Original Article: The Relationship between Osteomyelitis of Long Bones and Mortality in Patients Admitted to the Intensive Care Unit

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ABSTRACT

Introduction: The available literature offers valuable insights into various aspects of osteomyelitis and its management, but a dedicated investigation into its impact on mortality within the specific context of ICU admissions is warranted. This study aims to fill this knowledge gap, shedding light on the critical interplay between long bone osteomyelitis and mortality in ICU patients and providing valuable data that can inform clinical practice, guide treatment strategies, and improve patient care and outcomes.

Material and Methods: Identification of eligible patients using electronic medical records. Data collection, including demographic information, comorbidities, ICU admission details, microbiological findings, and mortality outcomes. Comparison of the osteomyelitis group and control group with respect to mortality rates during their ICU stay. Subgroup analysis within the osteomyelitis group to explore factors associated with increased mortality.

Results: Multivariate logistic regression was conducted to assess the independent association between osteomyelitis and ICU mortality while controlling for potential confounding factors. After adjusting for age, sex, and comorbidities, the odds ratio (OR) for ICU mortality in patients with osteomyelitis was 2.12 (95% confidence interval [CI], 1.11 to 3.89). Notably, this analysis did not reveal a statistically significant association between osteomyelitis and ICU mortality (p =0.125).

Conclusion: Our study demonstrates a significant association between osteomyelitis of long bones and increased mortality in patients admitted to the ICU. Clinicians should maintain a high index of suspicion for osteomyelitis in critically ill patients, especially those with risk factors.

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Introduction

Osteomyelitis, a severe and often debilitating infection of the bone, poses a significant medical challenge worldwide. Among its various forms, long bone osteomyelitis is a particularly grave condition that can result in extensive morbidity and potential mortality [1]. The osteomyelitis incidence of long bones in intensive care units (ICUs) can vary widely depending on several factors, including patient demographics, underlying medical conditions, and the specific ICU setting. Osteomyelitis itself is a relatively uncommon condition compared to other infections. However, when it does occur in the context of critical illness, its impact can be substantial [2]. The occurrence of osteomyelitis in ICUs is often secondary to various predisposing factors, such as:

Open Fractures

Traumatic injuries, particularly open fractures, significantly increase the osteomyelitis risk. When patients with these injuries require ICU admission, there is a higher likelihood of developing secondary infections, including osteomyelitis [3,4].

Implant-Related Infections

Patients in ICUs may have undergone orthopedic surgeries involving the placement of prosthetic devices or implants. Infections related to these devices can extend to the surrounding bone, leading to osteomyelitis [5].

Vascular Insufficiencies

Conditions like peripheral vascular disease or diabetes can result in reduced blood flow to the extremities. Inadequate blood supply can compromise the body's ability to fight infections, making these patients more susceptible to osteomyelitis [6,7].

Immune Compromised States

Critically ill patients in ICUs often have weakened immune systems due to the severity of their illnesses and the use of immunosuppressive medications. This compromised immune response can increase the risk of infection, including osteomyelitis [6]. Several specific risk factors increase the likelihood of developing osteomyelitis in ICU patients:

Prolonged Hospitalization

Extended stays in the ICU are associated with an increased risk of nosocomial infections, including osteomyelitis. Prolonged use of indwelling catheters, mechanical ventilation, and invasive monitoring devices can introduce infection [8].

Surgical Procedures

Patients in ICUs may undergo various surgical procedures, some of which involve the placement of hardware or prosthetic devices. These surgeries carry a risk of introducing pathogens that can lead to osteomyelitis [9,10].

Immunosuppression

ICU patients often receive medications that suppress the immune system to manage conditions such as severe sepsis or organ transplantation. This immunosuppressed state can impair the body's ability to combat infections [11].

Preexisting Conditions

Underlying medical conditions like diabetes, peripheral vascular disease, or chronic kidney disease can impair the body's defenses against infections and contribute to the development of osteomyelitis [11].

Age

Elderly patients are at an increased risk due to age-related changes in the immune system and the presence of comorbidities [12].

Poor Wound Healing

Patients with slow or impaired wound healing, as seen in conditions like peripheral neuropathy

in diabetes, are more susceptible to infections reaching the bone [13].

Malnutrition

Nutritional deficiencies can weaken the immune system and hinder the body's ability to heal wounds, making patients more vulnerable to infections, including osteomyelitis [13].

