



# Foot Ulcer a Devastating Complication of Diabetes Mellitus: A Single-Center Experience of 400 Patients

## Diyabetes Mellitusun Yıkıcı Bir Komplikasyonu Olan Ayak Ülseri: 400 Hastadan Oluşan Tek Merkez Deneyimi

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### Abstract

**Objective:** To identify the clinical predictors of amputation outcomes in patients with diabetic foot ulcers (DFUs) and the management of such patients. **Material and Methods:** Four hundred (273 men; 127 women) patients with DFUs, who were followed at our clinic between 2008-2014, were included. Patients' demographic characteristics, glycemic parameters, and diabetic complications were evaluated. The amputations were classified as minor (distal to metatarsus) and major (Chopart, and below or upper knee) amputations. **Results:** The mean age of the patients was 62.4±10.5 years. Three hundred and ninety-five patients had type 2 diabetes mellitus. The mean diabetes duration was 17±8 years. The rate of chronic diabetic complications consisting of neuropathy, nephropathy, and retinopathy were 97.5%, 81.3%, and 94.8%, respectively. Osteomyelitis and peripheral arterial disease rates were 327 (81.8%) and 265 (66%), respectively. The majority of the foot ulcers were of Wagner grade 3 (53.2%) and 4 (27.5%). According to the initial clinical considerations, 60% of the patients were administered empirical antibiotic therapy for infection. The minor and major amputation rates were 110 (25.5%) and 146 (36.3%), respectively. The average glycosylated hemoglobin value was 8.9±2.3%. Peripheral arterial disease [odds ratio (OR): 2.183, 95% confidence interval (CI): 1.242-3.837, p<0.001], osteomyelitis [OR: 5.062, 95% CI: 2.296-11.161, p<0.001] and Wagner grade (OR: 62.352, 95% CI: 7854-495.021, p<0.001) were found to increase the amputation risk. **Conclusion:** Diabetic neuropathy is still an underlying major risk factor for the development of DFUs. The presence of peripheral arterial disease, osteomyelitis, and high Wagner degree are negative prognostic factors for the need for amputation.

**Keywords:** Amputation; diabetic foot ulcer; diabetic complications; osteomyelitis; Wagner classification

### Özet

**Amaç:** Diyabetik ayak ülseri ile amputasyon sonuçlarının, klinik belirleyicilerini ve hastaların yönetimini sunmaktır. **Gereç ve Yöntemler:** Çalışmaya, 2008 ve 2014 yılları arasında kliniğimizde izlenen diyabetik ayak ülserli 400 (273 erkek, 127 kadın) hasta dâhil edildi. Hastaların demografik özellikleri, glisemik parametreleri ve diyabetik komplikasyonları değerlendirildi. Amputasyonlar, minör (metatarsın distalinde) ve majör (Chopart ve diz altı veya diz üstü) amputasyonlar olarak sınıflandırıldı. **Bulgular:** Hastaların yaş ortalaması 62,4±10,5 yıl idi ve 395'i tip 2 diyabetes mellituslu idi. Ortalama diyabet süresi 17±8 yıl idi. Kronik diyabetik komplikasyonlar olan nöropati, nefropati ve retinopati için oranlar sırasıyla %97,5; %81,3 ve %94,8 idi. Osteomyelit ve periferik arteriyel hastalık oranları, sırasıyla 327 (%81,8) ve 265 (%66) saptandı. Ayak ülserlerinin çoğu, Wagner 3 (%53,2) ve 4 (%27,5) düzeyinde bulundu. İlk klinik değerlendirmeye göre hastaların %60'ına enfeksiyon nedeniyle ampirik antibiyotik tedavisi verildi. Minör ve majör amputasyon oranları sırasıyla 110 (%25,5) ve 146 (%36,3) idi. Hastaların ortalama glikozile hemoglobin düzeyi 8,9±2,3 idi. Periferik arteriyel hastalık (olasılık oranı: 2,183; %95 güven aralığı: 1,242-3,837; p<0,001), osteomyelit (olasılık oranı: 5,062; %95 güven aralığı: 2,296-11,161; p<0,001) ve Wagner derecesi (olasılık oranı: 62,352; %95 güven aralığı: 7854-495,021; p<0,001), amputasyon riskini artıran faktörler olarak bulundu. **Sonuç:** Diyabetik nöropati, diyabetik ayak ülseri gelişimi için hâlâ temel risk faktörüdür. Periferik arteriyel hastalık, osteomyelit ve yüksek Wagner derecesi varlığı, amputasyon ihtiyacı için negatif prognostik faktörlerdir.

