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Analysis of Curative Effect of TTT Combined with PRP Treatment Technique in Limb Salvage of DFU

Chengcaihou[1], Ruiyan[2], Zhenli[3] , Dehengliu[4]*

[1]Department of Hand, Foot and Ankle Surgery, Zaozhuang Municipal Hospital, No. 41 Longtou Middle Road, Shizhong District, Zaozhuang City, Shandong Province 277100

[2]Shandong Provincial Hospital Group Taierzhuang Hospital, No. 1288, Taipei Middle Road, Taierzhuang District, 277400

[3]Department of Orthopedics, Yicheng District Hospital of Traditional Chinese Medicine, No. 389 Zhongxing Avenue, Yicheng District, Zaozhuang City, Shandong Province, 277300

[4]Department of hand and foot surgery, Qilu Hospital (Qingdao), Cheeloo College of Medicine, Shandong University, 758 Hefei Road, Qingdao, Shandong, 266035,China

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***Corresponding author:** Dehengliu, Department of Hand and Foot surgery, Qilu Hospital (Qingdao), Cheeloo College of Medicine, Shandong University, 758 Hefei Road, Qingdao, Shandong, 266035,China

ABSTRACT

To compare and analyze the clinical effects of Tibia Transverse Transport technique, Tibia Transverse Transport combined with Platelet-rich plasma treatment and conventional treatment on Diabetic Foot Ulceration.30 patients with Diabetic Foot Ulceration from January, 2021 to December, 2023 were randomly divided into three groups: Tibia Transverse Transport group, Tibia Transverse Transport combined with Platelet-rich plasma treatment group and routine treatment group, with 10 patients in each group. The routine treatment group was given basic clinical treatment, while the other two groups were treated with Tibia Transverse Transport combined with Platelet-rich plasma or Tibia Transverse Transport on the basis of routine treatment. The blood flow velocity of dorsal foot artery before and after treatment was detected by vascular doppler, and the skin temperature and Visual Analogue Scale pain score of foot before and after treatment were recorded to observe the healing of foot ulcer and compare the clinical effects of various methods. Compared with the conventional treatment group, the blood flow velocity of dorsalis pedis artery, the change of skin temperature of feet and the pain score in the Tibia Transverse Transport group and the Tibia Transverse Transport combined with Platelet-rich plasma group were significantly better than those in the conventional treatment group, and the Diabetic Foot Ulceration healing time in the Tibia Transverse Transport group was better than that in the Tibia Transverse Transport combined with Platelet-rich plasma group. However, the Visual Analogue Scale score of postoperative pain and the improvement of blood flow velocity of dorsalis pedis artery are similar. Diabetic Foot Ulceration brings huge psychological and mental burden to patients, and in the end the risk of amputation is often unavoidable. However, Tibia Transverse Transport can bring unexpected effects to patients, increasing limb

blood flow, increasing skin temperature, and reducing limb pain. Combined with platelet-rich plasma technology, it can increase therapeutic effects, improve quality of life, and avoid amputation.
Key words: Diabetic Foot Ulceration, Tibia Transverse Transport, PRP therapy

According to statistics, 1.7%-11.9% of diabetic patients are complicated with DFU, foot ulcer, infection and gangrene seriously affect the quality of life and even threaten the life of patients, which is the most serious complication of diabetes. The superposition of diabetic peripheral blood vessels and neuropathy promotes the formation of DFU [1,2,3]. The pathogenesis of DFU is complicated, which is a very difficult clinical problem for surgeons. At present, the main treatment measures are to improve local blood supply, promote DFU healing and prevent infection from getting worse, and severe cases need amputation [4]. Although there are many kinds of treatment methods, it is difficult to establish microcirculation of lower limbs, the curative effect is slow, and new complications will occur at the same time [5,6]. Therefore, re-establishing microcirculation of lower limbs is the focus of treatment. Ilizarov technique is a new treatment to reconstruct microcirculation of lower limbs [7]. In order to compare and analyze the clinical effects of TTT technique, TTT combined with PRP treatment and routine treatment of DFU, 30 patients from January 2021 to December 2025 were collected for prospective controlled clinical research.

