Amputation in diabetic foot patients: a prediction model

Merel JC Betman, Ingrid Hulst, Lucas C van Dijk, Hans van Overhagen, Randolph GS van Eps, Hugo TC Veger and Jan J Wever

The aim of this study was to evaluate the amputation frequency in a cohort of patients with a diabetic foot ulcer and to define risk factors for undergoing multiple amputations. The authors evaluated a cohort of 166 people with diabetes (115 males and 51 females) who were treated at the authors' multidisciplinary centre for a diabetic foot ulcer between 2007 and 2013. Baseline data were gathered on wound characteristics, neurovascular status and glycaemic control. Amputation frequencies were determined retrospectively until May 2017. Multivariate Poisson regression models were fit for all variables shown to be marginally associated in univariate analysis, and as a result a prediction model was formed. Four predictors influenced amputation frequency: peripheral arterial disease, Wagner grade, toe pressure and monofilament testing. The prediction model scored patients' risk for multiple amputations and formulated an estimated number of amputations per year, which correlated with observed amputation frequency (r=0.324, *P*<0.001). This study demonstrates that with a conservative approach to amputation comes a legitimate risk of secondary failure, and argues that a more radical approach may safeguard high-risk patients from a long and recurrent amputation process. In the population studied, the prediction model succeeded in identifying patients at high risk for multiple amputations. This model can serve as a decision-making aid to support the patient and surgeon in the difficult decision of determining amputation level. Additional prospective research is necessary to verify the effect of these predictors and validate the prediction model.

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Article points

1. Certain risk factors expose diabetic foot patients to multiple amputations.
2. This prediction model identifies patients at high risk of multiple amputions.
3. This model serves as a decision-making aid when determining amputation level.

Key words

- Amputation frequency
- Diabetic foot
- Multiple amputations
- Prediction model

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Diabetic foot patients are at increased risk of lower-extremity amputation (LEA). The incidence of lower-limb amputations is eight times higher in people with diabetes than those without it (Johannesson et al, 2009) and approximately 80% of diabetes-related lower-extremity amputations are preceded by a diabetic foot ulcer (DFU) (Hingorani et al, 2016).

Studies have proven the benefit of follow-up and adequate care from a multidisciplinary foot team in a hospital setting (Hingorani et al, 2016). Despite the many advances in care for a DFU, wounds frequently do not heal, exposing these patients to a risk of amputation. These patients are at higher risk of developing a new ulcer, once more exposing them to amputation. Needless to say, an amputation is a traumatic experience for a patient, often necessitating an intensive follow-up period. Not to mention, healthcare for these patients is very costly and lower-extremity amputations create an enormous burden on global healthcare (Ragnarson and Apelqvist, 2004; Boulton et al, 2005).

Many prediction models and classification systems have been developed, resulting in a considerable list of risk factors for a DFU, which make it possible to assess the chance of healing, limb

Page points

1. There are no previous studies published about risk factors for multiple amputations.
2. It is important to reduce health care costs and prevent patients from undergoing a long and recurrent amputation process.
3. A prediction model may define patients at high risk for multiple amputations.

Table 1. Demographics of study population (*n*=166).

Variables		All patients (*n*=166)	Categories			
			No Amputations	1 amputation	>1 amputation	Sig.
Age[1]		66 (12.3)	67 (11.9)	67 (12.4)	63 (15.1)	0.249
BMI[1]		30 (5.9)	30 (6.0)	30 (6.0)	28 (5.1)	0.131
Gender[2]	Male	115 (69.3)	66 (57.4)	22 (19.1)	27 (23.5)	0.464
	Female	51 (30.7)	35 (68.6)	7 (13.7)		
Ethnicity[2]	Caucasian	134 (80.7)	81 (81)	24 (82.8)	29 (80.6)	0.926
	African	4 (2.4)	3 (3)	0 (0)	1 (2.8)	
	Asian	27 (16.3)	16 (16)	5 (17.2)	6 (16.7)	
Total follow up[1] (years)		4.3 (2.1)	4.1 (2.2)	4.5 (2.4)	3.9 (2.2)	0.304
Deceased	Yes	64 (38.6)	36 (56.3)	14 (21.9)	14 (21.9)	0.490
	No	102 (61.4)	64 (63.7)	15 (14.7)	22 (21.6)	

All 166 patients were classified according to amputation frequency.
[1]Numerical variables are listed with mean and (SD).
[2]Categorical variables are listed with total number and (frequency in percentages).

