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M. H. Nabuurs-Franssen · M. S. P. Huijberts · A. C. Nieuwenhuijzen Kruseman · J. Willems · N. C. Schaper

Health-related quality of life of diabetic foot ulcer patients and their caregivers

Abstract *Aims/hypothesis:* The effect of a foot ulcer on health-related quality of life (HRQoL) of patients with diabetes mellitus and their caregivers is unclear, and was therefore evaluated prospectively in this multicentre study. *Methods:* HRQoL according to the 36-item health-related quality of life questionnaire (SF-36) of 294 patients (ulcer duration ≥4 weeks) and 153 caregivers was analysed at baseline (time-point zero [T0]), once the ulcer was healed or after 20 weeks (time-point 1 [T1]), and 3 months later (time-point 2 [T2]). Patients with severe ischaemia were excluded. *Results:* The mean age of the patients was 60 years, 72% were male, and time since diagnosis of diabetes was 17 years. Patients reported a low HRQoL on all SF-36 subscales. At T1, HRQoL scores in physical and social functioning were higher in patients with a healed vs a non-healed ulcer ($p<0.05$). At T2, these differences were larger, with higher scores for physical and social functioning, role physical and the physical summary score (all $p<0.05$). Within-group analysis revealed that HRQoL improved in different subscales in patients with a healed ulcer and worsened in patients with a persistent ulcer from T0 to T2 (all $p<0.05$). The caregivers of patients with a persisting ulcer had more emotional difficulties at T2. *Conclusions/interpretation:* Diabetic patients with a healed foot ulcer had a higher HRQoL than patients with a persisting ulcer. Healing of a foot ulcer resulted in a marked improvement of several SF-36 subscales 3 months after healing (from T0 to T2). HRQoL declined progressively when the ulcer did not heal. A diabetic foot ulcer appeared to be a large emotional burden on the patients' caregivers, as well.

Keywords Diabetes mellitus · Foot · Ulcer · Quality of life · Health-related quality of life · Caregiver · Healing · Prospective

Abbreviations HRQoL: health-related quality of life · HU: healed ulcer · PU: persisting ulcer · SF-36: short form 36-item health-related quality of life questionnaire · T0: time-point zero · T1: time-point 1 · T2: time-point 2 · tcpO$_2$: transcutaneous oxygen pressure

Introduction

Diabetic foot ulcers are one of the major complications of diabetes mellitus and have a large impact on the health status of the affected patients [1]. These ulcers heal slowly, usually within 2 to 5 months, require intensive treatment [2] and are associated with major health-care consumption and high costs [3]. In recent decades, understanding of the pathogenesis, treatment and prevention has improved [4]. In contrast, our knowledge of the impact of a foot ulcer on the quality of life of a diabetic patient and his or her immediate caregivers is limited. A few cross-sectional studies, with a small sample size [5–7] or a selected group [8] of patients reported a lower quality of life [5–9]. However, as these patients usually have other diabetic complications influencing health-related quality of life (HRQoL) [1, 10, 11], the effect of an ulcer itself on HRQoL is still unclear. In addition, a diabetic foot ulcer is probably a major burden for the (non-paid) individuals from the patient's family and friends, as these caregivers frequently assist in wound care and support the patient in coping with the physical disabilities and emotional distress [6]. Therefore, the aim of the present study was to determine

M. H. Nabuurs-Franssen (✉) · M. S. P. Huijberts ·
A. C. Nieuwenhuijzen Kruseman · J. Willems · N. C. Schaper
Division of Endocrinology,
Department of Internal Medicine,
University Hospital Maastricht,
PO Box 5800, 6202 AZ Maastricht, The Netherlands
e-mail: marrigje.nabuurs@gmail.com
Tel.: +31-43-3877019
Fax: +31-43-3875006

the impact of healing of a foot ulcer on the HRQoL of diabetic patients and their caregivers.

Subjects, materials and methods

Methods

This study was part of a prospective, randomised, double-blind, placebo-controlled trial testing the efficacy and safety of recombinant human platelet-derived growth factor BB (becaplermin). Eighty-one centres in the USA, the UK and Europe participated. Both patients and caregivers were asked to fill in the short form 36-item health-related quality of life questionnaire (SF-36) at three time-points: study entry (time-point zero [T0]), once the ulcer was healed or after 20 weeks (whichever occurred first) (time-point 1 [T1]), and 12 weeks after T1 (time-point 2 [T2]). The difference in HRQoL at T2 between the subjects with a healed ulcer and the subjects with a persisting ulcer was defined as the primary endpoint.

