

Effectiveness of Angioplasty in Treatment of Diabetic Foot Patients with Infragenicular Multiple Stenosis or Occlusion: A Prospective Study

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ABSTRACT

Background: Diabetic foot is one of the most serious and debilitating consequences of diabetes, and it is described as an ulcerated foot in a diabetic patient with neuropathy and/or peripheral artery disease of the lower limb. Diabetic foot ulceration affects 4–10% of diabetic patients, with the condition affecting older patients more frequently.

Objectives: In this study, we aimed to assess the effectiveness of angioplasty in the treatment of diabetic foot patients with infragenicular multiple stenosis or occlusion.

Patients and Methods: We performed a prospective cohort investigation that recruited diabetic patient with infragenicular critical limb ischemia (CLI) with or without supragenicular lesion at Vascular Surgery Department in Aswan University Hospital through the period from January 2019 to June 2020. 20 patients were included if they were older than 18 years old, diabetic, had diabetic foot, and had confirmed diagnosis of CLI.

Results: Seventeen patients (85%) had immediate success, they remained patent after one month. After three and six months, 14 patients (70%) and 13 (65%) remained patent, respectively ($p > 0.05$). With regard to limb salvage by the end of six months, 15 patients (75%) had limb salvage in the form of rest pain relief in 3/4 patients (75%), minor ulcer healing in 10/10 patients (100%), and healing of tissue after debridement or minor amputation 2/6 patients (33.3%). The remaining five patients had non-salvaged limbs. As regarding amputations, three patients (15%) underwent major amputation. A total of four patients (20%) had complications.

Conclusion: In conclusion, infragenicular angioplasty exhibited efficacy in CLI management in diabetic patients, with an acceptable patency rate and safety profile.

Keywords: Diabetes, Diabetic Foot, Infragenicular Angioplasty, Limb Ischemia.

INTRODUCTION

Diabetic foot ulcers are common complications of diabetes mellitus (DM), affecting more than 15% of all diabetic patients during their lifetime ⁽¹⁾. It was estimated that about 15 – 20% of patients with such conditions would need an amputation ^(2,3). The most significant risk factor for foot ulcers is peripheral sensory neuropathy, which is accompanied by peripheral vascular disease (PVD) ⁽³⁾. PVD affects the arterial tree at all levels, but atheroma seems to prefer some locations, such as bifurcations where hemodynamic shear stress is low or flow separation occurs ⁽⁴⁾. The infragenicular arteries are often involved in patients with diabetes, resulting in multiple stenosis or occlusion ⁽⁵⁾. Patients with critical limb ischemia (CLI) are becoming older and sicker with the more complex distal disease.

Revascularization is mandatory for patients with evident peripheral ischemia because sufficient blood flow is essential for the healing of injuries and the resolution of the underlying infection ⁽⁶⁾.

A surgical bypass is a popular form of treatment of ischemic limbs, which has recorded good long-term findings ⁽⁷⁾. In cases of multiple occlusions, revascularization is required at each stage to restore blood flow and raise the likelihood of limb regeneration ⁽⁸⁾. In combination with surgical bypass on the distal extremity, transluminal angioplasty of iliac arteries can be performed, and effectiveness has been demonstrated in diabetic patients. Transluminal angioplasty is also an ideal alternative for single stenotic injuries ⁽⁹⁾.

A large meta-analysis of 52 studies demonstrated the efficacy of angioplasty in managing infrapopliteal atherosclerotic lesions, with an overall success rate of 91.1% ⁽¹⁰⁾. In this study, we aimed to assess the effectiveness of angioplasty in the treatment of diabetic foot patients with infragenicular multiple stenosis or occlusion.

MATERIAL AND METHODS

We performed a prospective cohort investigation that recruited diabetic patient with infragenicular CLI with or without supragenicular lesion at Vascular Surgery Department in Aswan University Hospital through the period from January 2019 to June 2020. 20 patients were included if they were older than 18 years old, diabetic, had diabetic foot, and had confirmed diagnosis of CLI. We included patients with type B the Trans-Atlantic Inter-Society Consensus Document (TASC), defined as “multiple stenosis each equal or less than 5 cm in length with total length less than 10 cm, or single occlusion equal or less than 10 cm in length 5 cm in the target tibial artery with occlusion or stenosis similar or worse in severity in the other tibial arteries”.

The diagnosis of diabetic foot was based on clinical presentation and supporting imaging modalities ⁽¹¹⁾. While the CLI was defined as Rutherford category of equal or more than four ⁽¹²⁾. Patients were excluded if they had extensive lower limb infections, full-thickness gangrene, primary vascular etiology, and/or mental or



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cognitive impairment. Besides, we excluded patients who were not eligible for two revascularization strategies.

