Diabetes Care Publish Ahead of Print, published online April 4, 2008

Long Term Outcome and Disability of Diabetic Patients Hospitalised for Diabetic Foot Ulcers: A 6.5 Year Follow-up Study

[1,2]Edouard Ghanassia, MD, [1,2]Laetitia Villon, MD, [1,2]Jean-François Thuan dit Dieudonné, MD, [1]Catherine Boegner, MD, [1,2]Antoine Avignon, MD, [1,2]Ariane Sultan, MD

[1]CHU Montpellier, Montpellier, F-34000 France
[2]Université Montpellier1, UFR de Médecine, EA 4202, Montpellier, F-34000 France

Corresponding author:
Antoine Avignon
Metabolic Disease Department, Lapeyronie Hospital
371, Av Doyen G. Giraud
34295, Montpellier Cedex 5
E-mail: a-avignon@chu-montpellier.fr

Received for publication 07 November 2007 and accepted in revised form 01 April 2008.

Objective– The long-term outcome and functional status of subjects hospitalised for diabetic foot ulcers have been poorly studied and thus are the topics of this study.

Research design and methods– Ninety-four consecutive diabetic subjects hospitalized for diabetic foot ulcers between January 1998 and December 2000 were prospectively followed for 79.5±13.3 months. We calculated rates of primary healing, new ulcers, amputations, mortality, and disability and evaluated the global therapeutic success (GTS) of foot care management as defined by the association of primary healing without recurrence or disability at the end of follow-up.

Results– Follow-up was successful in 89/94 subjects (63 men/31 women, mean age 63.7±10.8 years). Of these, 69 (77.5%) experienced primary healing without major amputation, 39 (43.8%) underwent amputation (24 minor/15 major) and 46 died (51.7%), including 23 from cardiovascular events. Forty-two out of 69 patients who experienced primary healing (60.9%) had ulcer recurrence. At the end of the follow-up period, 25 patients (28.1%) were dependent and 40 subjects (44.9%) had achieved GTS. Multivariate analysis showed the independent role of age as a predictor of GTS ($p<0.05$) and of impaired renal function/albuminuria as independent predictors of healing failure, 1st amputation and mortality ($p<0.01$).

Conclusions – Despite a satisfactory initial healing rate, the global long-term outcome of patients hospitalised for diabetic foot ulcers was poor. Nephropathy appears to be an important predictor of long-term outcome. Further studies are needed to establish recognised criteria for therapeutic success going beyond just the evaluation of healing rate in the management of diabetic foot ulcers.

Diabetic foot ulcers represent a major public health concern (1) and are commonly viewed as a lower extremity disease associated with a high amputation rate (2). However, they are generally associated with advanced micro- and macroangiopathy, resulting in excessively high morbidity and mortality (3).

Pathogenic mechanisms and therapeutic options for foot ulcers have been extensively studied, leading to an international consensus in 1999 (4). However, most studies have focused on ulcer-related outcomes conducted over short periods of time (healing, change in area or amputations), rather than evaluating long term patient-related outcomes (5-7). Recently, Jeffcoate *et al* used the association of survival, absence of any amputation, and freedom from ulcers as an estimate of patient-related outcomes, showing that ulcer-related outcomes may extensively underestimate the true morbidity and mortality associated with diabetic foot disease (8). However, these authors did not evaluate functional outcome, and the measurements were confined to the first year after initial registration in their clinic. The aim of the present study was to analyze the long-term outcome of diabetic patients after hospitalization for foot ulcers using a scale for disability (9), and to investigate possible prognostic factors.

RESEARCH DESIGN AND METHODS

From January 1998 to December 2000, all patients hospitalized in our department for diabetic foot ulcers were included in a cohort. Admission for inpatient treatment was ordered if a limb-threatening infection and/or non-favourable evolution of the wound despite standard outpatient care was observed, according to international recommendations (4). Limb-threatening infection was defined by the presence of full-thickness ulcer, >2 cm of cellulitis with or without lymphangitis, bone or joint involvement, or systemic toxicity. Standard out-patients care included pressure offloading, treatment of infection including debridement, local wound care, podiatric care, adapted footwear when needed and, metabolic control and treatment of comorbidities and associated risk-factors including smoking, hypertension and dyslipidemia. The evolution of the wound was considered as non-favourable in the case of an aggravation at 2 consecutive visits or in the absence in any improvement after 1 month of care. During that period of time, 94 patients were included in the cohort.

