Original Research Article

Assessment of limb salvage in peripheral arterial disease in diabetic foot ulcer: A prospective study

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Abstract

Introduction: The association of peripheral arterial disease in diabetic foot ulcer is an emerging risk factor for accelerated limb amputations. Presence of ischemia delays the wound healing increasing the likelihood of limb loss. Most amputations can be prevented and limbs salvaged through a multimodal treatment of infection control, wound debridement and revascularization procedures.

Materials and methods: This was a prospective study which involved type 2 diabetic patients with isolated foot ulcer (DFU). WIFI- G score was incorporated in the wound assessment. A total of 100 patients were evaluated in this study. Once diagnosed with PAD, patients underwent vascular surgery consultation and were put on appropriate treatment. The patients were followed up for a period of 3 months from definitive procedure to assess the ulcer healing and limb salvage.

Results: There was significant association of PAD with high WIFI index. Osteomyelitis was strongly associated with PAD (59%, p=0.003). PAD was associated with higher amputation rates (53.8%, p=0.003). Of minor lower limb amputations, only 47% were associated with PAD whereas of all major amputations, 87% were associated with PAD (p= 0.002). Also higher amputation rates correlated with a high WIFI score (p<0.0001).

Conclusion: Revascularization limits the level of amputation and facilitates healing of stump. Major amputations were reduced to half with revascularization. Revascularization if indicated should be done at the earliest onset to attain the benefit of limb salvage.

Key words

Diabetic foot ulcer, Peripheral arterial disease, Ischemia, Osteomyelitis, Amputation, Revascularization.

Introduction

The association of peripheral arterial disease in diabetic foot ulcer is an emerging risk factor for accelerated limb amputations. Presence of ischemia delays the wound healing increasing the likelihood of limb loss. It involves a multimodal approach to diagnose ischemia at the earliest and intervene at appropriate time with individualized treatment [1].

The indications for revascularization of an ischemic limb are incapacitating claudication and critical limb ischemia (CLI). Disabling claudication is a relative indication and one has to weigh the existing quality of life against the risk of procedure during selection of suitable patient and it requires significant patient counseling. Revascularization in some ischemic limbs may be deferred if no target vessel present or unavailability of an autogenous vein. Even irreversible gangrene progressing beyond midfoot may preclude revascularization. In such patients a choice must be made between prolonged medical management and primary amputation [2].

Major amputation in an ischemic foot is indicated only when there is life threatening sepsis or when arterial occlusion causing extensive necrosis has destroyed the foot [3].

Most amputations can be prevented and limbs salvaged through a multimodal treatment of infection control, wound debridement and revascularization procedures. However amputation may warrant a good quality of life, if a prolonged treatment course is anticipated with minimal likelihood of healing. All diabetic patients should be offered full and active rehabilitation following limb amputation [4].

Medical management of PAD in DFU

Asymptomatic PAD

Life style modification

This involves modification of daily activities and dietary pattern.

Tobacco Smoking

Counseling of patients to abstain from all tobacco products is the first and most essential step. In PAD, tobacco is believed to increase progression of the atherosclerotic disease and hence increases amputation risk.

Blood sugar control

Adequate glycemic control to a tune of HbA1c < 7% is needed to prevent microvascular complications.

Hyperlipidemia

Many studies conclude that lipid lowering agents slow the disease progression and bring down deaths due to cardiovascular events.

Antiplatelets

Aspirin low dose exhibits antithrombotic effects and also slows down the clot propagation and reduce the cardiovascular complication. Those allergic to aspirin are put on clopidogrel [5].

Management of symptomatic PAD

Exercise

Moderate exercise within the limits of claudication distance is advised to improve the collateral blood supply and cardiovascular risk factor profile.

Drug therapies

Heparin is used to interfere with clotting mechanism and prevent further clot formation. However it does not act on existing clot.

Pentoxifylline is a hemorheologic modifier which is said to improve microcirculation by decreasing the blood viscosity.

Cilostazol is a phosphodiesterase III inhibitor acting as a vasodilator. It is contraindicated in heart failure.

Foot care

Patients should be counseling on foot care involving hygiene and specialized foot wear.

Regular supervision reduces the risk of foot complications.

Treatment of ischemic foot

Critical limb ischemia characterized by rest pain, tissue loss or gangrene is a limb-threatening condition which warrants emergent treatment. Peripheral neuropathy blunts the pain perception causing PAD to manifest late in a diabetic patient. Contrarily PAD accelerated nerve ischemia and worsened neuropathy [6].

