.7	<0.001
Oxygen Saturation (SpO2 %)	96.4 ± 5.4	97.6 ± 2.1	<0.001
Negative T waves, n (%)	16 (12.6)	79 (12)	0.03
ST Amplitude (mm)	0.85 ± 0.8	0.5 ± 0.4	<0.001
ACTION ICU Score (mean)	5.5 ± 2.7	4.2 ± 2.8	<0.001
GRACE Score (mean)	127.9 ± 34.7	112.4 ± 33.8	<0.001
TIMI Score (mean)	3.0 ± 1.2	2.5 ± 1.4	<0.001

Our results demonstrate that while the GRACE score remains effective for predicting long-term MACE, the ACTION ICU score significantly outperforms both the GRACE and TIMI scores in identifying patients at high risk of immediate, in-hospital complications during their ED stay. With an Area Under the Curve (AUC) of 0.88 and an optimal cut-off value of 5.5, the ACTION ICU score presents as a highly sensitive and specific tool to guide acute triage and intensive care unit (ICU) admissions.

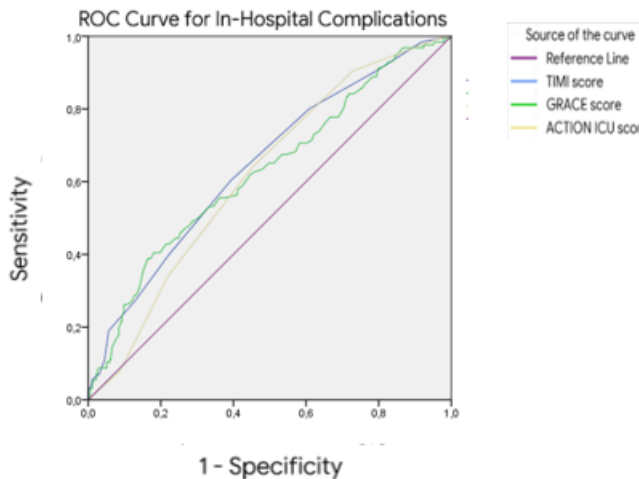


Figure 3: ROC Curves comparing the predictive accuracy of ACTION ICU, GRACE, and TIMI scores for Major Adverse Cardiovascular Events (MACE) at 6 months.

Baseline Demographic and Clinical Characteristics

Our cohort presented a mean age of 60 ± 12 years with a male predominance, which is comparable to data from the SCAAR (Swedish Coronary Angiography and Angioplasty Registry) registry (8). In comparison, data from an Egyptian registry reported a mean age of 62.6 years with a sex ratio of 1.17 (9). These metrics are consistent with a 2017 study conducted in our department, which reported a mean age of 61 years and a sex ratio of 1.46 (10). Conversely, Western populations typically present at an older age; statistics from the American Heart Association indicate the mean age for a first myocardial infarction is 65.6 years for men and 72 years for women (11). This earlier onset in our population may reflect different genetic predispositions or earlier exposure to unmanaged cardiovascular risk factors, notably hypertension, diabetes and smoking.

The high prevalence of hypertension in our study (57.1%) is consistent with international data. An analysis of the TIMI trials encompassing over 15,000 patients revealed an incidence of hypertension exceeding 70% among those with

coronary syndromes, while the SCAAR registry in Sweden observed hypertension in 63% of patients (8). Physiologically, chronic hypertension accelerates atherosclerosis through endothelial microtrauma and increased low-density lipoprotein (LDL) permeability, thereby increasing the vulnerability of coronary plaques (12).

During the initial ED management, 6.3% of our patients developed complications, the most frequent being acute pulmonary edema (3.5%). This complication rate is lower than some historical cohorts, such as the MOSCA-FRAIL study (13), which may be attributed to our exclusion of patients presenting initially with cardiogenic shock or cardiac arrest, as our goal was to evaluate initially stable patients requiring triage.

The central finding of our study is the superior performance of the ACTION ICU score in predicting these acute in-hospital events. With an AUC of 0.88, the score demonstrated excellent discriminatory power. This finding strongly corroborates recent international literature. A large Chinese cohort of 4,012 NSTEMI patients similarly reported the ACTION ICU score as the most accurate predictor of in-hospital mortality, with an AUC of 0.931 (14). Furthermore, a German study of 1,002 NSTEMI patients found the ACTION ICU score to outperform the GRACE model (AUC 0.87 vs. 0.84, respectively; $p=0.018$) for predicting in-hospital mortality (15).

In our analysis, a cut-off score of 5.5 provided a sensitivity of 80% and a specificity of 77.39%. This is clinically relevant. In the original derivation study by Fanaroff et al.(5), the score was designed to identify patients who genuinely required ICU care versus those who could be safely managed in step-down units. By demonstrating a high Negative Predictive Value (98.29%), our data suggests that an ACTION ICU score < 5.5 can reliably identify patients at low risk of acute deterioration, potentially

preventing unnecessary ICU admissions and optimizing resource allocation in constrained healthcare environments.

The GRACE score (AUC 0.77) and TIMI score (AUC 0.59) were less effective for immediate risk prediction. This is unsurprising, as the TIMI score was initially designed to predict events up to 14 days post-admission (16) while the GRACE score was primarily validated for in-hospital and 6-month mortality rather than acute procedural or hemodynamic complications in the immediate hours following ED presentation (17).

At the six-month follow-up, 16% of patients experienced MACE. For this long-term endpoint, the GRACE score demonstrated superior predictive performance (AUC 0.707) compared to ACTION ICU (AUC 0.643) and TIMI (AUC 0.624).

This validates the current European Society of Cardiology guidelines, which recommend the GRACE score (specifically GRACE 2.0) for long-term risk stratification (17).

Strengths and Limitations

This study benefits from a large, prospective data collection methodology over a nine-year period, allowing for a precise objective evaluation of NSTEMI-ACS epidemiology in an ED setting. Furthermore, conducting the study in a hospital without an integrated cardiology department necessitated meticulous clinical triage and prolonged ED observation, providing highly accurate data on acute in-hospital complications. However, we acknowledge several critical limitations. First, comparing the ACTION ICU score to the GRACE and TIMI scores introduces a comparability bias, as these tools were not designed for the same chronological endpoints or clinical purposes. Second, while baseline characteristics significantly differed between the complication + and complication- groups (Table 1), this does not constitute a true confounding bias. Instead, these differences naturally reflect the expected clinical predictors of acute events,

many of which are already partially integrated into the scoring systems being evaluated. Third, patient selection limits generalizability, as excluding patients with initial complications or missing angiographic data creates a selection bias. Finally, the retrospective monocentric design, reliance on telephone follow-ups, and the 2016 transition to high-sensitivity troponin assays carry inherent risks of reporting and methodological biases.

Clinical implications and perspectives

Our findings advocate for a dual-score strategy in the emergency department. While the GRACE score remains the gold standard for defining the long-term therapeutic strategy and timing of revascularization, the ACTION ICU score should be systematically integrated into the immediate triage process for NSTEMI-ACS patients. Implementing the ACTION ICU score in ED protocols could safely reduce unwarranted ICU admissions, thereby decreasing healthcare costs and freeing critical beds without additional risk to the patient particularly vital strategy in developing countries. . Prospective multicenter studies are strictly warranted to validate a triage algorithm utilizing this score before clinical implementation.

Non-ST-segment elevation acute coronary syndromes (NSTEMI-ACS) account for a substantial burden of cardiovascular hospitalizations, requiring precise risk stratification to optimize emergency department triage. This study demonstrates that while the GRACE score remains a robust tool for predicting long-term (6-month) Major Adverse Cardiovascular Events (MACE), the ACTION ICU offers superior accuracy for identifying immediate, in-hospital complications at the emergency department.

Specifically, the ACTION ICU score achieved an Area Under the Curve (AUC) of 0.88, significantly outperforming the GRACE (AUC:0.77) and TIMI (AUC:0.59). At an

optimal cut-off of 5.5, ACTION ICU score provided high sensitivity (80%) and specificity (77.39%), coupled with an excellent negative predictive value (98.29%), making it a highly reliable tool to rule out the need for immediate intensive care. These findings suggest that the ACTION ICU score can effectively guide emergency physicians in rationalizing intensive care unit admissions. Given the limitations of our retrospective design and potential population disparities, prospective multicenter validation is essential before integrating this score into routine clinical protocols.

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Value of Nonspecific Severity Scores in Predicting Mortality in Severe Traumatic Brain Injury

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Abstract

Introduction: Severe traumatic brain injury (sTBI) is a leading cause of mortality in young adults. Neurological scores alone, such as the Glasgow Coma Scale (GCS), may be insufficient due to associated organ dysfunction. This study evaluated the predictive value of nonspecific severity scores (APACHE II, SAPS II) and organ dysfunction scores (SOFA, LODS, and MODS) for mortality in ICU patients with sTBI.

Methods: Prospective descriptive and analytical study over 10 months in a 22-bed multidisciplinary ICU at Habib Bourguiba University Hospital, Sfax. We included adult patients (≥ 18 years) admitted to the ICU with both isolated severe traumatic brain injury and polytrauma patients with severe traumatic brain injury (Glasgow Coma Scale ≤ 8 after initial resuscitation). Patients who died before day 5 were excluded, and organ dysfunction scores were calculated whenever data were available on days 1, 3, and 5. Data collected included demographics, neurological and biological status, imaging, interventions, initial severity scores, and organ dysfunction scores on days 1, 3, and 5. Univariate and multivariate analyses were performed to identify factors associated with mortality. Predictive performance was assessed using ROC curves (AUC, sensitivity, specificity).

Results: Thirty-seven patients were included, with a median age of 40 years and 86% male. Road traffic accidents accounted for 86%. ICU mortality was 16.2%. Non-survivors had higher SAPS II and APACHE II scores ($p < 0.01$). LODS and MODS scores on days 1, 3, and 5 were significantly associated with mortality. ROC analyses showed excellent discrimination, particularly for LODS on day 5 (AUC 0.911). Multivariate analysis revealed MODS day 1, LODS day 3, and LODS day 5 as autonomous predictors of mortality.

Conclusion: Nonspecific severity scores and serial organ dysfunction scores are reliable tools for predicting ICU mortality in sTBI. Dynamic assessment enhances prognostic accuracy and may guide clinical decision-making.

Keywords: Severe traumatic brain injury, mortality prediction, APACHE II, SAPS II, SOFA, LODS, MODS, intensive care unit

INTRODUCTION

Trauma represents the leading cause of mortality before the age of 45 years(1). Approximately half of trauma-related deaths are due to traumatic brain injuries (TBI)(1). Every day, intensivists face difficulties in the management of severe traumatic brain injury (sTBI) patients (2) and must decide which patients should be admitted to the intensive care unit. Although TBI-specific prognostic models, particularly IMPACT and CRASH, demonstrate good discriminatory ability, they primarily predict long-term neurological outcomes and inadequately account for extracranial organ dysfunction or the dynamic course of critical illness. Therefore, routinely used nonspecific ICU severity scores may provide a more comprehensive assessment of mortality risk in patients with severe TBI(3). Patients with severe TBI admitted to the ICU often present not only with neurological dysfunction, assessed by specific scores such as the Glasgow Coma Scale (GCS) and the Glasgow Outcome Scale (GOS) (4), but also with dysfunction of at least one other major organ system. Therefore, predicting outcomes and mortality in severe TBI patients admitted to the ICU based on the number, severity, and duration of organ failures has become increasingly relevant (5). Several scoring systems have been developed, among the most recent being the Multiple Organ Dysfunction Score (MODS) (6), the Logistic Organ Dysfunction Score (LODS) (7), and the Sequential Organ Failure Assessment (SOFA) score (8). The main objective of our study was to evaluate the predictive value of two antiepileptic drugs, anti-edema therapy, and surgery), imaging findings, biological data at admission, systemic secondary brain insults at admission, initial severity scores at admission (GCS (9), SAPS II(10), and APACHE II (11)), and organ dysfunction scores (SOFA (8), MODS (6), and LODS (7)) calculated on day 1, day 3, and day 5. Additional variables included the need for tracheostomy, length of ICU stay, duration of mechanical ventilation, and mortality.

types of nonspecific severity scores—initial severity scores (APACHE II and SAPS II) and organ dysfunction scores (SOFA, LODS, and MODS) in predicting mortality after severe traumatic brain injury.