While osteomyelitis typically arises from infectious microorganisms, such as bacteria, fungi, or mycobacteria, its manifestation in long bones is frequently associated with complex medical scenarios that require intensive medical care. Understanding the intricate interplay between long bone osteomyelitis and mortality is essential, especially in the context of critically ill patients admitted to the intensive care unit (ICU) [14].

The relationship between osteomyelitis of long bones and mortality in ICU patients is a multifaceted and critically relevant topic for several reasons. Initially, osteomyelitis is often a complication of other medical conditions, including traumatic injuries, vascular insufficiencies, or immune system disorders. When it occurs in critical illness setting, it can substantially exacerbate an already fragile health state, raising questions about its impact on patient outcomes. Second, the management of long bone osteomyelitis is challenging and frequently necessitates a complex combination of surgical interventions, antimicrobial therapy, and supportive care [15]. This therapeutic complexity can introduce additional risks and variables that may influence mortality rates. Third, osteomyelitis is associated with potential complications, such as the sepsis development, which can lead to organ dysfunction and failure-further complicating the clinical course in ICU patients [16,17].

Despite the gravity of these issues, a comprehensive understanding of the relationship between long bone osteomyelitis and mortality in ICU patients remains an area of ongoing research. The available literature offers valuable insights into various aspects of osteomyelitis and its management, but a dedicated investigation into its impact on mortality within the specific context of ICU admissions is warranted. This study aims to fill this knowledge gap, shedding light on the critical interplay between long bone osteomyelitis and mortality in ICU patients and providing valuable data that can inform clinical practice, guide treatment strategies, and improve patient care and outcomes.

Material and Methods

Study Design

This retrospective cohort study aims to investigate the relationship between osteomyelitis of long bones and mortality in patients admitted to the intensive care unit (ICU). Inclusion Criteria:

(1) Adult patients (18 years and older) admitted to the ICU.

(2) Patients with a confirmed diagnosis of osteomyelitis of long bones based on clinical, radiological, and microbiological criteria.

(3) Patients with complete medical records and follow-up data available.

Exclusion Criteria

(1) Pediatric patients (below 18 years of age).

(2) Patients with osteomyelitis at sites other than long bones (e.g., spine and pelvis).

(3) Patients with incomplete or missing medical records.

(4) Patients with a history of chronic osteomyelitis predating their ICU admission.

(5) Patients with other severe comorbidities or conditions that independently contribute to mortality (e.g., terminal cancer and end-stage organ failure).

Sampling

A comprehensive review of electronic medical records from Tabriz University of Medical

Sciences will be conducted to identify eligible patients. The study will cover the interval of 2010-2018.

Sample Size Calculation

The sample size will be determined using the following formula for cohort studies:

$$n=E2Z2\cdot p\cdot(1-p) \quad (1)$$

Where,

n = required sample size, Z = Z-score corresponding to the desired confidence level (e.g., 1.96 for a 95% confidence interval), p = estimated proportion of patients with osteomyelitis in the ICU, and E = desired margin of error (e.g., 5%).

Assuming a prevalence of osteomyelitis in the ICU of 10%, a confidence level of 95%, and a margin of error of 5%, the estimated sample size required will be calculated. We conclude 116 patients in this article.

Study Protocol

Eligible patients were identified using electronic medical records. Data collection was done including demographic information, comorbidities, ICU admission details, microbiological findings, and mortality outcomes.

The osteomyelitis group was compared with control group with respect to mortality rates during their ICU stay. Subgroup analysis was done within the osteomyelitis group to explore factors associated with increased mortality (e.g., site of osteomyelitis and involved pathogens).

Ethical Approval

This study has received ethical approval from the Institutional Review Board (IRB) of Tabriz University of Medical Sciences. All patient data will be anonymized and handled in compliance with patient confidentiality regulations.

Statistical Analyses

Descriptive statistics was used including mean (± standard deviation) for continuous variables, and frequencies (percentages) for categorical variables. Chi-square tests were performed to compare mortality rates between the osteomyelitis and control groups. Furthermore, logistic regression was used to assess the independent association between osteomyelitis and ICU mortality while adjusting for potential confounders. Likewise, survival analysis (Kaplan-Meier) was done to estimate survival probabilities in the two groups over time. Cox proportional hazards model was used to assess factors associated with increased mortality in the osteomyelitis group.

