

ORIGINAL RESEARCH

Risk Factors Associated with In-hospital Poor Outcomes in Patients with Acute Limb Ischemia

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ABSTRACT

Background: Acute limb ischemia (ALI) is a vascular emergency characterized by a sudden reduction in limb perfusion, most commonly resulting from thromboembolism or thrombosis at the site of an atherosclerotic plaque. This study aimed to analyze and identify risk factors associated with major amputation and in-hospital mortality in patients with ALI.

Material and methods: We retrospectively analyzed 177 patients diagnosed with upper or lower limb ALI admitted to the Vascular Surgery Clinic between January 2019 and December 2024. Data collected from electronic medical records included demographic variables, cardiovascular comorbidities, chronic kidney disease, diabetes mellitus, malignancies, preoperative laboratory parameters (within the first 12 h of admission), type of surgical intervention, and anesthesia type. **Results:** Patients with lower limb ischemia were significantly older than those with upper limb involvement ($p = 0.041$). Lower limb ischemia was also associated with a higher prevalence of ischemic heart disease ($p = 0.030$), chronic heart failure ($p = 0.013$), and peripheral arterial disease ($p < 0.001$). Laboratory findings revealed lower red blood cell counts ($p = 0.034$), hemoglobin ($p = 0.010$), and hematocrit ($p = 0.011$), along with higher creatine kinase ($p = 0.013$), neutrophil ($p = 0.017$), and monocyte levels ($p = 0.034$) in patients with lower limb ALI. While surgical intervention types did not differ significantly, lower limb ALI patients underwent local anesthesia less frequently ($p < 0.001$) and general anesthesia more frequently ($p < 0.001$). Univariate analysis identified peripheral arterial disease (OR: 2.45, $p = 0.046$) as a predictor of major amputation, while chronic heart failure (OR: 2.77, $p = 0.033$), prior myocardial infarction (OR: 3.85, $p = 0.024$), and diabetes mellitus (OR: 3.23, $p = 0.012$) were significantly associated with in-hospital mortality. **Conclusions:** These findings highlight the critical role of aggressive cardiovascular risk factor management in patients with ALI to improve outcomes following surgical revascularization.

Keywords: acute limb ischemia, major amputation, mortality, vascular surgery, open revascularization

ARTICLE HISTORY

Received: February 12, 2024

Accepted: May 5, 2025

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INTRODUCTION

Acute limb ischemia (ALI) is a vascular emergency characterized by a sudden reduction in limb perfusion, most commonly caused by thromboembolism or in situ thrombosis over an atherosclerotic plaque.^{1–4} In recent years, various minimally invasive treatment methods have been proposed, including catheter-directed thrombolysis (CDT),⁵ percutaneous thromboaspiration,⁶ and percutaneous mechanical thrombectomy.⁷ However, the reported results have been inconsistent. Furthermore, a meta-analysis by Enezate *et al.*,⁸ which included six clinical trials, compared the short- and medium-term outcomes of endovascular versus surgical interventions and found no significant differences in postoperative results. Notably, during the COVID-19 pandemic, an increase in thromboembolic events and ALI cases has been reported.^{9–12}

Several risk factors have been associated with poor outcomes after revascularization, including advanced clinical stages,^{13,14} elevated systemic inflammation,^{13–17} heart failure,¹⁷ and renal failure.¹⁷ Although multiple biomarkers have been investigated for their potential to predict short- and long-term outcomes in patients with ALI, none have yet been integrated into clinical practice.^{13–17}

The primary aim of this study was to identify and analyze risk factors associated with major amputation and in-hospital mortality among patients with ALI.

METHODS

STUDY DESIGN

This study included all patients diagnosed with ALI of the upper or lower extremities who were admitted to the Vascular Surgery Clinic of Târgu Mureș County Emergency Clinical Hospital between January 2019 and December 2024. Patients who did not undergo open surgery or had incomplete clinical data were excluded. Due to its negative impact on outcomes,^{9–12,18–22} patients diagnosed with COVID-19 at admission were also excluded. A total of 177 patients met the inclusion criteria, of whom 60 (33.89%) were diagnosed with upper limb ALI and 117 (66.11%) with lower limb ALI.

