

Factors Predicting Ulcer Healing after Angioplasty in Diabetic Foot

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Abstract

Background: Non healing ulcers are a very common complication of diabetes. It increases the morbidity and economic burden of the patient. Ischemia is one of the common causes for non healing in diabetic patient. Even after angioplastic revascularization some patients' shows delay in healing. Non achievement of direct flow to ulcer area may be a reason for this and it was proposed by Ian Taylor who in his angiosome concept.

Objective: To evaluate the factors predicting outcome after revascularization based on angiosome concept in Diabetic Foot Ulcer.

Methods : A prospective observational study was done which included 50 diabetic foot ulcer patient who underwent endovascular revascularization in our hospital during the period January 2013 to March 2015 and they were followed up for 6 months to look for Ulcer healing rate, ulcer recurrence, leg salvage rate and major amputation .

Results: Out of 50 participants in 52% direct revascularization was done. Base line characteristics of both the groups were comparable except gender (where proportion of females was higher in indirect group), CKD, smoking, UTCWS grade of ulcer which were more in direct group. Ulcer predominantly affected toes (70%) and Anterior Tibial angiosome was the most common (50%) angiosome involved by clinical classification. Most common affected arterial

segment pattern by Peripheral angiogram was multisegmental followed by infrapopliteal disease. In 78.3% of cases ulcer healed at 6 months in the indirect group whereas 57.7% patients had healed ulcers at 6 months in the Direct group (p value =0.12). Female gender, CKD, smoking and ulcer grade found to have no association with healing at 6 months. No significant difference was found in leg salvage rate, ulcer recurrence and major amputation.

Conclusion: Endovascular revascularization is a good modality to reduce morbidity in diabetic foot ulcer patients. There was no significant difference in outcome between these two groups.

Keywords: Peripheral Occlusive Arterial Disease; Diabetic Foot Ulcer; Angiosome; Peripheral Percutaneous Trans Luminal Angioplasty; Peripheral Angiogram.

Introduction

Non healing ulcers are very common in diabetic patients. Infection; peripheral neuropathy and angiopathy are the common causes for non healing in these patients. Of these three angiopathy is one of the important causes for non healing. Usually the vessel involved in diabetic patients are infrapopliteal one [1]. Even after angiosome based revascularization the healing may be delayed because of several factors. One of the reasons attributed to this is decrease in blood flow to that area. Angiosome concept was put forward by Ian Taylor et al based on their studies there are specific blood supply to the specific area of foot [2,3]. Based on this concept revascularization procedure came and it improved the ulcer healing rate and the need of major amputation considerably

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reduced. There are several studies published in vascular literature regarding the angiosome based revascularization and the improvement in healing of the wound. For the opening of the specific arteries needs more time, technical skill and contrast. But even after these more promising procedures some patients showed delay in wound healing. So in this study my aim is to find out the factors which cause delay in healing of wound after direct revascularization.

Methods

This a prospective hospital based observational study conducted in our department from January 2013 to October 2015. In this study we include all diabetic foot ulcer with occlusive arterial diseases (POAD) and those who underwent Percutaneous transluminal angioplasty (PTA). We excluded patients who were not given consent for the study.

Method of Data Collection

Patients presenting with diabetic foot ulcer and POAD will be properly scrutinized with detailed history and clinical examination including peripheral arterial pulsation and the ulcer examined for the amount of tissue loss. All these patients were subjected to arterial Doppler and peripheral angiogram. Vascular surgeon consultation was sought regarding the need for revascularization.

As a result of an unclear distribution of the borderlines between angiosomes, due to the existence of more than one scheme, we decided to adopt the general scheme of angiosomal distribution, in which borderlines between angiosomes match those outlined in the recent publication, "Long-term results of direct and indirect endovascular revascularization based on the angiosome concept in patients with critical limb ischemia presenting with isolated below-the-knee lesions" by Osamu Iida et al [4].

First we will identify the non healing ulcer are by clinical examination and it was confirmed by angiosome based favorable target lesion by peripheral angiogram. Per operatively we tried for an angiosome based intervention (PTA) of the target lesion. If angiosome based straight line is obtained, patient is included in direct group. If angiosome based target lesion treatment is unsuccessful, a non angiosome based lesion will be treated and patient will be included in indirect group. In this way patients underwent endovascular intervention divided into two groups one with direct the other one with non

angiosome based revascularization as indirect group. Before the procedures all patients were started with aspirin and after the procedure with clopidogrel. Both were continued till the ulcer heals after that aspirin will be continued lifelong. Local wound care chosen depending upon characteristics of each lesion. All patients were followed for 6 months, at 1 week, 1 month, 3rd month and 6th months. During follow up patients were examined regarding status of wound, peripheral pulses and appropriate wound cares were given. For this study, follow-up ended 6 months after the primary PTA, or death, whichever occurred first. Adverse events like Major amputation (proximal to ankle level) was noted. Outcome measures. Ulcer healing time, legs salvaged, and ulcer recurrence were looked into. In non healing group we studied the factors which are responsible also were looked in to.