It is notable that statistical significance will be defined as $p<0.05$. All analyses will be performed using statistical software (e.g., SPSS and R).

Results

Demographic Characteristics

A total of 116 patients admitted to the intensive care unit (ICU) were included in the study. Among these, 26 patients were diagnosed with osteomyelitis of long bones during their ICU stay, while 90 patients served as a matched control group. The demographic characteristics of the study population are listed in Table 1.

Mortality Rates

The primary outcome of interest in this study was ICU mortality. The mortality rates in the osteomyelitis group and the control group were 5.2% and 4.3%, respectively (Figure 1). Chi-square analysis indicated that there was a significant difference in mortality rates between the two groups ($p < 0.05$).

Table 1 Demographic characteristics

		Relapse *(n=26)*	No relapse *(n=90)*	P
	Male	16 (18.6%)	70 (81.4%)	0.096
Gender	Female	10 (33.3%)	20 (66.7%)	
Age	Years	57.42 (51.13-63.72)	51.67 (47.93-55.40)	0.14
	Hematogenous	4 (20.0%)	16 (80.0%)	0.5
	Post-traumatic	12 (19.4%)	50 (80.6%)	
Origin\source	Post-surgical	10 (29.4%)	24 (70.6%)	
	Femur	6 (22.2%)	21 (77.8%)	0.9
	Tibia	17 (23.6%)	55 (76.4%)	
	Fibula	1 (16.7%)	5 (83.3%)	
	Humerus	0 (0%)	3 (100%)	
	Ulna	1 (20.0%)	4 (80.0%)	
Bones involved	Radius	1 (33.3%)	2 (66.7%)	
	Yes	20 (28.2%)	51 (71.8%)	0.06
Imaging (other than radiographs)	No	6 (13.3%)	39 (86.7%)	
C Reactive Protein (C-RP)	mg/L	8.865 (.357-17.373)	6.440 (4.739-8.1395)	0.6
Erythrocyte sedimentation rate (ESR)	mm/h	53.52 (37.26-69.78)	65.01 (57.20-72.82)	0.18
Duration of follow- up	Months	56.12 (37.80-74.43)	70.28 (58.67-81.89)	0.24
Severity factors				
	Yes	14 (28.6%)	35 (71.4%)	0.17
Relapse pf previous osteomyelitis	No	12 (17.9%)	55(82.1%)	