The SF-36 [12, 13] is a short, 36-item questionnaire which measures eight multi-item general health scales, ranging from 0 (worst possible health status) to 100 (best possible health status). The scores on the eight subscales can be aggregated in two distinct summary scores: physical component summary (physical functioning, role physical, bodily pain, general health) and mental component summary (vitality, social functioning, role emotional, mental health). In the physical functioning scale, physical impairments are assessed; in the role physical scale the burden of these impairments in daily life is addressed. In the role emotional scale, the subject is questioned about impairments in daily life due to emotional problems. The investigators were instructed not to help the patients in interpreting or answering any question. Data were also obtained on patient demographics, relevant medical details and foot ulcer severity according to clinical criteria. All participants gave written informed consent and the hospital's medical ethics committee approved the study, which was carried out in accordance with the Declaration of Helsinki as revised in 2000.

Patients and caregivers

Diabetic patients with a chronic (ulcer duration at least 4 weeks), full-thickness lower extremity ulcer, ranging from 0.5 to 30 cm^2 after debridement, were included. Patients were ≥18 years of age and had type 1 or type 2 diabetes. Patients with more than three foot ulcers, with ulcers not related to diabetes or with poor metabolic control (HbA_1c >11.0%) were excluded. In addition, patients with severe peripheral ischaemia (transcutaneous oxygen pressure [$tcpO_2$] of the dorsum of the foot <30 mmHg), any malignancy, connective tissue diseases, chronic alcohol or drug abuse, or signs of infection and/or osteomyelitis at study entry were excluded. The caregiver was defined as a significant, non-paid person who had regular contact with the subject and was responsible for and/or engaged in caregiving activities with the subject (e.g. health-care, housekeeping, shopping, transport). No information about clinical characteristics of the caregiver was obtained.

The study population is shown in the flow chart (Fig. 1). HRQoL data were obtained in 486 patients at baseline; 32 were excluded from the analyses because they developed a major disease during the study or were hospitalised during completion of the SF-36 questionnaire. At T1 the ulcer was still present in 230 patients and was healed in 224 patients. Between T1 and T2 the ulcer healed or recurred in 81 patients, and 79 patients were lost to follow-up. For all analyses, we used the HRQoL data of the 132 patients with a per-

Fig. 1 Flow chart of the study population. *T0*=study entry; *T1*=time-point at which ulcer was healed or still persisted at 20 weeks; *T2*=12 weeks after *T1*; *48 patients lost to follow-up; #31 patients lost to follow-up

Flow chart study population
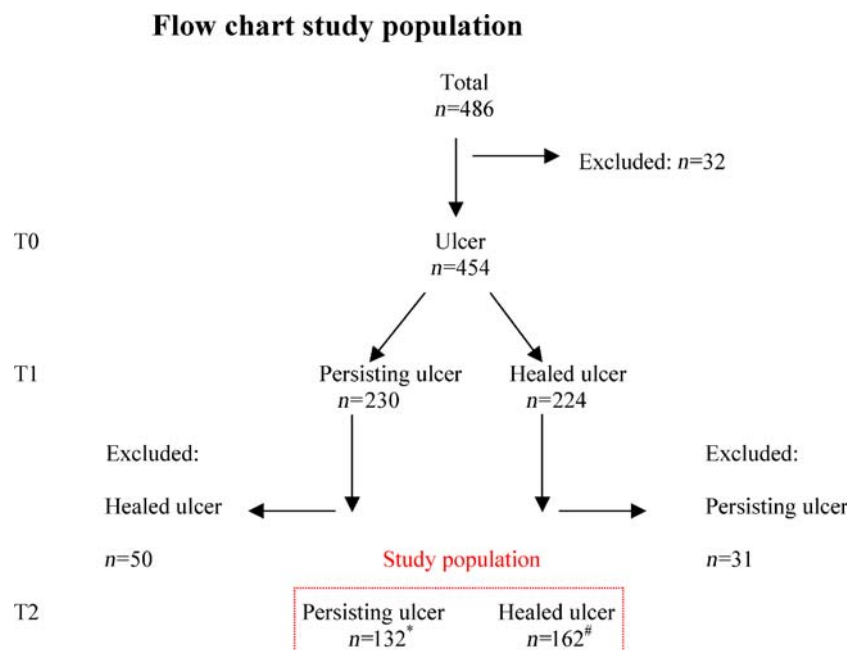
sisting ulcer (PU) during the course of the study (from T0 to T2) and of the 162 patients with a healed ulcer (HU) at both T1 and T2 (in total 294 subjects). Since numbers were too small, we excluded from the analyses patients in whom the ulcer healed or recurred between T1 and T2. No differences in clinical characteristics were observed between the included and excluded patients. HRQoL data of 153 caregivers was obtained. This number was smaller than the number of patients (n=294), as many did not have a caregiver or the caregiver did not want to participate.

