Article

AMERICAN ORTHOPAEDIC FOOT & ANKLE SOCIETY

Foot & Ankle Orthopaedics
2023, Vol. 8(3) 1–7
© The Author(s) 2023
DOI: 10.1177/24730114231182656
journals.sagepub.com/home/fao

Risk Factors for Failure After Surgery in Patients With Diabetic Foot Syndrome

Helen Anwander, MD[1], David Vonwyl[1], Verena Hecht, MD[1], Moritz Tannast, MD[2], Christophe Kurze, MD[1], and Fabian Krause, MD[1]

Abstract

Background: In the present study, we aimed to identify risk factors for failure (defined as reoperation within 60 days) after debridement or amputation at the lower extremity in patients with diabetic foot syndrome and to develop a model using the significant risk factors to predict the success rate at different levels of amputation.

Methods: Between September 2012 and November 2016, we performed a prospective observational cohort study of 174 surgeries in 105 patients with diabetic foot syndrome. In all patients, debridement or the level of amputation, need for reoperation, time to reoperation, and potential risk factors were assessed. A cox regression analysis, dependent on the level of amputation, with the endpoint reoperation within 60 days defined as failure and a predictive model for the significant risk factors were conducted.

Results: We identified the following 5 independent risk factors: More than 1 ulcer (hazard ratio [HR] 3.8), peripheral artery disease (PAD, HR 3.1), C-reactive protein > 100 mg/L (HR 2.9), diabetic peripheral neuropathy (HR 2.9), and nonpalpable foot pulses (HR 2.7) are the 5 independent risk factors for failure, which were identified. Patients with no or 1 risk factor have a high success rate independent of the level of amputation. A patient with up to 2 risk factors undergoing debridement will achieve a success rate of < 60%. However, a patient with 3 risk factors undergoing debridement will need further surgery in > 80%. In patients with 4 risk factors a transmetatarsal amputation and in patients with 5 risk factors a lower leg amputation is needed for a success rate > 50%.

Conclusion: Reoperation for diabetic foot syndrome occurs in 1 of 4 patients. Risk factors include presence of more than 1 ulcer, PAD, CRP > 100, peripheral neuropathy, and nonpalpable foot pulses. The more risk factors are present, the lower the success rate at a certain level of amputation.

Level of Evidence: Level II, prospective observational cohort study.

Keywords: Diabetic foot syndrome, diabetes, foot ulcer, non-healing, risk factor, failure, amputation, reamputation

Introduction

Diabetes mellitus (DM) is a rising global problem affecting more than half a billion people worldwide.[20] One in 4 patients with DM will develop diabetic foot syndrome.[15] Diabetic foot syndrome is a multifactorial disease including diabetic peripheral neuropathy, peripheral arterial disease (PAD), ulcers, and infection. Diabetic foot syndrome is defined by the World Health Organization as "ulceration of the foot (distally from the ankle and including the ankle) associated with neuropathy and different grades of ischemia and infection."[7] Diabetic peripheral neuropathy with loss of protective sensation results in unconscious local pressure overload and trauma to the foot. PAD is present in 1 of 2 patients with diabetic foot ulcers. It is a known risk factor

[1]Department of Orthopaedic Surgery and Traumatology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
[2]HFR Freiburg – Kantonsspital, Fribourg, Switzerland

Corresponding Author:
Helen Anwander, MD, Department of Orthopaedic Surgery and Traumatology, Inselspital, Bern University Hospital, University of Bern, Freiburgstrasse 10, Bern, 3010, Switzerland.
Email: Helen.anwander@insel.ch

for ulcer development, impaired healing, infection, and finally amputations.[10,11,13,21] The incidence of developing ulcers in a diabetic patient is 19% to 34%.[3] The worldwide prevalence of diabetic foot ulcer is 6.3%.[22] More than half of all ulcers become infected, known as diabetic foot infection.[13]

The current standard of care for diabetic foot syndrome includes an interdisciplinary approach. Important cornerstones are pressure relief, restoration of tissue perfusion, wound care, and control of the infection and metabolic situation. Pressure relief can be achieved with orthopaedic shoes and insoles custom made for the patient, total contact casts, or knee-high devices such as a boot. Dependent on the location and size of the ulcer, partial weightbearing may be required. The vascular status must be assessed. Studies have shown that a large toe pressure of >30 mm Hg must be present for adequate wound healing. In patients with ankle pressure <50 mm Hg, toe pressure <30 mm Hg, or ankle brachial index <0.5, revascularization should be considered. If infection is present, infection control must be initiated by surgical debridement or amputation. Empiric intravenous antibiotic therapy is initiated, adapted to culture-directed antibiotics after acquiring biopsy, and later antibiotic treatment is changed to oral.

