Developing a foot ulcer risk model

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Developing a foot ulcer risk model: what is needed to do this in a real-world primary care setting?

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What's new?

- Foot ulceration is the most common complication in diabetes, with a lifetime risk of 25%. The condition portends significant excess morbidity and mortality in individuals with diabetes already facing reduced life expectancy and unfavourable prognosis.
- Our aim was to determine how data collected in the course of diabetes reviews of patients in UK primary care can inform a risk model to predict *de novo* foot ulcer presentation.
- People with foot ulcers were significantly older than those without, and had higher HbA_{1c} concentration, raised creatinine levels, and greater social disadvantage. Absence of monofilament sensation was more common in people with a foot ulcer, as was absence of foot pulses. More accurate determination of foot deformity and pedal circulation in the UK general practice setting may improve the predictive value of a future risk model for use in primary care.

Abstract

Aim To determine how routinely collected data can inform a risk model to predict *de novo* foot ulcer presentation in the primary care setting.

Methods Data were available on 15 727 individuals without foot ulcers and 1125 individuals with new foot ulcers over a 12-year follow-up in UK primary care. We examined known risk factors and added putative risk factors in our logistic model.

Results People with foot ulcers were 4.2 years older (95% CI 3.1–5.2) than those without, and had a higher HbA_{1c} concentration [+0.45 (95% CI 0.33–0.56), creatinine level [+6.9 μmol/L (95% CI 4.1–9.8)] and Townsend score [+0.055 (95% CI 0.033–0.077)]. Absence of monofilament sensation was

more common in people with foot ulcers (28% vs 21%; *P*<0.0001), as was absence of foot pulses (6.4% vs 4.8%; *P*=0.017). There was no difference between people with or without foot ulcers in smoking status, gender, history of stroke or foot deformity, although foot deformity was extremely rare (0.4% in people with foot ulcers, 0.6% in people without foot ulcers). Combining risk factors in a single logistic regression model gave modest predictive power, with an area under the receiver-operating characteristic curve of 0.65 (95% CI 0.62–0.67). The prevalence of ulceration in the bottom decile of risk was 1.8% and in the top decile it was 13.4% (compared with an overall prevalence of 6.5%); thus, the presence of all six risk factors gave a relative risk of 7.4 for development of a foot ulcer over 12 years.

Conclusion We have made some progress towards defining a variable set that can be used to create a foot ulcer prediction model. More accurate determination of foot deformity/pedal circulation in primary care may improve the predictive value of such a future risk model, as will identification of additional risk variables.

Introduction

Foot ulceration is the most common complication in diabetes, with a lifetime risk of 25% [1]. The condition portends significant excess morbidity and mortality in people with diabetes already facing reduced life expectancy and unfavorable prognosis [1–3]. Established aetiological risk factors for foot ulceration in diabetes are sub-optimally controlled diabetes, peripheral neuropathy, peripheral vascular disease, foot deformity and previous foot ulceration.

The incidence of foot ulcers is ~2.2% per annum in the UK, with an average 7000 people with diabetes undergoing leg, foot or toe amputation each year [4]. The financial burden is significant in terms of healthcare costs and long-term consequences. The annual NHS

expenditure on diabetes foot-related care is estimated to be £639 m to £662 m [5]. Consequently, better precision in understanding the risk calculus in relation to the development of diabetic foot ulcers and the likelihood of death in such individuals will result in reduced health service costs, with potential cost savings in the longer term.

The National Institute for Health and Care Excellence (NICE) guideline NG19, published in August 2015 [6], on the management of diabetes foot problems indicated that there is still no good evidence to support any particular schedule for monitoring and foot examination in relation to prediction of risk of diabetes foot ulceration. We aimed to provide an evidence base to address this gap.

The recently published PODUS study [7] has shown that risk assessment procedures recommended by NICE can be simplified. This was discussed by Monteiro-Soares *et al*. [8], who concluded that, although all the existing classifications were valid in a high-risk clinical context and had a very high capacity to categorize as low risk those individuals with diabetes who will not develop a foot ulcer, further research is needed in the primary care setting in this area.

A validated risk assessment tool that can be applied in primary care has the potential to lead to improvements in patient care and in the cost-effectiveness of screening for diabetes foot complications. The aim of the present study was to determine how data collected in the course of diabetes reviews of people in UK primary care could inform what additional data need to be collected in order to create a model for foot ulcer risk prediction that could be applied in the primary care setting. Data on previous foot ulceration were not included because people with a history of this are already closely monitored and are at greatly elevated risk of further ulceration [9].