DATA COLLECTION

Data were collected retrospectively from the hospital's electronic medical records and included demographic variables (age, sex), cardiovascular comorbidities, chronic kidney disease, diabetes mellitus, malignancies, and

other common risk factors. Preoperative laboratory results obtained within the first 12 h of admission were also recorded. Additionally, the type of surgical intervention (embolectomy, endarterectomy, or bypass) and the type of anesthesia (local, regional block, or general anesthesia) were documented. All patients underwent preoperative computed tomography angiography (CTA), from which the occluded arteries were identified.

STUDY ENDPOINTS

The primary endpoints were the incidence of major amputation, defined as any amputation above the ankle, and in-hospital mortality.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS v.29.0.2.0 (SPSS). Continuous variables were expressed as mean \pm s.d., and categorical data as frequencies and percentages. The chi-squared test was used to compare categorical variables between patients with upper and lower limb ischemia, and the Mann-Whitney U test and Student's t-test were used to compare continuous variables. Univariate analysis was conducted to identify risk factors associated with in-hospital major amputation and mortality.

RESULTS

In total, 177 patients were enrolled in the study, with a mean age of 71.37 ± 14.48 years, comprising 90 men (50.85%) and 87 women (49.15%). The most common comorbidity was hypertension, present in 133 patients (75.14%), followed by ischemic heart disease in 88 patients (49.72%), atrial fibrillation in 77 patients (43.50%), and diabetes mellitus in 50 patients (28.25%) (Table 1). Regarding surgical interventions, 156 patients (88.14%) underwent embolectomy using a Fogarty catheter, 14 patients (7.91%) required bypass grafting, and 7 patients (3.95%) underwent endarterectomy. In terms of anesthesia, the majority of patients (56.50%) received general anesthesia, one-third (33.33%) underwent local anesthesia, and 6.12% received regional block anesthesia. During hospitalization, 27 patients (15.25%) underwent major amputation, and 22 patients (12.43%) died (Table 1).

We observed that patients with lower limb ALI were significantly older than those with upper limb ALI (73.0 ± 14.19 vs. 68.21 ± 14.63 years; $p = 0.041$). Additionally, patients with lower limb ALI had a higher prevalence of ischemic heart disease (55.56% vs. 38.33%; $p = 0.030$),

TABLE 1. Baseline characteristics of the study population, based on the location of ALI

