Screening diabetic patients at risk for foot ulceration. A multi-centre hospital-based study in France

D Malgrange, JL Richard, F Leymarie, on behalf of the French Working Group on the Diabetic Foot (GFPD, Groupe Français Pied Diabétique)

SUMMARY

Background: To determine the prevalence of risk factors for diabetic foot ulceration in diabetic patients free of active pedal ulceration in a hospital setting.

Methods: In sixteen French diabetology centres, a survey was conducted on a given day in all diabetic people attending the units, both as in- or out-patients.

Results: 664 patients were evaluated: 105 had an active foot ulcer and were excluded from the analysis as were four other patients due to lack of reliable data. From the 555 assessable patients, 40 (7.2%) had a history of foot ulcer or lower-limb amputation. Sensory neuropathy with loss of protective sensation, as measured by the 5.07 (10 g) Semmes-Weinstein monofilament testing, was present in 27.1% of patients, whereas 17% had a peripheral arterial disease mainly based on the clinical examination. On addition, foot deformities were found in 117 patients (21.1%). According to the classification system of the International Working Group on the Diabetic Foot, 72.8% of patients were at low-risk for pedal ulceration (grade 0) and 17.5% were in the higher-risk groups (grade 2 & 3). If patients with isolated peripheral arterial disease were considered as a separate risk group (as was those with isolated neuropathy), percentage of low-risk patients decreased to 65.6%. There was a clear trend between the increasing severity of the staging and age, duration of diabetes, prevalence of nephropathy and retinopathy.

Conclusions: Prevalence of risk factors for foot ulceration is rather high in a hospital-based diabetic population, emphasising the need for implementing screening and preventive strategies to decrease the burden of diabetic foot problems and to improve the quality of life for people with diabetes.

Key-words: Diabetic foot ulcer - Screening - Risk factors - Classification.

RéSUMÉ

Dépistage des patients diabétiques à risque de lésion du pied : résultats d’une étude multicentrique française

Objectif : Déterminer la prévalence des facteurs de risque d’ulcération du pied chez les diabétiques sans lésion ouverte du pied, vus dans un contexte hospitalier.

Méthode : Une enquête a été réalisée un jour donné auprès de tous les diabétiques vus en hospitalisation ou en consultation dans seize centres de diabétopathologie français.

Résultats : Sur 664 patients examinés, 105 (15,8 %) présentaient une ulcération et ont été exclus de l’analyse ainsi que 4 autres en raison de données ininterprétables. Quarante des 555 patients évaluables (7,2 %) avaient un antécédent d’ulcère ou d’amputation. Une neuropathie sensitive avec perte de la sensation de protection jugée par le test au monofilament de 10 g, était notée chez 27,1 % des patients ; une artériopathie des membres inférieurs, jugée essentiellement sur des critères cliniques, était présente chez 17 % et des déformations du pied chez 21,1 %. D’après la classification du Groupe d’Étude International sur le Pied Diabétique, 72,8 % de la population étudiée était considéré comme à faible risque d’ulcération (classe 0), alors que 17,5 % étaient à haut risque (classes 2 et 3). En faisant de l’artériopathie isolée une classe de risque séparée, le pourcentage des patients à risque faible diminuait à 65,4 %. Il existait une association nette entre l’âge et la durée du diabète, la prévalence de la néphropathie et de la rétinopathie, d’autre part.

Conclusion : La prévalence des facteurs de risque podologique apparaît élevée dans une population diabétique hospitalière, justifiant la nécessité de la mise en pratique d’une politique réelle de dépistage et de prévention.

Mots-clés : Pied diabétique - Dépistage - Facteurs de risque - Classification.

1 Clinique Médicale B, Hôpital Robert Debré, CHU, Reims, France
2 Service des Maladies de la Nutrition et Diabétologie, Centre Médical, Le Grau du Roi, France
3 Département de l’Information Médicale, CHU, Reims, France
4 See list of participating centres on the last page.