Data Collection:

The following data were obtained from every eligible patient:

- Demographic characteristics.
- Risk factors for CLI and diabetic foot
- History of previous peripheral artery disease (PAD) procedures or leg amputation.
- Findings of the physical examination.
- Routine laboratory findings.
- Imaging findings, including duplex ultrasound, computerized tomography angiography (CTA), magnetic resonance angiography (MRA), and digital subtraction angiography (DUS).

Study Procedures:

Patients were instructed to take clopidogrel five days preoperatively. Alternatively, a periprocedure loading dose of 300 mg was administrated. The angioplasty technique was performed according to the institute’s protocol and all procedures were performed under local anesthesia. The access through the artery was guided by preoperative imaging and done by either antegrade or cross-over techniques of common femoral artery puncture. Then, F sheath was inserted, and a dye-guided angiography was performed to identify the lesion. To cross the stenosis, guidewires were introduced and a drilling motion of the guidewire was performed, followed by insertion of coaxial catheter balloon. Then, a 2-3.5 mm balloons were inserted and inflated. After balloon deflation, a 100 ug of nitroglycerin was injected intra-arterially. Then, an angiogram was performed. A success technique was defined as less than 30% residual stenosis of the target tibial artery and restoration of the pulse. Patients were managed postoperatively according to the institute’s protocol and maintained on cilostazol 100 mg twice/day, acetylsalicylic acid 150 mg/day, and /or clopidogrel 75 mg/day after hospital discharge. All patients were followed up for six months procedure.

Study Endpoints:

The primary endpoint in our study was the primary patency rate at the end of the sixth month of follow-up, the patency was determined by palpation of the pulse and Duplex ultrasound. The secondary endpoints included the rate of clinical success, limb salvage, rest pain restoration, and postoperative complications.

Ethical consent:

An approval of the study was obtained from Aswan University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of the operation. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analyses

The statistical analyses were employed using SPSS software (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) version 22 for Microsoft Windows. The mean ±standard deviation (±SD) and median were used to describe numerical variables. Frequencies with percentages were applied to present categorical variables. The level of significance was set at a probability critical value (p-value) lower than 0.05.

RESULTS

The baseline data of the study are shown in table 1.

Table (1): Baseline data in both groups

Variables	Patients (n= 20)	
	No.	%
Sex		
Male	15	75.0
Female	5	25.0
Age (years)		
Min. – Max.	52.0 – 82.0	
Mean ± SD.	67.05 ± 9.34	
Median	67.0	
Smoking	14	7
Diabetes mellitus	16	80
Hypertension	15	75
Ischemic heart disease	12	60
HLIP	13	65
Stroke	4	20
Previous angioplasty	5	25
Rutherford		
4	4	20.0
5	10	50.0
6	6	30.0
Min. – Max.	4.0 – 6.0	
Mean ± SD.	5.10 ± 0.72	
Median	5.0	

Three patients (15%) underwent major amputation and a total of four patients (20%) had complications (Table 2).

Table (2): Amputations and complications in both groups

Variables	Patients (n= 20)	
	No.	%
Amputation	No	17 85
	Yes	3 15
Complications	Major	1 5
	Acute thrombosis	0 0
	Severe hemorrhage	0 0
	Severe graft infection	0 0
	Huge hematoma and pseudo-aneurysm	1 5
	Minor	3 15
	Edema	0 0
	Infection	0 0
	Hematoma	3 15
	Contracture scar at knee	0 0

There were no significant associations between patency rate and age, risk factors, co-morbidities, symptomatic presentation, and lesion morphology. Patients with IHD and a history of previous angioplasty had significantly lower patency rate ($p < 0.05$).

DISCUSSION

The incidence of critical limb ischemia (CLI) is reported to be 10 per 10,000 population, with about 27% due to infragenicular disease⁽⁷⁾. Because of aging, persistently elevated levels of smoking, and the rapid increase in diabetes mellitus rates, the incidence of infragenicular disease continues to increase⁽¹³⁾. Recently, a growing body of evidence highlighted promising results of infragenicular angioplasty in diabetic patients with CLI; it was shown that infragenicular angioplasty achieved high patency rates and limb salvage in diabetic patients, which were comparable to non-diabetic patients⁽¹⁴⁾. Nonetheless, limited data are available about the safety and efficacy of infragenicular angioplasty in limited-resource areas like Egypt. Accordingly, our study aims to examine the effectiveness and safety of infragenicular angioplasty in diabetic patients with critical limb ischemia.

