



# Risk factors and rates of revision amputation following ischemic lower major limb amputations: A 10-year retrospective analysis

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In recent years, conditions such as peripheral arterial disease (PAD) and diabetes mellitus (DM) have become the primary causes of lower limb amputations (LLAs) worldwide.<sup>[1]</sup> Peripheral arterial disease is encountered in 3 to 10% of the population, which increases to 15 to 20% in individuals over the age of 70.<sup>[2,3]</sup> This progressive condition results in amputation in 20 to 50% of these patients.<sup>[4,5]</sup>

Lower limb amputations profoundly impact patients and their families socially, psychologically, and economically. Notably, between 78 and 90% of LLAs in developed countries are attributed to PAD and DM.<sup>[4,6]</sup> Despite advancements in surgical and percutaneous interventions, as well as improvements in primary diabetic foot care, LLA remains a last resort option.<sup>[7]</sup>

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## ABSTRACT

**Objectives:** This study aimed to evaluate the rates and risk factors associated with revision amputation following ischemic lower major limb amputations, focusing on cases related to peripheral arterial disease.

**Patients and methods:** This retrospective study included 253 patients (174 males, 79 females; mean age: 73.1±12.2 years; range, 44 to 99 years) who underwent ischemic foot amputation between December 2012 and December 2022. Eligible patients were over 18 years old and had major lower extremity amputations due to peripheral arterial disease or chronic arterial occlusion. Exclusions were made for amputations due to diabetic foot conditions, trauma, tumors, or osteomyelitis and minor lower extremity amputations.

**Results:** Above-knee amputations were the most common type of amputation, accounting for 56.5% (n=143) of cases. Revision amputations occurred in 27.3% (n=69) of patients, with significantly higher rates in those with open wounds at first admission (chi-square [ $\chi^2$ ]=9.81, p=0.002). Patients with occlusion at the popliteal artery level had a higher rate of revision amputation following below-knee amputation (p=0.034). Each additional year of age decreased the likelihood of revision amputation by 2.3% (p=0.049). Vacuum-assisted closure therapy was associated with higher revision rates ( $\chi^2=22.71$ , p<0.001). Patients who developed infections (n=40) had a significantly higher rate of revision amputations (n=26, p<0.001). Elevated preoperative C-reactive protein levels were also correlated with an increased risk of revision (p=0.006).

**Conclusion:** Patients with ischemic lower limb amputations, particularly those presenting with open wounds, are at higher risk for revision amputation. Elevated preoperative C-reactive protein levels, infections, age, and the initial level of amputation significantly impact the likelihood of reamputation.

**Keywords:** Amputation, chronic limb threatening ischemia, reoperation, risk factors, peripheral arterial disease.

Peripheral arterial disease and DM often coexist and can influence each other's development. However, amputations due to DM typically involve minor amputations and have a distinct clinic compared to those due to PAD-related critical limb ischemia.<sup>[8]</sup> Current literature explores the effects of DM and PAD on the same LLA population.<sup>[9,10]</sup> Some studies have included all causes of amputation (traumatic, malignant, and infectious) in their analyses. Furthermore, the majority of the literature focuses predominantly on the diabetic foot population.<sup>[11]</sup>

As a result, it has been challenging to evaluate isolated PAD-related ischemia in terms of prognosis and revision amputations in the existing literature. This research gap is critical, considering the high morbidity and mortality rates associated with major amputations. Unplanned reoperations, linked to increased morbidity and hospital readmissions, directly affect the quality of postamputation care and the patient's quality of life.<sup>[12]</sup> Therefore, this study aimed to evaluate the rates and risk factors of revision amputation following ischemic major LLAs.

