Predictive factors for successful limb salvage surgery among patients with diabetic foot in Capitol Medical Center, Philippines





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Abstract: The role of limb salvage is to restore and maintain stability and ambulation. Some surgeons, who are advocates of limb salvage procedures, often delay amputation, leading to worsening of patients' clinical condition and to multiple operative procedures, eventually resulting in a major limb amputation. Other clinicians do an outright major limb amputation even in mild to moderate diabetic foot syndrome. The goal of this study is to establish predictive factors of the success or failure of a limb saving procedures among patients with diabetic foot ulcers. The result of this study showed that the higher the grade of PEDIS classification increases the probability of the failure of limb salvage procedures Non-significant predictors of failure of limb salvage procedures included age, gender, presence of foot ischaemia, presence of peripheral neuropathy, presence of myocardial infarction and the presence of diabetic nephropathy. Despite the identification of the variables probability to the outcome of limb salvage procedures, the results have limited clinical use. It is recommended that this will be validated with a larger group of patients, to determine if the factors affect the result of limb saving procedures.

Key words:

- Amputation
- Diabetic foot ulcers
- Limb salvage procedures
- Wound healing

Maria Ellaine P Briones, is a GS resident, Capitol Medical Center Luinio S. Tongson, FPCS, FPSGS, CWSP, Capitol Medical Center; Luinio S Tongson, FPCS, FPSGS, CWSP, Capitol Medical Center oot problems are an important cause of morbidity in patients with diabetes mellitus. The lifetime risk of a foot ulcer in patients with diabetes (type 1 or 2) may be as high as 34%. The management of diabetic foot ulcers (DFU) accounts for a large number of in-patient stays, has a high rate of hospital readmission, and is associated with a 2.5-fold risk of death compared with patients with diabetes without foot ulcers (Wexler et al, 2006). Amputations of the foot, many of which are preventable with early recognition and therapy, may be required in up to 20% of DFUs (Weledji and Fokam, 2014).

One of the most important strategies for the management of the diabetic foot is to prevent complications that may necessitate a major limb amputation. Even with appropriate treatment, some patients must undergo major amputation or a limb salvage operations. These operations are not only a huge emotional and social burden to the patients due to physical impairment, but also a financial burden.

The key to limb salvage surgery is maximal retention of the limb and minimisation of the amputation level. Successful limb salvage, defined as a stump fit for functional ambulation, is mostly determined by the level of amputation. It is mostly affected by preservation of the talus and calcaneus because it minimises limb length discrepancy and preserves the heel pad. The level of Chopart amputation is the most proximal among lower limb amputation locations that preserve the talus and calcaneus. Although disputable, the Chopart amputation has been defined as the threshold of successful limb salvage (Suk, 2014).

The incidence of reamputation following first toe or transmetatarsal amputation associated with diabetes mellitus has been found to be nearly one-third. Nearly 40% of patients with DFUs who had amputations at the foot level have a history of previous amputation. Surgeons should preserve as much limb length as possible. However, it is also important to avoid reamputation, since it is a massive surgical

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burden to diabetic patients, who usually already are in a poor general condition and face financial difficulties.

Surgeons who are advocates of limb salvage procedure, often delay amputation, leading to worsening of patients' clinical condition, prolonging hospital stay, which in turn can lead to multiple operative procedures, and eventually major limb amputation. While others decide to do outright major limb amputation even in mild to moderate diabetic foot severity.

In 2007, there was a study conducted at Mary Johnston Hospital, entitled "*Prognostic factors associated with limb saving procedures in diabetic foot patients*". This study was published at University of the East Ramon Magsaysay Memorial Medical Center (Tongson, 2007). It was able to formulate a scoring system based on factors that significantly affect success or failure of limb saving procedure in diabetic foot. Once the scoring system has been validated, this will then augment and support the decision of surgeon in the surgical management of DFUs.

Currently, there is no available scoring system evaluating success of a limb salvage procedure. It was proposed in a study of Weledji that a structured clinical and vascular assessment would help clinical decision-making as to which patients to hospitalise and recommend surgical intervention (Weledji and Fokam, 2014).

Literature review

Diabetic foot syndrome is one of the most common long-term complications of chronic hyperglycaemia and a major source of morbidity and mortality. More than 60% of nontraumatic amputations are attributed to diabetes, 80% of which are preceded by a DFU (Singh et al, 2006).