Variable	All patients (n = 177)	Upper limb (n = 60)	Lower limb (n = 117)	p value
Age, mean ± s.d.	71.37 ± 14.48	68.21 ± 14.63	73.0 ± 14.19	0.041
Male, n (%)	90 (50.85%)	32 (53.33%)	58 (49.57%)	0.636
Comorbidities and risk factors, n (%)				
Hypertension	133 (75.14%)	44 (73.33%)	89 (76.07%)	0.690
Ischemic heart disease	88 (49.72%)	23 (38.33%)	65 (55.56%)	0.030
Chronic heart failure	40 (22.60%)	7 (11.67%)	33 (28.21%)	0.013
Chronic kidney disease	31 (17.51%)	8 (13.33%)	23 (19.66%)	0.295
Peripheral arterial disease	39 (22.03%)	3 (5.00%)	36 (30.77%)	<0.001
Atrial fibrillation	77 (43.50%)	22 (36.67%)	55 (47.01%)	0.189
Diabetes	50 (28.25%)	12 (20.0%)	38 (32.48%)	0.138
History of myocardial infarction	16 (9.04%)	3 (5.00%)	13 (11.11%)	0.180
History of stroke	26 (14.69%)	8 (13.33%)	18 (15.38%)	0.715
Malignancy	17 (9.60%)	6 (10.00%)	11 (9.40%)	0.898
Active smoking	34 (19.21%)	11 (18.33%)	23 (19.66%)	0.832
Dyslipidemia	25 (14.12%)	10 (16.67%)	15 (12.82%)	0.487
Laboratory data, median (Q1–Q3)				
WBCs	11.11 (8.34–13.75)	10.60 (8.25–12.56)	11.41 (8.51–14.41)	0.167
Red blood cells	4.47 (4.01–4.85)	4.63 (4.16–4.96)	4.37 (3.97–4.79)	0.034
K, mmol/l	4.15 (3.78–4.61)	4.14 (3.81–4.71)	4.16 (3.78–4.55)	0.843
Na, mmol/l	140 (137–142)	141 (138–142)	140 (137–142)	0.293
Glucose, mg/dl	118.0 (98.0–164.9)	111.0 (95.0–141.95)	121.0 (100.0–169.75)	0.100
Urea, mg/dl	42.80 (32.1–59.92)	44.94 (31.35–60.46)	42.40 (34.24–59.71)	0.849
Creatinine, mg/dl	0.95 (0.78–1.33)	0.97 (0.78–1.21)	0.93 (0.79–1.37)	0.929
Creatin kinase	277.5 (88.6–1920.25)	159.0 (86.2–481.0)	500.0 (100.0–3079.0)	0.013
Hemoglobin, g/dl	13.38 (11.9–14.58)	14.10 (12.3–15.45)	13.10 (11.8–14.3)	0.010
Hematocrit, %	40.51 (36.9–43.9)	41.86 (38.61–46.0)	40.10 (35.99–42.93)	0.011
Neutrophils, × 10 ³ /μl	8.91 (5.69–11.49)	7.57 (5.39–10.05)	9.34 (5.94–12.07)	0.017
Lymphocytes, × 10 ³ /μl	1.70 (1.21–2.29)	1.66 (1.14–2.32)	1.72 (1.29–2.24)	0.858
Monocytes, × 10 ³ /μl	0.75 (0.55–1.08)	0.68 (0.51–0.87)	0.80 (0.59–1.12)	0.034
Platelets, × 10 ³ /μl	234.70 (188.5–310.0)	231.0 (191.0–279.5)	238.0 (188.25–334.0)	0.207
Surgical interventions, n (%)				
Embolectomy	156 (88.14%)	51 (85.00%)	104 (89.74%)	0.356
Endarterectomy	7 (3.95%)	1 (1.67%)	6 (5.13%)	0.263
Bypass	14 (7.91%)	2 (3.33%)	12 (10.26%)	0.106
Anesthesia, n (%)				
Local anesthesia	59 (33.33%)	38 (63.33%)	21 (17.95%)	<0.001
Regional block anesthesia	11 (6.21%)	1 (1.67%)	10 (8.55%)	0.053
General anesthesia	100 (56.50%)	15 (25.00%)	85 (72.65%)	<0.001
Major amputation, n (%)	27 (15.25%)	4 (6.67%)	23 (19.66%)	0.023
In-hospital mortality, n (%)	22 (12.43%)	4 (6.67%)	18 (15.38%)	0.096
Length of stay, days, mean ± s.d.	6.78 ± 8.96	4.37 ± 3.35	8.02 ± 10.56	<0.001

BUN, blood urea nitrogen; GFR, glomerular filtration rate; GOT, glutamic oxaloacetic transaminase; GPT, glutamate-pyruvate transaminase; INR, international normalized ratio

chronic heart failure (28.21% vs. 11.67%; $p = 0.013$), and peripheral arterial disease (30.77% vs. 5.0%; $p < 0.001$) (Table 1). Regarding laboratory parameters, patients with lower limb ALI had significantly red blood cell count ($p = 0.034$), hemoglobin ($p = 0.010$), and hematocrit ($p = 0.011$), along with higher levels of creatin kinase ($p = 0.013$), neu-

trophils ($p = 0.017$), and monocytes ($p = 0.034$) (Table 1). Although the types of surgical interventions did not differ significantly between groups, patients with lower limb ALI underwent local anesthesia less frequently (17.95% vs. 63.33%; $p < 0.001$) and general anesthesia more frequently (72.65% vs. 25.0%; $p < 0.001$).