Each patient gave oral informed consent, in accordance with the European directives as edited in 2001 (available from http://europa.eu.int/eur-lex/pri/en/oj/dat/2001/l_121/l_12120010501en00340044.pdf), which require no approval from an ethics committee for a study design as described herein.

Participants were considered to have type 2 diabetes if they had no history of ketosis and if they did not commence insulin treatment either in the 2 years following the diagnosis or before the age of 40 years. Otherwise, they were considered to have type 1 diabetes.

Past history of myocardial infarction was determined using medical records and/or when an electrocardiographic Q wave was present. Hypertension was diagnosed if one of the following conditions was present: systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥80 mmHg and/or the presence of at least one antihypertensive medication. Patients were considered smokers if they were current smokers or if they stopped smoking less than 3 years before admittance.

Peripheral neuropathy was diagnosed when two criteria were met among the following: paresthesis, neuropathic pain, altered 10-g Semmes-Weinstein

monofilament test and diminished ankle reflexes.

A diagnosis of peripheral arterial disease (PAD) was made in case of the abolition of ≥2 peripheral pulses and/or ≥1 significant stenoses as diagnosed by Doppler ultrasound, or by a reduction of lumen diameter ≥50% or an occlusion of ≥1 artery as shown by angiogram.

Arterial stenoses diagnosed with Doppler ultrasound were deemed significant when occlusions, single or multiple stenoses, or diffuse stenotic disease in the femoropopliteal segments, individually or collectively, caused significant velocity change and flow disturbance locally, and resulted in loss of reverse flow distally or in the presence of occlusions of arteries below the knee. Lesions were classified as ischemic wounds (IW) when PAD was diagnosed or as non-ischemic wounds (NIW) otherwise.

Wounds were graded using Wagner's classification (10). The lesions were then categorized into 2 main clinical groups: skin ulcers (Wagner 1 and 2) and critical ulcers, including both deep tissue infections and suspected osteomyelitis (Wagner 3), and gangrenous lesions (Wagner 4 and 5).

We defined a foot infection by clinical criteria consistent with the International Working Group guidelines (4) (i.e., the presence of purulence or ≥2 other local signs of inflammation). We evaluated patients with an infection for the extent of soft tissue involvement and for evidence of bone involvement. Bone infection was suspected in the presence of positive bone-probing (11) and was confirmed either by resonance magnetic imaging or by a standard 99mTc [HMPAO]-leukocyte scan**.**

The biological and bacteriological data considered were the first realised after admittance. In the presence of clinical infection, culture specimens were obtained using deep swabbing and/or surgical debridement.

Glycated haemoglobin (HbA1c) was measured using high-performance liquid chromatography with an automated analyser (Menarini, Rungis Cedex, France). The instrument was calibrated against Diabetes Control and Complications Trial standards (reference range 4.1–5.7%). The urinary albumin excretion rate (UAER) was measured by radioimmunoassay on 24-h urine collections and diabetic nephropathy was defined by UAER≥ 30 mg per day. The serum creatinine level was measured and creatinine clearance was calculated according to Cockroft and Gault's formula. Renal impairment was defined as a creatinine clearance ≤60 ml/min.

Follow-up data were obtained during the month of July 2007 (which was 5.5 years after the last patient's inclusion) through a telephone interview of each patient's family physician or diabetologist, using a specifically designed questionnaire.

The clinical outcomes considered were primary wound healing, ulcer recurrence, major amputation, death, disability and global therapeutic success (GTS) for diabetic foot management, defined as the association of primary healing, absence of recurrence and no disability. In case of death during the follow-up period, GTS was considered if the three criteria were met at the time of death. Primary wound healing was considered to be achieved when total disappearance of the initial ulcer was reported without major amputation of the limb. Ulcer recurrence was reported when the subject developed a new ulcer after a successful primary healing. An amputation was considered as major if it was performed above the midtarsal level, and as minor otherwise (4). Cardiovascular death was defined as death caused by ischemic heart disease, acute pulmonary oedema, acute congestive heart failure, cardiogenic shock, stroke or sudden death. Death was considered wound-related when caused by immobilisation (pulmonary embolism), sepsis

secondary to wound infection or when occurring during wound related events like vascular surgery.

