L-lactate in acute mesenteric ischemia: a reliable biomarker for diagnosis and prognosis?

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Abstract

Acute mesenteric ischemia is a life-threatening condition with high mortality, often caused by arterial or venous hypoperfusion of the intestines. Early diagnosis remains challenging due to nonspecific clinical findings and the unreliability of laboratory biomarkers. Serum L-lactate, a marker of tissue hypoperfusion, has been investigated as a potential prognostic and diagnostic indicator in acute mesenteric ischemia. This retrospective study analyzed 75 patients who underwent emergency surgery for acute mesenteric ischemia between 2010 and 2015. Demographic data, comorbidities, preoperative serum L-lactate levels, operative details, intestinal resection length, and survival outcomes were collected and statistically evaluated. ROC analysis was used to assess the diagnostic power of L-lactate in predicting the extent of bowel resection and to define a cut-off value. The overall mortality rate was 62.7%. Mortality was significantly associated with age ≥65 (p=0.011) and the presence of diabetes mellitus (p=0.041). Preoperative serum L-lactate levels were significantly higher in non-survivors than in survivors (median: 4.88 mmol/L *vs.* 3.00 mmol/L; p=0.011). However, no significant correlation was found between L-lactate levels and bowel resection length (p=0.316). ROC analysis failed to identify a statistically significant cut-off value for L-lactate in predicting resection extent (AUC=0.580; p=0.316). Preoperative serum L-lactate levels are significantly associated with mortality in patients with acute mesenteric ischemia and may serve as a prognostic biomarker. However, they do not reliably predict the extent of intestinal resection. Larger, prospective studies are required to define clinically meaningful diagnostic thresholds for L-lactate in acute mesenteric ischemia.

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Introduction

Acute mesenteric ischemia is a critical clinical condition characterized by a sudden and severe hypoperfusion of the arterial or venous circulation of the small intestine, associated with high mortality rates. The pathogenesis may involve occlusive arterial obstruction, non-occlusive hypoperfusion, or venous outflow obstruction. While acute mesenteric ischemia predominantly affects the small intestine, it may also involve the colon in some cases. Delayed diagnosis can lead to irreversible tissue damage, intestinal infarction, and multiorgan failure, resulting in catastrophic clinical outcomes. Therefore, prompt and accurate diagnosis is crucial for altering the clinical course.

Approximately 60–70% of all mesenteric ischemia cases are attributed to arterial hypoperfusion, while the remainder are associated with chronic or colonic ischemia.[1] With the aging population and increasing prevalence of cardiovascular diseases, the incidence of acute mesenteric ischemia has markedly risen. Although the incidence of mesenteric ischemia among patients presenting with abdominal pain is about 1-2%, this rate can increase to as high as 18% in individuals over the age of 65.[2] Despite advancements in imaging techniques and intensive care capabilities, mortality rates associated with acute mesenteric ischemia remain between

60% and 90%.[3,4] This persistently high mortality is attributed not only to delays in diagnosis but also to factors such as advanced patient age, underlying comorbidities, and late presentation. One of the main challenges in achieving early diagnosis is the nonspecific nature of acute mesenteric ischemia symptoms and the lack of sufficiently reliable laboratory markers. The classic clinical triad of acute mesenteric ischemia — abdominal pain, hematochezia, and fever — is observed in only about one-third of patients.[5]

The most critical factor in reducing acute mesenteric ischemia-related mortality is the rapid restoration of blood flow through timely diagnosis and intervention. One of the significant diagnostic challenges in acute mesenteric ischemia is the absence of specific laboratory markers. Given that delays in diagnosis and treatment significantly increase mortality, the use of rapid and reliable biochemical markers has become increasingly important. Laboratory findings such as leukocytosis, increased anion gap, and elevated lactate levels are commonly observed but are limited in diagnostic specificity. L-lactate, a product of anaerobic glycolysis, is considered a biochemical indicator of tissue hypoperfusion.[6] Elevated serum L-lactate levels are frequently detected in acute mesenteric ischemia patients and have been reported to correlate with mortality. However, its diagnostic power and an optimal cut-off value predictive of mortality have not yet been established.

