A prospective study of risk factors for foot ulceration: The West of Ireland Diabetes Foot Study

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Summary

Background: This is the first study to examine risk factors for diabetic foot ulceration in Irish general practice.

Aim: To determine the prevalence of established risk factors for foot ulceration in a community-based cohort, and to explore the potential for estimated glomerular filtration rate (eGFR) to act as a novel risk factor.

Design: A prospective observational study.

Methods: Patients with diabetes attending 12 (of 17) invited general practices were invited for foot screening. Validated clinical tests were carried out at baseline to assess for vascular and sensory impairment and foot deformity. Ulcer incidence was ascertained by patient self-report and medical record. Patients were re-assessed 18 months later.

Results: Of 828 invitees, 563 (68%) attended screening. On examination 23–25% had sensory dysfunction and 18–39% had evidence of vascular impairment. Using the Scottish Intercollegiate Guidelines Network risk stratification system we found the proportion at moderate and high risk of future ulceration to be 25% and 11%, respectively. At follow-up 16/383 patients (4.2%) developed a new foot ulcer (annual incidence rate of 2.6%). We observed an increasing probability of abnormal vascular and sensory test results (pedal pulse palpation, doppler waveform assessment, 10g monofilament, vibration perception and neuropathy disability score) with declining eGFR levels. We were unable to show an independent association between new ulceration and reduced eGFR [Odds ratio 1.01; P=0.64].

Conclusions: Our data show the extent of foot complications in a representative sample of diabetes patients in Ireland. Use of eGFR did not improve identification of patients at risk of foot ulceration.

Introduction

Lower extremity amputation is among the most feared complications of diabetes. A recent Irish study reported an annual incidence of diabetes related lower extremity amputation between 145 and 176 per 100,000 people with diabetes. Prevention of diabetes related amputation involves good foot care including early intervention for new foot problems.

Current international guidelines recommend a comprehensive annual foot examination, and in the UK, diabetic foot screening is routinely carried out in general practice. With an increasing emphasis on primary-care-based diabetes care in Ireland, general practice seems the ideal setting for this
screening. To date, there are few published data on diabetic foot complications in Ireland. In a pilot study, our group reported sensory dysfunction in up to 30% of patients attending a single general practice and vascular impairment in 17%.5

Diabetic foot ulceration has a multi-factorial aetiology, with sensory dysfunction, vascular impairment and structural foot deformity contributing to risk.2 Poor glycaemic control has also been proposed as a risk factor6 and there is now an increasing recognition of the link between end-stage kidney disease and diabetic foot ulceration and amputation.7,8 Our aim was to look at the prevalence of established risk factors for foot ulceration in a community-based cohort in the West of Ireland, and to explore the relationship between sensory and vascular impairment with level of eGFR.

**Methods**

**Practice and participant recruitment**

We invited 17 general practices from a mix of urban and rural locations to participate in this prospective cohort study. We invited practices of varying list size that were known to have a practice nurse and a diabetes register.9 The study took place in the counties of Galway and North Clare, with patient recruitment taking place from February 2008 to September 2009. We obtained research ethics approval from the Irish College of General Practitioners Research Ethics Committee (REC) and the Galway University Hospitals REC. We offered practices training in diabetic foot assessment followed by mentoring by a podiatrist with assistance at foot screening clinics, as well as a financial reimbursement of €15 per screening visit.

From the practice diabetes register, we selected all adult patients with a diagnosis of type 1 or type 2 diabetes, except those with significant cognitive impairment identified by the practice team based on their knowledge of the patient. We sent letters of invitation to all eligible patients and if required, followed this up with a telephone call. A senior podiatrist trained the practice nurses in diabetes foot-screening techniques. This involved attendance at a workshop, followed by one-to-one mentoring by the podiatrist during at least two screening clinics at the practice.

**Measurement**

All screening clinics were held in general practice. Patients underwent a clinical foot examination and were asked questions regarding their social history. We reviewed the practice medical records to obtain details of patients’ medical history, comorbidities and most recent laboratory results. We documented HbA1c results as DCCT units and we later converted the mean HbA1c to IFCC units. To calculate eGFR, we used the most recent creatinine result in the abbreviated MDRD equation. We grouped participants according to eGFR level into eGFR ≥ 90 ml/min/1.73 m², eGFR 60–89 ml/min/1.73 m², eGFR 15–59 ml/min/1.73 m² and eGFR <15 ml/min/1.73 m².