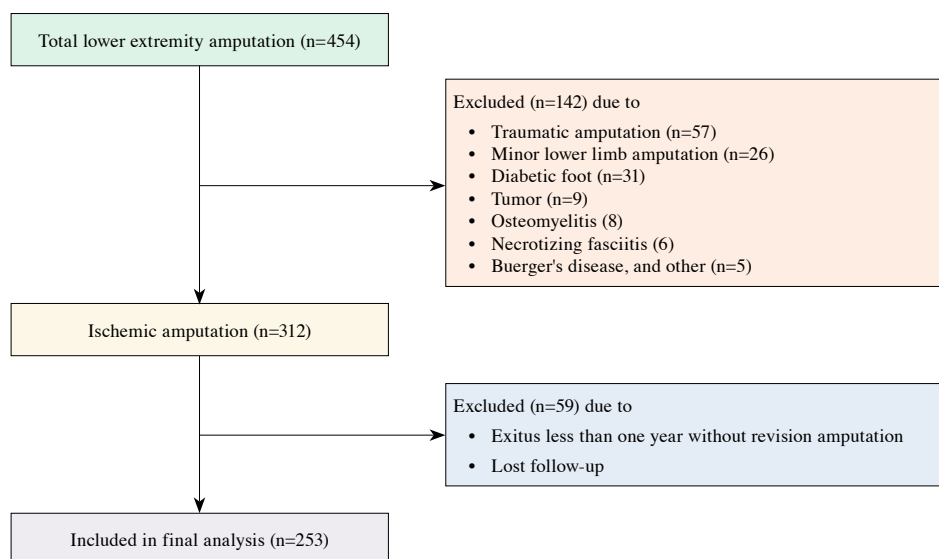
## PATIENTS AND METHODS

This retrospective study included 253 patients (174 males, 79 females; mean age: 73.1±12.2 years; range, 44 to 99 years) who underwent ischemic foot amputation at the Trakya University Faculty of Medicine between December 2012 and December 2022. The inclusion criteria were as follows: patients over 18 years of age who underwent major lower

extremity amputation due to underlying circulatory problems such as PAD or chronic arterial occlusion. The exclusion criteria were as follows: patients who underwent amputations due to diabetic foot conditions, traumatic amputation, tumors, osteomyelitis, necrotizing fasciitis, Buerger's disease, and minor lower extremity amputation. Patients who had less than one year of follow-up were also excluded. The flow chart for patient selection is shown in Figure 1. The study protocol was approved by the Trakya University Faculty of Medicine Non-Interventional Ethics Committee (date: 27.02.2023, no: 03/08). Written informed consent was obtained from all patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The demographic information of the patients, amputation levels, levels of vascular occlusion, vascular interventions, operation and consultation notes, laboratory information, comorbidities, preamputation mobilization levels, and the use of debridement and vacuum-assisted closure (VAC) were retrospectively collected from patient files and the hospital archive system.

By evaluating the consultation notes, whether the patients were ischemic and whether a vascular intervention was necessary before the operation were determined. Data on the presence of skin integrity disruption, necrosis, or open wounds in patients were collected, and the WIfI (wound, ischemia, and foot infection) classification score was completed. This classification is part of the Society for Vascular



**FIGURE 1.** Flowchart for patient selection.

Surgery lower extremity threatened limb classification system.

The level of primary amputation was determined by the orthopedic surgeon in consultation with a vascular surgeon, considering factors such as tissue viability, ischemic severity, and intraoperative findings, following a multidisciplinary approach to optimize patient outcomes.

The primary outcome measure was the occurrence of revision amputation, which we defined as a surgical procedure involving the removal of bone and other soft tissues at a level more proximal than the previous amputation site. Specifically, this involved an amputation performed at a higher anatomical level due to complications such as infection, necrosis, or poor healing of the residual limb. In cases where debridement and similar soft tissue procedures were deemed insufficient, a revision amputation was performed based on a consensus among the clinical team. Procedures that only addressed soft tissue issues without altering the bone level were excluded from this definition.

Major lower extremity amputations refer to those performed above the ankle level, including hip disarticulation, above-knee amputation (transfemoral), knee disarticulation, and below-knee amputation (transtibial).

