

Application of Ilizarov transverse tibial bone transport and microcirculation reconstruction in the treatment of chronic ischemic diseases in lower limbs

QIANG ZUO, FENG GAO, HUANGHE SONG and JINCHUN ZHOU

Department of Orthopedics, The First Affiliated Hospital of Nanjing Medical University,
Nanjing, Jiangsu 210029, P.R. China

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Abstract. The aim of the present study is to investigate the clinical value of Ilizarov transverse tibial bone transport and microcirculation reconstruction in the treatment of chronic ischemic diseases in lower limbs. A total of 90 patients with chronic ischemic diseases in lower limbs were selected and randomly divided into two groups: The observation group (n=45) and the control group (n=45). Those patients were treated with Ilizarov transverse tibial bone transport and microcirculation reconstruction, and percutaneous balloon angioplasty (PTBA), respectively. Changes in the diameter, blood flow of lower limb arteries in the paretic side, wound healing time, disappearance time of pains, dorsal foot skin temperature, and the expression area of vascular endothelial growth factors (VEGFs) were detected in both groups. Compared with control group, the diameters and blood flows of lower limb arteries were significantly larger ($P<0.05$), and the dorsal foot skin temperature was significantly higher at 1 day, 1 week and 1 month after operation, respectively. Meantime, the expression area of VEGFs in the observation group was significantly larger than that in the control group at 1 day, 1 week and 1 month, respectively. Furthermore, compared with control group, wound healing time and disappearance time of pains of patients were earlier in the observation group ($P<0.05$). At 1 month after operation, the intermittent claudication, rest pain and lower limb ulcer or gangrene among clinical symptoms of patients in the observation group improved significantly more than those in the control group ($P<0.05$). In conclusion, the application of Ilizarov transverse tibial bone transport and microcirculation reconstruction could achieve better outcomes in the treatment of chronic ischemic diseases in lower limbs.

Introduction

Thromboangiitis obliterans and arteriosclerotic occlusive disease are the most common ischemic diseases in lower limbs, which, due to chronic ischemia and hypoxia in lower limbs, are often accompanied by skin color changes (1) muscle atrophy and subcutaneous fat disappearance, thus leading to fibrous connective tissue hyperplasia (2) and eventually resulting in osteoporosis ischemic neuritis and vasculitis. The prolonged course of disease will aggravate tissue ischemia and hypoxia and lead to ulcer or even gangrene (3). Traditional drug therapy cannot fundamentally eradicate limb ischemia and hypoxia caused by vascular lesions, so people are not satisfied with the treatment results and eventually choose to be treated with amputation (4).

Through Ilizarov transverse tibial bone transport and microcirculation reconstruction technique, tibiae are formed into movable bone flaps to be transversely transported correspondingly, which repeatedly stimulates the regeneration of tibial bone marrows (5), promotes neovascularization and bone tissue formation, achieves the reconstruction of peripheral blood circulation (6), so as to improve limb blood supply, fundamentally eradicate the source of ischemic diseases in lower limbs and promote blood circulation, thus playing a role in clinical treatment (7). Although certain clinical effects have been achieved after it is applied in the treatment of diabetic foot, it has been applied in few studies to the treatment of chronic ischemic diseases in lower limbs. To make up for the above deficiencies, the clinical value of Ilizarov transverse tibial bone transport and microcirculation reconstruction technique in the treatment of chronic ischemic diseases in lower limbs was mainly explored in the present study.

Patients and methods

General data. A total of 90 patients with chronic ischemic diseases in the lower limbs admitted to The First Affiliated Hospital of Nanjing Medical University (Nanjing, China) from July 2015 to June 2017 were selected. All the patients were the confirmed cases diagnosed through comprehensive examinations such as clinical manifestation examination, biochemical tests and lower limb vascular ultrasound, and all of them had symptoms such as intermittent claudication, rest pain and lower

Correspondence to: Dr Jinchun Zhou, Department of Orthopedics, The First Affiliated Hospital of Nanjing Medical University, 300 Guangzhou Road, Nanjing, Jiangsu 210029, P.R. China
E-mail: htudt016@163.com

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Table I. Comparisons of main artery diameter and blood flow and dorsal foot skin temperature of lower limbs between two groups of patients (mean \pm SD).

