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Original Article

Lumbar sympathectomy combined endarterectomy and percutaneous transluminal balloon angioplasty in patients with TAO

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Abstract: This study aimed to investigate whether combination therapy of unilateral lumbar sympathectomy, endarterectomy and percutaneous transluminal balloon angioplasty had a better therapeutic effect than endarterectomy alone for patients with thromboangitis obliterans (TAO). From August 2009 to January 2014, a total of 114 patients with TAO who underwent surgical treatment were recruited. Totally, 78 patients of combination group received the lumbar sympathectomy combined endarterectomy and percutaneous transluminal balloon angioplasty, 36 patients of single group received endarterectomy. Ankle-brachial index (ABI) and patency rates were detected in the combination and single groups 1 week, 6 months, and 12 months after operation. The operative successful rates were 97% (76/78) and 100% (36/36) in the combination and single groups, respectively. The ABI value was significantly higher in the combination group than that in the single group ($P<0.05$) 1 week, 6 months and 12 months after operation, respectively. In addition, the patency rates were 85.5% (59/69) and 84.8% (28/33), respectively, in the combination and single groups 6 months after operation, as well as 75.4% (52/69) and 63.6% (21/33) 12 months after operation ($P<0.05$). The combination therapy of lumbar sympathectomy, endarterectomy and percutaneous transluminal balloon angioplasty might be superior to single endarterectomy for patients with TAO in the short term. However, more cases collection and the long-term follow-up data were necessary to further perfect therapeutic method for TAO.

Keywords: Combination therapy, lumbar sympathectomy, endarterectomy, percutaneous transluminal balloon angioplasty, thromboangiitis obliterans

Introduction

Thromboangiitis obliterans (TAO) is an chronic non-suppurative inflammatory disease that may result in amputation of the affected extremity [1]. TAO commonly occurs in a young male smokers of the age of 40-45 years [1]. The predominant clinical symptoms of TAO include intermittent claudication, rest pain, digital gangrene and ulcers [2]. Although this disease has been first reported in 1879, the etiology of TAO remains unclear. It is well known that tobacco consumption is closely associated with the initiation and persistence of TAO [3, 4]. Complete smoking cessation has been considered as the most important preventive and therapeutic method for TAO [5]. Currently, surgical treatments mainly include lumbar sympathectomy, revascularization, endarterectomy, Ilizarov techniques, and omentopexy [6]. Lumbar sympathectomy can relieve pain and promote wound healing in the short term [7, 8]. Lower limb endarterectomy is primarily aimed to reconstruct lower limb blood supply, improve the leg blood flow, and prevent limb ischemic necrosis, thereby achieving the goal of limb salvage [8, 9]. However, the current surgical treatment methods have a certain limitation, uncertainty and short-term character [8]. Therefore, combination therapy of multiple operation methods may improve the therapeutic effect. In this study, we compared the effects of combination therapy (unilateral lumbar sympathectomy combined endarterectomy and percutaneous transluminal balloon angioplasty) and single therapy (endarterectomy with sequential