#### Statistical analysis

Data were analyzed using IBM SPSS version 27.0 software (IBM Corp., Armonk, NY, USA) and R version 4.2.1 (R Foundation for Statistical Computing,

Vienna, Austria). The association between categorical variables was assessed using the chi-square ( $\chi^2$ ) test. Pairwise comparisons were conducted to determine the groups that showed significant differences based on the results of the  $\chi^2$  test. The Kaplan-Meier hazard function test was used to demonstrate the relationship between open wounds and the likelihood of undergoing a revision amputation within one year. Binary logistic regression was utilized to analyze the relationship between blood tests and the probability of revision amputation. A p-value <0.05 was considered statistically significant.

## RESULTS

The clinical characteristics are summarized in Table I. In the radiological evaluation presented, which included computed tomography angiography and Doppler ultrasonography, blood flow and arterial obstructions were assessed at the level of the ankle and the lower leg. Distal blood flow was observed in 12.6% of patients, while 54.5% had obstructions distal to the popliteal artery (Table II). A total of 108 patients underwent vascular intervention.

Patients with popliteal artery occlusion had higher revision rates after below-knee amputation (50%) compared to above-knee amputation (18.9%;  $\chi^2 [1, n=63]=4.495, p=0.034$ ). No significant differences were observed at other occlusion levels ( $p>0.005$ ).

The most common procedure performed on the patients was above-knee amputation, accounting for 56.5% ( $n=143$ ) of the cases, followed by below-knee

**TABLE I**  
Clinical characteristics and comorbidities in amputation patients ( $n=253$ )

|  | n   | %     |
|--|-----|-------|
| Open wound or necrosis at presentation                             | 143 | 56.5  |
| Cardiovascular outpatient clinic visit before amputation           | 199 | 78.7  |
| Vascular intervention before amputation (angioplasty, bypass etc.) | 107 | 42.63 |
| Anticoagulant  | 161 | 63.26 |
| Diabetes mellitus  | 98  | 38.7  |
| Insulin  | 44  | 17.4  |
| Neurological disease (stroke, Alzheimer etc.)                      | 48  | 19    |
| Renal dysfunction  | 23  | 9.1   |
| Mobilization   |     |       |
| Independent  | 211 | 83.4  |
| Mobilization with cane/assistive device                            | 30  | 11.9  |
| Immobile   | 12  | 4.7   |

| TABLE II<br>Vascular status and intervention |                              |  |  |  |               |
|--|------------------------------|--|--|--|---------------|
| Vascular intervention                        | Distal blood flow (+) (n=32) | Occlusion at distal (ATA, PTA) (n=132) | Occlusion at popliteal artery level (n=63) | Occlusion at femoral artery level (n=20) | Total (n=253) |
| Balloon angioplasty                          | 6                            | 21                                     | 9  | 4  | 40            |
| Embolectomy                                  | 2                            | 8                                      | 4  | 0  | 14            |
| Bypass                                       | 0                            | 25                                     | 4  | 4  | 33            |
| Endarterectomy                               | 0                            | 1                                      | 1  | 0  | 2             |
| Unknown procedure                            | 2                            | 7                                      | 10   | 1  | 20            |

ATA: Anterior tibial artery; PTA: Posterior tibial artery.

amputation, which comprised 43.5% (n=110) of the procedures. The median hospital stay for the patients was 5 days (interquartile range [IQR], 3 to 10 days).

The median WIfI stage of the patients was 3, and there was no statistical difference between the revision amputation group and the nonrevision group (p=0.182).

Due to wound site problems after amputation, debridement was performed on 12.6% (n=32) of

the patients. The mean time for debridement was 13.5 days (IQR, 7 to 26 days), and VAC was used in 5.1% (n=13) of the patients.

Revision amputation occurred in 27.3% (n=69) of patients. Rates peaked in the 70 to 79 age group before declining (Figure 2). Logistic regression showed a 2.3% decrease in revision risk per year of age (95% confidence interval 0.955-1.000, p=0.049).

