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Diabetic foot ulcers in the Hong Kong Chinese population: retrospective study

香港華人中的糖尿病足潰瘍：回顧研究

Objective. To assess the predictive power of various parameters on the final outcome of ulcerated diabetic feet among the Hong Kong Chinese population.
Design. Retrospective cohort study.
Setting. Regional public hospital, Hong Kong.
Patients. Medical records of 340 diabetic patients with foot ulcers (535) who were referred to the Diabetic Foot Clinic between July 1995 and June 2000 were reviewed.
Main outcome measures. Demographic and clinical data, including assessment of the foot and blood parameters.
Results. Increasing age, wound depth, the presence of ischaemia, a low albumin level, and the lack of simultaneous ulceration were determined by stepwise logistic regression analysis to be the most significant independent predictors of an unfavourable outcome.
Conclusions. Major amputation is more likely to occur in elderly patients, with progressive wound depth, and in the presence of ischaemia. A low albumin level was also noted to be an independent predictor of major amputation in the population studied.

目的：評定各種參數對香港華人中患有糖尿病足潰瘍的最終結果的預期能力。
設計：回顧隊列性研究。
安排：香港地區公立醫院。
患者：1995年7月至2000年6月期間被轉介到糖尿病足門診部就診的340名糖尿病足潰瘍患者的535個個案。
主要結果測量：人口統計學和臨床數據，包括足評價和血參數。
結果：由逐步回歸分析確定出年齡增長、傷口深度、局部缺血症狀、低白蛋白水平和缺乏潰瘍，是不良結果的最顯著的獨立指標。
結論：截肢手術很可能出現在較年老、有累積傷口深度、及局部缺血的患者中。低白蛋白水平也是所研究人口中進行截肢手術的一個獨立指標。

Key words:
Amputation;
Diabetes mellitus;
Diabetic foot;
Hong Kong;
Prognosis

關鍵詞：
切斷術；
糖尿病；
糖尿病足；
香港；
預後

HKMJ 2001;7:350-5

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Introduction

Amputation for non-traumatic causes is a frequent outcome in the diabetic foot.[1] The life-time risk for American diabetics was estimated at 5% to 15%, 15 times that of the non-diabetic population.[2,3] Local data on amputation rates for the Hong Kong Chinese population is lacking. However, the trend to western lifestyles, together with the similarity in diabetic prevalence[4] and disease pattern[5] in Hong Kong and the US make it a reasonable assumption that amputation figures will also be similar between the two localities.[6,7]

Limb amputation has a major impact on the individual—not only in distorting body image,[8] but also with regard to loss of productivity,[9] increasing dependency, and the cost of medical care.[10,11] Growing awareness of the economic cost of limb amputation,[12] together with recognition of the need for more holistic medical care for the diabetic population, has stimulated interest in identifying and systematically obviating risk factors for limb loss.[13] In the past decade, reported factors associated with amputation have included demographic factors,[1,14] limb and wound clinical assessment parameters,[15,16] blood parameters,[1,17-19] and radiological investigations, including angiography.[20] There has been, however, no consensus reached with regard to critical prognostic factors.

The objective of this retrospective cohort study was to assess the predictive power of various parameters on the outcome of the ulcerated diabetic foot in Hong Kong Chinese patients. Parameters included demographic information, details of foot assessment, and blood parameters.

Subjects and methods

Subjects

Kwong Wah Hospital established a multidisciplinary Diabetic Foot Clinic as early as 1995. The Clinic operates as a tertiary referral centre and provides care for a catchment area of 600 000 residents.

A retrospective evaluation was undertaken of 535 ulcers in 340 diabetic Hong Kong Chinese seen at the Diabetic Foot Clinic from July 1995 to June 2000. Fifty-two patients receiving conservative treatment, who failed to attend follow-up appointments during the study period, were excluded.

Data collection

Demographic data were collected for 340 patients, including sex, age, type of diabetes, and duration since diagnosis. Blood was taken in 351 episodes, and all patients had undergone a standardised evaluation to assess wound depth, presence of ischaemia, sensory neuropathy, infection, and co-existing ulceration. This was conducted conjointly by an orthopaedic surgeon and a nurse specialist, both with a special interest in diabetic foot care. The worst ulcer was chosen as the representative lesion. Following presentation, the patients had received conservative treatment, including foot care education and wound dressing. At this point, they were also referred to a vascular surgeon, to assess the feasibility of revascularisation if indicated. Minor local debridement was offered by podiatrists if required. More aggressive surgical intervention was adopted only when consensus was reached among two specialists and an advanced trainee.

