Title: Association of Serum Lactate Levels Measured in the Emergency Department with 30-Day Mortality in Elderly Patients with Unilateral Hip Fracture

Running Title: Serum Lactate Levels in Elderly Patients with Unilateral Hip Fracture

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Abstract

Background: Hip fractures are frequent injuries in older patients and are associated with high mortality rates. This study assessed the association between serum lactate level and 30-day mortality in older patients with unilateral hip fractures and examined the prognostic value of this association on the clinical outcomes of these patients.

Methods: This retrospective, single-center study included patients aged ≥65 years admitted to the emergency department due to low-energy trauma and diagnosed with unilateral hip fracture upon admission. The additional inclusion criteria were patients with independent ambulation or walker or cane assistance before the injury, with available data on serum lactate levels on venous blood gas analysis, and who underwent surgery.

Results: Among the 330 included patients, 30.9% experienced postoperative complications and 10.3% died within 30 days. Using a lactate cut-off value of 2 mmol/L to distinguish between living and deceased patients, the sensitivity and specificity were 41% and 88%, respectively. Multivariate logistic regression analysis revealed that high lactate and low albumin levels and male sex were associated with mortality.

Conclusion: Identifying risk factors for mortality in geriatric patients with hip fractures is important. Male sex, low albumin levels, and particularly increased lactate levels were independent predictors of short-term mortality in these patients.

Keywords: Hip fracture, emergency department, older adults, lactate concentration, 30-day mortality
1. Introduction

The older adult population has been increasing in developed countries in recent years due to prolonged lifespans.\(^1\) Hip fractures are a common injury among this population, and can lead to increased morbidity and mortality due to factors such as limited physiologic reserve, preoperative medical conditions, and major surgery.\(^2\) Approximately 1.6 million individuals experience hip fractures worldwide annually.\(^4\) These injuries usually result from low-energy trauma and present significant challenges to patients and their families. Factors such as rehabilitation processes and long-term care needs can affect cost and quality of life. Older patients treated for hip fractures have a shorter average survival time than those without.\(^1,3\) In this context, assessing the risk of mortality and morbidity in patients with hip fractures and identifying factors that may increase the chance of recovery is important.\(^4\)

Lactate is a commonly used marker for conditions such as cellular oxygen deficiency and circulatory disorders. Studies in recent years have investigated the relationship between lactate levels and clinical outcomes of patients. Blood gas analysis is a low-cost and easily accessible test, particularly in emergency services.\(^5,6\) Recent studies have demonstrated the value of lactate level as a prognostic indicator for evaluating trauma severity and predicting the prognosis of patients with multiple traumas.\(^5,7\) However, few studies have reported on lactate levels and trauma in geriatric patient groups.

Therefore, this study assessed the correlation between serum lactate levels and 30-day mortality in older patients with unilateral hip fractures and determined the potential prognostic value of this association in the clinical outcomes of these patients.

2. Materials and Methods

2.1. Study Design

This retrospective study was conducted in an emergency department with an annual average of 385,000 patient visits. After receiving approval from the local ethics committee (2012-KAEK-15/2843), data were collected from electronic health records and patient files.
2.2. Study Population

The study included patients diagnosed with unilateral hip fractures in the emergency department between January 10, 2020, and January 10, 2023. We used the hospital data system to identify patients with International Classification of Diseases, 10th revision (ICD-10) codes S72.00, S72.10, and S72.20. We included patients who experienced low-energy trauma (a fall from a level at or below body height), were able to walk independently or with the aid of a walker or cane before the injury, were aged ≥65 years, had available data on serum lactate levels measured during the emergency department evaluation, and who underwent surgery. We excluded patients who were <65 years of age, unable to care for themselves before the injury, had additional injuries other than hip fractures, were in the high-risk group (American Society of Anesthesiologists [ASA] grade V), had high-energy trauma, and had not undergone surgery. The fracture diagnoses and types were determined using pelvis/hip radiography and/or pelvic computed tomography. We classified the fracture types as femoral neck, pertrochanteric, and subtrochanteric fracture. An additional inclusion criterion was patients who had venous blood samples taken within the first hour of admission to the emergency department. The blood gas samples were analyzed using a Siemens RAPIDLab 1265 device within 5 min of collection. This study analyzed demographic data, comorbidities, medications, laboratory results, postoperative complications, and 30-day mortality. We classified postoperative complications according to the POSSUM score and included fever, pulmonary infection, wound infection, urinary tract infection, septicemia, heart failure, acute renal failure, arrhythmia, myocardial infarction, deep vein thrombosis, pulmonary embolism, and ischemic stroke. The primary and secondary outcomes of this study were 30-day mortality and postoperative complications, respectively.

