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Preoperative lactate, wound complications, and mortality following major amputation in patients with peripheral artery disease

Teguh Marfen Djajakusumah[1], Indra Prasetya Yarman[2], Azis Satrio Wibowo[3]

[1,2]Division of Vascular and Endovascular Surgery, Faculty of Medicine, Padjadjaran University/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

[3]Department of Surgery, Faculty of Medicine, Padjadjaran University/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

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ABSTRACT

Introduction: Peripheral Arterial Disease (PAD) is a leading cause of major lower-extremity amputation, particularly in patients with severe ischemia, gangrene, infection, or when revascularization is no longer feasible. Preoperative blood lactate is a biomarker reflecting tissue hypoperfusion and systemic metabolic stress, but its prognostic role in predicting postoperative wound complications and mortality after major amputation in PAD remains limited. Methods: This was an analytic observational study with a prospective cohort design conducted at Dr. Hasan Sadikin General Hospital between November 2024 and November 2025. Adult patients with PAD who underwent major amputation were enrolled using total sampling. Preoperative lactate levels were categorized into <2.5, 2.5–4, and >4 mmol/L, and associations with postoperative wound complications and mortality were analyzed using Fisher's Exact test. Results: A total of 51 patients met the study criteria; 60.8% were male and 52.9% were older than 60 years. Diabetes mellitus was the most common comorbidity (64.7%). Postoperative wound complications occurred in all patients with lactate >4 mmol/L, compared with 16 of 44 patients with lactate <2.5 mmol/L ($p = 0.016$). Mortality occurred in 4 of 5 patients with lactate >4 mmol/L, compared with 7 of 43 patients with lactate <2.5 mmol/L ($p = 0.001$). Discussion: Preoperative blood lactate is significantly associated with postoperative wound complications and mortality following major amputation in patients with PAD. Elevated lactate, particularly >4 mmol/L, identifies patients with worse postoperative outcomes, supporting its use as a simple, rapid, and accessible biomarker for perioperative risk stratification.

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Corresponding Author:

Teguh Marfen Djajakusumah,
Division of Vascular and Endovascular Surgery, Faculty of Medicine,
Padjadjaran University/Dr. Hasan Sadikin General Hospital,
Jl. Pasteur No. 38, Bandung 40161, Indonesia.
Email: marfen.djajakusumah@gmail.com

1. INTRODUCTION

Peripheral artery disease (PAD) is a progressive manifestation of systemic atherosclerosis characterized by chronic arterial insufficiency in the lower extremities. This disease affects more than 230 million people worldwide and is a leading cause of disability, reduced quality of life, and cardiovascular mortality (Criqui & Aboyans, 2015; Fowkes et al., 2017; Kullo & Rooke, 2016). As the disease progresses, many patients develop chronic limb-threatening ischemia (CLTI), the most severe stage of PAD characterized by ischemic rest pain, tissue loss, infection, and a high risk of major lower extremity amputation despite advances in revascularization techniques (Campia et al., 2019; Farber & Eberhardt, 2016). Major amputation remains an unavoidable treatment option for patients with non-salvageable limbs and is closely associated with significant postoperative morbidity, prolonged hospitalization, reduced functional status, and high short- and long-term mortality rates (Fortington et al., 2013; Moxey et al., 2011).

The success of postoperative recovery following major amputation depends heavily on adequate tissue perfusion and oxygen delivery. Chronic ischemia in patients with PAD disrupts microvascular circulation, exacerbates inflammatory and immune responses, reduces collagen synthesis, and slows wound healing, thereby increasing the risk of surgical site infection (SSI) and wound dehiscence (Bucataru et al., 2023; Sandy-Hodgetts et al., 2015; Zhang et al., 2021). These complications often require prolonged antibiotic therapy, revision surgery, increased healthcare costs, and may potentially increase postoperative mortality (Al-Saadi et al., 2024; Dutronc et al., 2013). Therefore, the identification of objective biomarkers that accurately reflect tissue perfusion and predict poor postoperative outcomes is of great clinical importance.

