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# The impact of diabetes on the outcomes of lower extremity arterial disease in patients with vascular surgical interventions in Kosovo

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#### Abstract

The study aims to enhance understanding of the link between type 2 diabetes mellitus (DM) and lower extremity arterial disease (LEAD) outcomes in patients treated with vascular surgical interventions to improve clinical practice and management. It includes patients with DM who underwent surgery for LEAD from November 2023 to April 2024 at the Vascular Surgery Clinic, University Clinical Center of Kosovo, Pristina. Data were collected from medical records and included demographics, comorbidities, smoking status, laboratory values, procedural details, outcomes, prior surgeries, and hospitalization duration. Categorical variables were analyzed using descriptive statistics, one-sample *t*-tests, bivariate, and chi-square tests. Ethical approval was obtained, and informed consent was secured. The largest patient group was aged 62-71 years (48.15%), predominantly male (62.96%), and mostly insulin-managed (96.3%). Ischemic toe gangrene requiring amputation occurred in 25.93% of cases; arterial ischemia with thrombosis was the most common preoperative complication (33.33%). Hospitalization was typically 6-10 days (40.74%), with combined anti-aggregation, anti-diabetic, and antibiotic therapy used in 81.48% of cases. LEAD remains a major global health concern, requiring personalized care strategies and ongoing patient education to reduce complications and amputations.

## Introduction

Lower extremity arterial disease (LEAD) represents a frequent clinical expression of atherosclerosis and is notably prevalent among individuals with type 2 diabetes mellitus (T2DM). Research demonstrates that people with T2DM face a two- to four-fold increased likelihood of developing LEAD compared with non-diabetic populations, resulting in elevated risks of lower limb amputation (LLA), cardiovascular events, and death. Although diagnostic and treatment options have advanced, LEAD in diabetic patients is often underrecognized and insufficiently managed, particularly in resource-limited regions. Worldwide, over 200 million people live with LEAD, including nearly 40 million in Europe. Its prevalence rises sharply with age, peaking in those over 65 years. In diabetes, arterial disease tends to be more widespread and involves distal vessels, leading to less favorable outcomes after revascularization. Ongoing ischemia, combined with infection and neuropathy, can progress to critical limb ischemia (CLI), demanding prompt surgical action to safeguard both limb function and survival. The present study's main goal was to assess how T2DM influences perioperative and early postoperative outcomes in LEAD patients undergoing surgery in Kosovo, aiming to define high-risk groups, evaluate surgical results, and highlight the need for tailored perioperative care in diabetic cases.

LEAD is common in patients with T2DM, associated with LLA, with frequency added 4-5 times higher.<sup>1,2</sup> Despite its severity, LEAD remains less studied than other diabetic vascular complications. LEAD affects over 200 million people worldwide, including 40 million living in Europe. It is 2-4 times more common in people with type 2 diabetes than in the general population.<sup>3-5</sup> The prevalence of LEAD varies in studies depending on differences in population characteristics, including the definition of LEAD, age, and ethnicity. Commonly discovered during the 5th decade of life, lead prevalence has increased exponentially after the age of 65.<sup>6-10</sup>

LEAD is one of the leading causes of diabetic foot. It is present in 49% of patients with diabetic legs in the European Study Group on Diabetes and the Lower Extremity (EURODIALE) study, and a third of the participants had both LEAD and infection. Diabetic patients with LEAD, compared to those without LEAD, also have a higher risk of cardiovascular disease (CVD) and cardiovascular mortality from all causes.<sup>2,10-13</sup> Pulse palpation (distal artery pedis, posterior tibial, popliteal, and femoral), a simple and free clinical examination, should be systematically performed in all patients with diabetes.

