

Risk Factors for Postsurgical Diabetic Foot Recurrence after Minor or Major Lower-Limb's Amputation

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Abstract

Background: Many previous studies on diabetic foot focus on ulceration and amputation, but few studies took on recurrent ulcer or wound infection with several years' follow-up after amputations and studying risk factors such as peripheral arterial disease (PAD), renal disease, cardiovascular disease, and environmental factors which may play a role and explain for that disease recurrence. **Aim:** The aim of this study was to assess the risk of recurrence of diabetic foot disease after different level of amputations. **Patients and Methods:** A prospective study was conducted for 32 patients presented with diabetic foot disease. This study started from September 2011 up to December 2016. Those patients who admitted for (minor or major) amputation with risk factor diseases were studied and followed up for any recurrence. **Results:** Among 32 patients, 17 cases did minor amputation (53.1%), whereas 15 cases (46.9%) did major amputations. The number of patients who developed recurrence was 11 cases distributed, as 8 cases (25%) developed wound infection and other 3 cases (9.4%) developed ulceration. Seven cases of those who developed wound infection (87.5%) after amputation had PAD. All patients who complained recurrent ulceration (100%) had PAD risk factor with $P = 0.0001^*$. Two cases (25%) of those with wound infection and also one case with ulceration had renal disease with $P = 0.039^*$. **Conclusion:** PAD, renal disease, and renal failure have significant risk factors for recurrence of wound infection and ulceration after diabetic foot–limb amputation.

Keywords: Amputation, diabetic foot, recurrence, risk factors

INTRODUCTION

The diabetic patients presented with gangrenous feet or limbs are not different from the patient suffers from incurable cancers. Those patients frequently presented late; therefore, in spite of doing operation properly, there may be recurrence or local spread of gangrene to the same limb. Hence, we consider a diabetic foot ulcer as malignant disease and the recurrence of limb gangrene as metastasis.^[1] In previous studies of recurrent ulceration after amputation shows vascular disorders and foot and joint abnormalities are important risk factors.^[2] Fifteen percent of the diabetic patients eventually suffer from foot ulceration; therefore, targeting those patients, lowers the chances to progress to end-stage disease.^[3]

The global prevalence of diabetes was estimated 2.8% in 2000 and expected to increase to 4.4% in 2030, that means, more than 366 million people will suffer from diabetes mellitus by that year. Diabetic foot ulcer complicates this disease in more than 15% of those patients during their lifetime.^[4]

Many previous studies on diabetic foot focus on ulceration and amputation, but few studies took on new (recurrent) ulcer after amputation, several years' follow-up, and correlation with risk factors (peripheral arterial disease [PAD], renal disease, cardiovascular disease, and environmental factors others) for those patients whose play a role for that recurrence.^[5] Therefore by predicting who at risk for developing recurrence and correction of these factors can reduce lower limb recurrence of ulceration and surgical complications.^[6]

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Foot ulceration may end with infection or gangrene; therefore, recurrent ulceration will significantly burden long-term costs for diabetic foot care.^[7]

The question why some diabetic patients with ulceration need lower-limb amputation, while other heals; previous studies reveal a duration of the disease, previous amputation, poor diabetes control, obesity, increasing age, and renal impairment as the probable causative factors. However, different studies show different results and the published articles that identify such risk factors for diabetes-related lower-limb amputation are limited.^[8]

It had been stated that every 30 s, there were somewhere in the world, a lower extremity is amputated due to diabetes mellitus.^[9]

We designed the study to assess the risk of recurrence of diabetic foot disease in form (ulceration, infection) after minor or major amputation.

PATIENTS AND METHODS

This study is a prospective study conducted from September 2011 to December 2016 over a period of 5 years.

Inclusion and exclusion criteria

All cases of trauma causation of amputation are excluded. All cases of diabetic neuropathy ulceration are excluded. The diabetic patients who presented with foot ulcer and were treated conservatively or by simple wound excision are also excluded from the study.

Reulceration is defined as an ulceration at the same level of the previous ulcer, whereas recurrent ulcer defined any secondary ulcer regardless of its location.^[10]

A total of 32 cases were selected; among whom, 17 cases had minor amputation, while the remaining 15 cases underwent major amputations.