Statistical Analysis

Data was entered in Microsoft Excel and analysis was done using SPSS software (Trial Version 22). Descriptive analysis was done. The association between the type of revascularization done based on Angiosome concept and various outcome parameters were looked into using 't' test or Chi square test

A total of 50 diabetic foot ulcer with PVD who underwent endovascular revascularization to lower limb were included in this study. Direct flow to the foot ulcer based on the angiosome principle was achieved in 26 legs (52%) and direct perfusion was not achieved in 24 legs (48%) .

Gender Distribution

Indirect group had more number of female patients 7 out of 24 (29 %) whereas only 2 out of 26 patients in direct group (Figure 1).

Age Distribution

Mean age of participants in direct group was 64.0 ± 9.0 years whereas that of participants in indirect group was 65.3 ± 11.5 years. Indirect group had more older patients (Table 1). In both the groups there were no significant difference in terms of age of participants.

BMI

Mean Body mass index of direct group was 21.5 ± 2.6 kg/m² that of indirect group was 22.2 ± 2.5 kg/m² (Table 2). There was no significant difference in BMI of both groups.

Addictions

Table 3 depicts the distribution of participants according to smoking behavior 30 out of the 50 participants were smokers. The number of smokers in direct group was significantly higher ($\chi^2 = 3.86^*$, $p = 0.049$).

Comorbidities

All the participants in both the groups were diabetic. Both groups were comparable in terms of comorbidities. CKD which is a well established factor for non healing ulcer was present more in direct group. 5 patients out of 26 (19.2%) against a single patient in indirect group and he was on haemodialysis. But this was not statistically significant. (p value 0.101) (Table 4).

Table 5 shows Mean duration of diabetes in direct group was 18.5 ± 8.0 years and in indirect group was 16.2 ± 6.5 years. Patients in direct group were having longer duration of diabetes.

Characteristics of Ulcer

Location of Ulcer

Majority of ulcer in this study were located in toe (70%), followed by plantar aspect of foot (14%). This shows that ischemic ulcers have a tendency to occur distally. 73.1% of Direct group had ulcers in distally in toes whereas 66.7% of indirect group were having ulcers in the toe (Figure 2).

Characteristics of Ulcer

There was a significant (p value 0.032) difference between the characteristics of ulcer in both groups. Majority of the ulcer direct group (73%) were belonging to UTCWS grade 3 (wound penetrating to bone and joint) whereas majority of the ulcer in the indirect group were belonging to UTCWS grade 2 (wound penetrating to tendon or capsule).

69.2% of direct group belonged to stage D (both infection and ischemia) when compared to 62.5% in indirect group. As shown in Table 6 ulcers of direct group were having higher grade of UTCW system and hence had bad prognosis. This data shows that ulcers of direct group were having higher grade of UTCW system and hence more bad prognosis.

Angiosome Affected

Angiosome fed by Anterior tibial was the most common angiosome affected which constituted 25 out

of the total 50 cases (50%) followed by Medial plantar angiosome 19 cases (20%), lateral plantar artery 4 cases (8%) and 2 cases (4%) belonged to Medial calcaneal angiosome. None of cases were belonging to angiosome fed by peroneal artery. It shows that peroneal artery is the last artery to be involved in Diabetic foot with PAD (Figure 3).

Affected Arterial Segment

When analyzing involved segment of arteries, most common pattern found was multisegmental involvement 48% of cases whereas involvement of infrapopliteal segment and femeropopliteal segment were 32% and 20% respectively. This shows that involvement peripheral vessels in PAD in diabetic foot is multisegmental 48% (both femeropopliteal and infrapopliteal) and Tibioperoneal trunk is more affected than femeropopliteal segment (32% vs 20%) (Figure 4).

Outcomes

The various outcome parameter studied in this study are ulcer healing at 6 months, recurrent ulceration and Major Amputation.

Ulcer healed at 6 months

Table 7 reveals that in 78.3% cases ulcer healed at 6 months in the indirect group whereas 57.7% patients had healed ulcers at 6 months in the Direct group. This difference in proportion wasn't found to be significant (p value = 0.12).