Disability was assessed by Katz's Index of Activities of Daily Living (ADL) (9). This index measures performance in six personal ADL: bathing, dressing, toileting, transfer, continence, and feeding. It consists of six items with binary quotations of 1 or 0 based on the person's ability to perform the corresponding activity without assistance by another person. Patients living with a partner were considered independent if they were able to perform the activity when left alone. A subject whose score was <3 was regarded as very dependent (12). Hence, in the present study, we defined disability as a Katz's Index score <3.

Statistical analysis was performed using StatView and StatBox Pro 6.0. The normality of the distribution of each quantitative parameter was assessed using the Kolmigorov-Smirnov's test. If normality was established, results were given as mean ± standard deviation, and comparisons were made using the Student's *t* test for unmatched series. Otherwise, the results were given as median (range), and comparisons were made using the non-parametric Mann-Whitney's *U* test. Discontinuous parameters were calculated as a frequency and expressed in percents. Univariate analyses between qualitative parameters were made using the χ^2 test with the Yates' test. We used logistic regression analyses to compute the relative risks (RRs) of an end-point associated with different factors. Multivariate analysis to identify independent predictive factors was made using Cox's logistic regression. The entry criterion was $p<0.1$, and the permanence criterion was $p<0.05$. Predictive value was expressed as RR with a 95% confidence interval (95%CI). Kaplan-Meier's curves were used to compare survival between two groups, and significance was assessed by LogRank's test. For all tests, significance was set at $p<0.05$.

RESULTS

Follow-up data were obtained in 89 of 94 (95%) patients. The main characteristics of the patients at inclusion are given in *Table 1*. Mean follow-up was 79.4 ± 13.3 months (66.1 to 92.6 months).

Of the 89 patients, 82 (92.1%) had sensorimotor diabetic neuropathy and 41 (46.1%) had IW; a total of 48 (53.9%) patients were considered purely neuropathic. Fifteen of the 89 patients in the cohort (20.3%) underwent vascular procedures.

Primary healing Primary healing was achieved in 69/89 patients (77.5%) (Table 2). Univariate predictors of healing failure were smoking (RR=2.89; 95%CI: 1.01–8.27; $p<0.05$) , popliteal stenosis (RR=3.6; 95%CI: 1.28–10.14; $p<0.02$) and renal impairment (RR=6.45; 95%CI: 2.17–10.83; $p<0.0001$) . All 14 patients (100%) with NIW and 55 of 75 patients (73.3%) with IW achieved primary healing ($p=0.06$). After introducing factors associated with healing failure at $p<0.1$ in univariate analysis into a multivariate model, renal impairment (RR=6.21; 95%CI: 1.28 – 31.05; $p<0.03$) and smoking (RR=6.11; 95%CI: 1.42 – 26.30; $p<0.02$) were found to be independent predictors of healing failure.

Ulcer recurrence Among the 69 patients who achieved primary healing, 42 (60.9%) developed a new ulcer during the follow-up period (Table 2). Insulin treatment before admission was the only predictor of ulcer recurrence, both in univariate analysis (RR=3.87; 95%CI: 1.37–10.98; $p<0.006$) and after adjusting for factors associated at $p<0.01$ in univariate analysis, i.e. ischemia and osteitis (RR=4.61; 95% CI: 1.35–15.79; $p=0.015$).

Amputations Thirty-nine out of the 89 patients in the whole cohort (43.8%) underwent an amputation (30 minor and 9

major) (Table 2). Univariate predictors of amputation were critical ulcers (RR=3.01; 95%CI: 1.26 – 7.21, p<0.01), IW (RR=6; 95%CI: 1.26 – 28.69; p<0.003), supra-popliteal (RR=14.4; 95%CI: 1.73–119.48; p<0.01) and popliteal stenosis (RR=4.03; 95%CI: 1.03–10.12; p<0.003). In multivariate analysis, popliteal stenosis was the only independent predictor of amputation (RR=3.67; 95%CI: 1.34–10.07; p≤0.01).

Regarding major amputations, past history of lower limb revascularization (RR=5.80; 95%CI: 1.38 – 24.40; p<0.02), previous amputation (either minor or major) (RR=5.52; 95%CI: 1.27 – 24.10; p<0.02) and critical ulcers (RR=11.15; 95%CI: 1.33 – 93.52; p<0.03) were found to be univariate predictors, but none of these factors remained as independent predictors in multivariate analysis.

Even though the rate of amputation was higher in the group of patients with a previous history of amputations (15/27 patients, 55.6%) in comparison to those who did not have a previous history of amputation (23/62 patients, 37.1%), the difference between these 2 groups did not reach the level of statistical significance.