The Brachial Index (ABI) has emerged as a relatively simple, non-invasive, and invasive tool for LEAD diagnosis. The American Diabetes Association recommends evaluating ABI as a noninvasive first-line test in patients with symptoms or signs of LEAD.<sup>14</sup>

CLI is defined as the presence of chronic ischemic pain for over 2 weeks, usually in the front of the leg, with or without ischemic or gangrenous lesions due to occlusive arterial disease. It is considered the last stage of the LEAD spectrum, with extremely high risk for CVD and death. <sup>15</sup> The American Heart Association and the American College of Cardiology recommend antihypertensive treatment in patients with LEAD to decrease cardiovascular pathology and stroke. 16 The European Society of Cardiology (ESC) and the European Society of Vascular Surgery (ESVS) recommended a low-density lipoprotein level less than 1.8 mmol/L (<70 mg/dL) or lowered by  $\ge 50\%$  if the initial value is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) for all patients with LEAD. 17 Reduction of atherothrombosis for continued health registry (REACH), statin use was associated with a 17% decrease in rates of unwanted cardiovascular events among individuals with LEAD, without heterogeneity regarding diabetes status.<sup>18</sup> However, the Fenofibrate Intervention and Event Lowering in Diabetes exhibited a 36% risk reduction for LLA in participants assigned to fenofibrate compared to those assigned to placebo. 19 Evolocumab use was also associated with a 42% reduction in LEAD-related events.<sup>20</sup> Meta-analyses by the Antithrombotic Trialists' Collaboration group showed that aspirin was protective in various populations with high vascular risk, including those with LEAD.<sup>21</sup> Treatment with rivaroxaban was also associated with a reduction in major limb events in patients with disease of the peripheral carotid or lower limb arteries. This benefit was reliable in participants with or without diabetes at the initial stage.<sup>22</sup> Contrary observations have

been reported regarding operating outcomes in patients with diabetes undergoing revascularization.<sup>23-27</sup> Recent studies have shown similar perioperative and postoperative mortality in patients with diabetes compared to those without diabetes, but diabetic patients had a higher risk of incomplete wound healing, major amputation, a longer duration of hospital stay, and more frequent hospitalizations.<sup>28</sup>

Surgical revascularization ensures good long-term outcomes, albeit with a longer hospital stay and an increased risk for postoperative complications and mortality compared to endovascular procedures.

# Research purpose

The purpose of the research is to identify known data regarding the impact of T2DM on outcomes of cardiac ischemic disease of lower extremities in patients with vascular surgical intervention, new connections, risk analysis of complications, and the effect of diabetes on the recovery and improvement of the condition in the patient after surgery. Identify specific risk factors that affect outcomes of cardiac ischemic diseases of the lower extremities in patients with diabetes following vascular surgery. Identifying age groups of patients who may need special care and closer monitoring.

## **Materials and Methods**

# Study design and population

This forward-looking observational research enrolled adult individuals with T2DM who underwent surgical management for LEAD from November 2023 to April 2024 at the Vascular Surgery Clinic, University Clinical Center of Kosovo. Eligibility criteria included a verified diagnosis of T2DM and a surgical procedure for LEAD (such as toe, transmetatarsal, or femoral amputation, peripheral bypass, or thrombectomy). Individuals without diabetes or those receiving only conservative therapy were not considered. The study cohort comprised patients who underwent various vascular surgical procedures, including toe amputation, crural amputation, femoral amputation, and vascular reconstructions such as thromboendarterectomy, peripheral bypass, and thrombectomy for stenosis, occlusion, or embolism of the lower extremity arteries. The diagnosis of vascular pathology was confirmed using appropriate diagnostic modalities, including conventional radiography, foot radiography, echocardiography of the lower extremity vascular system, computed tomography angiography (angio-CT), and magnetic resonance angiography.

Demographic, clinical, and procedural data were extracted from inpatient medical records, including age, sex, smoking status, and other lifestyle habits, comorbidities, medication use, preoperative laboratory values, procedural details, and postoperative outcomes. Additional variables included previous surgical interventions and length of hospital stay.

The primary outcome was procedural success, defined as the absence of intraoperative or postoperative complications and the non-occurrence of major adverse cardiovascular events (MACE), including myocardial infarction, stroke, or cardiovascular death—during hospitalization. Secondary outcomes included postoperative complications and the requirement for re-intervention. Statistical analyses were performed using SPSS v16.0. Categorical variables were expressed as descriptive statistics, and between-group comparisons were conducted using independent sample t-tests, bivariate correlations, and non-parametric chi-square tests.

The study protocol was reviewed and approved by the Ethical Affairs Commission of the Faculty of Medicine, University of Pristina, and the Ethical Affairs Commission of the Kosovo Chamber of Doctors. Written informed consent was obtained from all participating patients prior to inclusion.