**Anahtar kelimeler:** Amputasyon; diyabetik ayak ülseri; diyabetik komplikasyonlar; osteomyelit; Wagner sınıflandırması

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## Introduction

Diabetes mellitus (DM) is a worldwide epidemic disease with an increasing prevalence (1). The risk of foot ulcers in patients with diabetes during their life span is 12-25%. Except for traumatic amputations, the most frequent cause of limb amputation is diabetic foot ulcers (DFUs) (2,3). Delay in the treatment causes severe morbidities and mortalities and leads to increased amputation rates. The most important factor in the pathogenesis of DFU is neuropathy. Other factors such as peripheral vascular disease, foot deformities, and infections are also important for outcomes (4,5). The principal management of DFU is glycemic control, infection control, wound care, and debridement of necrotic tissues. If non-responsive to therapy, minor or major amputation has to be performed. Since the last decade, the use of hyperbaric oxygen, epidermal growth factors, platelet-derived growth factors, and wound bed preparation materials are also gaining attention in the management of DFU. The main objective is to decrease amputation (6-8).

Here, we present the management of the patients with DFU followed at our inpatient clinic for the last six years.

## Material And Methods

### Study design

The patients with DFU were regularly evaluated and monitored by the multidisciplinary diabetic foot council, including the specialists from departments of orthopedics, plastic surgery, vascular surgery, dermatology, infectious diseases, and endocrinology at our hospital since 2000. Patients followed up between 2008-2014 were included in the study. The age; sex; residential area; type and duration of DM; comorbid disease; chronic diabetic complication including neuropathy, nephropathy, and retinopathy; smoking history; anti-diabetic medicines; cause and location of DFU; results of the wound culture; imaging, treatment methods [antibiotic treatment, surgical debridement, vacuum aided wound closure system (VAC), and amputation]; and day of hospitalization stay were recorded. The study was approved by Çukurova University Faculty of Medicine Non-interventional Clinical Re-

searches Ethics Board (Approval No.: 102/07.08.2020). The study was conducted in accordance with the principles of the Declaration of Helsinki.

### Management of the patients

X-ray radiography of foot ulcer; if required, magnetic resonance imaging (MRI) was performed, and ulcer was graded according to the Wagner-Meggitt classification system (7). To maintain the glycemic control of the patients, those on oral agents were switched to intensive insulin treatment (basal-bolus) during the hospitalization period. On the first day of admission to the hospital, bacterial culture specimens were obtained from the wound from deep tissue. No anaerobic culture was performed. After the culture was obtained, if there were signs of infection (induration, erythema, and cellulitis), empirical antibiotics were initiated. According to the culture-antibiogram results, the necessary modifications were made.

The surgical interventions were divided into two groups of minor and major, depending on the level of amputation. The amputations from the distal phalanx and/or metatarsus levels were considered as minor, and the amputations from the heel, ankle, below-knee, or above the knee were accepted as major. Also, patients with and without amputation were compared for their characteristics.

### Laboratory and imaging

The plasma glucose, glycosylated hemoglobin (HbA1c), C-reactive protein, erythrocyte sedimentation rate, complete blood count were performed for all patients.