Statistics

The data were entered using a double-entry validation technique and are presented as means (95% confidence interval). As some of the data were not normally distributed, non-parametric tests were used. In the primary analyses we compared the HRQoL at each time point between the two groups (PU vs HU: Kruskal–Wallis test and the Mann–Whitney U-test). Changes over time within each group were analysed using the Wilcoxon rank sum test; correlations were calculated using the Spearman test. Statistical analyses were performed with the SPSS statistical package (SPSS, Chicago, IL, USA). A p-value of ≤0.05 was considered to indicate statistical significance.

Results

Patients

Seventy-one percent of the subjects with an HU and 76% of the subjects with a PU were men (NS). No differences were observed between patients with an HU and patients with a PU with respect to age (61 [95% CI 59–62] vs 60 [59–62] years), duration of diabetes (16 [15–18] vs 17 [15–19] years) and HbA$_1$c (mean of T0 and T1: 8.7 [8.5–9.0] vs 8.8 [8.6–9.1]%). The mean tcpO$_2$ was 54 mmHg in both groups. HU patients had a lower BMI than PU patients (28.2 [27.5–28.9] vs 29.6 [28.8–30.3] kg/m^2) and at baseline had smaller ulcers (3.7 vs 5.8 cm^2) with a shorter duration (32 vs 73 weeks) (all p<0.01).

At baseline (T0), no differences were observed in the HRQoL data between the HU and PU patients (see between-group analyses, Table 1). Compared with PU patients, HU patients had higher HRQoL scores at T1 for both physical and social functioning (p<0.05). At T2 these differences were more prominent, with higher scores for physical and social functioning, role physical and the physical summary score (all p<0.05). The changes over time within each group are also depicted in Table 1 and Fig. 2 (within-group analyses). In general, HRQoL improved in the different subscales in the patients with an HU and worsened in those with a PU patients. In the patients with an HU only, social functioning was improved at T1 (T1 vs T0, p<0.05). At T2, in these HU patients, social and physical functioning, role physical and the physical summary score were improved (T2 vs T1 and T0, both p≤0.05). In addition,

Table 1 SF-36 Score at three measurement time-points

SF-36 category	T0		T1		T2	
Patients	PU	HU	PU	HU	PU	HU
Physical functioning	39.2	44.7	38.3	47.5[a]	35.0[b]	51.1[a,c]
Social functioning	63.8	60.5	63.5	65.5[a,d]	58.0[c]	71.0[a,c]
Role physical	38.0	26.7	35.7	32.3	29.6[e]	43.4[a,c]
Role emotional	59.2	47.9	55.6	48.1	50.0[e]	55.5[e]
Mental health	70.1	65.9	67.9	66.4	67.9	68.7
Vitality	53.1	51.8	51.1	52.1	49.5[e]	53.3
Bodily pain	60.9	58.4	61.0	63.3	58.9	64.4[e]
General health	52.0	53.1	51.1	53.1	48.8	52.8
Physical component score	34.6	35.0	34.7	38.8	33.3[b]	38.3[a,c]
Mental component score	49.5	46.5	48.7	48.8	47.9	48.5
Caregivers	CPU	CHU	CPU	CHU	CPU	CHU
Physical functioning	77.0	65.1	76.4	60.0	67.0	65.9
Social functioning	78.7	74.1	74.7	70.7	73.0	73.5
Role physical	68.6	57.9	62.1	56.9	56.2	64.8
Role emotional	72.4	63.6	70.5	64.9	54.3[c]	77.0[a,c]
Mental health	70.7	67.4	71.2	69.2	70.6	70.9
Vitality	62.4	54.6	62.7	57.0	58.9	57.8
Bodily pain	77.4	65.2	74.3	65.0	69.0	65.1
General health	66.8	64.7	63.2	61.4	61.7	62.6
Physical component score	48.5	44.6	46.2	42.8	44.2	44.0
Mental component score	48.8	47.8	49.0	48.2	46.6	50.9[e]

