DOI:10.34084/bshr.1113655 e-ISSN 2587-1641

Journal of Biotechnology and Strategic Health Research

Araştırma Makalesi /Research Article

http://dergipark.org.tr/tr/pub/bshr

Examination of Underlying Lower Extremity Vascular Pathologies In Patients With Diabetic Foot Infection and Clinical Outcomes

Diyabetik Ayak Enfeksiyonu Olan Hastalarda Alt Ekstremite Damar Patolojilerinin Incelenmesi ve Klinik Sonuçları

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Geliş Tarihi / Received : 08-05-2022 **Kabul Tarihi / Accepted:** 01-07-2022 **Yayın Tarihi / Online Published:** 31-08-2022

Şahin S, Alkan S, Şener A. Examination of Underlying Lower Extremity Vascular Pathologies In Patients with Diabetic Foot Infection and Clinical Outcomes, J Biotechnol and Strategic Health Res. 2022;6(2):138-145

Abstract

Aim Diabetes and vascular disorders raise the risk of diabetic foot infection and lower extremity amputation. Although DFI risk factors and microbiological analyses have been thoroughly researched, data for this specific group is limited. This study aimed to examine the underlying vascular risk factors of patients who were followed up and treated with the diagnosis of DFIs and clinical outcomes.

Material and Method Clinical, demographic, laboratory, microbiological, and foot examination data for 153 patients referred to our center for DFI between 2016 and 2021 were collected retrospectively from the hospital information system.

Results A total of 153 DFI patients with a mean age of 67.71±15 years were included in the study. There were 104 patients in the non-vascular induced DFI group and 49 vascular induced DFI group. The top two comorbidities of DFI patients were cardiovascular disease and hypertension respectively. The rate of male patients was statistically higher in the vascular-induced DFI group (p=0.003). History of extremity amputation/debridement, having Wagner grade 5 DFI and Gram-negative microorganism growth in tissue cultures were more common in the vascular-induced DFI group (p=0.01, p=0.01, and p=0.0006). Extremity amputation/debridement rates were higher in the vascular-induced DFI group (p=0.01).

Conclusion DFIs cause an increased risk of amputation, prolonged antibiotic therapy, increased hospitalization, and increased healthcare costs as a result of investigations. Awareness of the vascular pathologies underlying DFIs can help clinicians manage the disease. The aim of this study is to emphasize the importance of vascular factors.

Keywords diabetic foot infection, vascular risk factors, clinical outcomes.

Özet

Amaç *Diyabet ve damar hastalıkları, diyabetik ayak enfeksiyonu (DAE) ve alt ekstremite amputasyonu riskini artırır. DAE risk faktörleri ve mikrobiyolojik analizler kapsamlı bir şekilde araştırılmış olmasına rağmen, bu özel grup için veriler sınırlıdır. Bu çalışma DAE tanısı ile takip ve tedavi edilen hastaların altta yatan vasküler risk faktörlerinin ve klinik sonuçlarını incelenmeyi amaçladı.*

Gereç ve Yöntem *2016-2021 yılları arasında DAE için merkezimize başvuran 153 hastanın klinik, demografik, laboratuvar, mikrobiyolojik ve ayak muayene verileri hastane bilgi sisteminden geriye dönük olarak toplandı.*

Bulgular *Çalışmaya yaş ortalaması 67.71±15 yıl olan toplam 153 DAE hastası dahil edildi. Vasküler kaynaklı olmayan DAE grubunda 104, vasküler kaynaklı DAE grubunda 49 hasta vardı. DAE hastalarının ilk iki komorbiditesi sırasıyla kardiyovasküler hastalık ve hipertansiyondu. Vasküler kaynaklı DAE grubunda erkek hasta oranı istatistiksel olarak daha yüksekti (p=0,003). Ekstremite amputasyonu/debridman öyküsü, Wagner grade 5 DAE ve doku kültürlerinde Gram negatif mikroorganizma üremesi vasküler kaynaklı DAE grubunda daha sıktı (p=0.01, p=0.01 ve p=0.0006). Vasküler kaynaklı DAE grubunda ekstremite amputasyon/debridman oranları daha yüksekti (p=0.01)*

Sonuç *DAE'ları, yüksek ampütasyon riski, uzun süreli antibiyotik tedavisi, artan hastane yatışı ve tetkikler sonucu artan sağlık maliyetlerine neden olur. DAE'larının altında yatan vasküler patolojilerin farkındalığı, klinisyenlerin hastalığı yönetmesine yardımcı olabilir. Bu çalışmada amaç vasküler faktörlerin önemini vurgulamaktadır.*

Anahtar Kelimeler *diyabetik ayak enfeksiyonu, vasküler risk faktörleri, klinik sonuçlar.*