## Data collection

Information was obtained on demographic factors (age, gender), clinical profile (tobacco use, existing comorbidities), laboratory parameters (pre-surgical blood glucose), applied treatments (insulin therapy, other medications), and procedural characteristics, all recorded through

standardized case report templates. The evaluated outcomes comprised surgical success (absence of intraoperative complications and major cardiovascular events during admission) and postoperative events (infections, thrombotic episodes, recurrence of ischemia).

## Statistical analysis

Continuous data are shown as mean  $\pm$  standard deviation, while categorical data are expressed as counts and percentages. Group comparisons were carried out using the chi-square test and Student's t-test, considering p-values <0.05 as statistically significant. Data analysis was executed with SPSS version 16 (IBM Corp., Armonk, NY, USA).

#### Results

The study was conducted on 27 patients diagnosed with T2DM and lower extremity ischemic arterial disease (LEAD) who were admitted to the Vascular Surgery Clinic in Pristina from November 2023 to April 2024. The descriptive parameters of ischemic arterial disease of the lower extremities, including age, gender, postoperative medications, blood glucose levels, diabetes management, length of hospitalization, and lifestyle habits, are presented in Table 1.

Table 2 presents data on ischemic arterial disease of the lower extremities, structured according to radiological and echographic imaging parameters, preoperative clinical diagnoses, and preoperative complications. Table 3 presents the most common types of surgical interventions applied in ischemic arterial disease of the lower extremities.

# Demographic and clinical characteristics

The age group most frequently affected by LEAD and requiring surgical intervention was 62-71 years (48.15%, p<0.05). Male patients predominated, accounting for 62.96% of the cases (p<0.05). A history of tobacco use was reported in 85.2% of patients (p<0.05).

In 96.3% of cases, diabetes was managed with insulin therapy (p<0.05), and a statistically significant association was observed between diabetes management and gender (p=0.0035) (Supplementary Figure 1). Blood glucose levels most often ranged from 6.1–10.0 mmol/L (40.8%, p<0.05), with a statistically significant correlation with age (p=0.039) (Supplementary Figure 2).

# Clinical and diagnostic findings

A statistically significant three-way association was found between diabetes management, gender, and occupation (p=0.002). LEAD medical check-ups and preoperative radiological imaging also demonstrated a statistically significant association (p=0.017). The overall analysis revealed significant correlations with age (p=0.017), days of hospitalization (p=0.004), occupation (p=0.05), and diabetes management (p=0.05) (Supplementary Figure 3).

The most frequently used imaging modality was angio-CT of the lower extremities (55.55%, p<0.05) (Supplementary Figure 4). Hospitalization most frequently lasted between 6 and 10 days (40.74%, p<0.05) (Supplementary Figure 5).

The leading preoperative clinical diagnosis was ischemic gangrene of the toes (25.93%, p<0.05), while acute arterial ischemia was the most common preoperative complication (33.33%, p<0.05) (Supplementary Figure 6).

# Surgical interventions and postoperative course

The most frequent surgical procedure was toe (1-5) amputation (25.92%, p<0.05), followed by thrombectomy and peripheral bypass operations. A statistically significant association was observed between the type of surgery and postoperative complications (p=0.002), as well as between clinical diagnosis and surgical intervention type (p=0.027) (Supplementary Figure 7).

The most common postoperative pharmacological regimen included anti-aggregants, antibiotics, and antidiabetic agents (81.48%).