The foot screening assessment comprised a series of tests of neuropathy symptoms [neuropathy symptoms score (NSS)10,11] and signs [cutaneous pressure perception (CPP) using a 10 g monofilament,2 modified neuropathy disability score (mNDS)11 and vibration perception threshold (VPT)12,13], vascular symptoms and signs [pedal pulse palpation, doppler waveform assessment and ankle brachial pressure index (ABPI)] as well as an assessment of foot deformity [the Manchester Hallux Abducto Valgus (HAV) scale14,15] where HAV deformity is graded against a set of standardised photographs as 1 (no deformity) to 4 (severe deformity). We selected the simple screening tests of CPP, pedal pulse palpation and severity of HAV deformity, as well as history of diabetic foot ulceration and amputation as the tools by which to stratify participants according to the Scottish Intercollegiate Guidelines Network (SIGN) risk stratification system.16 This risk stratification system has been shown to accurately predict foot ulceration.16,17

**Ascertainment of outcomes**

During screening clinics, we asked all patients and practice team members to report any new foot ulcer to the study team. We provided patients with a foot-wound alert card with a hotline number and sent reminder letters at 6 months and 12 months post-screening. At 18 months, following re-training of practice nurses, we invited all patients to attend for repeat clinical assessment. At the follow-up visit we questioned patients regarding their foot health to determine if any ulcer had developed and we repeated the vascular and sensory tests. For patients who reported a new ulcer but were unable to attend for re-assessment, we validated the ulcer (through medical record review and contact with members of the primary healthcare team) and obtained details of management and outcomes.

**Statistical analysis**

The number of practices invited to participate was based on pragmatic considerations (support of a single research podiatrist) and not on a formal sample size calculation. Baseline characteristics
were compared for the low-, moderate- and high-risk groups (based on SIGN score) using ANOVA for continuous variables and chi-square test for categorical variables. Two sample comparisons were performed using t-tests and the Mann–Whitney U-test when appropriate. As the percentage of missing data was small, multiple imputation was not deemed necessary. The number of patients developing a new ulcer was used to calculate the annual incidence of ulceration, as opposed to using the number of new ulcers. Binary logistic regression models were used for the analysis of binary responses, specifically to analyse the effect of eGFR on the probability of having abnormal vascular and sensory results. Binary logistic models were also fitted to determine the effect of different foot ulcer risk factors on the probability of developing new ulceration.

Results
Sample
Of the 17 invited practices, 12 (71%) responded and were recruited into our study. General practice diabetes registers were reviewed by practice nurses, and 828 patients were identified who fulfilled the study inclusion and exclusion criteria. Of these, 563 (68%) attended for screening. The flow of participants through the study is illustrated in Figure 1.

Baseline characteristics, clinical tests and risk categories

Demographic details of all patients attending for foot screening are displayed in Table 1. Over 95% of participants were Caucasian in origin. Over half of all participants were also attending the hospital for their diabetes care. A review of medical records revealed that 3% had previously documented neuropathy, 3.7% had previous foot ulceration and 1.6% had prior amputation.

Results of baseline clinical measurements are presented in Table 1. On examination of sensory function using CPP, mNDS and VPT, 23–25% had abnormal results. All three sensory tests were abnormal in 10% of participants. Vascular assessment revealed that 18% had ≥2 pedal pulses absent. On doppler waveform assessment, 40% had a monophasic or biphasic pulse and on further investigation 23% of these participants had an abnormal ankle brachial pressure index (ABPI). A total of 2.5% were referred for the first time to a vascular

Figure 1. Flow of participants through the study.
specialist. Moderate and severe HAV deformity was present in 16.3% and 2.4%, respectively.

Renal function

Of the 563 patients attending for foot screening, a recent creatinine result was available for 502 patients. Of these, 157 (31%) had an eGFR ≥ 90 ml/min/1.73 m², 238 (47%) had an eGFR 60–89 ml/min/1.73 m² and 107 (21%) had an eGFR 15–59 ml/min/1.73 m². No patient had an eGFR less than 15 ml/min/1.73 m². We observed a trend towards an increasing probability of impaired sensory and vascular function with declining eGFR; this is shown graphically in Figure 2 with eGFR represented as a continuous variable; a similar pattern was observed when eGFR was treated as a categorical variable (data not shown). The logistic regression model for CPP yielded an odds ratio of 0.99 (CI 0.98–0.998; P = 0.018) indicating that for every one unit decrease in eGFR we observed a 1% increase in the odds of having abnormal CPP. Similar results were observed for other sensory and vascular risk factors.

Ulcer incidence at follow-up

A total of 383 (68%) of 563 recruited patients were followed up at an average of 19.4 months. A total of 377 participants attended a follow-up clinic. A further six participants, for whom an ulcer had been reported but did not attend follow-up, were also included. The reason for non-attendance at the follow-up clinic was not determined. There was no significant difference in age, gender or duration of diabetes between those who did and those who did not attend the follow-up clinic.
however, non-attenders at follow-up had a higher median HbA1c at baseline than attenders at 7.2% vs. 6.9% (P=0.04). At follow-up 16/383 patients (4.2%) developed 19 ulcers. Of those patients who developed an ulcer 9 (56%) had a history of foot ulceration and 7 (44%) developed a foot ulcer for the first time. Ulcers were validated by the study podiatrist (n=11), community podiatrist (n=4) or public health nurse (n=1). Two participants underwent an amputation (1 trans-metatarsal and 1 below knee amputation). The annual incidence of ulceration and amputation were 2.6% (CI 1.6–4.1%) and 0.3% (CI 0.1–1.2%), respectively. Of the 16 participants who developed an ulcer, 2 died during the study period.