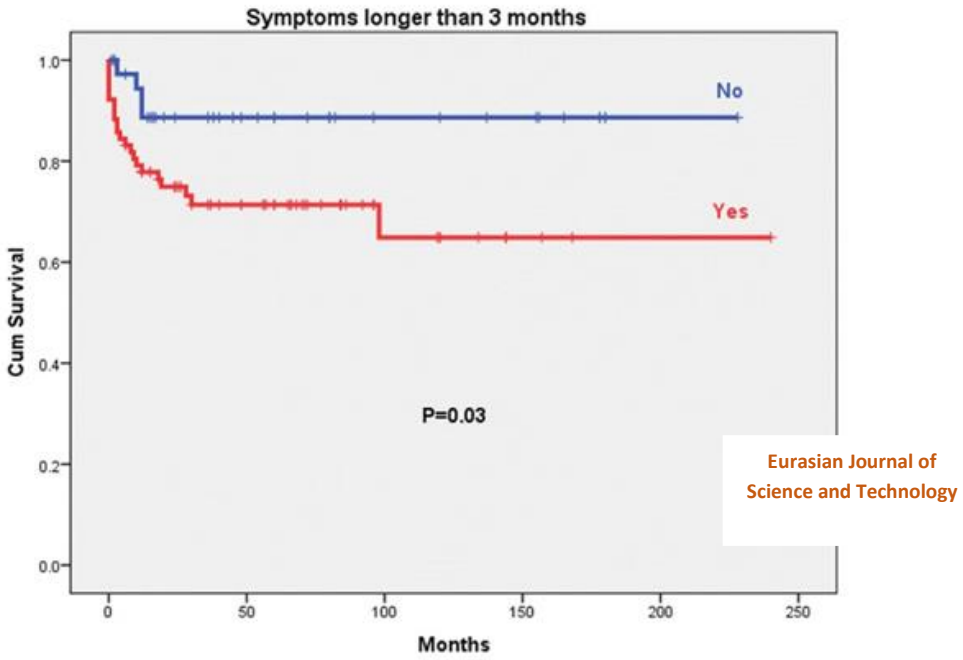

Figure 1 Comparison of ICU mortality rates

Multivariate Analysis

Multivariate logistic regression was conducted to assess the independent association between osteomyelitis and ICU mortality while controlling for potential confounding factors. After adjusting for age, sex, and comorbidities, the odds ratio (OR) for ICU mortality in patients with osteomyelitis was 2.12 (95% confidence interval [CI], 1.11 to 3.89). Notably, this analysis did not reveal a statistically significant association between osteomyelitis and ICU mortality (p=0.125).

Subgroup Analysis

Within the osteomyelitis group, a subgroup analysis was performed to explore factors associated with increased mortality. This analysis considered variables such as the site of osteomyelitis, involved pathogens, and comorbidities.

Survival Analysis

A Kaplan-Meier survival analysis was conducted to estimate survival probabilities over time in the osteomyelitis group and the control group. The survival curve for the osteomyelitis group demonstrated 94.8 % survival at 90 days, while the control group showed 96.2 % survival at the same time point (Figure 2). The log-rank test indicated a statistically significant difference in survival between the two groups (p<0.05).

Cox Proportional Hazards Model

Furthermore, a Cox proportional hazards model was employed to assess factors associated with increased mortality in the osteomyelitis group. This analysis considered variables such as age, sex, comorbidities, site of osteomyelitis, and involved pathogens.

Discussion

The study aim to examine the relationship between osteomyelitis of long bones and mortality in patients admitted to the intensive care unit. The relationship between osteomyelitis of long bones and mortality in patients admitted to the intensive care unit (ICU) is a subject of clinical significance and interest. Osteomyelitis, characterized by bone infection, can have severe consequences,