METHODS

Study Design: This was a prospective descriptive and analytical study conducted over 10 months (from November 1, 2024, to August 31, 2025) in the multidisciplinary intensive care unit of the Habib Bourguiba University Hospital in Sfax, which has 22 beds. We included adult patients (≥ 18 years) admitted to the ICU with both isolated severe traumatic brain injury and polytrauma patients with severe traumatic brain injury (Glasgow Coma Scale ≤ 8 after initial resuscitation). Patients who died before day 5 were excluded, and organ dysfunction scores were calculated whenever data were available on days 1, 3, and 5. We included all consecutive eligible patients admitted during the study period; no formal sample size calculation was performed. The requirement for informed consent was waived because of the anonymized data collection. All medical records of patients admitted during the study period were reviewed. Data were collected using a standardized file including: age, sex, medical history, mechanism of injury, neurological examination at admission (pupillary status and presence or absence of motor deficit), treatments used at admission (mechanical ventilation, catecholamine, fluid resuscitation, sedation,

Statistical Analysis: Data were entered and analyzed using SPSS software version 22. Results were presented as a descriptive study. Quantitative variables were expressed as mean $\pm$ standard deviation or median (IQR) depending on their distribution, while qualitative variables were expressed as number (percentage). For the analytical study, factors associated with mortality were evaluated. Comparisons of proportions

were performed using the Pearson Chi-square test or Fisher's exact test when appropriate. Comparisons of means were performed using the nonparametric Mann–Whitney U test. The level of statistical significance was set at $p < 0.05$. Multivariate analysis was performed using a stepwise ascending multiple logistic regression model, including variables with $p < 0.05$ in the univariate analysis. The optimal cut-off values were determined using receiver operating characteristic (ROC) curve analysis.

RESULTS

Descriptive Study: Patients assessed for eligibility were 50. Thirty-seven patients were included in our study (Figure 1). The median age was 40 years, with extremes ranging from 19 to 73 years. A male predominance was observed, with a sex ratio of 6. Most patients had no prior medical history (76%). The most frequent mechanism of injury was road traffic accident (86%). All included patients had a Glasgow Coma Scale (GCS) score ≤ 8 after initial resuscitation, with a median admission GCS of 6. The median SAPS II (IGS II) was 39, and the median APACHE II score was 17. The median SOFA score was 7, LODS was 5, and MODS was 5. Thirteen patients (35%) presented with motor deficits. Thirteen patients exhibited anisocoria (45%), and one patient had mydriasis. Twenty-one patients (56%) developed shock at admission, requiring catecholamine. Volume resuscitation was performed in 28 patients (75%), and all patients (100%) required mechanical ventilation from admission. Organ dysfunction scores were available for all 37 patients at each assessment time point (Day 1, Day 3, and Day 5), as no deaths occurred before Day 5. Table 1 details the severity and organ dysfunction scores on Day 3 and Day 5. All patients underwent a cranial CT scan on admission. The most common lesions were subdural hematoma ($n=21$; 56%) and epidural

hematoma ($n=12$; 32%). All patients received sedation (100%).

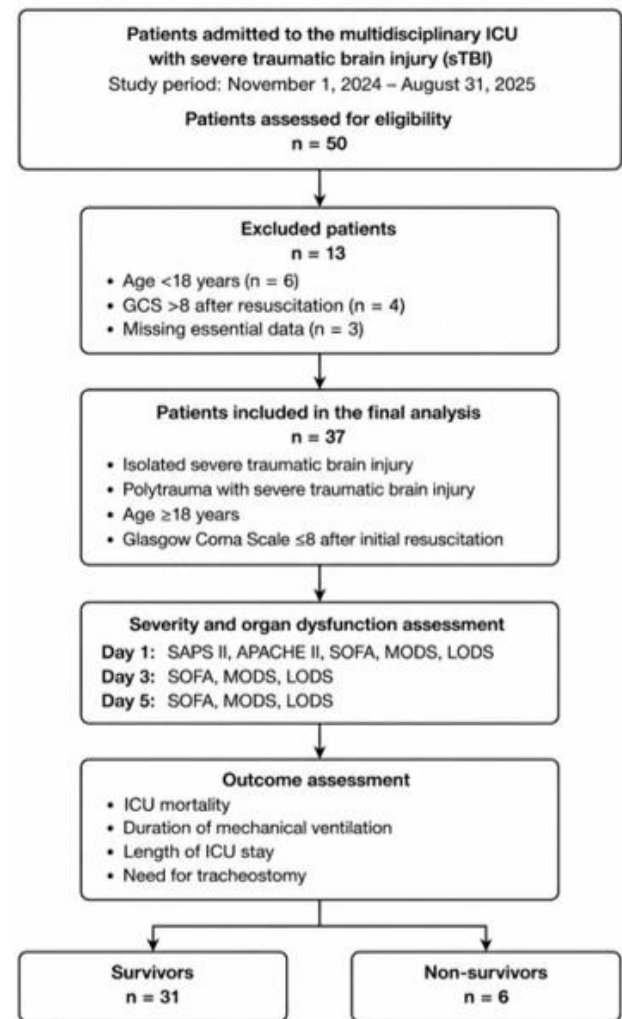


Figure 1: Flow chart of patient selection

Osmotherapy with 20% mannitol was indicated in 24 patients (64%), and antiepileptic treatment in 21 patients (56%). Tracheostomy was performed in 19 patients (51%) at a median of 10 days. Surgical decompressive craniectomy was performed in 10 patients (27%). Blood transfusion was indicated in 20 patients. The median duration of mechanical ventilation was 10 days, and the median ICU stay was 18 days. Overall mortality was 16% (6 patients).

Analytical Study: The median age of nonsurvivors was slightly higher than that of survivors (43 vs. 41 years; $p = 0.84$). The median SAPS II (IGS II) score was higher in nonsurvivor patients than in survivors (58 vs. 37; $p = 0.004$).

Table 1: Severity scores during ICU stay

	Median [IQR]
SOFA d 3	7 [5–9]
LODS d 3	4 [3–7]
MODS d 3	5 [4–8]
SOFA d 5	5 [3–8]
LODS d 5	4 [2–6]
MODS d 5	4 [2–7]

SOFA: Sequential Organ Failure Assessment Score, LODS: Logistic Organ Dysfunction System, MOD: Multiple Organ Dysfunction Score, d: day, IQR:interquartile

The median APACHE II score was also higher among nonsurvivors patients (24 vs. 16; $p = 0.001$). LODS and MODS scores on day 1 were higher in nonsurvivors compared to survivors, with significant differences ($p = 0.034$ for both). LODS and MODS on day 3, and SOFA, LODS, and MODS on day 5 were also significantly associated with mortality (Table 2).

ROC curve analysis showed that: SAPS II (IGS II) > 53.5 had an AUC of 0.823, with a sensitivity of 83% and specificity of 93% ($p = 0.013$) (Figure 2, curve A). APACHE II > 20.5 had an AUC of 0.836, with a sensitivity of 83% and specificity of 87% ($p = 0.01$) (Figure 2, curve B). LODS on day 1 > 6.5 had an AUC of 0.847, with a sensitivity of 83% and specificity of 87% ($p = 0.008$) (Figure 2, curve C). MODS on day 1 > 5.5 had an AUC of 0.815, with a sensitivity of 83% and specificity of 67% ($p = 0.016$) (Figure 2, curve D). MODS on day 3 > 6.5 had an AUC of 0.863, with a sensitivity of 83% and specificity of 90% ($p = 0.005$) (Figure 3, curve E).

LODS on day 3 > 6.5 had an AUC of 0.883, with a sensitivity of 83% and specificity of 93% ($p = 0.003$) (Figure 3, curve F). SOFA on day 5 > 6.5 had an AUC of 0.819, with a sensitivity of 83% and specificity of 79% ($p = 0.015$) (Figure 3, curve G).

Table 2: Univariate analysis of factors associated with mortality

Variables	Survivors (n=31)	Nonsurvivors (n=6)	<i>p</i>
Age (median)	41	43	0.84
Sex ; n(%)			
Male	26 (83)	6(100)	0.29
Female	5 (16)	0 (0)	

Factors associated with mortality in univariate analysis

GCS (median)	7	5	0.108
IGSII d1 (median)	37	58	0.004
APACHE II d1 (median)	16	24	0.001
SOFA d1 (median)	7	11	0.076
LODS d1 (median)	5	10	0.034
MODS d1 (median)	5	10	0.034

Systemic secondary brain insults (SBI) at admission

Shock (n ;%)	17(46)	4(66)	0.6
Anemia (n ;%)	8(25)	1(16)	0.6
Hypoxemia (n ;%)	16(51)	4(66)	0.6
Hypercapnia (n ;%)	12(38)	2(33)	0.8
Hyponatremia<135 mmol/l (n ;%)	1(3)	1(16)	0.3
Hyperglycemia ≥ 8 mmol/l (n ;%)	10(32)	2(33)	1

Severity scores and organ dysfunction scores during the ICU stay

SOFA d3 (median)	6	10	0.053
LODS d3 (median)	4	9	0.037
MODS d3 (median)	4	10	0.05
SOFA d 5 (median)	5	11	0.048
LODS d 5 (median)	3	9	0.02
MODS d 5 (median)	4	10	0.032

GCS: Glasgow coma score, IGSII: Indice de Gravité Simplifié II, APACHE: Acute Physiology and Chronic Health Evaluation, SOFA: Sequential Organ Failure Assessment Score, LODS: Logistic Organ Dysfunction System, MOD: Multiple Organ Dysfunction Score, d: day, ACSOS: agressions cérébrales secondaires d'origine systémiques, CIVD: coagulation intra vasculaire disséminée, pH: potentiel Hydrogène

LODS on day 5 > 6.5 had an AUC of 0.911, with a sensitivity of 83% and specificity of 93% ($p = 0.002$) (Figure 3, curve H). MODS on day 5 > 6.5 had an AUC of 0.855, with a sensitivity of 83% and specificity of 89% ($p = 0.003$) (Figure 3, curve I). Table 3 details the prognostic accuracy of severity scores for predicting ICU mortality.

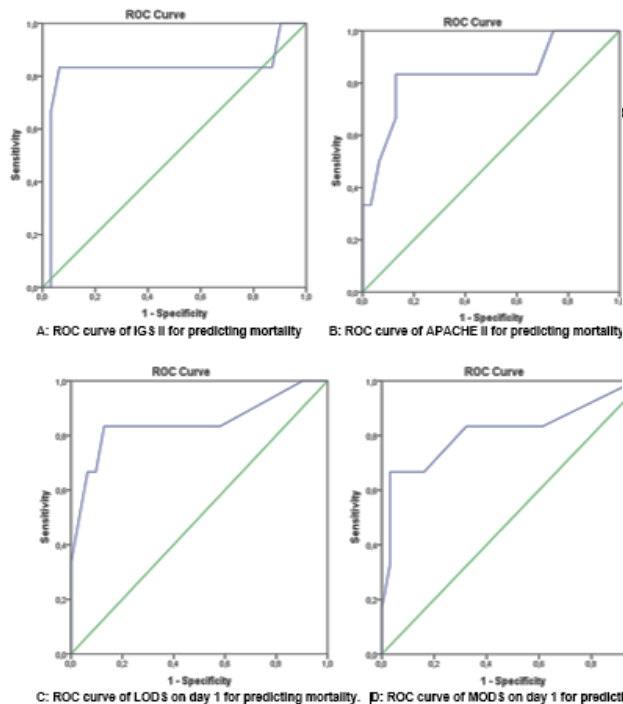


Figure 2: ROC curves of IGS II, APACHE II, and LODS (day 1), and MODS (day 1) for predicting mortality.