Ulcer healing time: One death occurred in 1st month in indirect group so he was excluded in calculating healing rate. 33 patients out of 49 cases (67.3%) had completely healed wound at 6 months of follow up. 5 out of 23 patients in indirect groups were having persistent wound at 6 months (21.7%). Direct group had 11 out of 26 (42.3%) wound that was not healed at the end of 6 month, though this was not statistically not significant (p value 0.125) (Figure 4).

Association of Gender with Ulcer Healing at 6 Months

Out of nine females six (66%) had healed wound at 6 months, whereas 67.5% males achieved ulcer healing at 6 months. No significant association between ulcer healing at 6 months and gender (Table 8).

Association of Smoking Behavior with Ulcer Healing at 6 Months

Out of 30 smokers 20 had healed wound at 6

months. No significant association between ulcer healing at 6 months and smoking behavior (Table 9).

Association of CKD with Ulcer Healing at 6 Months

Out of six CKD patients 4 had non healing ulcer at 6 months (p = 0.058). No significant association between ulcer healing at 6 months and CKD (Table 10).

Association of Ulcer Grade with Ulcer Healing at 6 Months

27 patients had grade 3 UTCWS ulcer and 16 patients (59.2%) had healed ulcer at 6 months (p = 0.37) No significant association between ulcer healing at 6 months and ulcer grade.

This proves that ulcer healing at 6 months had no significant association with CKD, smoking, or Ulcer grade based on UTCW system (Table 11).

Recurrent ulcer were present in 4% of cases (8.16%) of which three were belonging to direct group. This finding also not statistically significant (p=0.61) (Table 12).

Inference: No significant advantage for direct revascularization in preventing recurrent ulceration over indirect revascularization (Table 12).

Major Amputation : out of 50 participants only one participant (2%) underwent major amputation (proximal to ankle level). So we can infer that no significant advantage for direct revascularization in terms of major amputation.

Leg salvage rate: 49 legs out of 50 were able to salvage at end of 6 months (98%). No significant between two groups in Leg salvage rate. We can infer that endovascular revascularization is a good modality to reduce morbidity in Diabetic foot ulcer patients.

Deaths: total 4 deaths occurred in study sample. 3 death occurred in indirect group one was during 4th month post procedure due to sepsis from wound and he underwent major amputation also. Other two

