Predictors of further intervention after toe amputation in people with diabetes

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Article points

1. Toe amputation is the most common distal amputation of the foot used mainly to preserve the maximal mobility in patients who need surgical intervention.
2. This study aimed to determine the predictors of further intervention after toe amputation that may help in optimising and individualising the patient's treatment plan.

Key words

- Diabetic foot
- Toe amputation
- Wound healing

Authors

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Background: Diabetic foot is a major cause of morbidity among diabetic patients. Toe amputation is the most common distal amputation of the foot used mainly to preserve the maximal mobility in patients who need surgical intervention. Aim: This study aimed to determine the predictors of further intervention after toe amputation that may help in optimising and individualising the treatment plan. Methods: The authors retrospectively reviewed the results of 85 toe amputations for diabetic foot ulcers treated in a tertiary medical centre in Lebanon from 2008 to 2017. The outcome endpoint was requiring further intervention, either debridement or more proximal amputation. Results: Eighty-five patients (65 males, 20 females) with a mean age of 67 ± 12 years and a mean duration of diabetes of 18 ± 7 years were enrolled. Eighteen patients were lost to follow up. Out of the remaining 67 patients, 48 did not require further intervention and 19 did. Those who required further intervention were older and had more incidence of peripheral arterial disease (*P*=0.026 and 0.012 respectively). Toe pressure and Toe Brachial Index were significantly higher in the patients who did not require further intervention (*P*=0.027 for both). No difference was found between the two groups regarding glycemic control or glycosylated hemoglobin value. However, patients treated with insulin had a lower further intervention rate compared to those treated with oral antidiabetics only (OR: 0.245, *P*=0.026) and delayed primary closure was associated with lower further intervention rate compared to primary closure (OR: 0.147, *P*=0.027). Conclusion: Older age and low toe pressure were the main predictors of requiring further intervention after toe amputation. Diabetes treatment with insulin was associated with lower further intervention rates. Delayed primary closure was the preferred surgical wound closure option with the lowest further intervention rates.

Diabetic foot ulceration (DFU) is a common complication of diabetes that affects 15% of diabetic patients during their lifetimes (Amin and Doupis, 2016). Approximately 30% of patients with diabetic foot will need a minor amputation (Acar and Kacıra, 2017). Wound healing after minor amputation will save the patient's functional capacity and eliminates the need for prosthetic devices (Caruana et al, 2015). Thus the ability to predict wound healing after minor amputation will enable health care providers to make the proper choice of the amputation level reducing the need for amputation revision or amputation at a higher level The aim of this study was to identify the significant differences between the patients who needed further intervention after toe amputation and those who did not.

Patients and methods

This is a single-centre retrospective study of all patients who were admitted to the American University of Beirut Medical Center (AUBMC) in Beirut, Lebanon, with DFU and underwent toe amputation between January 2008 and June 2017. The charts of these patients were identified and reviewed. Any amputation performed for another reason, such as trauma or tumor and any more proximal amputation level were excluded from the study.

By reviewing the medical records, data were obtained about the general characteristics of the patients including age, gender, origin, Body Mass Index (BMI), and comorbidities (hypertension, dyslipidemia, chronic kidney disease, coronary artery disease, congestive heart failure). Diabetes history was reported including type, duration, treatment with oral medications only or with insulin and diabetes complications such as sensory neuropathy and peripheral artery disease.

Diabetic ulcers were classified according to the depth of the wound using the Wagner-Meggit classification (Jeon et al, 2017). The pathophysiologic status of the diabetic ulcers was also reported as neuropathic, neuro-ischemic or ischemic. The wound infectious status was classified according to the IWGDF and IDSA criteria (Lavery et al, 2007). Samples were obtained for culture by swabbing of the ulcer (swab culture) or deep tissue or bone biopsy (tissue culture). Antibiotics were given in consultation with the infectious diseases specialists. Empirical parenteral treatment was changed according to the culture results and antibiogram. Patients continued their antibiotic course after discharge.