This study aims to evaluate the prognostic and diagnostic value of preoperative serum L-lactate levels in patients diagnosed with acute mesenteric ischemia, and to determine a diagnostic "cut-off" level that can predict mortality risk.

Materials and Methods

This retrospective study included patients who underwent surgery with a preoperative diagnosis of acute mesenteric ischemia at the General Surgery Department of our hospital between 2010 and 2015. A total of 75 patients who underwent emergency surgical intervention for acute mesenteric ischemia during the five years were included in the study. Patients with incomplete or inaccessible medical records—such as missing operative notes, laboratory results, or outcome data—were excluded to ensure data integrity. This exclusion criterion may have introduced selection bias and should be taken into account when interpreting the study results. Data were collected through patient discharge summaries and hospital archive records. Ethics approval for the study was obtained from the Ethics Committee of Ankara Dışkapı Yıldırım Beyazıt Training and Research Hospital (Protocol 36125894, Date:02/03/2016). Demographic characteristics (age, sex), comorbidities, preoperative biochemical findings, type of surgical intervention, resected bowel segment and length according to pathology reports, length of hospital stay, and survival status were systematically recorded for each patient.

Preoperative serum L-lactate levels were obtained from the final arterial blood gas analysis performed before surgery. Samples were collected under anaerobic conditions using heparinized syringes, transported on ice, and analyzed within 30 minutes using an enzymatic amperometric method on a calibrated blood gas analyzer. Measurements were taken according to manufacturer guidelines, and internal quality controls were routinely applied. Due to lactate's instability, strict pre-analytical precautions were taken to minimize degradation. Patients were categorized based on survival status (survivors vs. non-survivors), age group (<65 years and ≥65 years), length of bowel resection (<3 cm *vs*. ≥3 cm), and resected bowel segment. In addition to L-lactate levels, other biochemical parameters were statistically analyzed about mortality and resection length.

Statistical analysis

All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 15.0. The distribution characteristics of continuous variables were assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. For normally distributed variables, comparisons were made using the independent samples t-test, whereas the Mann-Whitney U test was used for non-normally distributed data. Differences between categorical variables were analyzed using the Chi-square test or Fisher's Exact test when appropriate. Correlations between variables were assessed using Pearson and Spearman correlation coefficients, and statistical significance was reported using p-values.

Descriptive statistics were presented as mean ± standard deviation for normally distributed continuous variables and as median (minimum–maximum) for non-normally distributed data. Categorical variables were expressed as frequency (n) and percentage (%). A p-value of <0.05 was considered statistically significant for all analyses.

Results

A total of 75 patients who underwent surgery with a diagnosis of acute mesenteric ischemia were included in our study. Among these, 46 (61.3%) were male and 29 (38.7%) were female. The mean age was 66.07±13.03 years, ranging from 33 to 87 years. Thirty-four patients (45.3%) were younger than 65 years, while 41 (54.7%) were aged 65 years or older.

Regarding comorbidities, 29 patients (38.7%) had Coronary Artery Disease (CAD), 40 (53.3%) had Hypertension (HT), 21 (28%) had Diabetes Mellitus (DM), and 13 (17.3%) had Chronic Obstructive Pulmonary Disease (COPD). In addition, 35 patients (46.7%) had more than one comorbidity. Atrial Fibrillation (AF) was present in 19 patients (25.3%), Deep Vein Thrombosis (DVT) in 9 (12%), Pulmonary Thromboembolism (PTE) in 1 (1.3%), and Cerebrovascular Disease (CVD) in 12 (16%).

Of the 75 patients who underwent surgery for acute mesenteric ischemia, 28 (37.3%) were discharged without complications. However, 47 patients died within the first 7 days postoperatively, corresponding to an early postoperative mortality rate of 62.7%. The mortality rate was 60.9% among males and 65.5% among females. A second-look operation was performed in 18 patients (24%), and postoperative complications developed in 4 patients (5.3%). Bowel resections were categorized based on resection length: patients who underwent resections of <3 m were placed in Group 1, and those with resections of ≥3 m were placed in Group 2. This classification considered the risk of short bowel syndrome. Of the 75 patients who underwent laparotomy, 63 (84%) had bowel resection, while 12 (16%) had laparotomy only without resection. Among the 63 resected cases, 42 (56%) underwent resections of <3 m, and 21 (28%) had resections of ≥3 m.