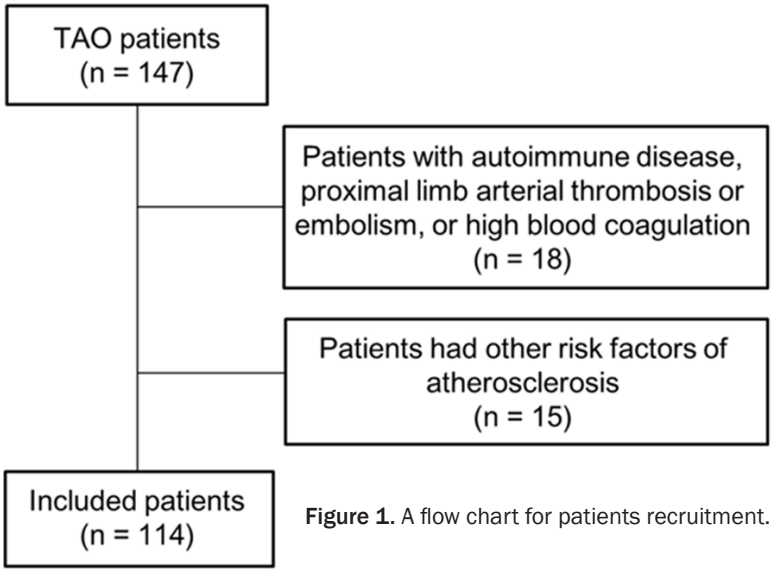

Figure 1. A flow chart for patients recruitment.

Table 1. The baseline characteristics in the combination and single groups

Index	Combination group (n = 78)	Single group (n = 36)	*t/chi square value*	*P* value
Age (years)	34.12±3.91	35.53±3.83	-1.8012	0.074
Gender			2.788	0.835
Male	66 (84.6%)	31 (86.1%)		
Female	12 (13.4%)	5 (13.9%)		
Course of disease (years)	6.75±2.14	5.83±3.02	1.8643	0.065
Claudication distance score	3.23±0.73	3.48±0.51	-1.8545	0.066

Claudication distance score 0: walk ≥1000 m; 1: walk at 500 m-999 m; 2: walk at 250 m-500 m; 3: walk at 100 m-249 m; 4: unable to walk or walk <100 m.

method), aimed to explore whether combination therapy had a better therapeutic effect for the patients with TAO.

Materials and methods

Patients

This retrospective nonrandomized controlled study recruited 147 consecutive patients with TAO who underwent surgical treatment in our hospital from August 2009 to January 2014. TAO was diagnosed by computed tomography angiography (CTA) of both lower limbs based on angiographic and clinical criteria published by Shinoya *et al.* [10] and Olin *et al.* [11]. Preoperative ankle-brachial index (ABI) was detected. The inclusion criteria included: (1) the onset age of patients was below 50 years old; (2) patients had infrapopliteal arterial obstructive lesions; (3) patients were accompanied by upper extremity artery occlusion or wandering phlebitis. The exclusion criteria were: (1) patients was accompanied by autoimmune diseases, proximal limb arterial thrombosis or embolism, or high blood coagulation state; (2) patients had other risk factors of atherosclerosis; (3) patients had surgical contraindications such as moderate and severe anemia, toe gangrene, hematological diseases, cardiopulmonary diseases, coagulation dysfunction, and hepatorenal dysfunction. As a result, a total of 114 patients were included in this study (**Figure 1**). The patients with TAO were divided into combination and single groups according to clinical staging and CTA. Patients with at least one distal outflow tract were included in the single group, while patients with poor distal outflow, severe claudication or gangrene were considered as the combination group. Among these 114 patients, 78 patients of combination group received the unilateral lumbar sympathectomy combined endarterectomy and percutaneous transluminal balloon angioplasty, 36 patients of single group received endarterectomy with sequential method. There were no significant differences in age, gender, course of disease, and claudication distance between the combination and single groups (**Table 1**). All of the patients had palpable femoral artery pulses, while dorsalis pedis artery and the posterior tibial artery pulse disappeared. In addition, only 5 patients had palpable popliteal artery pulses. Approval from the Ethics Committee of the first clinical medical college of Harbin medical university was obtained.