Peripheral neuropathy, peripheral vascular disease, ipsilateral foot ulcers, previous amputation, male gender, and insulin therapy have been reported as risk factors for lower extremity amputation (LEA). Limb preservation in patients with diabetes mellitus is a challenging process that aims to prevent major limb loss in a population often plagued by multiple comorbidities (Gambardella et al, 2013). Employing a multidisciplinary approach has proved advantageous in improving limb salvage rates in the diabetic population.

A US-wide study by Margolis et al (2011) found that 23% of new DFUs in people with diabetes led to immediate leg amputation. In tackling the problem, the expert group agreed that early intervention was key, with focus on: offloading; vascular assessment and

optimisation; and treatment of infection. It is vital that management strategies involve a multidisciplinary-focused approach to care, and the adoption of advanced therapies where appropriate (Attinger et al, 2018).

Prevention of diabetic foot disease through glycaemic control, periodic foot examinations, callus debridement, shoe-gear recommendations, deformity prevention and accommodation, and patient education is the first line of defence against amputation (Gambardella et al, 2013). However, surgical intervention frequently becomes necessary to eradicate infection, remove necrotic tissue, close chronic wounds, eliminate structural causes of tissue breakdown and reconstruct deformities.

The foot and ankle surgeon is one of the foremost players in the limb salvage effort, assuming the difficult tasks of preserving extremities through various surgical techniques and preventing and managing complications postoperatively. Providing each patient with a functional, biomechanically sound, and shoe-able foot that is free of infection, while minimising the risk of tissue breakdown and recurrent infection, is integral to a successfully salvaged limb. Efficiently achieving these objectives decreases the threat of a major LEA, prolongs survival, promotes independence, and evades quality of life (QoL) deterioration, as will be explained in detail below (Gambardella et al, 2013).

Limb salvage should be considered a first-line approach in treating most patients with an at-risk limb. It has been demonstrated that five-year mortality rates are higher in those with a diabetes-related LEA than those afflicted with breast cancer or prostate cancer.

Following below and above knee amputations, 30-day mortality rates of 6.3% and 13.3%, respectively, have been reported. Long-term survival rates have been documented as low as 62% at one year, 50% at two years, and 29% at five years. In patients with diabetes and endstage renal disease (ESRD) on haemodialysis, the one-year mortality rate approaches almost 50%. Conversely, significantly better mortality rates have been reported following partial foot amputations, which also spare patients the need for intensive rehabilitation. While increased energy expenditure and oxygen consumption during prosthetic gait in patients with transtibial and transfemoral amputations have been observed and considered a disadvantage of proximal amputation, other studies have been unable to find a statistically significant difference when compared with partial foot amputees (Goktepe et al, 2010).

Furthermore, major limb loss in older, diabetic, and dysvascular patients has been associated with a deteriorating QoL. Many amputees are unable to achieve premorbid levels of ambulatory mobility, they remain confined to their homes when without assistance, and require a wheelchair for mobilisation. They experience considerably more problems than age- and sex-matched controls with performing household chores and hobbies and maintaining social relationships due to their inability to be effectively rehabilitated into the community. Psychosocial effects, as well as a moderate risk for loss of the contralateral limb, are also concerns following LEA.

Similarly, DFUs can have a profound effect on QoL if not treated appropriately. Healing index wounds has been shown to preserve QoL, whereas those who fail to heal, or who develop recurrent ulcers, have reported deterioration on the physical functioning, general health, and mental health QoL domains of the Short Form-36 assessment tool. Ribu and colleagues (2008) demonstrated that QoL improved substantially for the social functioning and mental health domains of the SF-36 as DFUs healed. However, studies have revealed alarmingly high DFU recurrence rates, translating into continued office visits for serial debridements, wound reconstruction, and a prolonged modified ambulatory status. Plantar ulcer location, osteomyelitis, HbA1C levels of more than 7.5%, and elevated C-reactive protein levels have been associated with DFU recurrence in the diabetic population.

If wounds fail to heal due to compromised perfusion, become infected, or result in osteomyelitis, a minor amputation can be considered. Following partial foot amputation, patients exhibit fewer physical limitations than those with a chronic foot wound or transtibial amputation. However, with any pedal amputation, altered biomechanics must be addressed to prevent pathological gait patterns and tissue breakdown under areas of increased pressure.

During the course of our literature review, it became apparent there is no suitable existing scoring system for predicting the success or failure of limb saving procedures among patients with diabetes.