DISCUSSION

Severe traumatic brain injury (TBI) remains a leading cause of critical illness and mortality worldwide, particularly among young adults (12). Despite advancements in prehospital care and intensive care unit (ICU) management, predicting outcomes after severe TBI continues to be a clinical challenge (13). Early prognostication is essential for guiding therapeutic decisions, allocating resources, and informing families, yet reliance solely on neurological scores such as the Glasgow Coma Scale (GCS) may be insufficient given the systemic impact of severe TBI (12).

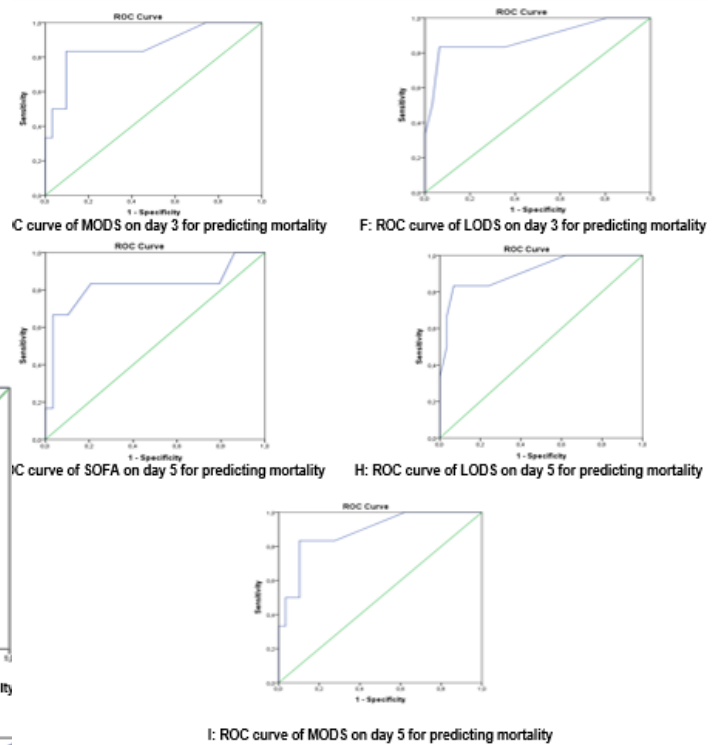


Figure 3: ROC curves of MODS (day 3), LODS (day 3), SOFA (day 5), LODS (day 5), and MODS (day 5) for predicting mortality.

Multivariate Analysis identified MODS on day 1, LODS on day 3, and LODS on day 5 as independent factors associated with mortality (Table 4).

In our cohort of 37 patients with severe sTBI, we observed an ICU mortality of 16.2%. Median admission severity scores (APACHE II: 17; SAPS II: 39) and organ dysfunction scores (SOFA: 7; LODS: 5; MODS: 5) were elevated, reflecting significant physiological disturbances. These findings corroborate prior studies demonstrating that severe TBI frequently results in multisystem dysfunction, which has a substantial influence on patient outcomes (14,15).

Our analyses indicate that both nonspecific severity scores (APACHE II, SAPS II) and organ dysfunction scores (SOFA, LODS, MODS) are significantly associated with mortality in severe TBI.

Table 3: Prognostic accuracy of severity scores for predicting ICU mortality

Severity score	Cut-off	AUC (95% CI)	Sensitivity (%)	Specificity (%)	P value
SAPS II	>53.5	0.823(0.66–0.98)	83	93	0.013
APACHE II	>20.5	0.836(0.68–0.99)	83	87	0.010
LODS Day 1	>6.5	0.847(0.70–0.99)	83	87	0.008
MODS Day 1	>5.5	0.815(0.65–0.98)	83	67	0.016
MODS Day 3	>6.5	0.863(0.73–0.99)	83	90	0.005
LODS Day 3	>6.5	0.883(0.75–1.00)	83	93	0.003
SOFA Day 5	>6.5	0.819(0.66–0.98)	83	79	0.015
LODS Day 5	>6.5	0.911(0.80–1.00)	83	93	0.002
MODS Day 5	>6.5	0.855(0.71–1.00)	83	89	0.003

AUC, area under the receiver operating characteristic (ROC) curve; SAPS II, Simplified Acute Physiology Score II; APACHE II, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; MODS, Multiple Organ Dysfunction Score; LODS, Logistic Organ Dysfunction System; CI, confidence interval.

Table 4: Multivariate analysis of severity and organ dysfunction scores associated with mortality

Variables	p	OR	Confidence Interval 95%
MODS D1	0.004	2.5	2.24-10.80
LODS D3	0.013	4.5	3.53-12.77
LODS D5	0.011	6.33	4.33-15.43

Univariate comparisons showed higher median values of these scores among nonsurvivors, and ROC curve analysis demonstrated excellent discriminative performance. Notably, LODS at day 5 yielded an AUC of 0.911, with high sensitivity and specificity, while scores such as MODS at day 3 (AUC 0.863) and SOFA at day 5 (AUC 0.819) also showed robust predictive value.

These results align with contemporary literature (15,16). Prior research has shown that commonly used ICU scoring systems traditionally developed for general critical illness can reliably predict mortality in TBI populations when applied dynamically (14,15). For example, recent comparative analyses indicate that APACHE II and SAPS II outperform GCS alone (17) in prognostic accuracy when predicting short- and medium-term mortality after TBI (14). In addition, the predictive validity of organ dysfunction scores such as SOFA, MODS, and LODS has been increasingly recognized, reflecting the systemic inflammatory response and secondary organ failures that commonly complicate severe TBI (15,18).

The selection of days 1, 3, and 5 for organ dysfunction assessment was intended to capture the dynamic evolution of multiple organ dysfunction during the early phase of critical illness. Day 1 reflects the initial physiological derangement at ICU admission, whereas day 3 corresponds to the period when secondary brain injury and systemic inflammatory responses may lead to the development or worsening of organ dysfunction. Day 5 allows evaluation of the persistence or resolution of organ failure following initial resuscitation and intensive care management. Serial assessment at these predefined time points provides a more comprehensive evaluation of disease progression than a single measurement and may improve the prognostic performance of organ dysfunction scores (19–21).

Our findings confirm that serial measurements of organ dysfunction scores provide additional prognostic value beyond initial admission scores. Several authors have emphasized that evaluating trends in organ failure over the early ICU period better captures the evolving pathophysiology after TBI and improves outcome prediction (18). This temporal dimension allows clinicians to detect progressive organ dysfunction and identify high-risk patients who may benefit from

intensified monitoring and tailored supportive therapies.

Multivariate analysis in our study identified MODS at day 1, LODS at day 3, and LODS at day 5 as independent predictors of mortality, underscoring the relevance of dynamic organ dysfunction assessment. These results are consistent with prior evidence suggesting that early and sustained organ failure represents a significant contributor to adverse outcomes in critically ill TBI patients (18). Whereas initial neurological severity provides important information about primary brain injury, systemic scores capture the cumulative burden of secondary insults such as shock, hypoxia, sepsis, and metabolic dysfunction that often determine survival.

Clinically, incorporating both nonspecific ICU severity scores and organ dysfunction scales into routine TBI assessment can enhance prognostic precision. Such integration can support multidisciplinary decision-making regarding escalation of care, resource utilization, and goals of treatment. For instance, high APACHE II or SAPS II scores combined with increasing LODS or MODS trajectories may indicate a poor prognosis, warranting early palliative care involvement or discussion of withdrawal of aggressive treatment modalities (15). Conversely, patients with stable organ function scores over the first ICU week may have better recovery potential.

Nevertheless, our study has limitations. The sample size is modest and derived from a single tertiary center, potentially limiting external validity. Additionally, although nonspecific severity and organ dysfunction scores provide valuable prognostic information, these tools should be interpreted within the broader clinical context including neuroimaging, comorbidities, and complications such as intracranial hypertension (13). Another important limitation of this study is the small number of deaths (6 events), which may have limited the robustness of the multivariable logistic regression analysis.

Future research should pursue larger, multicenter cohorts to validate prognostic models that combine neurological and systemic variables, potentially enhanced by advanced machine learning techniques (18).

CONCLUSION

Our findings support the use of nonspecific severity scores (APACHE II, SAPS II) and serial organ dysfunction scores (SOFA, LODS, MODS) as effective predictors of ICU mortality in severe TBI. Dynamic assessment over the first week after injury offers superior discrimination compared with single-time-point measurements. Integrating these scoring systems into clinical practice could improve prognostication, optimize care strategies, and facilitate informed decision-making in the management of severe TBI.

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Fatal Refractory Hypokalemic Paralysis Secondary to Occupational Toluene Exposure: A Case Report

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Abstract

Toluene is an aromatic hydrocarbon widely encountered in occupational settings, particularly in carpentry, painting, and furniture manufacturing. Chronic inhalational exposure can cause acquired distal renal tubular acidosis (dRTA), leading to severe hypokalemia and potentially fatal hypokalemic paralysis. We report the case of a 42-year-old male carpenter with a ten-year history of unprotected daily exposure to organic solvents, who presented with acute flaccid quadriplegia and severe hypokalemia (1.0 mmol/L) in the context of hyperchloremic metabolic acidosis with normal anion gap and renal potassium wasting, consistent with dRTA. Alternative etiologies were systematically excluded. Despite intensive intravenous potassium and magnesium replacement, hypokalemia remained refractory, necessitating mechanical ventilation on day 3 for progressive respiratory failure. Sustained ventricular tachycardia on day 4 was treated with intravenous amiodarone. In the early hours of day 5, the patient suffered a cardiac arrest refractory to advanced cardiopulmonary resuscitation, and no return of spontaneous circulation was achieved. This case illustrates the potentially fatal course of toluene-associated hypokalemic paralysis and underscores the critical importance of occupational history in the diagnostic evaluation of unexplained hypokalemia and acute flaccid paralysis.

Keywords: Toluene; Distal Renal Tubular Acidosis; Hypokalemic Paralysis; Occupational Exposure; Ventricular Arrhythmia

INTRODUCTION

Toluene, an aromatic hydrocarbon widely used in industrial solvents, adhesives, and paints, is a well-documented cause of acquired distal renal tubular acidosis (dRTA). Exposure may occur in recreational settings through deliberate inhalation or in occupational environments, particularly in poorly ventilated workplaces. (1–3)

Chronic toluene exposure is associated with hyperchloremic metabolic acidosis, renal potassium wasting, and severe hypokalemia, which may precipitate acute flaccid paralysis. (4–6)

The underlying mechanism involves hepatic biotransformation of toluene into benzoic acid and subsequently hippuric acid, which impairs distal tubular hydrogen ion secretion by the H⁺-ATPase pump, resulting in urinary acidification failure and renal potassium depletion. (7,8)

Although most reported cases are reversible with appropriate electrolyte replacement, severe and potentially fatal cardiac complications have been described. (9)

We report a fatal case of refractory hypokalemic paralysis possibly related to chronic occupational toluene exposure, illustrating the diagnostic challenges and the life-threatening risk of

malignant ventricular arrhythmias in this condition.