The demographic factors such as age, sex, and surgical history of diabetic foot ulcer and past medical history of hyperlipidemia and obesity and other comorbid illness such as hypertension, asthma, cerebrovascular disease, coronary artery disease, and heart failure were studied.

Other factors were evaluated to determine the level of amputation: (type of diabetes treatment [insulin, oral tablet]), the patient glycemic control by HbA1c%, other diabetic-related complications such as PAD including acute and chronic arterial limb occlusion or insufficiency by Doppler study of lower limb, nephropathy by renal function and general urine examination (GUE) for sugar, albumin, and urinary tract infection (if the patient on chronic hemodialysis or after nephrologist consultation). Usually, the patients with diabetic foot presented with anemia need correction of their anemic state.

All the patients sent for foot X-ray looking for osteomyelitis and any signs of gas gangrene or bony destruction.

After the operations, all the patients' follow-up visits were recorded and managed in the form of local wound care (change dressing, removal of stitches, using MEBO or other ointments, gel or lotions, control level of sugar by medication, correction of anemia, calcium supplement, and iron and folic acid in patient with renal impairment).

In this study, all the patients' wounds were examined and noticed for any diabetic foot recurrence and looking for any ulceration or nonhealing wound, any discharge, any sign of black discoloration of the amputee with repeating X-ray, repeating Doppler study for vascular assessment, and repeating the laboratory investigations to those who showing any of the above signs of recurrence.

Statistical analysis

Analysis of data was carried out using the available statistical package of Statistical Package for the Social Sciences Version 24 (IBM, Chicago, Illinois, USA).

Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

The significance of difference of different percentages (qualitative data) was tested using Pearson Chi-square test (two tests) with application of Yate's correction or Fisher's exact test whenever applicable. Statistical significance was considered whenever $P \leq 0.05$.

RESULTS

In this study, the patients were distributed according to the age and sex and type of their treatments for diabetes mellitus and any added local gel; ointments were used to improve the local wound healing after amputations and regarding age distribution, most of the patients were between 60-69 years, for gender, male patients were 22 while female patients were

Table 1: Distribution of demographic factors

	<i>n</i> (%)
Age (years)	
<50	8 (25.0)
50-59	7 (21.9)
60-69	11 (34.4)
≥70	6 (18.8)
Mean±SD (range)	59.4±10.8 (43-80)
Gender	
Male	22 (68.75)
Female	10 (31.25)
Type of treatment	
OHA	11 (34.4)
Insulin	20 (62.5)
OHA and insulin	1 (3.1)
Ointments, lotions, gels used	
Mebo	15 (46.9)
Others	17 (53.1)

SD: Standard deviation, OHA: Oral hypoglycemic agents

10. Most of the patients were on insulin therapy 20 (62.5%), as shown in Table 1.

The number of patients did minor amputations was 17 cases (53.1%) (six of them were in the big toe), while the remaining 15 cases (46.9%) did major amputations distributed as 10 cases (66.66%) above the knee and 5 cases below the knee (33.33%), as shown in Tables 2 and 3. In this study, 11 cases (34.4%) from that 32 cases who did amputations developed complications distributed into 8 cases (72.72%) developed wound infection and 3 cases (27.28%) developed recurrent ulceration as shown in Table 3.

The predominant risk factor in this study was PAD (peripheral arterial disease) found in 13 cases (40.6%), other risk factors such as renal disease and failure were 3 cases (9.4%) as shown in Table 4.

Table 2: Frequency and distribution of minor amputation

	<i>n (%)</i>
Minor amputation (toe)	
Yes	17 (53.1)
No	15 (46.9)
Minor amputation (toe)	
First big toe ulcer	6
First and second toes	4
Three fingers	1
Four fingers	1
Five fingers (blisters, ulcers in distal phalanges)	4
Bilateral foot ulceration	1

Table 3: Distribution of amputation and subsequent complication

	<i>n (%)</i>
Amputation	
Above the knee	10 (31.3)
Below the knee	5 (15.6)
Minor	17 (53.1)
Type of complication	
Wound infection	8 (25.0)
Ulceration	3 (9.4)
No	21 (65.6)

