The Prediction of Diabetic Neuropathic Foot Ulceration Using Vibration Perception Thresholds

A prospective study

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OBJECTIVE — To assess the ability of vibration perception threshold (VPT) to predict the development of diabetic foot ulceration.

RESEARCH DESIGN AND METHODS — A prospective follow-up study of consecutive patients with vibration perception measured by biothesiometry from April 1988 to March 1989. Patients were stratified in various risk groups.

RESULTS — Patients with a VPT <15 V had a cumulative incidence of foot ulceration of 2.9% compared with 19.8% in patients with a VPT >25 V, odds ratio (OR) 7.99 (3.65–17.5, 95% confidence intervals), $P < 0.01$. The incidence of ulceration increased with duration of diabetes, but even with this effect removed, the excess of ulceration persisted, OR 6.82 (2.75–16.92), $P < 0.01$.

CONCLUSIONS — VPT is an effective predictor of the risk of foot ulceration in diabetes and therefore could be used to target foot-care education to those patients most likely to benefit and, thereby, possibly improve its effectiveness.

The development of foot ulceration is a significant marker of the extent of diabetes complications and can have potentially serious consequences for life and limb. The financial cost of diabetic foot ulceration was estimated at £13.5 million in the U.K. in 1985–1986 (1), and foot ulceration is the most common reason for hospital admission of diabetic patients in the U.K. (2). Diabetic patients are 15 times more likely to have an amputation than are nondiabetic patients (3), and this has led the joint World Health Organization/International Diabetes Federation Declaration of St. Vincent to call for a 50% reduction in foot ulceration throughout Europe within 5 years (4). The effective prevention of foot ulceration through education and preventative treatment, however, is time-consuming and expensive (5–8). If the appropriate at-risk groups could be identified (9), educational resources could be concentrated on those patients at risk and possibly improve the effectiveness of foot-care programs. As peripheral vascular disease (PVD) and consequent gangrene are unlikely to be influenced by standard foot-care education, such programs are generally oriented to the prevention of neuropathic foot ulceration.

A number of factors have been identified in cross-sectional studies as being associated with foot ulceration, including a previous foot ulcer (5), peripheral neuropathy (10), diabetic nephropathy (11), limited joint mobility (12,13), and high dynamic plantar foot pressures (13–15). Of these, only high dynamic plantar foot pressures have been shown, prospectively, to predict an increased risk of foot ulceration (15). However, the measurement of dynamic foot pressures is principally a research tool and is not widely available in routine clinics. An increased vibration perception threshold (VPT) has been found in patients with diabetic foot ulceration (10). VPTs are regularly measured in diabetic patients attending hospital clinics and have been shown to equate with clinical scoring systems of neuropathy (16,17). This study, therefore, was designed to assess the effectiveness of VPT to predict patients at risk of foot ulceration over a 4-year period.

RESEARCH DESIGN AND METHODS

— After the setting up of a new diabetes center and diabetic foot clinic, as described previously (7), the regular screening of patients with VPT was established. VPT was assessed by biothesiometry (Arnold Horwell, Lon-

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VPT, vibration perception threshold; OR, odds ratio; CI, confidence interval; PVD, peripheral vascular disease.

Table 1—*Clinical characteristics of the subject groups*

	Group 1 VPT <15 V	Group 2 VPT 16–24 V	Group 3 VPT > 25 V	All patients
n	209	58	202	469
Sex (M/F)	86/123	24/34	118/84*	228/241
Mean years of age (range)	45 (17–77)	59 (26–85)†	61 (31–83)*	54 ((17–85)
Type I diabetes (%)	97 (46.4)	18 (31.0)	77 (38.1)	192 (40.9)
Type II diabetes (%)	112 (53.6)	40 (69.0)	125 (61.9)	277 (59.1)
Duration of diabetes (range) in years	10.1 (0–48)	10.5 (0–54)	15.6 (0–60)†	12.4 (0–60)
HbA_1 (normal <8%)	10.5 ± 2.2	11.0 ± 2.3	11.0 ± 2.4	10.7 ± 2.3
Creatinine (μM)	83.0 ± 21.7	94.1 ± 23.9	102.4 ± 56.0	92.0 ± 40.3

Data are means ± SD. *$P < 0.01$ group 3 vs. group 1. †$P < 0.05$ group 2 vs. group 1.

don, U.K.) at the great toe with the probe balanced vertically on the pulp of the toe. A mean of three readings was used to derive the value for each foot.

