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Life expectancy of patients with diabetic foot sepsis post-lower extremity amputation at a regional hospital in a South African setting. A retrospective cohort study

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A B S T R A C T

Background: Diabetes foot sepsis (DFS) is the leading cause of amputation of lower extremities. Over 50 % of patients who have had major lower extremity amputation due to DFS are dead within 4 years following the procedure.
Aim: To determine the life expectancy of patients following amputation for DFS at a regional hospital in South Africa.
Methods: We conducted an audit of patients who had DFS and were admitted over a 5-year period. The duration from admission to time of death was recorded in days. Occurrence of death was confirmed from family members of the deceased using structured telephonic interview questionnaires. Categorical findings were summarized using actual counts and percentages and compared using either the Chi-square or Fisher's exact test. We used the mean with standard deviation or median and range to compare parametric and non-parametric continuous data, respectively. The Shapiro-Wilk test was used to test normality of data. Multivariate logistic regression was done to establish factors that were strongly associated with the mortalities. Adjusted survival curves were added to compare the rate of occurrence of mortality between males and females with age as a confounder. Statistical significance was set at a p-value below 0.05.
Results: 197 were found of which 100 % of participants had Type 2 diabetes mellitus and 63.5 % were males. Associated comorbidities included hypertension in 73.6 %, obesity in 66 %, alcohol use in 64.5 % and smoking in 58.4 %. 190 participants had an amputation and 19.3 % died.
Conclusion: DFS was more common in males and 96 % of the patients had an amputation. Mortality rate within 4 years following amputation was 19.3 % and was higher in females and individuals with multiple comorbidities.

Introduction

Diabetes mellitus (DM) has become so prevalent that it is consuming a significant portion of the healthcare budget [1–4]. Complications of DM may involve the eyes, kidneys and the cardiovascular system [5–10]. Diabetes mellitus is one of the major risk factors of atherosclerosis and vascular territories which are commonly affected are the cerebrovascular, coronary, mesenteric, renal and the lower extremities. Affectation of the arterial system of the lower extremities in patients with DM is often complex, multilevel and challenging to treat, and frequently lead to major amputations [11] (see Fig. 2 and 3).

Diabetic foot sepsis is the main predisposing factor for amputation in individuals with DM, especially in low and middle income countries (LMICs) [12–14]. Worldwide, DM is the leading cause of non-traumatic amputations. Motor and sensory neuropathy, vasculopathy and immunopathy combined make a foot of a DM patient prone to ulceration [15–18]. Foot ulceration, if not detected and managed timeously, leads to sepsis which may spread rapidly and end up with major lower extremity amputation or even mortality [16,19].

Majority of lower extremity amputations due to DM are in LMICs. Amputation is a life changing event in most of the patients as some are not able to return to a productive life and close to 50 % die within 3 years following the amputation [19,20]. Furthermore, acquisition of prosthesis is a luxury which remains a theoretical dream for the majority of individuals residing in LMICs.

Prevention and management of diabetic foot ulceration and its complications should be by a multidisciplinary team (MDT) as it reduces the rate of major lower extremity amputations. Unfortunately, primary preventative strategies and MDT for management of foot ulceration and subsequent infection in DM patients are almost non-existent in the

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majority of LMICs. The aim of the study was to determine the life expectancy of patients following amputation for DFS at a regional hospital in a South African setting.