Table 4: Distribution of risk factors

	<i>n (%)</i>
PAD	13 (40.6)
Hypertension	10 (31.3)
Hyperlipidemia and obesity	7 (21.9)
Renal disease and failure	3 (9.4)
Previous amputation on opposite side	5 (15.6)
CVA	3 (9.4)
Other*	7 (21.9)

*Other includes four smokers, two retinopathy, and one IHD. PAD: Peripheral arterial disease, CVA: Coronary artery disease, IHD: Ischemic heart disease

In this study, there was statistical difference between type of complication with only one of the demographic factor which is age of the patients; in a form, that only one case whose age is <50 years developed wound infection (12.5%) while seven cases (87.5%) from total 8 cases who developed wound infection, their age were more than 50 years, while 2 out of 3 cases who develop ulceration their age was more than 50 and a case with age younger than 50.

Other demographic factors such as gender, type of treatment like oral hypoglycemic drug, insulin, or combined show no statistical differences, as shown in Table 5.

In addition, there was no statistical correlation between the type of amputations and development of complications, as four cases (23.5%) from a total of 17 cases who did minor amputations developed wound infection, 1 case only (5.9%) develop ulceration, while from those who did above knee; 3 (30%) from 10 cases developed wound infection with no ulceration. Regarding below the knee, 1 case (20%) developed wound infection and 2 cases developed recurrent ulceration from total 5 cases as shown in Table 5.

Furthermore, there was no statistical difference between the type of amputations whether minor or major with diseases risk factors as shown in Tables 6 and 7.

In this article, there was a statistical significance between PAD risk factor and risk of recurrence and wound infection in a form that 7 cases (87.5%) from total 8 cases developed wound infection, 3 cases (100%) developed recurrent ulceration with $P = 0.0001^*$, as shown in Table 8.

The second risk factor is the renal disease and failure; the results showed that 2 out of 8 cases (25%) developed wound infection, 1 out of 3 case (33.3%) developed recurrent ulceration; $P = 0.039^*$ was statistically significant, as shown in Table 8.

DISCUSSION

Diabetes is a debilitating disease; diabetic patients have 1.5–2.5-time fold higher risk of death at any age compared to nondiabetic persons, and also the prevalence of diabetes has been increased due to increase in socioeconomic state with lifestyle and diet changes for high-carbohydrate caloric diet and fast food.^[11] There is complexity of factors related to the outcome of patients after amputations.^[9] Hence, evaluation of these factors is important to improve the results after surgery and prevent future recurrence.

In our study, we try to focus on different factors and their effect on recurrence of disease after operation. Most of the previous studies were focusing on the effects of factors before the surgery; few studies till now and our recent study tries to assess the recurrence after surgical intervention. Many previous studies documented their management of diabetic feet and their success in preventing amputation in the future.^[12]

Table 5: Frequency of complication

	Type of complication			P
	Wound infection, n (%)	Ulceration, n (%)	No complication, n (%)	
Age (years)				
<50	1 (12.5)	1 (12.5)	6 (75)	0.041*
50-59	5 (71.4)	-	2 (28.6)	
60-69	2 (18.2)	2 (18.2)	7 (63.6)	
≥70	-	-	6 (100)	
Gender				
Male	6 (27.3)	2 (9.1)	14 (63.6)	0.908
Female	2 (20.0)	1 (10.0)	7 (70.0)	
Type of treatment				
OHA	2 (18.2)	1 (9.1)	8 (72.7)	0.891
Insulin	6 (30.0)	2 (10.0)	12 (60.0)	
OHA and insulin	-	-	1 (100)	
Drugs used				
Mebo	2 (13.3)	2 (13.3)	11 (73.3)	0.322
No	6 (35.3)	1 (5.9)	10 (58.8)	
Minor amputation (toe)				
Mebo	4 (23.5)	1 (5.9)	12 (70.6)	0.726
No	4 (26.7)	2 (13.3)	9 (60.0)	
Amputation				
Above the knee	3 (30.0)	-	7 (70.0)	0.140
Below the knee	1 (20.0)	2 (40.0)	2 (40.0)	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level. OHA: Oral hypoglycemic agents

