

Original Article

The efficacy and safety of percutaneous transluminal angioplasty of tibioperoneal arteries with DEEP Balloon in diabetic patients with critical limb ischemia: a pilot study

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Abstract: This pilot study was to investigate the efficacy and safety of percutaneous transluminal angioplasty (PTA) of tibioperoneal arteries with DEEP Balloon in diabetic patients with critical limb ischemia (CLI). 15 adults diabetic patients with CLI were recruited in this study. All patients underwent PTA of tibioperoneal arteries with DEEP Balloon and were followed up for 6 months post operation. Technical successful rate, ulcer cure rate and limb salvage rate were calculated after the operation; ankle brachial index (ABI), temperature of toes skin (TTS), rest pain visual analogue scale (VAS) was assessed pre, post the surgery, and at month 1 (M1), M3 as well M6. The overall technical successful rate and ulcer cure rate were 93% and 80% respectively. Limb salvage rate at M6 was 87%. Type 2 DM patients presented an increased technical successful rate (100%) compared to Type 1 DM (67%), $P=0.038$; as well as an elevated limb salvage rate (100% vs 33%, $P=0.002$). ABI was elevated immediately after PTA surgery compare with Pre-PTA ($P<0.001$) and M6 ($P=0.005$). TTS was increase post-PTA and at M6 compared to pre-PTA visit (all $P<0.001$). And rest pain VAS score was decreased post-PTA operation ($P<0.001$), but no difference was observed between pain VAS at M6 and pre-PTA ($P=0.192$). Arterial perforation occurred in 1 patient, and no other PTA operation related complications and death were illuminated. This study revealed that PTA of tibioperoneal arteries with DEEP Balloon was effective and well tolerated for diabetic patients with CLI.

Keywords: Percutaneous transluminal angioplasty (PTA), diabetic, critical limb ischemia (CLI), DEEP Balloon

Introduction

Diabetes mellitus (DM), as a chronic degenerative metabolic disease, has reached epidemic proportions in the recent decades with prevalence approaching 400 million people worldwide [1]. Due to peripheral neuropathy and ischemia, DM patients always present with foot problems [2]. Approximately 2-3% of DM patients are considered to suffer from active foot ulcer, and the lifetime risk of development of a foot ulcer for these patients is as high as about 25% [3, 4]. Patients with diabetic foot reveals a high mobility and mortality, which results from amputation, infection and other inducing complications such as microvascular as well as macrovascular disease [5, 6].

Critical limb ischemia (CLI), as one of the most severe problems in the management of diabet-

ic foot, brings about ischemic rest pain or ischemic skin lesions, either ulcers or gangrene, and is the leading cause of nontraumatic major amputations of the lower limbs, which eventually dramatically increases the disease burden of the patients [7-9]. Percutaneous transluminal angioplasty (PTA) of tibioperoneal arteries is considered to be an optional treatment for diabetic CLI, however, on account of extensive vasculopathy of DM and the necessity of revascularization of inflow tract, the application of conventional Balloon was limited.

DEEP Balloon (Invatec, Italy), benefits from its great abrasion resistance and compliance, is suitable to use in PTA operation of tibioperoneal arteries. This pilot study was to investigate the efficacy and safety of PTA of tibioperoneal arteries with DEEP Balloon in diabetic patients with CLI.

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Table 1. Characteristics of diabetic patients with CLI (N=15)

No.	Age (years)	Gender	DM type	DM duration	Lesion location	Wagner grade	ABI	TTS	Rest pain VAS
1	63	Female	1	16.5	ATA, PTA	1	0.08	34.57	3
2	70	Male	1	17.9	ATA	3	0.09	34.43	3
3	75	Male	1	14.2	PTA, PA	2	0.16	34.08	5
4	78	Female	2	12.5	ATA, PTA	3	0.47	33.82	6
5	71	Female	2	16.7	ATA, PA	3	0.40	33.86	4
6	64	Male	2	13.8	ATA, PTA, PA	4	0.58	33.42	7
7	60	Male	2	13.9	ATA, PTA	3	0.37	33.90	5
8	79	Male	2	12.3	ATA	1	0.19	34.27	5
9	80	Male	2	15.2	PTA, PA	4	0.54	33.60	6
10	80	Male	2	18.0	ATA	2	0.14	34.26	6
11	71	Male	2	15.4	ATA, PTA	1	0.08	34.50	4
12	75	Male	2	10.8	ATA, PTA	3	0.18	34.05	6
13	66	Male	2	12.3	ATA	3	0.17	34.06	5
14	66	Male	2	13.2	ATA, PTA	2	0.10	33.66	6
15	65	Male	2	15.1	ATA, PTA	4	0.52	33.95	6