Table 2. Predictors for multiple amputations per year. Poisson regression analysis, *P*< 0.05.

Variables	Sig.
Wagner grade 0–2 vs 3–5	0.002
PAD classification	0.011
Toe pressure	0.002
Monofilament test	0.012

Dependent variable: total amputation frequency.

salvage or amputation. A few studies have attempted to define risk factors for re-amputation and, among others, gangrene on admission, insulin-dependent diabetes, age >70 years, heel lesions and peripheral arterial disease (PAD) were proven to be significant (Dillingham et al, 2005; Izumi et al, 2006; Kono and Muder, 2012; Nerone et al, 2013). Between these studies, however, there is little consensus and study groups are small. Furthermore, none have attempted to define risk factors for multiple amputations or evaluate frequencies of amputation, focused solely on the diabetic foot. The results of these studies are too general to apply them to an individual patient or to make an estimated risk of multiple amputation for each patient.

Defining risk factors for multiple amputations contributes to formulating a more precise prognosis for diabetic foot patients at an early stage, supporting healing and limb salvage. More importantly, defining a risk profile for patients who may benefit from immediate major amputation instead of multiple minor amputations leading to the same result may be of great value. This approach potentially increases quality of life and considerably reduces healthcare costs.

The aim of this study is to define risk factors for undergoing multiple lower-extremity amputations as a consequence of a DFU, and to create a prediction model to determine the risk for undergoing multiple amputations for each patient with a DFU. The authors discuss if patients with a DFU and a high-risk profile for multiple amputations might benefit from a more proximal lower-extremity amputation at an earlier stage, thereby considering current standards for determining amputation level. A question could be raised if it is necessary to put patients through multiple minor amputations, which would eventually result in a major amputation to the same extent. Ultimately, the authors hypothesise that a prediction model will appoint the correct risk profile to each patient based upon the observed amount of amputations.

Research design and methods

In this retrospective cohort study, 166 diabetic patients with a foot lesion were referred to an outpatient diabetic foot clinic (DFC) in the Haga Teaching Hospital, the Netherlands, for treatment and regular follow-up. A DFU was defined as a sore or wound below the ankle. Baseline data were recorded prospectively between 2007 and 2013, and consisted of 40 variables assembled at the time patients had their first appointment at the DFC. Treatment lasted until wound healing was achieved, after which they were referred back to their general practitioner. The DFC consisted of a multidisciplinary foot care team, providing integrated care to address all aspects of management of the ulcer. Retrospectively, up until April and May 2017, data were collected on number of amputations, previous history of amputations or ulcers (before inclusion), and total follow-up period. All information was gathered and extracted from the medical records by IH and MB (authors).

The choice for baseline variables was determined by standard data collection for patients who were treated at the DFC, and because they were common risk factors for amputation and re-amputation in previous studies (Dillingham et al, 2005; Tseng et al, 2005; Izumi et al, 2006; Nather et al, 2008; Skoutas et al, 2009; Kono and Muder, 2012; Nerone et al, 2013).

Age, gender, ethnicity, smoking status and body mass index (BMI) were recorded at baseline. Patients were categorised as Caucasian, African or Asian, based upon their reported ethnicity.

Diabetes and kidney function

Concerning their underlying diabetes, it was recorded how long a patient had had diabetes and if patients were insulin-dependent, tablet-dependent or both. Hba_{1C} was measured to assess glycaemic control, and glomerular filtration rate (GFR) and creatinine to assess kidney function.

Wound characteristics

Ulcers were classified according to the Wagner wound classification system (Wagner, 1981). Further data gathered on wound characteristics were wound area in cm^2, location of the ulcer (plantar, non-plantar of interdigital), wound duration (in months) and presence of infection.

Table 3. Example of how scores are calculated with the prediction model, for two randomly chosen patients.

Predictors	Patient A		Patient B	
	value	B	value	B
Wagner grade	3	0.623	1	0
PAD classification	3 (severe PAD)	0.315	1 (no PAD)	0
Toe pressure[2]	27 mmHg	-0.008	188 mmHg	-0.008
Monofilament test	2 (positive)	1.188	1 (negative)	0
Score[1]		0.964		-2.065
Number of amputations per year[3]		0.25		0.01

[1]Score calculation was done by summation of all beta coefficients.
[2]Toe pressure multiplied by beta coefficient.
[3]Calculated by exponential function of (constant (-8.243) + score) x 365.