Methods

We examined pseudo-anonymized electronic health records in a retrospective cohort of all men and women aged 16–89 years, attending 46 general practices in Central and Eastern Cheshire and Derbyshire, UK. The total population of the geographical area studied was 475 000 people. The area is a mixed urban and rural environment with a wide range of socio-economic situations, from significantly disadvantaged urban areas to highly affluent suburbs and rural areas. The prevalence of significant social disadvantage (based on multiple measures) was 23% (Townsend score) [10].

Data were available on 15 926 individuals without foot ulcers and on 1127 individuals with new foot ulcers over the 12-year follow-up. This long follow-up period was chosen so as to enable a significant number of foot ulcer cases to be identified in relation to the modelling to be conducted.

We examined known risk factors and added putative risk factors to our logistic model: age; HbA_{1c} concentration; creatinine levels; Townsend score; smoking status; gender, absence of monofilament sensation; absence of foot pulse; and presence of foot deformity.

Individuals were eligible for inclusion if they had received a diagnosis of diabetes prior to cohort entry on 1 January 2004, to allow long-term follow-up. The participants had no history of foot ulceration. A data search was performed through the centralized data facility afforded by Egton Medical Information Systems (EMIS®), a commercial organization that provides health information for all but one general practice in Cheshire. Search terms included all relevant Read [11] codes for diabetes and foot ulceration, together with relevant Read codes for the variables included in the analysis. 'Missingness' in terms of any datapoint was defined as the variable not being available in the period 1 January 2004 to 31 December 2005. For the final model only individuals with all variables available were included. The data were exported from the EMIS database in '.CSV' format. Data cleaning was performed using STATA 13 (Stata Corp., College Station, TX, USA). The

predictors used in developing the multivariable prediction model were those routinely recorded in the primary care setting.

One author (A.H.) conducted the search, with the assistance of an experienced collaborator in search methodology using Read codes from EMIS. Permission to conduct this study was obtained from the local information governance committees.

Statistical analysis

Exploratory data analysis was performed using STATA 13 (Stata Corp.). Analysis included comparison of risk factors between people with or without foot ulcers and for prediction of risk, stepwise selection of predictors without pre-categorizing the continuous predictors. Participant-related data are presented as arithmetic means with standard deviation. Those people with a history of foot ulceration were excluded from logistic risk modelling. Goodness-of-fit was tested using the Hosmer–Lemeshow test.

Results

Foot ulcers occurred in 1127 of the 17 053 participants (7%), after a median (interquartile range) time of 5.0 (2.6–8.1) years. Those who developed foot ulcers were significantly older at baseline (age 77.9 ± 14.1 vs 73.8 ± 16.9 years) than those without, and had a higher mean ± SD HbA_{1c} concentration [63 ± 21 vs 59 ± 19 mmol/mol (7.9 ± 1.9% vs 7.5 ± 1.7%); $P<0.0001$] and creatinine level (100 ± 46 vs 93.0 ± 39 μmol/L; $P=0.0001$) and greater social disadvantage as measured by Townsend score, in which a higher score relates to greater social disadvantage (–0.72 ± 2.84 vs –1.14 ± 2.70; $P=0.02$). Absence of monofilament sensation was more common in people with a foot ulcer (left foot 21.5%; right foot 26.2%) than in people without a foot ulcer (left foot 16.5%; right foot 18.8%; $P<0.0001$), as was absence of one or more foot pulses ($P=0.017$; Table 1).

There was no difference between people with or without foot ulcers in smoking status, gender, history of stroke or foot deformity, although foot deformity was extremely rare (0.4% in people with foot ulcers, 0.6% in people without foot ulcers; Table 1).

The best prediction was obtained by stepwise selection of predictors in a logistic regression model without pre-categorizing the continuous predictors. In this case, the statistically significant predictors were: HbA_{1c}; age; absence of monofilament sensation; creatinine level; and history of stroke. This model, shown in Table 1, had modest predictive power, with an area under the receiver-operating characteristic curve of 0.65 (95% CI 0.62–0.67). The absolute risk of ulceration in the bottom decile of risk was 1.8%, and in the top decile it was 13.4%; thus, the presence of all six risk factors yielded a relative risk of 7.4 for development of a foot ulcer over 12 years. The final model where P = probability of a foot ulcer developing was:

$$Log\left(\frac{p}{1-p}\right) - 6.398 + \{0.217 \times \text{HbA1c}\} + \{0.023 \times \text{age}\} +$$
$$\{0.380 \times [\text{absence of monofilament sensation}]\} +$$
$$\{0.003 \times \text{creatinine}\}\{-0.505 \times [\text{history of stroke}]\} .$$