Patients and methods

This study was part of multidisciplinary research investigating the model to reduce the rate of lower extremity amputation in individuals with DM in the Gauteng Province of South Africa. We reviewed records of all the patients who were admitted and treated for DFS from 1st January 2016 to 31st December 2020 at Leratong hospital, a regional health institution in the west of Johannesburg. Data of patients who had amputation associated with DFS was collected from the hospital files and theatre records. Data retrieved included demographic information, duration of DM, comorbidities, site of ulcer, severity of DFS, laboratory results, in-hospital and death rate during follow-up. Occurrence of death was confirmed with family members of the deceased using a structured questionnaire, telephonically. Consent was obtained from patients telephonically and the clinical manager of the health facility approved of the access to the records. Ethics clearance for the study was received from the Human Research Ethics Committee (Medical) of University of the Witwatersrand (M190563). We used StataSE version 17.0 edition to analyze the data. Categorical data was summarized using percentages and continuous data using the median or mean. Comparison of categorical findings were compared using Chi-square or Fisher's exact and for continuous data using t-test or Mann-Whitney test. Shapiro-Wilk test was used to confirm normal distribution of continuous data. Multivariate logistic regression was conducted to establish the strength of the association between the co-morbidities and mortality. Adjusted survival curves (Kaplan Meier) were added to compare the rate of occurrence of mortality between males and females with age as a confounder. A p-value below 0.05 was deemed significant.

Results

The total participants in the study were 197 and 83.2 % (164/197) were blacks and 63.5 % (125/197) were males. All the participants had type 2 DM. Occurrence of death could not be ascertained in three subjects. The right lower limb was affected in 58.3 % (115/197) of the cases. Hundred and ninety (96.4 %%:190/197) participants had an amputation with 94.7 % being major amputations (Table 1).

Ninety-one (46.2 %: 91/197) of participants were below the age of 61 years. The overall mortality rate in the period of study was 19.3 % (38/197) and 97.4 % (37/38) of the deaths were in participants aged above 60 years (Table 2).

Table 1
Demography of participants who had diabetic foot sepsis (N = 197).

Modality	Category	Number (%)
Participants	Total	197 (100 %)
Gender	Male	125 (63.5 %)
	Female	72 (36.5 %)
Race	Black	164 (83.2 %)
	White	33 (16.8 %)
Laterization	Right	115 (58.3 %)
	Left	77 (39.1 %)
	Bilateral	5 (2.6 %)
Site of ulcer	Toe	15 (7.6 %)
	Foot	147 (74.6 %)
	Below knee	23 (11.6 %)
	Above Knee	12 (6.2 %)
Clinical findings	Septic	171 (86.8 %)
	Wet gangrene	10 (5.1 %)
	Dry gangrene	16 (8.1 %)
Type of Diabetes	Type 1	0 (0 %)
	Type 2	197 (100 %)
Outcome of limb	Amputation	190 (96.4 %)
	Salvaged	7 (3.6 %)
Type of amputation	Major	10 (5.3 %)
	Minor	180 (94.7 %)

Table 2
Breakdown of participants according to age groups and outcomes.

Age group	30–40	8 (4.1 %)
	41–50	30 (15.2 %)
	51–60	53 (26.9 %)
	61–70	73 (37.1 %)
	71–80	29 (14.7 %)
	81–90	3 (1.5 %)
	91–100	1 (0.5 %)
Post-operative status	Alive	159 (80.7 %)
	Demised	38 (19.3 %)
Death by gender	Males	16 (42.1 %)
	Females	22 (57.9 %)
Death by year	2016	7 (18.4 %)
	2017	9 (23.7 %)
	2018	9 (23.7 %)
	2019	5 (13.2 %)
	2020	8 (21 %)
Death by age	30–40	0 (0 %)
	41–50	0 (0 %)
	51–60	1 (2.6 %)
	61–70	15 (39.5 %)
	71–80	20 (52.7 %)
	81–90	1 (2.6 %)
	91–100	1 (2.6 %)

Comorbidities among the participants included hypertension in 73.6 % (145/197) and obesity in 66 % (130/197) (Fig. 1).

Eighty-eight (70.4 %: 88/125) of the male participants compared to 54.2 % (39/72) of females had a history of alcohol use. The difference in the rate of alcohol use among male and female participants was statistically significant (p-value: 0.022). Records of 2 % (4/197) of the participants showed that they were positive for human immunodeficiency virus (HIV) (Table 3).