1. DATA AND METHODS

1.1 Clinical data

Select patients with DFU from January 2021 to December 2023. Inclusion criteria: Type II diabetes; Clinical symptoms: Cold or fever, numbness, intermittent claudication, nocturnal rest pain and acupuncture pain. Physical examination: Cyanosis of legs, feet and toes, ulcer and infection; Color Doppler ultrasound or angiography: Stenosis or occlusion of blood vessels in lower limbs. Exclusion criteria: Patients over 76 years old; Patients with liver and kidney dysfunction, cardiac insufficiency, coagulation dysfunction, bleeding tendency and chronic basic diseases such as severe hyperglycemia, hypertension and hyperlipidemia will not receive surgical intervention; Patients who are allergic to contrast media, have myocardial infarction or cerebral infarction during acute cerebral hemorrhage or within 6 months. The present study was approved by the Ethics Committee of Zaozhuang Municipal Hospital, and written informed consent was obtained from all patients prior to enrollment in the present study.

1.2 Group divide of the experiment

The experimental groups were randomly divided into TTT combined with PRP treatment group, TTT treatment group and routine treatment group, with 10 cases in each group. After admission, the patients were classified according to wagner stage [8], and the general data of age, course of disease and smoking history of the three groups were compared.

1.3 Treatment methods of each group

1.3.1 Conventional treatment

①Drug therapy: Oral hypoglycemic drugs or insulin pump can control blood sugar about 6-8 mmol/L and 8-1 0 mmol/L; Take rivaroxaban orally to prevent thrombosis, take mecobalamin orally to nourish nerves and control blood pressure below 135/95 mm Hg; Intravenous alprostadil improves microcirculation.② Treatment of ulcer

surface: Thoroughly remove necrotic tissue, rinse with iodophor and hydrogen peroxide, and bandage with gauze. ③Physical therapy: Hyperbaric oxygen or laser therapy can effectively improve the hypoxic environment and promote DFU healing.

1.3.2 Preoperative preparation for tibia transport: Fasting blood glucose level of all patients is less than 7.8 mmol/L, and postprandial blood glucose is less than 10 mmol/L; Improve circulation; Nutritive nerve; Correct the imbalance of internal environment and control infection with antibiotics; Local debridement.

Surgical method of tibia transport and installation of tibia transport frame: After anesthesia, mark the tibia 5 cm below the tibial tuberosity of the affected limb, make an arc-shaped 5-7 cm incision on the inner side of the tibia, separate the periosteum, keep the periosteum intact and separate it to both sides passively, mark a tibia window of 2cm×5cm, drive two transport needles in the position of the tibia window, then swing the edge of the tibia window with a pendulum saw and slowly separate it with a osteotome. After the tibia transport window was successfully established, the fixed needles were respectively inserted into the upper and lower ends, the transport frame was installed, the skin was sutured, and the external dressing was applied **(Figure 1)**.

Figure1: Surgical operation process

A: Preoperative appearance photo;

B: Incision of skin during operation;

C: Exposure of periosteum;

D: Marking and opening the tibia window;

E: Install the tibia moving frame

Postoperative treatment: Antibiotics were used during the operation and one day after the operation, and the external fixation bracket was adjusted for tibia transport on the third day after the operation. First, the tibia block was moved outward at a speed of 1 mm/d, which was completed in three times. After 2 weeks, move back at the same speed; After 2 weeks, the external fixator can be removed after the tibia piece was reset, and it was moved laterally for 4 weeks.

1.3.3 TTT combined with PRP

PRP treatment: During the operation, 40-50 mL of peripheral venous blood was drawn, 5 mL of anticoagulant was mixed, injected into an anticoagulant tube, and centrifuged at 2000 r/min for 15 min to remove the lower red blood cells and white blood cells, leaving the plasma and platelet layer for 15 min to obtain PRP7-10 mL. Autologous PRP was directly applied to the DFU, and sterile gauze strips were placed. The DFU healing was

observed for 3 days, and the dressing was changed regularly for 7 days.

1.4 Index observation and evaluation method of curative effect

①Skin temperature of patients' feet: Skin temperature of the middle point of the back of patients' feet or toes is measured by skin temperature gun); ② The VAS scoring system was used to score the patients before and after treatment, with a score range of 0-10, which was divided into painless, slightly painful, obvious painful, severe painful and severe painful, and the score value was positively correlated with the pain [9]; ③ Using vascular Doppler to detect the velocity of dorsal foot artery before and after treatment, so as to understand the improvement of blood supply at the distal extremity; ④ Pulse oximeter was used to detect the oxygen saturation of the affected foot before and after treatment, so as to understand the oxygen saturation of the distal limb.

