ORIGINAL ARTICLE



Wound infections and recovery time among patients with diabetic foot ulcer living in multiethnic Suriname, a developing country: a retrospective cohort study among patients from the One Stop Shop for chronic diseases Paramaribo

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Abstract

The purpose of this study was to describe patient characteristics and clinical outcome among patients with diabetic foot ulcers under treatment of a multidisciplinary outpatient clinic in multiethnic Suriname, a developing country in South America. Retrospectively, all diabetes patients (> 18 years) with foot ulcers starting their treatment at the outpatient clinic between November 2013 and October 2014 were included and followed for at least 12 weeks. To assess differences in clinical outcome between subgroups, chi-square and incorporating time-related data, the log-rank test were used. One hundred patients were included (lost to follow-up, n = 20). Half of patients were males (n = 40). Mean age was 57.8 years. Nephropathy, peripheral arterial disease, and neuropathy were present in 90.9, 41.7, and 90.3%, respectively. Thirty-five percent of wounds healed within 12 weeks (median at 50 days, 13 visits). Sixty-eight percent of wounds were infected. No major but four minor amputations were carried out. Looking at subgroups, infection and ethnicity (African vs. Asian descent), but not gender or age, increased risk for delayed healing (p < 0.001 and p = 0.049, log-rank test). It seems of high priority to increase awareness and search for accurate preventive strategies for diabetic foot, and related wounds and infections, with special attention for ethnic disparities, in Suriname.

Keywords Diabetic foot ulcer · Infection · Recovery · Amputation · Developing country · Ethnic disparity

Introduction

The number of people with diabetes mellitus is increasing worldwide, in particular in developing countries [1-3]. This rise is most likely due to population growth, aging, urbanization, and increasing prevalence of obesity

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Ingrid S Krishnadath Ingrid.Krishnadath@uvs.edu and physical inactivity. The Suriname Health Study estimated that 13.2% of the Surinamese population between 15 and 65 years of age suffers from diabetes, including a prevalence of 23.3% for the Hindustani [4]. Worldwide, the prevalence of diabetes was estimated at 7.7% for 2030 [2].

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Suriname is located in the Northeast of South America and placed among the upper-middle-income countries (World Bank's list of economies [5]). The historical development of Suriname has resulted in a unique social structure, composed of a variety of cultures, religions, ethnicities, and economic units. The present population distribution in Suriname is as follows: Hindustani (27.4%), Maroons (21.7%), Creoles (15.7%), Javanese (15.7%), mixed (13.4%), and other ethnicities (8.2%) [6]. Diabetes mellitus is the fourth cause of death, with cardiovascular disease as the main cause [7].

A major complication of diabetes is the diabetic foot [8, 9]. One in every four up to ten individuals with diabetes will suffer from a foot ulcer during lifetime, with higher risk if other diabetes-related complications exist [8, 10, 11]. Many of these ulcers will need intensive treatment and hospitalization [12, 13]. Despite treatment, diabetic foot ulcers frequently lead to amputation of the foot, which is associated with higher mortality rates [8, 14]. Better diagnosis and prevention of diabetic foot ulcers can reduce amputation risk and health care costs also shown for developing countries in the region [9, 15-17]. Many multidisciplinary team-based practice models have been shown to decrease the frequency of major amputations by directing their interventions to infection, peripheral arterial disease (PAD), abnormal pressure loading caused by peripheral neuropathy, and limited joint mobility and by increasing the rate of minor amputations [8, 12, 15, 18-20]. From November 2013, the first multidisciplinary wound clinic to treat diabetic foot ulcers in Suriname was operational, located at the One Stop Shop for chronic diseases (OSS) in Paramaribo.

Data on the burden of diabetes-related complications such as diabetic foot ulcers from developing countries are lacking. Also for Suriname no data was reported. Therefore, this study aimed to describe patient characteristics and clinical outcome such as rates of infection, wound healing, amputations, and recovery time among diabetes patients with different ethnicities under treatment for diabetic foot ulcers provided at the OSS Paramaribo.

