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RESEARCH ARTICLE

Effectiveness of revascularization of the ulcerated foot in diabetic patients with peripheral artery disease for one year follow-up

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BACKGROUND: Diabetes is an important risk factor for atherosclerosis. The diabetic foot is characterized by the presence of arteriopathy and neuropathy.When ischemia is diagnosed, restoration of pulsatile blood flow by revascularization may be considered for salvaging the limb. The treatment options are angioplasty with or without stenting and surgical bypass or hybrid procedures combining the two.
AIMS: To evaluate the outcomes of severe ischemic diabetic foot ulcers for which percutaneous transluminal angioplasty (PTA) was considered as the first-line vascular procedure. Factors associated with successful PTA were also evaluated.
METHODS: In 80 consecutive diabetic patients with foot ulcers and severe limb ischemia, PTA was performed if feasible. All patients were followed until healing or for one year. Clinical and angiographic factors in fluencing outcomes after PTA were sought by univariate and multivariate analysis.
RESULTS: PTA was done in 73 of the 80 (91.2%) patients, and considered clinically succe ssful in 58(79.9%). Successful PTA was significantly higher in patients with Superficial femoral artery, posterior Tibialis and dorsalis pedis arteries involvement in the univariate analysis. Seven patients were expired during the study follow up due to MI, pulmonary thromboembolism and GI bleeding.
CONCLUSION: PTA in diabetic patients with severe ischemic foot ulcers provided favorable. Some parameters could be used for predicting PTA successfulness.

Keywords percutaneous transluminal angioplasty, revascularization, diabetes

Introduction

One of the most common complications associated with diabetes is diabetic foot syndrome. It is a severe chronic complication that raised from a lesion associated with diabetic neuropathy and peripheral arterial disease (PAD) in the lower limbs. Because of increasing in the diabetic patient life expectancy, the incidence of diabetic foot syndrome has also increased (Zhang et al., 2017). It has been estimated, up to 25% of diabetic patients suffered from foot ulcers that usually coexists with PAD (Markakis et al., 2016). It has also subsequently proceeded to a severe gangrene or infections and finally foot amputation. In fact, 85% of amputations in diabetic patients is due to diabetic foot (Lepäntalo et al., 2011). Foot ulcers and amputations lead to considerably decreased in patients quality of life that accompanied by raised morbidity and mortality rate. The most recent study has reported that about 4.5 million adult people were suffered from diabetes in Iran and its incidence estimated around 6.2% (Esteghamati et al., 2017).

Critical limb ischemia (CLI) presents in the late stage of PAD. In the situation, significant reduction of limb arterial blood supply has been occurred that threaten the viability of tissues. Indeed large arteries atherosclerosis caused an obstacle to blood flow and depleting the tissue oxygen and nutritions. CLI presented by rest pain, tissue necrosis, non-healing foot ulcers and gangrene. It could be caused high

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morbidity and poor prognosis (Jörneskog, 2012). It has been reported that five to ten percent of PAD developed to CLI whiten 5 years (Norgren et al., 2007). The best outcome in patients with CLI was occurred when immediately treated by revascularization, and if the attempt have failed, the probability of amputation is about 50% (Lumsden et al., 2009). Several procedures were proposed for revasculaization in diabetic foot including; bypasses and endovascular techniques such as Percutaneous Transluminal angioplasty (PTA) and Subintimal recanalization (Kota et al., 2013). The procedures provided the possibility of distal arterial revascularization to treat distal arterial stenosis and/or obstructions. They also are less invasive than open surgery. Moreover, it could be frequently used in patients who have failed during treatment (Uccioli et al., 2010).

Recently some investigators have evaluated the efficacy of PTA in management of diabetic patients with CLI in upper blow the knee arteries. As it shown several factors could be affected the treatment success (Faglia et al., 2008). In the current study we have tried to evaluate the outcome diabetic patients with ulcerated foot and PAD following treatment by PTA. We have also assessed the predictive factors associated with treatment success.