Patients underwent a variety of different evaluations during their admission, including physical examination, Doppler ultrasonography, Duplex scan, plain X-ray of the foot, and in a few cases, magnetic

Page points

1. This was a retrospective study of all patients admitted with diabetic foot ulceration who underwent toe amputation in a single centre.
2. All relevant clinical and descriptive data were collected from the Electronic Medical Records.
3. The main outcome was whether further treatment was required — either debridement of the wound or more proximal amputation.

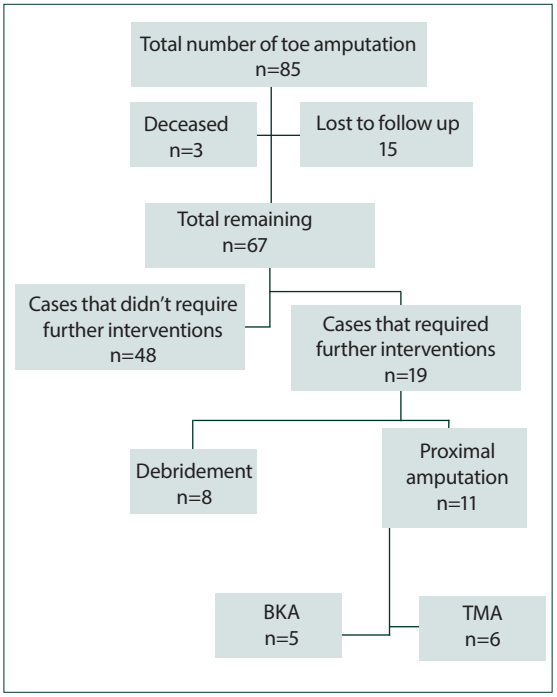

Figure 1. Flow chart showing the outcomes of 85 patients who underwent toe amputation.

resonance imaging (MRI). Various laboratory tests were done including; Glucose level, Glycosylated hemoglobin (HBA_{1C}), C-reactive Protein (CRP) and kidney function test.

Osteomyelitis was assessed by the presence of one of four determinants; plain X-ray finding indicative of osteomyelitis, MRI findings when available, positive bone culture or positive pathology results. Ankle Brachial Index (ABI) <0.9 or Toe Brachial Index (TBI) <0.7 diagnosed PAD when Doppler was done, and we depended on clinical assessment when Doppler was not done. Vascular surgeons evaluated the patients and vascular revascularisation such as balloon angioplasty or bypass was done when indicated.

The vascular surgeons's strategy was as follows: patients with poor blood supply were typically managed by attempted revascularisation followed by toe amputation unless the infectious process necessitated urgent/emergent toe amputation and foot debridement. Such patients underwent revascularisation after the amputation. Patients with good blood supply as evidenced by palpable pedal pulses or toe pressures greater than 50 mmHg underwent toe amputation first. Similarly, patients with borderline blood supply as evidenced by toe pressures between 30–50 mmHg underwent toe amputation first followed by wound assessment to determine further need for revascularisation.

All patients underwent toe amputation with or without excision of the metatarsal head depending on the extent of the infectious process. The wound was closed by primary closure in the same operation or delayed primary closure where the wound was not closed and packed with antibiotic gel for (1–3) days then taken back to the operating room where the wound was irrigated and closed primarily. In secondary closure, the wound was left to heal by secondary intension or with a skin graft at a later time. Patients with moderate to severe infections were not offered primary closure.

Statistical analysis:

Patients' data were entered and analysed using SPSS 24.0. Comparison between groups characteristics were made with chi-square test or student's t test. Binary logistic regression was used to calculate the odds ratio (OR) with a 95% confidence interval (CI). Statistical significance was defined at the 5 % ($P \leq .05$) level.

Results

Patients' demographics

Out of 384 patients admitted to AUBMC with the diagnosis of DFU, 85 (22%) patients underwent toe amputation including toe amputation at the proximal phalangeal level in 65 (76%) patients and ray amputation in 20 (24%) patients. *Table 1* shows the general characteristics of the patients upon admission.