Address correspondence and reprint requests to: JL Richard, Service des Maladies de la Nutrition et Diabétologie, Centre Médical, 30240 Le Grau du Roi, France.
jean.louis.richard@chu-nimes.fr

Received: October 21, 2002; revised: February 4, 2003
Foot problems are common in diabetic patients, often requiring prolonged and costly hospital stays and eventually leading to lower extremity amputation [1-3]. So, identification of patients at risk of foot ulceration is of paramount importance. Numerous risk factors have been implicated in the development of ulceration [2, 4, 5]: a history of ulceration or amputation is the factor most closely associated with the occurrence of a (new) ulceration [6-9]; so, according to Apelqvist et al. [10], 70% of foot ulcerations in diabetic patients might recur in the five-year period following initial healing. Peripheral neuropathy plays a major role in the pathogenesis of ulceration [5, 8, 9, 11-14] and is associated with an 8- to 18-fold higher risk of pedal ulcer [2]. High plantar foot pressure and foot deformity, often related to the peripheral neuropathy [2, 5, 15], are also strongly predictive of plantar ulceration [13, 15]. Finally, peripheral arterial disease (PAD) and group 3 (highest-risk group) those with a history of foot ulceration or a lower-limb amputation [1-3]. So, identification of patients at risk of foot ulceration is of paramount importance. Numerous risk factors have been implicated in the development of ulceration [2, 4, 5]: a history of ulceration or amputation is the factor most closely associated with the occurrence of a (new) ulceration [6-9]; so, according to Apelqvist et al. [10], 70% of foot ulcerations in diabetic patients might recur in the five-year period following initial healing. Peripheral neuropathy plays a major role in the pathogenesis of ulceration [5, 8, 9, 11-14] and is associated with an 8- to 18-fold higher risk of pedal ulcer [2]. High plantar foot pressure and foot deformity, often related to the peripheral neuropathy [2, 5, 15], are also strongly predictive of plantar ulceration [13, 15]. Finally, peripheral arterial disease (PAD) is recognised as a significant risk factor [11] but this remains challenged [6, 8, 11, 13, 16]. Additional general factors have been also described, like ageing, visual impairment, nephropathy or poor socioeconomic status [2, 6, 17, 18]. Recognition of such factors enables to classify patients according to systems of increasing risk categories [6, 8].

In 1999, the International Working Group on the Diabetic Foot (IWGDF) developed a new classification system [19] where four grades of increasing severity are identified: group 0 consisted of subjects without significant peripheral neuropathy as affirmed by their ability to feel the 5.07 Semmes-Weinstein monofilament (low-risk patients), group 1 included patients with isolated neuropathy, group 2 neuropathic patients with foot deformity or peripheral arterial disease (PAD) and group 3 (highest-risk group) those with a history of foot ulceration or a lower-limb amputation. Effectiveness of this system to predict foot complications was recently demonstrated in a prospective study [7], as three-year ulceration rate increased from 5.1% in grade 0 to 14.3, 18.8 and 55.8% in grade 1, 2 and 3, respectively. Moreover, the IWGDF system has the advantage of being based on practical and simple clinical data. On the other hand, patients suffering from an isolated PAD are not considered as a separated risk group although there actually are purely ischaemic diabetic foot ulcers [19].

In France, data on prevalence about diabetic people at risk for foot ulceration are scarce. Thus, the French Working Group on the Diabetic Foot (GFPD, Groupe Français Pied Diabétique) initiated a hospital-based survey 1) to determine the prevalence rate of such factors, 2) to precise the distribution of the patients in the various risk categories as described by the IWGDF, and 3) to evaluate the effect of taking into account an isolated PAD as an independent risk category.

**Patients and methods**

**Patients**

Sixteen French hospital departments specially involved in the diabetic foot management took part in the study. On a given day, in May 2001, all diabetic subjects attending the participating centres, both as in- and out-patients, were included. To record relevant data, a standardised form was worked out during preliminary discussions where at least one representative of each participating centre was present. The testing modalities were shown to all investigators before the start of the study.