Materials and methods

Subjects and design

To describe patient characteristics and clinical outcome at the OSS, a retrospective cohort study was conducted. Included were all diabetes patients (> 18 years) with foot ulcers starting their treatment at the OSS Paramaribo between November 1, 2013, and October 31, 2014. Excluded were patients with ulcus cruris or wounds above the ankle. The OSS is an outpatient health care center where diabetes mellitus and its diabetic foot are managed and treated by a multidisciplinary team of general practitioners, orthopedic surgeons, physiotherapists, nurses, podiatrists, and dieticians, with the international guide-lines as basis [12]. According to Boulton et al. [19], diabetic

foot ulcers can be expected to heal within 12 weeks utilizing a multidisciplinary approach. To give all patients at least 12 weeks to reach ulcer healing, each patient was followed up retrospectively for at least 12 weeks (= 84 days). At the end of the study period, patients were (1) discharged because of healed wounds, (2) still under treatment, (3) dead, or (4) lost to follow-up. A patient was considered lost to follow-up if the patient did not complete the minimal treatment period of 84 days without being recovered or deceased. The research proposal for this study was approved by the Ethics Committee of the Ministry of Health of Suriname.

Data collection

Patient characteristics (demographics and comorbidities). wound characteristics, and clinical outcomes were extracted from the patient medical files and electronic database of the outpatient wound clinic. Patient characteristics collected were gender, age, ethnicity, weight and height (body mass index; BMI), duration of diabetes mellitus (DM), presence of hypertension, nephropathy, PAD and neuropathy, Charcot neuroosteoarthropathy, multiple ulcers, and previous ulcers or amputation of the foot. Ethnicity and duration of DM were selfreported by the patients. BMI was calculated by dividing weight (kg) by squared height (m²). Body weight was measured at the first visit at the wound clinic using an electronic beam scale with digital readout to the nearest 0.1 kg (Seca, Germany). Body height was measured to the nearest 0.5 cm using a stadiometer (Seca, Germany). Status of comorbidities such as hypertension or nephropathy was reported by the referring specialist or general practitioner. In case the status of current comorbidities was unknown, diagnostics were performed at the OSS according to standard medical protocols (SPAOGS protocols http://www.spaogs.org/ accredited by the Ministry of Health Suriname). Diagnostics of diabetes-related complications of the foot were performed at the OSS. PAD was assessed at the OSS by vascular patency using Echo-Doppler. A mono phasic or no sound indicated PAD. Neuropathy was judged to be present if superficial sensibility disorder was diagnosed using monofilament test. Charcot neuro-osteoarthropathy was determined by X-ray of the foot when clinical signs were present such as pain, swelling, local temperature rise, or deformity. For this study, wound characteristics at baseline were described from the most severe ulcer per patient based on the Wagner classification, an ulcer severity scoring system based on wound depth, presence of infection, and gangrene [21]. Localization was defined by dividing the foot into single anatomic areas based on pressure load into hallux, lesser toes, fore foot, mid foot, and heel. Other sites on the foot where ulcers were seen were added to this list, such as dorsum, the lateral and medial edge of the foot, interdigital, and site of previous amputation. Multiple locations refer to small non-adjoining ulcerations located on different parts of the foot. Clinical outcome measures

were the occurrence of infection and osteomyelitis, diagnosed according to the international protocol [22], wounds healed within 12 weeks, recovery time, amount of visits, and minor and major amputation rates.

Statistical analysis

To describe patient characteristics and clinical outcome among diabetes patients treated for foot ulcers at the OSS Paramaribo, rates (frequencies and percentages) of infection, wound healed within 12 weeks, and amputations were presented. Recovery time and amount of visits were presented as medians. Differences in wound healing within 12 weeks were analyzed between subgroups (gender, age (> 60 years), ethnicity, infection) using the Pearson chi-square (trend) test. In order to include time-related information concerning recovery at the OSS, the dependent variable time till recovery was analyzed using the Kaplan-Meier Survival curve, with differences between subgroups tested with the log-rank test. A pvalue ≤ 0.05 was considered to indicate statistical significance. All statistical analyses were performed with SPSS (version 22.0, 2014, SPSS Inc., Chicago, IL).

Results

After initial screening of medical files, 100 patients were included, each of which had one or more foot ulcers as a complication of diabetes. Twenty patients were found lost to follow-up, and clinical outcome of these patients remained unknown. Gender, age, and ethnicity did not differ from the remaining 80 patients (data not reported). At the end of the study period (n = 80), 42 (53%) patients were recovered (median weeks to heal 10 (mean 15), range 2–56, with median of 17 visits (mean 23), range 2–138). The rest, 38 (47%) patients, were under treatment at the end of the study.