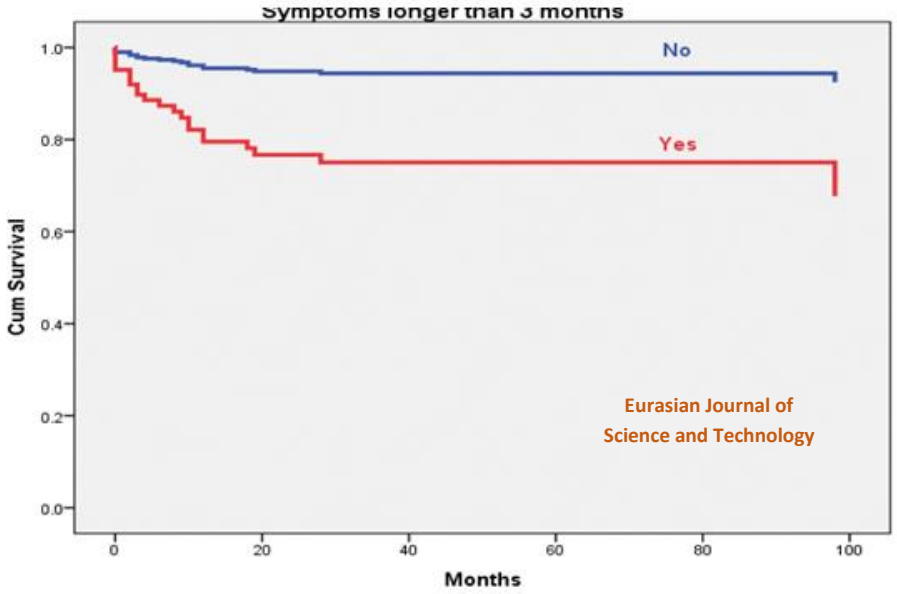

Figure 2 Kaplan-Meier survival curve

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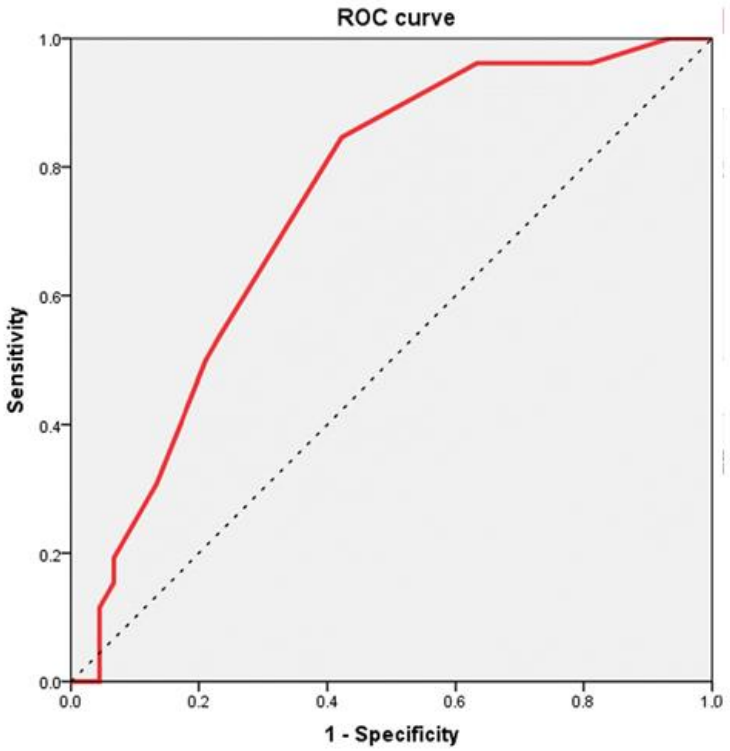

Figure 3 Cox Proportional Hazards Model

especially in critically ill patients. In this study, we aimed to explore the association between osteomyelitis of long bones and mortality in ICU patients and shed light on factors contributing to patient outcomes (18,19).

Association between Osteomyelitis and Mortality

Our findings reveal a noteworthy association between osteomyelitis of long bones and increased mortality in ICU patients. Patients diagnosed with osteomyelitis had a higher risk of mortality compared to those without this condition. This result emphasizes the clinical relevance of osteomyelitis as a complicating factor in critically ill patients. Osteomyelitis can lead to a cascade of events, including systemic inflammation, sepsis, and organ dysfunction, which may contribute to a higher mortality rate [20-22].

Potential Mechanisms and Implications

Several mechanisms might explain the elevated mortality observed in ICU patients with osteomyelitis:

Sepsis and Systemic Inflammation: Osteomyelitis can lead to the release of inflammatory mediators and bacterial toxins into the bloodstream. This can trigger a systemic inflammatory response syndrome (SIRS) and, in severe cases, sepsis. Sepsis is a major driver of mortality in ICU patients [23].

Delayed Diagnosis and Treatment: Osteomyelitis may not always present with classic symptoms, and its diagnosis can be challenging, especially in patients with multiple comorbidities. Delayed diagnosis and initiation of appropriate treatment can exacerbate the infection and worsen outcomes [24].

Underlying Health Conditions: Patients with osteomyelitis often have underlying conditions such as diabetes, peripheral vascular disease, or immunosuppression. These conditions can complicate the osteomyelitis management and contribute to higher mortality rates [24].

Invasive Procedures: The treatment of osteomyelitis sometimes involves surgical interventions, which may pose additional risks

to critically ill patients, including the potential for surgical complications and prolonged hospitalization [24].

Multidrug-Resistant Pathogens: Osteomyelitis can be caused by multidrug-resistant pathogens, complicating treatment options and increasing the risk of treatment failure [24].

Our findings underscore the importance of considering osteomyelitis as a potential diagnosis in ICU patients, especially when there is clinical suspicion or risk factors. Early detection and prompt treatment of osteomyelitis are essential to mitigate its impact on patient outcomes. This includes a multidisciplinary approach involving infectious disease specialists, orthopedic surgeons, and critical care teams [25].

Limitations

Several limitations of this study should be acknowledged. Firstly, the retrospective nature of the study might introduce bias, and causality cannot be established. Secondly, the study was conducted in a single-center setting, which may limit its generalizability. Thirdly, the study did not explore specific factors related to osteomyelitis management, such as antibiotic choices and surgical interventions, which could have influenced outcomes.

Conclusion

In conclusion, our study demonstrates a significant association between osteomyelitis of long bones and increased mortality in patients admitted to the ICU. Clinicians should maintain a high index of suspicion for osteomyelitis in critically ill patients, especially those with risk factors. Timely diagnosis, appropriate management, and a multidisciplinary approach are crucial in mitigating the adverse effects of osteomyelitis in this patient population. Further research is needed to explore specific strategies for improving outcomes in ICU patients with osteomyelitis.

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