**Diagnostic criteria**

They are detailed in Table 1. Presence of peripheral sensory neuropathy (PSN) was assessed using the 5.07 (10-g) Semmes-Weinstein monofilament, according to the technique suggested by the IWGDF [19, 20]. As shown in figure 1, three plantar sites were tested on both feet: at the apex of the hallux and under the 1st and 5th metatarsal head; at each site, test was repeated three times. PSN was deemed to be present if at any site, at least two out of three responses were wrong. A new identical filament was provided to every investigator to ensure uniformity and inter-rater reproducibility.

PVD was diagnosed according to the ANAES recommendations [21], mainly based on the medical history and clinical examination.

Due to difficulty to obtain precise information on the ophthalmologic status of every patient, retinopathy was defined as diabetic retinal lesions having required laser photocoagulation treatment.

Renal function was assessed by calculating creatinine clearance using Cockcroft’s formula [21] from the most recent (less than one year) serum creatinine level. Chronic renal failure was affirmed if creatinine clearance was less than 40 ml.min⁻¹ according to Fernando et al. [17] or in case of current dialysis or a history of renal transplantation.

**Statistical analysis**

All data were captured and analysed using the epidemiological software Epi-Info (version 6.04c). Lacking or questionable data were labelled as inadequate and not taken into account for calculating percentage. A preliminary univariate descriptive analysis was carried out. Thereafter patients were categorised according to the IWGDF and a modified
system. In the latter, group 1 was divided in two subgroups: 1A or 1N if PVD or PSN was isolated, respectively; criteria for grades 2 and 3 were identical for both classification systems. Comparison between risk groups was done using Pearson’s Chi² test for qualitative data and Student’s t test for quantitative variables. \( p \leq 0.05 \) was considered statistically significant.

Table I
Definition of the recorded data.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Type 1: Onset under the age of 30 years or insulin treatment initiated in the 2 year-period following diagnosis. Type 2: Onset over the age of 30 years and no insulin treatment or insulin treatment initiated later than 2 years after diagnosis. Other: Secondary, MODY or drug-induced.</td>
</tr>
<tr>
<td>History of foot ulceration</td>
<td>Healed foot ulceration of longer than 3 months of duration.</td>
</tr>
<tr>
<td>History of lower extremity</td>
<td>Non traumatic amputation, at any level of the lower limb.</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>Present: Intermittent claudication or a history of vascular reconstruction or of ischaemic foot lesion (necrosis, gangrene) or documented PAD (Doppler waveform evaluation and/or ankle-brachial index &lt; 0.90 and/or ToPO₂ on the dorsum of the foot &lt; 30 mm Hg). Absent: Absence of the above criteria and presence at least of 2 pedal pulses (on the same foot) and no arterial femoral or popliteal murmur.</td>
</tr>
<tr>
<td>Sensory neuropathy</td>
<td>Present: At least two out of three incorrect answers to 10-g monofilament application at one of the six tested sites (3 at each foot). Absent: At least two out of three correct answers at each of the six tested sites.</td>
</tr>
<tr>
<td>Hyperkeratosis</td>
<td>Presence of callus on the dorsal aspect of the toes and/or on the plantar aspect of the forefoot and/or on its edge (facing the 1st or 5th metatarsal head) and/or on the heel.</td>
</tr>
<tr>
<td>Foot deformity</td>
<td>Hallux valgus or hallux quintus and/or overlapping toes or fixed clawed toes and/or pes cavus or planus and/or neuroarthropathic changes (Charcot foot).</td>
</tr>
<tr>
<td>Intertrigo</td>
<td>Clinically evident lesions of the interdigital space due to yeasts.</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>A history of diabetic retinal lesion treated by laser photocoagulation.</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>Creatinine clearance( \leq 40 \text{ mL.min}^{-1} \text{ } \text{ or current dialysis or a history of renal transplantation.}</td>
</tr>
<tr>
<td>Poor psychosocial status</td>
<td>Patient living alone and/or alcohol excess and/or serious psychiatric illness and/or poor body hygiene.</td>
</tr>
</tbody>
</table>

\( \text{§ According to Cockroft's formula.} \)

Results

664 diabetic patients were initially examined by 58 diabetest specialists. An active ulcer was present in 105 patients (15.8%) who were therefore excluded for the subsequent analysis. Four other patients were excluded too, due to im-
the possibility to obtain reliable information. So, 555 diabetic were finally included whose clinical data are shown on Table II.