Neurovascular status

Peripheral pulses were palpated in both feet for the dorsal pedal artery and posterior tibial artery. Ankle-brachial pressure index (ABI) and toe pressure (mmHg) were measured by a registered vascular technologist in a noninvasive vascular laboratory. The presence or extent of PAD was determined by categorising patients into four groups defined as 'no PAD', 'mild', 'severe' or 'medial artery calcification' (MAC) (Hirsch et al, 2006; Spreen et al, 2016).

Testing for loss of sensation was achieved by two simple and effective tests for peripheral neuropathy; a 10-g Semmes-Weinstein monofilament evaluated tactile sensitivity (Bakker et al, 2012) and a standard 128 Hz tuning fork evaluated vibration perception.

Comorbidities and interventions in previous history

Relevant comorbidities were considered hypertension, hypercholesterolemia, coronary artery disease (CAD), stroke, transient ischaemic attack (TIA) and end stage renal disease. Hypertension was defined as a resting blood pressure equal to or over 140/90 mmHg. This condition was considered therapy-resistant if it had to be treated with three or more antihypertensive medications. Hypercholesterolemia was present in patients treated with a statin or with a total cholesterol higher than

Table 4. Poisson multivariate regression analysis with forward selection process. The variables highlighted in blue were proven significant (P< 0.05) in this analysis and are interpreted as being risk factors for undergoing multiple amputations per unit of time (days).

Variables	Generalised linear model	Forward selection 1	Forward selection 2	Forward selection 3	Forward selection 4	Forward selection 5
Smoking	0.243	0.014*	0.045*	0.275	0.131	0.059
Pulsatile ATP	0.054	0.188	0.800	0.273	0.144	0.053
Wagner score 0–2 vs 3–5	0.004*	0.000*				
PAD classification	0.002*	0.000*	0.000*			
Wound area in cm² (<1, 1-5, 5>)	0.490	0.009*	0.153	0.327	0.391	0.507
Wound infection	0.328	0.026*	0.782	0.577	0.406	0.248
Monofilament test	0.003*	0.000*	0.001*	0.008*	0.012*	
Tuning fork test	0.781	0.317	0.830	0.864	0.518	0.398
Previous history: amputation	0.131	0.029*	0.034	0.046*	0.101	0.127
Previous history: PTA	0.930	0.091	0.423	0.421	0.533	0.410
Previous history: none	0.507	0.281	0.480	0.531	0.688	0.397
Days treated	0.447	0.298	0.744	0.703	0.614	0.520
ABI left	0.744	0.017*	0.090	0.545	0.631	0.667
Toe pressure	0.001*	0.000*	0.000*	0.001*		

Predictors are highlighted in blue.

6.5 mmol/L. CAD included angina, myocardial infarction and sudden cardiac death. ESRD was present if patients had a GFR <15 ml/min and/or if they were dependent on dialysis. Finally, it was documented if the patient had had a stroke (ischaemic or haemorrhagic) or TIA.

Interventions in previous history were either peripheral arterial bypass surgery or percutaneous transluminal angioplasty (PTA) in the lower extremities. Amputations and ulcers in previous history were documented as well.

Amputation

In the follow-up period, patient charts were thoroughly reviewed for frequency of minor and major amputations. Indications for amputation were either persistent infection (clinical signs or confirmed by culture growth), osteomyelitis or gangrene (necrosis). Additionally, charts were reviewed for number of wound debridements. A debridement was considered equivalent to nettoyage and necrotectomy. It was performed either in the operating room or the inpatient ward, depending on the necessity of general anaesthesia. These soft tissue surgeries, including incision and drainage, were not considered an amputation, but totaled separately.

A differentiation was made between minor amputation (below the ankle) and major amputation (above the ankle). Minor amputations included partial or complete toe amputation, partial of complete ray resection or partial or complete foot amputation. Major amputations were considered as below-the-knee or above-the-knee amputations (Nather and Wong, 2013). Re-amputation was defined as any amputation on the lower extremity at a more proximal level. Stump revision procedures were included if the surgical report specifically mentioned shortening of the tibia or femur. Patient charts were reviewed thoroughly for amputations performed in a different centre.