Among the 62 patients without previous amputation, univariate predictors of 1st amputation were diabetic nephropathy (RR=5.54; 95%CI: 1.59 – 19.32; p<0.008) and IW (RR=8.54; 95%CI: 1.03 – 72.16; p<0.05) . After multivariate analysis, only diabetic nephropathy remained as an independent predictor of 1st amputation (RR=6; 95% CI: 1.62 – 22.21; p<0.01).

Disability Twenty-five subjects (28.1%) were considered as having a disability (Katz's index <3) at the end of the follow-up period or at the time of their death (Table 2). Patients with a disability were older at the time of entry into the study (70.1±8.3 *vs* 61.5±10.7 years, disability *vs* no disability, p<0.001). Other univariate associates of disability were, renal impairment (RR=3.76; 95%CI: 1.26 – 11.24; p<0.01) and history of amputation (RR=3.02; 95%CI: 1.14 – 7.99; p<0.03). . None of these factors remained as independent predictors of disability after multivariate analysis.

Global therapeutic success

GTS was achieved for 40 subjects (44.9%): 28 (31.5%) who were alive at the end of the follow-up period and 12 (13.4%) who had died (Table 2). In the subgroup of 43 patients still alive at the end of the follow-up period, the GTS rate was 65.1%. In the subgroup of 46 deceased patients, the GTS rate was 26.1% (p<0.001).

In univariate analysis, failure to reach GTS was associated with advanced age (66.6±9.3 vs 59.8±11.6, GTS *vs* no GTS, p<0.01), previous history of foot ulcers (RR=2.67; 95%CI: 1.03 – 6.91; p<0.05) and insulin therapy before admission (RR=2.63; 95%CI: 1.06 – 6.53; p<0.04) . In multivariate analysis, an age >70 years, was the only independent predictive factor that persisted (RR=2.8; 95%CI: 1.01 – 7.67; p<0.05).

Mortality

Forty-six patients (51.7%) died during the follow-up period, including 23 (25.8%) from a cardiovascular event, 9 (19.6%) from a wound-related event, 7 (15.2%) from malignancies and 7 (15.2%) from other causes (Table 2). In univariate analysis, mortality was associated with advanced age (68±9.1 vs 57.5±10.8 years, deceased *vs* alive, p<0.001), renal impairment (RR=6.93; 95%CI: 2.67 – 18.04, p<0.0001) and past history of amputation (RR=3.08; 95%CI: 1.17 – 8.59; p<0.03) . When disability, age, renal impairment and history of myocardial infarction were considered in a multivariate analysis, only renal impairment (RR=4.57 95% CI: 1.1 – 19.4; p<0.05) was identified as an independent predictor for mortality (*Figure 1)*.

After both univariate and multivariate analyses with the introduction of insulin therapy, renal impairment and history of

myocardial infarction into the model, we found the independent predictive factors for cardiovascular mortality to be insulin therapy before admittance (RR=13.14; 95% CI: 1.39 – 124.48; $p<0.05$) and renal impairment (RR=8.7; 95% CI 1.6 – 48; $p\leq0.01$).

CONCLUSIONS

Most previous studies evaluating diabetic foot ulcer outcome were short-term studies (<5years) and were limited to ulcer related end-points, such as healing and amputations. Thus, in the present report, we evaluated long term outcome (6.5 years), including disability as an end-point in a consecutive series of patients hospitalised at a single specialised centre for foot ulcers. Predictors of long-term outcome were further evaluated.

The primary healing rate was 77.5%, but the years following the initial event were marked by high rates of ulcer recurrence (60.9%) and amputations (43.8%). At the end of the follow-up period or at the time of their death, 28.1% of the patients were considered to have a disability leading to dependency, which is one of the essential criteria used to evaluate functional status (13). To our knowledge, no data concerning prospective evaluation of disability or dependency in diabetic subjects with foot ulcers are available, nor has it ever been considered as a therapeutic criterion in any previous study. Even though it was not specifically designed for diabetic subjects with foot ulcers, we chose Katz's index to evaluate disability for different reasons: (i) it is easy to use in routine clinical practice, (ii) the French version has been validated and (iii) it is widely used in the literature (12).