40 patients (7.2%) had a history of ulceration (n = 35) and/or amputation (n = 18, toe amputation in thirteen, below the knee in three and above the knee in two). As shown on figure 2, hyperkeratotic change was the most prevalent abnormality, found in 45% of patients. Prevalence rate of PSN was 27.1%, higher than that of PAD (17.0%), whereas foot deformity was seen in 21.1%.

21 patients were receiving dialysis or have a history of renal transplantation whereas 6.7% had a clearance < 40 mL.min⁻¹. 110 patients had a laser-treated retinopathy. Lastly, a poor psychosocial status was frequently noted (12.6%).

Figure 3 displays the repartition of patients according to the IWGDF and the modified classification system. 72.8% of patients were considered as having low-risk by the IWGDF classification, compared with 65.6% in the modified system. By both systems, 17.5% of the study population were at high-risk for pedal ulceration (grades 2 and 3). Comparison between the two grading systems revealed that making isolated PAD as a special risk category increased the number of patients in grade 1 to the detriment of grade 0: thus, 16.9% of diabetic subject were classified as grade 1 (1A + 1N) using the modified system compared with 9.7% by the IWGDF.

The increase in the risk severity was significantly associated with increase in age and diabetes duration, presence of hyperkeratosis, decrease in creatinine clearance and presence of retinopathy. Thus, compared to grade 0, patients in group 2 and 3 were significantly older, had diabetes of longer duration and more often of type 2; retinopathy and chronic renal failure was significantly more frequent as was poor psychosocial status (Tab III). On the contrary, sex ratio and BMI were not significantly different. Finally, distribution of patients into the various risk categories was not different between centres.

Discussion

To our knowledge, the present survey is the first done in France on a national scale aiming to precise the prevalence of risk factors for foot ulceration in a hospital-based diabetic population.

We are aware of limitations of the study, specially with regard to the patients’ selection and the screening methods we used. Patients were recruited from diabetes centres in several French hospitals; moreover, these departments are highly specialised in managing diabetic foot problems. This might explain the overrepresentation of type 1 and insulin-treated type 2 patients in the sample and the high prevalence of active ulceration. In addition, the participating centres are not representative of the French diabetes centres as a whole, considering first the strong involvement of the former in managing diabetic foot and second their geographical distribution, as some area were underrepresented or not represented at all. So, the results of our study can not be extrapolated to the general diabetic population in France. Regarding the diagnostic criteria we used, they had obvious weakness: some diabetic complications were very likely un-

Table II
Characteristics of the study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>Gender (M/F)</th>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
<th>Diabetes</th>
<th>Diabetes duration (years)</th>
<th>Creatinine clearance§</th>
<th>Chronic renal failure</th>
<th>Retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>555</td>
<td>286/269</td>
<td>56 ± 15 [14-89]</td>
<td>28.2 ± 6.5</td>
<td>138</td>
<td>13.0 ± 10.4 [&lt; 1-57]</td>
<td>88.7 ± 36.7</td>
<td>55¶</td>
<td>110</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Type 1</td>
<td>Type 2</td>
<td>Other type</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>138</td>
<td>377</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Type 2</td>
<td>Insulin-treated (%)</td>
<td>Non insulin-treated (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>53.6</td>
<td>46.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Insulin-treated (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>53.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Non insulin-treated (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>46.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Data are n or mean ± SD with range into square brackets. * n = 546, § n = 506, ¶ 21 patients are receiving dialysis or had a history of renal transplantation.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1
Testing with 5.07 (10 g) Semmes-Weinstein monofilament. On each foot, each of the three sites (hatched bars) was tested thrice, according to the IWGDF recommendations [19].