Based on a study conducted in 14 tertiary care hospitals in Europe including >1000 patients, 77% of diabetic foot ulcers healed within 1 year without major amputation, defined as amputation above the ankle. However, of those patients with healed ulcers, 17% had to undergo minor amputation. In the entire population, 5% underwent a major amputation, 12% of the feet did not heal, and 6% of the patients died within 1 year.[14]

As mentioned above, one known risk factor for nonhealing ulcer and amputation is PAD.[13] In patients with PAD, infection is an additional risk factor. Difficulty to ambulate independently leads to reduced ability to offload pressure and, as a result, impaired healing. Ulcer size, male gender, older age, and advanced end-organ disease such as congestive heart failure or end-stage renal disease have also been associated with poor ulcer healing.[14] A far-reaching problem is that many precipitating factors that led to the ulcer in the first place, such as peripheral neuropathy, increased plantar stress, and peripheral vascular disease, often remain unresolved after healing.[5]

In case of surgical treatment of diabetic foot ulcers, assessing the necessity of an amputation and, if so, assessing the adequate level of amputation is most fundamental and also difficult for the clinician. Unnecessary resection of healthy tissue or amputation in general should be avoided whenever possible; a too restrictive amputation on the other hand may lead to multiple surgeries. Identification of predictive parameters analyzed in this study could support the decision making of an appropriate resection height.

The aims of this study were as follows:

1. Assess the rate of surgical failure within 60 days in patients with diabetic foot syndrome.
2. Assess risk factors for failure (defined as reoperation within 60 days) after surgery.
3. Develop a model using the significant risk factors to predict the success rate on different levels of amputation.

Material and Methods

Between September 2012 and November 2016, we performed a prospective observational cohort study (level of evidence: II) of 105 patients with diabetic foot syndrome, who received a total of 174 surgeries (including revisions). Indications for surgical treatment of diabetic foot syndrome at our facility are signs of osteomyelitis, including probe-to-bone positive ulcers and radiographic osteolysis, local signs of infection such as pus, and ulcers that do not heal within 4-6 weeks despite consistent conservative treatment. Conservative treatment includes offloading as possible or orthopaedic shoes with insoles, total contact casts, or knee-high devices such as a boot and appropriate management of DM and, if present, PAD.

The following preoperative examinations are our standard: radiography of the foot under weightbearing in dorsoplantar and lateral view. In case of a more proximal amputation, for example, a lower leg amputation, the radiography is taken according to the planned height of the amputation. Screening for peripheral neuropathy is performed using the monofilament test (Semmes-Weinstein 0.1 N) plantar at the great toe. The presence of a PAD was defined by an ankle brachial index <0.9,[1] in the course of which we also assess vascular status in all patients, including palpation of the posterior tibial and dorsalis pedis arteries and measurement of systolic pressure of the great toe. Palpable arteries and a systolic pressure of at least 30 mm Hg in the great toe and >50 mm Hg in the ankle are considered sufficient for healing.[4] If time allows and no emergency abscess evacuation is necessary, patients failing these criteria are referred to a vascular specialist who evaluates the need for percutaneous transluminal angioplasty and/or stent implantation in the arteries of the affected leg. In addition, a laboratory chemistry test of the blood is performed. Patients with HbA_{1c} levels >7% are referred to a diabetologist for adjustment of antidiabetic treatment. In the event of an acute derailment during the inpatient stay, the diabetes was adjusted together with the doctors from the diabetology department. In addition, inflammatory parameters (white blood cell count and traditional C-reactive protein [CRP]) are determined.