Our findings showed an overall success rate of 85%, which persists for six months in about 65% of the included patients. Regarding limb salvage, 75% of the patients had limb salvage after six months in the form of rest pain relief, minor ulcer healing, and tissue healing after debridement or minor amputation. A large meta-analysis on 6769 patients demonstrated the efficacy of angioplasty in managing infrapopliteal atherosclerotic lesions with an overall success rate (primary patency rate) of 91.1%⁽¹⁰⁾. **Tartaglia et al.**⁽¹⁵⁾ conducted a retrospective study on 101 high-risk diabetic patients with CLI and reported that the primary patency was 67%, while the secondary patency was 83%. In terms of limb salvage rate and survival rate, it was 84% and 86%, respectively. In 63 patients with CLI due to Infrapopliteal (IP) lesions, **Park et al.**⁽¹⁶⁾ identified the primary patency rate was 75% in 1 year, and the limb salvage rate was 91%. **Ferraresi et al.**⁽¹⁷⁾ recorded a 97 percent survival rate and 91 percent limb salvage rate in 101 diabetic patients who presented with CLI and were treated with angioplasty. In contrast, **Sadaghianloo and his colleagues** reported a very low rate of primary and secondary patency after angioplasty, 13% and 32%, respectively. They found a significant association between the length of the occlusion and the success of the technique. Moreover, they demonstrated that the number of patent arteries at the end of the procedure is significantly associated with the rate of success; the larger number of patent arteries, the higher is the success rate⁽¹⁸⁾.

Ni and his colleagues⁽¹⁹⁾ reported that limb salvage rates were 75% at one year and reached 62% after 10 years. Compared to the **Adam et al.**⁽²⁰⁾ and **Iida et al.**⁽²¹⁾ studies, the limb salvage rate was lower in our study and Ni's study. The different populations could

explain the difference in findings between our study and both **Adam et al.**⁽²⁰⁾ and **Iida et al.**⁽²¹⁾. Ni's study and our study targeted mainly diabetic patients, while the aforementioned studies have fewer patients with diabetes. According to the regression analysis, DM was significantly correlated with lower-limb salvage rate and survival rate, which is confirmed by the previous literature. The multivariate analysis of **Ni et al.** demonstrated that DM was associated with a higher risk of major amputation OR 2.813, 95% (1.719–4.604), $p < 0.001$ ⁽¹⁹⁾.

Ten years ago, the most favored technique for endovascular diseases was to seek a clear blood circulation antegrade in the most accessible artery. However, **Peregrin et al.**⁽²²⁾ reported complete revascularization in diabetic patients with CLI if one, two, or three vessels were patent again, resulting in 1-year limb salvage of 73, 80, and 83 percent, respectively. In the case of multiple lesions on various arteries, it is recommended to target the angiosome-related artery to ensure maximum revascularization⁽²³⁾. Nevertheless, it is often difficult, particularly in heavily calcified lesions in diabetic patients⁽²⁴⁾.

Previous CLI research has mainly focused on patency and limb salvage rates, neglecting cost-effectiveness, clinical improvement, and functional status⁽²⁵⁾. The results of **Romiti et al.**'s⁽²⁶⁾ meta-analysis on 30 infrapopliteal angioplasty studies showed the futility of these endpoints and their ability to misinform patient outcomes. They observed a significant difference between secondary patency and limb salvage, showing that patency was not a requirement for avoiding amputation.

Regarding the safety of angioplasty, our findings showed that only 15% of the included patients had major amputation. To predict the risk of amputation, **Ni et al.**⁽¹⁹⁾ developed a predicting score consist of age < 69 years, DM, history of cerebral vascular disease, end-stage renal disease, Rutherford classification, repeat intervention, number of straight-line flows. Another method was suggested by **Suárez-Cuenca et al.**⁽²⁷⁾, who applied the Local Circulating Mononuclear Progenitor Cells to predict the amputation in angioplasty-treated patients with CLI. In terms of mortality, we did not record any case of death in this study; however, the mortality rate in the study of **Ni et al.**⁽¹⁹⁾ was 5.9%. One patient in our study was reported with a large hematoma and underwent pseudo-aneurysm. In the study of **Ni et al.**⁽¹⁹⁾, 3% had vessel perforation, 2% had distal embolization, and 1% of the patients had a hematoma.

We acknowledge that this prospective study has some limitations. All patients were recruited from one center only; therefore, these results may not be generalized to all patients. In addition, the small sample size and the lack of long-term follow-up are other limitations.

In conclusion, infragenicular angioplasty exhibited efficacy in CLI management in diabetic patients, with an acceptable patency rate and safety

profile. Nonetheless, the current published literature shows conflicting results, and further studies with multinational collaboration are required to assess the outcomes of infragenicular angioplasty.

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