In perioperative risk stratification, various biomarkers such as inflammatory markers (C-reactive protein, white blood cell count, or procalcitonin) and nutritional indicators (such as serum albumin) are frequently used. However, these parameters tend to be nonspecific, are easily influenced by the systemic acute-phase response, and do not directly reflect the dynamics of tissue perfusion. In contrast, blood lactate is a pathophysiologically validated biomarker for directly assessing tissue hypoperfusion and anaerobic metabolism (Li et al., 2022). When oxygen delivery to tissues is impaired due to microarterial insufficiency, pyruvate is preferentially converted to lactate via anaerobic glycolysis, resulting in lactate accumulation in the circulation. Lactate levels offer a mechanistic advantage because they accurately reflect the imbalance between systemic/local oxygen delivery and tissue metabolic demand in real time. In addition to these pathophysiological advantages, preoperative blood lactate testing is rapid (point-of-care), affordable, easily accessible through routine blood gas analysis, and provides an objective indicator of a patient's physiological reserve prior to surgery (Krähenbühl, 1980). In critical conditions, trauma, sepsis, and major vascular surgery, hyperlactatemia has consistently been shown to be associated with organ dysfunction and mortality (Ivashkiv, 2020; Kushimoto et al., 2016; ter Avest et al., 2020).

Several studies have shown that elevated preoperative and perioperative lactate levels predict postoperative mortality following major lower extremity amputation (Husain et al., 2017; Nair et al., 2020). Nevertheless, there is a fundamental scientific gap in previous studies. Most of the literature focuses exclusively on systemic mortality outcomes (He et al., 2023; Kong et al., 2023), whereas scientific evidence regarding the association between preoperative lactate levels and local surgical site complications—particularly wound dehiscence and SSI—remains very limited and inconsistent (Marcarelli et al., 2017; Muller-Sloof et al., 2024). However, in PAD patients with complex comorbidities such as diabetes mellitus and severe infections, tissue hypoperfusion as reflected by lactate levels has the potential to be a key determinant of surgical wound healing failure (Septiani et al., 2021; Yunir et al., 2022). Furthermore, empirical evidence from the Southeast Asian population remains extremely scarce, even though the clinical characteristics of patients in this region are often characterized by delayed presentation (late presentation with severe gangrene) and a different comorbidity profile compared to Western cohorts.

Clarifying the prognostic value of preoperative blood lactate levels in patients undergoing major amputation could strengthen perioperative risk stratification, facilitate early detection of patients at high risk for postoperative complications, and support more personalized perioperative management (Aitken et al., 2020; Thorud et al., 2016). Therefore, this prospective cohort study aims to evaluate the association between preoperative blood lactate levels and postoperative wound complications (specifically surgical site infections and wound dehiscence) as well as postoperative mortality in PAD patients undergoing major lower extremity amputation at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.

2. RESEARCH METHOD

This prospective cohort study was conducted at the Division of Vascular and Endovascular Surgery, Dr. Hasan Sadikin Central General Hospital (RSUP), Bandung, Indonesia, from November 2024 to November 2025. The aim of this study was to evaluate the association between preoperative blood lactate levels and postoperative wound complications as well as mortality in patients with peripheral arterial disease (PAD) undergoing major lower extremity amputation.

Adult patients (≥18 years) diagnosed with PAD based on clinical findings and/or imaging and who underwent elective or emergency major lower extremity amputation (below-knee or above-knee) during the study period were eligible for inclusion. Sampling was conducted using consecutive total sampling among all patients who met the criteria. Patients were excluded if they had conditions known to significantly affect blood lactate concentrations beyond ischemia/perfusion factors, including severe liver dysfunction (due to reduced lactate clearance), a history of seizures prior to lactate measurement, or current use of medications that induce hyperlactatemia (such as salbutamol, terbutaline, or epinephrine). Patients with a history of previous amputation within the same study period or those who had undergone massive resuscitation or intensive care prior to preoperative lactate measurement were also excluded to minimize distortion of baseline measurements.

Baseline demographic and clinical characteristics were recorded prospectively using a standardized case report form. Potential confounding factors collected included age, sex, systemic comorbidities (diabetes mellitus, hypertension, and cardiovascular disease), amputation level (above-knee vs. below-knee), and surgical indications (such as a dead limb/gangrene or a danger limb due to severe infection) (Aitken et al., 2020; Septiani et al., 2021; Yunir et al., 2022; Zhang et al., 2021). Control of metabolic and exogenous confounding factors was achieved through strict exclusion criteria, while comorbidities and clinical variables were measured in a structured manner to assess their distribution in relation to postoperative outcomes. Preoperative arterial blood lactate levels were measured immediately before surgery from arterial blood samples collected as part of routine perioperative evaluation. All patients were then followed up during their hospital stay to evaluate postoperative outcomes.