Table 1 shows characteristics of the patient population on initial visit at the OSS. The ethnic group that was mostly treated for foot ulcers were Hindustani. The average DM duration was 14.8 years; 38.8% of the patients underwent previously a minor amputation, and 2.5% a major amputation of the foot. Forty percent of patients had two or more ulcerations. Fifty-five percent of ulcers were classified as grade 1 indicating low complexity of the wound according to the Wagner classification (Table 1).

Table 2 shows that 35% (n = 28) of wounds healed within 12 weeks, with a median treatment duration till healing of 50 days and 13 visits. Sixty-eight percent of wounds (n = 54) were infected of which one third were diagnosed with osteomyelitis (n = 14). No major amputations were carried out. Four patients received a minor amputation. No association was found between gender, age, or ethnicity and healing within 12 weeks (Table 2,

Table 1 Characteristics of the patient population on initial evaluation at the OSS (n = 80)

	Study population <i>n</i> (%)	Missing n	
Sex		_	
Male	40 (50)		
Female	40 (50)		
Age (years) mean (min-max)	57.8 (31-82)	_	
Ethnicity		_	
Asians			
Hindustani	46 (57.5)		
Javanese	6 (7.5)		
Africans			
Creoles	19 (23.5)		
Maroon	2 (2.5)		
Others			
Mixed	5 (6.3)		
Amerindians	1 (1.3)		
Caucasian	1 (1.3)		
BMI			
Median (min-max) (kg/m ²)	27.2 (20.3–52.2)	18	
Duration of DM			
Median (min-max) (years)	14.0 (0.0-42)	7	
HbA1c			
Median (min-max) (%)	9.0 (5.6–15.2)	16	
HbA1c			
Median (min-max) (mmol/mol)	74 (38–143)	16	
Hypertension	53 (80.3)	14	
Nephropathy	50 (90.9)	25	
Overweight	17 (27.4)	18	
Obesity	22 (35.4)	18	
Smoking	11 (17.5)	17	
Alcohol	8 (14.3)	24	
Vascular patency		10	
No indication ^a	46 (65.7)/-		
Mono phasic	10 (12.5)/(41.7)		
Bi phasic	11 (13.8)/(45.8)		
Tri phasic	3 (3.8)/(12.5)		
Neuropathy	65 (90.3)	8	
Superficial sensibility disorder	5 (6.9)		
Deep sensibility disorder	2 (2.8)		
Both	60 (83.3)		
Charcot deformity	17 (21.3)	-	
Multiple ulcerations	32 (40)	1	
Previous ulcer	33 (68.8)	32	
Previous amputation		—	
Minor	31 (38.8)		
Major	2 (2.5)		
Wagner classification		6	
Grade 1	41 (55)		
Grade 2	22 (30)		

Table 1 (continued)

	Study population <i>n</i> (%)	Missing n
Grade 3	11 (15)	
Grade 4	0 (0)	
Location of wound		1
Forefoot	29 (37)	
Midfoot	12 (15)	
Heel	7 (9)	
Hallux	13 (16)	
Lesser toes	8 (10)	
Dorsum	4 (5)	
Lateral foot edge	2 (3)	
Interdigital	1 (1)	
Medial foot edge	1 (1)	
Multiple	1 (1)	
Site of prev. amp.	1 (1)	
Referrer ^b		_
Surgeon	42 (58.3)	
General practitioner	25 (34.7)	
"Walk-ins"	5 (6.9)	

^a No indication meant that PAD was judged not present based on palpation of the A dorsalis pedis and A tibialis posterior. In case of no indication, the Echo Doppler technic was not performed. Since the Echo-Doppler technic was available at the OSS, vascular patency was judged in every patient using the Echo-Doppler technic. The clinical practitioners doubt the value of no indication based on palpation. Therefore, the number of PAD was also calculated as if no indication were missing values. The number of patients with PAD (mono phasic) is therefore reported as 12.5 and 41.7%, respectively