Review with respect to the main outcome measure of major amputation, revealed that 93 amputations at, or proximal to the midfoot level, were scheduled within 6 months of first presentation. Four patients requiring amputation were not medically fit for surgery and died within a 4-week period. Five further patients initially declined the proposed amputation, with four subsequently proceeding to surgery; the remaining patient was documented to have persistent ulceration.

Parameter definitions

The depth of ulcer was categorised as:

(1) grade 1—ulceration extending to subcutaneous tissue;
(2) grade 2—ulceration involving the joint capsule or tendon; and
(3) grade 3—ulceration extending into bone or within a joint.

Gangrenous toes have full thickness tissue loss, hence were classified as grade 3 ulcers by definition.[21] The diagnosis of infection was made on clinical grounds rather than based on laboratory assessment.

Classification of ischaemic status is a controversial issue. Assessment of ischaemia ranges from symptomatology and subjective clinical assessment—cool skin temperature and pale colour, positive Buerger test and palpability of the peripheral pulses—to sophisticated objective measurement of the ankle-brachial or toe-brachial index, transcutaneous oxygen tension, duplex vascular study, and magnetic resonance angiography. The 1999 International Consensus on the Diabetic Foot[22] suggested that ischaemic status be taken as present when the ankle-brachial index is less than 0.9. This measure of ischaemia was utilised in this study. Sensory neuropathy was determined by use of the Semmes-Weinstein 10 g nylon monofilament test over four plantar sites for both feet, as recommended by the Lower Extremity Amputation Prevention programme and others,[21,23-26] including the International Working Group on the Diabetic Foot.[2] Simultaneous ulceration was defined as more than one lesion over the ipsilateral foot during the observation period. The main outcome measure was a major amputation, at midfoot level or higher, proposed within 6 months of initial assessment.

Statistical analysis

The Statistical Package for Social Science (SPSS) [Windows version 9.0; SPSS Inc., Chicago, US] was used for statistical analysis. Categorical data for amputees

and patients treated conservatively were compared using the Chi squared test, with the significance level set at $P<0.05$. Data considered in this analysis included sex, type of diabetes, the presence of ischaemia, infection, sensory neuropathy, simultaneous ulceration, and wound depth.

Continuous scale data including age, duration since diagnosis of diabetes, and levels for albumin, haemoglobin, lymphocyte count, and HbA_1C were analysed using the Student's *t* test. A stepwise logistic regression model was then created to determine the most significant independent predictive factors for diabetic foot ulcer, and their odds ratios. The appropriateness of the resulting model was evaluated by the Hosmer-Lemeshow goodness-of-fit test (SPSS Inc., Chicago, US).

Results

A total of 103 (30.3%) major amputations were proposed in the 340 patients—46 (44.7%) in male patients and 57 (55.3%) in female patients. The age of patients who underwent major amputation ranged from 24 to 95 years (mean, 68 years). Forty-five (13.2%) patients had type 1 diabetes, while the remainder (86.8%) had type 2 diabetes. Time from diagnosis to presentation with foot ulceration varied from at diagnosis to more than 40 years post-diagnosis (mean, 7.1 years). Of the 340 presenting ulcers, 303 (89.1%) were infected, and 158 (46.5%) ischaemic. Approximately one third (32.9%) of patients had more than one lesion evident on the ulcerated foot.

Sex ($P_{sex}=0.712$), type of diabetes ($P_{type}=0.840$), duration of diabetes ($P_{time\ elapse}=0.069$), and HbA_1C level ($P_{HbA1C}=0.962$), were not associated with outcome. The age of the patient was shown to be a significant determinant ($P_{age}<0.0005$) of outcome, however. Albumin level, haemoglobin level, and lymphocyte count were also shown to correlate with the outcome ($P_{alb}<0.0005$, $P_{Hb}<0.0005$, $P_{lymphocyte}=0.024$, respectively). A significant correlation between wound depth ($P_{depth}<0.0005$), infection ($P_{infection}<0.0005$), the presence of ischaemia ($P_{ischaemia}<0.0005$), and sensory neuropathy ($P_{neuropathy}=0.008$) and final outcome was also seen (Table 1).