INTRODUCTION

Diabetic foot infections (DFI) are caused by many reasons such as trauma, diabetic neuropathy, and peripheral vascular pathologies (arterial or venous). Neuropathy leads to foot deformities, and this causes higher pressure on the foot and may result in a foot ulcer. When ulcer formation occurs the limb is at high risk of invasive infection.[1] Although the etiology of DFI is complex, three major components are neuropathy, ischemia, and infection, all contribute to tissue necrosis and ulcer formation.[2]

DFIs are known to be a major diabetes mellitus (DM) complication, and they cause significant morbidities and fatalities. The fatality rate associated is predicted to be 5% in the first 12 months, with a 5-year fatality rate of 42%. Surgical debridement if needed, vascular evaluation, dressings to promote a moist wound environment and exudate control, off-loading, infection and glycemic controls are all routine practices in DFI therapy.[3]

DFI treatment can be challenging, and underlying patient comorbidities, as well as a lack of patient compliance, might impede recovery. Diabetes impairs healing by interfering with cell responses to cytokines and chemokines, macrophage function, angiogenesis, epidermal barrier function, and the creation of collagen and granulation tissue.[4] Medical and surgical management, and percutaneous transluminal angioplasty of stenosed or blocked lower extremities arteries are all options for diabetic ischaemic foot treatment. In diabetics, foot ulceration is the most common cause of amputation.5 Irresolvable rest pain and claudication, as well as nonhealing ulcers despite appropriate medical care, are indications for arterial reconstruction surgery.[4]

Critical leg ischemia in diabetic patients can be prevented with rapid vascular interventions. Diabetes and vascular disorders raise the risk of diabetic foot infection and lower extremity amputation. Although DFI risk factors and microbiological analyses have been thoroughly researched, data for this specific group is limited. In this study, it was aimed to examine the underlying vascular risk factors of DFIs patients and the outcomes.

MATERIAL and METHODS

This is a retrospective study that was performed on collected data from DFI patients, who were hospitalized in the Çanakkale Onsekiz Mart University Hospital, between 2016-2021. This study included adult patients who presented as DFI and were admitted to the in-patient clinic. A list of all patients diagnosed with DFI was retrieved from the hospital database. The list included 198 patients of which 45 patients were excluded from the study due to missing data. The patient's confidentiality was guaranteed by issuing each patient a number code for reference and the codes were only accessible to the authors. Demographic data, clinical symptoms, vital signs, underlying diseases, underlying vascular pathologies, recurrent DAI, duration of DM, a treatment used for DM (not receiving treatment, oral antidiabetic, insulin), DAI location, tissue or wound cultures, history of extremity amputation, lack of access to health care, patient compliance, uncontrolled diabetes, vascular insufficiency, peripheral motor neuropathy, neuro-osteo-arthropathic deformities, serum hemogram parameters, inflammatory parameters [C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)], glycated hemoglobin (Hb A1C) levels, imaging procedures and results, the length of hospitalization, the outcome of the treatment were examined in detail.

The Wagner classification was used to classify each patient's wound. The Wagner classification system uses the following grades to determine ulcer depth and the occurrence of osteomyelitis or gangrene: Grade 0 (no skin lesions, hyperkeratosis below or above bony prominences); degree 1 (partial/ full-thickness ulcer); grade 2 (probing to tendon or capsule); grade 3 (deep tissues always implicated, osteomyelitis may be present); grade 4 (partial foot gangrene); and grade 5 (whole foot gangrene) (whole foot gangrene).[6]

The mentioned department used magnetic resonance imaging (MRI), X-ray if available nuclear medicine imaging, or histopathologic examinations to identify osteomyelitis. At referral, peripheral arterial/venous disease was defined as a documented history of lower extremity revascularization and/or the presence of angiographically or Doppler ultrasonographically characterized peripheral vascular disease.

The patients were divided into two groups based on their clinical presentation: "vascular induced DFI group" and "non-vascular induced DFI group."

Inclusion criteria

- Being over the age of 18,
- Having a diagnosis of DAI,
- Inpatients,
- Cases who had at least one microbiological positive culture result,
- Cases who underwent doppler or computerized tomography angiography (CTA) scan

Exclusion criteria

- Being under the age of 18,
- Pregnancy,
- Outpatients,
- Missing data

Statistical analysis

The Statistical Package for Social Sciences (SPSS) statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA), was used for descriptive statistics. All nominal variables' frequencies and percentages, as well as the mean and range of all measurable variables, were determined. For all measurable variables, the t-test was employed for comparisons between the groups, whereas the chi-square test was utilized for all nominal variables. A p-value of under 0.05 was deemed significant.