Statistical analysis

Categorical variables were analysed with a χhi-squared test and presented as total number and frequency in percentages. Continuous variables were analysed using analysis of variance (one-way ANOVA) and presented as a mean with 95% confidence interval (CI) or standard deviation (SD).

A multivariate Poisson regression model was fit for all variables shown to be marginally associated in the univariate analysis. For multivariate analysis, all *P*-values <0.05 were considered to indicate statistical significance. Statistical analysis was performed using SPSS version 17.0 (SPSS Inc. Released 2008. SPSS Statistics for Windows, version 17.0. Chicago: SPSS Inc.).

Results

The general characteristics of the study population are summarised in *Table 1*.

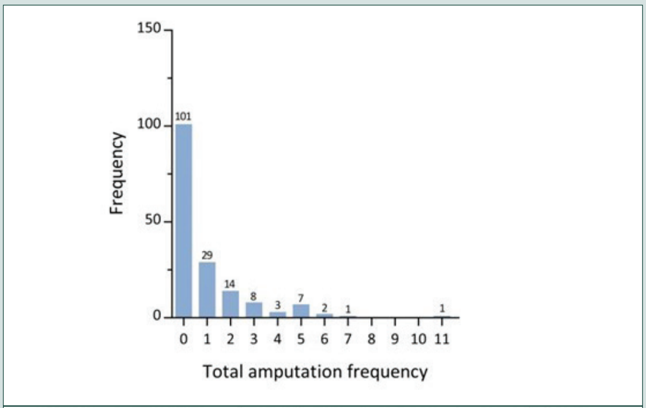
All included patients were diagnosed with diabetes mellitus type 1 or 2. A total of 164 patients were treated at the DFC for an ulcer of the foot. Two patients who presented with a Charcot foot were not excluded because both patients had a previous history of DFU and had a DFU in the study period.

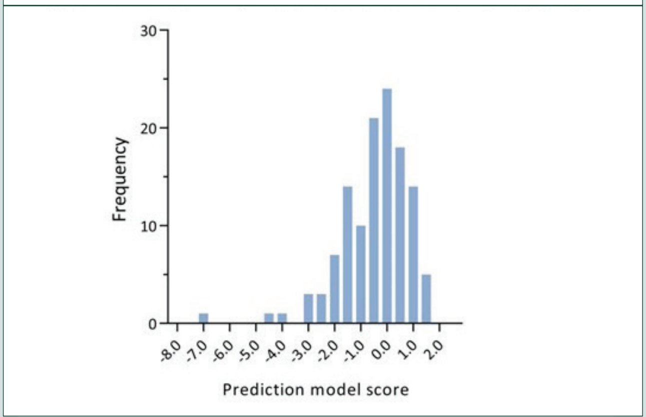
Of the total patient population, 87 patients (52.4%) completed follow-up and 64 patients (38.6%) had passed away. Among others, causes of death were coronary heart disease, stroke, and sepsis. Fifteen patients (9%) were lost to follow-up, either because they were transferred to a different hospital or because they missed follow-up appointments.

Amputation frequency

Men had relatively more amputations and re-amputations than women, but this was not statistically significant. As demonstrated in *Figure 1*, 101 patients had no amputation in the study period (60.8%), 29 had one amputation (17.5%) and 36 had one or more re-amputations (21.7%). Notably, in the group with no amputations, 15 patients had a history of previous amputation(s). In the group with one amputation, the same applied to 10 patients.

The distribution of number of amputations ranged from one to 11. In total, 125 debridements, 123 minor and 35 major amputations were performed. Furthermore, 52% had had an ulcer before inclusion and 31% a previous amputation. One patient had a minor amputation in another hospital. To the best of the authors' knowledge, no further patients received treatment for a DFU or had an amputation in a different hospital during the study period.