^b Patients visiting the One Stop Shop are referred by the general practitioner or the surgeon. It is also possible for patients to consult the OSS on own initiative. These patients are called walk-ins

p > 0.154, chi-square (trend) test). Analyzing the association between the occurrence of infection and wound healed within 12 weeks in the total group, it was found that of those wounds with an infection 22% (n = 12)healed within 12 weeks and of those without an infection 62% (n = 16) healed within 12 weeks (p = 0.001, chisquare test) (Table 2). In addition, looking at ethnicity in more depth by comparing only those patients from Asian descent (n = 52) with patients from African descent (n =21), it was seen that in patients of Asian descent a higher number of wounds healed within 12 weeks and less infections occurred; 42.3% of patients of Asian descent (n =22) recovered in 12 weeks vs. 19.0% of patients of African descent (n = 4) (p = 0.060, chi-square test); and 57.7% of patients of Asian descent had an infected wound vs. 81.0% of African descent (p = 0.060, chi-square test). Patients from African descent were at higher risk at baseline using the Wagner classification than those from Asian descent (grade 1 (32 vs. 65%), grade 2 (42 vs. 27%), and grade 3 (26 vs. 8%), p = 0.031, chi-square trend test). No other statistical differences between patients of African and Asian descent were found (data not reported).

Figure 1 shows part of diabetes patients healed over time under treatment of the OSS using the Kaplan-Meier curve. On the y-axis, part of patients healed is presented. At the start of treatment (x-axis, day 0), part of patients healed was logically 0. After 100 days, in about 35% of patients, their wound was healed. From the steeply decreasing course of the curve, it was seen that the highest healing rates were seen before 100 days of treatment. Wound healing rates over time dropped after 100 days of treatment. Figure 2 shows part of diabetes patients healed over time under treatment of the OSS with and without an infection

Table 2 Frequency and percentage of healed ulcer within 12 weeks, and average time and	Subgroup (<i>n</i>)	Healed ulcer in 12 weeks <i>n</i> (%)	Time till healing (days) Median (min–max)	Visits till healing Median (min–max)
amount of clinical visits for healed wound within 12 weeks	All (80)	28 (35)	50 (17-84)	13 (2–31)
	Gender			
	Male (40)	12 (30)	39 (19–73)	10 (2–27)
	Female (40)	16 (40)	52 (17-84)	12 (3–31)
	Age			
	≤60 (53)	19 (36)	52 (17-84)	11 (3–27)
	>60 (27)	9 (33)	48 (22-82)	12 (2–31)
	Ethnicity			
	Asians (52)	22 (42)	55 (19–84)	10 (2–31)
	Africans (21)	4 (19)	49 (17–71)	17 (5–22)
	Others (7)	2 (29)	44 (40–48)	16 (13–18)
	Infection			
	Yes (54)	12 (22) *	51 (25-82)	18 (10–31) **
	No (26)	16 (62)	45 (17–84)	8 (2–25)

*p < 0.05, chi-square test; **p < 0.05, non-parametric independent MWU test

Table 2 Frequency and



Fig. 1 Part of patients with diabetic foot ulcer recovered over time treated at the OSS

in separate curves. These curves show that patients with uninfected wounds have a higher healing rate than patients with infected wounds. After 100 days of treatment, almost 70% of patients with an uninfected wound healing were observed compared to about 25% of patients with an infected wound (p < 0.001, log-rank test). In both subgroups, wound healing rates drop after 100 days of treatment. Figure 3 shows part of diabetes patients healed over time under treatment of the OSS of Asian and African descent, separately. After 100 days of treatment in about 45% of patients of Asian descent, their wound was healed compared to about 20% of patients of African descent (p = 0.049, log-rank test). In both subgroups, wound healing rates drop after 100 days of treatment.



Fig. 2 Part of patients with an infected diabetic foot ulcer and without an infected foot ulcer recovered over time treated at the OSS. Full line represents the subgroup of diabetic patients with an infected foot ulcer; dotted line represents the subgroup of diabetic patients without an infected foot ulcer



Fig. 3 Part of patients with diabetic foot ulcer of Asian descent and of African descent recovered over time treated at the OSS. Full line represents the subgroup of diabetic patients with a foot ulcer of African descent; dotted line represents the subgroup of diabetic patients with a foot ulcer of Asian descent