Material and methods

Study design

The clinical trial study was carried out on the patients with ulcerated diabetic foot admitted to Razi hospital during the 2015 to 2017. The patients with absence of lower limb pulse and/or ulcerated foot included in the study. While, the patients with active infections and high level of creatinine were excluded. The patient preparation recommendations were as follow: Laboratory assessment of complete blood count (CBC), INR, PTT and PT, fasting for 12 h, starting Aspirin and Clopidogrel 3-5 days before surgery, Showering and shaving, Platelet count $>$ 75000 mcl, INR less than 1.5, stopping Warfarin at least 3 days before the procedure, Stop metformin from 48 h before to 48 h after the procedure. In heparinized patients the infusion must be stopped at least 2 h before the procedure. Moreover in the cases with higher than 1.1 mg/dl Cr, Saline infusion and N-Acetyl Cysteine 1200 mg were prescribed. The study was approved by ethical committee of Ahvaz Jundishapour University of Medical Sciences. The study protocol was explained for the patients and signed informed consent were given.

Lower-limb vascular assessment

To determine the lower-limb vascular conditions, color Doppler ultrasound (Accuson 2000, Simens,German) and/or computerized tomography angiography (CTA) were performed. Moreover, the demographic and clinical informations including: Age, Gender, Smoking, Hyperlipidemia, Hypertension, Coronary artery disease, Cerebrovascular accident and transient ischemic attack were collected by a questionnaire. Color Doppler ultrasound were repeated 1, 3, 6 and 12 months after PTA for the patients monitoring.

Angiography and percutaneous transluminal angioplasty

During the procedure, 3000-5000 IU of heparin administered intra arterially Angiography performed through femoral artery retrogradely or antegradely (based on the stenosis site). Hydrophilic guide 0.035 and 0.014, ballon and angioplastic stent were used. The balloon length and diameter were selected based on the vessel diameter and the lesion length. The antiplatelet medications (Aspirin 80 mg and Clopidogrel 75 mg per day) were prescribed for the patients for three months after PTA. The patients were recommended to consume Aspirin for a long time after PTA.

Statistically analysis

Statistical analysis performed by IBM SPSS Statistics version 22. The data obtained were showed by descriptive indicators; mean, standard deviations. Kolmogorov–Smirnov (K-S) used to test the normal distribution of data. To compare numerical variables between the groups, according to normality of data, *t*-test and Mann–Whitney were used. Chi square test was used to compare the categorical variables. A p-value less than 0.05 was considered significance

Results

During the study 80 diabetic patients with foot ulceration were evaluated. The mean age of patients was 66.5 year and 48.8% of them were male. The most common underlying diseases was CAD with 70% frequency that followed by HTN and HLP (Table 1). Posterior Tibialis artery and anterior tibial artery are the most prevalent involved arteries with frequency of 61% and 51%, respectively. While the less frequent involved artery was popliteal artery (Table 2). The mean length of involved arteries were shown in Table 3.

Angioplasty was successfully performed in more than 90% of patients. The one year outcome of patients were as below: 65% of patients completely treated, 7.5% partially treated, 3.8% non-treated, 6.3% relapsed and 8.8% were expired (Table 4, Figs. 1, 2).

The demographic characteristics including age, gender and BMI did not showed any significant differences between healed and non-healed patients. Among the clinical characteristics only hyperlipidemia was significantly higher in patients that successfully treated (Table 5).

The multivariable analysis showed that stenosis in Superficial femoral, posterior tibial and dorsals pedis arteries are associated with better outcome (Table 6).