In contrast to involvement of plantar aspect in neuropathic ulcers, ischemic ulcers commonly involve dorsum, edges of foot and toes. Conservative management includes wound debridement, ulcer offloading, appropriate dressing, and adjuvant wound healing methods.

Wound Debridement

Wound debridement should aim to remove all necrotic debris and slough to reduce infection. It should be done when there is presence of localized fluctuation, undermining of ulcer with slough, crepitus with gas in X-ray and need for drainage of pus.

Appropriate footwear

It is most important in case of a neuroischemic foot wear the aim is protection of foot from shear and pressure. Patients should be advised not to wear tight shoes. This would hinder ulcer healing. Ideal footwear should be long, deep and broad, designed to protect arch of foot and offload the pressure. This would automatically facilitate the ulcer healing.

Dressings

Dressing is applied to prevent tissue desiccation, absorb discharge, prevent external contamination. Occlusive dressing lowers risk of infection. Non adhesive dressings should cover foot ulcers at all times. Some properties like easy removability, accommodating foot pressures while walking and is desirable. Various available dressings include foams, hydrogels, absorbent polymers, alginates, growth factor and skin replacement agents.

Treatment of infection

In a diabetic foot, the signs and symptoms of foot infection are often diminished due to impaired neuroinflammatory response.

The isolates in diabetic foot sepsis are usually polymicrobial. Commonly streptococci, methicillin resistant staphylococcus (MRSA), enterobacteriaceae and pseudomonas are encountered. Often it is mixed infection with anaerobes.

Appropriate empirical antibiotics should act against both gram positive and gram negative organisms and provide both aerobic and anaerobic coverage. Such wounds require intravenous antibiotics and these patients should be hospitalized [7].

Patients with mild to moderate infection, superficial ulcers without sepsis, localized cellulitis can be treated with oral antibiotics on an outpatient basis. The empirical antibiotics should be started after initial cultures are taken and changed as needed.

Incision and drainage is the core of treatment for almost all diabetic foot infections. It may be supplemented with toe or ray amputation for facilitating drainage. Aggressive wound debridement and revascularization procedure usually make limb salvage possible.

Neuroischemic foot may complicate into dry and wet gangrene. Septic arteritis following soft tissue infection and ulceration leads to wet gangrene. If gas in soft tissue is noted, immediate open drainage of all potentially infected spaces is necessary along with broad spectrum I.V. antibiotics.

In acute on chronic limb ischemia, there is severe reduction in arterial perfusion leading to dry gangrene. Surgical wound debridement should be done only after revascularization if applicable. Only then the debrided foot will be perfused adequately to heal [8].

Revascularization

Revascularization can be carried out by open surgical technique or endovascular procedures. These two types of procedures are not mutually exclusive. They are combined in most of the cases like iliac angioplasty with bypass grafting with saphenous vein.

Endovascular procedures are preferred in focal segmental disease.
Aortoiliac disease usually managed effectively with open aortofemoral prosthetic bypass but endovascular stenting is gaining significant recognition as an alternative.
Superficial femoral artery stenosis can be treated by open femoropopliteal bypass.
Bypass grafting with autogenous great saphenous vein is the common procedure for tibial disease. Nevertheless, endovascular procedures are increasingly becoming popular due to technical advances allowing aggressive use of tibial angioplasty.

Major limb amputation is only indicated in case of life threatening sepsis in an ischemic foot. majority of limb amputations can be prevented by timely diagnosis and intervention by a combination of revascularization, wound debridement, infection control by antibiotics, and staged closure of wound.

WIFI-G Index
The society of vascular surgeons formulated a new wound classification system WIFI based on wound, ischemia and foot infection. It is useful for risk stratification like other classification systems like Wagner, PEDIS, Texas. This study aimed to incorporate this classification and test its correlation with PAD and limb amputation.

Objectives

- To assess the risk factors associated with lower limb amputation
- To test the correlation of WIFI-G score with severity of disease
- To assess the limb salvage in DFU with PAD
- To compare the results with previous similar studies

Materials and methods

Patient selection
In-patients admitted with isolated diabetic foot ulcer were randomly selected from the surgical wards on every 7th day. A total of 100 patients were sampled.
Study area: Department of General Surgery and Vascular Surgery, Govt. Stanley Hospital, Chennai.