The average period to death of the participants who demised (38) was 1250 days, which when upscaled to the whole study population (197) the average period to death was 395 days, equivalent to 1.1 years. Female participants had a higher mortality rate (p: 0.009) compared to males even though the study population had more males with DFS. Thirty-three (86.8 %: 33/38) of the participants who died had at least two comorbidities. All the comorbidities including alcohol use and smoking had no strong association with the mortality following multivariate logistic regression (Table 4).

Additionally, in accounting for the influence to compare the survival between males and females. Survival curves were drawn out using the Kaplan Miere analysis, with an adjusted curve applying age as a confounder.

From the analysis, the difference in the rate of occurrence to mortality between the two groups was statistically significant in the first 25 days post-amputation with a p.value:0.028. After that the difference bore no significance.

Discussion

The aim of the study was to determine the average life-expectancy in the patients who underwent minor or major amputation due to diabetic foot sepsis. The overall mortality in the study was 19 %, which is similar to the rate reported by Adeleye et al. (2020) in a study conducted in Nigeria. Adeleye et al. reported a mortality rate of 21.4 % [21]. In other similar studies Rigato et al. (2018) in a meta-analysis conducted in multiple parts of Africa reported a mortality of 14 %, this was the same as what Edo et al. (2013) reported in a study conducted in Benin (14 % mortality) [22,23]. An Indonesian study observed a mortality rate of 10.7 % [24]. While on the other hand, Ekpebegh et al., in 2009 reported a much higher mortality of 40.5 % in a single-center study conducted in Lagos, Nigeria [25]. The mortality rate of 19 % in close to 5 years is far lower than the predicted 50 % advanced by Walsh et al. (2016) [26].