CLI, critical limb ischemia; DM, diabetes mellitus; ATA, anterior tibial artery; PTA, posterior tibial artery; PA, peroneal artery; ABI, ankle brachial index; TTS, temperature of toes skin; VAS, visual analogue scale.

Methods

Participants

15 adult patients with DM between Sep. 2015 and Feb. 2016 from Ningbo No.2 Hospital (Zhejiang Province, China) were consecutively recruited in this pilot study. The inclusion criteria were: (1) diagnosed with DM and the disease duration above 10 years; (2) complicated with CLI according to TASC II recommendations [10]: presenting with persistent, recurring resting pain lasting more than 2 weeks that requires regular analgesia; an ankle systolic pressure <50 mmHg or an immeasurable ankle pressure level; and/or ulceration, gangrene, or non-healing wounds of the foot; (3) about to carry out PTA operation presenting with stenosis (decreasing vessel diameter more than 50%) or occlusion (less than 10 cm length). (3) Age above 18 years. The exclusion criteria were: (1) with severely uncontrolled DM (defined as A1C > 12%); (2) Dermatologic comorbid disease; (3) pregnancy, or breast feeding; (4) cognitive impairment or unable to understand or obey the protocol.

All the patients signed the informed consents, and this study was approved by the Ethics Committee of Ningbo No.2 Hospital.

Treatment

All patients underwent percutaneous transluminal angioplasty of tibioperoneal arteries with DEEP Balloon (Invatec, Italy). Ipsilateral common femoral artery puncture was performed, while ipsilateral puncture was unavailable, a crossover approach through the contralateral common femoral artery was used. Angiography was carried out firstly using 6F long-shaft sheath within the superficial femoral artery by introducing a 0.035 guidewire, in order to identify the location and features of the target lesions. 0.014 guidewire was subsequently introduced to cross distal lesions, and DEEP Balloon was guide to the lesions through 0.014 guidewire. 10-16 barometric pressure was conducted to operate the PTA by pressure pump according to the condition of stenosis. DEEP Balloon was kept inflated above 5 minutes each time, and inflated times was determined by the effect observed by angiography. All procedures were performed by two interventional radiologists who expert in peripheral vascular intervention.

Follow ups and assessments

Patients were followed up at month 1 (M1), month 3 (M3) and month 6 (M6) post the PTA operation. Technical successful rate, ulcer cure

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Table 2. Technical success rate, ulcer cure rate and limb salvage rate

	All patients (N=15)	Wagner grade 1-2 (N=6)	Wagner grade 3-4 (N=9)	P value	Type 1 DM (N=3)	Type 2 DM (N=12)	P value
Technical success rate	14 (93%)	6 (100%)	8 (89%)	0.398	2 (67%)	12 (100%)	0.038
Ulcer cure rate	12 (80%)	6 (100%)	6 (67%)	0.114	2 (67%)	10 (83%)	0.519
limb salvage rate	13 (87%)	6 (100%)	7 (78%)	0.215	1 (33%)	12 (100%)	0.002

Comparison was determined by Chi-square test.

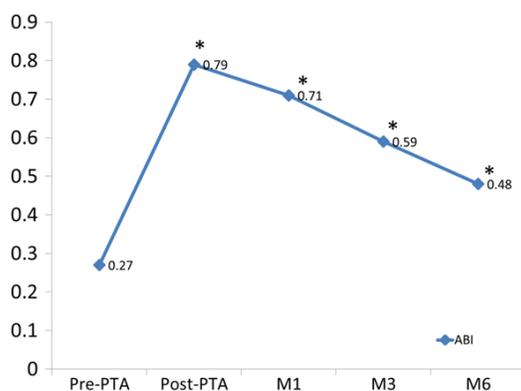


Figure 1. ABI value of patients at each visit.

