Research Article

Evaluation of angiosome based revascularization in diabetic foot ulcers

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ABSTRACT

Background: Diabetic foot ulcers are very common complication in diabetic patients and important cause of morbidity to patient and affect quality of life. Ischemia forms a major risk factor for non-healing ulcer. Even after revascularization these ulcers shows delay in healing. Based on studies by Ian Taylor who proposed angiosome concept, it is said that non achievement of direct flow to ulcer area may be a reason for this. Objective of this study was to evaluate the outcome in angiosome based revascularization in diabetic foot ulcer.

Methods: A prospective observational study was done which included 50 diabetic foot ulcer patient who underwent endovascular revascularization in department of general surgery in our hospital during the period October 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 multi segmental followed by infra popliteal 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.

Conclusions: 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

Foot ulcers are common in diabetic population. Ischemia, neuropathy, and infection forms etiological triad. Among these three, occlusive disease of the infra popliteal arteries are the most important factor preventing healing of diabetic foot ulcers.[1,2] Despite achievement of revascularization several factors cause delayed healing. Inadequate arterial flow to specific ulcer area may be one of the reason for delayed wound healing.[3] Ian Taylor et al put forward angiosome concept, which states specific source artery supplies specific areas of foot. This concept is adapted in vascular revascularization and multiple studies about wound healing have been published over the last decade in vascular literature showed promising results in terms of ulcer healing rates and amputation free survival. But in order to open a specific source artery to ulcer area requires more time, more skills, more contrast

and prolongs procedure time. This study is an attempt to know whether significant advantage exist for angiosome guided revascularization over non-angiosome guided revascularization.

METHODS

It's a prospective observational study conducted in our institution from October 2013 to October 2015 and included 50 foot ulcer patients with POVD who undergoes endovascular revascularization. The aim of our study was to evaluate the outcome in angiosome based revascularization in diabetic foot ulcer.

Inclusion criteria

Study population should satisfy following criteria

- Patients with diabetic foot ulcer having peripheral occlusive arterial disease (POAD)
- Patients who underwent percutaneous trans luminal angioplasty (PTA).

Exclusion criteria

- Patients who didn't give consent for the study
- Patient who underwent revision surgery

Method of data collection

Patients presenting with diabetic foot ulcer and POAD will be properly scrutinized with.

- Detailed history
- Clinical examination including each arterial pulsation
- Extent of tissue loss
- Duplex ultra sound imaging
- Peripheral angiogram
- Vascular surgeon opinion whether intervention indicated or not

As a result of an unclear distribution of the borderlines between angiosome, due to the existence of more than one scheme, we decided to adopt the general scheme of angiosome distribution, in which borderlines between angiosome 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] Schematic diagram is shown in (Figure 1).

Before intervention first confirms the location of non-healing ulcer by clinical examination and angiosome based favorable target lesion by peripheral angiogram. Per operatively we tried for an angiosome based intervention 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.

Figure 1: Schematic representation of the angiosomes of foot.

Antiplatelet therapy with Aspirin (150 mg daily) started prior to PTA and Clopidogrel (150 mg) started after the procedure. Clopidogrel and Aspirin continued till ulcer heals and aspirin continued for life long. 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 care was given. For this study, follow-up ended 6 months after the primary PTA, or death, whichever occurred first. An adverse event like major amputation (proximal to ankle level) was noted. Outcome measures of ulcer healing time, legs salvaged, and ulcer recurrence were looked into.

Parameters studied are

- Ulcer healing rate
- Ulcer recurrence
- Leg salvage rate
- Patients undergoing major amputation

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 .

RESULTS

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.

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 older patients (Table 1).

Table 1: Age distribution in both groups.

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

Both the groups were not significantly different 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).

Table 2: Comparison of groups based on BMI.