The primary outcomes of this study were postoperative wound complications and all-cause postoperative mortality. Postoperative wound complications included surgical site infection (SSI) and wound dehiscence diagnosed during the index hospitalization based on clinical examination by the attending surgical team (Kolasiński, 2018). Mortality is defined as death from any cause occurring during the postoperative hospital stay. The primary independent variable is preoperative blood lactate concentration, which was categorized for categorical analysis into three groups: <2.5 mmol/L, 2.5–4.0 mmol/L, and >4.0 mmol/L. This categorization is based on thresholds for physiological and clinical risk stratification that have been extensively validated in the critical care and surgical literature (Husain et al., 2017; Kruse et al., 2011; Kushimoto et al., 2016). Values <2.5 mmol/L represent the normal physiological range to minimal elevation; the 2.5–4.0 mmol/L range reflects mild–moderate hyperlactatemia or compensated tissue hypoperfusion (gray zone); while >4.0 mmol/L constitutes a critical threshold indicating severe tissue hypoperfusion, high anaerobic metabolic stress, and a significantly increased risk of organ failure and death (He et al., 2023; Kong et al., 2023; Nair et al., 2020).

Continuous variables were tested for normality using the Shapiro–Wilk test. Normally distributed variables are presented as mean ± standard deviation (SD), while non-normally distributed variables are presented as median with interquartile range (IQR). Categorical variables are presented as frequencies and percentages. The relationship between preoperative lactate categories and early postoperative outcomes was initially evaluated using the chi-square test. If the expected cell count was less than five, Fisher's exact test was applied. A two-tailed p-value <0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics software, version 26.0. This study received ethical approval from the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital, Bandung.

3. RESULTS AND DISCUSSION

A total of 51 consecutive patients with peripheral artery disease (PAD) who underwent major lower extremity amputation between November 2024 and November 2025 were prospectively enrolled. The majority of patients were male (31/51, 60.8%), while females accounted for 39.2% of the cohort. More than half of the patients were over 60 years of age (52.9%). Diabetes mellitus was the most common comorbidity (64.7%), followed by hypertension (41.2%) and cardiovascular disease (19.6%). Above-knee amputation was performed in 58.8% of patients, while 41.2% underwent below-knee amputation. Elevated preoperative blood lactate levels were identified in 9 patients (17.6%), while the remaining 42 patients (82.4%) had normal lactate concentrations. The primary indication for amputation was gangrene (78.4%), followed by limb threat due to severe infection (33.3%). Postoperative wound complications included surgical site infection (SSI) in 12 patients (23.5%) and necrotic stump in 1 patient (1.9%). Postoperative mortality occurred in 10 patients (19.6%), while 41 patients (80.4%) survived. Detailed characteristics of the study population are summarized in Table 1.

Table 1. Characteristics of the Study Population

Variable	n	%
Sex		
Male	31	60.8
Female	20	39.2
Age		
< 60 years	24	47.1
> 60 years	27	52.9
Comorbidities		
Diabetes mellitus	33	64.7
Hypertension	21	41.2
Heart disease	10	19.6
Preoperative Blood Lactate Level		
Normal (≤2.5 mmol/L)	42	82.4
Elevated (>2.5 mmol/L)	9	17.6
Level of Amputation		
Above-knee	30	58.8
Below-knee	21	41.2
Indication for Amputation		
Dead limb / gangrene	40	78.4
Danger limb / infection	17	33.3
Postoperative Wound Complication		
Surgical site infection	12	23.5
Necrotic stump	1	1.9
Postoperative Mortality		
Survived	41	80.4
Died	10	19.6

Table 2 presents the association between preoperative lactate level and postoperative wound complications. A statistically significant association was observed between preoperative blood lactate concentration and postoperative wound complications. Patients with severe hyperlactatemia (>4 mmol/L) experienced wound complications in 100% of cases (4 of 4 patients). In contrast, no wound complications occurred among patients with lactate concentrations between 2.5 and 4.0 mmol/L, whereas 16 of 44 patients with lactate concentrations below 2.5 mmol/L developed postoperative wound complications. The incidence of postoperative wound complications increased progressively with increasing preoperative lactate concentration. Fisher's exact test demonstrated a significant association between elevated lactate levels and postoperative wound complications (p = 0.016), indicating that patients presenting with higher preoperative lactate concentrations were at substantially greater risk of impaired postoperative wound healing.