CASE PRESENTATION

A 42-year-old male presented to the emergency department with a five-day history of progressive generalized weakness, preceded by several weeks of fatigue, muscle cramps, and increasing difficulty in ambulation. A detailed occupational history revealed that the patient had worked as a carpenter for approximately ten years, with chronic exposure to industrial solvents. He denied any history of medication use, toxic ingestion, or known past medical conditions. On physical examination, the patient was alert and oriented, with stable vital signs. Neurological assessment revealed severe flaccid quadriparesis with generalized areflexia, without sensory deficits, cranial nerve involvement, or sphincter dysfunction. Initial laboratory investigations demonstrated severe hypokalemia (1.0 mmol/L), hyperchloremic metabolic acidosis with a normal anion gap (9 mEq/L), preserved renal function, and hypomagnesemia. Urinalysis showed inappropriate renal potassium wasting (urine potassium: 17 mmol/L) with a urine pH of 5.5 (Table 1). Electrocardiography demonstrated classical hypokalemic changes, including flattened T waves, ST-segment depression, and prominent U waves (Figure 1). Cerebrospinal fluid analysis was normal, and electromyography showed no evidence of demyelinating or axonal neuropathy.

The metabolic profile, in the context of chronic occupational exposure to industrial solvents, strongly suggested toluene-induced distal renal tubular acidosis (dRTA). Urinary hippuric acid measurement was not performed due to assay unavailability.

The patient was transferred to the intensive care unit for continuous cardiac monitoring and correction of severe electrolyte disturbances. Intravenous potassium chloride was administered via a central venous catheter at 10–15 mmol/h, in combination with magnesium

sulfate infusion (1g/h). Despite ongoing replacement therapy, severe hypokalemia persisted, with serum potassium remaining below 1.5 mmol/L. On day 3, progressive respiratory muscle weakness led to acute ventilatory failure requiring endotracheal intubation and invasive mechanical ventilation. On day 4, the patient developed ventricular tachycardia, managed with intravenous amiodarone (300 mg over 30-60 minutes), followed by continuous infusion (900 mg over 24 hours). In the early hours of day 5, he suffered a cardiac arrest. Advanced life support was immediately initiated, including external chest compressions and repeated intravenous epinephrine (1 mg every 3-5 minutes). Despite 40 min of resuscitative efforts, return of spontaneous circulation was not achieved, and the patient was pronounced deceased.

Table 1. Patients' Laboratory findings on admission

Parameter	Value	Reference Range
Plasma		
Sodium (mmol/L)	139	136–145
Potassium (mmol/L)	1.0	3.5–5.0
Magnesium (mmol/L)	0.5	0.8–1.1
Chloride (mmol/L)	109	98–107
Bicarbonate (mmol/L)	12	22–29
Glucose (mmol/L)	5.6	3.9–6.1
Urea (mmol/L)	0.5	2.5–7.1
Creatinine (μmol/L)	84	62–115
Anion Gap (mEq/L)	9	8–12
Arterial pH	7.31	7.35–7.45
Urine		
Sodium (mmol/L)	15	—
Potassium (mmol/L)	17	—
pH	5.5	—

DISCUSSION

Toluene is a widely used aromatic hydrocarbon encountered in numerous industrial products. (1). Chronic inhalational exposure, particularly in poorly ventilated workplaces, may remain

unrecognized for prolonged periods before presenting with severe metabolic complications.(1–3)



Figure 1. Electrocardiogram showing hypokalemic changes (flattened T waves, ST-segment depression, and prominent U waves).

The renal toxicity of toluene is primarily mediated through its hepatic metabolism. Following absorption, toluene is oxidized to benzyl alcohol and subsequently converted to benzoic acid, which is conjugated to hippuric acid. The accumulation of hippurate anions impairs distal tubular hydrogen ion secretion, resulting in distal renal tubular acidosis. (7,8)

This disorder is characterized by hyperchloremic metabolic acidosis with a normal anion gap, impaired urinary acidification, and renal potassium wasting.(8)

Potassium depletion in this setting is multifactorial. Increased distal delivery of non-reabsorbable anions promotes renal potassium secretion, while secondary hyperaldosteronism further enhances urinary potassium losses. Concomitant hypomagnesemia, as observed in our patient, may aggravate potassium depletion and contribute to refractory hypokalemia by increasing renal potassium wasting.(10,11)

The resulting severe hypokalemia causes skeletal muscle membrane hyperpolarization, reducing neuromuscular excitability and leading to acute flaccid paralysis.(11)

In the present case, the patient's occupation as a carpenter with likely chronic inhalational exposure to toluene-containing solvents, combined with severe hypokalemia,

hyperchloremic normal anion gap metabolic acidosis, preserved renal function, and urinary potassium wasting, strongly supported the diagnosis of toluene-induced distal renal tubular acidosis (dRTA). However, because urinary hippuric acid measurement was unavailable, the diagnosis remained presumptive and alternative etiologies were carefully considered.

Acquired distal renal tubular acidosis may occur in association with autoimmune disorders, hypergammaglobulinemic states, and nephrotoxic drugs (1,7). In parallel, the differential diagnosis of hypokalemic paralysis is broad, including thyrotoxic periodic paralysis, gastrointestinal potassium losses, primary hyperaldosteronism, Bartter syndrome, and Gitelman syndrome (10,11). A systematic clinical and biochemical evaluation, encompassing acid–base status, urinary electrolytes, and renal function, is essential to narrow the diagnostic spectrum (10).

In this case, the absence of autoimmune features, endocrine abnormalities, renal dysfunction, metabolic alkalosis, and gastrointestinal potassium losses further supported toluene toxicity as the most likely diagnosis.

The acute flaccid quadriplegia with generalized areflexia initially raised concern for Guillain–Barré syndrome. However, normal cerebrospinal fluid analysis and the absence of demyelinating or axonal abnormalities on electroneuromyography effectively excluded this diagnosis. Similar presentations have been reported in several cases of toluene-induced hypokalemic paralysis (9,12,13).

According to international society guidelines, the management of severe and refractory hypokalemia is based on prompt and controlled potassium replacement, usually through continuous intravenous infusion under close ECG monitoring, together with magnesium supplementation to facilitate potassium correction and reduce the risk of arrhythmias (14).

In our case, this approach was applied using continuous intravenous potassium chloride (10–15 mmol/h via a central venous catheter) and intravenous magnesium sulfate, under continuous electrocardiographic monitoring.

Although aggressive electrolyte replacement and isotonic saline administration may theoretically influence hydro-electrolyte and acid–base balance, the severe hypokalemia, characteristic electrocardiographic abnormalities, and hyperchloremic metabolic acidosis were already present on admission, prior to any significant therapeutic intervention.

Therefore, the fatal outcome is more attributable to the severity of the underlying disease process rather than to iatrogenic factors.

Despite intensive treatment, serum potassium concentrations remained profoundly low, reflecting ongoing renal potassium losses secondary to persistent tubular dysfunction. The patient subsequently developed progressive respiratory muscle weakness requiring mechanical ventilation. Cardiac arrest occurred on day 5 and was managed immediately according to Advanced Life Support guidelines. (15) However, resuscitative efforts were unsuccessful, and the patient died. Similar fatal outcomes have been reported in the literature in severe cases of toluene intoxication. (5,6)

A major limitation of this report is the absence of direct toxicological confirmation. Urinary hippuric acid measurement, the standard biomarker of toluene exposure, was unavailable in our institution. Furthermore, no post-mortem toxicological investigation was performed. In resource-limited settings, diagnosis may therefore rely on the integration of occupational history, clinical presentation, and characteristic biochemical findings, an approach that has been accepted in comparable published reports. (6,9,13).

CONCLUSION

Toluene-induced distal renal tubular acidosis is a rare but potentially fatal . This case highlights

the diagnostic importance of systematically considering occupational toxic exposures in patients presenting with acute flaccid paralysis, hyperchloremic metabolic acidosis, and renal potassium wasting.

The diagnosis was established by clinical and biochemical exclusion of alternative etiologies, in the absence of direct toxicological confirmation. Clinicians should remain vigilant for the risk of malignant ventricular arrhythmias in severe refractory hypokalemia, and should consider the potential contribution of iatrogenic factors in the context of aggressive fluid and electrolyte therapy. Beyond individual patient management, such cases underscore the obligation to consider occupational disease declaration and workplace investigation to protect potentially co-exposed workers.

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

Informed consent: Informed consent was not obtained due to the patient's death. Patient anonymity has been strictly preserved, and no identifying information is included in this report.

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Severe upper airway obstruction and mediastinitis after accidental quaternary ammonium ingestion: highlighting the role of early parenteral nutrition

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Abstract

Quaternary ammonium compounds (QACs) are widely used disinfectants and surfactants. Poisoning following ingestion is rare but may threaten both airway and upper gastrointestinal integrity. We report a case of A 21-year-old woman with no prior medical history presented after accidental ingestion of a QAC-based disinfectant at work, with vomiting, hematemesis, hypersalivation, and progressive respiratory distress. Examination showed extensive oral mucosal necrosis and impending laryngeal edema requiring early intubation. Laboratory tests revealed leucocytosis, lymphopenia, hypocalcemia, prolonged prothrombin time, and elevated creatine kinase. Contrast-enhanced Computed Tomography (CT) demonstrated moderate esophagitis, mediastinitis, and gastritis with mild peritoneal effusion but no perforation. Treatment included proton pump inhibitors, corticosteroids, broad-spectrum antibiotics, and a total parenteral nutrition protocol ensuring nutritional intake during gastrointestinal rest. Laparoscopic exploration confirmed inflammatory peritoneal effusion without gastric perforation, and recovery was favorable. This case highlights the emergency medicine relevance of QAC ingestion, which may manifest as life-threatening airway compromise with mediastinitis and peritoneal effusion despite the absence of perforation, requiring rapid multidisciplinary management and tailored nutritional support.

Keywords : Caustic ingestion ; Mediastinitis ; Poisoning ; Quaternary ammonium; Nutrition

INTRODUCTION

Quaternary ammonium compounds (QACs) are cationic surfactants used in disinfectants, detergents, and personal care products, and are increasingly encountered in both domestic and occupational environments. Most reports of QAC toxicity describe inhalational or dermal exposure, while clinically significant ingestion remains rare and poorly characterized(1).

When ingested, QAC-based disinfectants behave as caustic agents and may induce liquefactive

necrosis of the oropharyngeal, esophageal, and gastric mucosa, with potential extension to the mediastinum and peritoneal cavity. Only a few case reports have described severe esophagitis, mediastinitis, and airway compromise after benzalkonium chloride or mixed QAC solutions (2–5).

We present an unusual case of accidental QAC ingestion in a young adult, complicated by severe upper airway obstruction and early mediastinitis

with intraperitoneal inflammatory effusion but without gastrointestinal perforation, and we discuss the diagnostic and therapeutic approach.

CASE PRESENTATION

A 21-year-old woman, working in a cleaning company, with no known medical, surgical, or psychiatric history, was brought to the emergency department after accidental oral ingestion of 75ml of an industrial disinfectant at her workplace. The ingested product was Bacticide Plus, a ready-to-use industrial disinfectant spray for non-porous surfaces, formulated with an alcohol base and benzalkonium chloride, with a declared active concentration of 0.1–0.2% benzalkonium chloride according to the manufacturer's datasheet. She had no history of caustic ingestion, substance misuse, or previous Ear, Nose and Throat (ENT) or gastrointestinal disease, and there was no suicidal intent.