Discussion

Compared to studies from different continents, patient characteristics such as gender, age, BMI, or duration of DM were alike [23-25]. However, presence of other risk factors differed largely from the population of the OSS Paramaribo. In the OSS, there were less smokers (17 vs. 41% in Brazil [25], 47% in Boston, and 52% in Italy [23]), but there was a higher prevalence of diabetes-related complications. Nephropathy was present among 91% of patients from the OSS vs. 62% in Brazil [25], 18% in Boston, and 25% in Italy [23]. PAD was present among 42% of patients in the OSS vs. 36% in Brazil [25] and 22% in Oslo [24]. Lastly, peripheral neuropathy was present among 93% of patients in the OSS vs. 59% in Brazil [25] and 12% in Oslo [24]. Higher rates of peripheral neuropathy were also reported in studies among other developing countries [26, 27]. The high rates of PAD found for the population of the OSS are in line with the current rising rates of diabetes mellitus and cardiovascular disease in upper-middleincome countries as Suriname, in contrast to low-income countries [9]. Looking at clinical outcome, it was seen that mean weeks to heal were higher at the OSS than at the centers in Boston or Pisa (15 vs. 7 and 11 weeks) as also the amount of mean visits (23 vs. 5 and 16) [23]. Hampered recovery among the OSS population might be a consequence of the higher prevalence of diabetes-related complications. However, it should be taken into account that duration of follow-up differed between the studies, and that mean and not median weeks to heal were presented. As also seen in other research, our data suggest that in case an ulcer was not healed within the first weeks, prognosis worsened [19]. Perhaps clinical decision-making should differ after several weeks of treatment without healing. Infection rates at the OSS, Boston, and Italy

were alike, about two thirds of ulcers [23]. Compared to the center in Oslo [24], more patients recovered at the OSS (53 vs. 37%). However, in Oslo 14% (n = 18) underwent an amputation (11 minor) which was much higher than in the OSS. And, in many cases, amputation is the most appropriate way towards recovery, instead of a mutilating failure. [28]. Wagner risk classification indicated that the wounds of patients at the OSS at baseline were as severe as the wounds of patients in Oslo. Clinical outcome of the center in Brazil [25] seemed most comparable with the OSS. At the center in Brazil, complete healing without amputation was observed in 31.8% of patients after 3 months of treatment and 51.1% (*n* = 48) after 6 months. Twelve percent (n = 11) underwent a minor amputation. There were no major amputations. Also in the Brazil study, infection was associated with recovery time as also described by others [25, 29]. In conclusion, clinical outcome data from the OSS did not seem to deviate much from numbers reported in other countries. However, because of large differences in the presence of patient characteristics such as lifestyle and diabetes-related complications, clinical outcome cannot be compared, especially not in low- vs. high-income countries with differing health care facilities. Factors such as ethnicity, wound complexity, diabetes-related complications, and treatment facilities in place differ largely, and all have their impact on recovery and amputation rates [8, 26, 27, 30-32].

The results of our study might suggest that patients of African descent were at higher risk for wound infections and lower healing rates than those from Asian descent. A study in Eurasian and African TBC patients living at the UK suggested the possibility of genetic disparities in relation to the inflammatory response in favor of Eurasians [33]. However, differences might be as well associated with other confounding risk factors such as differences in patient characteristics, social economic factors, or health seeking behavior. Future prospective research with a larger sample has to reveal if ethnic disparities appear with respect to wound healing.

This study faced some limitations. The retrospective design resulted in high amount of missing values among some of the baseline characteristics resulting in overreported or underreported numbers. Time to follow-up might have been relatively short to count all amputations eventually carried out. This single-center study is the first documentation of estimates of patient characteristics and clinical outcome among patients with diabetic foot ulcer in Suriname. To increase generalizability, further research should focus on multicenter studies including control groups without ulcer and larger sample size.

Conclusion

multiethnic Suriname, a developing country in South America. High prevalence of diabetes-related complications and two-thirds infection rate implicate that it is of high priority to increase awareness and search for preventive strategies for diabetic foot, and related wounds and infections, among the Surinamese population, with special attention to ethnic disparities. Because characteristics differ between developing and developed countries, it is of importance that developing countries invest in prospective data registration and research to increase effectiveness of care and reduce costs.