Surgical technique

General anesthesia was performed before operation. For patients of single group, arteri-

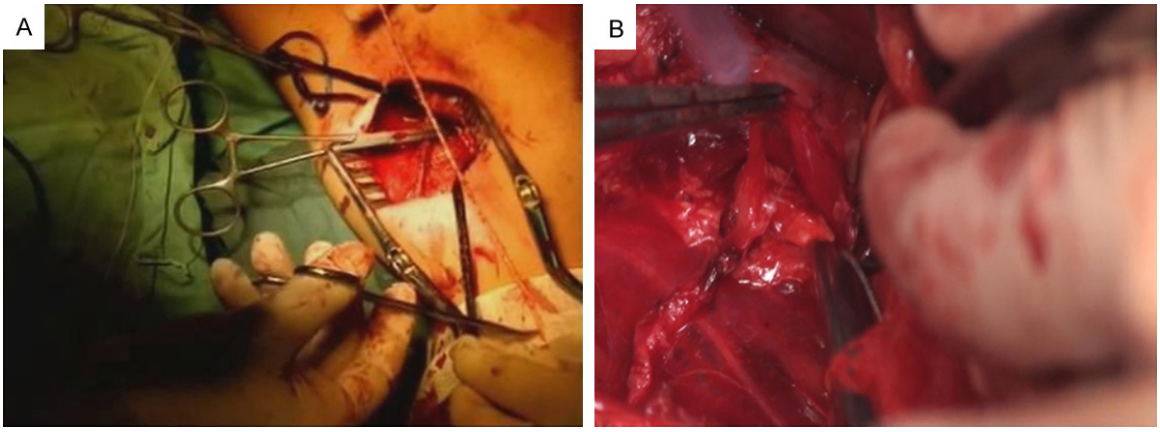

Figure 2. The photo of organized embolus stripped (A) and lumbar sympathetic ganglion removed (B).

Table 2. The reference range of multiple safety parameters to evaluate the pre-, intra- and post-operative risks

Safety parameters	Reference range
Peripheral blood cells	
Leucocyte ($\times 10^9$/L)	4-15
Neutrophil ratio (%)	50-75
Hematocrit (%)	M: 40-50; FM: 37-48
Hemoglobin (g/L)	M: 120-160; FM: 110-150
Platelet ($\times 10^9$/L)	100-300
Biochemical detection	
Creatinine clearance (%)	M: 53-106; FM: 44-97
Alanine aminotransferase (U/L)	≤40
Sodium ion (mM/L)	135-145
Potassium ion (mM/L)	3.5-5.5
Total serum protein (g/L)	60-80
Serum albumin (g/L)	40-55
Blood glucose (mM/L)	3.9-6.1
Triglyceride (mM/L)	<1.7
Total cholesterol (mM/L)	2.9-6.0
PH value	7.35-7.45
Coagulation test	
Prothrombin time (s)	11-14
Activated partial thromboplastin time (s)	25-37
Fibrinogen (g/L)	2-4
Activated clotting time (s)	180-240
Temperature (°C)	≤38.0
Mean arterial pressure (mmhg)	70-109
Ventricular rate (/min)	60-100
PaO_2	>75
Total blood loss (mL)	200

Male is abbreviated for "M", and female is for "FM".

otomy site were determined according to the different lesion location shown in CTA. If lesion involved in superficial femoral artery, incision was positioned in the inguinal region. Then, if catheter suffered the distal obstruction, incision was positioned in inner thigh above the knee, followed by the lower medial leg below the knee. After artery freed, the distal and proximal arteries were blocked using band-blockade, and intravenous heparinization (ordinary heparin 0.8 mg/kg) was performed. Artery walls with lesions were cut 1.5 cm long using a sharp knife, and then intraluminal organized thrombus (pale thrombus) were stripped using detacher. If the lesions were longer, thrombus should be stripped using 3F, 4F Fogarty catheter, even combined with the clamps when necessary (**Figure 2A**).

For patients of combination group, endarterectomy was performed as stated above. Meanwhile, unilateral lumbar sympathetic ganglion was removed (**Figure 2B**). In brief, abdomen was cut about 15 cm long, and then the peritoneal cavity and the fat were downward separated. Next, the inferior vena cava and ureter were pulled to the opposite side, and then lumbar sympathetic trunk was separated. Lumbar 2-4 sympathetic ganglion were removed and lumbar 1

Figure 3. Pre and post-operative computed tomography angiography (CTA).

sympathetic ganglion were reserved. Subsequently, angiography was performed to determine the lesion region, and then balloon dilatation were carried out using microcatheter combined with V18 or PTII guide wire. Artery incision was sutured using CV6 or CV7 vascular sutures.