Inclusion criteria
Age group 35- 65yrs
Both sexes
In-patient
Known diabetic
Isolated foot ulcer

Exclusion criteria
Out patients
Known case of peripheral vascular disease during admission
Ulcer other than in foot
Vasculitis

Methodology
This was a prospective study which involved type 2 diabetic patients with isolated foot ulcer (DFU). Their history and clinical parameters were noted and documented. WIFI- G score was incorporated in the wound assessment. A total of 100 patients were evaluated in this study. The patients were subjected to detailed history by administering questionnaires to assess the diabetic foot ulcer and associated risk factors. A thorough clinical examination was carried out followed by specific examination which included distal pulse assessment, ankle-brachial index (ABI) and duplex scan to evaluate PAD. Portable hand held Doppler was used to measure ABI.
Once diagnosed with PAD, patients underwent vascular surgery consultation and were put on appropriate treatment.

The patients were followed up for a period of 3 months from definitive procedure to assess the ulcer healing and limb salvage. The data was subjected to statistical analysis to find out association between parameters of interest.

Diagnosis criteria

Diabetic foot ulcer: A full thickness wound breaching the dermis below the level of ankle in a diabetic patient

Peripheral arterial disease: Any 2/3 criteria of the following

ankle brachial pressure index(ABI) <0.9

absent distal foot pulses

abnormal doppler flow/duplex scan

Fontaine classification:

Stage I asymptomatic

Stage IIa intermittent claudication >200m/mild

Stage IIb intermittent claudication <200m/moderate-severe/incapacitating

Stage III rest pain

Stage IV ulceration/gangrene

Proposed WIFI Index

Based upon existing validated systems or best available data with 4 point scales where

0 = none

1 = mild-moderate

2 = moderate-severe

3 = severe or advanced

WIFI index is intended to be analogous to the TNM staging system for cancer

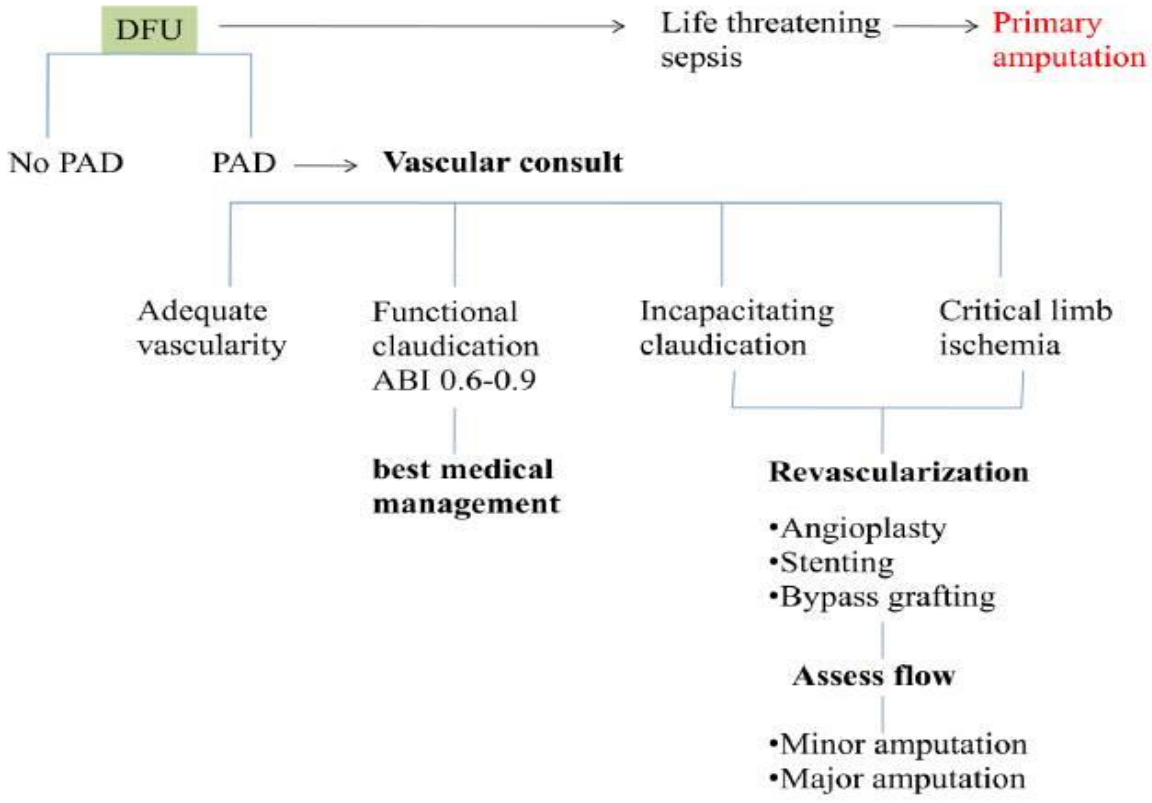
A patient with diabetes, a shallow superficial foot ulcer, early cellulitis and an ABI of 0.43 with a TP of 25 mm Hg would be classified as follows:

