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Temporal changes in the prevalence and associates of foot ulceration in type 2 diabetes: The Fremantle Diabetes Study

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ABSTRACT

Aims: To assess temporal changes in foot ulceration and its risk factors in community-based people with type 2 diabetes.
Methods: Baseline data from the longitudinal observational Fremantle Diabetes Study collected from 1993 to 1996 (Phase I) and 2008 to 2011 (Phase II) were analyzed. Generalized linear modeling was used to examine changes in foot ulcer prevalence and its associates between phases. Multiple logistic regression was used to determine associates of prevalent foot ulceration in individual and pooled phases.
Results: There were 16 foot ulcers among 1296 patients in Phase I (1.2%) and 23 in 1509 Phase II patients (1.5%; $P = 0.86$ after age, sex and race/ethnicity adjustment). Glycemic and non-glycemic cardiovascular risk factors were better in Phase II, but diabetes duration was longer, peripheral sensory neuropathy (PSN) was more prevalent and more patients were Aboriginal ($P < 0.001$) than in Phase I. In multivariable analysis of both phases and pooled data, diabetes duration and peripheral sensory neuropathy (PSN) were independent associates of foot ulceration ($P \leq 0.026$). Prior hospitalization for ulcer, intermittent claudication, any absent pedal pulse and Aboriginality were also significant in the pooled model ($P \leq 0.009$).
Conclusions: Strong associations between foot ulcer and diabetes duration, PSN, symptomatic and clinically-detectable peripheral vascular disease were observed. Aboriginality also proved an independent risk factor. Since all these risk factors apart from intermittent claudication and impalpable foot pulses were more prevalent in Phase II, improved community- and hospital-based foot care between phases are likely to have attenuated the risk of foot ulcers in Phase II patients.

1. Introduction

Diabetes management and prognosis have changed significantly over the past two decades. There is evidence that blood glucose-lowering strategies have intensified in the US (Dodd et al., 2009), the UK (Calvert, Shankar, McManus, Lester, & Freemantle, 2009) and Australia (Davis et al., 2012a), that other vascular risk factors including hypertension and dyslipidemia are also now better managed (Davis et al., 2012a; Ford, 2011), and that outcomes such as cardiovascular events and preventable hospitalizations have declined (Wang et al., 2009; Gregg et al., 2014). In the case of diabetes-related foot disease, most population-based studies have shown a reduction in lower extremity amputation (LEA) rates (Gregg et al., 2014; Margolis & Jeffcoate, 2013), but some have shown no change (Buckley et al., 2012; McCaslin, Hafez, & Stansby, 2007; Trautner, Haastert, Spraul, Giani, & Berger, 2001).

Equivalent temporal data relating to foot ulceration complicating diabetes, a potent precursor of LEA, are sparse. The decline in LEA rates observed in most geographic contexts (Margolis & Jeffcoate, 2013) could reflect better management of established foot ulcers by multi-disciplinary care that improves offloading, debridement, treatment of bacterial infection and revascularization, rather than a reduction in foot ulcer incidence over time through improvements in glycemia and non-glycemic vascular risk factors (Malik, Tesfaye, & Ziegler, 2013). In the light of issues complicating standardized ascertainment of foot ulceration and its risk factors (Crawford, Inkster, Kleijnen, & Fahey, 2007; Monteiro-Soares, Boyko, Ribeiro, Ribeiro, & Dinis-Ribeiro, 2012), valid examination of temporal changes in foot ulcer incidence and its determinants requires active surveillance of, and detailed data collection from, representative community-based cohorts.

Conflicts of interest: None declared.

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The aims of the present study were, therefore, i) to determine whether the prevalence of foot ulceration had changed in well-characterized representative cohorts of patients with type 2 diabetes resident in a large urban Australian population between 1993–1996 and 2008–2011, and ii) to assess the relationship between changes in established risk factors for ulceration and its prevalence over the same period. We hypothesized that improved cardiovascular risk management and implementation of better podiatric care over the 15 years between assessments would reduce foot ulcer prevalence.

2. Material and methods

2.1. Patients

We studied participants in both phases of the Fremantle Diabetes Study (FDS) which are longitudinal observational studies conducted in the same postcode-defined geographical area surrounding the city of Fremantle in the state of Western Australian state of (WA). Details of recruitment, sample characteristics including classification of diabetes type and non-recruited patients have been published previously (Davis, Bruce, & Davis, 2013). In brief, any patient resident in the study catchment area with clinician-verified diabetes was eligible for recruitment. Sources of identification and/or diagnostic data included public hospital inpatient/outpatient clinic lists and laboratory databases, notifications by local primary care/specialist physicians and allied health services including diabetes education, dietetics and podiatry, advertisements in pharmacies and local media, and word of mouth. The Phase I (FDS1) protocol was approved by the Fremantle Hospital Human Rights Committee, and Phase II (FDS2) was approved by the Human Research Ethics Committee of the Southern Metropolitan Area Health Service, Perth, WA. All subjects gave written informed consent before participation.