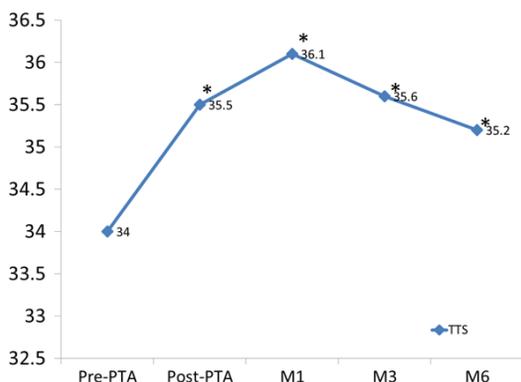


Figure 2. TTS value of patients at each visit.

rate and limb salvage rate were calculated after the operation; ankle brachial index (ABI), temperature of toes skin (TTS), rest pain visual analogue scale (VAS) was assessed pre, post the surgery, and at M1, M3 as well M6.

Technical success rate was defined as a direct flow to the ankle in at least one of the treated lesions by the control angiogram, without residual stenosis higher than 30%. Ulcer was graded by Meggitt-Wagner classification system, Ulcer cure rate was defined as the wound has healed during follow-up. The limb salvage rate was

defined as a survival rate without major amputation.

Statistics

Statistical analysis was performed by SPSS 21.0 (Chicago, USA) software. Data was present as mean and standard deviation, median and 1/4 to 3/4 quarter, or count and percentage. Comparison between each visit was determined by paired t test; comparison between two subgroups was determined by t test or Chi-square test. $P < 0.05$ was considered significant.

Results

Characteristics of patients

Detailed characteristics of 15 patients were presented in **Table 1**. The average age was 70.9 ± 6.7 years, with 12 males and 3 females. There were 3 patients with type 1 DM and 12 type 2 DM, and the median disease duration was 14.2 (12.5-16.5) years. Anterior tibial artery (ATA) lesion was observed in 13 patients, while posterior tibial artery (PTA) in 10 patients, and peroneal artery (PA) in 4 patients. Six patients presented grade 1-2 ulcer, and 9 with grade 3-4. The average ABI, TTS and rest pain VAS score were 0.27 ± 0.19 , $34.0 \pm 0.3^\circ\text{C}$ and 5.1 ± 1.2 before the operation, respectively.

Efficacy

As presented in **Table 2**. Technical success was achieved in 14 out of 15 patients after PTA operation with technical successful rate 93%, among which patients with type 2 DM had an increased technical successful rate (100%) compared to Type 1 DM (67%), $P = 0.038$. Overall ulcer cure rate was 80%, while patients with grade 1-2 ulcer (100%) achieved numerically higher ulcer cure rate compare to patients with grade 3-4 ulcer (67%) ($P = 0.114$). Limb salvage rate at M6 was 87% totally, and Type 2 DM

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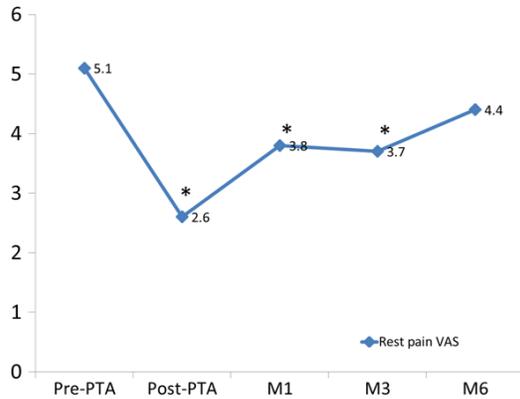


Figure 3. Rest pain VAS score of patients at each visit.

patients also revealed higher limb salvage rate than Type 1 DM patients (100% vs 33%, $P=0.002$).