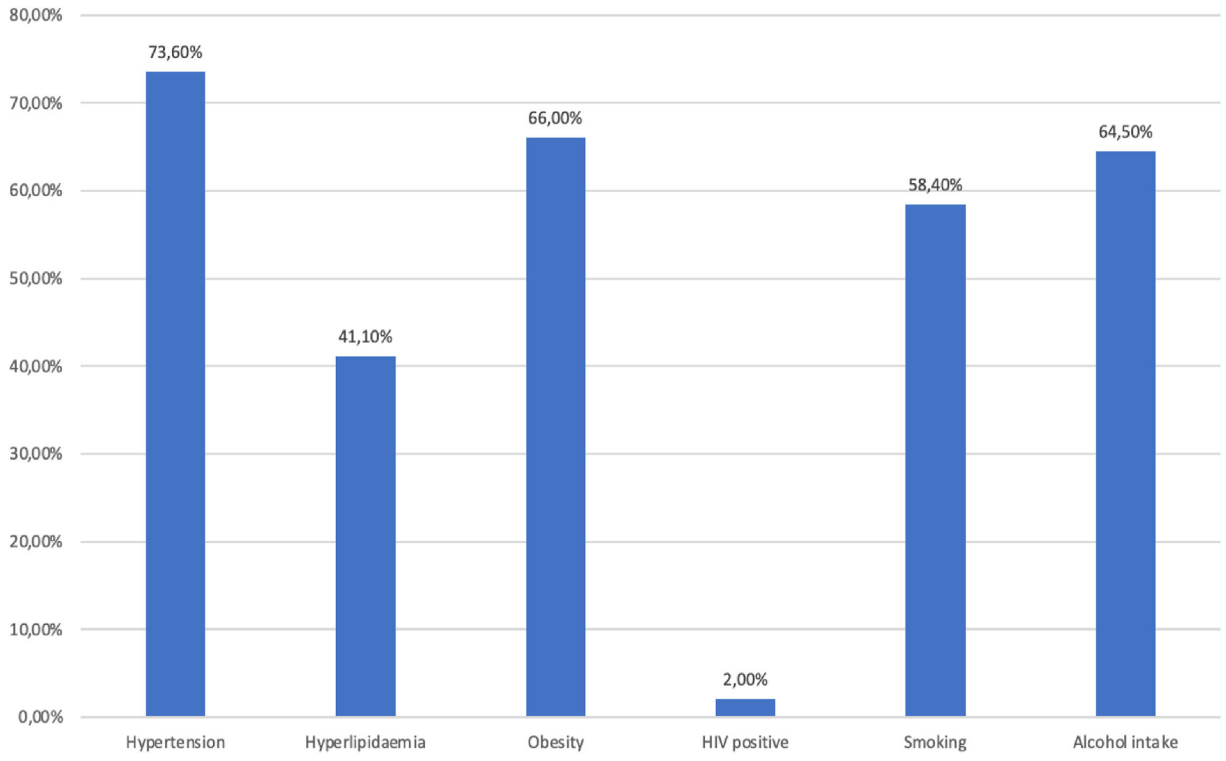

Fig. 1. Prevalence of comorbidities in patients with DFS.

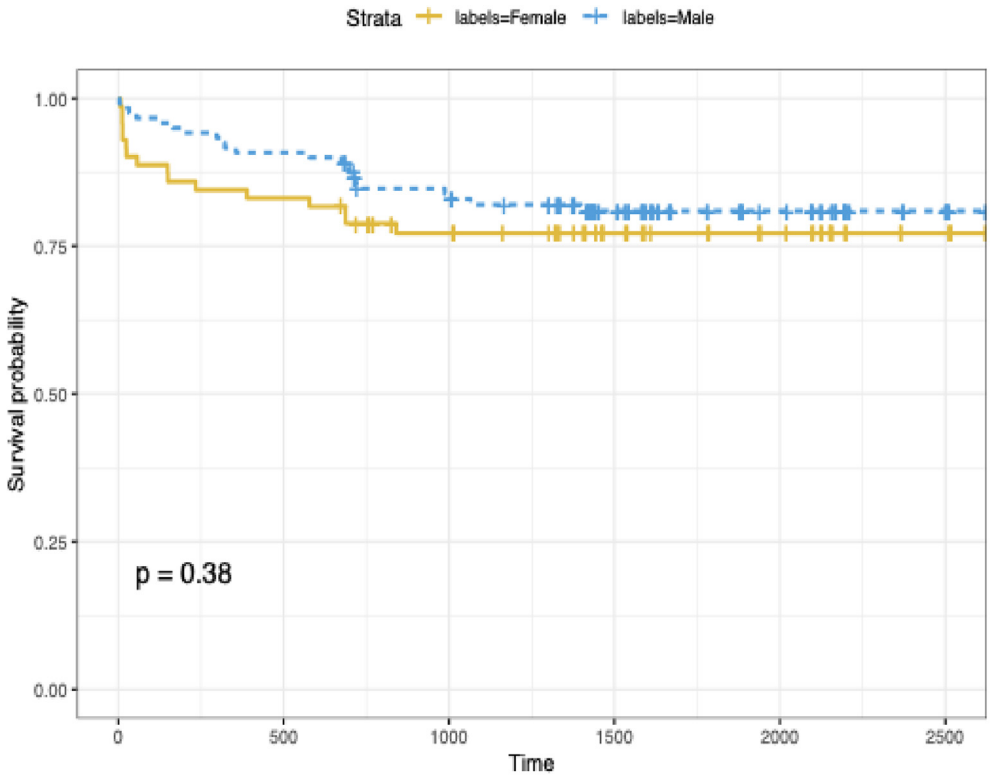

Fig. 2. Classic curve outlining the difference in the rate of mortality between males and female.