2.3. Data Analysis

We performed the data analysis using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to determine the normality
of the distributions of discrete and continuous numerical variables. Descriptive statistics include medians and interquartile range (IQR) for discrete and continuous numerical variables, and the number of cases and percentages for categorical variables. We evaluated categorical and continuous variables using the chi-square and Mann–Whitney U tests, respectively. We applied univariate tests to evaluate mortality predictors and included statistically significant variables (p<0.2) in a multivariate logistic regression model. The Hosmer–Lemeshow test was used to evaluate the fit of the multivariate regression model. We performed receiver operating characteristic (ROC) analysis and calculated the area under the curve (AUC) to determine the cut-off lactate level to distinguish between mortality and intensive care unit complications. Statistical significance was set at p<0.05.

3. Results

During the study period, we evaluated 579 patients diagnosed with hip fracture. Of these, we included 330 patients with complete data (Figure 1). Most patients were female (64.5%), and the median age was 81 years (IQR 75–87). The median lactate level was 1.26 mmol/L (IQR 25–75, 0.9–1.76). The most common fracture type was pertrochanteric (58.5%). Postoperative complications occurred in 30.9% of patients, with fever the most common complication (19.4%). The 30-day mortality was 10.3%. Demographic, laboratory, and clinical data and patient outcomes are shown in Table 1. Table 2 shows the results of the comparison between patients who did and did not die within 30 days. Advanced age, a history of hypertension, high lactate levels, and low albumin levels were significant factors associated with mortality (p<0.05). Additionally, postoperative complications and prolonged hospital stay were associated with mortality (p<0.05). Mortality did not differ significantly according to the type of fracture or surgery performed (p>0.05).

The results of the ROC analysis identified that a lactate level cut-off value of 2 mmol/L was differentiated between deceased and living patients with an AUC value of 0.712 (95% confidence interval [CI]; 0.615–0.810) (Figure 2) and a sensitivity and specificity of 41% and
88%, respectively. The lactate levels of patients who did and did not develop postoperative complications differed significantly (1.71 mmol [1.2–2.5] vs. 1.1 mmol [0.8–1.4, p<0.001). The ROC analysis to determine the lactate level threshold between patients with and without postoperative complications revealed an AUC of 0.744 (95% CI; 0.684–0.804) for a threshold of 2.1 mmol/L, with sensitivity and specificity of 31% and 96%, respectively (Figure 3). Multivariate logistic regression analysis was performed to examine the effects of the variables analyzed in Table 2 and lactate levels, together with other variables, on mortality. In the multivariate model, hypertension, dementia, lactate, and albumin levels (p≤0.2), as well as age, and sex were included. The results of the Hosmer–Lemeshow test demonstrated the fitness of the model, and the association of high lactate level, low albumin level, and male sex with mortality (p=0.043, p=0.001, and p=0.003, respectively) (Table 3).

4. Discussion

The results of our study demonstrated the value of serum lactate level as a prognostic indicator in older patients with isolated hip fractures. Moreover, lactate levels >2 mmol/L were associated with 30-day mortality and the risk of postoperative complications. In addition, older age, male sex, and low albumin levels were associated with 30-day mortality. Therefore, a lactate concentration of ≥2 mmol/L can be used as a biomarker to predict the short-term risk of death in older patients after hip fracture surgery. This biomarker may assist clinicians in the early identification of critically ill patients and the prediction of outcomes and management.

Hip fractures are a common consequence of the growing older adult population and the global osteoporosis epidemic. These fractures are associated with high morbidity and mortality. The reported 1-month, 6-month, and 1-year mortality rates are approximately 11%, 16%, and 35%, respectively.10-13) We also analyzed the demographic, laboratory, and clinical characteristics of the patients, especially the blood lactate level, to define the conditions associated with mortality and morbidity in hip fractures, which have a high incidence and mortality rate. In our study, the 30-day mortality rate was 10.3%, similar to that reported in the literature. Although our study
was limited to a patient population selected according to specific criteria, the similarity of mortality rates to those in the literature suggests that our data have general validity.

Lactate levels generally increase during trauma due to conditions such as tissue hypoperfusion, anaerobic metabolism, cellular damage, inflammation, mitochondrial dysfunction, and systemic inflammation that occur because of inadequate oxygen transport to tissues and impaired energy production processes. Recent studies have highlighted the clinical importance of lactate in shock, especially in patients with trauma, and have demonstrated the prognostic value of this biomarker. High lactate levels are also associated with mortality in hip fractures, especially in geriatric patients. One study reported that a lactate concentration of >2 mmol/L measured at the time of the patient’s initial presentation was a good prognostic indicator of 30-day mortality. In the present study, the sensitivity and specificity values for a lactate concentration of >2 mmol/L were 41% and 88%, respectively, to differentiate between living and deceased patients based on previous studies. The sensitivity and specificity values using a lactate cut-off value of 2.1 mmol/L for predicting the development of postoperative complications, were 31% and 96%, respectively. In the multivariate regression analysis, high lactate levels were associated with mortality. Our results showed that lactate levels >2 mmol/L were associated with a significant increase in the risks of mortality and complications. However, low lactate levels did not completely exclude these risks. This may be due to factors such as patient comorbidities, individual differences in lactate clearance, margin of error in laboratory testing, and the time elapsed between trauma and hospital arrival.