W1 I 2 FI 1 G 0 or WIFI-G 1210, with a Total Score of 4 (1+2+1=0)

The highest possible score would be in a patient with severe ischemia (TP 15 mm Hg), dorsal foot ulcer with penetration to bone, wet gangrene of 3 toes to the bases and systemic sepsis: W3 I3 FI3 G3, WIFI-G 3333, generating a Total Score of 12

It might be useful to analyze outcomes based on total as well as fractionated scores. Workup protocol used in study is as per **Chart – 1**.

Chart – 1: Workup protocol used in study.



Results

The prevalence of PAD in DFU was found to be 36% (**Table – 1, Figure - 1**). There was significant association of PAD with high WIFI index (**Table – 2, Figure - 2**). Osteomyelitis is strongly associated with PAD (59%, p=0.003) (**Table – 3, Figure - 3**). PAD was associated with higher amputation rates (53.8%, p=0.003) (**Table – 4, Figure - 4**). Of minor lower limb amputations, only 47% were associated with PAD whereas of all major amputations, 87% were associated with PAD (p= 0.002) (**Table – 5, Figure - 5**).

Table – 1: Prevalence of PAD.

		Count	Column N %
PAD	NO PAD	64	64.0%
	PAD	36	36.0%

Figure – 1: Prevalence of PAD.

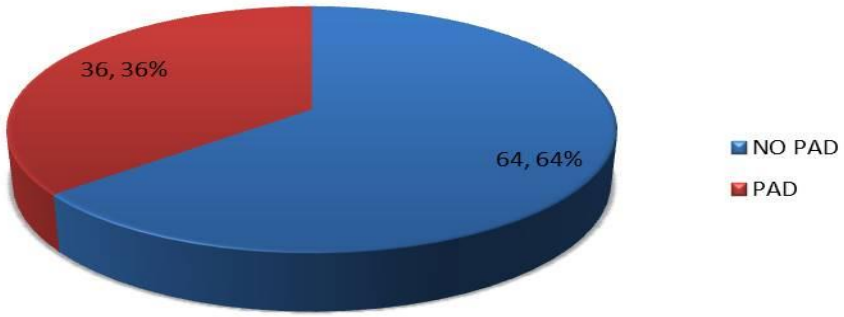


Table - 2: Ulcer duration and WIFI-G score correlation with PAD.

	NO PAD (64)			PAD (36)			
	Mean	**Median**	**SD**	**Mean**	**Median**	**SD**	**p**
Ulcer duration days	25.03	14.00	46.9	25.3	17.50	21.5	0.09
WIFIG Score	3.48	3.00	1.83	6.6	7.0	2.7	**<0.0001**

Figure – 2: Ulcer duration and WIFI-G score correlation with PAD.

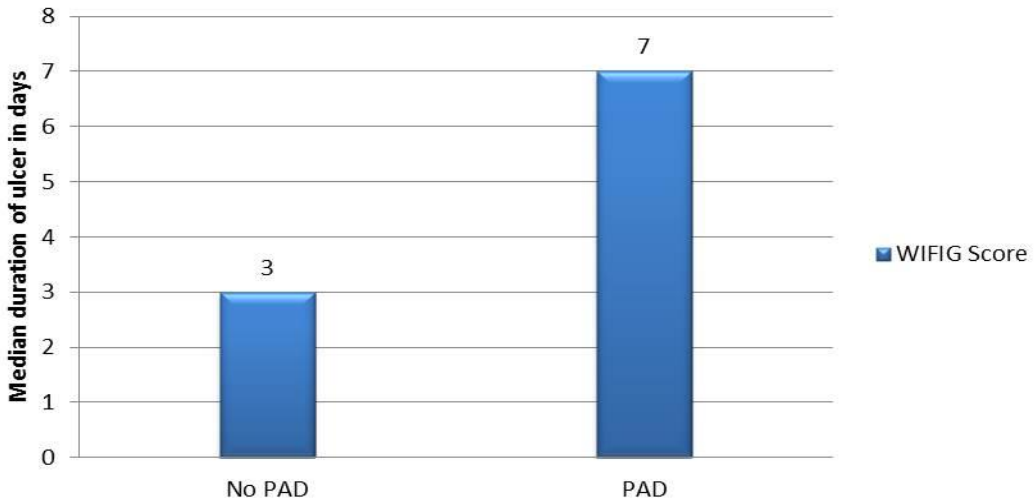


Table - 3: Osteomyelitis and PAD.