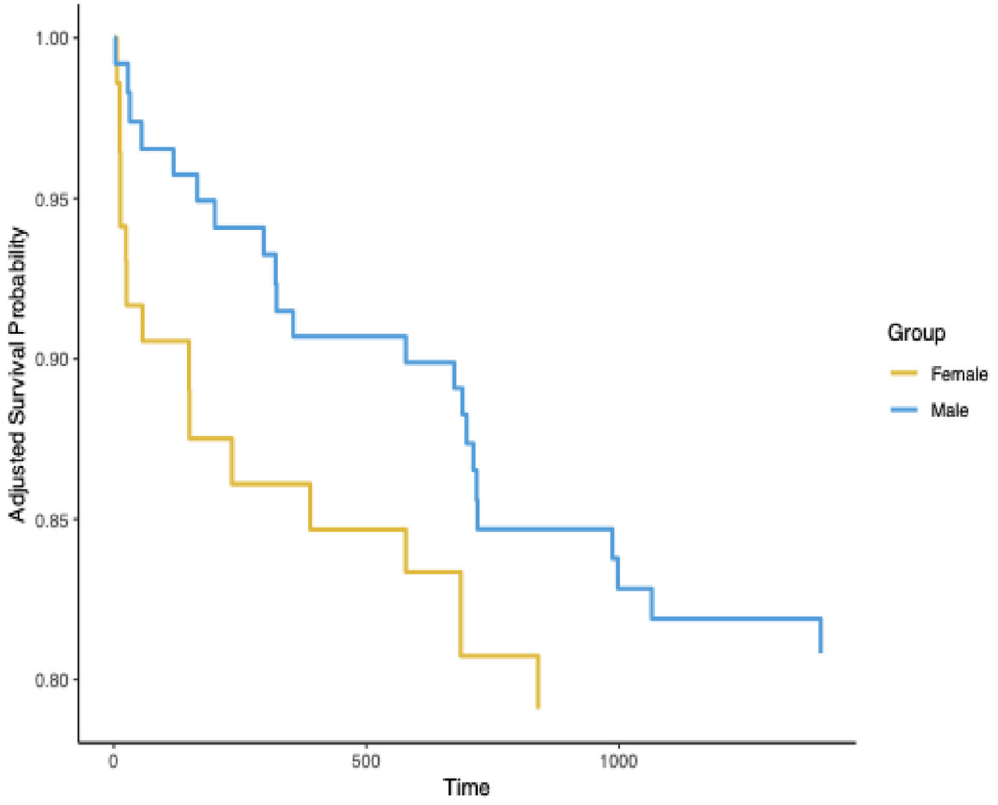

Fig. 3. Adjusted survival curve outlining the rate in moratlity, confounded by age.

Hoffman et al. (2015) found that 50 % of patients with DFS die within three years post amputation [20].

Although as recorded there were more men in the study with DFS, around 58 % of the mortalities occurred in women which is contrary to previous findings of Panuda et al. (2019). In the study 64 % (32/49) mortality was seen in males [27]. The likelihood of death after amputation for DFS is higher in patients who are above 60 years and/or have a longer history of DM. Aragón-Sánchez et al. (2014) and Costa et al. (2017) also reported higher mortality following amputation in patients older than 60 years [28,29]

Majority of the deaths in the study occurred in patients over 65 years. The duration of DM also translated to an increased chance of death as most of the deaths occurred in patients who had had the disease for more than 10 years [21,30]. The average duration of DM in women was about 27 years compared to 22 years in males, which might have contributed to the difference in the mortality rate between the two groups.

Though hypertension, dyslipidemia and the lifestyle habits (smoking, alcohol) when studied independently had no significance in the outcome of death. However, as a collective all comorbidities explored had a positively significant relationship to death occurrence with a p-value: 0.0156. This is further proven in the study where 87 % (33/38) of the demised patients had two or more of the above mentioned comorbidities.

Table 3
Comparison of clinical findings and prevalence of comorbidities in male and female participants who had DFS (N = 197).