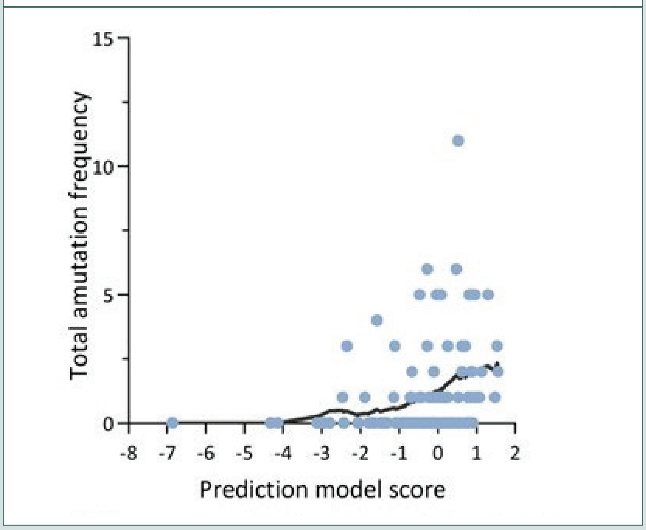


Figure 1 (top). Distribution of frequency of amputations among all patients. Figure 2 (middle). Distribution of prediction model scores in the study group. Figure 3 (bottom). Scatter plot of prediction model score versus amputation frequency.

Table 5. Parameter estimates with beta coefficients (B) from multivariate analysis.

Parameter	B	Std. error	Sig.
Constant	-8.243	0.542	0.000
Wagner grade 3–5	0.623	0.204	0.002
Wagner grade 0–2	0[a]	-	-
PAD classification 4	0.624	0.331	0.060
PAD classification 3	0.315	0.345	0.361
PAD classification 2	0.824	0.269	0.002
PAD classification 1	0[a]	-	-
Toe pressure	-0.008	0.003	0.002
Monofilament test abnormal	1.188	0.472	0.012
Monofilament test normal	0[a]	-	

Dependent variable: total amputation frequency.
[a] Set to zero because this parameter is redundant.

Six patients had a major amputation with no preliminary minor amputation. Indications for this were a flexion contracture of the knee, osteomyelitis, multiple ulcers or gangrene. Remarkably, for all these patients the amputation frequency was 1; neither in their previous history, nor in their entire follow-up period, had they had another amputation.

Univariate analysis

For univariate analysis, patients were divided into three groups depending on the number of amputations they had undergone: no amputations, one amputation or more than one amputation.

Multivariate analysis

Multivariate analysis was performed using Poisson regression. All variables proven to be significant in univariate analysis were eligible for multivariate analysis. To benefit this analysis, the variable Wagner grade was transformed into two categories (Wagner grade 0–2 or 3–5) and toe pressure of the left and right foot were converted to toe pressure of the foot where the initial ulcer was located. Through forward processing modeling, this ultimately resulted in four significant variables ($P<0.05$): Wagner grade, PAD severity, toe pressure and monofilament test, as demonstrated in *Table 2*. These factors were interpreted as being predictors for undergoing multiple amputations per year (hereafter referred to as predictors).

Prediction model

A prediction model was created to score each individual patient's risk of undergoing multiple amputations per year. Factors contributing to a higher score were:

- A higher Wagner grade (3 or higher)
- Mild PAD, severe PAD or MAC (progressively more influence from left to right, respectively)
- A lower toe pressure
- A positive monofilament test (neurosensory loss).

The higher a patient's score, the higher their risk was for multiple amputations. An example of how such a score was formulated is given in *Table 3*.

This prediction model provides a risk score that indicates the number of expected amputations per year for each individual patient. Patient A scored high (0.964) and was exposed to a risk of 0.25 amputations per year, or an expectation of one amputation every four years. Patient A had five amputations during a follow-up period of four years (1,481 days).

Patient B had a low score (-2.065) and was at risk of 0.01 amputations per year. This adds up to an expectation of one amputation every 100 years. Patient B had no amputations in the study period.

The overall distribution of patient scores is made visible in *Figure 2*. As demonstrated, most patients (82.3%) scored between -2.0 and 1.0. The mean score was -0.48 (SD 1,299) and on average patients had a risk of 0.059 amputations per year (one amputation every 16.8 years). In *Figure 3,* all prediction model scores and total amputation frequencies were plotted against each other, with a trend line drawn in ($r=0.324$, $P<0.001$). This clearly demonstrates that a significant, positive correlation exists between a higher score and more observed amputations.

The subgroup of six patients, who had a major amputation without preliminary minor amputations, as mentioned earlier, had an average score of 0.295 (range -0.671, 0.880). This gives an average risk of 0.13 amputations per year (one amputation every 7.7 years).

Discussion

In this retrospective study, the authors categorised patients according to their amputation frequency and identified four significant predictors for re-amputation. This is the first study to create a prediction model that estimates the risk of multiple amputations per year for each individual patient.