Table 1 Patients characteristics

Variables		Frequency	Percent
Age(mean±SD)		66.5±8.3 (48-82)	
Gender	Male	39	48.8%
	Female	41	51.2%
Underlying Diseases	HTN	54	67.5%
	HLP	52	65%
	CAD	55	68.8%
	CVA	6	7.5%
	Neuropathy	17	21.3%
	Nephropathy	14	17.5%
Ulcer Size	> 5	38	47.5%
	< 5	42	52.5%
BMI	> 30	33	41.3%
	< 30	47	58.8%
Smoking		30	37.5%

Discussion

Our results showed that could be successfully treated 72.5% of patients. While 3.8% not healed and 6.3% relapsed. Angioplasty was not possible in 8% of patients. Finally, 5 patients were expired during short time after the procedure due to GI bleeding, MI and PTE. The success rate in our study was similar to previous reports. Flagila et al. reported the 78% success rate of peripheral angioplasty in patients with previous history of bypass (Faglia et al., 2008). Actually in contrary with our study, they only included the patients with failing bypass graft or residual CLI after bypass graft. While we did not included such patients. In another study, Kassaian et al. evaluated the 6 months outcome of revisualization in diabetic patients with ulcerative foot. They reported that 59% of patients were successfully treated during 6 months follow up (Kassaian et al., 2013). In the other study with longer

Table 2 The severity of stenosis among involved arteries

Arteries	Variable	Frequency	Percent
Superficial femoral artery	Mild (50-70)	17	21.3%
	Moderate (70-90)	14	17.5%
	Severe (> 90)	7	8.8%
	Near Ocluded (99)	0	0
	Total	38	47.5%
Popliteal artery	Mild (50-70)	9	11.3%
	Moderate (70-90)	5	6.3%
	Sever	0	0
	Near Ocluded (99)	0	0
	Total	14	17.5%
Anterior Tibialis artery	Mild (50-70)	18	22.5%
	Moderate (70-90)	16	20%
	Severe (> 90)	0	0
	Near Ocluded (99)	7	8.8%
	Total	41	51.2%
Posterior Tibialis artery	Mild (50-70)	27	33.8%
	Moderate (70-90)	13	16.3%
	Severe (> 90)	3	3.8%
	Near Ocluded (99)	6	7.5%
	Total	49	61.3%
Proneal artery	Mild (50-70)	24	30%
	Moderate (70-90)	11	13.7%
	Severe (> 90)	0	0
	Near Ocluded (99)	0	0
	Total	35	43.7%
Dorsalis pedis artery	Mild (50-70)	17	21.3%
	Moderate (70-90)	9	11.3%
	Severe (> 90)	0	0
	Near Ocluded (99)	0	0
	Total	26	32.5%

Table 3 Mean length of involved arteries

Vessels	Mean	Std. Deviation	Minimum	Maximum
Superficial femoral artery	181.42	31.47	133	224
Popliteal artery	16.57	2.4	12	19
Anterior Tibialis artery	132.43	42.09	78	201
Posterior Tibialis artery	110.36	35.21	22	192
Proneal artery	107.51	14.83	68	137
Dorsalis pedis artery	42.26	7.23	30	52

Table 4 The outcome of participants

Outcomes		Frequency	Percent
Adverse Effects	None	73	91.3%
	Gi bleeding cuased by colopidogrol overdose (Expired)	3	3.8%
	MI(expired)	3	3.8%
	PTE(expired)	1	1.3%
Healing	Comprelet healing	52	65%
	Partial healing	6	7.5%
	Non-healing	3	3.8%
	Angioplasty not done	7	8.85
	Relapse	5	6.3%
	Expired	7	8.8%

Figure 1 Long segment stenosis of Anterior Tibialis arttry before and after angioplasty.

follow up time, Salas et al. reported the 69% of PTA success rate in treating CLI. The evaluated population in the study not limited to the diabetic patients (Salas et al., 2004). But surprising results were reported by Sun et al.(2013). They showed 100% treatment response without any adverse events.

During evaluation of risk factors associated with treatment response we have found that, demographic characteristics have no significantly correlation with treatment response. Forman et al. in the study evaluated the effect of age on angioplasty treatment response, they did not find any correlation between age and angioplasty success rate (Forman et al., 1992). Some other study were also reported similar results (Kassaian et al., 2013). In terms of clinical

Figure 2 Dorsalis pedis artery angioplasty.