#### Discussion

The main risk factors are similar to those associated with CVD, including age, gender, smoking, systolic blood pressure, and plasma lipid concentrations.<sup>29-31</sup> Smoking is an independent risk factor for LEAD.<sup>29-33</sup> LEAD risk may also vary according to differences in the region of origin. Despite a higher CVD rate, people from South Asia, compared to white Europeans, have a lower prevalence of LEAD. The explanation of this paradox has not yet been clearly clarified and may be suspected of genetic predisposition to LEAD.<sup>34</sup> Our findings in the study found that the most commonly associated factor with ischemic arterial disease of the lower extremities is 52-61 years of age at 48.15% (p<0.05); the most commonly affected sex is male at 62.96% (p<0.05); and smoking is 85.2% (p<0.05). These give them even more correspondence to the descriptions of different authors. Epidemiological studies and randomized clinical trials demonstrated the efficacy of intensive blood glucose control in reducing the development and progression of long-term microvascular complications in patients with diabetes.<sup>35,36</sup> Our blood glucose levels are 6.1-10.0 mmol/L with 40.8% (p<0.05). Exercise improves walking ability, physical function, vitality, and overall health.<sup>37</sup> Previous studies suggested the impact of nutrient quality on lead prevalence.<sup>38,39</sup> DM type 2 management in the researched cases is medication, diet + exercise, and insulin. Insulin is used at 96.3% (p<0.05). Ultrasound Doppler screening is a good performance imaging method of LEAD diagnosis, with 93% sensitivity and 97% specificity. 40 Angiography with computed tomography, magnetic resonance angiography, and angiography allows for an accurate topographic diagnosis and is often performed in pre-surgery work when large arterial containers are involved. Distal localization has been shown to be more common than proximal in patients with diabetes.<sup>41</sup> The most commonly used diagnostic imagery in our research is angio-CT of the lower extremities at 55.55% (p<0.05). We have a correlation between diabetes management and insulin use with sex (gender) up to 96.3% (p<0.05), as well as gender, management, and occupation, which are at the top of retirement (p<0.05). The correlation rate between the days of hospitalization from 6 to 10 10 days is 40.7%; age and occupation are important (p<0.002).

The development of new techniques in recent decades has driven the implementation of endovascular therapy in patients with LEAD. The various options for revascularization depend on several factors, including the anatomic location, extent, and length of the arterial lesion; the general health status of each patient and associated diseases; as well as the experience of the center and the surgeon. Endovascular revascularization may be a good strategy for short stenosis below 5 cm or closure of the iliac arteries, providing a good long-term cavity.<sup>41</sup> Hybrid procedures (endarterectomy or bypass at the femoropopliteal level combined with endovascular therapy) may be indicated for iliofemoral laziness.<sup>42</sup> Aortofemoral bypass is the first-line strategy in aortoiliac occlusions in patients adapting for surgery, 43 while an endovascular procedure should be considered in long or bilateral occlusions in patients with severe comorbidities. 40,44 In our research findings, the most frequently diagnosed clinical pathology was ischemic gangrene of the toe with 25.93% (p<0.05). The most common preoperative complication was acute arterial ischemia of the lower extremities with 33.33% (p<0.05). An endovascular revascularization may also be considered as a first strategy for aortoiliac occlusive lesions if done by an experienced team without compromising subsequent surgical options. 45 In femoropopliteal stenosis/occlusion below 25 cm, an endovascular revascularization can be considered first-line therapy, and a primary stent implant has been associated with further morphological benefits. 45,46 If occlusion stenosis is more than 25 cm, surgical bypass may be a suitable option with better long-term capacity, especially when using the large saphenous vein. Infrapopliteal artery disease is a common lead appearance in patients with diabetes. The ESC and ESVS recommend endovascular therapy as the first choice for infrapopliteal artery disease with stenotic lesions and short occlusions, while bypass surgery with an autologous vein can be considered for long occlusions. However, endovascular therapy can be tested in patients with long occlusions if the surgical risk is assessed as high or in the absence of an autologous. The concept of angiosome, which targets ischemic tissue, can also be considered. 44-46 Our study findings on the types of surgical interventions, surgical amputation of fingers 1, 1, 2, 3,

and 5 of the toe, were up to 25.92% (p<0.05). The connection of surgical operations (p=0.024) and postoperative complications (p=0.002) is evident. Correlate between clinical diagnoses and surgical and representative operations (p=0.027).