1.5 Statistical treatment

Statistical data were processed and analyzed by SPSS19.0. The data of skin temperature, VAS score, blood oxygen saturation and blood flow velocity of dorsalis pedis artery were expressed in the form of mean standard deviation. The statistical data were analyzed by one-way ANOVA, and pairwise multiple comparisons were made among the groups (LSD method), with $P<0.05$ being statistically significant.

2. RESULT

2.1 There is no significant difference in general data such as patients' age, course of disease and smoking history (P>0.0 5). **(Table 1, Table 2)**

Table 1. The basic clinical information of the patients (n =30)

Group	Age	Course of diabetes mellitus (year)	Course of DFU (month)	Smoking history (year)	BMI(kg/m(2))
Conventional treatment group	57.12±3.89	7.59±2.31	7.49±1.56	14.37±5.10	26.10±1.11
TTT treatment group	61.10±3.01	8.16±3.14	8.12±1.64	14.10±3.11	27.01±1.13
TTT combined treatment PRP	62.36±4.01	8.21±3.37	8.46±1.37	15.71±4.10	25.79±1.21

Table 2. Classification of DFU in patients (Wagner level)

Group	Number of cases	Level 0	Grade I	Grade II	Grade III	Grade IV	Grade V
Conventional treatment group	10	0	five	four	one		
TTT treatment group	10	0	2	four	three	one	
TTT combined	10	0	one	four	four	one	

PRP treatment group							

2.2 Single factor analysis of variance was made on skin temperature, pain, oxygen saturation and blood flow index of patients, and the results of each evaluation index were statistically different (P<0.05). The comparison between groups (LSD method) showed that the blood flow velocity of dorsalis pedis artery after operation, the change of skin temperature of feet after operation and the pain score in TTT treatment group and TTT combined with PRP treatment group were significantly better than those in conventional treatment group (P<0.05). However, the VAS score of postoperative pain and the improvement of blood flow velocity of dorsalis pedis artery were similar (P>0.05, **(Table 3)**.

Table 3. Comparison of the relevant indicators of patients in the three groups

Group	Cases No.	Postoperative skin temperature (℃)	Postoperative VAS	Postoperative oxygen saturation	Postoperative dorsalis pedis blood flow velocity (cm/s)
TTT treatment group	10	31.01±0.96	1.16±0.19	92.16±4.75	34.78±3.71
TTT combined PRP treatment group	10	31.10±0.82	1.10±0.11	93.12±3.79	34.78±3.71
Conventional treatment group	10	27.51±0.86	3.46±0.24	93.56±3.21	29.18±4.31
F		7.313	21. 012	28.7	5.918
P		＜0.001	＜0.001	＜0.001	＜0.001

2.3 Typical cases: 30 cases are followed up for an average of 6 months (3-13 months), and the ulcer DFU begin to shrink after 3-4 weeks in the TTT treatment group, and it shrink obviously after 2-3 weeks in the TTT treatment group and TTT combined with PRP group. All the DFUs of 30 patients are healed in 3 months after operation, and the temperature, touch and pain of the affected limbs are obviously improved **(Figure 2, Figure 3)**.

Figure 2

A: Preoperative appearance photo;

B and C: Right lower extremity arteriography photo before operation;

D: Transverse transport photo of the right tibia during operation;

E: Appearance photo of right toe 1 month after operation;

F: Lateral X-ray photo 4 weeks after operation (traction for 2 weeks, retraction for 2 weeks);

G: Appearance photo of right toe 3 years after operation.

Figure 3

A: Preoperative appearance photo;

B: Postoperative DFU photo;

C: Tibia transplantation photo after operation;

D: Photos of the DFU surface 4 days after operation;

E: X-ray photo of the tibia block is moved one week after operation;

F: X-ray photo of tibia block was moved 3 weeks after operation;

G: Photos of the left foot DFU surface 3 weeks after operation.