Groups	Femoral artery diameter (cm)	Popliteal artery diameter (cm)	Posterior tibial artery diameter (cm)	Dorsalis pedis artery diameter (cm)	Femoral artery blood flow (ml/min)	Popliteal artery blood flow (ml/min)	Posterior tibial artery blood flow (ml/min)	Dorsalis pedis artery blood flow (ml/min)	Dorsal foot skin temperature
Observation	0.58 \pm 0.04	0.49 \pm 0.03	0.13 \pm 0.01	0.15 \pm 0.01	456.5 \pm 8.3	158.6 \pm 6.0	40.2 \pm 2.1	33.0 \pm 2.1	27.1 \pm 0.2
Control	0.59 \pm 0.04	0.48 \pm 0.03	0.13 \pm 0.01	0.15 \pm 0.01	456.1 \pm 8.3	159.1 \pm 5.9	40.3 \pm 2.0	33.1 \pm 2.0	27.2 \pm 0.3
t or χ^2	1.186	1.342	<0.001	<0.001	0.229	0.399	0.231	0.231	1.861
P-value	0.239	0.183	1.000	1.000	0.820	0.691	0.818	0.818	0.007

limb ulcer or gangrene. Before the inclusion, all the patients signed the informed consent, and the study was approved by the Ethics Committee of The First Affiliated Hospital of Nanjing Medical University. Patients were aged 18-60 years old with no past history of diseases. Patients combined with lower limb fractures, knee dislocation, liver and kidney dysfunction, diabetes, coronary heart disease, immune system diseases, systemic infection, malignant tumors, mental illness, systemic immune system diseases were excluded. Through a random number table, the patients were divided into two groups with 45 patients each. In the observation group, there were 25 males and 20 females, aged 18-60 years old with the mean age of 53.2 \pm 1.8 years old; the course of disease endured 3 months to 1 year with the mean time of 5.1 \pm 0.3 months. In the control group, there were 24 males and 21 females, aged 18-60 years old with the mean age of 53.1 \pm 1.7 years old; the course of disease endured 3 months to 1 year with the mean time of 5.0 \pm 0.3 months. Differences in comparisons of sex, age, course of disease, the diameters and blood flows of the femoral, popliteal, posterior tibial and dorsalis pedis artery and dorsal foot skin temperature were not statistically significant (Table I).

Methods. Surgical methods in the observation group: Patients in the observation group were treated with Ilizarov traverse tibial bone transport and microcirculation reconstruction, during which patients were in the supine position. The operation was performed under the spinal anesthesia, and the incision was made at 15-18 cm in the medial margin of the middle and lower tibia. The tibial osteotomy distance was determined after the fascia was exposed by blunt dissection. Generally, it is appropriate to set the length of tibial osteotomy as 10-12 cm and width as 1.5-2.0 cm. The periosteum was opened after being longitudinally cut in the middle osteotomy area, so that the osteotomy area was completely exposed. Then the bone cortex was cut using a pendulum saw to form the active bone flap. An \sim 2 mm Schanz needle was inserted into the upper and lower parts of the fenestrate bone flap, respectively, for the traverse bone traction. Then two 4 mm Schanz needles were inserted in a parallel direction into both ends of the tibia, and the external fixation bracket was installed. Finally, two movable transverse tractors were fitted on the external fixation bracket and fixed with the traction needle. After operation, the hemostasis was conducted, and wounds were sutured. Patients in the control group were treated with percutaneous balloon angioplasty (PTBA) mainly for the parts with ulcer and (or)

gangrene. Treating the femoral artery with PTBA improved and strengthened the lower limb blood supply.

Observation indexes. Changes in the diameter and blood flow of lower limb arteries in the paretic side after intervention were compared between two groups of patients. Wound healing time and disappearance time of pains in the two groups were counted. The variation trends of dorsal foot skin temperature and the expression area of vascular endothelial growth factors (VEGFs) at different observation time-points in the two groups were compared so as to know the improvement degree of clinical symptoms at 1 month after operation in the two groups.