Table 1. Characteristics of the study population on referral

		Amputation		P value
		No*	Yes*	
Sex	Male	111 (70.7)	46 (29.3)	0.712
	Female	126 (68.9)	57 (31.1)	
	Total	**237 (69.7)**	**103 (30.3)**	
Age (years)	No. of patients	237	103	<0.0005
	Mean (SD)	67.25 (11.54)	74.41 (10.28)	
Type of diabetes	Type 1	32 (71.1%)	13 (28.9%)	0.840
	Type 2	205 (69.5%)	90 (30.5%)	
	Total	**236 (69.8%)**	**102 (30.2%)**	
Time since diagnosis (years)	No. of patients	204	73	0.069
	Mean (SD)	8.61 (7.15)	10.49 (8.55)	
Ischaemia	No	148 (81.3)	34 (18.7)	<0.0005
	Yes	89 (56.3)	69 (43.7)	
	Total	**237 (69.7)**	**103 (30.3)**	
Neuropathy	No	48 (84.2)	9 (15.8)	0.008
	Yes	177 (66.3)	90 (33.7)	
	Total	**225 (69.4)**	**99 (30.6)**	
Infection	No	36 (97.3)	1 (2.7)	0.0005
	Yes	201 (66.3)	102 (33.7)	
	Total	**237 (69.7)**	**103 (30.3)**	
Wound depth	Grade 1	43 (100)	0 (0)	<0.0005
	Grade 2	107 (90.7)	11 (9.3)	
	Grade 3	87 (48.6)	92 (51.4)	
	Total	**237 (69.7)**	**103 (30.3)**	
Multiple simultaneous ulcers	No	154 (67.5)	74 (32.5)	0.216
	Yes	83 (74.1)	29 (25.9)	
	Total	**237 (69.7)**	**103 (30.3)**	
Albumin (g/L)	Level	218	98	<0.0005
	Mean (SD)	34.97 (6.19)	29.32 (6.36)	
Haemoglobin (g/L)	Level	222	98	<0.0005
	Mean (SD)	114.0 (21.0)	102.8 (16.8)	
Lymphocyte count ($x10^9$ /L)	No. of patients	149	79	0.024
	Mean (SD)	1.57 (0.58)	1.38 (0.63)	
HbA_1C (%)	No. of patients	136	60	0.962
	Mean (SD)	9.19 (2.93)	9.21 (3.51)	

* Results are expressed as No. (%) except where indicated

Table 2. Stepwise logistic regression analysis adjusting for age

Factors	Odds ratio (95% CI)
Wound depth	14.44 (6.43-32.44) (grade 3 versus 1 and 2)
Ischaemia	2.32 (1.19-4.52)
Age	1.068 (1.033-1.105)
Albumin	0.86 (0.81-0.91)
Multiple ulcers	0.46 (0.23-0.92)

A stepwise logistic regression model was then created to determine the most significant independent predictors of wound outcome. Results are shown in Table 2. The Hosmer-Lemeshow goodness-of-fit test statistic (4.733 with 8 degrees of freedom, P=0.786) did not indicate the model created was an inappropriate fit for the data.

Age, wound depth, ischaemic status, and albumin level were selected as independent predictors of the main outcome measure. With elimination of confounding factors, multiplicity of ulceration was also found to correlate with outcome. Haemoglobin level and lymphocyte count, as well as infection status and neuropathy were deemed dependent predictors.

Discussion

This retrospective cohort study identified five independent predictors for major amputation, namely age, wound depth, presence of ischaemia, albumin level, and multiplicity of ulcer. Presence of infection, neuropathy and blood parameters, specifically lymphocyte count and haemoglobin level, were dependent risk factors for the ultimate amputation, that is, these latter factors correlated with the outcome by association with other factors. Sex, duration and type of diabetes, and HbA_1C levels were not correlated with final outcome.