Discussion

We have made progress in defining the data that need to be collected to develop a viable model for foot ulcer prediction. Importantly, we did not rely on history of ulceration as a risk factor in the model, given the very strong association already known. More accurate determination of foot deformity and pedal circulation in the UK general practice setting may improve the positive predictive value of the model. Previous studies suggest that these and other risk factors may have predictive value. It is clear that vascular dysfunction must be severe in order to predispose to ulcer formation;

however, diminished sensation appears to be implicit in ulcer formation. An insensate foot means that trauma, even minor is not sensed [1,3].

We have shown that age >55 years, serum creatinine level >150 μmol/L, HbA_{1c} concentration > 80 mmol/mol (9.5%), social disadvantage, absent monofilament sensation and absent foot pulse are relevant to evaluation of the risk of foot ulceration. Other factors, including smoking status, gender and foot deformity, were not associated with the development of a foot ulcer. This compares with the findings of study from Seattle in US Veterans [12], which identified a similar group of risk factors including impaired vision, tinea pedis and onychomycosis. The model in that study, however, also included previous foot ulcer and prior amputation, both of which are associated with a very significantly elevated risk of future ulceration. In the PODUS meta-analysis of 16 cohort studies [7], including >16 000 people, female sex was protective when the data in the PODUS dataset were analysed, but this effect was not maintained in the validation analysis using the external cohort dataset. The PODUS investigators did not find serum creatinine, HbA_{1c} or age to be predictive of foot ulceration.

Readily available clinical information has substantial predictive power for the development of diabetic foot ulcers [7,8,10] and may help in accurately targeting people at high risk of this outcome for preventive interventions. In 2006, Boyko *et al.* [12] found HbA_{1c}, impaired vision, prior foot ulcer, prior amputation, monofilament insensitivity, tinea pedis and onychomycosis to be predictive factors for future foot ulceration. In a systematic review (PODUS study) of individual patient data in 2015, Crawford *et al.* [7] found that the 10-g monofilament test most consistently identifies those people with diabetes who are at risk of foot ulceration, regardless of whether they are at low, moderate or high risk of ulceration. An

inability to feel a 10-g monofilament was at least as predictive as the groups of tests currently recommended in national and international clinical guidelines.

Monteiro-Soares *et al.* [8] showed differences between participants' characteristics and classification accuracy according to the setting. The great majority of the variables were associated with higher diabetes foot ulcer risk. Importantly, diabetes duration (since diagnosis) was considered to be associated with foot ulcer development in univariate analysis. Diabetes duration is not currently included in any classification.

The lack of significant contribution of vascular supply to the likelihood of foot ulceration is relevant to healing processes, but perfusion has to be severely reduced to compromise the integrity of the soft tissues and predispose to ulceration. Furthermore determination of absence of foot pulses may be less accurate than determination of loss of sensation using a monofilament. The difference in laterality of the foot in relation to the risk prediction model in our findings is intriguing, but may simply relate to the low frequency of pulse absence in people with foot ulcers. It may also be the case that, in the primary care setting, there is sometimes inaccurate evaluation of foot condition, which could potentially be addressed through use of arterial Doppler studies. Irrespective of this, the modelling indicates that we can identify some clear risk factors that predict future foot ulceration.

Additional risk variables will need to be identified to improve prediction to clinically useful levels to predict foot ulcers. We suggest that inability to see or reach the foot be added as a risk factor, as should accurate recording of foot deformity; however, this and other putative risk factors need to be tested in a prospective study, possibly with a more precise measure of vascular supply; for example,

arterial Doppler studies which are now straightforward to perform. Type of footwear, including new shoes, is another potential risk factor that will be included in a future model.

In relation to foot deformity, we propose that there is training of practice nurses with regard to the accurate recording of minor but still clinically significant foot deformity by the local podiatry team.

We accept that there are limitations to the dataset that was collected; however, this does reflect the way that data are routinely collected in UK primary care at diabetes reviews. There are caveats with regard to the drawing of conclusions from routinely collected data [13–15]. The point of the present study was to describe how we can make the most of those data and improve their quality.