Within a few hours after ingestion, the patient developed multiple episodes of vomiting, followed by moderate hematemesis, sore throat, odynophagia, and progressive dyspnea.

On arrival in the emergency department, initial assessment followed the ABCDE approach.

The patient presented with marked hypersalivation, halitosis, and extensive erosive and necrotic lesions of the oral cavity, while ENT examination revealed severe pharyngo-laryngeal mucosal necrosis with an imminent risk of laryngeal edema and upper airway obstruction. She also developed progressive dyspnea with an oxygen saturation of 86% on room air, tachypnea, and signs of respiratory distress, prompting early endotracheal intubation and mechanical ventilation to secure the airway and ensure adequate oxygenation. Hemodynamically, her heart rate was 110 bpm and blood pressure was 100/70 mmHg under crystalloid infusion, with no clinical evidence of shock, and fluid resuscitation was adjusted to maintain stability.

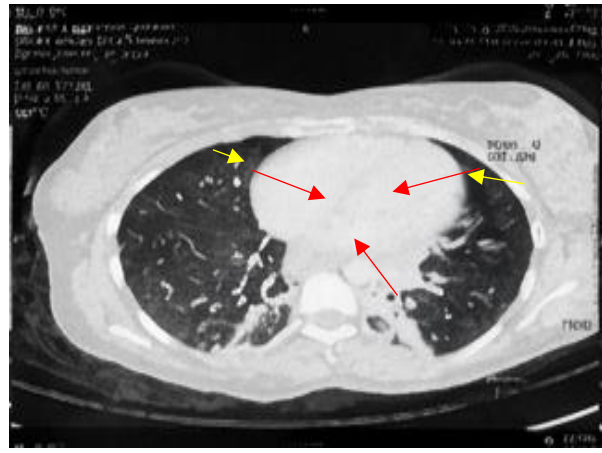
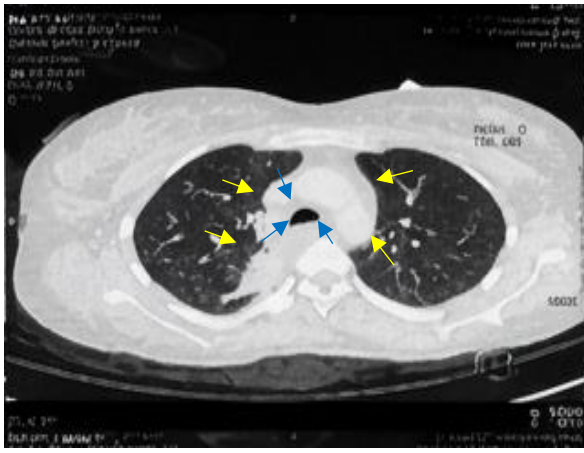
She was initially conscious but anxious, then became progressively drowsy, requiring close neurological monitoring for possible toxic or hypoxic encephalopathy. A complete examination found no cutaneous burns or subcutaneous emphysema, and attention focused on the upper aerodigestive tract and abdominal findings to guide further imaging and possible surgical exploration.

Overall, this clinical assessment prioritized airway protection and respiratory support while simultaneously addressing circulatory status, neurological surveillance, and the extent of caustic exposure, thereby informing subsequent CT imaging, pharmacologic therapy, and nutritional management.

Laboratory evaluation showed leukocytosis with lymphopenia, normal serum electrolytes and creatinine, normal C-reactive protein, prolonged prothrombin time at 51%, mild hypocalcemia at 2.08 mmol/L, and elevated creatine kinase at 312 U/L.

Contrast-enhanced thoracoabdominal CT demonstrated circumferential esophageal wall thickening compatible with moderate esophagitis, mediastinal fat stranding suggestive of mediastinitis, gastric wall thickening with focal mucosal enhancement defects, and a small volume of intraperitoneal effusion, without pneumomediastinum or free intraperitoneal air. CT was used as first-line imaging to assess depth and extension of injury, in line with caustic ingestion recommendations (Figure 1).

Upper endoscopy was deferred because of unstable airway conditions and the risk of worsening mucosal injury in this severely damaged upper tract. No alternative cause such as infectious mediastinitis or peptic perforation was suggested by clinical or imaging findings. Given the progressive clinical and radiological improvement, and after multidisciplinary discussion, no endoscopy was performed during the acute phase, and the patient was scheduled for



A: Upper thoracic CT slice showing esophagitis (blue) and mediastinitis (yellow)

B: Lower thoracic and upper abdominal CT slice showing caustic gastritis (red)

Figure 1. Contrast-enhanced thoracoabdominal CT showing esophagitis, mediastinitis, and gastritis following caustic quaternary ammonium ingestion

delayed endoscopic follow-up to detect late esophageal sequelae.

The patient was intubated early and mechanically ventilated because of progressive upper airway obstruction related to laryngeal edema and persistent hypoxemia. She received high-dose intravenous proton pump inhibitor (omeprazole 80 mg), systemic corticosteroids to reduce laryngeal edema, and broad-spectrum antibiotics (ceftriaxone and metronidazole) to cover mediastinitis and prevent secondary infection.

Because of severe odynophagia, extensive upper gastrointestinal mucosal injury, and the high risk of esophageal and gastric complications, oral and enteral feeding were initially contraindicated. Total parenteral nutrition (TPN) was started within the first 24 hours through a central venous catheter, using a standard three-in-one admixture providing approximately 25 kcal/kg/day and 1.2–1.5 g/kg/day of amino acids, with 20–30% of non-protein calories as lipids and the remainder as glucose. Micronutrients (electrolytes, vitamins, and trace elements) were added according to current critical care recommendations, and infusion was delivered over 24 hours using an infusion pump with strict aseptic precautions. Daily reassessment of weight, fluid balance, serum electrolytes, liver

and renal function, and capillary glucose allowed progressive adjustment of TPN composition and rate, with reduction of parenteral intake as soon as cautious enteral feeding became feasible.

Despite the absence of pneumomediastinum or free intraperitoneal air on CT, the combination of circumferential esophagitis, mediastinitis, gastric wall thickening with mucosal defects, and intraperitoneal effusion raised concern for occult transmural injury. In a multidisciplinary meeting involving intensivists, surgeons, and gastroenterologists, we considered that the risk of missed perforation or rapidly progressing necrosis outweighed the morbidity of a minimally invasive procedure, and diagnostic laparoscopy was therefore selected as a proactive strategy.

Laparoscopic exploration confirmed inflammatory peritoneal effusion without gastric perforation or transmural necrosis, and submucosal edema of the lesser curvature, which was managed by lavage and close monitoring (Figure 2, Figure 3).

ICU care focused on ventilatory support, fluid and electrolyte balance, analgesia, and prevention of nosocomial infections, following current principles of caustic ingestion management.

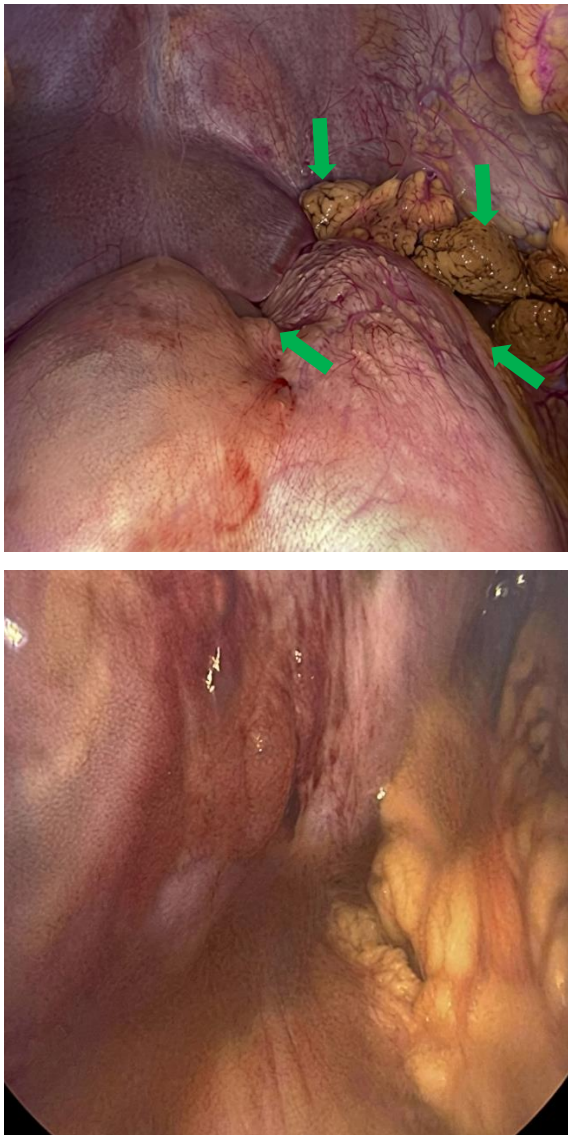


Figure 2. Laparoscopic view showing inflammatory intraperitoneal effusion without visible gastrointestinal leakage (green)

On postoperative day 1, the patient remained hemodynamically stable, with no new respiratory or abdominal complications. Follow-up CT showed regression of esophageal and gastric wall edema and partial improvement of mediastinal and abdominal fat stranding, without new collections or perforation.

Her respiratory status improved, allowing stepwise ventilator weaning, and nutritional support was progressively adapted from parenteral to enteral feeding.

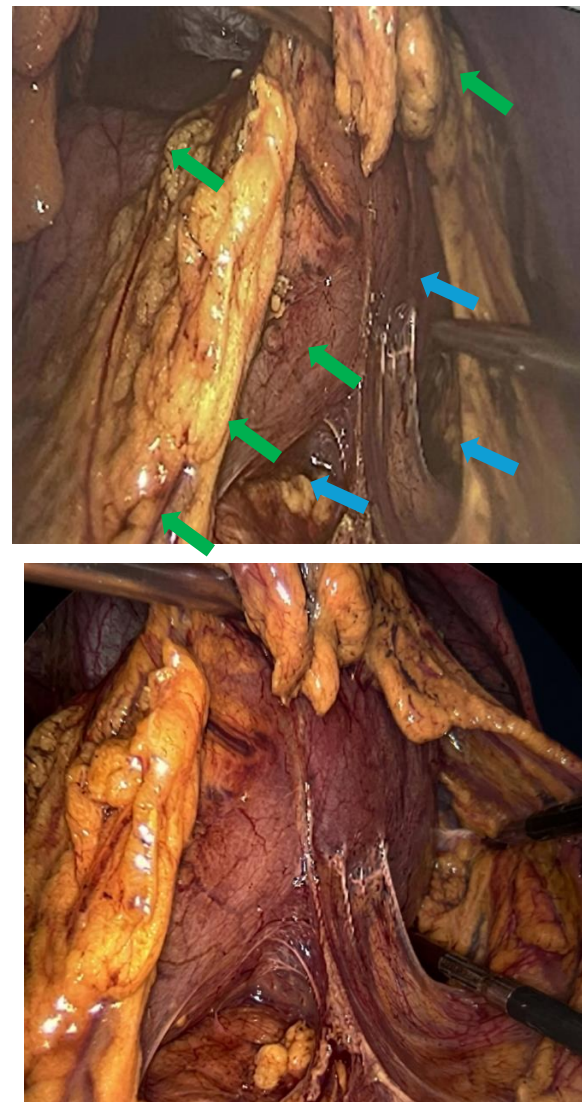


Figure 3. Laparoscopic exploration of the lesser sac confirming the absence of perforation of the posterior gastric wall and the posterior cavity of the omentum (orange)

Long-term endoscopic surveillance was planned to detect late esophageal sequelae.