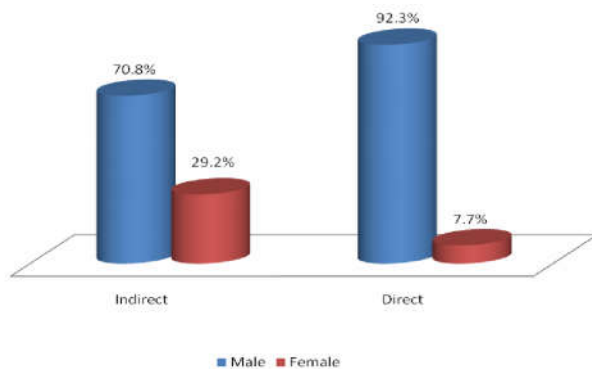


Fig. 1: Gender distribution

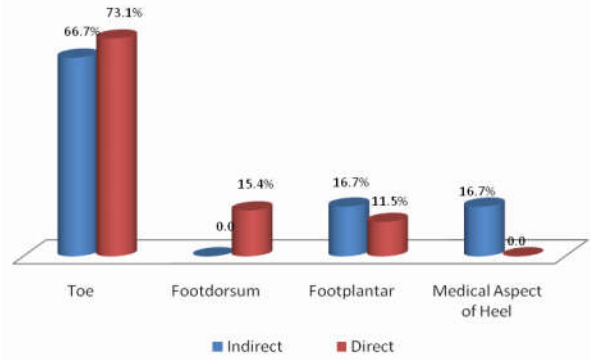


Fig. 2: Comparison of group based on ulcer Location

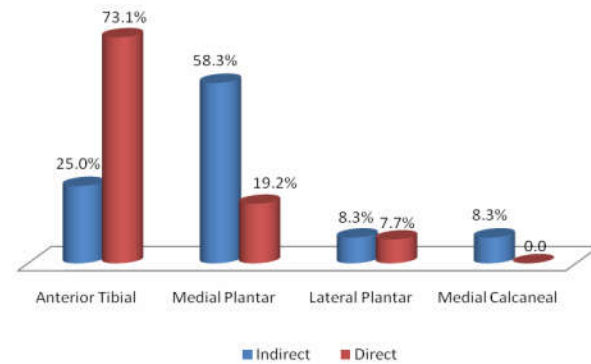


Fig. 3: Distribution of angiosome affected in both group

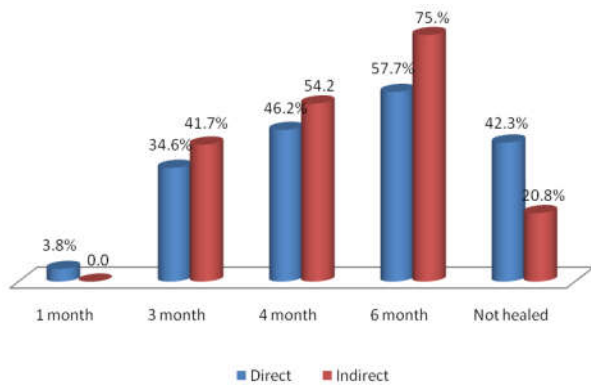


Fig. 4: Comparison ulcer healing time in both group

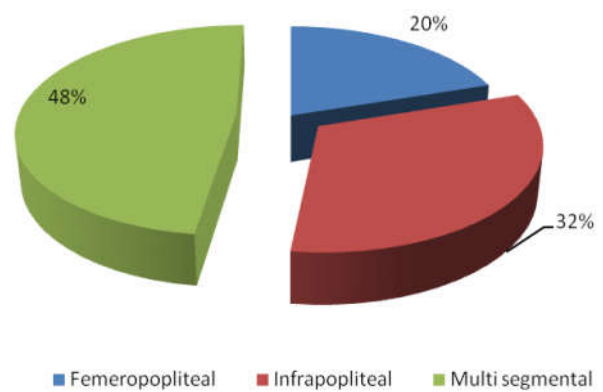


Fig. 4: Pattern of affected arterial segment in this study

Table 1: Age distribution in both groups

Age (in years)	Indirect		Direct		χ^2	P
	Count	Percent	Count	Percent		
< 65	13	54.2	13	50.0	0.09	0.768
≥ 65	11	45.8	13	50.0		
Mean ± SD	65.3 ± 11.5		64.0 ± 9.0			

Table 2: Comparison of groups based on BMI

BMI (kg/m ²)	Indirect		Direct		χ^2	p
	Count	Percent	Count	Percent		
Under weight	1	4.2	4	15.4	2.62	0.270
Normal weight	21	87.5	18	69.2		
Over weight	2	8.3	4	15.4		
Mean ± SD	22.2 ± 2.5		21.5 ± 2.6			

Table 3: Distribution according to smoking

Smoking	Indirect		Direct	
	Count	Percent	Count	Percent
No	13	54.2	7	26.9
Yes	11	45.8	19	73.1

Table 4: Distribution of participants based on comorbidities

Comorbidities	Indirect		Direct		χ^2	p
	Count	Percent	Count	Percent		
DM	24	100	26	100		
Hypertension	12	50.0	17	65.4	1.21	0.271
Hyperlipidemia	12	50.0	16	61.5	0.67	0.412
Chronic Kidney Disease	1	4.2	5	19.2	2.68	0.101
Coronary Artery Disease	6	25.0	10	38.5	1.04	0.308
Cerebral Vascular Disease	3	12.5	0	0.0	3.46	0.063
Chronic Obstructive Pulmonary Disease	3	12.5	1	3.8	1.27	0.260

Table 5: Distribution according to duration of Diabetes Mellitus

Duration of Diabetes Mellitus (in years)	Indirect		Direct	
	Count	Percent	Count	Percent
≤ 10	7	29.2	6	23.1
11 - 15	5	20.8	6	23.1
16 - 20	7	29.2	7	26.9
> 20	5	20.8	7	26.9
Mean ± SD	16.2 ± 6.5		18.5 ± 8.0	

Table 6: Comparison of both groups based on characteristics of wound

Characteristics of wound	Indirect		Direct		χ^2	p	
	Count	Percent	Count	Percent			
UTCWS Classification	Grade 1	4	16.7	3	11.5	6.91*	0.032
	Grade 2	11	45.8	4	15.4		
	Grade 3	9	37.5	19	73.1		
UTCWS Classification	Stage C	9	37.5	8	30.8	0.25	0.616
	Stage D	15	62.5	18	69.2		

Table 7: Comparison of groups based on proportion of ulcer healed at 6 months

Whether healed at 6 months	Indirect		Direct		χ^2	p
	Count	Percent	Count	Percent		
No	5	21.7	11	42.3	2.35	0.125
Yes	18	78.3	15	57.7		