Evaluation methods. The diameter and blood flow of lower limb arteries in the paretic side were detected using the Philips Hdiixe Doppler blood vessel diagnostic apparatus with the probe frequency of 7-10 MHz. During the detection, patients were in the supine and prone position, and the femoral, popliteal, posterior tibial and dorsalis pedis artery were measured for detecting the artery inner diameter and arterial stenosis. The diameter measurement position includes 1 cm away from the bifurcation proximal site of the femoral artery and popliteal artery, 1 cm at the starting site of the posterior tibial artery and 1 cm away from the distal junction site of the ankle joint and the dorsalis pedis artery; the pain degree was assessed with the visual analogue score as the standard, and the total score ranged from 10 points (unbearable pain) to 0 point (painless). The higher the score was, the higher the pain degree would be. Rest pain refers to that people feel pain when the affected limb is kept still, and rest pain score <3 points indicates that clinical symptoms are improved. Disappearance time of pains was examined with the score of rest pain and pain on motion <3 points as the standard. The positive detection rate of VEGFs was detected using enzyme-linked immunosorbent assay (the kit was provided by Qingdao Wolsen Biotechnology Co., Ltd., Qingdao, China), and its expression level was assessed using the HPIAS-1000 image analyzer. The main criterion for assessment was the ratio of the area of positive substances in cells to the gray value in the background.

Statistical analysis. SPSS 13.0 (SPSS, Inc., Chicago, IL, USA) was used in this study. Measurement data were expressed as mean \pm standard deviation (mean \pm SD), and the t-test was used for mean comparisons between the two groups. χ^2 test

Table II. Comparison of the diameters of lower limb arteries in the paretic side between the two groups (cm, mean \pm SD).

Groups	Femoral artery	Popliteal artery	Posterior tibial artery	Dorsalis pedis artery
Observation	0.72 \pm 0.08	0.60 \pm 0.05	0.23 \pm 0.01	0.21 \pm 0.01
Control	0.63 \pm 0.05	0.48 \pm 0.03	0.15 \pm 0.01	0.16 \pm 0.01
t	6.034	13.016	35.777	22.361
P-value	<0.001	<0.001	<0.001	<0.001

Table III. Comparison of the blood flow of lower limb arteries in the paretic side between the two groups after intervention (ml/min, mean \pm SD).

Groups	Femoral artery	Popliteal artery	Posterior tibial artery	Dorsalis pedis artery
Observation	766.5 \pm 15.3	458.6 \pm 11.1	80.2 \pm 3.1	73.6 \pm 2.8
Control	698.8 \pm 12.7	323.2 \pm 5.9	53.5 \pm 2.0	43.1 \pm 2.5
t	21.533	68.123	45.773	51.389
P-value	<0.001	<0.001	<0.001	<0.001

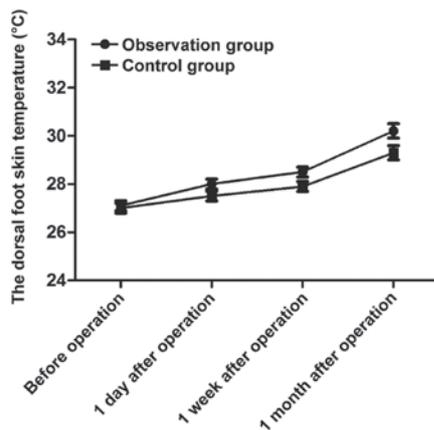


Figure 1. Comparison of the dorsal foot skin temperature at different observation time-points between the two groups. The dorsal foot skin temperature in the observation group at 1 day, 1 week and 1 month after operation is significantly higher than that in the control group (t=11.180, 13.416 and 13.416; p<0.05).

was used for ratio comparisons. P<0.05 represented that the difference was statistically significant.

Results

Comparison of the diameters of lower limb arteries in the paretic side between the two groups after intervention. After intervention, diameters of the femoral artery, popliteal artery, posterior tibial artery and dorsalis pedis artery of patients in the observation group were significantly larger than those of patients in the control group (P<0.05) (Table II).

Comparison of the blood flow of lower limbs in the paretic side between the two groups after intervention. Blood flows of the femoral artery, popliteal artery, posterior tibial artery and dorsalis pedis artery of patients in the observation group were significantly higher than those of patients in the control group (P<0.05) (Table III).