At baseline, all patients groups (no amputation, one amputation, >1 amputation) were normally distributed regarding descriptive characteristics. Although there were notably more men in the study population (69.3%), the difference was not significant and this gender distribution was comparable with previous studies reporting that men with diabetes have a higher incidence of amputation than diabetic women (Kanade et al, 2007; Johannesson et al, 2009). A meta-analysis by Tang et al (2014) reported similar results and concluded that this could be attributed to men commonly being more reluctant to seek medical consultation (Tang et al, 2014). However, higher prevalence of smoking among men could apply as well (Kattainen et al, 2005). Regarding ethnicity, a large proportion was Caucasian (80.7%) and only four patients were of African origin. Unfortunately, it was not possible to discriminate between African/Asian and South-American, and the authors were unable to determine if any patients were Surinamese of Indian subcontinent ancestry, since previous studies have demonstrated that South-Asian Surinamese (Hindu) have a four times higher risk of diabetes than ethnic Dutch (Admiraal et al, 2014).

This study showed that 21.7% of patients required re-amputation in a mean follow-up period of 4.3 years. This is broadly in accord with previous reports which show that diabetics have high rates of re-amputation, mostly within 6–12 months after a primary amputation (Izumi et al, 2006; Snyder et al, 2006; Johannesson et al, 2009; Skoutas et al, 2009). Murdoch et al (1997) reported a 10-year re-amputation rate of 60%. Izumi et al (2006)'s study showed a re-amputation rate of 60% in 5 years, and in Skoutas et al (2009)'s study a re-amputation incidence of 21.5% in 18 months was found. In the latter study, it was also stated that re-amputation occurred more in patients whom initially had one or two toes amputated than those who had been amputated at the foot level or below the knee. Patients with an above-knee amputation did not need additional amputations, which is in accordance with another study by Dillingham et al (2005), which stated than progression to a higher level of limb loss occurred most frequently (34.5%) among persons with an initial foot or ankle amputation (Dillingham et al, 2005). In a different study, it was stated that a large proportion of patients receiving minor amputations received higher level amputations in the first year following the initial amputation (Murdoch et al, 1997). Additionally, the risk of distal amputation for the contra-lateral lower extremity was raised. On the same note, in Izumi et al (2006) an increase in one level of amputation for first-time amputation decreased the risk of re-amputation by 34%. These results clearly demonstrate that with a conservative approach comes a legitimate risk of secondary failure. This further implies that initial transtibial or transfemoral amputations may provide the highest probability of successful wound healing.

An important finding from univariate analysis is that as many as 15 variables had an effect on amputation frequency, providing a solid foundation for further multivariate analysis. The major focus in this study was to determine if there are risk factors for undergoing multiple amputations. The most interesting finding to emerge from the analysis is that these indeed exist: multivariate analysis resulted in four predictors generating a prediction model. These predictors, Wagner grade, PAD classification, toe pressure and monofilament testing (peripheral sensory neuropathy), are affirmative with previous studies, and additionally a completely new insight is given by the formation of a prediction model and risk score for multiple amputations. These major observations are discussed further later in the article.

Wagner grade

For benefit of the analysis we split this variable into two groups, 0–2 and 3–5, with the latter category being a significant predictor for multiple amputations. This has been confirmed in previous studies, where an association between Wagner grade and risk of LEA was consistently observed (Monteiro-Soares et al, 2014). Another study reported that all patients who underwent diabetes-related LEA were classified as grade 4 or 5 (Al-Tawfiq and Johndrow, 2009). The cut-off point in this variable, from Wagner grade 2 to 3, was determined by the involvement of infection. It is, therefore, surprising that the variable describing presence of infection proved not to be significant.

Although the Wagner system is well established, it does not fully address infection and ischaemia (Oyibo et al, 2001). At the time of inclusion, the Wagner classification system was used for DFU classification, however, the shortcomings of this system lead to the use of the University of Texas Classification as current standard practice in the authors' medical centre.

Peripheral arterial disease

Mild PAD, severe PAD and MAC were progressively associated with a higher score. In Nerone et al (2013)'s study, a group of patients who underwent major amputation proved to have significantly more patients with severe PAD compared to patient undergoing only minor amputation (71% versus 25%, respectively). The prevalence of major amputation after initial minor amputation was statistically significantly associated with the presence of PAD (Nerone et al, 2013).