BMI (kg/m²)	Indirect		Direct		χ^2	p
	Count	%	Count	%		
Under weight	1	4.2	4	15.4		
Normal weight	21	87.5	18	69.2	2.62	0.270
Over weight	2	8.3	4	15.4		
Mean±SD	22.2±2.5		21.5±2.6			

There was no significant difference in BMI of both groups.

Addictions

Depicts the distribution of participants according to smoking behavior (Table 3).

Table 3: Distribution according to smoking.

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

30 out of the 50 participants were smokers. The number of smokers in direct group was significantly higher (X^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 hemodialysis. But this was not statistically significant (P value 0.101) (Table 4).

Table 4: Distribution of participants based on comorbidities.

Comorbid-ities	Indirect		Direct		χ^2	p
	Count	%	Count	%		
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	%	Count	%
≤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	

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

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 (Figure 2).
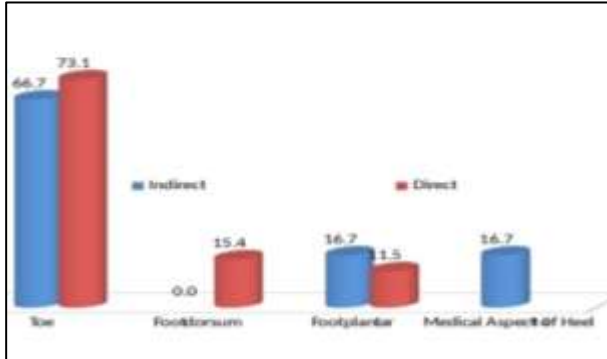

Figure 2: Comparison of group based on ulcer location.

73.1% of direct group had ulcers in distally in toes whereas 66.7% of indirect group were having ulcers in the toe.

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 bad prognosis.

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

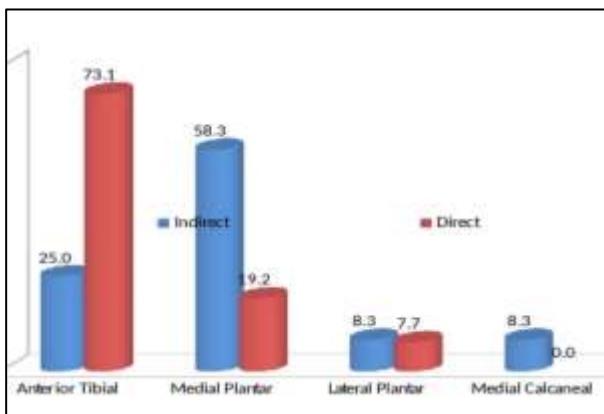| Characteristics of wound		Indirect		Direct		χ^2	p
		Count	Percent (%)	Count	Percent (%)		
UTCWS Classification	Grade 1	4	16.7	3	11.5	6.91*	0.032
	Grade 2	11	45.8	4	15.4		
	Grade 3	9	37.5	19	73.1		
UTCWS Classification	Stage C	9	37.5	8	30.8	0.25	0.616
	Stage D	15	62.5	18	69.2		

Angiosome affected

Figure 3: Distribution of angiosome affected in both group.

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).
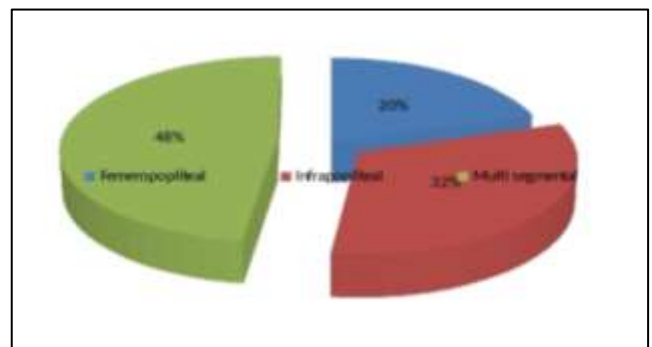
Affected arterial segment

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

When analysing involved segment of arteries, most common pattern found was multisegmental involvement 48% of cases whereas involvement of infra popliteal segment and femeropopliteal segment were 32% and 20% respectively (Figure 4).