Variable	Males	Females	P-value
Duration of diabetes			0.976
Median	6–42	2–46	
Range in years			
Clinical findings			0.572
Wet gangrene	7 (3.5 %)	3 (1.5 %)	
Dry gangrene	12 (6.1 %)	4 (2 %)	
Septic	106 (53.8 %)	65 (33.1 %)	
Hypertension			0.315
Yes	95 (48.2 %)	50 (25.3 %)	
No	30 (15.2 %)	22 (11.3 %)	
Dyslipidaemia			0.905
Yes	51 (25.9 %)	30 (15.2 %)	
No	74 (37.5 %)	42 (21.4 %)	
HIV status			0.139
Positive	1 (0.5 %)	3 (1.5 %)	
Negative	124 (62.9 %%)	69 (351 %)	
Smoking			0.226
Yes	77 (39 %)	38 (19.3 %)	
No	48 (24.3 %)	34 (17.4 %)	
Alcohol			0.022
Yes	88 (44.7 %)	39 (19.8 %)	
No	37 (18.8 %)	33 (16.7 %)	
Obesity			0.161
Yes	78 (39.6 %)	52 (26.4 %)	
No	47 (23.9 %)	20 (10.1 %)	

Limitations

The data collected was mainly from hospital theatre records, administration records, patient files and telephonic conversations of family members to confirm the occurrence of death. The latter meant that in some patients, the occurrence of death could not be confirmed. Due to this limitation, some other essential data relating to patients' biochemistry results, classification of ulcers and treatment prescribed could not be ascertained. This data, though not weighty in the aim of study, would have been pivotal in the interrogation to determine patterns of association to support the research question.

Secondly, it is a single centre study. The data and trends determined are not reflective when scaled to a broader outlook. Though there is diversity in the demographics of the study, it is not large enough to capture in accuracy and precision the confidence to institutionalize the conclusions. This is a more microscopic view which in principle could add to a more greater outlook.

Table 4
Multivariate logistic regression for the influence of comorbidities on the occurrence of morality.

Logistic regression				Number of obs = 197	
				LR chi2 (8) = 18.87	
				Prob > chi2 = 0.0156	
Log likelihood: −87.171463				Pseudo R2 = 0.0977	
Death Yes1 No0	odds ratio	Std. err.	z	P>|z|	95 % conf. interval
Age	0.91	0.03	−3.08	0.002	0.85–0.96
Gender M1F0	0.35	0.14	−2.62	0.009	0.16–0.77
Duration of diabetes in years	1.11	0.05	2.35	0.019	1.02–1.22
Hypertension Yes1No0	1.81	0.87	1.25	0.210	0.71–4.63
Smoking Yes1No0	1.03	0.40	0.07	0.947	0.48–2.20
Alcohol Yes1No0	1.40	0.58	0.81	0.418	0.62–3.18
Obesity Yes1No0	0.84	0.36	−0.40	0.686	0.37–1.9
Hyperlipidaemia Yes1No0	0.84	0.34	−0.43	0.665	0.3743741–1.871428
_cons	12.30	17.02	1.81	0.70	0.8173196–185.2319

Note: _cons estimates baseline odds.

Conclusion

Common comorbidities included hypertension, obesity and dyslipidemia; with each being concurrent in at least 50 % of the patients. At least 20 % of patients with DM smoke cigarettes and drink alcohol. Over 97 % admitted for DFS end up with an amputation. Around 19 % of the patients who are admitted and get an amputation die within 4 years following surgery. Although DFS is more common in men, close to 60 % of mortalities occur more in women.

Recommendation

The study was retrospective and some of the records might have been missed. Outcomes of single-centre studies are not accurately representative to the entire population. So, as a more ambitious intent to reach a broader representation, multiple centres within different regions could conduct a similar study such that a meta-analysis could be set. This would be beneficial in showing trends of similarity and how from this, just as within the greater study to reduce amputations, could give insight toward the initiation and application of a preventive method to achieve the desired outcome.

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Authorship and contributions

MTC: Data collection, data analysis, drafting of manuscript and review of the manuscript.

SV: Conception and literature review compilation.

MED: Data collection and review of the manuscript.

LTE: Application of ethics, data analysis and review of the manuscript.

Declaration of competing interest

None of the authors have a conflict to declare.