Postoperative management

First, ordinary heparinization was continued for at least one week, and active coagulative time (ACT) was controlled at 180-250 s through adjusting the dose of heparin. Second, the arteriopalmus of wounded limb, skin color, skin temperature and ABI were observed. Third, antiplatelet therapy was performed at the same time of anticoagulation. After one week, heparin was gradually replaced with oral warfarin, as well as blood routine and blood coagulation were regularly monitored. The international normalized ratio was 1.8-3.0. Patients were advised to take the long time warfarin, but patients who had fertility requirements should be considered to stop. In addition, adjuvant drugs such as alprostadil and argatroban were administered both in the two groups. All the patients were told to quit smoking. The routine follow-up such as symptoms, physical sign, arterial ultrasonic Doppler and CTA were performed for 12-65 months.

Evaluation index

ABI were detected in all the patients 1 week, 6 months and 12 months after operation, respectively. The patency rates were calculated according to the examination results of arterial ultrasonic Doppler and CTA 1 week, 6 months and 12 months after operation, respectively. In addition, multiple safety parameters, including peripheral blood cells, biochemical detection, coagulation test, temperature, mean arterial pressure, ventricular rate, PaO_2, total blood loss, were measured to evaluate the pre-, intra- and post-operative risks (**Table 2**).

Statistical analysis

The statistical analysis was performed using SPSS software (version 17.0; SPSS for Windows, Chicago, IL, USA). Measurement data were represented as mean ± standard deviation (SD). The comparison between two groups was performed using *t* test. Enumeration data were analyzed using chi-square test. *P* values of less than 0.05 were considered statistically significant.

Results

Operation results

The operative successful rate (technical successful rate) was 97% (76/78) and 100% (36/36) in the combination and single groups, respectively. Two patients underwent failed surgery; one patient did not observe blood reflux in distal extremity after organized thrombus stripped, and then outflow tract was not found because catheter probing could not pass to ankle, which resulted in postoperative infrapopliteal amputation; one patient performed infrapopliteal amputation due to acute thrombosis 24 h after operation. These two patients emerged postoperatively incision hemorrhage, and then symptomatic treatments such as pressure bandaging were used for hemostasis. Postoperative symptoms of patients obviously improved compared with preoperative symptoms based on CTA (**Figure 3**). In the combination group, 57 patients had palpable distal limb artery pulse; 10 patients with regional anabrosis showed obvious bleeding wound, while

Table 3. Pre and post-operative ankle-brachial index (ABI) in the combination and single groups

Index	Combination group (n = 69)	Single group (n = 33)	*t* value	*P* value
Preoperative ABI	0.10±0.13	0.11±0.12	-0.239	0.811
Postoperative ABI				
1 week	0.89±0.15	0.59±0.18	8.866	0.000
6 months	0.90±0.12	0.58±0.15	11.185	0.000
12 months	0.89±0.13	0.58±0.13	10.957	0.000

wound cured after treatment with by vacuum sealing drainage; 6 of 9 patients with digit gangrene performed cut toe surgery due to obviously local pain. In addition, allpre-, intra- and post-operative safety parameters were in the reference range, and there was no any difference between the two groups regarding to all safety parameters.

Following-up

The follow-up rates were 90.8% (69/76) and 91.7% (33/36) in the combination and single groups, respectively. The follow-up duration ranged from 12-65 months (mean 34 months). All patients had no smoking during the follow-up period. Two patients in the single group performed amputation due to repeated arterial occlusion 10 and 12 months after operation, respectively. The ABI value was significantly increased in the combination group compared with the single group ($P<0.05$) 1 week, 6 months and 12 months after operation, respectively (**Table 3**). The patency rates were 85.5% (59/69) and 84.8% (28/33), respectively, in the combination and single groups 6 months after operation, as well as 75.4% (52/69) and 63.6% (21/33) 12 months after operation ($P<0.05$).