		PAD			
		NO PAD		PAD	
		Count	Row N %	Count	Row N %
Osteomyelitis	no	53	72.6	20	27.4
	yes	11	40.7	16	59.3

Figure – 3: Osteomyelitis and PAD.

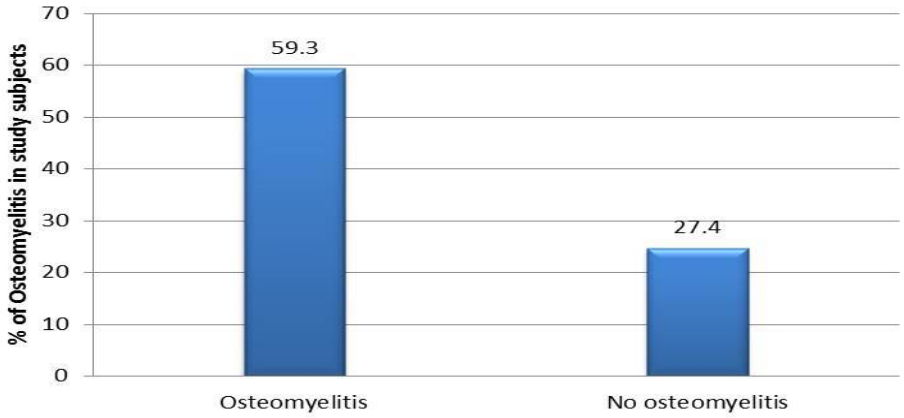


Table - 4: Lower limb amputation in PAD.

		PAD			
		NO PAD		PAD	
		Count	Row N %	Count	Row N %
amputation	no	46	75.4	15	24.6
	yes	18	46.2	21	53.8

Figure – 4: Lower limb amputation in PAD.

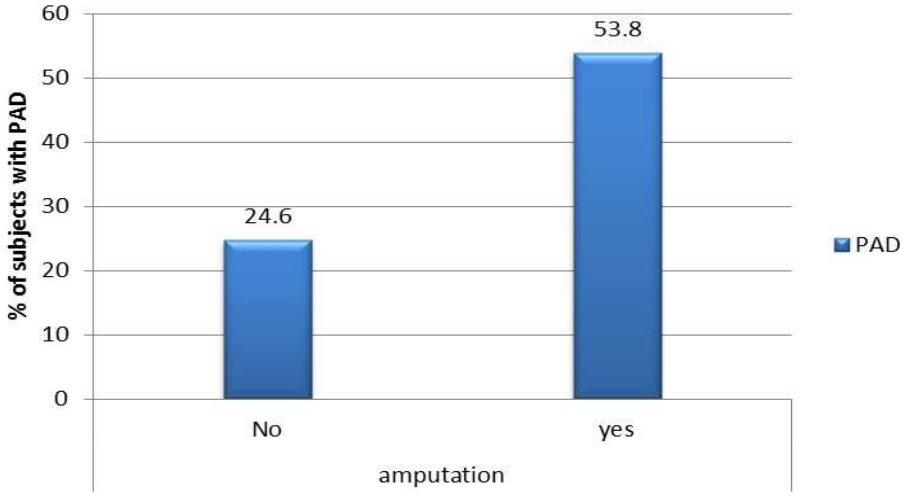
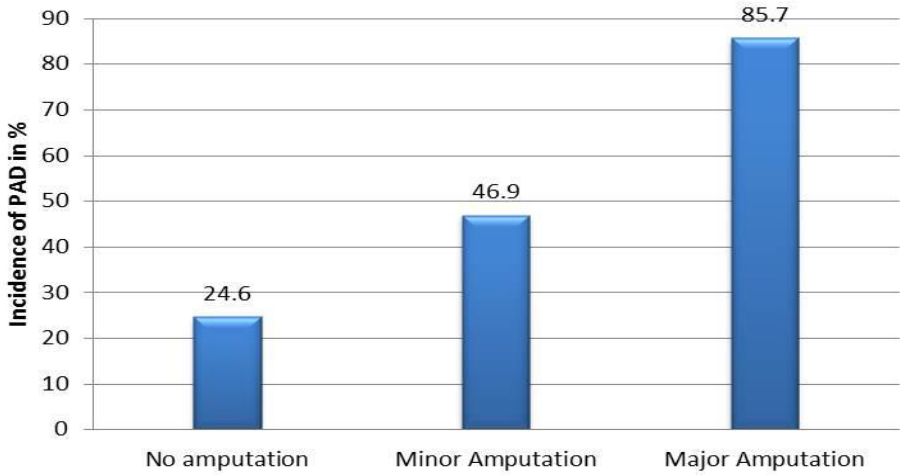