Between April 1988 and March 1989, 469 consecutive patients, as described below, were screened. These patients were then followed until 31 March 1992 in the diabetes center and foot clinic as appropriate. All foot ulcers, regardless of cause, were recorded either in the patient record, chiropody notes, or foot hospital notes and included in the analysis.

The 469 patients had no history of previous foot ulceration, and all had at least one pedal pulse in each foot, which excluded those with significant ischemia at the start of the study. The overall mean age was 53.7 years (range 17–85), and mean duration of diabetes was 12.4 years (range 0–60); men and women were equal in number, and 58% had type II diabetes.

For the analysis of results, the patients were divided into three groups on the basis of vibration perception: group 1 had a vibration perception of <15 V in both feet; group 2 had a VPT between 16–24 V in both feet; and group 3 had a VPT >25 V in either foot (Table 1). These groups were chosen on the basis that a VPT <15 V was unlikely to be associated with significant neuropathy, a VPT of >25 V has been shown to be associated with foot ulceration in cross-sectional studies (10), and the group with VPT 16–24 V were thought to be at intermediate risk.

Statistical analysis

Results were analyzed using SAS software (SAS, Cary, NC) and Minitab software (Minitab, State College, PA). Parametric tests were used throughout. χ^2 and Fisher's exact test were used to compare the ulcer frequencies among groups. Multiple logistic regression was performed following initial data assessment using CUSUM plots (18). In addition to VPT, subject age, duration of diabetes, type of diabetes, and sex were all presented to the multiple logistic regression model. The incidence of an ulcer was taken as the incidence of first ulcer only. Recurrent ulceration was not included in the regression model.

RESULTS

VPT

The incidence of the first ulcer in a patient for each group is described in Table 2. No significant difference was observed between the 4-year cumulative ulcer incidence in the group of diabetic patients with a VPT <15 and a VPT 16–24 V (2.9 vs. 3.4%, odds ratio [OR] 1.21, 0.24–6.15, 95% confidence interval [CI], NS), but the patients in group 3, with a VPT >25 had a cumulative ulcer incidence of

Table 2—*Annual number of first ulcers in each group*

	Year 1	Year 2	Year 3	Year 4	Total ulcers	Total incidence (%)	Annual incidence/year (%)
VPT							
<15V	2	1	2	1	6	3.0	0.75
16–24V	1	1	0	0	2	3.4*	0.85
>25V	14	13	6	7	40	19.8†	4.95

*P = NS, group 2 vs. group 1. †P <0.01, group 3 vs. group 1.

Table 3—*Results of logistic regression analysis for the risk of foot ulceration*

Model	Degrees of freedom	Deviance	Change in deviance	*P* value
Intercept	1	281.447		
Diabetes duration (positive)	1	265.458	15.989	<0.01
Group (positive)	2	239.513	25.945	<0.01

19.8%, OR 7.99 (3.65–17.5), ($P < 0.01$) versus patients with VPT <15 V.

Recurrent ulceration only occurred in those patients with a VPT >25 V (group 3). In total, 70 ulcers were detected in 4 years in this group, (17.5 ulcers/year, incidence rate 8.3%/year).

Sex, age, height, type, and duration of diabetes

Overall, men had a higher incidence of foot ulceration than women did, 13.2 vs. 7.5%, $P < 0.01$. Men were over-represented in the group of patients with a VPT >25 (Table 1).

The proportion of patients who developed foot ulceration during the study period increased with age, duration of diabetes, and height. However, the increase with age and height did not reach statistical significance. A diabetes duration of 45–55 years was associated with a seven-times-higher proportion of patients with foot ulceration than that in patients with 0–10 years duration, $P < 0.01$ (Fig. 1). Overall, type I diabetic patients had a higher incidence of foot ulceration than did type II diabetic patients, 14.1 vs. 7.6%, $P < 0.01$. In the patients with a VPT >25, this was 29.9 vs. 13.6%, $P < 0.01$.

Logistic regression

Initial stepwise logistic regression was performed. After adjusting for VPT group, only diabetes duration remained as a significant single predictor of the incidence of ulceration. The model was then refitted by first fitting diabetes duration and then VPT group. After adjusting for diabetes duration as the covariate of interest, a significant VPT group effect remained (Table 3). The adjusted OR for the 4-year cumulative incidence of foot ulceration in the VPT >25 vs. VPT <15 was 6.82 (2.75–16.92), $P < 0.01$.

