

Risk factors for recurrent diabetic foot ulcers: Site matters

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Introduction

The rate of recurrent ulceration in diabetic patients with a history of foot complications is high.(1-6) The purpose of this study was to evaluate the outcome of diabetic foot ulcers and to study the risk factors for recurrent foot ulcers in a high-risk setting such as a specialized tertiary diabetic foot center.

Research design and methods

The study was set up as a prospective cohort study to evaluate risk factors for secondary diabetic foot ulcers. At enrollment 81 subjects presented with an ulcer distal to the ankle and were sequentially enrolled from a high-risk foot clinic at an urban teaching institution. Patients without follow up visit at the diabetic foot clinic were excluded from the study. All patients were assessed at the foot clinic at intervals necessary for either treatment or for regular care according to international standards.(7) Part of the data of this cohort of patients has been previously published.(8) Tactile, vibratory nerve function, three-step mean plantar pressure, range of motion and multiple vascular parameters were assessed using previously described techniques.(1; 9-11) Plantar peak pressures $> 70 \text{ N/cm}^2$ were defined as elevated.(1; 3; 8; 12-15)

The presence of risk factors in the group of patients that developed an ulcer in the follow-up period was compared to the presence of these factors in the group of patients without a follow-up ulcer. Secondary points were: incidence of amputation, recurrent ulcers, the amputation level, reamputations and necessity for peripheral arterial bypass. A reulceration was defined as an ulcer at the same location as a previous one. A recurrent ulcer was defined as any secondary ulcer regardless of its

location. For purposes of analysis, the foot was divided into four different regions.

Results

Of the initially presenting ulcers, 71.6% healed, 12.3% were not healed at the end of the follow-up period, and 16.0% had led to a lower extremity amputation. The median duration of follow up was 31.5 months (mean $27.1 \text{ months} \pm 9.2$).

Of the total population, 60.5% of the patients developed an ulcer in the follow up period. The incidence of ulceration was 26.8/100 patients per year. If multiple ulcers were counted as separate events, the incidence rose to 56.3/100 per year. Of the 24 patients with a plantar first ray ulcer, 7.7% (2/24) required an amputation during the follow up period compared to 20% (11/44) of patients with an ulcer at a different location ($p > 0.05$). Plantar peak pressures for patients with a first ray ulcer were $86.0 \pm 22.0 \text{ N/cm}^2$ compared to $84.2 \pm 25.0 \text{ N/cm}^2$ ($p > 0.05$) for patients with any other ulceration at enrollment. 14.3% of patients with an ulcer in the follow up period received a peripheral artery bypass, compared to none of the patients without follow up ulcer (odds ratio 1.17 (CI 1.04-1,31), $p = 0.025$). Eight reamputations were performed in the follow-up period.

The majority of the ulcers at the lesser toes occurred on the dorsal aspect (91%, $n = 32$). All of the ulcers at the great toe were plantar. Compared to all other groups combined, patients with plantar hallux ulcers developed significantly more ulcers in the follow-up period (83.3% $n = 18$ compared to 54.0% $n = 63$, $p = 0.025$, odds ratio (OR) 4.3, confidence interval (CI) 4.1-4.5). Compared to other groups, ulcers at the lesser toes were least likely to heal during the period of

follow-up (65.6% n=32 compared to 77.1% n=49, p=0.24, OR 1.6, CI 1.6-1.7) and a large percentage of lesser toe ulcers ended with an amputation (25.0% n=32 compared to 10.2% n=49, p=0.073, OR 2.9, CI 2.8-3.1).

Patients with a plantar hallux ulceration were most likely to get another ulceration at the same location (reulceration) as the index ulcer compared to the other groups (50.0% n=18 compared to 14.3% n=63, p=0.002, OR 6.0, CI 5.8-6.2). In further analysis, patients were grouped in either a group of patients with a plantar hallux or submetatarsal ulcer (both plantar forefoot ulcers) or a group of patients with ulcers at another location. Reulceration at the same location was more likely in the group of patients with a plantar hallux or submetatarsal ulcer at enrollment compared to ulcers at any other location (43.2% n=37 vs. 4.5% n=44, p=0.002, OR 9.1, CI 8.6-9.5). History of amputation, history of first ray amputation or presence of hallux rigidus was not significantly more prevalent in patients with a recurrent ulceration.

Risk factors for recurrent ulceration in a univariate analysis are shown in Table 1. Risk factors with p<0.20 from the univariate analyses were taken to construct a logistic regression model. Location of ulceration was also included in this model. Significant risk factors from the logistic regression analysis were: Peripheral vascular disease (p=0.006, estimated odds ratio 10.1), location of the index ulcer at the plantar aspect of a toe (p=0.038, estimated odds ratio 5.3).