Table - 5: Lower limb amputation type and PAD.

		PAD			
		NO PAD		PAD	
		Count	Row N %	Count	Row N %
ampute	No amputation	46	75.4	15	24.6
	Minor Amputation	17	53.1	15	46.9
	Major Amputation	1	14.3	6	85.7

Figure – 5: Lower limb amputation type and PAD.



In a 3 month follow up (**Table – 13**), the ulcer healing was delayed in patients with PAD compared to non-PAD.

36 DFU patients diagnosed with PAD were referred for vascular surgery consultation, out of which 10 patients had severe ischemia were taken up for revascularization. After a 3 month follow up, complete ulcer healing without any amputation occurred in 3 patients, 2 patients had toe amputation with complete healing of wound, one patient had a subsequent BKA with complete healing of the stump and one patient subsequently expired after angioplasty due to MI. 2 patients were lost to follow up. Therefore 60% limb salvage was possible.

Among the rest of 26 patients with PAD, 6 patients who were assessed to have adequate vascularity were put on best medical management and had complete ulcer healing (**Table – 14**).

Out of the 20 patients with PAD, 6 underwent toe amputation, one patient underwent forefoot amputation with complete healing, 9 patients underwent BKA with complete healing of stump, 3 patients underwent AKA with complete healing, and one patient was lost to follow up. Since it is a tertiary setting, the referral was late and hence primary amputation was done as a life saving measure in these patients.

Major amputations were associated more with plantar foot ulcer (16%) whereas minor amputations were associated more with dorsal foot ulcer (33%) (**Table – 10**). About 47% of ulcers involving whole of foot went in for major amputation while forefoot ulcers (33%) and mid foot ulcers (25%) commonly went in for minor amputations ($p<0.0001$) (**Table – 11**).

Also higher amputation rates correlated with a high WIFI score ($p<0.0001$) (**Table – 6, Figure - 6**) and higher Fontaine grades (**Table - 7**). Mean diabetic duration (9.8 years) (**Table - 6**) was found higher in those who underwent amputation ($p=0.006$).

Association of risk factors with lower limb amputation in DFU was as per **Table – 8**. Association of Fontaine grade with lower limb amputation in DFU was as per **Figure – 7**. Distribution of Osteomyelitis and lower limb amputation in DFU was as per **Table – 9**. Revascularization and amputation was as per **Table – 12**. Association of Amputation with revascularization was as per **Figure – 8**.

Discussion

One study reported that ischemic patients without revascularization had the worst outcomes [9]. One study reported a limb salvage rate of 36% in revascularized patients [10].

Table - 6: Correlation of WIFI-G score and diabetic duration with lower limb amputation in DFU.

	no			yes			
	Mean	Median	Standard Deviation	Mean	Median	SD	p
WIFIG Score	2.98	2.00	1.27	7.15	7.00	2.11	**<0.0001**
Diabetes duration years	7.6	5.0	5.9	9.8	8.0	6.5	0.06

Figure - 6: Correlation of WIFI-G score with lower limb amputation in DFU.