In conclusion, we aimed to determine what variable could be used in a systematic study looking at the determinants of foot ulceration in a primary care setting. Derivation of a predictive algorithm would come out of the data generated by such a study. Our findings will inform what additional data should be collected in primary care to enable model development for prediction of future foot ulceration. More accurate determination of foot deformity and pedal circulation in the primary care setting should improve the positive and negative predictive value of any future model, as will identification of additional risk variables.

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Competing interests

None declared.

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Table 1 Differences between individuals who did and did not develop a foot ulcer for categorical variables

Variable	Non-cases *n* (%)	Cases *n* (%)	OR (95% CI)	*P* value for difference
Smoking status				
Never smoked	3782 (38.55)	287 (39.81)	Reference	
Not current	1257 (12.81)	87 (12.07)	0.91 (0.71, 1.17)	
Ex-smoker	3174 (32.35)	232 (32.18)	0.96 (0.81, 1.15)	
Current smoker	1598 (16.29)	115 (15.95)	0.95 (0.76, 1.19)	0.8917
History of stroke				
No	14676 (92.15)	1046 (92.81)	Reference	
Yes	1250 (7.85)	81 (7.19)	0.91 (0.72, 1.15)	0.4236
Gender				
Female	7160 (45.51)	522 (46.32)	Reference	
Male	8574 (54.49)	605 (53.68)	0.97 (0.86, 1.09)	0.5974
Absence of monofilament sensation: L				
No	13298 (83.50)	886 (78.62)	Reference	
Yes	2628 (16.50)	241 (21.38)	1.38 (1.19, 1.60)	<0.0001

Absence of monofilament sensation: R				
No	12936 (81.23)	832 (73.82)	Reference	
Yes	2990 (18.77)	295 (26.18)	1.53 (1.34, 1.76)	<0.0001
Foot pulse absent: L				
No	15297 (96.05)	1066 (94.59)	Reference	
Yes	629 (3.95)	61 (5.41)	1.39 (1.06, 1.82)	0.0160
Foot pulse absent: R				
No	15296 (96.04)	1074 (95.30)	Reference	
Yes	630 (3.96)	53 (4.70)	1.20 (0.90, 1.60)	0.2165
Foot deformity: L				
No	15845 (99.49)	1125 (99.82)	Reference	
Yes	81 (0.51)	2 (0.18)	0.35 (0.09, 1.42)	0.1227
Foot deformity: R				
No	15846 (99.50)	1123 (99.65)	Reference	
Yes	80 (0.50)	4 (0.35)	0.71 (0.26, 1.93)	0.4946
Absence of monofilament sensation on ≥ 1 foot				
0	12619 (79.24)	812 (72.05)	Reference	

1	3307 (20.76)	315 (27.95)	1.48 (1.29, 1.70)	<0.0001
Foot pulses absent on ≥ 1 foot				
0	15162 (95.20)	1055 (93.61)	Reference	
1	764 (4.80)	72 (6.39)	1.35 (1.06, 1.74)	0.0168
Deformity on on ≥ 1 foot				
0	15832 (99.41)	1123 (99.65)	Reference	
1	94 (0.59)	0.40 (0.35)	0.60 (0.22, 1.63)	0.3125
HbA_{1c} >80 mmol/mol (9.5%)				
No	11672 (89.17)	727 (83.28)	Reference	
Yes	1418 (10.83)	146 (16.72)	1.65 (1.37, 1.99)	<0.0001
Creatinine > 150 μmol/L				
No	9921 (96.12)	744 (93.23)	Reference	
Yes	401 (3.88)	54 (6.77)	1.80 (1.34, 2.41)	0.0001
Age >55 years				
No	2245 (14.27)	83 (7.36)	Reference	
Yes	13489 (85.73)	1044 (92.64)	2.09 (1.67, 2.63)	<0.0001

Townsend score > 1				
No	11935 (74.94)	798 (70.81)	Reference	
Yes	3991 (25.06)	329 (29.19)	1.23 (1.08, 1.41)	0.0020
Variable	**Non-cases** **Mean (SD)**	**Cases** **Mean (SD)**	**OR per SD increase** (95% CI)	***P* value for difference**
HbA_{1c}, %	7.48 (1.67)	7.92 (1.93)	1.26 (1.19, 1.34)	0.0001
Creatinine	92.97 (39.28)	99.91 (45.52)	1.12 (1.06, 1.17)	0.0001
Age	73.77 (16.86)	77.92 (14.06)	1.31 (1.23, 1.40)	0.0001
Townsend score	–1.14 (2.70)	–0.72 (2.84)	1.16 (1.09, 1.23)	0.0001

L, left foot; OR, odds ratio; R, right foot.