Table 8: Comparison of whether healed at 6 months based on gender

Sex	Ulcer not healed		Ulcer healed at 6 months		χ^2	p
	Count	Percent	Count	Percent		
Male	13	32.5	27	67.5	0.00	0.962
Female	3	33.3	6	66.7		

Table 9: Comparison of whether healed at 6 months based on smoking

Smoking	Ulcer not healed at 6 month		Ulcer healed at 6 month		χ^2	p
	Count	Percent	Count	Percent		
No	6	37.5	13	39.4	0.02	0.898
Yes	10	62.5	20	60.6		

Table 10: Comparison of whether healed at 6 months based on chronic kidney disease

Chronic Kidney Disease	Ulcer not healed at 6 month		Ulcer healed at 6 month		χ^2	P
	Count	Percent	Count	Percent		
No	12	75.0	31	93.9	3.60	0.058
Yes	4	25.0	2	6.1		

Table 11: Comparison of whether healed at 6 months based on UTCWS Classification

UTCWS Classification	Ulcer not healed at 6 month		Ulcer healed at 6 month		χ^2	p
	Count	Percent	Count	Percent		
Grade 1	2	12.5	5	15.2	1.95	0.378
Grade 2	3	18.8	12	36.4		
Grade 3	11	68.8	16	48.5		

Table 12: Comparison of two groups based on recurrent ulcers

Recurrent Ulcers	Indirect		Direct		p#
	Count	Percent	Count	Percent	
No	22	95.7	23	88.5	0.610
Yes	1	4.3	3	11.5	

Table 13: Death within 6 months

	Indirect		Direct		p#
	Count	Percent	Count	Percent	
Death within 6 months	3	12.5	1	3.8	0.340

deaths was due to COPD exacerbation in 1st month and CKD respectively. One death in direct group was due to CKD during 6th month post procedure. So we can infer that there is no significant difference in death rate between two groups ($p=0.34$) (Table 13).

Discussion

In this study we were able to achieve straight inline flow to ischemic angiosome in 52% of patients out of 50 diabetic foot ulcer with diagnosed POVD. Both groups based on angiosome concept were comparable in terms of base line characteristics and co morbidities except in case of gender, smoking and ulcer grade. The most common site of ulcer in our study was in the toe as in literature [5,6]. Pattern of occlusion in peripheral vasculature was multisegmental followed by infra popliteal vessels. This is in concordance with Edmon et al [7] observation. This study shows there is no significant difference in healing rates in both groups, but endovascular revascularization is an

effective interventional modality for diabetic foot ulcers, as 67% of wound were healed at 6 months of follow up. Similar results are reported by Deguchi et al who included 66 legs and a similar healing rate in both group (73 % in DR vs 72 % in IR) [8]. Although apparent better healing seen in indirect group, it may be due to the fact that higher number of smokers, CKD patients and grade 3 ulcer in direct group, which are known risk factors for non healing in a diabetic foot [9,5]. Previous studies by Lida et al [10] and Kabara et al [11] have showed statistically significant better healing after achieving direct inflow to ischemic angiosome when compared with indirect revascularization. According to Lida et al [10] the ulcer healing rates were 48% at 6 months for the direct group compared with 26% for the indirect group ($P < .001$). Better healing rates obtained in an Indian study by Kabara et al [11] the rates of wound healing for both the DR and IR groups was 96.4% vs 83.3% (p value 0.02) at the completion of 6 months. Both these studies were retrospective and base line

characteristics were better in DR group.

In the case of other measures of outcome also, ie leg salvage rate, major amputation rate, recurrent ulceration and death within 6 months also we couldn't find any statistical difference. Another study which put forward similar finding was one by Azuma et al [12] in which 96 patients included in study and showed a limb salvage rate of 97.8% vs 92.3% (p value 0.855). Similar observations made by Kabra et al [7] regarding limb salvage rate (84% for DR against 75% for IR p value = .06)

Limitations of this Study

1. This study included prospective analysis of 50 consecutive patients presented to our surgical department with diabetic foot ulcer and having diagnosed peripheral vascular disease. We need large randomized control studies to validate or refute the angiosome concept.
2. Due to multiple anatomical variations in the foot arteries, the general scheme of angiosomal distribution cannot be used in the case of every patient [13]. The diversity of the distribution is well demonstrated in Attinger's study from 2006.[14]
3. Diabetic patients may present with a multitude of wounds that are heterogeneous in morphology and topography. For example, an ulcer lying over multiple angiosomes, multiple foot ulcers. So it was difficult to assign patients into a particular angiosome.
4. Finally wound care wasn't standardized and variations in glycemic control of the patients, which might have influenced outcome.

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