In addition to revascularization strategies, antithrombotic therapy plays a critical role in secondary prevention for patients with diabetes and LEAD. The COMPASS trial demonstrated that the combination of low-dose rivaroxaban (2.5 mg twice daily) with aspirin significantly reduced the risk of MACE and major adverse limb events compared with aspirin alone in patients with stable atherosclerotic vascular disease, including those with diabetes and peripheral artery disease. Importantly, this intensified regimen showed a consistent benefit in reducing acute limb ischemia, major amputations, myocardial infarction, and stroke, albeit with an increased risk of major bleeding (but not fatal or intracranial bleeding). In the context of our study population, where the prevalence of smoking, insulin use, and severe arterial lesions is high, integrating a dual-pathway inhibition strategy, as supported by COMPASS, may offer substantial improvements in both limb salvage and overall survival. Tailoring therapy based on bleeding risk assessment remains essential to optimize patient outcomes. 47-49

This research underscores the complex perioperative care of LEAD in T2DM patients in Kosovo. In agreement with existing evidence, advanced age, male gender, tobacco use, and insulin therapy emerged as common risk factors linked to worse LEAD outcomes. Our results support prior observations that diabetic individuals undergo more amputations and experience longer hospital stays than non-diabetic patients.

The lack of a non-diabetic comparator group restricts causal conclusions; nevertheless, the descriptive results stress the urgency of targeted risk-factor control and enhanced surgical strategies. Further investigations with broader samples and comparative arms are needed.

#### Conclusion

LEAD is one of the most severe conditions observed in diabetes patients. It leads to excess risk of death, CVD, and limb loss and is responsible for disabilities and a significant socio-economic burden. The implementation of personalized care strategies and patient continuing education is key to successful management and reduction of complications associated with diabetes mellitus and LEAD. Peripheral vascular reconstruction plays a crucial role in managing diabetic patients with peripheral vascular disease, providing opportunities for limb rescue, symptom relief, and improved quality of life. However, its success depends on careful patient selection, comprehensive presurgery evaluation, long-term follow-up, and a multidisciplinary approach to addressing the complex needs of these patients. Patients with T2DM who receive surgery for LEAD face notable perioperative risk and frequent postoperative complications. Prompt detection, strict glycemic regulation, and individualized multidisciplinary care are essential to enhance intervention results and patient treatment.

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Online supplementary material:

Supplementary Figure 1. Correlation between gender and diabetes management in patients with lower extremity ischemic artery disease.

Supplementary Figure 2. Correlation between patient age and blood glucose levels in the group of patients with type 2 diabetes mellitus and lower extremity ischemic artery disease.

Supplementary Figure 3. Statistically significant correlation between gender, diabetes management and occupation.

Supplementary Figure 4. Correlation between the control of lower extremity ischemic arterial disease and preoperative images.

Supplementary Figure 5. Interaction between patient age, which is a key factor in the progression of lower extremity ischemic artery disease, and the mode of hospitalization and days of hospitalization that reflect the complexity of treatment and postoperative course.

Supplementary Figure 6. Distribution of preoperative complications in patients undergoing various vascular and lower extremity surgical interventions, where the vertical axis lists the types of operations (such as amputations at different levels, thrombectomy, peripheral bypass, and aneurysmectomy) and the horizontal axis indicates the number of cases.

Supplementary Figure 7. Correlation between clinical diagnoses and surgical interventions in patients with type 2 diabetes mellitus and lower extremity ischemic artery disease.

Table 1. Descriptive parameters of patients with ischemic arterial disease of the lower extremities for age, gender, postoperative medications, blood glucose level, diabetes

management, days of hospitalization, and habits are presented.

Age (years)	Case (n)	Percentage (%)	р				
50-51	2	7.40	>0.05				
52-61	3	11.11	>0.05				
62-71	13	48.15	< 0.05				
72-81	6	22.22	>0.05				
82-91	3	11.11	>0.05				
Gender							
Male	17	62.96	< 0.05				
Female	10	37.04	>0.05				
Postoperative medications							
Antiplatelet agents (aspirin, clopidogrel)	0	0	>0.05				
Anticoagulants (Xarelto, Sintrom, Warfarin)	0	0	>0.05				
Statins	0	0	>0.05				
Antihypertensive	0	0	>0.05				
Antidiabetics (orally, insulin)	0	0	>0.05				
Antibiotics	0	0	>0.05				
Antiaggregant + Antidiabetics + Antibiotics	22	81.5	< 0.05				
Antiaggregant + Antidiabetics + Antibiotics + Antihypertensive	4	14.8	>0.05				
Anticoagulants + Antidiabetics + Antibiotics	1	3.7	>0.05				
Blood glucose levels (mmol/L)							
4.5-6.0	0	0	>0.05				
6.1-10.0	11	40.8	< 0.05				
10.1-15.0	4	14.8	>0.05				
15.1-20	6	22.2	>0.05				
>20.1	6	22	>0.05				
Management of type 2 diabetes mellitus							
Medication	1	3.7	>0.05				
Diet + Exercise	0	0	>0.05				
Insulin	26	96.3	< 0.05				
Days of hospitalization							
1-5	8	28.6	>0.05				
6-10	11	40.7	< 0.05				
11-20	6	22.3	>0.05				
21-30	1	3.7	>0.05				
>31	1	3.7	>0.05				
Expression	•						
Alcohol	3	11.1	>0.05				
Drugs	0	0	>0.05				
Tobacco	23	85.2	< 0.05				
Alcohol + Drugs	1	3.7	>0.05				