At 3-month clinical follow-up, the patient reported normal swallowing function, with no dysphagia for solids or liquids and no odynophagia. Her body weight and nutritional markers remained stable, and she had resumed her usual occupational activities without functional limitations. A delayed upper endoscopy performed at month 6 showed no significant esophageal strictures, only mild residual mucosal irregularities in the distal

esophagus and antral region, requiring no endoscopic intervention.

DISCUSSION

This case illustrates an uncommon but severe presentation of QAC-based disinfectant ingestion, combining extensive oropharyngeal burns, high-grade risk of laryngeal edema, mediastinitis, and intraperitoneal inflammatory effusion without documented perforation. Most published QAC poisonings involve inhalation or dermal exposure, while clinically significant ingestion is rarely reported and often associated with benzalkonium chloride or mixed biocide solutions(1,2,4–6).

Several case reports have described benzalkonium chloride or mixed QAC ingestion with severe esophageal or airway injury across different age groups : Kumar et al. reported an adult with dilute benzalkonium chloride ingestion complicated by severe esophagitis and chemical pneumonitis, Civan et al. described corrosive esophagitis due to benzalkonium chloride in a neonate, Nițescu et al. detailed a pediatric case with a particularly severe course, Perera et al. reported laryngeal edema and metabolic acidosis after ingestion, and Spiller described a fatal ingestion of a 10% benzalkonium chloride solution (3,4,6,8).

Compared with these observations, our case is distinctive in combining high-grade risk of upper airway obstruction with CT-documented mediastinitis and intraperitoneal inflammatory effusion in the absence of radiological perforation. Also, in highlighting the role of early laparoscopic exploration and structured nutritional support in an emergency setting, with early mediastinal and peritoneal involvement suggesting deep mucosal and submucosal necrosis with inflammatory spread rather than open transmural rupture and raising questions about thresholds for surgical exploration when CT findings are equivocal, as also discussed in caustic esophagogastritis with mediastinitis managed conservatively (6).

In our patient, the estimated ingested volume of around 75 ml is consistent with severe caustic injury, as larger volumes of QAC-based disinfectants are more likely to produce deep mucosal damage and systemic inflammatory response. Although precise dose–response relationships for benzalkonium chloride ingestion are not well established, this quantity clearly exceeds incidental exposure and supports the severity of the clinical course.

Airway compromise is a major determinant of prognosis in caustic ingestions. In our patient, hypersalivation, extensive oral necrosis, and dyspnea were early warnings of impending airway obstruction, justifying prompt intubation before complete diagnostic workup. This decision is consistent with recommendations that emphasize airway and hemodynamic stabilization as the first priorities in caustic injuries(6,8).

In emergency practice, a systematic ABCDE approach is crucial in caustic ingestions, as it ensures rapid identification and treatment of life-threatening airway and breathing compromise before secondary diagnostic procedures. In our patient, early recognition of airway obstruction risk at the A and B steps led to prompt intubation and ventilation, while simultaneous evaluation of circulation, neurological status, and overall exposure guided fluid management, monitoring, and the decision to proceed to CT imaging and laparoscopy. Emphasizing ABCDE in such toxicological emergencies may therefore improve time-critical decisions and reduce delays in securing the airway and assessing the extent of injury (9).

CT now plays a central role in evaluating caustic injuries, as it can detect wall thickening, fat stranding, and free air or fluid, and help stratify the risk of perforation and guide surgical decisions. In our case, CT findings prompted laparoscopic exploration, which confirmed inflammation without perforation and avoided unnecessary resection (6,8).

In fact, in the absence of radiologically proven perforation, conservative management could have been considered, as described in other series of caustic esophagogastritis with mediastinitis. However, in our case, the coexistence of mediastinal and intraperitoneal inflammation with focal gastric enhancement defects led the team to favor early surgical exploration to avoid delayed recognition of perforation, while still aiming to preserve the stomach and esophagus whenever possible. This decision illustrates the delicate balance between active surgical assessment and close conservative monitoring in severe caustic injuries, and supports an individualized, CT-guided approach.

Management of QAC ingestion is mainly supportive, as no specific antidote exists. Core measures include airway protection, acid suppression, pain control, infection prevention, and early nutritional support. Systemic corticosteroids remain controversial for esophageal injury but may be justified for severe laryngeal edema threatening airway patency, as in this case (1,4,7,9).

In this context, early TPN was used as a temporary bridge to cover energy and protein needs while keeping the upper gastrointestinal tract at rest, in line with recommendations that reserve parenteral nutrition for situations where enteral nutrition is contraindicated or impossible. The chosen regimen, targeting around 25 kcal/kg/day and 1.2–1.5 g/kg/day of amino acids with a balanced lipid–glucose ratio, is consistent with current expert guidelines for critically ill patients and aimed at limiting both catabolism and metabolic complications (11).

CONCLUSION

This case shows that accidental ingestion of quaternary ammonium–based disinfectant can cause severe caustic injury with combined upper airway obstruction, mediastinitis, and significant nutritional vulnerability. Early airway protection, rapid CT-based assessment, and timely surgical evaluation were essential to rule out perforation

and to guide a conservative but closely monitored strategy. In this context of extensive upper digestive tract damage and odynophagia, early, carefully supervised parenteral nutrition played a key supportive role by covering energy and protein needs while allowing functional rest of the injured mucosa. Overall, this observation underlines the importance of a multidisciplinary approach integrating toxicology, emergency medicine, intensive care, surgery, ENT, and nutrition to reduce morbidity and improve short-term outcomes after severe caustic ingestions.

Informed consent

Informed consent was obtained from the patient for publication of this case report and its anonymized images.

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A new electrocardiographic pattern suggestive of occlusion myocardial infarction: a report of two cases.

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Abstract

Background: Classical teaching assumes that the location of ST-segment elevation (STE) on the electrocardiogram (ECG) reflects the site of myocardial infarction (MI), and current guidelines require STE in two contiguous leads to diagnose ST-elevation MI (STEMI). This framework can miss high-risk occlusive infarctions presenting with atypical, non-contiguous STE.

Methods: We retrospectively describe two patients presenting with acute coronary syndrome whose initial 12-lead ECG displayed the Aslanger pattern: isolated STE in lead III, ST-segment depression in leads V4-V6, and STE in V1 greater than in V2.

Results: Both patients were diagnosed with a STEMI-equivalent Aslanger pattern and underwent urgent coronary angiography. The first, with known multivessel disease, had critical left anterior descending (LAD) artery stenosis; the second presented in cardiogenic shock with an occlusive thrombus in the right coronary artery. Both were successfully treated with percutaneous coronary intervention.

Conclusion: The Aslanger pattern is a high-risk STEMI-equivalent that can be missed under conventional STE criteria. Our cases, including an atypical LAD culprit lesion, support incorporating this pattern into routine ECG interpretation and emergency training to enable timely reperfusion.

Keywords: Aslanger pattern; STEMI-equivalent; acute coronary occlusion; electrocardiogram.

INTRODUCTION

For more than a century, the electrocardiogram (ECG) has been the most accessible clinical tool for diagnosing and localizing acute myocardial infarction (MI). Classical teaching assumes the infarct lies beneath the leads showing ST-segment elevation (STE), and international guidelines accordingly require STE in two contiguous leads of the same localization group (anterior, lateral, or inferior) to diagnose and localize STEMI (1). However, this framework is more intuitive than evidence-based, and recent studies show that the leads demonstrating STE do not reliably indicate the location of the infarcted myocardium (2,3). Instinctively assigning lead groups to specific infarct locations may misclassify MI location (4) and often requires

unsupported explanations, such as a single infarct-related artery supplying two coronary territories (5), to account for atypical STE patterns.

Moreover, this requirement reduces STEMI sensitivity in certain configurations (6,7) and may obscure novel ECG patterns that nonetheless signal acute coronary occlusion requiring emergent reperfusion.

We report two cases presenting with acute coronary syndrome whose initial 12-lead electrocardiogram (ECG) met the diagnostic triad described by Aslanger et al. (8): isolated ST-segment elevation (STE) in lead III, ST-segment depression in leads V4-V6, and STE in V1 greater than in V2. Clinical presentation, ECG tracings, laboratory results, and coronary

angiography findings were extracted from the patients' medical records. Informed consent was obtained for the anonymized publication of clinical data and images.

CASE PRESENTATION

Case 1: A 71-year-old man with a history of hypertension, heart failure, and a prior NSTEMI two months earlier due to critical triple-vessel disease (including distal left main stenosis) for which he had declined percutaneous coronary intervention (PCI), presented to the emergency department with rest angina and acute dyspnoea. On admission, the patient was assessed following the ABCDE approach. A (Airway): patent, able to speak in short sentences. B (Breathing): acute respiratory distress with bilateral pulmonary crackles; respiratory rate 20 breaths/min) and SpO₂ 96% on room air. C (Circulation): markedly hypertensive (220/110 mmHg) and tachycardic (110 bpm), with clinical signs of acute pulmonary oedema. D (Disability): Glasgow Coma Scale 15/15; capillary glucose 1 g/L, no focal neurological deficit. E (Exposure): temperature 37 °C; no other relevant findings on complete exposure.

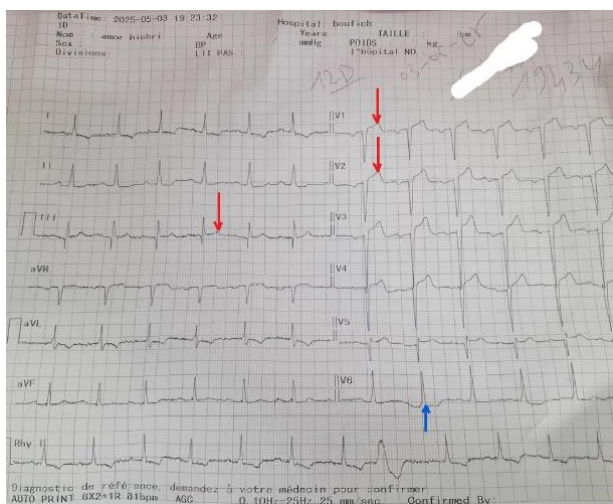


Figure 1: The first case's prehospital ECG.

↓ ST-segment elevation in lead III, V1, and V2 (V1 > V2).
↑ ST-segment depression at the J point in lead V6.

The initial ECG demonstrated an isolated ST-segment elevation in lead III, ST-segment

elevation in V1 greater than that in V2, and ST-segment depression in leads V4-V6, which is a triad characteristic of the Aslanger pattern. The high-sensitivity troponin I level was elevated to 2000 ng/L. Chest radiography confirmed pulmonary oedema and cardiomegaly (Figure 1). The patient was diagnosed with ST-elevation myocardial infarction (STEMI) equivalent due to the Aslanger pattern. The patient was stabilized with non-invasive ventilation, intravenous diuretics, and nitrates. Subsequent coronary angiography confirmed severe multivessel disease, including critical distal left main and proximal left anterior descending (LAD) artery stenoses. The patient successfully underwent PCI with drug-eluting stent implantation into the LAD (Figure 2).