The presence of vascular stenosis was evaluated using distal foot pulses and Doppler ultrasonography (USG), and if needed, magnetic resonance angiography (MRA) or conventional angiography was performed particularly for those who had undergone possible balloon angiography or intra-arterial stent implantation. The existence of osteomyelitis was determined using X-ray radiography and/or MRI. The localized demineralization accompanying the bone erosion or soft tissue infections on radiographs was interpreted as osteomyelitis. The diabetic neuropathy was revealed using superficial and deep sensation feel tests (light touch

microfilament test and neuropathy symptoms), deep tendon reflex, and, in some patients, using electromyography. For nephropathy, the albuminuria level was measured in the 24-h collected urine; normal <30 mg/24-h, micro-albuminuria 30-300 mg/24-h, and macro-albuminuria >300 mg/24-h (9).

### Statistical analysis

SPSS-19 software package program was used for the statistical analysis. Descriptive tests and frequency analysis were performed.  $p < 0.05$  was accepted as statistically significant. Chi-square and Student's t-tests were used for comparison of the groups. For the evaluation of the differences in subgroups, a one-way analysis of variance was performed. Logistic regression analysis was performed for variables found below  $p$  value 0.05 as a result of paired comparison, and the risk increases were evaluated within a 95% confidence interval (CI).

### Results

In the study, there were 400 patients (273 men, 127 women) with DFU, and the mean age was  $62.4 \pm 10.5$  years (range 23-88

years). Of all the patients, 395 were type 2 diabetic (98.8%), five were type 1 diabetic (1.3%), and the duration of DM was  $17 \pm 8$  years (range 1-40 years). The most common comorbidities were hypertension (20.8%), coronary artery disease (14.8%), and coexistence of both diseases (15%). In the past medical history, 18 (4.5%) patients were taking oral anti-diabetic drugs, 31 (7.8%) were taking oral anti-diabetic drugs+insulin, and 350 (87.5%) were taking only insulin treatment for glycemic control. One hundred and 61 (41%) patients had a smoking history when admitted to the hospital. However, 19.3% of participants had a history of trauma. The frequency of ulcer localization was most at the phalanx, metatarsus, cruris, and heel (38%, 27%, 11.8%, and 11.3%, respectively). In 28 (7%) patients, the heel and metatarsus regions were affected together.

The clinical characteristics, diabetes complications, and amputation type of the patients are shown in Table 1.

There was no bacterial growth in 225 (56.3%) cultures obtained from foot ulcers. However, the most frequent bacterial growth in the culture-positive participants was

Table 1. Demographic and clinical characteristics of diabetic patients with and without amputation.

	Non-amputated n (%)	Amputated n (%)	p*
Nephropathy	113 (78.5)	212 (82.8)	0.28
Retinopathy	134 (93.1)	245 (95.7)	0.25
Neuropathy	140 (97.2)	250 (97.7)	0.79
Peripheral vascular disease	70 (48.6)	195 (76)	<0.001
Osteomyelitis	73 (50.7)	254 (99)	<0.001
	<b>Mean±SD</b>	<b>Mean±SD</b>	
DM duration (year)	15.99±7.9	17.8±7.9	0.027
Age (year)	61.8±11	62.7±10.2	0.4
Glucose (mg/dL)	202.8±87	186±78	0.02
HbA1c (%)	9.5±2.5	8.6±2.0	0.001
Htc (%)	34±6.1	31.6±5.6	<0.001
WBC (µL)	9,664±3,812	11,924±6,987	<0.001
ESR (mm/h)	52.5±28	65±39	<0.001
CRP (mg/dL)	14.8±30.4	31.5±59	<0.001
Hospitalization (day)	25.2 ±19.2	24.9±15	0.84
TOTAL	144 (36)	256 (64)	

SD: Standard deviation; DM: Diabetes mellitus; Htc: Hematocrit; WBC: White blood cell; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; \* $p < 0.05$ : Accepted as statistically significant.