Management and follow up

Out of the 85 patients who underwent toe amputation, 22 (26%) patients had multiple toes amputation and the rest had amputation of one toe, most commonly the first toe in 29 (34%) patients. The wound was closed using three strategies including; primary closure in the same operation in 28 (33%) patients, delayed primary closure after few days in 20 (24%) patients and the wound was left open to heal by secondary intervention in 37 (44%) patients.

All the patients received parenteral antibiotics according to the infectious diseases specialists' consultation. Angiography was done in 18(21%) patients and accordingly some patients underwent different vascular interventions including balloon angioplasty in 9 (11%) patients and Bypass surgery in 8 (9%) patients.

In this study, 3 (4%) patients died (two due to cardiac causes and 1 due to uro-sepsis) and 15 (18%) patients were lost to follow up. From the remaining 67 patients, 19 patients required further intervention. Of these, 11 patients required more proximal amputation including Below Knee Amputation (BKA) in five patients and Trans Metatarsal Amputation (TMA) in six patients and eight patients underwent further debridement and ultimately healed (*Figure 1*).

Predictors of further intervention

Forty-eight (72%) did not require further intervention, and 19 (28%) patients did. Compared to the no-further intervention group, the further intervention group patients were significantly older (*P*=0.026), and were more frequently on oral antidiabetic medications only (*P*=0.021). No significant difference between the two groups based on comorbidities or glycemic control was observed.

The further intervention group had significantly higher frequency of peripheral vascular disease (*P*=0.012). In order to assess vascular parameters we excluded the patients who underwent vascular interventions (Angioplasty or bypass surgery) as the perfusion to the foot would have altered significantly from the baseline tests done preoperatively and there was no documented Doppler results post vascular interventions. We found that Toe pressure (TP) and Toe Brachial index (TBI) were significantly lower in the further intervention group (*P*=0.027 for both), whereas no significant difference in Ankle Brachial Index (ABI) was found.

By comparing the three types of wound closure, the further intervention group had significantly lower frequency of delayed primary closure (p: 0.041). In addition, there was no significant difference between the groups in infection severity as classified by IWGDF/IDSA. Wagner classification and the pathophysiologic classification were not also significantly different between the groups. *Table 2* shows comparison between further intervention and no further intervention groups

By using the binary logistic regression, the odds ratio (OR) for further intervention with older age was 1.058 with 95% confidence interval (1.005–1.114), *P*=0.031. The OR for further intervention in patients on insulin compared to those on oral medication was 0.245 with 95% CI (0.071–0.848), *P*=0.026. The OR for further intervention after delayed primary closure compared to primary closure was 0.147 with 95% CI (0.027 – 0.808), *P*=0.027, the OR was also lower when comparing delayed primary closure to secondary closure 0.419, but not significant statistically (*P*=0.317).

Table 1. General characteristics of the 85 patients who underwent toe amputation.

		Total: 85 (100)
Age	(M ± SD)	66.52 ± 11.82 years
Origin	Lebanese	51 (60)
	Non-Lebanese	34 (40)
Gender	Male	65 (77)
	Female	20 (24)
DM treatment	Oral medications	47 (55)
	Insulin	38 (45)
DM duration	(M ± SD)	17.77 ± 6.73 years
Pathophysiological classification	Ischaemic	30(35)
	Neuropathic	13(15)
	Neuro-ischemic	37(44)
Wagner Classification	2	5(6)
	3	10(12)
	4	70(82)
IWGDF/IDSA*	No infection	3(4)
	Mild infection	17(20)
	Moderate infection	62(73)
	Severe infection	3(4)

*International Working Group for Diabetic Foot/ Infectious Diseases Society of America.