Table 1. Parameters Assessed as Possible Risk Factors for Failure.[a]

Group	Parameters
Demographic factors	Gender, age >75 y, body mass index >30, side of the affected foot
Diabetic foot	Peripheral neuropathy, HbA_{1c} >6%, Charcot foot, forefoot deformity, prior interventions
Vascular status	Palpability of foot pulses, peripheral artery disease over stage 2 according to the Fontaine and the Rutherford systems
Signs of infection	Ulcer probe-to-bone positive, signs of osteomyelitis on the standard radiograph, CRP >100 mg/L, white blood cell count >10 000/µL, duration of antibiotic treatment (in wk)
Ulcer specification	Time since ulcer appearance (longer than 30 d), ulcer depth (deeper than subcutaneous), size of ulcer (>5 cm^2), more than 1 ulcer
Foot scores	Wagner score (>2), Infectious Diseases Society of America PEDIS score >2, Site, Ischemia, Neuropathy, Bacterial Infection and Depth (SINBAD) classification system grade (>3), Wound Ischemia and Foot Infection score (>4)
Comorbidities	Renal insufficiency, creatinine in the blood (>200 µmol/L), arterial hypertension, arterial fibrillation, history of myocardial infarction, coronary artery disease, nicotine abuse

Abbreviation: CRP, C-reactive protein; PEDIS, Perfusion, extent, depth, infection and sensation.
[a]In parameters that are nonbinary, thresholds were defined.

If surgery can be performed within the first 24 hours after admission, the start of antibiotic treatment in nonseptic patients will not be initiated until deep microbiological samples have been taken. If surgery is delayed, for example, because a vascular procedure is required preoperatively or in septic patients, antibiotic treatment is started immediately. The antibiotic of choice in patients without penicillin allergy is co-amoxicillin. The level of amputation was defined by the border of the necrotic tissue; always the most distal level of amputation was chosen with which the necrotic tissue was resected.

Postoperatively, patients remain in bed until the wound is dry. If fluid secretion persists >5 days, wound healing is delayed, or there are signs of spreading infection, revision surgery is performed. If bony samples taken from proximal to the amputation are positive, the antibiotic therapy was prolonged and adapted depending on the bacteria detected.

Patients are asked to mobilize with partial weightbearing, if possible. Three weeks after surgery, patients are monitored in the outpatient clinic. As soon as the wound has healed, the non resorbable sutures are removed and patients can bear full weight in an orthopaedic shoe with a soft custom-made insole.

In all patients, the level of amputation or debridement, reoperation, time to reoperation, and potential risk factors were assessed. Reoperations were categorized into the following levels: ulcer debridement, toe and toes amputation, partial ray amputation, complete ray amputation, transmetatarsal amputation, amputation at a level between Lisfranc and Syme, lower leg amputation, thigh amputation, and exitus letalis. Failure was defined as reoperation with debridement or amputation at a more proximal level of the same foot within 60 days of the last operation. As potential risk factors, a total of 30 parameters were assessed and extracted from the clinical information system, including demographic factors, peripheral neuropathy, vascular status, signs of infection, ulcer specification, and comorbidities (Table 1). This included the following 30 parameters: demographic factors (gender, age >75 years, body mass index >30, side of the affected foot), diabetic foot (peripheral neuropathy, HbA_{1c} >6 percent, Charcot foot, forefoot deformity, and prior interventions), Vascular status (palpability of foot pulses, PAD over stage 2 according to the Fontaine and the Rutherford systems), signs of infection (ulcer probe-to-bone positive, signs of osteomyelitis on the standard radiograph, CRP >100 mg/L, white blood cell count >10 000/µL, duration of antibiotic treatment [in weeks]), ulcer specification (time since ulcer appearance >30 days, ulcer depth [deeper than subcutaneous], size of ulcer >5 cm^2, more than 1 ulcer), foot scores (Wagner score >2, Infectious Diseases Society of America PEDIS score >2, Site, Ischemia, Neuropathy, Bacterial Infection and Depth (SINBAD) classification system grade >3, Wound Ischemia and Foot Infection score >4), comorbidities (renal insufficiency, creatinine in the blood [>200 µmol/L], arterial hypertension, arterial fibrillation, history of myocardial infarction, coronary artery disease, and nicotine abuse). Quantitative values were either handled numerically (antibiotic treatment [weeks]) or a threshold was defined.