3. DISCUSSION

DFU refers to the skin infection, ulcer and deep tissue destruction of lower far-end limbs caused by vascular and neuropathy in diabetic patients, which has the characteristics of high incidence, high disability rate, high mortality and high cost. The clinical types include DFU, arteriosclerosis obliterans of lower limbs and thromboangiitis obliterans [9]. According to statistics, about 15% of diabetic patients will have DFU ulcers, and

90% of diabetic amputees are related to DFU ulcers, chronic osteomyelitis and foot gangrene [10]; 45% of DFU is Wagner grade 3 or above, most of them are accompanied by refractory foot ulcer and chronic tibia infection, and the total amputation rate with poor prognosisis as high as 18%~28% [11].

The condition of DFU is complicated, the treatment effect is poor, and amputation is needed in the later stage, but the best choice for DFU is limb salvage treatment. Vascular diseases caused by abnormal glucose metabolism and neurological function lead to ischemia of the distal limb [12], slow vascular regeneration and long healing time, which is a great problem in the field of ulcer DFU healing, suggesting that the current treatment methods have not fundamentally solved the problem of amputation. In 1989, Dr. Ilizarov put forward the “tension-stress rule”, which is an effective clinical scheme for tissue regeneration. Later, many doctors at home and abroad used this clinical scheme to cure a large number of difficult orthopedic cases that could not be treated by conventional techniques [13,14]. During this period, Dr. Ilizarov discovered the phenomenon of vascular regeneration, suggesting that this rule can be used to treat ischemic diseases. In 2000, Dr. Qu Long successfully treated vasculitis obliterans with the technique of tibial transverse transport (TTT) based on the “tension-stress law” for the first time. After long-term clinical follow-up, it showed that it had a good effect in treating vasculitis obliterans [15]. In 2013, Professor Hua Qikai used TTT technology to treat DFU for the first time. At present, there are more than 500 cases and good results have been achieved [16].

Clinical studies have found that transverse tibia transfer technology can increase the number of small blood vessels in distal limbs, rebuild microcirculation and promote DFU healing [17,18,19]. TTT is operated on the lower leg, and the DFU at the distal end of the limb is finally cured, which is called “summoning phenomenon”. The basic research on this phenomenon shows that: 1. Mobilize tibia marrow-derived stem cells (hematopoietic stem cells, mesenchymal stem cells, endothelial progenitor cells, etc.) to promote proliferation and survival, increase the number of M2 macrophages, reduce the proportion of M1 and M2 macrophages, and form an inflammatory balance and tissue regeneration for chronic unhealed DFU [20], which provides a good foundation for DFU healing. 2. Activation of P13K/AKT signaling pathway mediated by SDF1 / CXCIu axis can increase the expression level of P13K and Akt [22,23,24], which is involved in regulating the transport, differentiation and survival of tibia marrow-derived stem cells and promoting the healing of DFU ulcers. The basic research also shows that the TTT technique often causes the proliferation of arteriovenous system and microcirculation system, and promotes the establishment of microcirculation at the distal end of limbs, but there is no evidence that the middle artery system can be regenerated. If the middle artery cannot be reconnected, this method cannot achieve the desired effect.

PRP is a kind of plasma concentrate rich in platelets. Platelets are concentrated and aggregated in the supernatant by high-speed centrifugation of autologous whole blood, so that PRP preparation can be obtained, and its platelet concentration is 3-6 times higher than that before preparation. Studies have shown that once activated, platelets in PRP will release a large number of growth factors such as platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF) [25]. Platelet-derived growth factor (PDGF) can induce target cells to divide and proliferate in vivo, and chemotaxis into fibroblasts and neutrophils to gather in the DFU, increasing the number of DFU cells and promoting DFU healing. Vascular endothelial growth factor (VEGF) is a landmark indicator of angiogenesis, which plays a specific role in the process of DFU treatment. Its main mechanism is to induce mitosis of vascular endothelial cells, provide a matrix for vascular endothelial

migration and blood vessel formation, promote angiogenesis, and accelerate the reconstruction of blood vessels and nerves, thus improving DFU microcirculation and accelerating DFU healing [26,27].

To sum up, combined treatment of DFU with TTT technique and PRP can effectively increase the expression of platelet-derived growth factor protein receptor, shorten the healing time of ulcer DFU, improve the treatment effect and improve the quality of life.

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