Discussion

Although many studies discussed the outcomes of major amputation in people with diabetes, few reports described toe amputation outcomes. In the authors' cohort of 384 patients with a diabetic foot ulcer, 85 (22%) underwent toe amputation, which is the most common type of amputation in people with diabetes.

Table 2. Comparison between further intervention and no further intervention groups.							
		N (total)	No-further intervention		Further intervention		P-value
		67	**48**	**72%**	**19**	**28%**	
Age (years)		67	64.92 ± 11.14		72.02 ± 12.35		0.026
Gender	Male	54	36	67%	18	33%	0.066
	Female	13	12	92%	1	8%	
Origin	Lebanese	45	30	67%	15	33%	0.196
	Non-Lebanese	22	18	82%	4	18%	
BMI(kg/m²)		57	27.72 ± 4.71		26.08 ± 5.28		0.246
DM Duration (years)		47	17.14 ± 6.97		20.45 ± 7.41		0.207
HBA_{1c} %		52	8.87 ± 1.93		8.48 ± 2.17		0.551
DM treatment	Oral	38	23	60%	15	40%	0.021
	Insulin	29	25	86%	4	14%	
Hypertension (yes)		56	38	68%	18	32%	0.121
Dyslipidemia (yes)		49	33	67%	16	33%	0.198
Coronary artery disease (yes)		33	21	64%	12	36%	0.152
Congestive heart failure (yes)		12	7	58%	5	42%	0.259
Neuropathy (yes)		34	23	68%	11	32%	0.317
Peripheral arterial disease		54	35	65%	19	35%	0.012
Duplex	TP	23	64.70 ± 54		25.67 ± 22.6		0.027
	TBI	22	0.48 ± 0.3		0.17 ± 0.2		0.027
	ABI	24	1.14 ± 0.4		0.99 ± 0.4		0.369
Wound closure	Primary	21	11	10	48%		0.041
	Delayed	17	15	2	12%		
	Secondary	29	22	7	24%		
IWGDF/IDSA classification	No infection	2	2	100%	0	0%	0.731
	Mild	13	9	69%	4	31%	
	Moderate	50	36	72%	14	28%	
	Severe	2	1	50%	1	50%	
Tissue culture	Positive	53	34	64%	19		0.202
	Negative	3	3	100%	0	36%0%	

Table 2 (continued). Comparison between further intervention and no further intervention groups.							
		N (total)	No-further intervention		Further intervention		*P*-value
Wagner classification	2	4	4	100%	0	0%	0.213
	3	8	7	88%	1	12%	
	4	55	37	67%	18	33%	
Pathophysiological classification	Neuropathic	7	7	100%	0	0%	0.079
	Ischaemic	28	20	71%	8	29%	
	Neuro-	27	16	59%	11	41%	
	Unclassified	5	5	100%	0	0%	
All continuous variables were presented as Mean ± Standard deviation, (IWGDF/IDSA) International Working Group for Diabetic Foot/ Infectious Diseases Society of America, TP: Toe Pressure, TBI: Toe Brachial Index, ABI: Ankle Brachial Index, MPSV: Mean Peak Systolic Velocity. BMI: Body Mass Index.							

A total of 72% of the patients in this study had adequate wound healing and did not require any further debridement or proximal amputation which is comparable to the healing rate of 64% and 82% reported in other studies (Caruana et al, 2015; Chu et al, 2016).

In the authors' study study, five patients ended up with BKA, which is one of the worst outcomes in DFU patients. This outcome could be related to presenting with high-grade ulcers; as those patients had Grade 4 ulcers according to Wagner classification and moderate to severe infection according to IWGDF/IDSA classification. In addition, the severity of peripheral artery disease was greater in this group as revascularisation was not an option in three patients and two patients failed to heal despite angioplasty and bypass surgery.

The negative effect of aging on wound healing has been previously reported (Guo and DiPietro, 2010). In concordance with this study, Vitti et al (1994) found that age was a negative predictor of wound healing.