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Authors' contributions LK coordinated this study together with ISK and LMN-vV. LMN-vV conducted statistical analysis, reviewed the data and results, and wrote the manuscript. CP and BA assisted in the data collection and statistical analyses. CP, BA, EB, ISK, and LK collaborated with the interpretation of data, and reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standards of the national research committee, the Ethics Committee of the Ministry of Health of Suriname, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Because of the retrospective study design, informed consent was not obtained from the subjects. All data were gathered primarily for standard clinical care. To guaranty confidentiality, analyses were on group level and anonymized by coding.

References

- Aguiree F, Brown A, Cho NH, Dahlquist G, Dodd S, Dunning T, et al. IDF Diabetes Atlas Sixth edition. Basel: International Diabetes Federation; 2013.
- Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2009;87(1):4–14. https://doi.org/10.1016/j.diabres.2009.10.007.
- Nishida C, Uauy R, Kumanyika H, Shetty P. The Joint WHO/FAO Expert Consultation on diet, nutrition and the prevention of chronic diseases: process, product and policy implications. Public Health Nutr. 2004;7(1A):245–50.
- Krishnadath IS, Nahar-van Venrooij LM, Jaddoe VW, Toelsie JR. Ethnic differences in diabetes and prediabetes in Suriname. BMJ Open Diabetes Res Care. 2016;4(1):e000186. https://doi.org/10. 1136/bmjdrc-2015-000186.
- World Bank. Countries and economies. Washington, DC: World Bank; 2014.

- Algemeen Bureau voor de Statistiek, Censuskantoor. Resultaten Achtste (8e) Volks- En Woningtelling in Suriname (Volume I) Demografische en Sociale Karakteristieken en Migratie, 294/013. Paramaribo: General Bureau of Statistics Suriname; 2013.
- Punwasi W. In: Ministry of Health, Bureau of Public Health, editor. Doodsoorzaken in Suriname 2007-2011. Paramaribo: Ministerie van Volksgezondheid, Bureau Openbare gezondheidszorg; 2011.
- Jeffcoate WJ, Harding KG. Diabetic foot ulcers. Lancet. 2003;361(9368):1545–51.
- Unwin N. The diabetic foot in the developing world. Diabetes Metab Res Rev. 2008;24(Suppl 1):S31–3. https://doi.org/10.1002/ dmrr.857.
- Reiber GE, Lipsky BA, Gibbons GW. The burden of diabetic foot ulcers. Am J Surg. 1998;176(2):5S–10S. https://doi.org/10.1016/ S0002-9610(98)00181-0.
- Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293(2):217–28. https://doi. org/10.1001/jama.293.2.217.
- Bakker K, Apelqvist J, Schaper NC. Practical guidelines on the management and prevention of the diabetic foot 2011. Diabetes Metab Res Rev. 2012;28:225–31. https://doi.org/10.1002/dmrr. 2253.
- Lipsky BA, Peters EJG, Berendt AR, Senneville E, Bakker K, Embil JM, et al. Specific guidelines for the treatment of diabetic foot infections 2011. Diabetes Metab Res Rev. 2012;28:234–5. https://doi.org/10.1002/dmrr.2251.
- Tentolouris N, Al-Sabbagh S, Walker MG, Boulton AJ, Jude EB. Mortality in diabetic and nondiabetic patients after amputations performed from 1990 to 1995: a 5-year follow-up study. Diabetes Care. 2004;27(7):1598–604. https://doi.org/10.2337/diacare.27.7. 1598.
- Lowe J, Sibbald RG, Taha NY, Lebovic G, Rambaran M, Martin C, et al. The Guyana diabetes and foot care project: improved diabetic foot evaluation reduces amputation rates by two-thirds in a lower middle income country. Int J Endocrinol. 2015;2015:920124. https://doi.org/10.1155/2015/920124.
- Bertoldi AD, Kanavos P, Franca GV, Carraro A, Tejada CA, Hallal PC, et al. Epidemiology, management, complications and costs associated with type 2 diabetes in Brazil: a comprehensive literature review. Glob Health. 2013;9(1):62. https://doi.org/10.1186/1744-8603-9-62.
- Ollendorf DA, Kotsanos JG, Wishner WJ, Friedman M, Cooper T, Bittoni M, et al. Potential economic benefits of lower-extremity amputation prevention strategies in diabetes. Diabetes Care. 1998;21(8):1240–5. https://doi.org/10.2337/diacare.21.8.1240.
- Vartanian SM, Robinson KD, Ofili K, Eichler CM, Hiramoto JS, Reyzelman AM, et al. Outcomes of neuroischemic wounds treated by a multidisciplinary amputation prevention service. Ann Vasc Surg. 2015;29(3):534–42. https://doi.org/10.1016/j.avsg.2014.10. 030.
- Boulton AJ, Meneses P, Ennis WJ. Diabetic foot ulcers: a framework for prevention and care. Wound Rep Reg. 1999;7(1):7–16. https://doi.org/10.1046/j.1524-475X.1999.00007.x.
- 20. Faglia E, Favales F, Aldeghi A, Calia P, Quarantiello A, Barbano P, et al. Change in major amputation rate in a center dedicated to diabetic foot care during the 1980s: prognostic determinants for