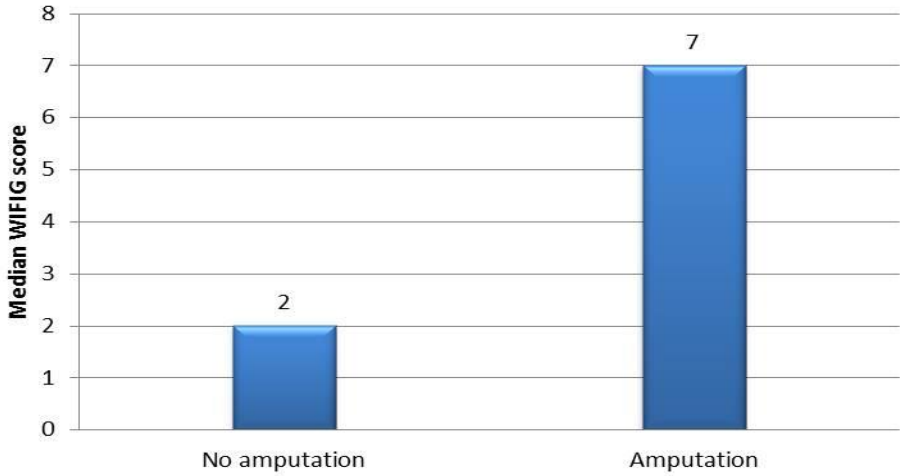


Table - 7: Association of risk factors with lower limb amputation in DFU.

		Amputation				
		No		Yes		
		n	%	n	%	P
Age	<40	2	40.0	3	60.0	0.2
	41-50	11	57.9	8	42.1	
	51-60	34	72.3	13	27.7	
	>61	14	48.3	15	51.7	
Sex	Male	43	64.2	24	35.8	0.6
	Female	18	54.5	15	45.5	
Fontaine grade	.00	46	71.9	18	28.1	
	1.00	5	71.4	2	28.6	**0.02**
	2.00	3	30.0	7	70.0	
	3.00	3	37.5	5	62.5	
	4.00	4	36.4	7	63.6	
CAD	no	57	61.3	36	38.7	0.9
	yes	4	57.1	3	42.9	
prev_amput	no	51	63.8	29	36.3	
	yes	10	50.0	10	50.0	0.3

In a 3 month follow up in our study, the ulcer healing was delayed in patients with PAD compared to non-PAD. 60% limb salvage was possible with revascularization. The amputation rates were higher (65%) in the non-revascularized group [11]. Ulcer healing occurred in revascularized and non-revascularized group of patients and was quicker in the revascularized group (PAD). The mean hospital stay duration and drug expenditure was lower in the revascularized patients [12].

Table - 8: Association of risk factors with lower limb amputation in DFU.

		Amputation				
		No		Yes		
		n	%	n	%	P
Age	<40	2	40.0	3	60.0	0.2
	41-50	11	57.9	8	42.1	
	51-60	34	72.3	13	27.7	
	>61	14	48.3	15	51.7	
Sex	Male	43	64.2	24	35.8	0.6
	Female	18	54.5	15	45.5	
Fontaine grade	.00	46	71.9	18	28.1	
	1.00	5	71.4	2	28.6	**0.02**
	2.00	3	30.0	7	70.0	
	3.00	3	37.5	5	62.5	
	4.00	4	36.4	7	63.6	
CAD	no	57	61.3	36	38.7	0.9
	yes	4	57.1	3	42.9	
prev_amput	no	51	63.8	29	36.3	
	yes	10	50.0	10	50.0	0.3

Figure - 7: Association of Fontaine grade with lower limb amputation in DFU.

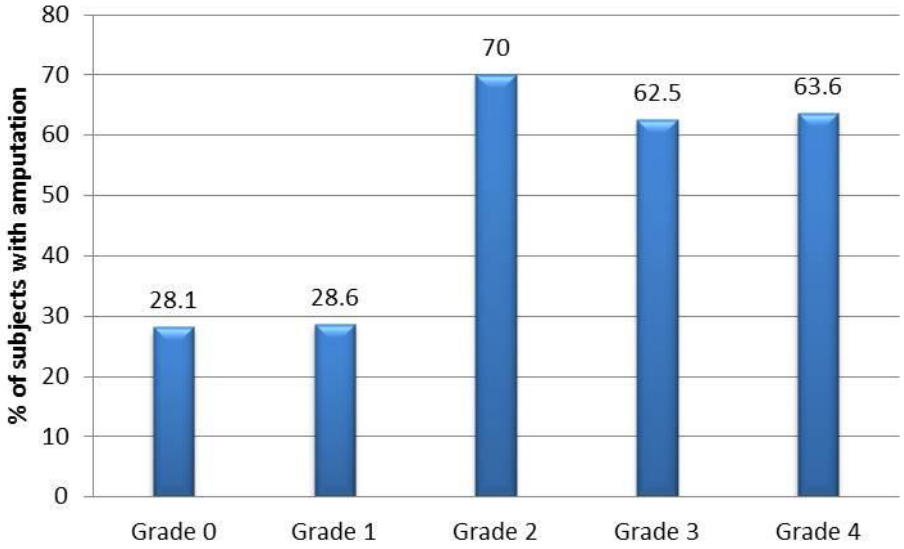


Table - 9: Distribution of Osteomyelitis and lower limb amputation in DFU.