Comparison of the dorsal foot skin temperature at different observation time-points between the two groups. The dorsal foot skin temperature in the observation group before operation (27.0 \pm 0.2°C) and at 1 day (28.0 \pm 0.2°C), 1 week (28.5 \pm 0.2°C), and 1 month (30.2 \pm 0.3°C) after operation was significantly higher than that in the control group before operation (27.0 \pm 0.2°C) and at 1 day (27.5 \pm 0.2°C), 1 week (27.9 \pm 0.2°C) and 1 month (29.3 \pm 0.3°C) after operation (t=11.180, 13.416 and 13.416; P<0.001<0.05 in all comparisons) (Fig. 1).

Comparison of the expression area of VEGFs during intervention between the two groups. The expression area of VEGFs in the observation group before operation (15.6 \pm 1.1 μ m²) and at 1 day (23.5 \pm 2.4 μ m²), at 1 week (35.6 \pm 2.9 μ m²) and at 1 month (33.5 \pm 2.8 μ m²) after operation was significantly larger than that in the control group before operation (15.5 \pm 1.1 μ m²) and at 1 day (18.5 \pm 2.3 μ m²), at 1 week (26.5 \pm 2.5 μ m²) and at 1 month (24.3 \pm 2.3 μ m²) after operation (t=9.513, 14.866 and 16.058; P<0.001<0.05 in all comparisons) (Fig. 2).

Comparisons of wound healing time and disappearance time of pains between the two groups. Wound healing time and disappearance time of pains of patients in the observation group were earlier than those of patients in the control group (P<0.05) (Table IV).

Comparison of the improvement degree of clinical symptoms at 1 month after operation between the two groups. At 1 month after operation, the improvement degree of intermittent claudication, rest pain, lower limb ulcers or gangrene among clinical symptoms in the observation group were significantly higher than that in the control group (P<0.05) (Table V).

Discussion

Lower limb ischemic disease is the most common cause of lower limb dysfunction or even amputation in present

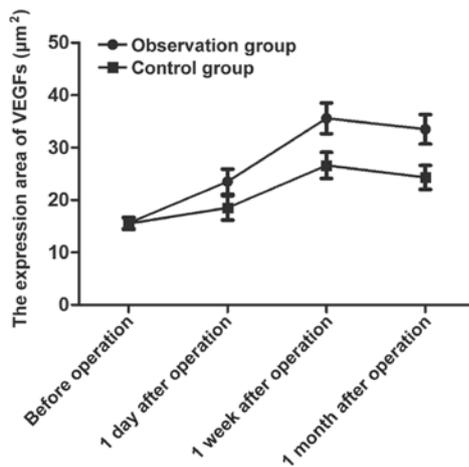


Figure 2. Comparison of the expression area of VEGFs during intervention between the two groups. The expression area of VEGFs in the observation group at 1 day, 1 week and 1 month after operation is significantly higher than that in the control group ($t=9.513, 14.866$ and 16.058 ; $P<0.05$).

Table IV. Comparisons of wound healing time and disappearance time of pains between the two groups (day, mean \pm SD).

Groups	Wound healing time	Disappearance time of pains
Observation	15.3 \pm 0.6	12.1 \pm 0.5
Control	26.5 \pm 1.5	25.6 \pm 1.3
t	43.846	61.300
P-value	<0.001	<0.001

Table V. Comparison of the improvement degree of clinical symptoms at 1 month after operation between the two groups (effective case/total case).

Groups	Intermittent claudication	Rest pain	Lower limb ulcers or gangrene
Observation	39/45	44/45	38/45
Control	25/45	30/45	11/45
χ^2	10.601	12.846	32.658
P-value	<0.001	<0.001	<0.001

clinical practices. The incidence rate of the disease is high, and its morbidity and mortality rate are in a certain degree, which will significantly reduce the quality of life of patients and threaten the safety of them (8). At present, the clinical treatment includes conservative drug therapy and minimally invasive vascular intervention, whose curative effects have to be further improved, so patients have to receive surgical treatments (9). Although Ilizarov transverse tibial bone transport and vascular regeneration and circulation reconstruction is still in the promotion stage clinically, it has been widely recognized that the transport can stimulate the regeneration of periosteum and tibial bone marrow (10), thus

promoting local micro-arterial regeneration to reconstruct the mechanism of lateral circulation network. In some studies, this technique has been applied to the treatment of the diabetic foot (11), which achieves significant curative effects with the advantages of minimal trauma, rapid postoperative recovery and low treatment cost, and it can effectively reduce and avoid the risk of amputation (12). In this study, it was applied to the treatment of lower limb ischemic diseases.