This shows that involvement peripheral vessels in pad in diabetic foot is multisegmental 48% (both femeropopliteal and infra popliteal) and tibioperoneal trunk is more affected than femeropopliteal segment (32% versus 20%).

Percutaneous trans luminal angioplasty was commonly done to superficial femoral artery in indirect group whereas anterior tibial was the commonly treated artery in direct group.

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

Ulcer healed at 6 months

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) (Table 7).

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

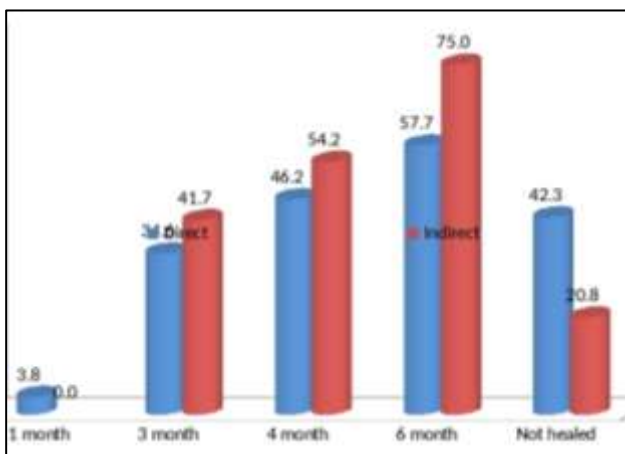| Whether healed at 6 months	Indirect		Direct		χ^2	p
	Count	%	Count	%		
No	5	21.7	11	42.3	2.35	0.125
Yes	18	78.3	15	57.7		

Ulcer healing time

Figure 5: Comparison ulcer healing time in both group.

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 5).

Association of Gender with ulcer healing at 6 months

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	%	Count	%		
Male	13	32.5	27	67.5	0.00	0.962
Female	3	33.3	6	66.7		

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.

Association of smoking behaviour with ulcer healing at 6 months

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

Smok-ing	Ulcer not healed at 6 month		Ulcer healed at 6 month		χ^2	p
	Count	%	Count	%		
No	6	37.5	13	39.4	0.02	0.898
Yes	10	62.5	20	60.6		

Out of 30 smokers 20 had healed wound at 6 months. No significant association between ulcer healing at 6 months and smoking behaviour.

Association of CKD with ulcer healing at 6 months

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	%	Count	%		
No	12	75.0	31	93.9	3.6	0.0
Yes	4	25.0	2	6.1	0	58

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.

Association of ulcer grade with ulcer healing at 6 months

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

UTCWS Classificati on-ion	Ulcer not healed at 6 month		Ulcer healed at 6 month		χ^2	p
	Count	%	Count	%		
Grade 1	2	12.5	5	15.2		
Grade 2	3	18.8	12	36.4	1.95	0.378
Grade 3	11	68.8	16	48.5		

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.

Recurrent ulcers were present in 4% of cases (8.16%) of which three was belonging to direct group. This finding also not statistically significant (P = 0.61).

Table 12: Comparison of two groups based on recurrent ulcers.

Recurrent ulcers	Indirect		Direct		p#
	Count	%	Count	%	
No	22	95.7	23	88.5	0.61
Yes	1	4.3	3	11.5	0

Inference no significant advantage for direct revascularization in preventing recurrent ulceration over indirect revascularization.

Major Amputation out of 50 participant's 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.

Table 13: Death within 6 months.

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

Deaths total 4 deaths occurred in study sample. 3 deaths occurred in indirect group one was during 4th month post

procedure due to sepsis from wound and he underwent major amputation also. Other two deaths were 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).

DISCUSSION

Diabetic foot ulcers are very common complication in diabetic patients and important cause of morbidity to patient and affect quality of life. Ischemia forms a major risk factor for a non-healing ulcer. Even after successful revascularization these ulcers show delay in healing. Based on studies by Ian Taylor who proposed angiosome concept, it is said that non achievement of direct flow to ulcer area may be a reason for this.