RESULTS

The present center collected a total of 153 DFI patients over 5 years this period. There were 86 males and 67 women with a mean age of 67.71±15 years. There were 104 patients in the non-vascular induced DFI group and 49 vascular induced DFI group. The vascular-induced DFI group consisted of cases diagnosed as a peripheral arterial disease (documented history of lower extremity revascularization and/or the presence of angiographically or Doppler ultrasonographically characterized peripheral arterial disease). The top two comorbidities of DFI patients were cardiovascular disease and hypertension respectively. The summary of characteristics of 153 DFI patients were given in Table 1.

The rate of male patients was statistically higher in the vascular-induced DFI group (p=0.003). Also, hypertension and cardiovascular disease were more common in the vascular-induced DFI group (p=0.0006, p=0.01). History of extremity amputation/debridement, having Wagner grade 5 DFI, and Gram-negative microorganism growth in tissue cultures were more common in the vascular-induced DFI group (p=0.01, p=0.01, and p=0.0006). Extremity amputation/debridement rates were higher in the vascular-induced DFI group (p=0.01) (Table 2).

Table 1. Summary of clinical characteristics of 153 DFI patients	
Age, mean (years)	67.71±15 years
Sex, male (%)	86(56.2)
Body mass index (kg/m2), mean ± SD	25.8 ± 5.78
Diabetes duration (years), mean ± SD	12±0.2
Diabetes medication, n (%)	
-only insulin	65(42.5)
-only oral antidiabetics	72(47)
- Insulin plus oral antidiabetics	16(10.4)
Uncontrolled diabetes	18(11.8)
Comorbidities	
- Hypertension	72(47)
- Cardiovascular disease	42(27.5)
- Chronic lung disease	13(8.5)
-Malignancy	3(2)
History of mechanical trauma/injuries	13(8.5)
Foot deformities	18(11.8)
Previously diagnosed as diabetic neuropathy	42(27.5)
Wound location, n (%)	
-Forefoot	72(47)
-Midfoot	42(27.5)
-Hindfoot	30(19.6)
-Entire foot	9(5.9)
History of extremity amputation/debridement (6 months)	42(27.5)
Orally antibiotics treatment before admission (15 days (%))	46(30.1)
Sepsis at admission	18(11.8)
Fever at admission	36(23.5)
Localization of DFI	
Left	70(45.8)
Right	80(52.2)
Bilateral	3(2)
Type of vascular disease (total:49)	
arterial	30(19.6)
venous	12(7.8)
both arterial and venous	7(4.6)
Wagner classification	
-grade 2	12(7.8)
-grade 3	53(34.6)
-grade 4	46(30.1)
-grade 5	42(27.5)
tissue cultures,	
Gram negative microorganism, n (%)	72(47)
Gram positive microorganism, n (%)	80(52.2)
Fungal microorganism, n (%)	1(0.7)
Interval between onset of DFI symptoms and referral, days, mean ± SD)	25.24± 15.1
Extremity amputation/debridement	70(45.8)
Hospitalization days	18.6±12.3
Mortality	4(2.8)
Abbreviations: DFI, diabetic foot infection; SD: standard deviation.	

Table 2. Characteristics of patients with DFI

Patient characteristics	Group 1 (non-vascular induced DFI group) (n=104)	Group 2 (vascular induced DFI group) (n=49)	P-value
Male (%)	50 (48)	36 (73)	0.003
Age (years) (SD)	66 ±15	62±15	0.019
Weight, kg	70±22	73±26	0.46
Hypertension	39 (38)	33 (67)	0.0006
Cardiovascular disease	22 (21)	20 (41)	0.01
Chronic renal failure	11 (11)	7 (14)	0.51
Chronic lung disease	9 (9)	4 (8)	0.99
History of mechanical trauma/injuries	9 (9)	4 (8)	0.99
Foot deformities	11 (11)	7 (14)	0.51
Duration of diabetes (years)	12 ± 4	12 ± 5	0.94
Insulin treatment for diabetes	44 (42)	21 (43)	0.95
Uncontrolled diabetes	11 (11)	7 (14)	0.51
Previously diagnosed as diabetic neuropathy	22 (21)	20 (41)	0.01
History of extremity amputation/debridement (6 months)	22 (21)	20 (41)	0.01
Orally antibiotics treatment before admission (15 days (%))	26 (25)	10 (20)	0.53
Sepsis at admission	11 (11)	7 (14)	0.51
Fever at admission	26 (25)	10 (20)	0.53
Wagner grade 5	22 (21	20 (41)	0.01
Gram negative microorganism growth in tissue cultures, n (%)	39 (38)	33 (67)	0.0006
DFI symptoms before admission, days, mean ± SD)	15 ±33	47 ±46	<0.0001
Extremity amputation/debridement	40 (39)	30 (60)	0.01
Hospitalization days	17± 20	22 ±16	0.09
Mortality	4 (4)	0 (0)	0.31
C- reaktive protein (mg/dl)	3.3 ±4.2	4.9± 4.3	0.03
Erythrocyte sedimentation rate (mean ± SD)	89± 24	87± 25	0.64
White blood cell (K/µL) (mean ± SD)	12±4	12 ± 5	0.94
Hemoglobin(103/µL) (mean ± SD)	12 ± 5	12 ± 5	0.71
HbA1c, % (mean ± SD)	9.5 ±5.3	9.4 ±4.2	0.93