CONCLUSIONS — This study examined the ability of a baseline VPT measurement to predict foot ulceration over a 4-year period. A VPT of >25 V was strongly associated with the risk of foot ulceration.

The potential benefits to be gained from accurately predicting those at risk for foot ulceration are great, in both financial and social terms. Foot ulceration accounts for the largest number of bed occupancy days of all the complications in diabetic patients (2), despite the increasing trend towards out-patient treatment (7,8). The loss of mobility during healing and the potential loss of a limb have severe social consequences, in addition to the financial costs (1). Education and foot care have been shown to reduce foot ulceration and amputation rates in specialist clinics, and the accurate targeting of preventative care is likely to improve its effectiveness further (7,8).

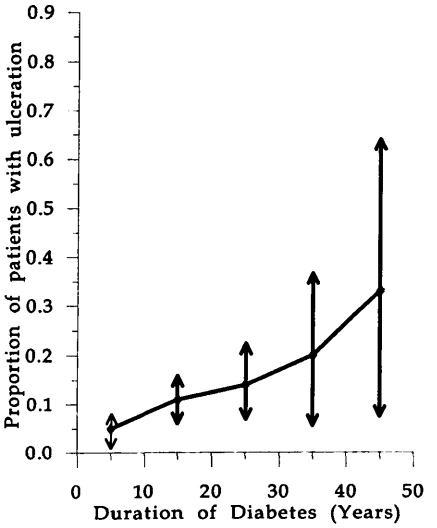

Figure 1—*Proportion of patients developing ulceration over the 4-year follow-up against duration of diabetes for each decade of increasing duration, with 95% CI. The increase in foot ulceration with increasing duration of diabetes was statistically significant ($P < 0.01$).*

Little prospective data are currently available to support the cross-sectional surveys of risk factors for diabetic neuropathic foot ulceration. Factors such as diabetic peripheral neuropathy (9), on clinical or quantitative testing, increasing age (7), limited joint mobility (12,13), diabetic nephropathy (11), and elevated dynamic plantar foot pressures (13–15) have all been identified more commonly in patients with foot ulcers than in diabetic patients without a history of foot ulceration. Of these, only elevated plantar foot pressure has previously been studied prospectively as a predictive factor for foot ulceration (15). In this study, 15 of 43 (35%) patients with high dynamic plantar pressures developed a plantar ulcer during the 30-month study period. All these patients had an abnormal VPT at the follow-up visit, when compared with age-related normal values. The measurement of plantar pressures is time consuming and the equipment too costly for routine clinical use, and thus a simpler, more widely available technique would be required for screening in most clinics.

The measurement of vibration perception using a biothesiometer is a long-established method of screening diabetic patients for neuropathy (19). A raised VPT has been found in diabetic patients with foot ulceration compared with nondiabetic and diabetic patients without foot ulcers (10). Measurements of VPTs have been shown to correlate with clinical scoring systems in a number of epidemiological surveys of neuropathy (16,17). Therefore, in routine clinical practice, es-

pecially where a biothesiometer is not available, for example, in the general practice mini-clinic, impairment of routine vibration testing using a tuning fork should also be taken to place a patient in a high-risk group.

The higher incidence of foot ulceration in men is in keeping with referral patterns to specialist diabetic foot clinics (7,8). However, the higher incidence of foot ulceration in type I diabetic patients overall, and particularly in those with a VPT >25 V, is unusual and may be partly caused by the exclusion of patients with PVD at the start of the study, because PVD is more prevalent in type II diabetic patients (20), and partly by the longer duration of diabetes in type I diabetic patients.

The greater age of the patients with a VPT of >25 V reflects the increase in vibration perception with age in the normal population (21), the increase in neuropathy with age, and duration of diabetes found in most epidemiological surveys (17). However, even after correcting for the increased duration of diabetes in the patients with a VPT >25 V, vibration perception remained a strong predictor of the risk of foot ulceration.

In conclusion, this study demonstrates prospectively that VPT is able to predict those diabetic patients at increased risk of foot ulceration and that a VPT of >25 V carries a sevenfold risk of foot ulceration compared with a VPT of <15 V. The measurement of vibration perception with a biothesiometer, or tuning fork, can therefore be used to target foot education and care to the population that is most likely to benefit. This may, in turn, help to meet the St. Vincent target of a reduction in amputations and reduce the appalling toll of limb loss in diabetes.