Dependency is plurifactorial and one of today's crucial issues is the identification of easily measurable predictive markers in order to undertake effective interventions for its prevention. In our study as well as in the literature, disability was associated with aging (13; 14). Thus, even though the primary healing rate observed in our series might be considered satisfactory and is in agreement with those of published prospective studies with a similar follow-up duration (5; 6; 15), global therapeutic success for foot care as defined by healing, absence of recurrence and of disability occurred in less than 50% of the patients (44.9%). The definition we used for GTS in the present study was based on a pragmatic basis as we wanted it to be simple enough to be used in everyday clinical practice, but other definitions, including more criteria, could have been used.

Vital status was not included as a success criterion for foot ulcer management in the present study since in this population of diabetic patients, a number of deaths were unrelated to diabetic foot care with, for example, only 9 out of 46 deaths being directly related to a foot ulcer complication, whereas 7 deaths were related to malignancies. However, at the end of the follow-up period, 46 patients had died, half of these deaths being due to a cardiovascular event. Thus, as few as 28 patients (31.5%) were both alive and considered to have achieved GTS at the end of the study.

Ulcer recurrence in the present study is also in agreement with the current literature (5; 15), even though Faglia *et al* (6) report a much lower value (12.75%). These authors explain their particularly good results as resulting from the fact that all of their subjects had therapeutic shoes with an adapted sole and that their families were educated on foot care. Of course, all of our subjects were also directed to wear adapted shoes and soles and received education regarding foot care. However, patients in France are somewhat reluctant to buy devices that are not covered by the social security, as is the case for therapeutic shoes and soles, limiting their use. This could explain the difference in rate of ulcer recurrence between Faglia’s study and ours.

Similarly, Moulik *et al* (7) report a limited rate (19%) of amputations for all levels after 5 years contrasting with our amputation rate of 43.8%, which is nevertheless similar to other studies (5; 6; 15). The lower amputation rate in that latter study could be explained by the fact that Moulik *et al* included only patients with new ulcerations.

Diabetic nephropathy appears to be an important marker of long-term prognosis, with impaired renal function being an independent predictor of healing failure, of all causes mortality and of cardiovascular death, and with albuminuria being associated with amputations. This latter point is in agreement with a previous study by Apelqvist *et al* (16). These results confirm the importance of diabetic nephropathy as a marker of extended angiopathy in patients with diabetic foot ulcers.

Ischemia, as defined in the present study, was a univariate associate of amputation, but was not found to be an independent predictive factor after correcting for confounding factors. However, other markers of macroangiopathy were associated with long-term outcomes, with popliteal stenosis as an independent predictor of amputation confirming that vascular involvement in diabetic patients with foot ulcers is particularly important (17). Thus, our results do not deny the crucial role of macroangiopathy in the long-term global prognosis of these subjects (7).

Insulin therapy before admittance also appears as a central marker, as it is an independent predictive factor of ulcer recurrence and cardiovascular mortality. Insulin is generally needed after a long diabetes duration associated with poor glycaemic control, with both being major risk factors for micro- and macroangiopathic complications (18). Insulin must thus be considered more as a marker of the severity of the disease rather than a risk factor *per se.*

Although one of the limitations of our study is that data were collected via a telephone interview and not face to face, we feel that this does not limit the validity or importance of these results.

In conclusion, we found that despite a satisfactory initial healing rate, the global long-term outcome of patients hospitalised for diabetic foot ulcers was poor. These observations confirm the need to establish recognised criteria, going beyond just healing rate, for the long-term evaluation of diabetic foot ulcers. Multicenter trials are needed in this respect. Our results also stress the importance of impaired renal function as a predictor of diabetic foot ulcer outcome and the need to pay particular attention to patients with this condition.