The median time for revision amputation was 21 days (IQR, 10 to 35 days). Fifty (72.4%) of the revision amputation occurred within the first five weeks, as shown in Figure 3. Of the 69 patients who underwent revision amputation, 72.5% (n=50) had open wounds upon hospital admission. In contrast, 35.3% (n=65) of patients who did not undergo revision amputation had open wounds. Open wounds or necrosis at admission significantly increased revision amputation risk ( $\chi^2[1, n=253]=9.81$ ,

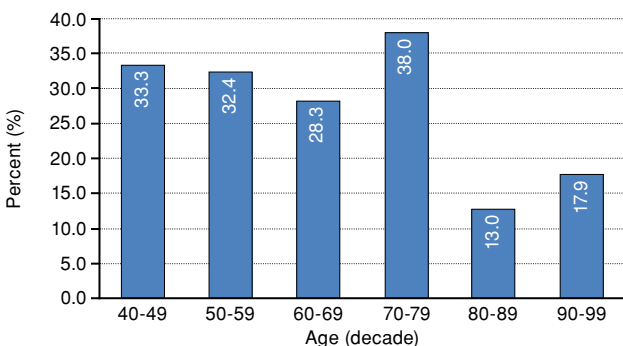


FIGURE 2. Revision amputation rates by age (decade).

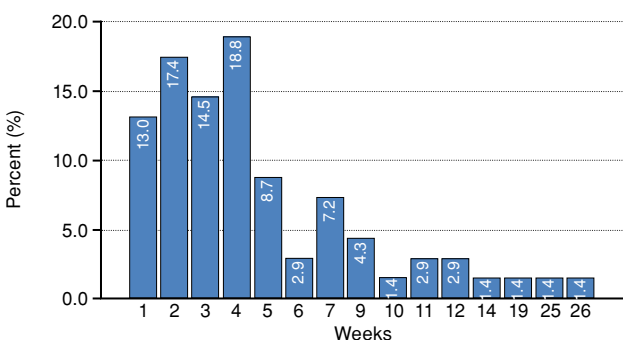


FIGURE 3. Timing of revision amputations.

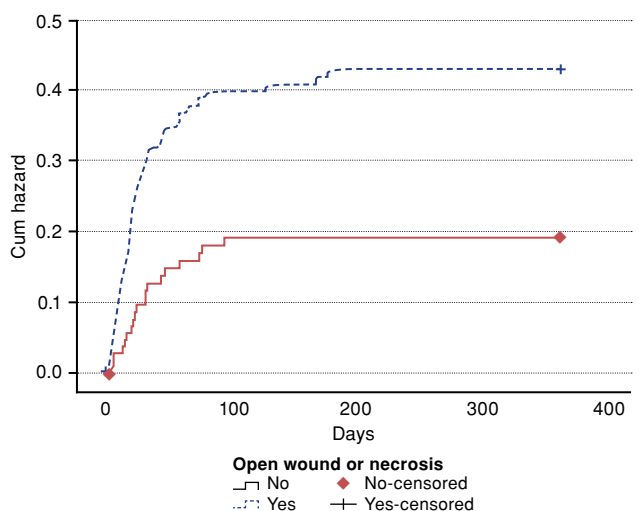


FIGURE 4. Kaplan-Meier hazard function: Relationship between open wounds and revision amputation.

p=0.002). The relationship between open wounds and revision amputation within the first year is shown in Figure 4 using the Kaplan-Meier hazard function test (log rank  $\chi^2=9.99$ , p=0.002).

In our study, it was observed that 17.3% (n=12) of patients who underwent revision amputation had previously undergone debridement. Conversely, among patients without a revision amputation, only 10.8% (n=20) required debridement. The analysis revealed no significant relationship between the necessity for postamputation debridement and revision amputation ( $\chi^2 [1, n=253]=1.93$ , p=0.165).