Table 5 Comparison between healed and non-healed patients

Variables		Healing (n = 58)	Non-healing (n = 15)	P-value
Age		65.18±7.6	66.6±8.6	0.519
Gender	Male	24(41.4%)	10(66.7%)	0.072
	Female	34(58.6%)	5(33.3%)	
Arteries	Superficial	183.7273± 30.32	172.4±30.32	0.32
	Popliteal	17.3333±1.7	16	0.147
	Anterior Tibialis	135.6667± 37.32	155.7273± 43.35	0.152
	Posterioi Tibialis	101.0588± 24.25	117.8125± 35.05	0.055
	Dorsalis	40.4444±5.7	40.6364±8.5	0.955
	Proneal artery	105.13±8.93	109.64±11	0.295
BMI	BMI > 30	27(46.6%)	5(33.3%)	0.267
	BMI < 30	31(53.4%)	10(66.7%)	
HTN	Yes	40(69%)	11(73.3%)	0.5
	No	18(31%)	4(26.7%)	
Neuropathy	Yes	12(20.7%	2(13.3%)	0.40
	No	46(79.3%)	13(86.7%)	
Nephropathy	Yes	9(15.5%)	5(33.3%)	0.20
	No	49(84.5%)	10(66.7%)	
CAD	Yes	33(56.9%)	13(86.7%)	0.11
	No	25(43.1%)	2(13.3%)	
CVA	Yes	3(5.2%)	3(20%)	0.097
	No	55(94.5%)	12(80%)	
Hyperlipidemia	Yes	38(65.5%)	9(60%)	0.4
	No	20(34.5%)	6(40%)	
Smoking	Yes	16(27.6%)	9(60%)	0.02*
	N0	42(72.4%)	6(40%)	
Ulcer Size	> 5	25(43.1%)	8(53.3%)	0.33
	< 5	33(56.9%)	7(46.7%)	

Table 6 Multivariable analysis between involved arteries and treatment response

Arteries	B	Sig.	Odds ratio	95% C.I.for EXP(B)	
				Lower	Upper
Superficial femoral artery	2.854	0.007	17.354	2.180	138.138
Popliteal artery	1.712	0.113	5.538	0.666	46.055
Anterior Tibialis artery	−0.430	0.576	0.651	0.144	2.937
Posterior Tibialis artery	2.921	0.007	18.553	2.210	155.723
Proneal artery	1.100	0.151	1.467	0.631	11.530
Dorsalis pedis artery	2.600	0.013	13.467	1.729	104.910

characteristics of patients we have found that hyperlipidemia is associated with better treatment response, this finding was in line with previous study (Kassaian et al., 2013). Exist scientific evidences did not support this result. Based on that, hyperlipidemia could decreases the angioplasty success rate thorough decreasing the endothelium-dependent vasomotor response (Forman et al., 1992). More studies needed to find out the distinct effect of hyperlipidemia on the PTA outcome.

The thrombotic events are the major causes of dead in our study. Although these events could be associated with angioplasty procedure, it has also must be considered that so many studies reported that CLI represented as a marker for predicting cardiovascular disease and generalized atherosclerosis (Gottsäter, 2006). Moreover, recently a study compared the cardiovascular events in CLI patients under treatment either Bypass or angioplasty and showed non-significantly differences between the groups (Flu et al., 2009). Three patients were also died due to GI bleeding. It has been thought it caused by anti-platelet overdose.

Conclusion

Our findings in line with previous studies showed that PTA could be effectively used in management of diabetic patients with CLI. Moreover, the adverse events of the treatment were relatively low.

Study limitations

The monthly evaluation of patients did not registered to determine pattern of changing the patients' clinical features. Moreover the date of admission and adverse events occurrence did not registered to perform survival analysis.

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Compliance with ethical standards

The authors declared no conflict of interest. All procedures have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Informed consent was signed prior to participation in the study.

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