The correlation seen between amputation and deeper wound depth, as well as the presence of ischaemia of the affected limb is not surprising. Older age is well known to be associated with both neuropathic ulcer,[27,28] and peripheral vascular disease.[29] The association between age and the risk of amputation has not been reported in some research,[26,30] however, these studies used a cut-off point of the age of 75 years to divide subjects into subgroups. The authors claimed that subjects living until their eighties were relatively more healthy than their younger counterparts. In their corresponding population mortality study,[2,31] however, no excessive mortality was seen to support use of the cut-off age and the authors' assertion.[32] In addition, the reluctance of surgeons to operate on the older elderly was not considered.[33] In this study, amputees were found to have a mean age of 74 years, compared with 67 years for patients with salvaged limbs. Had the earlier studies mentioned used age data as a continuous scale rather than as categorical data, it is possible that the association noted in this study would have been observed. A low albumin level was shown to be an independent risk factor for amputation in concordance with a previous published report.[3]

Male sex has been reported to be associated with a poorer outcome in studies completed in the West.[1,14,17,26] In this study, however, males were not shown to be at higher risk. Similarly, duration of diabetes,[34-38] type of diabetes,[30] and glycosylated haemoglobin level[1,39,40] have been reported as risk factors but were not shown to be significant risk factors in this study. A possible explanation for the current findings is that the detrimental effect of pre-existing poor diabetic control at the entry point of the study was off-set by the more aggressive treatment during the time of follow-up.

The presence of sensory neuropathy and infection correlated with a poorer outcome, a point of almost universal agreement among scholars and studies.[22] However, unexpectedly they were found to have no independent effect on the final outcome as determined by statistical analysis. It has been suggested that although the presence of neuropathy may precipitate an ulcer, it is the vasculopathy that inhibits the ulcer from healing.[30] Further, with modern potent antimicrobial therapy, the presence of infection should be controllable if the delivery of the drug, that is vascular supply, is not jeopardised. This may explain their position as dependent rather than independent risk factors.

Haemoglobin level was not shown to be an independent risk factor despite its well-known association with chronic ill health.[39,41,42] Previous studies have shown that a lower haemoglobin level is associated with major amputation.[19,43] Possibly the high prevalence of thalassaemia in local Hong Kong Chinese[44] may have a bearing on this finding. Also relevant is that the degree of anaemia is not in proportion to the severity of diabetic disease.

Lymphocyte count has long been suggested as a laboratory index of nutritional status and immunological competence. Its association with amputation was established in a study by Kay et al.[45] The results of this study agree with Kay et al's findings and suggest that the correlation observed is based on an association with other factors.

Table 3. Cross tabulation of multiple ulcers versus wound depth*

		Wound depth No. (%)			Total
		Grade 1	Grade 2	Grade 3	
Multiple ulcers	No	35 (81.4)	87 (73.7)	106 (59.2)	228 (67.1)
	Yes	8 (18.6)	31 (26.3)	73 (40.8)	112 (32.9)
Total		43 (100)	118 (100)	179 (100)	340 (100)

* P=0.003

Multiplicity of ulceration was associated with deeper ulcers (Table 3). A 'protective' effect offered by the presence of simultaneous lesions was noted on statistical analysis. This appears to be a chance finding in the absence of any more obvious explanation.

Limitations of the study

The follow-up period was selected arbitrarily as 6 months, thus failing to take into account any non-healing ulcers resulting in amputation after this time. In addition, as subjects were selected from a tertiary referral clinic registry, they may differ from patients seen in general practice, and generalisation of study findings to all diabetic foot ulcers might be erroneous.

Conclusions

The outcome for diabetic foot ulcer is poorer in elderly patients and with progressive wound depth. The presence of ischaemia and a low albumin level makes the outcome of major amputation more likely. Surprisingly, the presence of simultaneous ulceration was seen to be negatively associated with major amputation within the 6-month study period. Possibly however, patients with simultaneous ulceration may have undergone amputation at a later time, after the observation period.

Short of prevention of diabetes itself, this study along with others implies that early intervention before the ulcer has penetrated deeply,[12,13,46-48] more aggressive management of ischaemia by referral of patients to vascular surgeons for possible bypass[49] or other intervention,[50] and better attention to nutritional status,[51] might help prevent major amputation, although the evidence from the current study is indirect. At the same time, this study indicates that the presence of infection, neuropathy, anaemia, and chronicity and difficulty in disease control in itself should not preclude the pursuit of limb conserving treatment options.

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