TABLE 2. Characterization of thrombosed arterial segments in patients with ALI affecting both upper and lower extremities

Upper limb (n = 60), n (%)	
Subclavian artery	6 (10.0%)
Axillary artery	15 (25.0%)
Brachial artery	45 (75.0%)
Radial artery	32 (53.33%)
Ulnar artery	30 (50.0%)
1 artery involved	21 (35.0%)
>1 artery involved	39 (65.0%)
>2 arteries involved	27 (45.0%)
>3 arteries involved	5 (8.33%)
Lower limb (n = 117), n (%)	
Common iliac artery	20 (17.09%)
External iliac artery	25 (21.36%)
Common femoral artery	49 (41.88%)
Superficial femoral artery	88 (75.21%)
Profunda femoral artery	33 (28.20%)
Popliteal artery	95 (81.19%)
1 artery involved	25 (21.37%)
>1 artery involved	92 (78.63%)
>2 arteries involved	58 (49.57%)
>3 arteries involved	32 (27.35%)
>4 arteries involved	9 (7.69%)

Regarding thrombosis localization, in the upper limb, the brachial artery was most commonly affected, with involvement in 45 patients (75.0%), followed by the radial artery in 32 patients (53.33%) and again the radial artery

TABLE 4. Risk factors associated with in-hospital mortality following open revascularization in patients with ALI

Variables	In-hospital mortality		
	OR	95% CI	p value
Age	1.14	0.72–1.82	0.573
Ischemic heart disease	1.92	0.76–4.82	0.168
Chronic heart failure	2.77	1.08–7.06	0.033
Peripheral arterial disease	0.52	0.15–1.86	0.317
History of myocardial infarction	3.85	1.19–12.41	0.024
Diabetes mellitus	3.23	1.29–8.03	0.012
WBCs	1.51	1.02–2.24	0.041
Neutrophils	1.98	1.32–2.97	<0.001
Lymphocytes	0.58	0.34–0.98	0.042
Monocytes	1.19	0.79–1.80	0.399
Platelets	1.37	0.91–2.06	0.128
Upper limb ALI	0.39	0.13–1.22	0.106

TABLE 3. Risk factors associated with major amputation following open revascularization in patients with ALI

Variables	Major amputation		
	OR	95% CI	p value
Age	0.92	0.61–1.37	0.674
Ischemic heart disease	1.32	0.58–3.01	0.511
Chronic heart failure	0.74	0.26–2.12	0.583
Peripheral arterial disease	2.45	1.02–5.92	0.046
History of myocardial infarction	0.77	0.16–3.63	0.749
Diabetes mellitus	1.16	0.48–2.79	0.729
WBCs	1.92	1.29–2.85	0.001
Neutrophils	1.44	0.98–2.12	0.057
Lymphocytes	1.14	0.75–1.73	0.536
Monocytes	1.67	1.15–2.43	0.007
Platelets	1.51	1.04–2.21	0.031
Upper limb ALI	0.29	0.09–0.88	0.030

in 30 patients (50.0%). Thrombosis of the axillary artery occurred in 15 patients (25.0%) and of the subclavian artery in 6 patients (10.0%) (Table 2). In the lower limb, the popliteal artery was most frequently involved, affecting 95 patients (81.19%), followed by the superficial femoral artery in 88 patients (75.21%) and the common femoral artery in 49 patients (41.88%). Thrombosis also involved the deep femoral artery in 33 patients (28.20%), the external iliac artery in 25 patients (21.36%), and the common iliac artery in 20 patients (17.09%) (Table 2).

Furthermore, univariate analysis identified several predictive factors associated with major amputation and in-hospital mortality. As shown in Table 3, peripheral arterial disease (OR 2.45; $p = 0.046$), elevated baseline WBC count (OR 1.92; $p = 0.001$), increased monocyte levels (OR: 1.67, $p = 0.007$), and platelet count (OR 1.51; $p = 0.031$) were significantly associated with an increased risk of major amputation during hospitalization.