To reduce the potential sources of bias, the respective operations were performed only by 3 trained foot surgeons. Data collection was performed by one research assistant and independently controlled by another. If they did not agree, a third person was consulted and the majority decided.

Statistical analysis

Statistical analysis was conducted on Winstat.

A sample size calculation was conducted with the following numbers: level of confidence, 95%; expected incidence (of failure with need of minor or major amputation), 22%[14]; and precision ±8°, which led to a required minimum number of 103 patients. We included a total of 105 patients. The units of analysis were the 174 surgeries.

Patients for whom data were missing were excluded from the calculation.

A Cox regression analysis, dependent on the level of amputation (ie, debridement, toe/toes amputation, partial ray amputation, complete ray amputation, transmetatarsal amputation, amputation at a level between Lisfranc and Syme, lower leg amputation, or thigh amputation), was conducted with the endpoint reoperation within 60 days.

A predictive model for the significant risk factors was conducted. The reference group to estimate HRs were patients with none of the significant risk factors. The model building strategy was to build a mathematical relationship between the significant risk factors, and the failure rate using the level of amputation. A *P* value of .05 was used to assess significance.

Results

A total of 174 operations were performed in 105 patients. Figure 1 shows a study flowchart according to STROBE guidelines.[6]

These 174 operations were performed in a maximum care hospital in Switzerland. Eighty-five percent of the participating patients were male and 15% female. Thirty-nine percent of the patients were smokers and 33% had a body mass index >30. The mean follow-up time was 3.65 years. The minimum documented follow-up time was 15 months. We included a total of 174 surgeries including 41 debridements, 57 toe(s) amputations, 21 partial ray amputations, 6 complete ray amputations, 14 transmetatarsal amputations, 10 amputations at a level between Lisfranc and Symes, 19 lower leg amputations, and 6 thigh amputations. A patient could be classified into more than 1 group if they failed after the first attempt and the revision was conducted on a more proximal level.

Thirty-one patients (18%) required reoperation within 60 days of initial surgery; these surgeries are considered failures.

The following 5 independent risk factors for failure were identified: >1 ulcer, PAD, CRP>100 mg/L, diabetic peripheral neuropathy, and nonpalpable foot pulses (Table 2). The highest risk was associated with more than 1 ulcer, leading to a hazard ratio [HR] of 3.8. Arterial vascular disease was found to be critical: nonpalpable foot pulses lead to an HR of 2.7, and PAD over stage 2 according to the Fontaine and the Rutherford systems defined as ischemic resting pain leads to an HR of 3.1. CRP> 100 mg/L and peripheral neuropathy both come with a hazard ratio of 2.9. We could not identify the other 25 parameters to be risk factors for revision surgery in our study group.

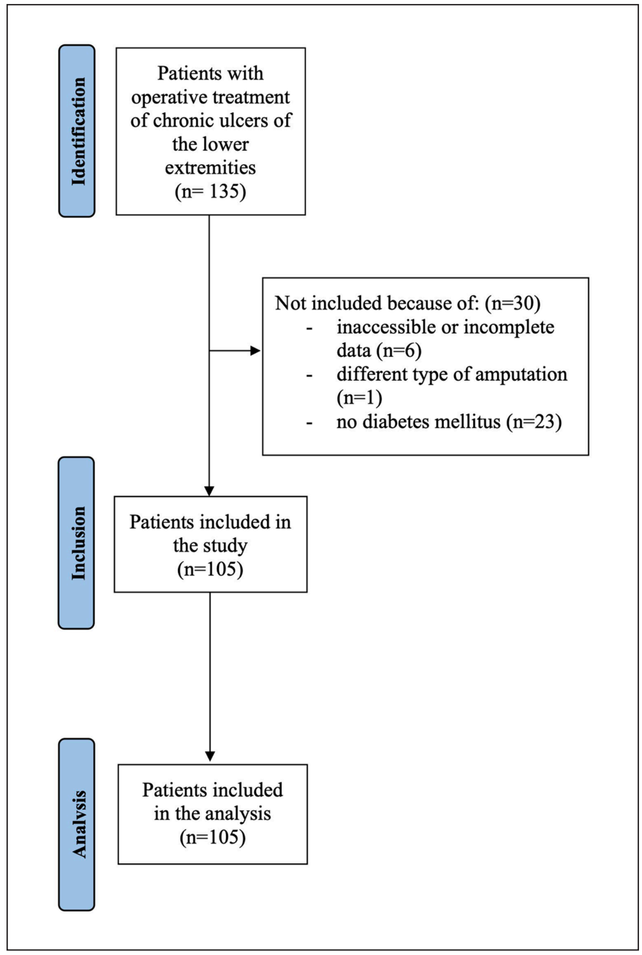

Figure 1. Study flowchart according to STROBE guidelines.[6]

Table 2. Risk Factors for Failure After Surgical Treatment of Diabetic Foot Syndrome.