DISCUSSION

Diabetic patients are more prone to foot ulcers caused by neuropathy, ischemia, and weakened immunity. Ischemia lowers local defenses against infections by reducing the flow of oxygen, vital nutrients, and growth factors to tissues. Because of the nature of the foot's compartments, tendon sheaths, and neurovascular systems, DFIs spread quickly.[7] Diabetes and vascular disorders raise the risk of DFIs and lower extremity amputation. Although DFI risk factors and microbiological analyses have been thoroughly researched, data for this specific group is limited.[5,7,8] In this study, it was aimed to examine the underlying vascular risk factors of patients who were followed up and treated with the diagnosis of DFIs and outcomes.

Our findings support the findings of Patil and Mane9, who observed that diabetes individuals between the ages of 51 and 60 developed foot ulcers. In the present study, there mean age of the patients was 67.71±15 years.

A similar study performed in the Kingdom of Saudi Arabia[8] found that the majority of DFIs were caused by non-vascular etiology. The factors that were substantially related to DFIs due to arterial disease were senility, a history of coronary artery disease, or peripheral artery disease in the unaffected limb. In our study, group 1 (non-vascular induced DFI group) patients were older than group 2 (vascular-induced DFI group) patients. Hypertension and cardiovascular disease were more common in the vascular-induced DFI group.

Modern data on the microbiologic characteristics of DFIs have produced conflicting results. Geographic distribution, meteorological circumstances, and socioeconomic level were all connected with the results. Whereas gram-positive isolates with high Staphylococcus aureus isolation rates predominated in the Western literature, more recent research from the Middle East and the Far East, as well as African countries, demonstrated gram-negative predominance with high Pseudomonas aeruginosa isolation rates.[7,9-15] The high prevalence of P. aeruginosa as a causal pathogen was also noted in our country's the National Consensus Report for the Diagnosis, Treatment, and Prevention of Diabetic Foot Wounds and Infections, and these findings were recommended to be taken into account in the empirical treatment of DFI patients.[16]

It has also been reported that polymicrobial infections are to blame for persistent wounds and more complex infections.[11,15] Körpınar[17] reported that the most common pathogens identified in deep wound cultures from DFIs in end-stage renal disease patients were S. aureus and P. aeruginosa, accounting for 27 (21.2%) and 16 (12.5%) of all 127 isolates, respectively. In our study, the most common pathogens were gram-positive isolates (52.2%). But gram-negative microorganism growth in tissue cultures was more common in the vascular-induced DFI group.

It has been found that limbs with chronic wounds (>6 weeks) attain full healing in only 57% of cases after a year.[18] Furthermore, chronic wounds usually have an underlying etiology that contributes to their nonhealing, which is either infectious or ischemic in etiology.[19] In our study, underlying vascular pathology was found in 49 (32%) of 153 patients with DFI. Of all cases, 19.6% had arterial, 7.8% had venous, and 4.6% had both arterial and venous vascular disorders. However, this number represented cases with radiological evidence. Since the involvement at the microvascular level will not show any radiological findings, this situation may have caused bias.

In the comparison between these two groups, a history of extremity amputation/debridement and Wagner grade 5 DFI were more common in the vascular-induced DFI group. Limb amputation/debridement rates were higher in the vascular-induced DFI group. Mortality rates were higher in the non-vascular-induced DFI group. This data on mortality can be attributed to the many different etiologies of mortality. However, mortality-related risk factors were not examined in detail in our study.

CONCLUSIONS

A dedicated facility offering vascular assessment, a multidisciplinary pre-coordinated strategy, and vascular management will be more effective in managing a diabetic patient with a foot wound. To reduce the number of major amputations in the diabetic community, better arterial evaluation and treatment are required (vascular functional testing and revascularization when possible). Peripheral vascular disease is highly curable if intervention is initiated promptly and collaboratively.

Ethical consideration

The Institutional Review Board Committee of Çanakkale Onsekiz Mart University approved this study (Decision Date: 19.01.2022; Decision No: 2022-02)

Conflict of interest

The authors declare no personal or financial conflict of interest.

Disclosure

No financial support was received.

Author Contributions

Main idea/Planning- SŞ, SA, Analysis/Comment- SŞ
Data provision- All authors, Spelling- SŞ, SA, AŞ, Review and Correction- AŞ, Literature Search- SŞ, SA, Writing - SŞ, SA, Confirmation-All authors

Limitatitons

This is a retrospective, single center study. The vascular pathology informations depends on radiological findings.

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