REFERENCES

1. Davis WA, Norman PE, Bruce DG, Davis TM: Predictors, consequences and costs of diabetes-related lower extremity amputation complicating type 2 diabetes: the Fremantle Diabetes Study. *Diabetologia* 49:2634-2641, 2006
2. Wrobel JS, Mayfield JA, Reiber GE: Geographic variation of lower-extremity major amputation in individuals with and without diabetes in the Medicare population. *Diabetes Care* 24:860-864, 2001
3. Boulton AJ, Vileikyte L, Ragnarson-Tennvall G, Apelqvist J: The global burden of diabetic foot disease. *Lancet* 366:1719-1724, 2005
4. Apelqvist J, Bakker K, van Houtum WH, Nabuurs-Franssen MH, Schaper NC: International consensus and practical guidelines on the management and the prevention of the diabetic foot. International Working Group on the Diabetic Foot. *Diabetes Metab Res Rev* 16 Suppl 1:S84-92, 2000
5. Apelqvist J, Larsson J, Agardh CD: Long-term prognosis for diabetic patients with foot ulcers. *J Intern Med* 233:485-491, 1993
6. Faglia E, Favales F, Morabito A: New ulceration, new major amputation, and survival rates in diabetic subjects hospitalized for foot ulceration from 1990 to 1993: a 6.5-year follow-up. *Diabetes Care* 24:78-83, 2001
7. Moulik PK, Mtonga R, Gill GV: Amputation and mortality in new-onset diabetic foot ulcers stratified by etiology. *Diabetes Care* 26:491-494, 2003
8. Jeffcoate WJ, Chipchase SY, Ince P, Game FL: Assessing the outcome of the management of diabetic foot ulcers using ulcer-related and person-related measures. *Diabetes Care* 29:1784-1787, 2006
9. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW: Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function. *JAMA* 185:914-919, 1963
10. Wagner FW, Jr.: The dysvascular foot: a system for diagnosis and treatment. *Foot Ankle* 2:64-122, 1981
11. Shone A, Burnside J, Chipchase S, Game F, Jeffcoate W: Probing the validity of the probe-to-bone test in the diagnosis of osteomyelitis of the foot in diabetes. *Diabetes Care* 29:945, 2006
12. Benaim C, Froger J, Compan B, Pelissier J: [The assessment of autonomy in elderly people]. *Ann Readapt Med Phys* 48:336-340, 2005
13. Valensi P, Girod I, Baron F, Moreau-Defarges T, Guillon P: Quality of life and clinical correlates in patients with diabetic foot ulcers. *Diabetes Metab* 31:263-271, 2005
14. Bourdel-Marchasson I, Berrut G: Caring the elderly diabetic patient with respect to concepts of successful aging and frailty. *Diabetes Metab* 31 Spec No 2:5S13-15S19, 2005
15. Pound N, Chipchase S, Treece K, Game F, Jeffcoate W: Ulcer-free survival following management of foot ulcers in diabetes. *Diabet Med* 22:1306-1309, 2005
16. Apelqvist J, Agardh CD: The association between clinical risk factors and outcome of diabetic foot ulcers. *Diabetes Res Clin Pract* 18:43-53, 1992
17. Graziani L, Silvestro A, Bertone V, Manara E, Andreini R, Sigala A, Mingardi R, De Giglio R: Vascular involvement in diabetic subjects with ischemic foot ulcer: a new morphologic categorization of disease severity. *Eur J Vasc Endovasc Surg* 33:453-460, 2007

18. Varma R, Macias GL, Torres M, Klein R, Pena FY, Azen SP: Biologic risk factors associated with diabetic retinopathy: the Los Angeles Latino Eye Study. *Ophthalmology* 114:1332-1340, 2007

Table 1: Patients' baseline characteristics. Values are mean ± SD or number (%)

	Total (n=89)
Male gender	62 (69.7)
Age (years)	63.8 ± 10.8
Diabetes duration (years)	24.0 ± 11.3
Type 1 diabetes (%)	11 (12.4)
Past history of Myocardial Infarction	21 (23.6)
Past history of amputation	27 (30.4)
Minor	18 (20.3)
Major	9 (10.1)
BMI (kg/m²)	26.6 ± 4
Ischaemic wounds (%)	75 (84.3)
Critical wounds (Wagner≥3)	41 (46.1)
HbA1c	9.2 ± 1.7%
Insulin therapy	60 (67.4)
Retinopathy	65 (75.3)
Nephropathy	52 (58.4)
Creatinine clearance (ml/min)	73.3 ± 30
High blood pressure	84 (94.4)
Dyslipidemia	74 (83.1)

Table 2: Main outcomes. Values are numbers (%). *percentage is calculated in proportion to the 69 patients who reached primary healing

	Total (n=89)
Primary healing	69 (77.5)
Recurrent ulceration	42 (60.9)
Amputations	39 (43.8)
Minor	30 (33.7)
Major	9 (10.1
All-cause mortality	46 (51.7)
Cardiovascular mortality	23 (25.8)
GTS for diabetic foot management	40 (44.9)

Figure 1. Kaplan-Meier's survival curves comparing survival rate in patients without (plain line) or with (dotted line) impaired renal function.