Risk factor	Hazard Ratio (95% CI)
More than 1 ulcer	3.8 (2.9-4.7)
Peripheral artery disease	3.1 (2.3-3.8)
CRP >100 mg/L	2.9 (2.2-3.7)
Peripheral neuropathy	2.9 (1.9-4.0)
Nonpalpable foot pulses	2.7 (1.9-3.5)

Abbreviation: CRP, C-reactive protein.

In a second statistical analyses, a predictive model was created including these 5 significant risk factors (Figure 2). Taking into account how many risk factors the patient had, the succes on each level of amputation was calculated. Patients with no or 1 risk factor have a high success rate independent on the level of amputation. A patient with 2 risk factors undergoing debridement would achieve a success rate of just below 60%. On undergoing toe amputation, the success rate increases to 75%. However, a patient with 3

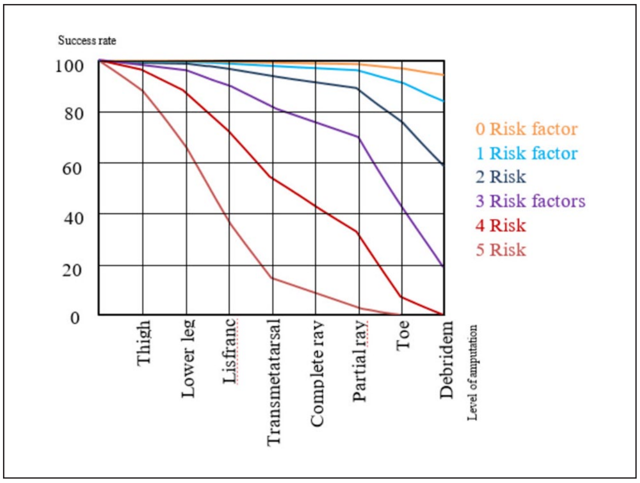

Figure 2. Predictive model for success rate after diabetic foot surgery as a function of level of amputation. The following risk factors were included: >1 ulcer, peripheral arterial disease (PAD), CRP > 100 mg/L, peripheral neuropathy, and nonpalpable foot pulses.

risk factors undergoing debridement will need further surgery in >80%. After toe amputation, the success rate is slightly over 40%, and after partial ray amputation around 70%. In patients with 4 risk factors, a transmetatarsal amputation is needed for a success rate >50%, and in patients with all 5 risk factors, no minor amputation (below the ankle joint) reaches a success rate of >40%.

Discussion

Diabetic foot syndrome and the resulting ulcerations are increasing in frequency and are a challenge. In case of infection and after failure of conservative treatment, surgery is advised, including debridement or amputation. In our study group, the overall failure rate after surgical treatment of a diabetic ulcer was 18%, which is comparable with the literature (20%-65%).[12,17-19]

Previous studies have paid particular attention to the potential risk factors that can lead to amputation. In this regard, it is known that the risk of amputation is significantly increased by the presence of PAD in diabetic foot syndrome.[16] In our study, we found PAD and nonpalpable foot pulses to be risk factors for failure after surgery. This confirms the need for an interdisciplinary approach involving a vascular specialist to increase the chances of success. In addition to a vascular disease (PAD and nonpalpable pulses), our study also found that having more than 1 ulcer, CRP > 100 mg/L, and peripheral neuropathy increased the risk of failure. In the literature it has been found that the risk of reamputation is also significantly increased by smoking, ankle brachial index <0.4, coronary artery disease, and an elevated HbA_{1c}.[9] Another study was able to show that smoking cessation significantly reduces the risk of reamputation.[8] The finding of CRP as a sign of infection and peripheral neuropathy as a risk facture for reamputation is consistent with the literature.[2] To our knowledge, no other study has evaluated the situation with more than 1 ulcer as a potential risk factor. Regarding gender, the literature is divided as to whether men[2] or women[12] have a higher risk of failure. Higher age, nicotine abuse, and hypertension were also found as risk factures in the literature, but none of those parameters were found to be relevant in our study.