There was no statistically significant difference in preoperative lactate levels between patients with resection lengths <3 m and ≥3 m (p=0.316). Additionally, resection length was not significantly associated with age, gender, white blood cell count, INR levels, blood pH, comorbidities (CAD, HT, DM, COPD), history of thrombosis (AF, DVT, PTE, CVD), ICU stay duration, hospital length of stay, second-look operations, postoperative complications, or time to death (Table 1).

The median preoperative lactate level was 3.00 mmol/L (range: 0.71–10.67) in survivors, while it was 4.88 mmol/L (range: 1.12–27.77) in non-survivors (Table 2). Elevated lactate levels were significantly associated with increased mortality (p=0.011), and a direct correlation was observed between lactate levels and mortality rates. However, lactate levels did not differ significantly among age groups, the need for a second-look operation, or the occurrence of postoperative complications.

Patients were further categorized based on the site of bowel resection into three groups: small intestine only, colon only, and both small intestine and colon. There was no significant difference in lactate levels among these groups (p=0.396). Additionally, no significant association was found between the resection site and the presence of AF or DVT; AF was evenly distributed across different resection sites.

A statistically significant difference in mortality was observed between age groups (<65 *vs.* ≥65 years), with advanced age being associated with higher mortality (p=0.011). The presence of diabetes mellitus was also found to increase mortality (p=0.041) significantly. Conversely, no statistically significant differences in mortality were observed based on gender, resection length (<3 m *vs.* ≥3 m), presence of comorbidities (CAD, HT, COPD), history of thrombotic events (AF, DVT, PTE, CVD), or whether bowel resection was performed during surgery. To evaluate potential predictors of mortality, clinical and laboratory variables were compared between survivors and non-survivors. The comparisons included demographic features, comorbid conditions, thrombotic history, operative variables, and preoperative serum L-lactate levels. The statistical significance of differences between groups was assessed using appropriate tests (Chi-square or Fisher's exact test for categorical variables, and Mann-Whitney U test for continuous variables). The results are summarized in Table 3.

The ability of lactate level to distinguish patients who underwent resection ≥3 m from those with <3 m was assessed using the Receiver Operating Characteristic (ROC) curve. The Area Under the Curve (AUC) was calculated as 0.580 with a standard error of 0.080. Based on a 95% confidence interval, the AUC was estimated to lie between 0.423 and 0.737 in similar samples. This result was not statistically significant (p=0.316), suggesting that lactate level does not have sufficient diagnostic power to predict resection length, and therefore, no cut-off value could be calculated (Figure 1). The diagnostic accuracy of lactate for this purpose was deemed inadequate.

Similarly, when patients were grouped based on a resection length of <2 meters and ≥2 meters, the AUC was also not statistically significant (p=0.202), indicating that a cut-off value could not be calculated for this grouping either.

Discussion

Acute mesenteric ischemia is a life-threatening condition marked by sudden gastrointestinal hypoperfusion and high mortality. It predominantly affects the small intestine and arises from either occlusive or non-occlusive vascular compromise. The main etiologic subtypes include arterial embolism (most common), arterial thrombosis, mesenteric venous thrombosis, and non-occlusive ischemia. Literature suggests that 60–70% of acute mesenteric ischemia cases are due to acute mesenteric blood flow insufficiency, while the remainder result from chronic or colonic ischemia.[1]

Early diagnosis plays a crucial role in the management of acute mesenteric ischemia. Patients typically present with acute abdominal pain, minimal physical signs, and metabolic acidosis. Delayed recognition often leads to bowel necrosis, sepsis, and multiorgan failure. Given the nonspecific nature of symptoms, particularly in high-risk individuals, maintaining a high level of clinical suspicion is essential. The diagnostic challenge significantly contributes to the condition's high mortality.