Objectives

To establish a predictive factors that affect the success or failure of a limb saving procedures among patients with DFUs in Capitol Medical Center, specifically:

- To determine if the age of the patient contributes significantly to the success or failure of a limb saving procedures
- To determine if gender is a risk factor to the success or failure of limb saving procedures
- To determine whether patients with diabetes and peripheral occlusive disease and/or foot ischaemia contribute significantly to the failure of a limb saving procedure
- To determine whether increased severity of infection increases the chance of failure of limb salvage procedure
- To determine whether presence of peripheral neuropathy contributes significantly to the success or failure of a limb salvage procedure
- To determine whether increased Wagner grade increases the chance of failure of limb salvage procedure
- To determine whether presence of a myocardial infarction contributes significantly to the success or failure of a limb salvage procedure
- To determine whether the severity of diabetic nephropathy contributes significantly to the success or failure of a limb salvage procedure.

Method

Approval for retrospective cross-sectional study will be obtained from the Institutional Review Board on Human Subjects Research and the Ethics Committee. The study population will be composed of patients with diabetic foot who underwent limb salvage and major amputation. Limb salvage procedures consist of all amputations located below the malleolus with the intention of the surgeon to retain the anatomic structure of the viable foot.

Records will be retrieved of patients with a diabetic foot who underwent a lower extremity amputation at Capitol Medical Center form January 2017 to June 2021 (sample size=148). The inclusion criteria were: ulceration of the distal foot (distal to the metatarsophalangeal joint) that required hospitalisation and amputation. The exclusion criteria were patients with complete healing without amputation, patients with venous ulcers, vasculopathies, malignant ulcers of the lower extremities and trauma to the lower extremities. The patients will be divided into two groups based on their latest amputation level. The group with successful limb salvage will consist of patients with a preserved talus and calcaneus after amputation at the Chopart level or distal to it. The other group will comprise of patients who underwent limb salvage surgery and subsequently subjected to major amputation in whom the limb could not be preserved. The patients of this group are the ones that required reamputation more proximal than the Chopart level following an unsuccessful limb salvage operation.

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During the chart review, the following data was collected:

- Age of the subjects
- Gender of the subjects
- Presence of foot ischaemia
- Presence of infection and its severity
- Presence of peripheral neuropathy
- Wagner grade classification
- Presence of myocardial infarction
- Presence of diabetic nephropathy

Subjects included in the study will be graded accordingly using the scoring system that will be generated from the multivariate logistic regression.

In lieu of the Data Privacy Act, data preservation will be at the most one year or until this research has been published.

Definition of Terms

1. Limb saving procedures: Limb salvage procedures for diabetic foot are considered as the operation of the lower extremity located inframalleolar intended to save or retain the anatomic structure of a viable foot.

Success – Inframalleolar operation or sequential operations of the diabetic foot that eventually lead to complete closure of the skin or complete healing of the primary wound without a time frame saving the extremity below the malleolus.

Failure – Inframalleolar operation or sequential operation of the primary wound of the diabetic foot that eventually result to a major amputation, such as below knee amputation or above knee amputation.

- 2. Major Amputation: Amputation proximal to the inframalleolar (i.e. below knee amputation, above knee amputation).
- 3. Myocardial Infarction(MI) is diagnosed within six months before the operation or during

the present hospitalisation, and the presence of any two of the following:

- ECG findings: ST segment elevation, presence of Q wave or T wave inversion
- (+) CKMB enzymes
- (+) Troponin
- Chest pain
- 4. Diabetic nephropathy is defined by the presence of micro/ macroalbuminuria in 2 of 3 tests after excluding other causes.
- No signs of renal impairment
- (+) with chronic renal insufficiency (serum creatinine 1.5 mg/dl) but not on dialysis
- (+) with chronic renal insufficiency (serum creatinine 1.5 mg/dl) but on dialysis
- 5. PEDIS Grade: diabetic foot infection is classified as shown in *Table 1*.

Data analysis

Data that was collected will be analysed using multivariate logistic regression. Collected variables from both study population will be evaluated whether it can significantly predict the success or failure of limb salvage procedure. Also, descriptive binary will be used to analyse the scoring system whether it can be an effective tool for predicting the outcome of limb salvage procedure. Coding manual will be used for data entry. The Statistical Software for the Social Science (SPSS 16.0) will be used for data processing and analysis.

Data will be analysed using the Crude odds ratios to determine the association of each factor to the success or failure of limb salvage procedures. Analysis of individual independent variables will be undertaken. Logistic regression will be used to determine the degree of association between the different factors that lead to the success or failure of limb salvage procedure.