*Staphylococcus aureus* (9.5%) and *Enterococcus faecalis* (7.8%). Initially, 60% of the patients were administered antibiotic therapy (ciprofloxacin+clindamycin combination). The patients given empirical antibiotics who switched to antibiotic treatments were revised according to the culture results (12.3% piperacillin/tazobactam, 6.3% carbapenem, 3.3% carbapenem+aminoglycoside, and 3.3% third-generation cephalosporin).

Arterial vascular disease was detected in 265 of 369 (72%) patients undergoing Doppler USG. Conventional angiography was performed in 44 patients; *A. tibialis* posterior stenosis was detected in 14 patients, *A. poplitealis* stenosis in eight patients, *A. dorsalis* pedis stenosis in two, superficial femoral artery occlusion or stenosis in 15, and diffuse atherosclerosis were detected in five patients. On comparing the patients with and without amputation, peripheral arterial disease was observed in 76% with amputation and 48.6% without amputation ( $p<0.001$ ). Among the patients who had a major amputation, lower extremity arterial stenosis was present in 82% of patients ( $p<0.001$ ).

Osteomyelitis was found in 327 (81.8%) patients, and of these, 78% underwent amputation. Osteomyelitis was present in 254 patients (99%) with amputation and 73 patients (50.7%) without amputation ( $p<0.001$ ).

A large number of the patients had higher grades of Wagner scores ( $>3$ ). Major amputation was performed commonly in patients of Wagner grade 4 ( $p<0.001$ ). For patients with Wagner grade 3, there was no difference in major and minor amputation need ( $p>0.05$ ). The results of DFU of the patients according to Wagner classification and the

amputation ratios are shown in Table 2.

As a surgical intervention, minor amputation was performed in 25.5% of the patients, major amputation in 36.3%, and local wound debridement in 21.3%. VAC treatment to improve the wound was performed in 18 patients after amputation and/or debridement (Table 3).

In patients who underwent an amputation (minor or major), the HbA1c and glucose levels were lower than those who did not undergo an amputation ( $p<0.001$  and  $p=0.02$ ). While there were no significant differences between patients with and without amputation in terms of age, sex, jobs, anti-diabetic therapy, the duration of diabetes in the patients with amputation was significantly longer ( $p=0.027$ ) than those without amputation.

Neuropathy, nephropathy, and retinopathy ratios were similar in patients with and without amputation ( $p>0.05$ ). The existence of other comorbidities such as hypertension, coronary artery disease, and chronic renal disease was found to be a risk factor with the increase in Wagner grade ( $p<0.001$ ), and also the amputation ratio was significantly higher in these patients ( $p=0.025$ ).

Duration of hospitalization was found significantly longer in patients with major amputation in comparison to those with minor amputation ( $p=0.048$ ). Table 3 illustrates the relationship between the patient's age, diabetes duration, and glycemic status with the treatment methods.

There were no significant differences between amputation and sex diversity ( $p>0.05$ ). However, smoking was found to be higher in men ( $p<0.001$ ) than in women. No significant difference was seen between smokers and non-smokers in terms of amputation ( $p>0.05$ ).

Table 2. Grades of foot ulcers of the patients according to Wagner classification.

Wagner classification	Number of patients n (%)	Number of amputation n (%)
Wagner 1 (superficial lesion)	5 (1.2)	0 (0)
Wagner 2 (lesion invasive to subcutaneous tissue)	67 (16.8)	0 (0)
Wagner 3 (osteitis, abscess, osteomyelitis)	213 (53.2)	151 (70.8)
Wagner 4 (localized gangrene)	110 (27.5)	100 (90.1)
Wagner 5 (generalized gangrene)	5 (1.2)	5 (100)
Total (n)	400	256

Table 3. Relation of treatment methods applied to the patients with age, diabetes duration, and glycemic status.