Regarding in-hospital mortality, univariate analysis revealed that chronic heart failure (OR 2.77; $p = 0.033$), history of myocardial infarction (OR 3.85; $p = 0.024$), and diabetes mellitus (OR 3.23; $p = 0.012$) were significantly associated with poor postoperative outcomes. In addition, elevated baseline WBC count (OR 1.51; $p = 0.041$) and neutrophil levels (OR 1.98; $p < 0.001$) were also predictive of mortality (Table 4).

DISCUSSION

This study investigated the risk factors linked to major amputation and in-hospital mortality in patients with

ALI affecting both upper and lower limbs. We provided a detailed analysis of the affected arterial segments, anesthesia methods, and surgical interventions performed at our center. Our short-term clinical outcomes, summarized in Table 1, revealed an amputation-free survival rate of 84.75% and a post-revascularization survival rate of 87.57%. Notably, among cardiovascular comorbidities, peripheral arterial disease was associated with an increased risk of major amputation, while chronic heart failure, previous myocardial infarction, and diabetes mellitus were correlated with higher in-hospital mortality rates. Therefore, stringent management of these comorbidities and preventive measures against their onset and progression might lower the long-term risk of ALI.

In a recent study published by El-Sayed *et al.*²³, the authors analyzed technical success, functional limb outcomes, and amputation risk in a cohort of 96 patients with upper limb ischemia, reporting a technical success rate of 76.4% and an in-hospital mortality rate of 7.3%. Similarly, in our cohort, patients with upper limb ischemia had a 6.67% rate of major amputation and in-hospital mortality. Additionally, Bae *et al.*²⁴ identified prolonged symptom duration (OR 1.251; $p = 0.046$) and elevated lactate dehydrogenase levels (OR 1.001; $p = 0.031$) as predictors of functional sequelae in patients with ALI. Regarding revascularization strategies in ALI, numerous studies have compared surgical, endovascular, and hybrid treatments, with inconsistent findings regarding short- and long-term benefits.^{25–30} While Taha *et al.*,²⁷ Kolte *et al.*,²⁸ and Grip *et al.*³⁰ reported a higher short-term amputation rate following open revascularization compared to endovascular treatment, Davis *et al.*²⁵ and Veenstra *et al.*²⁶ found no significant differences between the two approaches.

This study has several limitations. Firstly, it was conducted on a relatively small patient cohort from a single tertiary center, which may limit the generalizability of the findings. Future research should include prospective, multicenter studies to assess whether addressing the identified risk factors can improve long-term outcomes. Secondly, patient follow-up was restricted to the in-hospital period; we aim to extend this in future studies to incorporate medium- and long-term outcomes. Additionally, the study exclusively included patients who underwent surgical revascularization, excluding those treated with endovascular approaches. Consequently, our findings cannot be generalized to all patients with ALI, highlighting the need for additional studies with larger patient groups.

CONCLUSIONS

Poor outcomes following surgical revascularization for both upper and lower limb ischemia are strongly associated with underlying cardiovascular comorbidities, including peripheral arterial disease, chronic heart failure, diabetes mellitus, and prior myocardial infarction. These findings underscore the importance of aggressive management of cardiovascular risk factors in patients with ALI to improve outcomes following surgical revascularization.

CONFLICT OF INTEREST

Nothing to declare.

ETHICS APPROVAL

This research was carried out in accordance with the principles stated in the Declaration of Helsinki and was approved by the ethics committee of the County Emergency Clinical Hospital of Târgu Mureș, Romania (approval no. 4531/04.03.2025).

FUNDING

This work was supported by the George Emil Palade University of Medicine, Pharmacy, Science and Technology of Târgu Mureș, Romania (research grant no. 170/2/09.01.2024).

AUTHOR CONTRIBUTIONS

E-M.A. and M.C.C. conceptualized the study, developed the methodology, and prepared the original draft. E-M.A., A.M., and N.A.L. performed the formal analysis. E-M.A., A.M., N.A.L., I.G.B., R.B., L.A.S., and B.C.B. conducted the investigation. E-M.A., N.A.L., I.G.B., and M.T.C. curated the data. Eliza-M.A. performed review and editing. A.V.M. and E.R. created the visualizations, supervised the project, and managed project administration. All authors have read and approved the final version of the manuscript.

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