Computation of patients' scores using adjusted ratios of each factor will be obtained

Table 1. PEDIS Grade, diabetic foot infection is classified as follows						
Clinical manifestations of infection	Infection severity	PEDIS grade				
Wound lacking purulence or any manifestations of inflammation	Uninfected	1				
	Mild	2				
Infection (as above) in a patient who is systemically well and metabolically stable but which has >1 of the following characteristics: cellulitis extending >2cm, lymphangitic streaking, spread beneath the superficial fascia, deep-tissue abscess, gangrene, and involvement of muscle, tendon, joint or bone	Moderate	3				
Infection in a patient with systemic toxicity or metabolic instability (e.g., fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, severe hyperglycaemia, or azotemia)	Severe	4				

Demographic	Success	Success		Failure	
	n=131	%	n=17	%	
Gender					
Male	86	66	9	53	0.42
Female	45	34	8	47	
Age					
<50	17	13	2	12	
50-60	45	34	6	35	0.83
61–70	48	37	5	29	
>70	21	16	4	24	

Presence of foot ischaemia	Success		Failure	Failure	
	n=131	%	n=17	%	
Foot ischaemia - gangrene/necrosis					
Present	111	85	16	94	0.47
Absent	20	15	1	6	
Foot ischaemia - absent distal pulses					
Present	-	-	-	-	-
Absent	131	100	17	100	
Foot ischaemia - abnormal ankle brachial index					
Present	14	11	1	9	1.00
Absent	117	89	16	64	

Presence of infection	Success	Success		Failure	
	n=131	%	n=17	%	
PEDIS class					
Pedis grade 1	-	-	-	-	
Pedis grade 2	-	-	-	-	0.037
Pedis grade 3	118	90	12	71	
Pedia grade 4	13	10	5	26	
C-reactive protein (CRP)					
CRP elevated	-	-	1	5.9	-
CRP Normal	-	-	-	-	

from logistic regression and identification of best cut-off score that determines the success or failure of limb salvage procedure.

Results

Data consisted of a total of 148 medical records of patients with diabetic feet who underwent a limb salvage procedure from January 2017 to June 2021. The patients' demographic characteristics in terms of age, gender, and clinical status are shown in *Tables 2–6*. A total of 131 limb salvage procedures (89%) were considered successful while 17 were considered "failure" (11%).

Tables 2–6 also present the different independent variables groups according to the success or failure of limb salvage procedures.

There was no significant difference in terms of age distribution across the limb salvage procedure outcomes (p=0.83), there were more 61–70 years old patients who had successful outcomes than failure (37% versus 29%). There was no significant difference in terms of gender distribution across limb salvage procedure outcomes, although there were more males than females who had successful outcomes (66% versus 34%; p=0.42).

Wagner grade classification	Success	Success		Failure	
	n=131	%	n=17	%	
Wagner grade					
Grade 0	-	-	-	-	
Grade 1	20	15	1	6	
Grade 2	2	2	-	-	1.00
Grade 3	11	8	3	18	
Grade 4	94	72	7	41	
Grade 5	4	3	6	35	
Grade 1–3	33	25	4	24	1.00
Grade 4–5	98	75	13	76	1.00

Others	Current	Suggest Es		Failure	
	Success	Success		rallure	
	n=131	%	n=17	%	
Peripheral nephropathy					
Present	124	95	17	100	1.00
Absent	7	5	-	-	
Myocardial infarction					
Present	4	3	1	6	0.46
Absent	127	97	16	94	
Nephropathy					
Present	39	30	7	41	0.41
Absent	92	70	10	59	
On dialysis					
Yes	4	10	1	14	1.00
No	35	90	6	86	

More patients whom the limb salvage procedures failed had gangrene/necrosis foot ischaemia when compared with those who had successful outcomes (94% versus 85%; p=0.47; *Table 3*).

No significant difference was noted in terms of the distribution of patients who had peripheral neuropathy across treatment success and failure was noted (100% versus 95%; *p*=1.00, respectively). A significant higher proportion of patients with successful limb salvage procedures had only moderate infection (PEDIS Class 3; 90% versus 71%; *p*=0.037).

Among those with failed limb salvage procedures, a slightly higher proportion of patients had a Wagner rating of 4–5, but this was not statistically significant (76% versus 75%; p=1.00).

Among those who had successful limb salvage procedures, 39 subjects (30%) had diabetic nephropathy, of whom four (10%) were on haemodialysis (*Table 6*). Among those whose

limb salvage procedures failed, seven (41%) had diabetic nephropathy, of whom only one patient (14%) was undergoing dialysis. This distribution of patients with and without nephropathy did not statistically differed between the two outcomes (p=0.41; *Table 6*). A total of five patients (3%) had previous myocardial infarction (*Tables 6*), but the difference across limb salvage procedure outcomes did not significantly vary (p=0.46).