We identified 2258 eligible FDS1 subjects during the three-year period between 1993 and 1996 in the local population of 120,000 (crude prevalence 1.9%) and recruited 1426 (63%). In the case of FDS2, 4639 patients with diabetes were identified over the same time period between 2008 and 2011 from a population of 157,000 (crude prevalence 3.0%) and 1668 (36%) were recruited including 326 surviving FDS1 patients. For FDS1, 1296 (90.9%) of the cohort had type 2 diabetes and, for FDS2, the equivalent figure was 1509 (89.4%). The two cohorts had similar age, gender distribution, type of diabetes and race/ethnicity to those of the non-recruited patients (Davis et al., 2013).

2.2. Data collection methods

Each FDS1 participant was assessed in detail at baseline and invited to attend annual reviews for ≥5 years. For FDS2, comprehensive baseline assessments are followed by face-to-face assessments biennially with questionnaire follow-up in alternate years. We performed only a comparative analysis of baseline data from both phases in the present study. This was primarily because we wished to determine, using the most complete cross-sectional FDS data available, changes in foot ulcer prevalence and associates over the 15 years between recruitment periods but, in addition, we have previously published data relating to the prevalence and incidence of foot ulcer in FDS1 patients followed for up to 18 years (Baba, Davis, & Davis, 2014) while the average follow-up in FDS2 is currently only 4.5 years (Davis et al., 2013).

All FDS face-to-face assessments comprise a comprehensive questionnaire, physical examination and standard fasting biochemical tests (Davis et al., 2013). For both phases, diabetes type was assessed from diabetes treatment history, BMI, age at diagnosis, nature of first presentation, and/or self-identification, and case records were consulted for evidence of ketonemia, as well as islet cell antibody, glutamic acid decarboxylase antibodies, serum insulin and C-peptide concentrations, if available. Ethnic background was assessed from self-selection, country/countries of birth and parents' birth, language(s) spoken at home and, for FDS2, country of grandparents' birth. Intermittent claudication was ascertained by determining whether pain in the calves came on during walking, caused the patient to slow down or stop, and resolved with rest. In addition to other procedures, a trained nurse palpated the dorsalis pedis and posterior tibial pulses, measured the ankle brachial index (ABI), assessed peripheral sensory neuropathy (PSN) using the clinical features of the Michigan Neuropathy Screening Instrument (MNSI), and performed a general foot inspection to detect the presence or absence of ulceration (defined, for the purposes of the present study, as located at or below the level of the malleoli), deformity, corns or callus, skin fissures, infections and nail pathology (Baba et al., 2014).

Chronic complications were ascertained using standard criteria. Peripheral arterial disease (PAD) was considered present if the ABI was ≤0.90 on either leg or a diabetes-related amputation (attributable to PSN and/or PAD) was present. PSN was defined as a score of >2/8 on the clinical portion of the MNSI. Patients were considered to have coronary heart disease if there was a self-reported history of, or hospitalization for, myocardial infarction, angina, coronary artery bypass grafting or angioplasty. Self-reported stroke and transient ischemic attack were amalgamated with prior hospitalizations to define baseline cerebrovascular disease status. Retinopathy comprised grade, including maculopathy, as detected by direct and/or indirect ophthalmoscopy in one or both eyes and/or on more detailed assessment by an ophthalmologist. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (Levey et al., 2009).

Biochemical testing in both FDS phases was carried out in the same nationally accredited laboratory. Between-run imprecision for all methods was <3.5%, except for urine albumin and serum HDL-cholesterol in FDS2 for which it was <5.0%. Serum LDL-cholesterol was estimated using the Friedewald equation. For assays that changed subsequent to 1993, calibration equations were applied to standardize all concentrations to current assays used for FDS2 (Davis et al., 2012b).

2.3. Statistical analysis

The computer package IBM SPSS Statistics 21 (IBM Corporation, Somers, NY, US) was used for statistical analysis. Data are presented as proportions, mean ± SD, geometric mean (SD range), or, median and interquartile range [IQR] in the case of variables that did not conform to the normal or log-normal distribution. For independent samples, two way comparisons for proportions were performed by Fisher's exact test, Student's *t*-test for normally distributed variables, and the Mann–Whitney *U*-test for variables that were not normally distributed. A two-tailed *P*-value of <0.05 was considered significant. Multiple logistic regression was used to determine independent associates of prevalent foot ulceration, with all clinically plausible variables $P < 0.20$ considered for entry into the model. Generalized linear modeling with adjustment for age, sex and ethnicity was used to determine whether baseline associates had changed between phases.

3. Results

3.1. Patient characteristics

Demographic, socioeconomic, anthropometric and diabetes-specific details of participants with type 2 diabetes recruited to the two phases are summarized in Table 1. Those in FDS2 were older and there were proportionately more males than females than in FDS1. There were fewer Anglo-Celts and Southern Europeans, but a greater proportion of Aborigines and those with an ethnic/racial background outside the major groups. The FDS2 patients were diagnosed at a younger age and had a longer duration of diabetes. More FDS2 participants had received