Table 6: Correlation between risk factors and minor amputation

	Minor amputation (toe)		P
	Yes, n (%)	No, n (%)	
PAD			
Yes	5 (29.4)	8 (53.3)	0.169
No	12 (70.6)	7 (46.7)	
Hypertension			
Yes	7 (41.2)	3 (20.0)	0.197
No	10 (58.8)	12 (80.0)	
Hyperlipidemia and obesity			
Yes	4 (23.5)	3 (20.0)	0.810
No	13 (76.5)	12 (80.0)	
Renal disease and failure			
Yes	2 (11.8)	1 (6.7)	0.621
No	15 (88.2)	14 (93.3)	
Previous amputation on the opposite side			
Yes	3 (17.6)	2 (13.3)	0.737
No	14 (82.4)	13 (86.7)	
CVA			
Yes	2 (11.8)	1 (6.7)	0.621
No	15 (88.2)	14 (93.3)	
Other			
Yes	5 (29.4)	2 (13.3)	0.272
No	12 (70.6)	13 (86.7)	
Other types			
Smoking	2 (40.0)	2 (100.0)	-
Retinopathy	2 (40.0)	-	
IHD	1 (20.0)	-	

* Means significant difference etc.. between proportions using Pearson Chi-square test at 0.05 level. PAD: Peripheral arterial disease, CVA: Coronary artery disease, IHD: Ischemic heart disease

Table 7: Correlation between risk factors and minor amputation

	Amputation			P
	Above knee, n (%)	Below knee, n (%)	Minor, n (%)	
PAD				
Yes	4 (40.0)	4 (80.0)	5 (29.4)	0.129
No	6 (60.0)	1 (20.0)	12 (70.6)	
Hypertension				
Yes	2 (20.0)	1 (20.0)	7 (41.2)	0.435
No	8 (80.0)	4 (80.0)	10 (58.8)	
Hyperlipidemia and obesity				
Yes	2 (20.0)	1 (20.0)	4 (23.5)	0.971
No	8 (80.0)	4 (80.0)	13 (76.5)	
Renal disease and failure				
Yes	1 (10.0)	-	2 (11.8)	0.728
No	9 (90.0)	5 (100)	15 (88.2)	
Previous amputation on opposite side				
Yes	-	2 (40.0)	3 (17.6)	0.125
No	10 (100)	3 (60.0)	14 (82.4)	
CVA				
Yes	1 (10.0)	-	2 (11.8)	0.728
No	9 (90.0)	5 (100)	15 (88.2)	
Other				
Yes	-	2 (40.0)	5 (29.4)	0.115
No	10 (100)	3 (60.0)	12 (70.6)	
Others type				
Smoking	-	2 (100)	2 (40.0)	
Retinopathy	-	-	2 (40.0)	
IHD	-	-	1 (20.0)	

* Means significant difference etc., between proportions using Pearson Chi-square test at 0.05 level. PAD: Peripheral arterial disease, CVA: Coronary artery disease, IHD: Ischemic heart disease

Our study is focusing on postamputation period as the patients should adopt on the change of their life, for example, depend on crutches and wheelchairs, the hope of the patient to prepare their amputee for artificial limb prosthesis. Hence, any recurrence of the disease will bring frustrations to those patients; in addition to that, most of those patients need time after surgery for complete healing of their wounds.

Many risk factors for amputation have been cited in the papers. Carlson *et al.*^[13] demonstrate that digital deformity, diabetic neuropathy, and ischemia significantly increase amputation rate. Markowitz *et al.*^[14] in a retrospective case-control study observed that amputation was significantly increased by male gender, renal disease, and peripheral vascular disease. Chaturvedi *et al.*^[15] stated that retinopathy, PAD with hyperglycemia, and triglyceridemia are themselves risk for amputations. Miyajima *et al.*^[16] reported that PAD, hemodialysis, and increased HbA1c were risk factors for major amputation. Abolfazl Shojaiefard *et al.*^[12] concluded nephropathy, ischemic diabetic foot, and first fasting blood glucose >200 mg/dl are independent predictors of limb amputation in patients hospitalized for diabetic foot lesions. Lavery *et al.*^[2] have been concluded from the study on 225 patient for risk factors for foot ulceration that neuropathy, foot deformity, high planter pressure, and history of amputation are significantly associated with the presence of foot ulceration,

while vascular disease and renal disease although delay wound healing, they are not significant risk factors.