Mesenteric vascular diseases account for approximately 1–2% of all gastrointestinal diseases. However, with increasing clinical awareness and the aging population, the incidence of acute mesenteric ischemia has shown a notable rise in recent years. Elderly individuals, particularly those with significant cardiovascular or systemic comorbidities, are more susceptible to this condition. Although some literature has suggested that acute mesenteric ischemia accounts for up to 18% of abdominal pain presentations in patients aged ≥65 years,[2] this figure may be an overestimation.

Table 1. Comparison of clinical and laboratory variables according to resection length (<3 m *vs.* ≥3 m).

Variables	<3 m Median (Min–Max)	≥3 m Median (Min–Max)	p
Age (years)	65 (33-84)	70 (38-85)	0.461
White blood cell count (mm³)	13,675 (3,900-50,300)	18,190 (6,200-33,200)	0.117
INR	1.29 (0.90-5.69)	1.28 (0.96-2.24)	0.884
Lactate (mmol/L)	3.56 (1.12-26.00)	4.69 (0.86-17.10)	0.316
pH	7.39 (6.99-7.57)	7.37 (7.07-7.47)	0.556
ICU stay (days)	3 (0-49)	2 (1-62)	0.935
Total follow-up duration (days)	7 (0-49)	8 (1-62)	0.417
Time to death (days)	2.5 (0-49)	2 (1-62)	0.976

Table 2. Distribution of lactate levels according to survival status.

Survival Status	Mean (mmol/L)	Standard Error	Median	Min	Max	n
Survived	3.48	2.38	3.00	0.71	10.67	26
Deceased	6.44	5.73	4.88	1.12	27.77	45
Total	5.35	4.97	4.00	0.71	27.77	71

In an extensive retrospective analysis of 5,340 patients presenting with acute abdominal pain in an urban emergency department, Cervellin *et al.* reported considerably lower rates of mesenteric ischemia,[7] highlighting the rarity and diagnostic challenge of acute mesenteric ischemia in real-world settings. According to this trend, 54.7% (n=41) of the patients in our study were 65 years or older, with a mean age of 66 years for the cohort. Analysis by age group revealed that mortality was significantly higher in the ≥65 age group (p=0.011), reinforcing the role of advanced age as an independent risk factor for mortality in acute mesenteric ischemia. Age-related vascular changes, including loss of elasticity, the presence of atherosclerotic plaques, and multiple comorbidities, increase susceptibility to ischemia and negatively impact treatment outcomes.[8]

In our study, 46.7% of patients had multiple comorbidities, with HT (53.3%), CAD (38.7%), DM (28%), and COPD (17.3%) being most common. DM was significantly associated with mortality (p=0.041). Its impact may be explained by microvascular damage, endothelial dysfunction, and impaired immune response, which increase susceptibility to ischemia and accelerate progression to necrosis. These results align with prior studies identifying diabetes as an independent predictor of mortality in acute mesenteric ischemia.[9]

Despite advancements in diagnosis and treatment, acute mesenteric ischemia continues to carry a high mortality rate, often exceeding 60%.[1] Oldenburg *et al.* reported mortality rates of 44% in mesenteric venous thrombosis, 66% in arterial occlusions, and 89% in non-occlusive cases.[8] Similarly, our study found a mortality rate of 62.7%, likely influenced by factors such as delayed diagnosis, advanced age, comorbidities, and late hospital admission.

A distinctive feature of our study is its assessment of the prognostic utility of preoperative L-lactate levels in acute mesenteric ischemia. As a recognized indicator of hypoperfusion and anaerobic metabolism, L-lactate was evaluated about both mortality and bowel resection extent. Despite its relevance, no single non-invasive biomarker currently demonstrates sufficient sensitivity and specificity for the early diagnosis of acute mesenteric ischemia, prompting continued investigation into novel candidates in recent literature.