Table 2. Data on diseases with ischemic arterial disease of the lower extremities based on radiological and eco-diagnostic imaging parameters, preoperative clinical diagnoses, and

preoperative complications.

Images	Cases(n)	Percentage (%)	р	
Angio-CT of lower extremities	15	55.55	< 0.05	
ECHO Doppler	0	0	>0.05	
X-ray the sole	5	18.52	>0.05	
Angio-MRI	1	3.70	>0.05	
Angio-CT of the lower extremities + Echo Doppler	1	3.70	>0.05	
Angio-CT of the lower extremities + Echo Doppler + X-ray of	2	7.41	>0.05	
the sole.  Angio-CT of the lower extremities + X-ray of the sole	3	11.11	>0.05	
Clinical diagnoses of preoperative vascular diseases	<u>J</u>	11.11	7 0.03	
HTA (arterial hypertension)	2	7.41	>0.05	
Gangrene ischemic digitorum pedis	7	25.93	< 0.05	
FAV (arterio-venosum fistulae)	0	0	>0.05	
Arterial Occlusion	2	7.41	>0.05	
Arterial thrombosis	4	14.81	>0.05	
Arterial aneurysms	2	7.41	>0.05	
Other	2	7.41	>0.05	
HTA + Gangrene ischemic digitorum pedis	1	3.7	>0.05	
HTA+ Gangrene ischemic digitorum pedis + Arterial thrombosis	1	3.7	>0.05	
Gangrene ischemic digitorum pedis + FAV (arteriovenous fistulae))	1	3.7	>0.05	
Gangrene ischemic digitorum pedis + Arterial Occlusion	2	7.41	>0.05	
Gangrene ischemic digitorum pedis + Arterial thrombosis	1	3.7	>0.05	
Arterial Occlusion + Arterial thrombosis	1	3.7	>0.05	
Complications of preoperative				
Hemorrhage	1	3.70	>0.05	
Thrombosis	1	3.70	>0.05	
Embolism	0	0	>0.05	
Infection	0	0	>0.05	
Arterial ischemia in the lower extremities	9	33.33	< 0.05	
Other	2	7.4	>0.05	
Thrombosis + Embolism	1	3.70	>0.05	
Thrombosis + Arterial ischemia in the lower extremities	9	33.33	< 0.05	
Infection + Arterial ischemia in the lower extremities	4	14.81	>0.05	

Table 3. Most common types of surgical interventions in ischemic arterial disease of extremities.

Types of surgical interventions	Cases (n)	Percentage (%)	р
Amputatio digitorum 1,2,3,4,5 pedis	7	25.92	< 0.05
Amputatio regio cruris	2	7.41	>0.05
Amputatio regio femoralis	1	3.1	>0.05
Bypass periphericus	2	7.41	>0.05
Thrombectomia arterialis	2	7.41	>0.05
Incisio et necroctomia plantae pedis	1	3.1	>0.05
Aneurysmectomia et interpositio grafti	2	7.41	>0.05
Amputatio T-M (transmetatarsal) pedis	1	3.1	>0.05
Amputatio regio femoralis + thrombectomia arterialis	3	11.11	>0.05
Amputatio digitorum 1,2,3,4,5 pedis + incisio et necrectomia plantae pedis	2	7.41	>0.05
Amputatio regio cruris + Amputatio T-M pedis	1	3.1	>0.05