Compared with those who did not develop a foot ulcer, those who did develop a new ulcer were more likely to be older (P=0.06) and male (P=0.08) but these differences were not statistically significant. However those who developed a new ulcer had a significantly higher HbA1c and higher rates of neuropathy, vascular impairment and previous ulceration (Table 2). There was no significant effect of eGFR on the probability of developing new foot ulceration; OR 1.01 (CI 0.98–1.03; P=0.64). Variable selection procedures were used for the determination of a multivariate model considering, in addition to the variables described above, other possible risk factors such as duration of diabetes, smoking status, gender, cardiovascular disease, cerebrovascular disease, retinopathy, diabetic nephropathy and HAV. The final model included CPP, PP palpation, age and HbA1c with adjusted P-values <0.001, 0.005, 0.096 and 0.017, respectively. Based on these results it seems that impaired CPP and abnormal PP palpation have the strongest effect on the probability of developing a foot ulcer both individually and after adjusting for other significant risk factors.

**Risk stratification**

Applying the results of CPP, pedal pulse palpation, severe (Grade 4) HAV deformity, previous ulceration and previous amputation to the SIGN risk stratification system meant that 64%, 25% and 11% of the full cohort screened were assigned low, moderate and high risk of future foot ulceration, respectively. There was a significant difference in age, history of cerebro- and cardiovascular disease, signs and symptoms of neuropathy and signs and symptoms of vascular disease between the ulcer risk categories.

At follow-up 81% of those who developed an ulcer had been classified as high risk with the remainder (19%) classified as moderate risk. The high-risk group displayed the highest probability of developing a new ulcer (28.6%) compared to the probability of patients in the combined moderate- and low-risk category (3.2%).

**Discussion**

In this prospective study we report (for the first time in an Irish setting) the prevalence of risk factors for
foot ulceration and the incidence of new foot ulceration in a community-based cohort of adults with diabetes. Using the SIGN risk classification system we found that 11% of diabetes patients were at high risk of future foot ulceration. We observed a 2.6% annual incidence of new foot ulceration with the majority of incident ulcer patients (81%) being identified by SIGN as high risk at baseline. We noted a marked discrepancy between documentation of peripheral neuropathy in the GP record (3%) and the true prevalence of neuropathy symptoms (32%) and signs of sensory impairment (23–25%) in our cohort. While awaiting widespread uptake of foot screening by general practitioners and/or practice nurses in Ireland we believe that alternative ways of identifying patients at high risk of foot ulceration are required. Although not conclusive our data suggest that the level of eGFR (which is increasingly being provided routinely to GP surgeries as part of biochemistry testing) is worth exploring as a potential indicator of increased foot risk.

Our prevalence data for vascular and sensory dysfunction are consistent with other community-based studies. Scottish and English data report abnormal pedal pulse palpation in 17% to 21% and impaired CPP in 21% to 23% of patients.\textsuperscript{10,17} As well as neuropathy and vascular impairment, prior ulceration, prior amputation and structural deformity are all well recognized risk factors for ulceration.\textsuperscript{2} In this study the rate of prior ulceration was 3.7% which is in line with previous reported rates of 3.1–4.9% in the UK.\textsuperscript{10,17} The rate of previous amputation in our study was 1.7% which is consistent with the 1.3% reported by Abbott et al.\textsuperscript{10} in the North West Diabetic Foot Care Study. The annual incidence of ulceration in this study was 2.6% which is also broadly similar to that reported in other community-based studies.

Muller et al.\textsuperscript{18} reported an annual incidence of 2.1%, Abbott et al.\textsuperscript{10} reported an annual ulcer incidence rate of 2.2%, and Crawford et al.\textsuperscript{19} recently reported an annual incidence of 1.9%. We found that 19% had either moderate or severe HAV deformity. This is the first time the HAV scale has been used to screen for foot deformity. We chose this method of assessing deformity due to its simplicity to use with little training or experience, and it has been tested for reliability and validity.\textsuperscript{14,15} However a limitation of this method is that it only assesses one type of foot deformity.