		Count	Column N %
Osteomyelitis	no	73	73.0%
	yes	27	27.0%
amputation	no	61	61.0%
	yes	39	39.0%

Table - 10: Site of ulcer and amputation.

		dorsum_plantar			
		dorsum		plantar	
		Count	Column N %	Count	Column N %
amputation	No amputation	50	61.7%	11	57.9%
	Minor Amputation	27	33.3%	5	26.3%
	Major Amputation	4	4.9%	3	15.8%

Table - 11: Site of ulcer and amputation type.

		Location of foot							
		forefoot		hindfoot		midfoot		whole foot	
		Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %
ampute	No amputation	48	63.2%	5	100%	3	75.0%	5	33.3%
	Minor Amputation	28	36.8%	0	.0%	1	25.0%	3	20.0%
	Major Amputation	0	.0%	0	.0%	0	.0%	7	46.7%

Table - 12: Revascularization and amputation.

		Revascular			
		No		Yes	
		Count	Column N %	Count	Column N %
ampute	No amputation	53	58.9%	8	80.0%
	Minor Amputation	30	33.3%	2	20.0%
	Major Amputation	7	7.8%	0	.0%

Table - 13: 3 month follow up in revascularized group.

PAD	Revascularization for severe ischemia (vascular consult)	Complete healing without amputation	Toe amputation	BKA	Expired (MI)	Lost to follow up	LIMB SALVAGE
36	10	3	3	1	1	2	60%

Conclusion

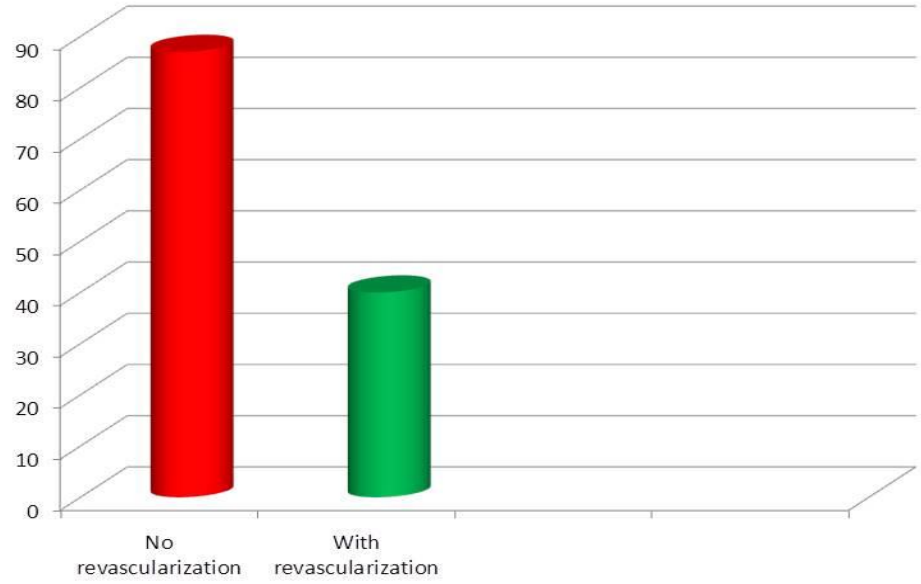
Increasing age and longer duration of diabetes are strong risk factors for PAD. Patients with high risk factors like male, age>40 years, high WIFI-G score should be dealt with a strong suspicion of PAD. WIFI-G scoring should be incorporated in the clinical assessment of wound due to its positive correlation with wound severity. The use of hand held Doppler will increase sensitivity of diagnosis and should be routinely employed. Based on the bacteriological data, institutional antibiotic protocol should be formed for empirical treatment of the diabetic foot to counter

the antibiotic resistance. Patients with PAD had delayed ulcer healing and higher amputation rates. Major amputations were reduced to half with revascularization. Revascularization limits the level of amputation and facilitates healing of stump. Revascularization if indicated should be done at the earliest onset to attain the benefit of limb salvage.

Table - 14: 3 month follow up in non-revascularized group.

PAD	Best medical management alone	toe amputation	Fore foot	BKA	AKA	Lost to follow up	LIMB SALVAGE
26	6	6	1	9	3	1	35%

Figure - 8: Association of Amputation with revascularization.



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