References

1. Connor H: The economic impact of diabetic foot disease. In *The Foot in Diabetes*. Connor H, Boulton AJM, Ward JD, Eds. Chichester, England, John Wiley and Sons, 1987, p. 145–149
2. Williams DRR: Hospital admissions of diabetic patients: information from hospital activity analysis. *Diabetic Med* 2:27–32, 1985
3. Bild DE, Selby JV, Sinnock P, Browner WS, Braveman P, Showstack JA: Lower extremity amputation in people with diabetes: epidemiology and prevention. *Diabetes Care* 12:24–31, 1989
4. World Health Organization/International Diabetes Federation: Diabetes care and research in Europe: the St. Vincent Declaration. *Diabetic Med* 7:360, 1990
5. Barth R, Campbell LV, Allen S, Jupp JJ, Chisholm DJ: Intensive education improves knowledge, compliance, and foot problems in type II diabetes. *Diabetic Med* 8:111–117, 1991
6. Day JL: Patient education: how may recurrence be prevented? In *The Foot in Diabetes*. Connor H, Boulton AJM, Eds. Chichester, England, John Wiley and Sons, 1987, p. 135–143
7. Thomson FJ, Veves A, Ashe H, Knowles EA, Gem J, Walker MG, Hirst P, Boulton AJM: A team approach to diabetic foot care: the Manchester experience. *The Foot* 2:75–82, 1991
8. Edmonds ME, Blundell MP, Morris HE, Maelor-Thomas E, Cotton LT, Watkins PJ: Improved survival of the diabetic foot: the role of the specialist foot clinic. *Q J Med* 232:763–771, 1986
9. Young MJ, Boulton AJM: Identification of the "at risk" foot in diabetes. *Pract Diabetes* 8:103–105, 1991
10. Boulton AJM, Kubrusly DB, Bowker JH, Gadia MT, Quintero L, Becker DM, Skyler JS, Sosenko JM: Impaired vibratory perception and diabetic foot ulceration. *Diabetic Med* 3:335–337, 1986
11. Fernando DJS, Hutchison A, Veves A, Gokal R, Boulton AJM: Risk factors for non-ischaemic foot ulceration in diabetic nephropathy. *Diabetic Med* 8:223–225, 1991
12. Delbridge L, Perry P, Marr S, Arnold N, Yue DK, Turtle JR, Reeve TS: Limited joint mobility in the diabetic foot: relationship to neuropathic ulceration. *Diabetic Med* 5:333–337, 1988
13. Fernando DJS, Masson EA, Veves A, Boulton AJM: Relationship of limited joint mobility to abnormal foot pressures and diabetic foot ulceration. *Diabetes Care* 14:8–11, 1991
14. Duckworth T, Boulton AJM, Betts RP, Franks CI, Ward JD: Plantar pressure measurements and the prevention of ulceration in the diabetic foot. *J Bone JT Surg* 67:79–85, 1985
15. Veves A, Murray HJ, Young MJ, Boulton AJM: The risk of foot ulceration in diabetic patients with high foot pressure: a prospective study. *Diabetologia* 35:660–663, 1992
16. Franklin GM, Kahn LB, Baxter J, Marshall JA, Hamman RF: Sensory neuropathy in non-insulin-dependent diabetes mellitus: the San Luis Valley study. *Am J Epidemiol* 131:633–643, 1990
17. Young MJ, Boulton AJM, Macleod AF, Williams DRR, Sonksen PH: A multicentre study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population. *Diabetologia* 36:150–154, 1993
18. Royston P: The use of CUSUMs and other techniques in modelling continous variables in logistic regression. *Statistics in Medicine* 11:1115–1129, 1992
19. Steiness IB: Vibratory perception in diabetics. *Acta Med Scand* 158:327–355, 1957
20. Ganda OP: Pathogenesis of accelerated atherosclerosis in diabetes. In *Management of Diabetic Foot Problems*. Kozak GP, Hoar CS, Eds. Philadelphia PA, WB Saunders, 1984, p. 17–26
21. Wiles PG, Pearce SM, Rice PJS, Mitchell JMO: Vibration perception threshold: influence of age, height, sex, and smoking, and calculation of accurate centile values. *Diabetic Med* 8:157–161, 1991