Long-term Prognosis of Diabetic Patients with a First Foot Ulcer in a Portuguese Tertiary Care Unit

Prognóstico a Longo Prazo de Doentes com uma Primeira Úlcera de Pé Diabético numa Unidade Portuguesa de Cuidados Terciários

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Abstract

Introduction: Diabetic foot ulcer (DFU) is a major cause of morbidity and mortality in diabetic patients. Our aim was to evaluate the 5-year outcome of patients with a first DFU and to analyze variables related with mortality.

Methods: Retrospective analysis of clinical data of patients with a first DFU attending the Diabetic Foot Clinic at Hospital de Santo António during 2008 with determination of outcomes (amputation and death) until December-2014.

Results: The study included 248 patients. The median age at presentation was 70 years and the median diabetes duration was 15 years. Ulcers were neuroischemic/ischemic in 62.5%. During the 5-year period, 31.9% (95% CI, 24.1-39.7) of the patients had at least one minor amputation and 23.7% (95% CI, 16.6-30.9) one major amputation. The 5-year all-cause mortality rate was 45.6% (95% CI, 39.3-51.8). Patients with neuroischemic/ischemic foot had higher mortality rate (p<0.001), as well as older patients (p<0.001) and those with longer diabetes duration (p=0.03). Other factors associated with higher mortality were ischemic heart disease (p=0.005), cerebrovascular disease (p<0.001), peripheral arterial disease (p<0.001) and hypertension (p=0.001).

Conclusion: DFU is associated with high 5-year rates of amputation and mortality, especially among older patients with longer diabetes duration, hypertension and established macrovascular disease.

Keywords: diabetic foot ulcer, diabetes duration, neuroischemic/ischemic foot, minor amputation, major amputation, mortality.

Resumo

Introdução: As úlceras de pé diabético são uma causa importante de morbidade e mortalidade nos doentes com diabetes mellitus.

Objetivos: Avaliar os desfechos aos 5 anos dos doentes com primeira úlcera de pé diabético e analisar as variáveis associadas à mortalidade.

Métodos: Análise retrospectiva de dados clínicos dos doentes com primeira úlcera de pé diabético que recorreram à consulta do Pé Diabético do Hospital de Santo António durante 2008, com determinação dos desfechos (amputação e morte) até dezembro-2014.

Resultados: Incluíram 248 doentes, 62.5% com pé neuroisquémico/isquémico, idade mediana à apresentação de 70 anos e duração mediana da diabetes de 15 anos. Durante os 5 anos de seguimento, 31.9% (IC 95%, 24.1-39.7) dos doentes foram submetidos a amputação menor e 23.7% (IC 95%, 16.6-30.9) a amputação maior. A taxa de mortalidade aos 5 anos foi de 45.6% (IC 95%, 39.3-51.8). Os doentes com pé neuroisquémico/isquémico apresentaram uma taxa de mortalidade superior (p<0.001), assim como os doentes mais velhos (p<0.001) e aqueles com mais anos de diagnóstico de diabetes (p=0,03). Outros fatores associados a uma maior taxa de mortalidade foram: doença cardíaca isquémica (p=0,005), doença cerebrovascular (p<0,001), doença arterial periférica (p<0,001) e hipertensão (p=0,001).

Conclusão: As úlceras de pé diabético estão associadas a uma elevada taxa de amputação e mortalidade aos 5 anos, especialmente entre indivíduos mais velhos, maior duração da diabetes, hipertensão arterial e doença macrovascular estabelecida.

Palavras-chave: úlcera de pé diabético, duração da diabetes, pé neuroisquémico/isquémico, amputação menor, amputação major, mortalidade.
> MATERIAL AND METHODS

We have conducted a retrospective data analysis of all patients with a first DFU attending the Diabetic Foot Clinic of Hospital de Santo António/Centro Hospitalar do Porto, a Portuguese tertiary care unit, during 2008. Data on outcome (mortality, minor and major amputation) were collected from hospital records and national mortality register up to December 2014. Cause of death was not ascertained. For determination of amputation rate we included only patients with history of amputation and/or available clinical records for the 5-year follow-up period. Patients with history of previous DFU and those with missing relevant data were excluded from the analysis.

Demographic variables obtained included gender and age at first clinic attendance. Clinical data included type of diabetes, duration of diabetes, HbA1c, metabolic and microvascular complications (diabetic neuropathy, diabetic nephropathy and diabetic ophthalmopathy), macrovascular disease (ischemic heart disease, peripheral artery disease, cerebrovascular disease), hypertension, dyslipidemia and smoking habits (smoker/ex-smoker vs non-smoker). Peripheral neuropathy was assessed through Semmes-Weinstein monofilament testing and peripheral vascular disease was considered present if dorsalis pedis and posterior tibial pulses were absent by palpation in the affected limb. Based on this, ulcers were classified as neuropathic or neuroischemic/ischemic (grouped due to the rarity of purely ischemic ulcers identified). Minor amputation and major amputation was defined as below or above the ankle, respectively. Duration of diabetes was self-reported, as were diabetic nephropathy, diabetic ophthalmopathy, ischemic heart disease, cerebrovascular disease, hypertension and dyslipidemia. HbA1c concentrations were measured using Siemens DCA 2000 (Siemens Healthcare Diagnostics, Deerfield, IL) (immunoassay).