Figure 2

deresized, as was retinopathy only recognised when treated by laser photocoagulation. Diagnostic criteria for PAD are also open to criticism, but there are no consensus to define it probably explaining why PAD is not always recognised as a significant risk factor for foot ulceration in diabetic patients [6, 8, 11, 16, 22]. So, whereas absence of peripheral pulses had a good predictive value for ulceration and amputation [14, 18, 23], a normal clinical examination does not completely rule out a PAD and conversely absence of a foot pulse may be of congenital origin [2, 24]. Finally, reproducibility of pulse palpation is rather poor. Non-invasive vascular tests have limitations as well [2] and the predictive value of a diminished ankle-brachial index for foot ulceration remains debated [6, 14, 16]. Whereas a TcPO2 value less than 30 mmHg was the most important risk factor for ulceration in the study by McNeely et al. [16], measuring TcPO2 is time-consuming and expensive and so can not constitute a screening tool. All these arguments explain why our screening criteria for PAD were mainly clinical, according to the ANAES recommendations.

The most important point of the study was the high prevalence of risk factors for foot ulceration. 7.2% of our patients had a history of ulceration and/or amputation and were therefore at very high-risk of (re)ulceration. This high prevalence might be explained by the hospital recruitment bias, as above emphasised. Nevertheless, this figure compares well with data published in Scandinavia or in the UK, where prevalence is estimated between 5 to 10% [25]. Moreover our population was mainly type 2 aged diabetic patients where amputation and ulceration rate are notably elevated [19].

Inability to feel the 5.07 nylon monofilament was noted in 27.1% of the patients and is in our opinion the most important clue to identify at risk patients, indicating that PSN is severe enough to favour foot ulceration. Advantages of testing light touch by the 10-g Semmes-Weinstein monofilament include simplicity, rapidity, low cost and reasonable reproducibility [4, 26], making it a specially accurate tool for routine screening [6, 13]. Due to differences in the performance according to the length and repetitive use of filaments [27, 28], every investigator was provided with a new and identical filament. Predictive value of insensitivity to the 10-g monofilament for foot ulceration has been demonstrated by prospective studies [8, 12-14] but methodology

Figure 2
Prevalence of risk factors (white bars) and aggravating factors (black bars) for foot ulceration in the study population.
varied between studies according to the location and number of sites to be tested, the way to ask patients and the definition of abnormality [4]. The technique suggested by the IWGDF [19, 20] takes the advantage of being easy and rapid; moreover, this methodology was used in the prospective study of Litzelman et al., in which insensitivity to the monofilament appeared as the only clinical criterion predictive of foot ulceration [14].

High plantar foot pressures have been implicated in the pathogenesis of diabetic foot ulceration [2, 5] and are a good predictor of plantar ulceration [13, 15], but pressures measurement is difficult, time-consuming and requires sophisticated and costly devices. As increased plantar pressure is often associated with foot deformity and callus [29], clinical inspection of the foot is of the utmost importance for assessing the risk of a subsequent ulceration. Indeed presence of callus is highly predictive of a future ulceration [30]. Only few data had been published about prevalence of such risk factors in diabetic patients. Prevalence rate for hammer toe deformity was 32%, according to Holewski et al. in non selected diabetic outpatients [31] and about 50% for Borsén in a population-based epidemiological study [32] and for Ahroni et al. in a cohort of diabetic veterans free of active ulcer [29]. In our study, the prevalence rate of foot deformity was less important (21.1%), probably due to differences in patient’s age and diabetes duration but also to imprecise clinical definition and subjective aspect of diagnosis. On the opposite, prevalence rate of hyperkeratosis in the present study (45%) is close to this reported by the former authors. So, hyperkeratosis and in a lesser extent, foot deformity are frequent in diabetic people and must be systematically detected through clinical examination.