In the authors' study, the categorisation of PAD was based on ABI and toe pressure. Mild and severe PAD were scored as having progressively lower ABI and toe pressure. The highest score, however, was attributed to patients with an ABI >1.3 and a toe pressure >200 mmHg. This represents poorly compressible or incompressible arteries in the lower extremities, and it is thought that medial artery calcification may play an important role in the aetiology. This is in accordance with a recent study by Spreen et al (2016), showing that higher ABIs (>1.4) are associated with an increased risk of major amputation.

Toe pressure

Toe pressure of the foot where the DFU, for which patients were included in this study, was located, proved to be a predictor as well. In a study by Stone et al (2005), toe pressure >50 mmHg had a positive predictive value of 91% for determining healing of midfoot amputations (Stone et al, 2005). This is in accordance with the authors' results, which state that the lower the toe pressure, the higher each patient's risk was for multiple amputations. However, this does not take into account that very high toe pressures, >250 mmHg, may be an indication of poorly compressible arteries (MAC, as previously mentioned) (Spreen et al, 2016).

Monofilament test

A positive monofilament test was interpreted as neurosensory loss, in particular, a loss of protective sensation, resulting in an inability to sense minor trauma to the feet and altered plantar pressure due to foot deformities, leading to ulceration. Diabetic peripheral sensory neuropathy is an important aetiologic factor of diabetic foot ulcers. A systematic review by Feng et al (2011) concluded that a positive monofilament test result is associated with foot ulceration and was also found to be an indicator of increased risk of LEA, confirming the results of this analysis that a positive monofilament test is a predictor of multiple amputations.

Prediction model

This study has shown that the predictors influence amputation frequency. Additionally, a Pearson correlation analysis showed that a positive correlation was present between higher scores on the prediction model and a higher observed number of amputations in the study period. This confirms that the model succeeds in appointing a high score at baseline to a patient observed to have undergone multiple amputations.

Despite that these predictors create a successful prediction model, previous reports have mentioned other baseline variables to influence re-amputation as well. Poor glycemic control (Hba_{1c} >75 mmol/mol) has been regularly mentioned as a risk factor for ulceration and foot amputation (Boyko et al, 1999; Lehto et al, 1999; Chu et al, 2016), but the results from the present study do not demonstrate Hba_{1c} as an independent risk factor. Furthermore, gangrene on admission and insulin-dependent diabetes (Kono and Muder, 2012), age of >70 years, heel lesions, male gender (Skoutas et al, 2009; Chu et al, 2016), and previous LEA (Adler et al, 1999) were proven to be independent risk factors for re-amputation. Dialysis and revision of the index amputation to a higher level were associated with a subsequent contralateral re-amputation (Shah et al, 2013). These variables have not come forth as predictors for re-amputations in this study, which can be attributed to the relatively small amount of patients included who had one or more amputations (*n*=65).

Further limitations of this study are mostly inherent to it partially being a retrospective study. Despite standardised examination, in some patient charts there was a lack of documentation. As a result, for 42 patients no score could be determined from the prediction model. Some variables, mentioned in other studies as affecting the outcome, were not considered or recorded in the patient chart. Among others, these include retinopathy, high serum phosphorus (Kaminski et al, 2015), lower temperature of the amputation site (Ohsawa et al, 2001) and arteriosclerosis obliterans (Miyajima et al, 2006). Furthermore, no intervals to amputation were assessed although this was a commonly documented and analysed variable in other studies regarding the same topic. Within this study, however, the aim was to focus on amputation frequency, and for this analysis intervals to amputation were irrelevant.

Decisions on level of amputation and amputation type likely varied slightly among attending surgeons, which may have affected the outcomes. However, all procedures were performed in the same surgical centre, which means the same protocols applied. Another aspect that needs to be considered is that several patients with no or one amputation had a history of at least one previous amputation. This obviously had an influence on the allocation of patients to the amputation frequency categories and has possibly affected further analysis.

Despite these limitations, this study has resulted in a prediction model, successfully providing individual patients with an estimated risk for multiple amputations. The present study examined the number of amputations in a population of patients with a diabetic foot ulcer and a range of risk factors for amputation. It was hypothesised that those patients with multiple amputations in the study period would have certain risk factors at the time of inclusion. The results confirm this, and suggest that the aforementioned predictors predispose patients to a higher probability of multiple amputations.