Another relevant factor in the literature for reamputation is the level of the initial amputation, with the highest risk of reamputation in patients after a distal amputation such as at toe level.[19] It is a well-known problem for any foot and ankle surgeon to define the adequate level of amputation: amputation that is too distal may lead to multiple reoperations, but we do not want to unnecessarily amputate healthy tissue. We calculated a predictive model for success rate after diabetic foot surgery as a function of level of amputation and dependent on the number of risk factors. We found a high success rate of >80% at all levels of surgery in patients with zero or 1 risk factor. With 2 risk factors, toe amputation is required for a 75% success rate. With 3 risk factors, partial ray amputation is required for a 70% success rate. In patients with 4 risk factors, a transmetatarsal amputation is needed for a success rate >50%, and in patients with all 5 risk factors, no minor amputation achieved a success rate >40%. Subsequently, the level of successful amputation is significantly more proximal with increased number of risk factors. As mentioned above, the decision making of the level of amputation is always difficult. Several factors have to be taken into account, including patient's age and general health, the location of the ulcer, the presence of osteomyelitis, and the patient's consent. However, the presence or absence of the 5 relevant risk factors found in this study may help to predict the outcome and subsequently guide decision making. In the presence of multiple risk factors, patients might be counseled to choose a more proximal amputation level as a more distal will likely lead to failure and thereby to 1 or more avoidable reoperation(s).

The present study has several limitations. Because it is a single-center study, selection bias may be present. Our hospital is a tertiary referral center for complex diabetic foot ulcers, subsequently the results of this study may not be generalizable to the general population or primary care centers. Furthermore, the number of patients with 105 patients within 4 years is limited. Surgeries were conducted by 3 different foot and ankle surgeons. They all underwent the same training, however small differences in the operation technique cannot be excluded. There are 2 statistical limitations: Patients with more than 1 surgery were included, leading to a potential bias for correlated observations. As we assessed 30 risk factors with 31 events, we can only make statements about the risk factors that proved significant. However, risk factors that were not found significant in this study may still be significant in a bigger study group.

In conclusion, reoperations and reamputations for diabetic foot syndrome occur in 1 of 4 patients. Risk factors include presence of more than 1 ulcer, PAD, CRP > 100, peripheral neuropathy, and nonpalpable foot pulses. The more risk factors are present, the lower the success rate at a certain level of amputation. Although patients with zero or 1 risk factor will have a high success rate at any level of amputation or debridement, patients with all 5 risk factors do not achieve a success rate > 40% with a minor amputation, defined as below the ankle. The decision on the level of amputation is clearly patient dependent; however, the above-mentioned 5 risk factors can provide guidance in decision making for both patient and surgeon.

Ethical Approval

Ethical approval for this study was obtained from the Bernese Ethics Committee (Kantonale Ethikkomission Bern, no. 2021-00479).

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ICMJE forms for all authors are available online.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Verena Hecht, MD https://orcid.org/0000-0002-0818-3863