The high prevalence of PSN and foot deformity in our population explains that 27% of the patients were at risk and 7.7% were classified in the highest-risk category, according to the IWGDF system. Other classification systems have been proposed: one of the most frequently used was published by Rith-Najarian ten years ago [8]. This system, based on perception of the 10-g monofilament, presence of foot deformity and a history of foot complications, was validated by a prospective study showing over a 32-month follow-up, a progressive increase in incidence of plantar ulceration by category, from 6 per 1000 diabetic person-year in the low-risk group up to 330 in the highest-risk group. In a case-control study using a similar system, Lavery et al. [6] showed that diabetic patients with an isolated PSN had a risk for ulceration 1.7-fold higher than patients without PSN; this risk was 12.1-fold higher if the PSN was associated with foot deformity and 36.4-fold higher if PSN and foot deformity were combined with a history of ulceration or amputation. The merit of the IWGDF system is to be simple and to have been recently validated [7]. Moreover, this system incorporates the possible presence of PAD to define the risk grade but does not accept isolated PAD to identify a special risk
group. In our study, 17% of patients suffered from PAD which was isolated (i.e. without neuropathy) in a high percentage (7.2% of the whole population). In our opinion, these latter patients are not free of risk for (ischaemic) foot ulceration and must benefit from preventive measures. A prospective study is therefore needed to confirm that diabetic patients with PAD but without neuropathy are prone to ulceration and to estimate the extent of the risk.

Finally, there was a clear trend between increasing severity category and age, diabetes duration, presence of severe retinopathy and nephropathy, confirming results of previous studies [6, 7, 16, 33]. Moreover, a poor psychosocial status was noted more frequently in high-risk patients emphasising the important role of patients’ environment [18] for occurrence of foot ulceration.

From a practical point of view, typical high-risk patients are frequently old type 2 diabetic patients with a disease of long duration often complicated by renal and retinal manifestations. As neuropathy is frequently asymptomatic, screening regularly this population is of utmost importance. As shown in this study, screening and classifying patients in a risk category is simple, rapid and inexpensive. So, it is urgent to implement screening strategy, specially in the primary care setting and to develop specialised multidisciplinary foot centres for an effective management of the diabetic foot before occurrence of ulceration and amputation.

List of participating centres — Service de Diabétologie et Nutrition, CHU de Grenoble (Dr Sylvie Pradines) — Fédération des Affections Métaboliques & Endocrinienes, CHU de Nîmes (Dr Jean-Louis Richard, Le Grau du Roi ; Dr. Nathalie Jourdan, Nîmes) — Service de Diabétologie, CHU de Lille (Dr Marc Lepeut, CH de Roubaix ; Dr Dominique Tsirtsikolou, CH de Boulogne ; Dr Catherine Fermon, CH de Lille ; Dr Armelle Fayard, CH d’Arras ; Dr Marie Velliet, CH de Tourcoing ; Dr Fabrice Devévy, CH de Lens ; Dr Christophe Schoonberg, CH de Béthune) — Service de Médecine Interne, CHU Lyon Sud (Dr Paul Michon) — Service d’Endocrinologie, CHU de Lyon (Dr Marie-Pierre Larmandaud) — Service de Diabétologie, CHU de Nancy (Dr Isabelle Got) — Service de Diabétologie, CHU Pitétière, Paris (Dr. Georges Ha Van) — Service d’Endocrinologie, Maladies Métaboliques & Médecine Interne, CHU de Reims (Dr Dominique Malgrange) — Service d’Endocrinologie et Diabétologie, CHU de Strasbourg (Dr Laurence Kessler) — Service de Diabétologie, CHU de Toulouse (Dr Jacques Martini).

Acknowledgements — The authors wish to thank Aventis Pharmaceuticals for providing the monofilaments and Mrs C. Thébaut for her logistical help.

References