In the present study, comparisons of the diameter and blood flow of lower limb arteries in the paretic side between the two groups after intervention showed that compared with the effect of expanding the femoral artery with PTBA, diameters and blood flows of the femoral, popliteal, posterior tibial and dorsalis pedis artery of patients after intervention in the observation group were significantly larger than those of patients in the control group, suggesting that the application of Ilizarov transverse tibial bone transport and microcirculation reconstruction to lower limb ischemic diseases can effectively expand the diameter of main lower limb arteries and improve the blood flow. At the same time, the analysis on the variation trends of dorsal foot skin temperature and the expression area of VEGFs in the two groups at different observation time-points manifested that dorsal foot skin temperature at 1 day, 1 week and 1 month after operation in patients in the observation group was significantly higher than that in patients in the control group, and the expression area of VEGFs was significantly larger than that in patients in the control group, suggesting that the application of Ilizarov transverse tibial bone transport and microcirculation reconstruction to lower limb ischemic diseases can effectively elevate the lower limb temperature, and the significantly increased expression level of VEGFs promoting vascular regeneration contributes to the revascularization of the lower limbs and improves clinical symptoms of patients. Besides, comparisons of wound healing time and disappearance time of pains between the two groups indicated that wound healing time and disappearance time of pains in the observation group were earlier than those in the control group, suggesting that Ilizarov transverse tibial bone transport and microcirculation reconstruction is of great significance for promoting the healing of lower limb ulcer and (or) gangrene and relieving lower limb pains. Finally, comparison of the improvement degree of clinical symptoms at 1 month after operation between the two groups revealed that the improvement degree of intermittent claudication, rest pain and lower limb ulcers or gangrene in the observation group was significantly higher than that in the control group, suggesting that the application of Ilizarov transverse tibial bone transport and microcirculation reconstruction to lower limb ischemic diseases is of more significant clinical importance for improving the clinical symptoms of patients than PTBA intervention treatment.

The principle of Ilizarov bone transport technique is to repeatedly stimulate the tibial bone marrow, the mitosis of vascular endothelial cells and tissue regeneration through the tension-stress effect so as to reconstruct blood circulation and avoid amputation (13). Fenestration operation was conducted on the tibia, which effectively reduced the bone pressure and relieved the occurrence of spasm in the small and medium blood vessels, and it had great value for improving lower limb pains, limb numbness and other symptoms (14).

Meanwhile, the bone transport effectively relieved rest pain and local swelling and improved the skin color, which were considered to be related to the reconstruction of new vessels in the lower limbs and the formation of lateral circulation (15). In addition, in combination with external fixation therapy (16), the bone transport could be repeatedly adjusted and modified during treatment, thus contributing to better microcirculation construction after the transport, while the both sides of the end ring could be separated from the main rod at any time, which was conducive to debridement, dressing change and wound observation, and even to the reduction of complications such as postoperative infection (17). In order to improve the operation results, it was advised in this study to avoid using the tourniquet and electric knife during operation so as to avoid the stimulation and damage of iatrogenic injuries to lower limb vessels (18). Besides, in the process of fenestration operation on periosteum, the periosteum should be kept integrated as much as possible, and it would be sutured at the end of operation (19). In the process of osteotomy, the protection of periosteum and bone marrow should be strengthened (20).

In conclusion, Ilizarov traverse tibial bone transport and microcirculation reconstruction in the treatment of lower limb ischemic diseases effectively improves the blood supply of lower limb arteries, enhances local vascular growth ability, improves local temperature, relieves clinical symptoms and promotes wound healing.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

QZ and JZ designed the study and performed the experiments, QZ, FG and HS collected the data, QZ and FG analyzed the data, QZ and JZ prepared the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of The First Affiliated Hospital of Nanjing Medical University (Nanjing, China). All the patients signed the informed consent

Patient consent for publication

Not applicable.

Competing interests

All authors have no conflict of interest to declare.

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