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References

[1] Commons RJ, Robinson CH, Gawler D, Davis JS, Price RN. High burden of diabetic foot infections in the top end of Australia: an emerging health crisis (DEFINE study). Diabetes Res Clin Pract 2015;110:147–57. https://doi.org/10.1016/j.diabres.2015.09.016.

[2] Skrepnek GH, Mills JL, Armstrong DG. A diabetic emergency one million feet long: disparities and burdens of illness among diabetic foot ulcer within emergency departments in the United States. PLOS ONE|DOI 2006-2010. https://doi.org/10.1371/journal.pone.0134914.

[3] Andrew C. Foot complications in diabetes are serious and costly. SAMJ 2010;28(4):181–5.

[4] Kim CH, Moon JS, Chung SM, Kong EJ, Park CH, Yoon WS, et al. The changes of trends in the diagnosis and treatment of diabetic foot ulcer over a 10-year period: single center study. Diabetes Metab J 2018;42:308–19. https://doi.org/10.4093/dmj.2017.0076.

[5] Tuttolomondo A, Maida C, Pinto. Diabetic foot syndrome: immune-inflammatory features as possible cardiovascular markers in diabetes. World J Orthopaedics 2015;6(1):62–76. https://doi.org/10.5312/wjo.v6.i1.62.

[6] Tresierra-Ayala MA, Rojas AG. Association between peripheral arterial disease and diabetic foot ulcers in patients with diabetes mellitus type 2. Med Univ 2017;19(76):123–6. https://doi.org/10.1016/j.rmu.2017.07.002.

[7] Abdul-Ghani M, DeFronzo RA, Del Prato S, Chilton R, Singh R, Ryder REJ. Cardiovascular disease and type 2 diabetes: has the dawn of a new era arrived? Diabetes Care 2017;40:813–20. https://doi.org/10.2337/dc16-2736.

[8] Tobe SW, Gilbert RE, Jones C, Leiter LA, Prebtani APH, Woo V. Treatment of hypertension. Can J Diabetes 2018;42:S186–9. https://doi.org/10.1016/j.jcjd.2017.10.011.

[9] Yokoyama H, Araki SI, Kawai K, Yamazaki K, Tomonaga O, Shirabe SI, et al. Declining trends of diabetic nephropathy, retinopathy and neuropathy with improving diabetes care indicators in Japanese patients with type 2 and type 2 diabetes (JDDM 46). BMJ Open Diabetes Research & Care 2018;6. https://doi.org/10.1136/bmjdrc-2018-000521.

[10] Altomare F, Kherani A, Lovshin J. Retinopathy. Can J Diabetes 2018;42:S210–6. https://doi.org/10.1016/j.jcjd.2017.10.027.

[11] Jeffcoate WJ, Van Houtum WH. Amputation as a marker of the quality of foot care in diabetes. Diabetologia 2004;(47):2051–8.

[12] Fiorito J, Trinidad-Hernandez M, Leykum B, Smith D, Mills JL, Armstrong DG. A tale of two soles: sociomechanical and biomechanical considerations in diabetic limb salvage and amputation decision-making in the worst of times. Diabet Foot Ankle 2012;3. https://doi.org/10.3402/dfa.v3i0.18633.

[13] Wukich DK, Hobizal KB, Brooks MM. Severity of diabetic foot infection and rate of limb salvage. Foot Ankle Int 2013;34(3):351–8. https://doi.org/10.1177/1071100712467980.

[14] Kim TG, Moon SY, Park MS, Kwon SS, Jung KJ, Lee T, et al. Factors affecting length of hospital stay and mortality in infected diabetic foot ulcers undergoing surgical drainage without major amputation. J Kor Med Sci 2016;31:120–4. https://doi.org/10.3346/jkms.2016.31.1.120.

[15] Boulton AJM, Vileiyte L, Tennvall R, Apelqvist J. The global burden of diabetic foot disease. Lancet 2005;366:1719–24.

[16] Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJG, Armstrong DG, et al. Infectious diseases society of America clinical practice guidelines for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis 2012;54(12):132–73. https://doi.org/10.1093/cid/cis346. 2012.