SF-36, short form 36-item health-related quality of life questionnaire; T0, study entry; T1, time point at which ulcer was healed or still persisted at 20 weeks; T2, 12 weeks after T1
PU persisting ulcer patients; *HU* healed ulcer patients; *CPU* caregiver of persisting ulcer patients; *CHU* caregiver of healed ulcer patients
Data are shown as means
[a]p≤0.05, HU vs PU; [b]p≤0.05, T2 vs T1; [c]p≤0.05, T2 vs T1 and T0; [d]p≤0.05, T1 vs T0; [e]p≤0.05, T2 vs T0

the role emotional improved and these patients with an HU experienced fewer problems with bodily pain relative to baseline (T2 vs T0, p<0.05). In the patients with a PU, no differences were observed at T1 compared with baseline, but at T2 social functioning (T2 vs T1 and T0, both p≤0.05), role physical and role emotional (T2 vs T0, p≤0.05) had worsened. The patients with a PU reported more problems with vitality at T2 compared with baseline (p<0.05). Analysing the 36 questions separately, the most marked difference between the two groups was observed in questions related to mobility: patients with an HU experienced fewer problems with walking and with performing moderate or vigorous activities compared to patients with a PU.

Caregivers

Between the caregivers of the patients with an HU and those with a PU, no differences were observed in the reported quality of life at study entry. At T2, the subscale role emotional was markedly higher in the HU caregivers
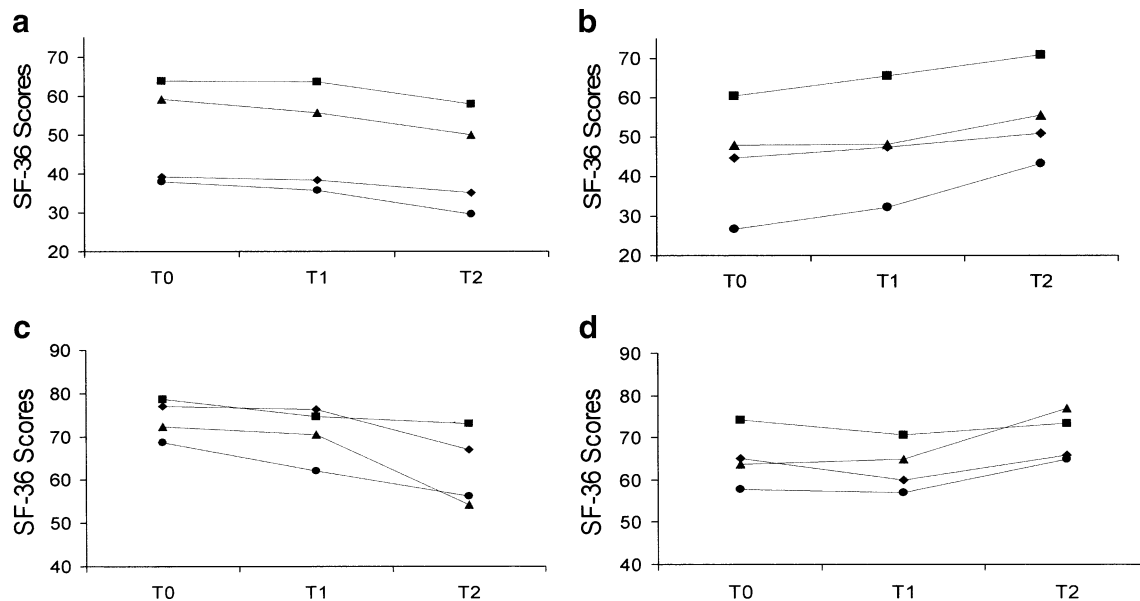
Fig. 2 Changes in SF-36 Scores for patients with persistent (**a**) and healed (**b**) ulcers and for caregivers of the former (**c**) and the latter (**d**) between baseline (*T0*) and final visit (*T2*). SF-36, short form 36- item health-related quality of life questionnaire. *Diamonds*, physical functioning; *squares*, social functioning; *circles*, role physical; *triangles*, role emotional

compared with the PU caregivers ($p \leq 0.05$). Analysing the changes over time (within-group analyses), the subscale role emotional improved in the HU caregivers and worsened in the PU caregivers (T2 vs T0 and T1 $p \leq 0.05$). In addition, the mental summary score was improved in the caregivers of patients with an HU at T2 compared with baseline ($p \leq 0.05$).