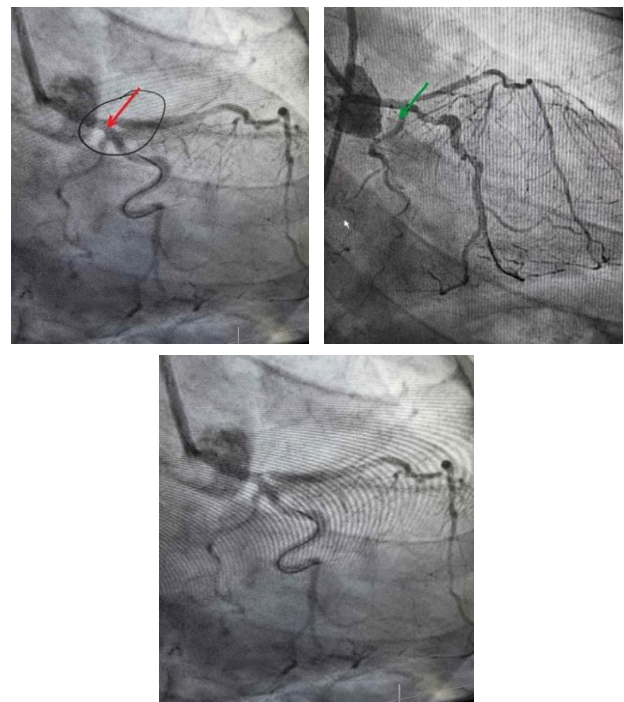


Figure 2: Coronary Angiography of the Left Anterior Descending Artery

↙ site of the acute LAD occlusion (pre-PCI). ↘ restored antegrade flow after PCI, showing resolution of the occlusion.

Antithrombotic loading doses: aspirin 300 mg, clopidogrel 600 mg, and anticoagulation with unfractionated heparin (70–100 IU/kg IV bolus) were administered. Reperfusion timing: door-to-ECG 10 min and door-to-reperfusion (door-to-

balloon) 40 min. Clinical course and outcome: short-term evolution was favourable with haemodynamic and respiratory stabilization; the patient was discharged on day 5 in stable condition.

Case 2: A 62-year-old woman with a history of heart failure and chronic respiratory disease was admitted to the primary emergency department with severe respiratory distress. On admission, she was assessed following the ABCDE approach. A (Airway): patent. B (Breathing): severe respiratory distress with tachypnoea (30 breaths/min), critical hypoxaemia (SpO₂ 67% on room air) and bilateral pulmonary crackles. C (Circulation): hypotension (BP 90/50 mmHg) and tachycardia (HR 110 bpm) with peripheral oedema, consistent with cardiogenic shock. D (Disability): Glasgow Coma Scale 14/15; capillary glucose 0.9 g/L. E (Exposure): temperature 37 °C; no other relevant findings. The initial ECG showed ST-segment elevation in leads III and V1 with complete right bundle branch block (Figure 3).

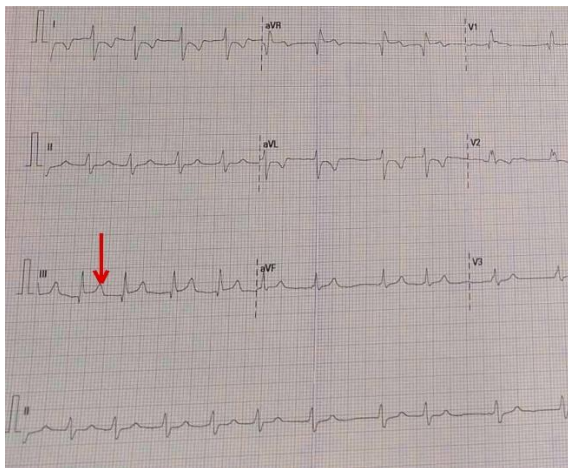


Figure 3: The second case's prehospital ECG.

The patient was managed for cardiogenic shock secondary to suspected acute coronary occlusion. She was placed in a semi-recumbent position and started on Continuous Positive Airway Pressure (CPAP) for respiratory support. The patient was stabilized and transferred to a tertiary hospital for further critical care and urgent coronary

angiography. Haemodynamic management: Given the cardiogenic shock, continuous intravenous noradrenaline (4 mg/h) combined with dobutamine (5 µg/kg/min) was initiated and maintained for 72 h, with dose adjustments according to haemodynamic response and end-organ perfusion; Antithrombotic loading doses: aspirin 300 mg, clopidogrel 600 mg and anticoagulation with unfractionated heparin (70–100 IU/kg IV bolus). Reperfusion timing: door-to-ECG 8 min and door-to-reperfusion 60 min. Clinical course and outcome: after PCI with stent implantation in the right coronary artery, the short-term evolution was favourable, and the patient was discharged on day 6.

This case underscores the significance of the Aslanger pattern as a critical STEMI-equivalent that can manifest with profound haemodynamic instability. Its recognition is essential for triggering urgent reperfusion strategies. Subsequent coronary angiography confirmed the diagnosis, revealing an occlusive thrombus in the right coronary artery, which was successfully treated with stent implantation. This case highlights that this pattern, despite its subtlety, signifies a high-risk occlusive myocardial infarction that can be misdiagnosed because of the absence of widespread ST-segment elevation.

DISCUSSION

The findings from our case series and the original study by Aslanger et al. collectively challenge the long-standing paradigm of electrocardiographic interpretation of acute myocardial infarction. For decades, the diagnosis of STEMI has been predicated on an intuitive yet incompletely evidence-based framework that requires ST-segment elevation (STE) in two contiguous leads, with the infarct location assumed to reside beneath those leads (3,8). However, recent evidence has confirmed that the location of STE does not reliably indicate the location of the infarcted myocardium, and rigid adherence to contiguous lead criteria can result in the

misclassification of MI location and a failure to recognize high-risk occlusive patterns (3,4). The Aslanger pattern serves as a critical example of this limitation. This demonstrates that STE in a single inferior lead (DIII) can possess profound clinical value, signifying an acute atherothrombotic event that frequently results in an occlusive MI (8). This atypical pattern, characterized by non-contiguous STE, arises when the frontal ST vector is oriented towards the edges of the standard 12-lead coverage. The underlying pathophysiology is theorized to be a summation of vectors: the ST vector of the inferior MI, directed inferiorly and rightwards, combined with the ST vector of concomitant subendocardial ischaemia from critical multivessel disease, which is characteristically directed towards lead aVR. The resultant average ST vector is directed rightward, projecting into the positive poles of leads III and aVR, while projecting into the negative poles of leads I and II, and appearing nearly isoelectric in aVF (8). This elegant vectorial explanation accounts for the full ECG picture: STE in III and aVR, ST depression in I and II, and ST depression in the lateral chest leads (V4-V6) as the vector points away from them.

This brings us to a pivotal question raised by the subsequent commentary: Should STE in aVR be formally incorporated into the pattern's definition? (9) While the original diagnostic triad (STE in DIII, STD in V4-V6, STE in V1 > V2) is highly specific, the pathophysiological model and example tracings consistently show accompanying STE in aVR. Therefore, while the triad remains the diagnostic cornerstone, the presence of STE in aVR should be recognized as a common and supportive feature that reinforces the vectorial diagnosis and may aid in the pattern recognition.

Clinically, the implications of missing this pattern are significant. The data of Aslanger et al. indicate that 13.3% of inferior MIs may present with this pattern and be incorrectly labelled as

NSTEMI, thereby depriving them of emergent revascularization therapy (8). These patients are not low-risk; they have a high frequency of multivessel disease, often involving the circumflex artery, and exhibit increased short- and long-term mortality risk comparable to patients with classical inferior STEMI (8). Therefore, an immediate invasive strategy is crucial to decrease morbidity and mortality in this patient group (8,9). Therefore, the Aslanger pattern is a high-risk STEMI-equivalent that underscores the limitations of the traditional ECG interpretation. Its recognition is paramount for triggering urgent reperfusion therapy. By educating clinicians on this pattern and its vectorial basis, rapid diagnosis in emergency settings can be improved, ultimately reducing major adverse cardiovascular events through appropriate and timely treatment. In contrast to the literature, which most frequently implicates the right coronary or circumflex arteries, our first case uniquely identified the left anterior descending (LAD) artery as the culprit vessel. This finding challenges the conventional anatomical association of this pattern and opens the door for a new discussion regarding its potential variability.

Our two cases directly illustrate these principles. In Case 1, recognition of the Aslanger pattern prompted urgent angiography that revealed critical distal left main and proximal LAD disease, enabling life-saving PCI in a patient who had previously declined revascularization, and showing that the culprit vessel is not invariably the RCA or circumflex. In Case 2, the same pattern identified an occlusive RCA thrombus in a patient presenting in cardiogenic shock, underscoring that the pattern can herald haemodynamic collapse and must trigger immediate reperfusion. Together, the cases support our central message that the Aslanger pattern should be managed as a STEMI-equivalent regardless of the culprit artery or the initial haemodynamic status.

The LAD culprit lesion observed in Case 1 warrants a mechanistic explanation. The Aslanger pattern reflects the summation of an inferior injury vector with a vector of concomitant subendocardial ischaemia from multivessel disease. In our patient, several non-exclusive mechanisms may account for an LAD culprit producing this pattern: (i) a long, wrap-around (type III) LAD supplying the inferior wall, which can generate inferior ST changes when occluded distally (5); (ii) proximal LAD stenosis superimposed on critical distal left main and triple-vessel disease, so that diffuse subendocardial ischaemia orients the average ST vector rightward toward leads III and aVR (8); and (iii) mid-anterior or diagonal involvement, known to produce ST-elevation in non-contiguous leads (6,7).

CONCLUSION

The Aslanger pattern is a significant advance in the electrocardiographic diagnosis of acute MI, demonstrating that high-risk occlusive coronary disease can present without the classic requirement of contiguous ST-segment elevation. Its hallmark triad—STE in lead III, STD in V4-V6, and STE greater in V1 than V2—identifies acute inferior MI, almost always in the setting of multivessel disease and concomitant critical stenosis. Our case series confirms the high clinical stakes of this pattern, with infarct sizes and mortality rates rivalling classical inferior STEMI, while the LAD culprit lesion in our first case suggests its underlying anatomy may be more variable than initially described. Failure to recognize this pattern risks misclassification as NSTEMI and delayed revascularization.

We therefore advocate integrating the Aslanger pattern into emergency medicine and cardiology training, and encourage future guidelines to formally adopt it as a STEMI-equivalent to ensure high-risk patients receive timely reperfusion.

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A Rare Case of Chest Wall Osteolipoma Presenting as a Paravertebral Mass

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Abstract

Osteolipoma is an extremely rare histological variant of conventional lipoma. While lipomas are the most common soft tissue tumors in adults, the occurrence of an osteolipoma in the chest wall is exceedingly uncommon and presents unique diagnostic challenges.

We report the case of a 62-year-old male patient who presented with a progressively enlarging right dorsal paravertebral mass over a three-year period. Computed tomography and magnetic resonance imaging identified a well-circumscribed, heterogeneous fatty mass containing significant ossified components, located deep to the paraspinal muscles without rib or vertebral invasion. The patient underwent a complete en-bloc surgical excision without preoperative biopsy. Histopathological examination confirmed the diagnosis of a benign osteolipoma. After a 12-month follow-up, no recurrence or complications were observed.

Although rare, a thorough radiological and pathological correlation is essential to differentiate this benign entity from more aggressive ossifying neoplasms, such as liposarcoma or myositis ossificans. Surgical excision remains the treatment of choice.

Keywords : Osteolipoma ; Lipoma ; Chest Wall ; Rare Diseases

INTRODUCTION

Lipomas are the most common benign soft tissue neoplasms in adults(1). While usually composed of mature adipose tissue, they can rarely incorporate other mesenchymal elements(2). Osteolipoma, or ossifying lipoma, is an extremely rare histological variant characterized by the presence of mature lamellar bone within the tumor, accounting for less than 1% of all lipomatous lesions(3).

The occurrence of osteolipoma in the chest wall is exceedingly uncommon, often posing diagnostic challenges(2). Its pathogenesis is attributed either to osseous metaplasia of mesenchymal cells within a pre-existing lipoma or to the direct differentiation of multipotent

fibroblasts into osteoblasts(4). Due to its radiodensity, it can mimic malignant ossifying neoplasms such as extraskeletal osteosarcoma or well-differentiated liposarcoma(5).