Another study reported a significant difference in 30-day mortality rates between patients with lactate levels <3 mmol/L and >3 mmol/L (6.8% vs. 28%). Moreover, lactate levels >1.2 mmol/L and pH <7.35 measured just before surgery in patients with hip fractures, are associated with 90-day mortality, as well as worsening hypovolemia, anemia, or decreased cardiac output while awaiting surgery. In a study by Jonsson using the 2 mmol/L threshold for lactate in a similar patient population, lactate was not predictive of 30-day mortality and postoperative
complications. The author suggested that high lactate levels may be secondary to factors other than trauma-induced hypoperfusion and factors other than tissue hypoxia may be more important for outcomes in older patients with hip fracture. Although conflicting opinions are reported in the literature, various studies have demonstrated the association of high lactate levels with mortality and morbidity in patients with isolated hip fractures. The use of a specific lactate cutoff for mortality prediction has significant potential in clinical settings; however, a comprehensive view of its efficacy across different clinical settings and patient demographics is imperative. Factors such as age, sex, comorbidities, and treatment history can significantly alter the impact of lactate level on mortality prediction. The results of the present study may catalyze further investigation to determine whether a specific lactate cutoff value should be universally considered as a tool for mortality prediction.

In geriatric patients with trauma, the risk of mortality is higher in men and with increasing age. The results of our regression analysis for mortality, in addition to similar predictors, revealed the significant association of high lactate levels with mortality. In addition, lactate levels at admission were significantly higher in patients who developed postoperative complications than in those who did not. Thus, patients with high lactate levels should be monitored closely during the postoperative period and carefully managed for potential complications.

5. Limitations

Our study has various limitations. First, this was a retrospective and single-center study, and the results cannot be generalized to other centers. We included patients whose lactate levels were measured within the first hour of admission to the emergency department. However, the time between presenting to the emergency department and experiencing trauma varies among patients, which may impact lactate levels and, thus, the study results. Because lactate levels were not measured in all patients with hip fractures, not all patients were included in the study.
However, the patients in our study had demographic characteristics similar to those in other studies.

6. Conclusion

Identifying risk factors for mortality in geriatric patients with hip fractures is important. Our study results showed that in older patients with isolated hip fractures, a serum lactate level of >2 mmol/L was associated with 30-day mortality and the risk of postoperative complications. Male sex, low albumin levels, and particularly increased lactate levels were independent predictors of short-term mortality in geriatric patients with isolated hip fractures.

SUMMARY

Background: The older adult population has been increasing in developed countries in recent years owing to the prolonged human lifespan. Hip fractures are common injuries in this population and can lead to increased morbidity and mortality rates due to factors such as limited physiologic reserve, preoperative medical conditions, and major surgery. This study assessed the association between serum lactate levels and 30-day mortality in older patients with unilateral hip fractures and examined the prognostic value of this association in the clinical outcomes of these patients.

Methods: This retrospective, single-center study included patients aged ≥65 years admitted to the emergency department due to low-energy trauma and diagnosed with unilateral hip fracture in the emergency department. We also included patients who could walk independently or with the help of a walker or cane before the injury, had serum lactate levels on venous blood gas analysis, and underwent surgery. The fracture diagnoses and types were determined using pelvis/hip radiography and/or pelvic computed tomography. We classified the fracture types as femoral neck, pertrochanteric, or subtrochanteric.

Results: Among 330 included patients, 30.9% experienced postoperative complications and 10.3% died within 30 days. Pertrochanteric fracture was the most common (58.5%). Using a
lactate cut-off value of 2 mmol/L to distinguish between living and deceased patients, the sensitivity and specificity were 41% and 88%, respectively. Using the best cut-off value of lactate for predicting the development of postoperative complications of 2.1 mmol/L, the sensitivity and specificity values were 31% and 96%, respectively. Multivariate logistic regression analysis revealed that high lactate and low albumin levels and male sex were associated with mortality.

**Conclusion:** Identifying risk factors for mortality in geriatric patients with hip fractures is important. The results of our study showed that in older patients with isolated hip fractures, a serum lactate level of > 2 mmol/L was associated with 30-day mortality and the risk of postoperative complications. Male sex, low albumin levels, and particularly increased lactate levels were independent predictors of short-term mortality in geriatric patients with isolated hip fractures.

**Informed Consent:** Retrospective study.

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