Our dataset enabled us to explore (in a prospective manner) the relationship between renal function and traditional risk factors for foot ulceration as well as incident foot ulceration. A total of 21% of our cohort had an eGFR of $<60$ ml/min/1.73 m$^2$. This compares with 26% reported in diabetes populations in UK primary care and 27.5% reported in combined primary and secondary care.\textsuperscript{7,20} Previous Irish data shows a 16.6% CKD rate (defined as eGFR $<60$) in general practice populations.\textsuperscript{21} We found a statistically significant relationship between declining levels of eGFR and the probability of having abnormal sensory or vascular function on foot screening. We believe that our findings are worthy of further exploration in a larger cohort and (if substantiated) would have relevance to clinical practice. Nephropathy was found to predict ulceration in the North West Diabetes Foot Care Study\textsuperscript{10} and more recently Leese et al.\textsuperscript{17} suggested that proteinuria could be added to risk stratification tools. While there is now an established association between renal disease and diabetic foot ulceration, the causative mechanism is less well established. Peripheral arterial disease (PAD) is believed to be an important underlying cause however the

### Table 2 Characteristics of patients developing a new foot ulcer

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>n</th>
<th>No</th>
<th>n</th>
<th>$P$-value</th>
</tr>
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<tbody>
<tr>
<td>New ulcer</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>69.9 (7.7)</td>
<td>16</td>
<td>64.3 (12.6)</td>
<td>370</td>
<td>0.064</td>
</tr>
<tr>
<td>Men (%)</td>
<td>81</td>
<td>16</td>
<td>60</td>
<td>370</td>
<td>0.081</td>
</tr>
<tr>
<td>Primary education only (%)</td>
<td>73</td>
<td>15</td>
<td>47</td>
<td>357</td>
<td>0.041</td>
</tr>
<tr>
<td>Duration of diabetes in years [Median (IQR)]</td>
<td>5.5 (14)</td>
<td>16</td>
<td>5 (9)</td>
<td>352</td>
<td>0.318</td>
</tr>
<tr>
<td>Mean HbA$_1c$ (SD)</td>
<td>7.8 (0.8)</td>
<td>16</td>
<td>7.2 (1.3)</td>
<td>365</td>
<td>0.038</td>
</tr>
<tr>
<td>eGFR (SD)</td>
<td>81.1 (30.4)</td>
<td>15</td>
<td>78.1 (24.2)</td>
<td>333</td>
<td>0.648</td>
</tr>
<tr>
<td>Abnormal CPP (%)</td>
<td>87.5</td>
<td>16</td>
<td>22.2</td>
<td>370</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal PP palpation (%)</td>
<td>50.0</td>
<td>16</td>
<td>14.9</td>
<td>370</td>
<td>0.001</td>
</tr>
<tr>
<td>Severe HAV deformity (%)</td>
<td>0</td>
<td>14</td>
<td>2.2</td>
<td>363</td>
<td>0.737</td>
</tr>
<tr>
<td>Previous ulcer (%)</td>
<td>56.2</td>
<td>16</td>
<td>2.7</td>
<td>370</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Previous amputation (%)</td>
<td>37.5</td>
<td>16</td>
<td>0.5</td>
<td>370</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
association has also been shown to exist in the absence of clinically apparent PAD. Because eGFR is itself a calculated variable (combining age and a biochemical measure of renal function) it represents a potentially attractive way of identifying individuals in a practice at high risk of foot ulceration. This approach to screening (i.e. using existing data from the practice clinical information system as an initial ‘filter’) has been used in approaches to screening for type 2 diabetes.

Our study has several limitations. We only invited practices with a practice nurse and a diabetes register to participate in the study. This may have resulted in a degree of selection bias. A further limitation of our study was our 32% rate of loss to follow-up. Individuals who did not attend for follow-up at 18 months tended to have poorer glycaemic control but were otherwise similar to those who did attend. Our analyses of foot ulcer prediction are limited by the relatively small number of outcomes that we observed. Ideally, when exploring relationships between risk factors and clinical events, investigators should have at least 10 outcomes for every independent variable explored in the model. For us this would have required in the region of 110 foot ulcers as opposed to the 19 ulcers we observed. For this reason we believe that the findings of our multivariate analysis should be interpreted with caution.

An important strength of our study is that foot screening was undertaken in a busy general practice setting by practice nurses trained in diabetic foot screening by a single podiatrist. Our pragmatic approach to screening reflects the realities of day-to-day clinical practice.

In conclusion, our data show for the first time the extent of sensory dysfunction and vascular impairment in a representative sample of patients with diabetes in Irish general practice. Simple screening tests such as cutaneous pressure perception, pedal pulse palpation, foot deformity assessment, previous ulceration and previous amputation, applied to the SIGN risk stratification system, appears to be a good predictor of risk. As the Irish health service is re-steering diabetes care towards general practice, our data can help inform policy and resource planning in this area.

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Conflict of interest: None declared.

References


11. Young MJ, Boulton AJ, MacLeod AF, Williams DR, Sonksen PH. A multicentre study of the prevalence of
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