In this study, our result showed significant increase risk of recurrence of wound infection and ulceration in patients with PAD and renal disease and age more than 50 years, whereas other risk factors such as hypertension, hyperlipidemia, and obesity failed to show any association with recurrence of the disease. The explanation regarding vascular disease has been cited and agreed by many authors that the diabetic patient has poor blood flow and this essential for healing and reaching of antibiotic to treat the severe infection that attacks the amputee, and there is impossible spontaneous revascularization.^[12,14,15] Our explanation for renal disease is compatible with Prompers *et al.*^[17] that renal disease and renal failure is poor prognostic factors for wound healing and also poor host-defense mechanism for more resistant microorganism; if the patient had both PAD and renal disease on hemodialysis, this accompanied by diffuse microcalcification for both leg and foot arteries, this will impair microvasculature, and this will lead to the recurrence of disease. Regarding age factor and its significance, it is explained by increase in atherosclerosis of the vessels, increase in impairment of renal function, increase in weight due to lack of physical activity after retirement, and also

Table 8: Correlation between risk factors and complications

	Type of complication			P
	Wound infection, n (%)	Ulceration, n (%)	No, n (%)	
PAD				
Yes	7 (87.5)	3 (100)	3 (14.3)	0.0001*
No	1 (12.5)	-	18 (85.7)	
Hypertension				
Yes	2 (25.0)	1 (33.3)	7 (33.3)	0.908
No	6 (75.0)	2 (66.7)	14 (66.7)	
Hyperlipidemia and obesity				
Yes	3 (37.5)	1 (33.3)	3 (14.3)	0.353
No	5 (62.5)	2 (66.7)	18 (85.7)	
Renal disease and failure				
Yes	2 (25.0)	1 (33.3)	-	0.039*
No	6 (75.0)	2 (66.7)	21 (100)	
Previous amputation on the opposite side				
Yes	1 (12.5)	1 (33.3)	3 (14.3)	0.670
No	7 (87.5)	2 (66.7)	18 (85.7)	
CVA				
Yes	1 (12.5)	-	2 (9.5)	0.818
No	7 (87.5)	3 (100)	19 (90.5)	
Other				
Yes	1 (12.5)	1 (33.3)	5 (23.8)	0.709
No	7 (87.5)	2 (66.7)	16 (76.2)	
Other types				
Smoking	1 (100)	1 (100)	2 (40.0)	-
Retinopathy	-	-	2 (40.0)	
IHD	-	-	1 (20.0)	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level. PAD: Peripheral arterial disease, CVA: Coronary artery disease, IHD: Ischemic heart disease

neglecting foot care from the patient and the family leading to increase the chance of recurrence after amputation.

Limitation of this study

1. Diabetic neuropathic patients were excluded from this study, this is due to nonavailability of tests to measure the diabetic sensory perception, for example, monofilament tests for pressure sensation and also vibration perception threshold test using biothesiometer,^[18] this had led to decreasing number of patients in this study
2. Adding patient with foot deformity for risk factors of diabetic foot recurrence, especially after minor amputations.

Recommendations

1. Constituting a tertiary referral hospital center includes patients' data collection to treat complex diabetic foot and ankle disease with multidisciplinary team (diabetologist, nephrologist, microbiologist, radiologist, physiotherapist, and for limb prosthesis designer postamputation), all work with coordination with surgeons
2. Focusing on early case of diabetic foot ulceration due to PAD with detection mild narrowing and stenosis with the availability of portable hand Doppler assist test for surgeon with measuring Ankle–Brachial Index, this open way for

endostenting or vascular grafting for revascularization and prevents amputation

3. Foot care in a diabetic foot clinic, especially for those among elderly and illiterate patient or those whom blind or foot deformity by encouraging them to wear diabetic medical special shoes adding topical gels or cream for rough and dry skin area.

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Conflicts of interest

There are no conflicts of interest.

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