Typical laboratory findings in intestinal ischemia, such as leukocytosis, elevated hematocrit, metabolic acidosis, and increased serum lactate, often appear in advanced stages, limiting their value for early diagnosis.[10] L-lactate rises due to anaerobic metabolism during hypoperfusion but lacks disease specificity, as it can elevate in other critical conditions like sepsis or organ failure.[11] Although serum lactate shows high sensitivity (~86%) for acute mesenteric ischemia, its low specificity (~44%) limits its standalone diagnostic utility. While animal models support L-lactate elevation following superior mesenteric artery occlusion,[12,13] human data remain inconsistent.[14] D-lactate, a stereoisomer produced by gut bacteria, may serve as a more specific marker, though its clinical use is limited by delayed elevation and methodological challenges.[6,15]

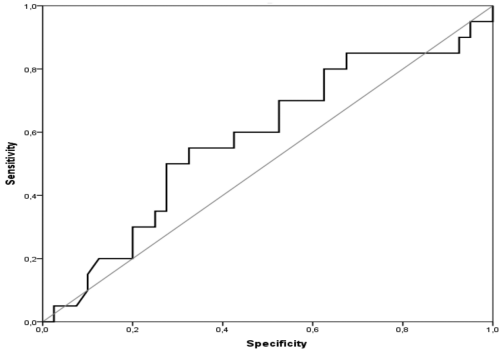
In our study, L-lactate demonstrated limited diagnostic utility for predicting bowel resection length. ROC analysis yielded an AUC of 0.58 (p=0.316), and no significant difference was observed for a ≥2 m resection threshold (p=0.202). These findings align with previous meta-analyses suggesting that serum lactate is a nonspecific marker for early ischemic injury.[16]

Nevertheless, in our study, preoperative L-lactate levels were found to be significantly associated with mortality (p=0.011). This suggests that elevated preoperative L-lactate levels may reflect poorer prognosis and increased mortality risk in acute mesenteric ischemia patients. Similar associations between elevated serum lactate and in-hospital mortality have been reported in several previous studies.[17] In this context, L-lactate may be better interpreted as a prognostic marker rather than a diagnostic one. However, no ROC analysis was performed to determine an optimal cut-off value for predicting mortality, primarily due to the limited sample size, which could compromise statistical robustness. Moreover, L-lactate was measured only once in the preoperative period. Serial or dynamic lactate monitoring may provide more accurate prognostic

Table 3. Summary of clinical variables and their association with mortality.

Variable	p	Interpretation
Age (<65 *vs.* ≥65)	0.011	Significant
Gender (male *vs.* female)	ns	Not significant
Coronary artery disease	ns	Not significant
Hypertension	ns	Not significant
Diabetes mellitus	0.041	Significant
Chronic obstructive pulmonary disease	ns	Not significant
Atrial fibrillation	ns	Not significant
Deep vein thrombosis	ns	Not significant
Pulmonary thromboembolism	ns	Not significant
Cerebrovascular disease	ns	Not significant
Bowel Resection (Yes vs. No)	ns	Not significant
Resection Length (<3 m *vs.* ≥3 m)	ns	Not significant
Second-look Operation	ns	Not significant
Postoperative complications	ns	Not significant
Preoperative L-lactate Level	0.011	Significant

Note: "ns" denotes non-significant results (p > 0.05). Statistical tests included Chi-square, Fisher's exact test, and Mann–Whitney U test, depending on variable type.



AUC (Area Under Curve)	Standard Error	p-value	95% Confidence Interval	
			Lower	Upper
0.580	0.080	0.316	0.423	0.737

Figure 1. ROC curve evaluating the diagnostic performance of preoperative serum L-lactate levels in predicting the need for ≥3 meters of intestinal resection. The area under the curve (AUC) was 0.580 (Standard Error: 0.080; p=0.316; 95% Confidence Interval: 0.423-0.737).

insights by capturing ongoing perfusion changes and clinical responses.

In recent years, a variety of novel biomarkers have been investigated for their potential utility in diagnosing intestinal ischemia. These include alpha-Glutathione S-Transferase (α-GST), Intestinal Fatty Acid-Binding Protein (I-FABP), Cobalt-Albumin Binding Assay (CABA), Ischemia-Modified Albumin (IMA), Diamine Oxidase (DAO), citrulline, and C-Reactive Protein (CRP).[18-20] While many of these biomarkers have shown promising results in experimental or early-phase clinical studies, sufficient validation and standardization for routine clinical use have not yet been established.