Treatment methods	n	Age	Hospitalization period	*DM duration	**FPG	Hb1Ac
		(mean±SD) (year)	(mean±SD) (day)	(mean±SD) (year)	(mg/dL)	(%)
None	48	62.8±11.6	14.2±9.3	16.6±6.5	202.8±87	9.0±2.4
***VAC or debridement	96	61.2±10.7	30.6±20.5	15.9±8.5	208±86.4	9.7±2.6
#Minor amputation	110	60.1±10.5	25.8±15.3	17.2±7.1	199±80.5	9.2±2.1
&Major amputation	146	64.6±9.6	24.1±15.4	18.3±8.5	177.5±75	8.2±1.9
p value		>0.05	<0.001	>0.05	0.02	<0.001
Total	400	62.3±10.5	25±16	17.1±8	194±81.5	8.9±2.3

SD: Standard deviation; \*DM: Diabetes mellitus; \*\*FPG: Fasting plasma glucose; \*\*\*VAC: Vacuum aided wound closure system; #Minor amputation: Amputations at distal phalanx, phalanx, and/or metatarsus levels; &Major amputation: Amputations at heel, ankle, below-knee, and above-knee levels.

Table 4. Logistic regression analysis of the patients for peripheral artery stenosis, osteomyelitis, Wagner grades, and duration of diabetes mellitus.

	B	SE	Wald	Sig.	Exp (B)	95.0% CI for EXP(B)	
						Lower	Upper
Peripheral artery stenosis	0.781	0.288	7.354	0.007	2.183	1.242	3,837
Wagner	4.133	1.057	15.286	0.000	62.352	7,854	495.021
Osteomyelitis	1.62	0.403	16.157	0.000	5.062	2,296	11.161
Diabetes mellitus duration	0.027	0.017	2.303	0.129	1.027	0,992	1.063
Constant	-5.297	1.084	23.877	0.000	0.005		

B: Beta coefficient, SE: Standart Error, Wald: Chi square statistics, Sig: Significance (P value), Exp: Odds ratio, CI: Confidence Interval.

By using logistic regression analysis for paired comparison (peripheral arterial disease, osteomyelitis, Wagner grade, and diabetes duration), Wagner grade, osteomyelitis, and peripheral arterial disease were found to increase the amputation risk (Table 4).

### Discussion

DFU is one of the most devastating of DM, resulting in limb amputation and/or high-cost treatment, morbidity, and mortality. In many studies, it was shown that the duration of DM, the status of blood glucose regulation, and chronic complications such as neuropathy, peripheral vascular disease, nephropathy, and retinopathy could increase the risk of DFU development (5,6,10,11). In this relatively large study on foot ulcer management through nearly two decades, we would like to underline the outcomes of this important complication and share our findings and experiences.

Approximately all patients with Type 2 DM (T2DM) were present with a long diabetes history (17±8 years) and comorbidities. Similarly, the diabetes duration in patients who underwent amputation was found to be significantly longer than those without amputation. Moreover, the blood glucose and HbA1c levels of the patients with amputation, particularly major amputation, were found to be significantly lower than the other patients. However, some important points should be considered in this evaluation: HbA1c shows the glycemic status of the last 2-3 months; however, it does not provide information about the metabolic control status of the ongoing previous years. Also, other causes such as anemia and kidney failure in patients are conditions that may lead to measurement variability. Also, insulin sensitivity increases, and glycemic levels are low due to nephropathy in patients. Although the glycemic values were found to be lower in our patients who were

statistically amputated, it should be noted that the HbA1c levels of both groups were above the target values (Section  $8.6\% \pm 2.0$  and  $9.5 \pm 2.5$ ).

In a study conducted in Egypt where 2000 patients with diabetes were scanned, the development of DFU was also found to be correlated to diabetes duration, history of coronary artery disease, peripheral vascular disease, sensational neuropathy, and renal replacement treatment (10).