In various reports, non-invasive vascular parameters were identified as predictors of healing after minor amputation in people with diabetes, such as TP and TBI. In concordance with our study, Caruana et al. and Vitti et al (1994) found that TP and TBI are better predictors of healing after minor amputation than ABI (Vitti et al, 1994; Caruana et al, 2015).

Although ABI is used traditionally to assess lower extremity circulation, its reliability in diabetic patients is limited due to the high prevalence of large arteries calcification in those patients that gives falsely elevated results. Medial arterial calcification affects 35–56% of diabetic patients but it spares the small arteries of the toe which makes toe pressure and toe brachial index more recommended in diabetic patients for assessment of peripheral vascular disease severity (Vitti et al, 1994; Scanlon et al, 2012).

The association between glycemic control and wound healing is highly reported. Several studies showed strong association between higher HbA1C level preoperatively and the outcomes such as impaired wound healing, re-ulceration and re-amputation and postoperative complications (Humphers et al, 2014; Chu et al, 2016). The authors' study, however, did not find significant difference in HbA_{1C} value between further intervention and no further intervention groups. This may be due to insufficient data, as HbA_{1C} was not taken in 21% of the patients.

Our study showed that patients treated with insulin had lower further intervention rate compared to those treated with oral medications only. This effect of insulin on wound healing is well known as insulin has been used to treat bed-sores in non-diabetic patients since the 1930s, and it was shown to improve healing in patients with gangrene and decubitus ulcers (Emanuelli et al, 2016). In addition, patients on insulin may be achieving better glycemic control than those on oral hypoglycaemic therapy. Whether insulin should be recommended for diabetic patients with foot

ulcers who are only on oral hypoglycaemic therapy remains to be determined but may be encouraged.

After toe amputation, the main problem that the surgeons face is the management of soft tissue wound. Our study showed decrease in further intervention rate with delayed primary closure compared to primary closure. When compared to secondary closure, delayed primary closure was also associated with lower further intervention rate but it was not statistically significant. Berceli et al, 2006 compared the three types of wound closure in diabetic and non-diabetic patients who had forefoot osteomyelitis and found that delayed primary closure was associated with fourfold decrease in time to healing and a 50% reduction in both early major amputation and the need for repeat intervention. However, primary closure was associated with good results as 38 out of 40 elective toe amputation healed well after primary closure in (Lakstein et al, 2014), but this study excluded patients with abscesses or extensive cellulites or those who required vascular intervention. The advantage of the delayed primary closure is that it allows the infection and oedema to settle and avoids closing the wound in a clean contaminated or contaminated setting.

Many studies suggested that DFU infection is associated with high amputation rate and poor outcome (Yesil et al, 2009; Pickwell et al, 2015), but after undergoing minor amputation no association was defined between the infectious status of the wound pre-amputation and the re-intervention rate. In this study, the severity of the infection measured by (IWGDF/IDSA) and the depth of the ulcer measured by Wagner classification were not associated with significant difference in re-intervention rate after toe amputation. In the presence of moderate or severe infection, primary closure should be avoided and a strong consideration for delayed primary closure or leaving the wound open for secondary closure.

The main limitation of this study is in its retrospective nature and having to depend on the medical records to obtain the needed information, as some important data were not uniformly reported in the charts such as neuropathy. In addition, not all the patient had Duplex/Doppler or laboratory test done during their admission especially in the presence of palpable pedal pulses or depending on the clinical assessment of the treating surgeon. Furthermore, the sample size was also relatively small (n=85) but our results were consistent with findings reported in the literature. Finally, a selection bias may affect the type of closure chosen. However, this selection bias could favour using primary closure for the more favourable wound and despite that potential favoritism the primary closure wounds had a higher re-intervention rates.

Conclusion

Older age and low toe pressure were the main predictors of requiring further intervention after toe amputation. Diabetes treatment with insulin was associated with lower further intervention rates. Delayed primary closure was the preferred surgical wound closure option with the lowest further intervention rates. Verification of these findings by a prospective study with more rigorous data recording may be required. ■

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