Table 2. Association between preoperative lactate level and postoperative wound complications

Preoperative Lactate Level	Wound Complication: Yes	Wound Complication: No	p-value
> 4 mmol/L	4	0	
2.5 – 4 mmol/L	0	3	
< 2.5 mmol/L	16	28	0.016

Table 3. Association between preoperative lactate level and postoperative mortality

Preoperative Lactate Level	Mortality: Yes	Mortality: No	p-value
> 4 mmol/L	4	1	
2.5 – 4 mmol/L	1	2	
< 2.5 mmol/L	7	36	0.001

Table 3 presents the association between preoperative lactate level and postoperative mortality. Preoperative hyperlactatemia was significantly associated with postoperative mortality following major lower-extremity amputation. Mortality was highest among patients with lactate levels >4 mmol/L, occurring in 4 of 5 patients, compared with 1 of 3 patients in the lactate 2.5–4 mmol/L group and 7 of 43 patients in the lactate <2.5 mmol/L group. Fisher's exact test confirmed a significant relationship between elevated preoperative lactate and postoperative mortality (p = 0.001), suggesting that serum lactate reflects systemic hypoperfusion and physiological derangement before surgery.

Collectively, these findings demonstrate that preoperative blood lactate is significantly associated with both postoperative wound complications and mortality in patients undergoing major lower-extremity amputation for PAD. Patients presenting with elevated lactate levels experienced worse postoperative outcomes than those with normal lactate concentrations, supporting the role of serum lactate as a readily available perioperative prognostic biomarker (Husain et al., 2017; Kong et al., 2023; Nair et al., 2020).

The results of this study are consistent with and expand upon previous literature findings regarding the prognostic role of lactate. Regarding mortality outcomes, our finding showing a strong association between high lactate levels and postoperative death (p = 0.001) is highly consistent with reports from vascular surgery and critical care cohorts in Western countries (Husain et al., 2017; Nair et al., 2020). Studies by (Husain et al., 2017; Nair et al., 2020) confirmed that perioperative hyperlactatemia is an independent predictor of postoperative mortality in major vascular surgery. Similar trends were also reported by (He et al., 2023; Kong et al., 2023) in critical care and trauma populations, confirming that a lactate threshold >4 mmol/L reflects a point of systemic physiological failure. However, a significant difference is observed in the evaluation of local wound complications. While most previous studies focused exclusively on systemic mortality or organ dysfunction (He et al., 2023; Kong et al., 2023; Kruse et al., 2011), evidence regarding the association between lactate and local complications such as wound dehiscence and SSI remains very limited and inconsistent in the vascular surgery literature (Marcarelli et al., 2017; Muller-Sloof et al., 2024; Zhang et al., 2021). In our study, all patients (100%) with lactate levels >4 mmol/L experienced postoperative wound complications. The novelty of this finding demonstrates that preoperative lactate serves not only as a marker of systemic survival but also as a sensitive predictor of local microvascular healing failure at the amputation stump. This difference in complication rates can be explained by the high burden of comorbid diabetes mellitus (64.7%) and the severity of tissue ischemia/infection in our study population in Indonesia compared to Western cohorts (Septiani et al., 2021; Yunir et al., 2022).

The physiological rationale for these findings is closely linked to the role of lactate as a direct biomarker of tissue hypoperfusion and anaerobic glycolysis. In patients with advanced PAD and CLTI, the combination of chronic arterial occlusion and secondary infection reduces microvascular oxygen delivery to distal tissues. When oxygen supply fails to meet cellular metabolic demands, lactate accumulates (Blaisdell, 2002; Li et al., 2022). This persistent tissue hypoxia inhibits collagen synthesis, impairs local immune phagocytosis, and slows epithelialization, which directly triggers the onset of surgical site infections (SSIs) and post-amputation wound dehiscence (Bucataru et al., 2023; Khalil et al., 2006; Sandy-Hodgetts et al., 2015).