Discussion

Because TAO was related to digital ulcers and even amputation, it frequently resulted in social problems and affected the quality of life of the patients [12]. It is urgent to search for a better effective therapeutic method than the current ones in order to manage patients with TAO. Our study showed that both combination therapy and single therapy could improve clinical symptoms and patency rates of patients, and patients underwent combination therapy had higher ABI value than that in the single group 1 week, 6 months and 12 months after operation.

A variety of surgical methods were applied to treat the patients with TAO. Previous study had shown that 1-year limb salvage rate and patency rates were 71% and 46%, respectively, in the patients underwent venous arterialization, which did not conform conventional artery-arterial blood reconstruction principle, thus many patients had to accept amputation [13]. Spinal cord stimulation had been used in patients with rest pain or trophic lesions [14]; however, therapeutic value remains to be demonstrated. Vascular bypass reconstructive surgery had been considered as relatively effective treatments for TAO in the early years [15]. However, due to the lack of appropriate distal outflow, the patients underwent artery bypass surgery were less than 10% and the long-term patency rate was unsatisfactory [12, 16]. Dilege *et al.* [9] demonstrated that the patency rates at the 12th, were 59.2%, while the patency rates at the 24th and 36th months were continuously decreased in patients underwent revascularization procedures. Vascular gene therapy might be useful by inducing angiogenesis using vascular endothelial growth factor or basic fibroblast growth factor [17, 18]. Unfortunately, few patients performed vascular gene therapy due to expensive cost. Several studies had reported lumbar sympathectomy and the mechanism of lumbar sympathectomy was that the connection of peripheral vascular and central reflection (2-4 lumbar sympathetic ganglion) were cut off, then alleviated the vascular spasm, established collateral circulation, eventually improved the state of limb ischemia [19, 20]. Bozkurt *et al.* [21] reported 161 patients with TAO underwent sympathectomy and the operative successful rate (symptoms improved) was 52.3%, suggesting that the treatment effect of single lumbar sympathectomy was not obvious. Graziani *et al.* [22] suggested that the patients underwent percutaneous transluminal balloon angioplasty had sustained clinical improvement rates and high amputation-free survival, indicating that percutaneous transluminal balloon angioplasty was a feasible and effective revascularization method for the treatment of TAO. Our study found that arterial patency rate slightly higher after operation for 6 months than that patency rate after 12 months, which suggested that some patients appeared again thrombotic

occlusion with the extension of time. Furthermore, we demonstrated that the unilateral lumbar sympathectomy combined endarterectomy and percutaneous transluminal balloon angioplasty had a better therapeutic effect than single endarterectomy for patients with TAO in the short term.

In the present study, we found that the nature of the detached thrombus was different due to the different courses of disease. For patients with the course of disease of 1-2 years, Fogarty catheter or forceps operation were proposed. For patients with the longer course of disease, forceps operation accompanied by intracavitary therapy was suitable. Although the application of balloon expansion might cause restenosis of lesion vessels, it increased the precious time for the establishment of collateral circulation. In view of the age of patients with TAO was relatively small with less systemic diseases, perioperative risk was low. But postoperative anticoagulation and antiplatelet therapy should be focused. Generally, oral warfarin for anticoagulation was advised at least 1 year, and antiplatelet drugs such as aspirin were also necessary for the patients with the high risk of thrombosis.

In summary, the combination therapy of lumbar sympathectomy, endarterectomy and percutaneous transluminal balloon angioplasty might be superior to single endarterectomy for patients with TAO in the short term. However, more cases collection and the long-term follow-up data were necessary to further perfect therapeutic method for TAO.

Disclosure of conflict of interest

None.

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