Vacuum-assisted closure therapy was used in 13 patients. Out of these 13 patients who received VAC therapy, 11 underwent revision amputation. The statistical analysis showed that patients treated with VAC therapy following their initial amputation

were more likely to need a subsequent revision amputation. This relationship was statistically significant ( $\chi^2 [1, n=253]=22.71$ , p<0.001).

Table III shows a significant relationship between amputation level and revision likelihood ( $\chi^2 [1, n=253]=8.30$ , p=0.016), with below-knee amputations more likely to require revision than above-knee amputations.

Binary logistic regression identified C-reactive protein (CRP) to be significantly associated with revision amputation (p=0.006), with a 6.2% increased risk for every 10-unit increase in CRP (Table IV). Multicollinearity was not an issue (tolerance, 0.323-0.980).

A total of 40 patients were found to have infections, and 26 of them underwent revision amputations.

**TABLE III**  
Amputation levels and revision amputation ratios

| Amputation levels | No revision amputation |      | Revision amputation |      | Total number of patient |
|-------------------|------------------------|------|---------------------|------|-------------------------|
|                   | n                      | %    | n                   | %    | n                       |
| Major amputation  | 184                    | 72.8 | 69                  | 27.2 | 253                     |
| Above knee        | 112                    | 78.3 | 31                  | 21.7 | 143                     |
| Below knee        | 72                     | 65.5 | 38                  | 34.5 | 110                     |

**TABLE IV**  
Regression analysis results of variables associated with revision amputation

| Effect                         | B     | SE    | Beta   | 95% CI |       | p            |
|--------------------------------|-------|-------|--------|--------|-------|--------------|
|                                |       |       |        | LL     | UL    |              |
| White blood cell               | 1.000 | 0.000 | 0.000  | 1.000  | 1.000 | 0.472        |
| Hemoglobin                     | 1.004 | 0.077 | 0.004  | 0.864  | 1.167 | 0.957        |
| Urea                           | 0.998 | 0.006 | -0.002 | 0.987  | 1.009 | 0.708        |
| Creatine                       | 0.916 | 0.206 | -0.088 | 0.612  | 1.371 | 0.670        |
| C-reactive protein             | 1.006 | 0.002 | 0.006  | 1.002  | 1.011 | <b>0.006</b> |
| International normalized ratio | 1.163 | 0.124 | 0.151  | 0.912  | 1.481 | 0.223        |

CI: Confidence interval; LL: Lower limit; UL: Upper limit; p indicates the significance level.

**TABLE V**  
Factors affecting revision amputation

| Variables          | Odds Ratio | 95% CI       | p     |
|--------------------|------------|--------------|-------|
| Age                | 0.977      | 0.955-1.000  | 0.049 |
| C-reactive protein | 1.062      | 1.018-1.107  | 0.006 |
| Open wound         | 4.157      | 2.178-7.932  | 0.002 |
| VAC therapy        | 9.824      | 4.183-23.056 | 0.001 |
| Infection          | 2.543      | 1.505-4.297  | 0.001 |

CI: Confidence interval; VAC: Vacuum-assisted closure.

Statistically, patients who developed infections had a significantly higher rate of revision amputations ( $\chi^2$  [1, n=253]=33.841,  $p<0.001$ ). Factors affecting revision amputation are shown in Table V.

Patients' preamputation mobility status, visits to the cardiovascular outpatient clinic before the amputation, vascular interventions prior to amputation (e.g., angioplasty and bypass), diabetes mellitus, insulin use, neurological diseases (e.g., stroke and Alzheimer disease), and renal dysfunction are not related to revision amputation (all  $p$ -values  $>0.05$ ).