The findings of this study have important clinical implications for translating perioperative risk stratification into everyday surgical practice (Aitken et al., 2020; Thorud et al., 2016): (1) Implementation of Rapid Screening Tools (Point-of-Care Testing): Preoperative lactate testing can be integrated as a standard routine test through blood gas analysis prior to major amputation procedures. Because it is quick and inexpensive, the lactate level provides an objective indication of the patient's physiological reserve in real time. (2) Lactate-Based Stratified Management Protocol; (a) High-Risk Category (>4.0 mmol/L), patients in this group are at risk for severe wound complications (100%) and have a very high mortality rate (80%). In this group, non-emergency surgery should be postponed briefly, if possible, to allow for targeted hemodynamic optimization, correction of dehydration/hypovolemia, administration of oxygen therapy, and aggressive control of the source of infection. Patients should also be prioritized for intensive monitoring in the ICU or High Dependency Unit postoperatively, as well as stricter wound care protocols. (b) Moderate Risk Category (2.5–4.0 mmol/L), requires monitoring of systemic perfusion and strict preoperative optimization of diabetes and cardiovascular comorbidities. (c) Low Risk Category (<2.5 mmol/L), patients can be managed using standard postoperative care protocols. (3) Multidisciplinary Decision-Making and Patient Counseling: Preoperative lactate levels provide an objective quantitative measure to help the multidisciplinary team (vascular surgery, critical care, anesthesia, and metabolic-endocrinology) plan the level of postoperative care, as well as facilitate honest and transparent communication with the patient's family regarding the risks of wound complications and death before surgery is performed.

This study has several limitations. The single-center design and relatively small sample size—particularly in the group with severe lactate elevation—may limit the precision of the effect estimates. Nevertheless, the consistent and statistically significant associations for both primary outcomes underscore the potential clinical utility of preoperative blood lactate as an affordable prognostic biomarker.

4. CONCLUSION

Preoperative blood lactate levels are a simple, objective, and clinically accessible biomarker for predicting postoperative outcomes in patients with peripheral arterial disease (PAD) undergoing major lower extremity amputation. Elevated preoperative lactate levels, particularly those >4.0 mmol/L, are significantly associated with an increased incidence of postoperative wound complications and postoperative mortality.

The key contribution of this study lies in expanding the scope of perioperative risk stratification in PAD patients undergoing major amputation. This study demonstrates that preoperative blood lactate levels serve not only as a marker of systemic mortality but also as a sensitive indicator of the development of local postoperative wound complications, such as surgical site infections (SSIs) and wound dehiscence. Furthermore, this study provides crucial empirical evidence from the Southeast Asian population—a region with specific clinical characteristics, including a high prevalence of diabetes mellitus and a phenomenon of late presentation with gangrene and severe infections—which has been underrepresented in the global vascular surgery literature. Thus, this study reinforces the role of preoperative lactate as an objective, point-of-care screening tool for identifying high-risk patients prior to surgery.

Based on these findings, several practical recommendations for the implementation of preoperative lactate testing in clinical practice include: (1) Integration into Routine *Point-of-Care* Testing. Blood lactate testing via arterial blood gas analysis is recommended as a standard component of routine preoperative evaluation for all PAD patients scheduled to undergo major amputation. (2) Implementation of a *Tiered Clinical Pathway*; (a) Lactate >4.0 mmol/L (High Risk): Indicates a brief postponement of non-emergency surgery (if possible) to allow for fluid resuscitation and targeted hemodynamic optimization, administration of broad-spectrum antibiotics, as well as postoperative allocation to an intensive care unit (ICU/High Dependency Unit) and extra-strict wound monitoring. (b) Lactate 2.5–4.0 mmol/L (Moderate Risk): Requires monitoring of microvascular circulation and strict metabolic control. (c) Lactate <2.5 mmol/L (Low Risk): Standard postoperative care protocols are applied. (3) *Multidisciplinary Decision-Making and Counseling*. Use preoperative lactate levels as an objective indicator to facilitate multidisciplinary team discussions (vascular surgery, anesthesia, critical care) and to explicitly convey information regarding the risk of complications and mortality to patients and their families.

To improve the internal validity, external validity, and generalizability of these findings in the future, the following directions for further research are recommended: (1) Prospective Multicenter Study. Conduct a multicenter study involving a larger sample size to externally confirm and validate lactate cutoff values across various patient populations. (2) Dynamic Lactate Clearance Monitoring. Measure lactate levels serially (preoperative, intraoperative, and postoperative) to assess the dynamics of lactate clearance and the effectiveness of resuscitation measures in improving tissue perfusion. (3) Advanced Multivariate Adjustment Analysis: Applying multivariate modeling to account for various complex confounding variables, such as the severity of sepsis, prior revascularization status, and the degree of glycemic control.

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