major amputation. J Diab Comp. 1998;12(2):96–102. https://doi.org/10.1016/S1056-8727(97)98004-1.

- Oyibo SO, Jude EB, Tarawneh I, Nguyen HC, Harkless LB, Boulton AJA. Comparison of two diabetic foot ulcer classification systems: the Wagner and the University of Texas wound classification systems. Diabetes Care. 2001;24(1):84–8. https://doi.org/10. 2337/diacare.24.1.84.
- Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54(12):e132–73. https://doi.org/ 10.1093/cid/cis346.
- Frykberg RG, Piagessi A, Donaghue VM, Schipani E, Haberschaw GM, Navalesi R, et al. Difference in treatment of foot ulcerations in Boston, USA and Pisa, Italy. Diabetes Res Clin Pract. 1997;35(1): 21–6. https://doi.org/10.1016/S0168-8227(96)01359-9.
- Ribu L, Birkeland K, Hanestad BR, Moum T, Rustoen TA. Longitudinal study of patients with diabetes and foot ulcers and their health-related quality of life: wound healing and quality-oflife changes. J Diabetes Complicat. 2008;22(6):400–7. https://doi. org/10.1016/j.jdiacomp.2007.06.006.
- Parisi MC, Zantut-Wittmann DE, Pavin EJ, Machado H, Nery M, Jeffcoate WJ. Comparison of three systems of classification in predicting the outcome of diabetic foot ulcers in a Brazilian population. Eur J Endocrinol. 2008;159(4):417–22. https://doi.org/10. 1530/EJE-07-0841.
- Morbach S, Lutale JK, Viswanathan V, Mollenberg J, Ochs HR, Rajashekar S, et al. Regional differences in risk factors and clinical presentation of diabetic foot lesions. Diabet Med. 2004;21(1):91–5. https://doi.org/10.1046/j.1464-5491.2003.01069.x.
- Ince P, Kendrick D, Game F, Jeffcoate WJ. Use of the SINBAD classification system and score in comparing outcome of foot ulcer management on three continents. Diabetes Care. 2008;31(5):964–7. https://doi.org/10.2337/dc07-2367.
- Weledji EP, Fokam P. Treatment of the diabetic foot to amputate or not? BMC Surg. 2014;14:83. https://doi.org/10.1186/1471-2482-14-83.
- Richard JL, Lavigne JP, Sotto A. Diabetes and foot infection: more than double trouble. Diabetes Metab Res Rev. 2012;28:46–53. https://doi.org/10.1002/dmrr.2234.
- Bos M, Agyemang C. Prevalence and complications of diabetes mellitus in Northern Africa, a systematic review. BMC Public Health. 2013;13(1):387. https://doi.org/10.1186/1471-2458-13-387.
- Prompers L, Apelqvist J. High prevalence of ischemia, infection, and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. Diabetologia. 2007;50(1):18–25. https://doi.org/10.1007/s00125-006-0491-1.
- 32. Lazo Mde L, Bernabe-Ortiz A, Pinto ME, Ticse R, Malaga G, Sacksteder K, et al. Diabetic peripheral neuropathy in ambulatory patients with type 2 diabetes in a general hospital in a middle income country: a cross-sectional study. PLoS One. 2014;9(5): e95403. https://doi.org/10.1371/journal.pone.0095403.
- Coussons AK, Wilkinson RJ, Nikolayevskyy V, Elkington PT, Hanifa Y, Islam K, et al. Ethnic variation in inflammatory profile in tuberculosis. PLoS Pathog. 2013;9(7):e1003468. https://doi.org/ 10.1371/journal.ppat.1003468.