Conclusions

Risk factors that were identified in our study were peripheral vascular disease and location of index ulcer. It is uncertain whether these

risk factors play an etiological role in the development of an ulcer. In this perspective it might be better to speak of *indicators* for potential recurrent ulceration instead of *risk factors*. The methods and definitions were based on previous publications and the recommendations of the International Working Group on the Diabetic Foot.(7) Only a few reports are available on the risk of new ulcers after an ulcer has occurred.(16-19) While many had relatively long follow-ups, the studies were either retrospective in nature or did not include robust multivariate analyses, with none specifically evaluating location as a factor.

Patients with plantar hallux ulcers were significantly more likely to develop additional ulcers. Ulcers on the bottom of the foot are generally believed to be due to repetitive injury to an insensitive foot.(20) In contrast with ulcers on the great toe, most of the ulcers on the lesser toes were on the dorsum. These dorsal wounds are usually the result of ill-fitting shoes. Once this mechanism of injury is identified, simply providing shoes that have an adequate toe box is probably a sufficient remedy to avoid re-injury. This simple prevention measure is probably more effective to reduce re-ulceration.

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	Follow up ulcer (n=49)	No follow up ulcer (n=32)	p-value	Odds Ratio (CI)	Coefficient (logistic regression)	Estimated Odds Ratio (logistic regression)
Male gender	73.5%	81.3%	> 0.3			
Age > 60 years	20.4%	34.4%	0.161	0.5 (0.2-1,3)		
Age (years)	52.6	53.5	> 0.3			
Type 2 diabetes mellitus	95.9%	93.8%	> 0.3			
Duration of DM > 10 years	73.5%	56.3%	0.11	0.2 (0.1-1.6)		
Alcohol abuse past and present	46.9%	50.0%	> 0.3			
Tobacco abuse past and present	55.1%	65.6%	> 0.3			
Nephropathy (at least micro albuminuria)	56.3%	50.0%	> 0.3			
Retinopathy (at least background changes)	86.1%	79.2%	> 0.3			
History of amputation	40.8%	34.3%	> 0.3			
HbA _{1c} > 9%	70.5%	66.7%	> 0.3			
Plantar peak pressure > 80 N·cm ⁻²	60.0%	55.2%	> 0.3			
Peak pressure forefoot (N·cm ⁻²)	85.7	83.7	> 0.3			
TcpO ₂ < 30mmHg	41.9%	25.0%	0.15	0.2 (0.1-1.5)		
TcpO ² (mmHg)	38.8	42.3	> 0.3			
Neuropathy (swm missing or VPT>25)	91.7%	90.6%	> 0.3			
Vibratory Perception Threshold (Volts)	39.1	34.9	0.11			
PVD (any pedal pulse missing or ABI < 0.8)	42.9%	9.4%	< 0.001	0.3 (0.1-3.2)		
Ankle-Brachial index	0.93	1.10	> 0.3			
Rigid toe deformity or charcot deformity	87.8%	81.3%	> 0.3			
Hallux rigidus	28.6%	15.6%	0.18	0.1 (0.1-1.3)		
Pes equinus	36.7%	28.1%	> 0.3			
Any rigid deformity	73.5%	65.6%	> 0.3			
Body Mass Index (kg/m ²)	29.8	29.8	> 0.3			
Cholesterol (mg/dl)	196	182	0.21			
Smoking: Pack year history (years)	17.4	15.8	> 0.3			
Years of education (years)	11.2	9.1	> 0.3			
Peripheral vascular disease (multivariate)			0.006		2.3	10.1
Location of index ulcer at plantar hallux (multivariate)			0.038		1.7	5.3

Table legend

Univariate and subsequent multivariate analysis of risk factors for an ulcer in the follow-up period. CI = confidence interval, DM = diabetes mellitus, HbA_{1c} = glycated hemoglobin, TcpO₂ = transcutaneous partial oxygen pressure, VPT = Vibratory Perception Threshold, PVD = peripheral vascular disease, ABI = Ankle-Brachial Index. The factors for foot ulceration after a previous ulceration entered into logistic regression analysis model included were: age > 60 years, duration of diabetes > 10 years, peripheral vascular disease (any missing pulse or Ankle-brachial index <0.8), presence of hallux rigidus and location of index. Variables with p<0.2 are displayed. The chi-square of the Hosmer and Lemeshow goodness-of-fit-test was 3.8 with p = 0.81, indicating that the model was well calibrated and that the data fit well.