Prognostic factors for successful limb salvage procedures

Different clinical variables were analysed that could be independent predictors of successful or failure of limb salvage procedures. Clinical factors presented are non-significant predictors of failing limb salvage procedures including gender, age, ischaemia, PEDIS grade classification, Wagner grade, peripheral nephropathy, myocardial infarction, nephropathy having dialysis or not.

Table 7. Overall regression analysis of factors contributing to failure of limb salvage procedures in diabetic foot, analysis of 148 patients Capitol Medical Center, January 2017 to June 2021

Clinical factors	ß-Coefficent	Odd's ratio	95% confid	ence interval	<i>p</i> -value	Comment
			Lowest	Highest		
Gender	-0.888	0.411	0.127	1.338	0.140	NS
Age	0.025	1.025	0.969	1.085	0.386	NS
Foot ischaemia - gangrene/necrosis	-2.083	0.125	0.010	1.603	0.110	NS
PEDIS Class	-1.285	0.277	0.069	1.116	0.071	NS
Wagner Grade	1.154	3.170	0.660	15.221	0.150	NS
Peripheral nephropathy	-19.750	0.000	0.000	-	0.999	NS
Myocardial infarction	-0.184	0.832	0.064	10.766	0.888	NS
Nephropathy	0.259	1.296	0.395	4.256	0.669	NS
On dialysis	0.184	1.203	0.093	15.505	0.888	NS
*Significant predictor if OR is $>$ 1 and $p>$ 0.05, by b	inary logistic regression, stepwi	se technique				

Table 8. Score transformation from standardized beta coefficients from variables for failure of limb salvage procedure in diabetic foot. Capitol Medical Center, January 2017 to June 2021

Clinical factors	ß-coefficent	Transformed coefficent	Calculated coefficent	Assigned raw score
Gender	-0.888	-35.52	-	0
Age	0.025	1.00	-	0
Foot Ischaemia - gangrene/necrosis	-2.083	-83.32	-	0
PEDIS Class	-1.285	-51.40	-	0
Wagner Grade	1.154	46.16	-	0
Peripheral nephropathy	—19.750	-790.00	-	0
Myocardial infarction	-0.184	-7.36	-	0
Nephropathy	0.259	10.36	-	0
On dialysis	0.184	7.36	-	0

Formulation of scoring system to predict failure of limb salvage procedure: regression coefficient transformation and assignment of raw scores

A second run of logistic regression was done to obtain the standardised beta coefficients. These coefficients were divided by the smallest coefficient obtained (0.025) to derive the transformed coefficient (Tables 7–8).

Discussion

Many DFU classification systems have been proposed to predict clinical outcome; however, most of these systems have limitations. A validated classification system of DFUs may help health professionals in assessment and management of patients, as well as researchers in the development and assessment of new therapies.

This study classifies patients who may benefit from a limb salvage procedure or outright amputation considering the clinical factors present on the subjects. The demographic, clinical and medical factors were included in this paper that will be of help to the physician in the management of the diabetic foot.

As to age, although the elderly can heal most wounds, they have a slower healing process, and all phases of wound healing are affected. The inflammatory response is decreased or delayed, as is the proliferative response (Gersteinet al, 1993). The results in this study showed that age was not a significant factor on the outcome of the procedure. A higher portion of older patients (>70 years old) who underwent limb salvage procedures were considered failure outcomes rather than successful (24% versus 16%) but this was not statistically significant. Age-related variables in the population must be excluded as fully as possible when or causal relationships are being examined.

As to gender, in this study there were no significant differences to the outcome of the procedure. There was no significant difference in

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terms of gender distribution across limb salvage procedure outcomes, although there were more males than females who had successful outcomes (66% versus 34%; *p*=0.42). However, a published data reported that increasing age and being male (Deshpande et al, 2008) are some of the several risk factors for LEA.

The result of this study showed that the higher the grade of PEDIS classification increases the probability of failure of limb salvage procedure in patients with diabetic foot.

Non-significant predictors of failure of limb salvage procedures include age, gender, presence of foot ischaemia, presence of peripheral neuropathy, Wagner grade classification, presence of myocardial infarction and presence of diabetic nephropathy.

Conclusions and recommendations

Despite the identification of the variables probability to effect the outcome of limb salvage procedures, the results have limited clinical use. This study provides only probabilities and do not accurately predict the outcome of a limb salvage procedure as there are other factors that could determine the success or failure.

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