There are different systems for the classification of DFU. Wagner-Meggitt classification classifies the wound according to the depth and extent of the ulcer (7,12). The ulcers in our patients with DFU were mostly found at Wagner grades 3 and 4; consequently, our patient's amputation ratios were found to be high. Additionally, long-term ulcer history (approximately >one month), late reporting at our clinic, or the presence of a physician without DFU experience were factors for amputation need. Our clinic is accepted as a reference center in this region for DFU follow-up; therefore, the patients treated in other clinics are referred to our clinic when the ulcer gets worsened. Generally, other clinics refer the patients to our clinic in case of amputation need. Thus, in this study, it was shown that high Wagner grades were associated with 60 times more amputation risk.

Diabetic neuropathy has been reported in approximately 60-70% of patients with T2DM (12,13). In our patients with DFU, the neuropathy rate was 97.5%, and the most frequent form was distal symmetric neuropathy. Among our patients, the neuropathy incidence was found with similar rates in patients with and without amputation.

The risk of peripheral vascular disease (macrovascular disease/atherosclerosis) increased in patients with diabetes, and this factor is one of the most important causes underlying the foot ulcer development; and its healing problems and affect the outcomes of the foot ulcer (6,14). In our patients, Doppler USG, MRA, or conventional angiography have been used for vascular assessment in clinical practice according to patient's clinical status and needs.

In general, peripheral arterial disease is observed in approximately 20-40% of diabetic patients. It was generally multi-segmental

and relatively medium and small size arterial contrary to atherosclerosis observed in non-diabetics. This characteristic of vascular disease in patients with diabetes could limit the invasive vascular application (15,16). Consequently, due to poor tissue perfusion related to atherosclerosis and decreased angiogenesis in patients with diabetes, ischemic ulcers may develop after trauma, and in this ulcer, both the recovery is delayed, and the response to infection is impaired (17). The coexistence of DFU and peripheral arterial disease also increases the amputation risk. In the previous study conducted with 135 DFU patients at our clinic, the rate of peripheral artery disease was observed as 45% and the amputation rate was 33.3%. The peripheral arterial disease was detected in 82.3% of patients who underwent amputation (18).

In this study, peripheral arterial stenosis was found in 66% of patients, and the amputation rate in patients with peripheral arterial disease was 76%. It was shown that peripheral arterial stenosis increased the amputation risk by 2.183 times. Since the last decade, there has been significant development in the field of invasive vascular radiology, and more and more patients have the chance to undergo balloon angioplasty, intra-arterial stent implantation, or by-pass surgery (14). However, in this study, relatively a small group of patients had the chance of invasive vascular process owing to their clinical status and vascular structure.

Osteomyelitis is observed in approximately two-thirds of the patients with DFU, and the existence of osteomyelitis makes the treatment challenging and an important cause leading to the amputation risk (19). Osteomyelitis should be excluded, particularly from a chronic, non-healing, and deepened wound (20). Since the last decade, MRI is preferred in the diagnosis of osteomyelitis as it is non-invasive and applied easily with a specificity above 90% (21). In this study, X-ray and/or MRI were used in the diagnosis of osteomyelitis, and it was observed in 81.8% of the patients. In our study, it was revealed that the existence of osteomyelitis increased the amputation risk by 5.062 times. Despite medical treatment, our patients had to undergo minor or major amputation due to worsening of osteomyelitis

and ongoing severe gangrene or necrosis, not improved peripheral vascular insufficiency, or worsening of the patient's general condition (sepsis and decompensated heart failure). Orthopedists also decided on the type of surgery based on the perfusion or necrosis level of the foot after discussion. However, patients with osteomyelitis and Wagner 3 grade ulcers constituted 58% of the amputated patients. In our previous study comprising 135 patients, the osteomyelitis ratio was 32.5%; however, 84% of the patients underwent amputation (18). This osteomyelitis ratio is similar to our present study.