ABI was elevated immediately after PTA surgery compare with Pre-PTA ($P<0.001$, **Figure 1**), although ABI showed a declined trend from post-PTA to M6, ABI was higher at M6 compared to Pre-PTA as well ($P=0.005$). TTS was increase post-PTA and at M6 compared to pre-PTA visit (all $P<0.001$, **Figure 2**). As to rest pain VAS score, it was decreased post-PTA operation ($P<0.001$), but no difference was observed between pain VAS at M6 and pre-PTA ($P=0.192$, **Figure 3**).

Safety

Arterial perforation occurred in 1 patient, and no other PTA operation related complications and death were illuminated.

Discussion

In this present study, we found treatment of PTA with DEEP Balloon revealed a good technical successful rate, ulcer cure rate as well as limb salvage rate; in the meanwhile, symptoms were also dramatically improved including ABI, TTS and rest pain VAS score. And PTA with DEEP Balloon was well tolerated.

DM, as a great current public health challenge, always leads to long-term complications which affect eyes, kidneys, peripheral and autonomic nervous system [11]. Diabetic foot is one of the most severe complications of DM, which influences range 2% to 15% diabetic patients in

various areas around the world [5, 12-16]. Multi factors have been reported to involve in the etiology of diabetic foot lesion, including neuropathy, infection and arterial, which results in foot ulceration, sepsis, rest and night pain, and eventual amputation [17, 18]. Despite of the health and economic burden, diabetic foot are correlated with high morbidity and mortality: diabetic patients with foot wounds or amputations have been reported to illustrate worse outcomes compared to some forms of cancers, and the mortality risk is even higher in diabetic foot patients receiving dialysis than almost all cancers [19, 20].

CLI, a most severe form of peripheral artery disease (PAD) associated with diabetic foot, occurred when the supply from arterial perfusion is sufficient for the metabolic demand of limb, which accounts for limb-threatening symptoms [7, 21]. Traditional medical treatment such as anticoagulant and vasodilation drugs usually lack efficacy in treating CLI, while surgical interventions were priority for CLI treatment [7, 22]. Bypass surgery is an option for CLI to postpone or even prevent an amputation; however it presents little benefits in complicated wound healing [23]. Thus, PTA is regarded as a good solution for CLI with fewer invasions and is largely applied in the treatment of CLI in diabetic patients with long duration [24].

DEEP Balloon, also named AMPHIRION DEEP, is appropriate for PTA of tibioperoneal arteries, characterized by: 1. low plasticity, only a few increments of diameter under higher pressure; 2. good abrasion resistance, Balloon broken would be avoided when passing through calcification area; 3. sustained extensibility, efficacy of PTA would be increased by prolonged inflation of the Balloon; 4. high bursting pressure with the maximum 20 atmospheric pressure; 5. Long length, extensive lesions would be dilated at one time [25, 26]. Benefits from these features of DEEP Balloon, it's a good option for PTA operation. In this study, we found PTA with DEEP Balloon in diabetic patients with CLI achieved a good technical successful rate (93%), ulcer cure rate (80%) as well as limb salvage rate (87%). The technical successful rate seems numerically higher than PTA with traditional Balloon in previous reports which was 83% [27]. Interestingly, we observed that patients with type 2 DM disclosed an increased

technical successful rate and limb salvage rate compared to type 1 DM patients, which might due to the more severe disease condition of type 1 DM and insulin dependence. And ulcer cure rate was found to be numerically elevated in Wagner grade 1-2 patients compared to Wagner grade 3-4 patients as well. And we also found the symptoms improved immediately after the PTA operation with DEEP balloon including rest pain, ABI and TTS.

There were some limitations in this study. First of all, the sample size was small, thus some significance might not be discovered such as the influence of ulcer Wagner grade on clinical outcomes; Secondly, this was a single armed study, which lacks the controls to assess the comparative efficacy of traditional treatment, and the bias of patients condition and disease progress on the outcomes could not be avoided; Thirdly, the follow-up time was short with 6 months, and longer observation was needed.

In conclusion, this study revealed that PTA of tibioperoneal arteries with DEEP Balloon was effective and well tolerated for diabetic patients with CLI.

Disclosure of conflict of interest

None.

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