A prospective observational study was done which included 50 diabetic foot ulcer patient who underwent endovascular revascularization (PTA) in our institution during the period October 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.

A total of 50 diabetic foot ulcer with PAD 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%). Indirect group had more number of female patients 7 out of 24 (29 %) whereas only 2 out of 26 patients in direct group. 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. Mean Body mass index of direct group was 21.5±2.6 kg/m^2 that of indirect group was 22.2±2.5 kg/m^2. 30 out of the 50 participants were smokers. The number of smokers in direct group was significantly higher (P = 0.049). All the participants in both the groups were diabetic. 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. 5 patients out of 26 (19.2%) against a single patient in indirect group and he was on hemodialysis.

Majority of ulcer in this study were located in toe (70%), followed by plantar aspect of foot (14%).This was in accordance with the literature.[5,6] 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 whereas majority of the ulcer in the indirect group were belonging to UTCWS grade 2, 69.2% of direct group belonged to stage D (both infection and ischemia). 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. When analyzing involved segment of arteries, most common pattern found was multi segmental involvement 48% of cases whereas involvement of infra popliteal segment and femeropopliteal segment were 32% and 20% respectively. This is in accordance with Edmon et al observation.[7]

The various outcome parameter studied in this study are ulcer healing at 6 months, recurrent ulceration and major amputation. 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). No significant association was found between ulcer healing at 6 months and gender (P value = 0.962). Out of 30 smokers 20 had healed wound at 6 months. No significant association between ulcer healing at 6 months and smoking behavior was seen in this study (P = 0.89). Out of six CKD patients 4 had non healing ulcer at 6 months (P = 0.058). This study couldn't find any significant association between ulcer healing at 6 months and CKD. 27 patients had grade 3 UTCWS ulcer and 16 patients (59.2%) had healed ulcer at 6 months (P = 0.37). This proves that ulcer healing at 6 months had no significant association with CKD, smoking, or ulcer grade based on UTCW system.

Recurrent ulcers were present in 4% of cases (8.16%) of which three was belonging to direct group. This finding is also not statistically significant (P = 0.61). 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. 49 legs out of 50 were able to salvage at end of 6 months (98%). No significant between two groups in leg salvage rate. 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 deaths was due to COPD exacerbation in 1st month and CKD in 5th month respectively. One death in direct group was due to CKD during 6th month post procedure.

Similar ulcer healing rates are reported by Deguchi et al who included 66 legs and a similar healing rate in both group (73% in DR versus 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. Kabra et al and Azuma et al provided a similar leg salvage rate at 6 months post procedure we can conclude that, there is no significant advantage of achieving direct pulsatile blood flow to an ischemic angiosome during endovascular revascularization in diabetic foot ulcers over revascularization in which direct flow can't be attained in terms ulcer healing rate, limb salvage or survival rate.

But we need a large multicenteric trials to refute the Angiosome concept.[5,9-11]

The limitations of this study was total number of patient here is only 50. We need large randomized control studies to validate or refute the angiosome concept. Due to multiple anatomical variations in the foot arteries, the general scheme of angiosomal distribution cannot used in the case of every patient. The diversity of the distribution is well demonstrated in Attinger's study from 2006.[12,13] Diabetic patients may present with a multitude of wounds that are heterogeneous in morphology and topography. So it was difficult to assign patients into a particular angiosome.

CONCLUSION

Endovascular revascularization is a good modality for treating ischemic diabetic foot ulcers to reduce the morbidity. From this study we can conclude that, there is no significant advantage of achieving direct pulsatile blood flow to an ischemic angiosome during endovascular revascularization in diabetic foot ulcers when compared to revascularization in which direct flow can't be attained in terms ulcer healing rate, limb salvage or survival rate. But we need large multicenteric trials to refute the angiosome concept.

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