Another aspect of osteomyelitis is that it also requires long-term antibiotic therapy with associated side effects and cost. More than 50% of DFU are complicated with infectious agents, requiring hospitalization and specific therapy (5,22). In general, the most isolated bacteria in foot ulcers are aerobic gram-positive cocci. In severe diabetic foot infections, a polymicrobial infection generally exists consisting of aerobic gram-positive, gram-negative, and anaerobic microorganisms. *S. aureus* and particularly group B streptococci are common in infected foot ulcers (13,23,24). Similarly, we also mostly isolated these bacteria. Saltoglu et al. mostly reported gram-positive and gram-negative cocci and no isolate in 10% of their study patients (25). In the present study, 56% of the wound cultures were negative for any bacteria. This result may be owing to the presence of non-infected ulcers (ischemic-gangrenous wound) or antibiotics used in other previous clinics.

Management of infection with drainage, debridement of infected necrotic tissues, dressing if needed VAC-application, as well antibiotic therapy (oral or enteral) based on culture results. Despite the medical therapy, if osteomyelitis and severe gangrene or necrosis continue to worsen, minor or major amputation is required (8,22,26).

Retrospective observational studies reported that 15-24% of surgical amputations were required in DFU, and these ratios vary among the centers. It is highly challenging to make any comparison between the studies on DFU as many parameters are affecting the outcomes, which prevent head-to-head comparisons such as patient's

age, Wagner grades, comorbid conditions, presence of infection, glycemic control, and smoking. Extensive retrospective studies indicate that multidisciplinary follow-up of DFUs provides a decrease in major amputations by 75% (5,27). We evaluated the DFU patients through the multidisciplinary diabetic foot care team, including endocrinologists, radiologists, orthopedists, plastic surgeons, dermatologists, and infectious disease specialists for better management of DFU.

#### Study limitations

The most important limitations of our study were that the patients reported delayed to our clinic with the stage of amputation and the wound culture results were negative in the majority of patients; therefore, treatment was challenging. Moreover, fewer interventional radiology procedures were performed in these years.

#### Conclusion

Our patients were monitored using a multidisciplinary approach at our clinic; empirical antibiotic treatment was initiated with a majority of them, even with the considerable part of those with major amputation; and revascularization, tissue debridement, and VAC treatment were performed on patients considered necessary. Despite these approaches, 64% of patients underwent amputations, with 36.3% major amputations. The possible reasons for the high amputation rate are the length of the diabetes duration, insufficient glycemic control, referral of patients with advanced ulcers, and who reached to amputation stage at our hospital. The majority of these ulcers were at Wagner 2, 3, or 4 levels, and the insufficient peripheral arterial circulation delayed the wound recovery and increased the amputation risk. Consequently, DFUs are an important health issue at our clinic and region. In our study, the presence of peripheral arterial disease, osteomyelitis, and high Wagner degree are negative prognostic factors requiring amputation.

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### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

Idea/Concept: Mehtap Evran, Murat Sert, Tamer Tetiker; Design: Murat Sert, Tamer Tetiker; Control/Supervision: Mehtap Evran, Murat Sert, Tamer Tetiker, Ömer Sunkar Biçer, Erol Kesiktaş, Behice Kurtaran, Erol Aksungur; Data Collection and/or Processing: Mehtap Evran, Murat Sert, Tamer Tetiker, Gamze Akkuş, Behice Kurtaran, Erol Aksungur; Analysis and/or Interpretation: Mehtap Evran, Gamze Akkuş; Literature Review: Mehtap Evran, Gamze Akkuş; Writing the Article: Mehtap Evran, Murat Sert, Tamer Tetiker; Critical Review: Murat Sert; References and Fundings: Mehtap Evran, Murat Sert, Gamze Akkuş, Ömer Sunkar Biçer, Erol Kesiktaş, Behice Kurtaran, Erol Aksungur, Tamer Tetiker; Materials: Behice Kurtaran, Ömer Sunkar Biçer, Erol Kesiktaş, Mehtap Evran.

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