This report describes a rare case of a large chest wall osteolipoma in a 62-year-old male, emphasizing the role of radiological and pathological correlation in achieving an accurate diagnosis.

CASE REPORT

A 62-year-old male patient presented to our department with a slow-growing, painless mass located in the right dorsal paravertebral region. The lesion had been progressively enlarging over the past three years, causing local discomfort but

no neurological symptoms. There was no history of prior trauma, weight loss, or constitutional symptoms.

Physical examination revealed a voluminous, firm, and non-tender mass measuring approximately 12 x 6 cm. The lesion was fixed to the underlying posterior chest wall at the T7–T9 vertebral levels. The overlying skin appeared normal, with no signs of inflammation, ulceration, or dilated veins. Neurological and respiratory examinations were unremarkable.

A chest computed tomography (CT) scan was performed, identifying a well-circumscribed, heterogeneous mass (3.3 x 5.8 x 10.7 cm) characterized by low-attenuation fat density (-80 to -100 HU) interspersed with significant ossified components (Figure 1) and showing no enhancement after contrast injection.

The lesion was located deep to the paraspinal muscles, abutting the adjacent ribs and vertebral bodies without signs of cortical erosion or invasion. Magnetic resonance imaging (MRI) further characterized the lesion, showing high signal intensity on both T1- and T2-weighted sequences, consistent with mature adipose tissue (Figure 2). The FAT SAT sequence showed heterogeneous signal suppression. Irregular thick septa and enhanced nodules were noted following dynamic gadolinium injection. The patient underwent surgical management under general anesthesia. An elective longitudinal incision was made over the mass, allowing for an en-bloc excision without preoperative biopsy. Intraoperatively, the tumor was found to be well-encapsulated, with no continuity or adherence to the adjacent bony structures or musculature (Figure 3). Due to the significant residual cavity in the paravertebral area, a Redon drain was placed to prevent seroma formation.

Gross pathological examination of the specimen revealed an encapsulated mass with a yellow, fatty cut surface containing gritty, hard calcified areas.

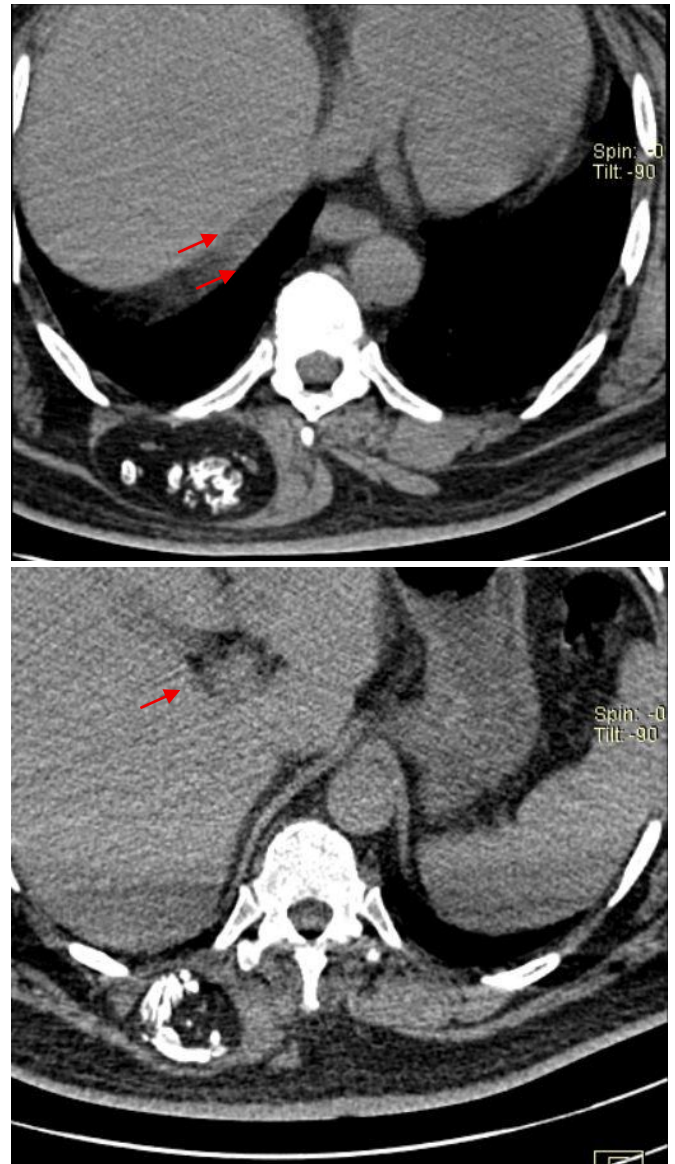


Figure 1: A CT scan showing a well-circumscribed, heterogeneous mass characterized by low-attenuation fat density interspersed with significant ossified components (arrows)

Microscopic analysis showed mature adipocytes interspersed with lamellar trabecular bone and occasional hematopoietic marrow. No cytologic atypia, mitotic activity, or necrosis were identified. Cyclin-Dependent Kinase 4 (CDK4) expression was negative. These findings confirmed the diagnosis of a benign chest wall osteolipoma.

At the 12-month follow-up, the patient remained asymptomatic with no clinical evidence of recurrence.

The postoperative course was uneventful; the patient was discharged on the first postoperative day, and the drain was removed 10 days later.

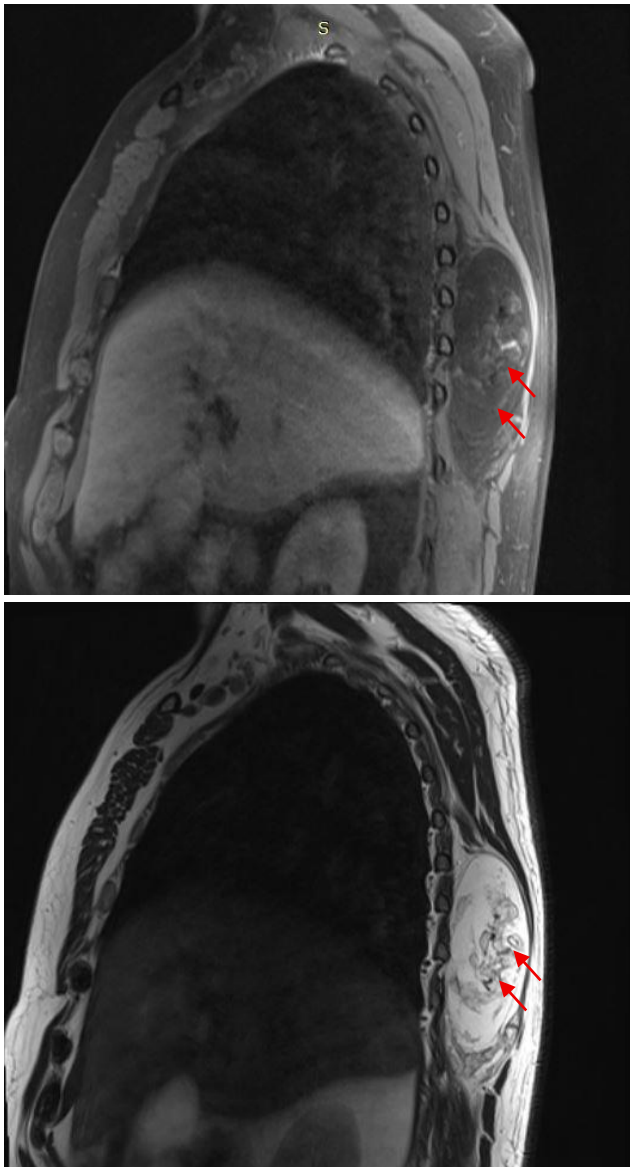


Figure 2: Magnetic resonance imaging characterizing the lesion, showing high signal intensity on both T1- and T2-weighted sequences with multiple thickened and nodular septa (arrows)



Figure 3: specimen after complete en-bloc resection

DISCUSSION

Osteolipoma is a rare histological variant of conventional lipoma, representing less than 1% of all lipomatous tumors(3). While lipomas are common soft tissue neoplasms, the presence of mature lamellar bone within the fatty matrix (as seen in our 62-year-old patient) distinguishes osteolipoma as a unique clinical and pathological entity(2). Although these lesions can occur in various anatomical sites, their manifestation in the chest wall is particularly rare and requires careful differentiation from other ossifying soft tissue masses(2).

The pathogenesis of osteolipoma remains a subject of ongoing discussion. Two main theories have been proposed in the literature. The "metaplastic theory" suggests that mesenchymal cells within a pre-existing lipoma undergo osseous metaplasia, often triggered by chronic mechanical stress, trauma, or local ischemia(4). Alternatively, the "fibroblast differentiation theory" posits that multipotent fibroblasts in the tumor tissue directly differentiate into osteoblasts(1). In our case, the three-year history of a progressively enlarging mass in a paravertebral location (an area subject to movement) could support the theory of

metaplastic change, although no specific trauma was reported.

Radiological evaluation is crucial for the preoperative assessment of chest wall osteolipomas. CT scans typically reveal a well-circumscribed mass with low-attenuation fat density containing irregular, mature bone components, as observed in our patient(2). MRI is particularly effective in identifying the fatty nature of the tumor through high signal intensity on T1- and T2-weighted sequences, while also highlighting the internal architecture and relationship with adjacent structures(2). However, the presence of ossification can complicate the radiological diagnosis, mimicking more aggressive lesions such as extraskeletal osteosarcoma, myositis ossificans, or well-differentiated liposarcoma(6).

The definitive diagnosis of osteolipoma is established through histopathological examination. The hallmark of this tumor is the presence of mature lamellar trabecular bone within a benign adipocytic neoplasm(2). The absence of cytologic atypia, mitotic activity, and lipoblasts is essential to rule out malignancy, particularly atypical lipomatous tumors or liposarcomas(7). In our case, the microscopic presence of hematopoietic marrow within the bone trabeculae further confirmed the benign, mature nature of the ossification.

In the management of atypical chest wall masses, a preoperative core needle biopsy is typically indicated to rule out malignancy. In our case, an upfront en-bloc surgical excision was performed without a prior biopsy for two main reasons. First, the lesion was well-circumscribed and lacked radiologic signs of local invasion or rib destruction, strongly suggesting a resectable process. Second, due to the highly heterogeneous composition of the mass (mature fat interspersed with lamellar bone), a core needle biopsy carried a high risk of sampling error, potentially yielding false-negative results (8). Furthermore, because complete en-bloc excision remains the definitive

curative treatment for both benign osteolipomas and low-grade liposarcomas, immediate resection was deemed the most definitive, cost-effective diagnostic and therapeutic strategy for this patient (9).

Surgical management via complete en-bloc excision remains the gold standard treatment for chest wall osteolipoma(3). This approach is generally curative. Recurrence appears to be rare after complete excision (10). However, long-term data are limited. In this case, the successful surgical outcome and the absence of recurrence after 12 months of follow-up align with the known clinical behavior of this rare tumor.

CONCLUSION

Chest wall paravertebral osteolipoma is a rare benign tumor that may clinically and radiologically mimic malignancy. Accurate diagnosis relies on the combination of imaging characteristics and definitive histopathological analysis. Surgical excision is curative and outcomes are excellent with minimal risk of recurrence. Awareness of this entity is important to guide appropriate management.

Conflict of Interest

The authors declare no conflict of interest associated with this publication.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Author Contributions

All authors have contributed to the clinical management, data collection, and the drafting of the manuscript. All authors have read and approved the final version of the manuscript.

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