Thromboembolic events of cardiac origin, particularly atrial fibrillation, are a significant cause of acute mesenteric ischemia.[21] In our cohort, 25.3% had AF, 12% DVT, 1.3% PTE, and 16% CVD, underscoring the role of cardiovascular comorbidities in acute mesenteric ischemia pathogenesis. However, AF was not significantly associated with mortality, potentially due to limitations in preoperative documentation or incomplete clinical data.

The mean hospital stay was 10 days, with an average ICU stay of 7.8 days. These durations are shorter than the ~23-day hospital stays reported in the literature,[22] possibly due to variations in patient selection, surgical timing, or institutional practices.

Second-look laparotomy was performed in 24% of cases. In most initially borderline viable segments, progression to necrosis required further resection. While second-look surgery may increase morbidity, literature supports its role in enabling timely necrosis management and improving long-term outcomes.[22]

Recent studies have demonstrated the prognostic significance of elevated L-lactate levels in acute mesenteric ischemia.[23] The updated guidelines of the World Society of Emergency Surgery (WSES) emphasize the adjunctive role of serum biomarkers, particularly in cases of high clinical suspicion.[24] Our findings make a meaningful contribution to this growing body of evidence.

One of the main strengths of this study is its focused assessment of preoperative L-lactate levels as a prognostic marker in acute mesenteric ischemia, specifically regarding mortality and the length of bowel resection. Few studies have evaluated these parameters concurrently, making this research a valuable contribution to the field. Additionally, a comprehensive analysis of clinical, laboratory, and operative data identified advanced age and diabetes mellitus as significant mortality-related factors, aiding in the early identification of high-risk patients.

However, this study also has several limitations. Primarily, its retrospective and single-center design restricts the generalizability of the findings. Additionally, the relatively small sample size may have limited the statistical power, particularly in the ROC analysis used to determine diagnostic accuracy. Another limitation stems from the incomplete availability of some preoperative clinical data, which constrained the comprehensive evaluation of comorbid conditions. Moreover, L-lactate levels were measured at a single time point only, which precluded assessment of their dynamic changes over time.

Furthermore, acute mesenteric ischemia was analyzed as a single entity without stratification by etiology (e.g., embolism, thrombosis, non-occlusive), which may have masked differences in biomarker behavior across subtypes. It should also be noted that elevated L-lactate levels are not specific to acute mesenteric ischemia and may be observed in various systemic conditions such as sepsis, shock, or hepatic dysfunction. As these potential confounding factors were not fully controlled in our study, the interpretation of L-lactate as a prognostic biomarker should be approached with caution. Therefore, to determine a clinically meaningful "cut-off" value for L-lactate and to enhance its utility in clinical decision-making, larger, multicenter, prospective studies are warranted.

Conclusions

In this study, the mortality rate among patients who underwent surgical treatment for acute mesenteric ischemia was 62.7%, which is consistent with the high mortality rates reported in the literature. Advanced age and the presence of diabetes mellitus were significantly associated with mortality, suggesting that these two variables may serve as independent risk factors influencing the prognosis of acute mesenteric ischemia.

Preoperative serum L-lactate levels were also found to be significantly associated with mortality. This finding supports the potential use of L-lactate as a prognostic biomarker for predicting adverse clinical outcomes in acute mesenteric ischemia. However, L-lactate failed to predict the extent of intestinal resection, as the ROC analysis did not yield a statistically significant cut-off value ($p=0.316$), limiting its diagnostic utility in this context.

These findings highlight the importance of early diagnosis and prompt intervention, particularly in elderly or diabetic patients. While L-lactate may aid in risk stratification, it remains insufficient for guiding surgical decisions. Further large-scale, prospective studies are needed to establish reliable thresholds and identify more specific biomarkers. A high index of suspicion, multidisciplinary assessment, and improved diagnostic tools remain essential to optimize outcomes in acute mesenteric ischemia.

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