[17] Sumpio BE. Contemporary evaluation and management of the diabetic foot. Scientifica 2012. https://doi.org/10.6064/2012/435487.

[18] Amin N, Doupis J. Diabetic foot disease: from evaluation of the “foot at risk” to the novel diabetic ulcer treatment modalities. World J Diabetes 2016;7(7):153–64. https://doi.org/10.4239/wjd.v7.i7.153.

[19] Chammas NK, Hill RLR, Edmonds ME. Increased mortality in diabetic foot ulcer patients: the significance of ulcer type. J Diabetes Res 2016. https://doi.org/10.1155/2016/2879809.

[20] Hoffmann M, Kujath P, Flemming A, Moritz P, Begum N, Zimmermann M, et al. Survival of diabetes patients with major amputation is comparable to malignant disease. Diabetes Vasc Dis Res 2015:1–7. https://doi.org/10.1177/1479164115579005.

[21] Adeleye OO, Ugwu ET, Gezawa ID, Okpe I, Ezeani I, Enamino M. Predictors of intra-hospital mortality in patients with diabetic foot ulcers in Nigeria: data from the MEDFUN study. 2020. https://doi.org/10.21203/rs.2.16549/v2.

[22] Rigato M, Pizzol D, Tiago A, Putoto G, Avogaro A, Fadini GP. Characteristics, prevalence, and outcomes of diabetic foot ulcers in Africa. A systematic review and meta-analysis. Diabetes Res Clin Pract 2018;142:63–73.

[23] Edo A, Edo G, Ezeani I. Risk factors, ulcer grade and management outcome of diabetic foot ulcers in a Tropical Tertiary Care Hospital. Niger Med J 2013;54(1):59–63.

[24] Pemayun TGD, Naibaho RM. Clinical profile and outcome of diabetic foot ulcer, a view from tertiary care hospital in Semarang, Indonesia. Diabet Foot Ankle 2017;8(1):1312974.

[25] Ekpebegh CO, Iwuala SO, Fasanmade OA, Ogbera AO, Igumbor E, Ohwovoriole AE. Diabetes foot ulceration in a Nigerian hospital: in-hospital mortality in relation to the presenting demographic, clinical and laboratory features. Int Wound J 2009;6(5):381–5.

[26] Walsh JW, Hoffstad OJ, Sullivan MO, Margolis DJ. Association of diabetic foot ulcer and death in a population-based cohort from the United Kingdom. Diabet Med 2016;33(11):1493–8.

[27] 1 Panuda JP, Macalalad-Josue AA, Buenaluz-Sedurante M. Factors associated with in-hospital mortality among patients with diabetes admitted for lower extremity infections. Journal of the ASEAN Federation of Endocrine Societies 2019;34(1):36–43. https://doi.org/10.15605/jafes.034.01.07.

[28] Aragón-Sánchez J, Lázaro-Martínez J, García-Álvarez Y, Morales EG, Hernández-Herrero MJ. Albuminuria is a predictive factor of in-hospital mortality in patients with diabetes admitted for foot disease. Diabetes Res Clin Pract 2014;104(1):e23–5. https://doi.org/10.1016/j.diabres.2014.01.006. PMID: 24530117.

[29] Costa RHR, Cardosa NA, Procópio RJ, Navarro TP, Dardik A, de Loiola Cisneros L. Diabetic foot ulcer carries high amputation and mortality rates, particularly in the presence of advanced age, peripheral artery disease and anemia. Diabetes Metabol Syndr 2017;S583–7. https://doi.org/10.1016/j.dsx.2017.04.008. PMID: 28465149.

[30] Martins-Mendes D, Monteiro-Soares M, Boyko EJ, Ribeiro M, Barata P, Lima J, et al. The independent contribution of diabetic foot ulcer on lower extremity amputation and mortality risk. J Diabetes Complicat 2014;28(5):632–8.