Correlations

The following correlations (Spearman correlation coefficient) were found between the reported HRQoL of the patients and the caregivers for the following scales and summary scores: physical functioning, 0.21; social functioning, 0.46; role physical, 0.35; role emotional, 0.46; and mental summary score, 0.55 (all $p < 0.03$).

Discussion

Neuropathic foot ulcers are characterised by loss of sensation and usually patients have very few specific complaints [2]. However, we demonstrated in this study that the HRQoL of patients with chronic neuropathic and neuroischaemic foot ulcers, without critical limb ischaemia, is poor and comparable with, for instance, the HRQoL of patients with recurrent (breast) cancer [14]. At T2, patients with an HU had a higher HRQoL than patients with a PU. Analyses over time revealed that this poor HRQoL improved after healing of the ulcer but deteriorated amongst the patients with a non-healing ulcer as well as their caregivers. We used the SF-36, which is a generic, not disease-specific, instrument, to measure quality of life [15]. Ideally, both a generic and a foot ulcer-specific instrument

should be used, but a foot ulcer-specific instrument, such as the NeuroQol, was not available at the time of the study [16]. Despite these limitations, the SF-36 has several advantages. It can be used in caregivers as well, and changes in HRQoL can be interpreted clinically [17]. The smallest relevant change in the physical component summary and mental component summary is approximately 2–2.5 points [18]. In our study, healing was associated with an improvement of 4.6 points in the physical summary score and of 11–25 points in the various subscales, underlining the large impact of a diabetic foot ulcer on different dimensions of HRQoL.

A foot ulcer is frequently a sign of a poor health status and cross-sectional studies suggest that at least part of the loss of HRQoL in these patients is related to diabetic complications such as neuropathy [19–21]. This study indicates that the presence of an ulcer has an independent and relatively large effect on HRQoL of both patients and caregivers. The largest loss of HRQoL was observed in the scores and specific items related to mobility. For example, the low scores on the physical functioning scale indicate impairments in walking or climbing stairs. In addition, there was deterioration in the role physical scale in patients with persisting ulcers (between T0 and T2). This part of the SF-36 questionnaire reports how patients experience physical impairments, suggesting that the longer an ulcer is present, the greater the burden to the patient. In parallel, our patients seemed to become more socially isolated, given the loss in the social functioning scale.

In comparison with baseline, we found a moderate improvement of HRQoL as soon as the ulcer was healed (T1) and further improvement was observed 3 months after healing (T2). The relative small improvement at T1 could be related to the design of the SF-36 instrument, since many questions are related to the health status of the patient

in the last 4 weeks. During this period most patients were still treated with an off-loading device, which was not specified in our study. However, an off-loading device [22, 23], such as a cast or half-shoe, can result in loss of physical functioning, in particular mobility, as observed in the majority of our patients. After healing of the ulcer these devices are usually discontinued, which could have contributed to the improvement in mobility and HRQoL 3 months after healing. Various off-loading devices are currently used, with possibly different impacts on mobility and HRQoL. However, further investigation is necessary on this count.

The treatment of diabetic foot ulcers poses a great burden not only on the patient but also on the patient's caregivers [6]. In particular, healing was associated with a large improvement in the subscale related to emotional difficulties of the caregivers. Moreover, HRQoL of the caregivers were correlated with the HRQoL of the patients. Several factors are probably responsible for the loss of HRQoL of the caregivers, such as wound care, impaired mobility, frequent hospital visits and fear of amputation. A limitation of our study was the relatively small number of caregivers (n=153) compared with the number of patients (n=294); this may have been due to social isolation or to unwillingness to fill in the questionnaire. We cannot exclude the possibility that the HRQoL of these possible non-participants was less affected by taking care of a diabetic patient with a foot ulcer. However, time and attention should be offered to these caregivers in the busy foot clinics, given their important role in treatment and the large emotional burden foot ulcers pose on the patients' immediate caregivers and family.

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