As previously mentioned, an interesting subgroup in this patient population consisted of six patients who had all had a single major amputation without preceding or following amputations. Although this group was too small to qualify for any form of statistical analysis and concluding anything from this is somewhat presumptuous, it is worth considering that such a radical approach may have safeguarded these patients from a long and recurrent amputation process.

Conclusion

This study succeeded in defining risk factors for multiple amputations and creating a prediction model, which provides each individual patient with an estimated risk for multiple amputations based on the presence and extent of four predictors: Wagner grade, PAD, toe pressure and monofilament testing. It is the intention of this study to serve as a first step in the process of defining a realistic prognosis for patients with a diabetic foot ulcer and to re-evaluate current decision making in level of amputation. Ultimately, the aim is to find an optimal amputation level that allows preservation of as much limb length as possible with an acceptable risk of re-amputation. When determining the level of amputation, achieving primary healing of the surgical wound should be as much a priority as limb salvage. Selection of amputation level remains a complex process, but this model can serve as a decision-making aid to support the patient and surgeon in this difficult decision.

It goes without saying that this subject calls for further prospective investigation. Subsequent studies should document amputation frequencies and this study's results and prediction model should be validated in large patient groups. ■

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1. According to Hingorani et al, what APPROXIMATE percentage of diabetes-related lower-extremity amputations are preceded by a foot ulcer? Select ONE option only.

   A. 40
   B. 50
   C. 60
   D. 70
   E. 80

2. According to Johannesson et al, the incidence of lower-limb amputations in people with diabetes is HOW MUCH HIGHER compared to people without diabetes? Select ONE option only.

   A. x4
   B. x8
   C. x12
   D. x16
   E. x32

3. All of the listed people with diabetes have had a previous lower-limb amputation due to diabetes-related complications

   Which person is LEAST at risk of re-amputation? Select ONE option only.

   A. 35-year-old woman with gangrene on admission to hospital
   B. A 50-year-old man with type 2 diabetes requiring three oral antidiabetic agents to reach acceptable glycaemic control
   C. A 60-year-old woman with type 1 diabetes
   D. A 75-year-old man with type 2 diabetes and an HbA_{1c} of 59 mmol/mol
   E. An 80-year-old woman with a heel ulcer

4. Which SINGLE ONE of the following research methodologies is LEAST likely to provide clinicians with evidence to change their clinical practice? Select ONE option only.

   A. Meta-analysis
   B. Prospective randomised controlled study
   C. Randomised controlled study with non-definitive results
   D. Retrospective cohort study
   E. Systematic review

5. In the study of 164 patients with diabetes by Betman et al, what APPROXIMATE percentage could NOT have their prediction score calculated due to inadequate clinical documentation? Select ONE option only.

   A. 10
   B. 25
   C. 33
   D. 50
   E. 66

6. In the 2007–2013 cohort study by Betman et al, what APPROXIMATE percentage of patients completed follow up? Select ONE option only.

   A. 33
   B. 50
   C. 66
   D. 75
   E. 90

7. According to the recent prediction model study published by Betman et al, which SINGLE ONE of the following variables was NOT a significant predictor for undergoing multiple amputations? Select ONE option only.

   A. Male gender
   B. Medial artery calcification (MAC)
   C. Positive monofilament test (sensory loss)
   D. Lower toe pressures
   E. Wagner grade 3–5

8. According to Betman's prediction model, a 51-year-old woman with type diabetes has a low-risk score. She is defined as being at risk of 0.02 amputations per year.

   What is her predicted 10-year amputation rate? Select ONE option only.

   A. 0.02
   B. 0.2
   C. 0.5
   D. 2
   E. 5

9. According to Skoutas et al, which amputation site is MOST likely to be associated with a re-amputation risk in people with diabetes? Select ONE option only.

   A. Digit
   B. Forefoot
   C. Ankle
   D. Below-knee
   E. Above-knee

10. A 68-year-old woman with type 2 diabetes has a non-healing foot ulcer for 6 weeks. The practice nurse undertakes Doppler blood flow measurements.

    According to Betman et al, which ABPI result has the HIGHEST risk prediction score for multiple amputations? Select ONE option only.

    A. <0.5
    B. 0.5–0.79
    C. 0.8–0.99
    D. 1–1.29
    E. >1.3