Statistical analysis was performed using SPSS for Windows v20.0, through descriptive and inferential statistics with Chi-squared test and Mann–Whitney U test, as appropriate. Values of p ≤ 0.05 were considered statistically significant.

> RESULTS

During 2008, a total of 248 patients with first DFU were seen at the Diabetic Foot Clinic. The male to female ratio was 1.2:1 and the median age at presentation was 70.0 years old (interquartile range, IQR, 61.0-76.5). Most of the patients had type 2 diabetes (94.4%). The median diabetes duration was 15 years (IQR, 8.0-22.0) and the median HbA1c was 8.0% (IQR, 6.8-9.9). Ulcers were exclusively neuropathic in 37.5% of patients and neuroischemic/ischemic in 62.5% (Table I).

During the 5-year period of follow up, 44.8% (95% CI, 36.6-53.0) of patients were submitted to amputation (65/145); 31.9% (95% CI, 24.1-39.7) had at least one minor amputation (45/141) and 23.7% (95% CI, 16.6-30.9) had at least one major amputation (33/139). Minor amputations were more frequent in neuroischemic/ischemic foot ulcers (75.6%, p 0.04) and major amputations happened almost exclusively in neuroischemic/ischemic foot ulcers (97.0%, p <0.001). The 5-year all-cause mortality rate was 45.6% (95% CI, 39.3-51.8) for the entire group (113/248). Patients with neuroischemic/ischemic foot had a higher mortality rate than those with neuropathic foot [54.8% (95% CI, 46.9-62.8) vs 29.0% (95% CI, 20.6-39.6), p<0.001]. Patients who died during the 5 year period were also older at presentation [median age 75.0 years (IQR, 69.0-81.0) vs 64 years (IQR, 56.0-72.0); p<0.001] and had longer diabetes duration [15 years (IQR, 10.0-29.5) vs 13 years (IQR, 5.0-20.0); p=0.03]. Other factors associated with mortality were: ischemic heart disease (p=0.005), cerebrovascular disease (p<0.001), peripheral arterial disease (p<0.001) and hypertension (p 0.001). None of the other clinical and demographic variables tested were related with this outcome (Table 1).

> DISCUSSION

DFU are a common complication of diabetes and it can be seen as the tip of an iceberg, as it is often a sign of overall poor health and prognosis. In our study, a first DFU was associated with a 5-year amputation rate of 44.8% and a mortality rate of 45.6%, in a population that included mostly elderly men with long standing and poorly controlled diabetes with several comorbidities. The same population, mostly elderly males with long-standing diabetes and a poor health status with an increasing prevalence of peripheral artery disease and neuroischemic foot ulcers, was also found in the pioneering Eurodiale study where over 1,000 diabetic foot ulcer patients referred to 14 different European hospitals were evaluated. This increasing prevalence of diabetic foot ulceration in patients with peripheral artery disease is a common pattern recognized by several other observational studies. Overall, diabetic patients have a 30 times greater lifetime risk of having an amputation than patients without diabetes. Few studies have assessed long term outcome of patients presenting with new-onset DFU. Our
5-year amputation rate [44.8% (95% CI, 36.6-53.0)] was much higher than that reported by other studies. Moulik et al. examined the 5-year outcome of 185 patients with new-onset DFU and reported an amputation rates of 19% [8] and Ramsey et al. calculated a 15.6% 3-year amputation rate among 514 patients also with first DFU. [9] These differences may be explained by the higher prevalence of neuroischemic foot ulcers in our series, as they are known risk factor for subsequent amputation. Likewise, though not addressed in this study, the high amputation rate could probably also reflect a referral bias, since more patients are being treated exclusively in primary care settings and only the patients with peripheral artery disease and/or moderate to severe infection...
are being referred to our tertiary clinic. In support to this hypothesis, similar amputations rates have only been described when diabetic patients hospitalized for acute diabetic foot syndromes are included.\(^{[10]}\)

In our study, patients with first DFU were found to have a high 5-year mortality rate (45.6% (95% CI, 39.3–51.8)), in agreement with previous observations regarding new-onset DFU (mortality rates reported between 36.4 and 44.0%).\(^{[8,11]}\)

As expected, the prognosis was worse among older patients with longer diabetes duration, history of macrovascular disease and hypertension. The excess risk of mortality found can be partly explained by the increased CVD risk observed in these DFU patients. Other factors, like greater diabetes burden and non-cardiovascular complications of foot ulceration, may also contribute for the excess mortality observed.\(^{[2]}\)

Addressing total burden of disease and preventing further deterioration of general health status of DFU patients should be one of our major efforts.

To our knowledge, this is the first Portuguese study concerning exclusively long-term outcome of diabetic patients with new-onset DFU. We included only patients with first DFU to avoid overestimation of disease severity that could occur if we also included recurrent DFU cases. Despite being a retrospective study and its many bias, our outcome results may be regarded as accurate, since we reviewed all hospital records and the national mortality register.

> CONCLUSION

In summary, this study confirms the great morbidity, brought by amputation, of patients with DFU, as well as the associated high mortality. This points out the need for an aggressive approach to new onset DFU patients, through a careful follow-up and management by multidisciplinary teams. In this population, addressing foot problems is essential, but we also should not forget to engage control of cardiovascular risk factors and other comorbid conditions. Hopefully, in the future, we will have new and prospective data from the multicentric Portuguese Registry of Patients with Diabetic Foot Infection (RENAPEDI) to better understand all prognosis predictive factors.

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REFERENCES