Fabian Krause, MD https://orcid.org/0000-0002-5668-0733

References

1. Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS): document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries. Endorsed by: the European Stroke Organization (ESO), the Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J*. 2018;39(9):763-816. doi:10.1093/eurheartj/ehx095
2. Acar E, Kacira BK. Predictors of lower extremity amputation and reamputation associated with the diabetic foot. *J Foot Ankle Surg*. 2017;56(6):1218-1222. doi:10.1053/j.jfas.2017.06.004
3. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. *N Engl J Med*. 2017;376(24):2367-2375. doi:10.1056/NEJMra1615439
4. Balletshofer B, Ito W, Lawall H, et al. Position paper on the diagnosis and treatment of peripheral arterial disease (PAD) in people with diabetes mellitus. *Exp Clin Endocrinol Diabetes*. 2019;127(Suppl 01):S105-S113. doi:10.1055/a-1018-9250
5. Bus SA. Priorities in offloading the diabetic foot. *Diabetes Metab Res Rev*. 2012;28(Suppl 1):54-59. doi:10.1002/dmrr.2240
6. Cuschieri S. The STROBE guidelines. *Saudi J Anaesth*. 2019;13(Suppl 1):S31-S34. doi:10.4103/sja.SJA_543_18
7. Jeffcoate WJ, Macfarlane RM, Fletcher EM. The description and classification of diabetic foot lesions. *Diabet Med*. 1993;10(7):676-679. doi:10.1111/j.1464-5491.1993.tb00144.x
8. Liu M, Zhang W, Yan Z, Yuan X. Smoking increases the risk of diabetic foot amputation: a meta-analysis. *Exp Ther Med*. 2018;15(2):1680-1685. doi:10.3892/etm.2017.5538
9. Lu Q, Wang J, Wei X, Wang G, Xu Y. Risk factors for major amputation in diabetic foot ulcer patients. *Diabetes Metab Syndr Obes*. 2021;14:2019-2027. doi:10.2147/DMSO.S307815
10. Mills JL Sr, Conte MS, Armstrong DG, et al. The society for vascular surgery lower extremity threatened limb classification system: risk stratification based on wound, ischemia, and foot infection (WIFI). *J Vasc Surg*. 2014;59(1):220-234.e1-2. doi:10.1016/j.jvs.2013.08.003
11. Monteiro-Soares M, Boyko EJ, Ribeiro J, Ribeiro I, Dinis-Ribeiro M. Predictive factors for diabetic foot ulceration: a systematic review. *Diabetes Metab Res Rev*. 2012;28(7):574-600. doi:10.1002/dmrr.2319
12. Ohsawa S, Inamori Y, Fukuda K, Hirotuji M. Lower limb amputation for diabetic foot. *Arch Orthop Trauma Surg*. 2001;121(4):186-190. doi:10.1007/s004020000207
13. Prompers L, Huijberts M, Apelqvist J, et al. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the EURODIALE study. *Diabetologia*. 2007;50(1):18-25. doi:10.1007/s00125-006-0491-1
14. Prompers L, Schaper N, Apelqvist J, et al. Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and without peripheral arterial disease. The EURODIALE Study. *Diabetologia*. 2008;51(5):747-755. doi:10.1007/s00125-008-0940-0
15. Rumenapf G, Morbach S, Rother U, et al. Diabetic foot syndrome—part 1: definition, pathophysiology, diagnostics and classification. Article in German. *Chirurg*. 2021;92(1):81-94. doi:10.1007/s00104-020-01301-9.
16. Sayiner ZA, Can FI, Akarsu E. Patients' clinical characteristics and predictors for diabetic foot amputation. *Prim Care Diabetes*. 2019;13(3):247-251. doi:10.1016/j.pcd.2018.12.002
17. Schaper N, Van Netten J, Apelqvist J, et al. IWGDF Practical guidelines on the prevention and management of diabetic foot disease. *Diabetes Metab Res Rev*. 2020; 36 (Suppl 1):1:e3266. doi: 10.1002/dmrr.3266
18. Seckin MF, Ozcan C, Camur S, Polat O, Batar S. Predictive factors and amputation level for reamputation in patients with diabetic foot: a retrospective case-control study. *J Foot Ankle Surg*. 2022;61(1):43-47. doi:10.1053/j.jfas.2021.06.006
19. Skoutas D, Papanas N, Georgiadis GS, et al. Risk factors for ipsilateral reamputation in patients with diabetic foot lesions. *Int J Low Extrem Wounds*. 2009;8(2):69-74. doi:10.1177/1534734609334808

20. Sun H, Saeedi P, Karuranga S, et al. IDF diabetes atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*. 2022;183:109119. doi:10.1016/j.diabres.2021.109119
21. Ward R, Dunn J, Clavijo L, Shavelle D, Rowe V, Woo K. Outcomes of critical limb ischemia in an urban, safety net hospital population with high WIfI amputation scores. *Ann Vasc Surg*. 2017;38:84-89. doi:10.1016/j.avsg.2016.08.005
22. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis (dagger). *Ann Med*. 2017;49(2):106-116. doi:10.1080/07853890.2016.1231932