## DISCUSSION

Determining the appropriate level of amputation in a progressive disease such as PAD can prevent unplanned revision surgeries and reduce morbidity and mortality. Therefore, identifying amputations that lead to revision can guide clinicians in adopting a more conservative or aggressive approach to determining the level of amputation. In this study, the main finding was that patients presenting with compromised skin integrity, such as necrosis or an open wound, were more likely to undergo revision amputation.<sup>[13]</sup> The observed high reamputation rate (72.5%) among patients presenting with open wounds or necrosis at hospital admission highlights the critical importance of early and aggressive wound management strategies. This is consistent with findings from similar studies that emphasize the role of wound site conditions in postsurgical outcomes and the need for vigilant preoperative assessment and prompt intervention.<sup>[14]</sup>

Our findings suggest a nuanced pathway for patient outcomes following initial amputation procedures, where the mean age, sex distribution, and predominance of above-knee amputations echo patterns observed in broader populations dealing with critical limb-threatening ischemia.<sup>[15]</sup> The present study's insights into the differential rates of reamputation based on the level of initial amputation add a valuable perspective to the existing literature, suggesting that the site of the initial amputation could be an important consideration in postoperative care plans and risk stratification. This finding aligns with current discussions in the field, advocating for tailored therapeutic strategies based on amputation level to optimize outcomes and possibly reduce the need for further surgical interventions.<sup>[16]</sup>

The current study found that revision rates decreased with aging, contrary to the expectation that higher CRP levels with age would lead to

increased revisions. This suggests that elevated CRP levels are linked more directly to amputation than to age.<sup>[17]</sup> C-reactive protein emerged as a significant predictor of reamputation risk, aligning with previous studies that identified CRP as a marker for poor healing and complications after amputation.<sup>[18]</sup> This highlights the role of systemic inflammation in postoperative outcomes and supports the use of CRP as an objective measure for assessing complication risks.

The results indicate a clear association between open wounds at the time of hospital admission and the likelihood of undergoing revision amputation, a finding significantly reinforced by the logistic regression analysis illustrating the decrease in revision amputation probability with increasing age. In younger patients, we may tend to adopt a more conservative approach by attempting amputations at more distal levels, aiming to preserve as much limb function as possible. This correlation underscores the vulnerability of patients with compromised skin integrity and aligns with the broader literature on the diabetic foot, where the presence of ulcers significantly escalates the risk of amputation.<sup>[19]</sup> While our study focuses on a nondiabetic cohort, the implications for proactive wound management and the potential for intervention to prevent revision amputations remain pertinent.

Interestingly, the increased likelihood of revision amputation following VAC therapy in our study presents a paradoxical scenario. While VAC therapy is traditionally viewed as enhancing wound healing, its association with higher revision amputation rates may reflect a selection bias, where more severe cases are chosen for this intervention. This observation warrants further investigation and echoes the complex decision-making framework in treating ischemic foot conditions, as described by Graziani and Piaggese<sup>[20]</sup> in their review of endovascular therapy outcomes for below-knee ischemia.

The paradoxical relationship between VAC therapy and higher revision rates likely reflects a selection bias, as VAC therapy is typically reserved for patients with more severe wounds or advanced tissue ischemia, which are conditions already associated with poor outcomes. Additionally, the timing and criteria for initiating VAC therapy may play a role; delayed application in ischemic settings might limit its effectiveness. This finding aligns with studies suggesting that VAC is often used for complex, high-risk wounds that inherently

carry greater risks of complications. Alternatively, the mechanical effects of VAC, while promoting granulation tissue formation, may not adequately address the underlying vascular or infectious issues that drive wound deterioration in ischemic patients.<sup>[21]</sup> Further research is needed to explore whether combining VAC with revascularization or enhanced infection control strategies could reduce revision rates and improve outcomes.

The primary limitation of this study was the exclusion of diabetic patients and other common causes of LLA, which reduces the generalizability of our findings to broader populations. This may limit the applicability of our results in diverse clinical settings and should be considered when interpreting our conclusions.

In conclusion, to mitigate the risk of reamputation in major ischemic foot conditions, it is crucial to conduct rigorous preoperative evaluations, strategically select the level of amputation, and carefully monitor skin integrity and inflammatory markers.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Concept, design, control, analysis, writing the article: E.S.; Data collection, analysis, literature review: M.E., S.Y.; Supervision, critical review, materials: C.Ç., M.Ç.; Data collection, materials: D.E.

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