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*Original Article*

# Lower limb deep vein thrombosis treatment by comprehensive interventional therapy through jugular vein

Qianjin Hua[1*], Jianmin Shen[1*], Wugen Kang[1*], Maoheng Zu[2], Linyou Wang[1], Liang Wu[1], Jinhui Lin[1]

*[1]Department of Medical Imaging, Taizhou Municipal Hospital, Taizhou University School of Medicine, Taizhou 318000, Zhejiang, China; [2]Department of Interventional Radiology, Affiliated Hospital of Xuzhou Medical College, Xuzhou 221002, Jiangsu, China. [*]Equal contributors.*

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**Abstract:** Objective: To evaluate the efficacy of comprehensive interventional therapy through jugular vein for lower limb deep vein thrombosis (DVT). Methods: Fifty-eight patients with DVT were treated at the Department of Interventional Radiology of Taizhou Municipal hospital. Pulmonary, inferior vena cava (IVC) and the ipsilateral iliac vein angiography were performed in all patients. According to angiography results, the following selected interventional therapies were performed for treatment: indwelling catheter-directed thrombolysis, IVC filter implantation, balloon dilatation, endovascular stent implantation, and dorsal foot vein pressure thrombolysis. Results: All 58 patients received indwelling catheter-directed thrombolysis through jugular vein; and among these patients, 28 cases were combined with IVC filter implantation (in which filters in 26 cases were removed), 18 cases were combined with balloon dilatation (in which 13 cases received stent implantation after balloon dilatation), and 10 cases were combined with dorsal foot vein pressure thrombolysis. According to the expert consensus on DVT interventional treatment standards of the Chinese Society of Interventional Radiology, curative effect was evaluated (based on four grades) prior to discharge. Venous patency was evaluated by color Doppler ultrasound and stent (or filter) shape was evaluated by abdominal X-ray in one, three, six and 12 months after discharge. After treatment with thrombolysis, clinical symptoms of all 58 cases before discharge achieved satisfactory grades. One patient had recurrent thrombosis and one patient had in-stent occlusion after one year follow-up. Conclusion: Comprehensive interventional treatments through jugular vein for lower limb DVT is a safe and effective method.

**Keywords:** Interventional therapy, deep vein thrombosis, thrombolysis, transjugular

## Introduction

Lower limb deep vein thrombosis (DVT) is a common peripheral vascular disease; wherein, a mass of coagulated blood or thrombus is present in deep veins that return blood to the heart [1]. The incidence for lower limb DVT is approximately 40% of peripheral vascular diseases [2]. Blood clots in the vein could break and lodge in the lungs, which block blood flow and result in pulmonary embolism (PE). Recent studies have suggested that DVT and PE are two stages of the same kind of disease. DVT is mainly treated by immediate anticoagulation with unfractionated or low-molecular-weight heparin followed by warfarin therapy for a certain period of time [3, 4]. However, anticoagulation alone is not completely effective in alleviating or preventing early and late clinical sequelae associated with lower limb DVT such as PE. For partial patients with thrombosis, natural fibrinolysis reduces volume of thrombi and can relieve outflow obstruction without use of interventional thrombolysis; Although anticoagulation could prevent thrombus propagation and recurrent venous thrombosis, but there is still a part of patients failed in dissolving the occluding thrombus or reducing venous outflow obstructions with the help of anticoagulation drugs; which is one of the important reasons for the occurrence of post-phlebitic syndrome. Catheter-directed thrombolysis (CDT) with direct delivery of a concentrated lytic agent into the clot has been proposed as an alternative therapy to anticoagulation [5, 6].

So far, there is no unified method or standard for interventional DVT therapy [7, 8]. A total of 58 cases were treated for DVT through jugular vein approach combined with comprehensive interventional methods from January 2011 to August 2014. This study evaluates the efficacy of comprehensive interventional therapy through jugular vein for lower limb DVT.

## Materials and methods

### *Ethics consideration*

This retrospective analysis was approved by the Ethics Committee of Taizhou Municipal Hospital including screening, treatments and follow-up of subjects. Signed written informed consent was obtained from all subjects. All works were undertaken following the provisions of the Declaration of Helsinki.

### *Patients*

Fifty-eight DVT patients treated in our hospital from January 2010 to August 2014 were enrolled in this study; wherein, 23 patients were male and 35 patients were female. Patient age ranged from 24 to 81 years old with an average age of 52.8 years old. Limited by the insidious onset of deep venous thrombosis and the economic conditions of the patients, patients' time from onset to interventional therapy was 2-90 days with an average of 6.5 days, and was less than two weeks in 23 cases. All patients had different degrees of limb swelling, which was accompanied by pain in some patients. Patients had different degrees of tightness in the chest. Color Doppler ultrasound for the lower limb vein was performed on all patients before operation; pulmonary artery CT angiograms were performed on patients with chest symptoms such as wheezing, cough, etc. The CT pulmonary angiography (CTA) was performed in the right lower limb and chest of DVT patients. After their diagnosis, low molecular weight heparin (5000 IU) was injected subcutaneously to each patients. Chinese patent medicines Ginkgo extract and Radix Salvia Miltiorrhiza were administered 2 times per day.

### *Indications for threshold for right heart strain and PE clot lysis*

PE is likely to occur in arteries and branches of pulmonary. In this study, right heart catheter diagnosis standard was adopted: mild, moderate and severe high-pulmonary pressures in pulmonary artery were defined as contraction pressure of 30~50 mmHg, >50~80 mmHg and >80 mmHg (1 mmHg = 0.133 kpa); the cut off value of $SpO_2$ was defined as 95%, when below 95%, the patients suffer from respiratory function been affected by PE.

### *Pulmonary, inferior vena cava (IVC) and ipsilateral iliac vein angiography*

A 4-5F pigtail catheter was first inserted directly to the main pulmonary artery through the right internal jugular vein, and 25-30 ml of contrast agent (Visipaque, GE Healthcare, Ireland) was injected with a speed of 15 ml/s. During this process, the presence of PE was checked. Then, the pigtail catheter was placed back to the right atrium down to the contralateral iliac vein. IVC angiography was performed to check the presence of thrombus, confirm the opening location of the left and right common iliac vein, and verify the existence of Cockett syndrome. PE in patients was confirmed by CTA, and IVC filters were implanted after IVC angiography once pulmonary embolism was confirmed by pulmonary angiography. After filter implantation, a 4-5F single curved catheter was placed into the ipsilateral iliac vein; and a deep femoral vein sectional contrast was performed to determine the characters of the thrombus.

### *Placement of the IVC filter*

Among the 58 patients enrolled in this study, 49 patients were confirmed with left lower limb DVT and nine cases were confirmed right lower limb DVT. Among the 49 patients confirmed with left lower limb DVT, 34 patients had Cockett syndrome, while 15 cases did not have Cockett syndrome. IVC filters were implanted in 24 patients with right iliac femoral venous thrombosis, left femoral vein thrombosis, and left iliac vein patency; wherein, 17 patients also had PE, the other 7 patients with left DVT and the openings is not compressed, there is a risk of thrombosis PE. During the operation, IVC filters were placed according to IVC angiography results (inferior vena cava thrombosis, diameter and renal vein opening position). If there was no thrombosis in the IVC, the filter was placed below the renal vein opening. If the thrombosis existed in the inferior vena cava, but does not exceed the renal vein opening, the

filter was placed in the renal vein. Among the 24 filters implanted, 22 filters were retrieved within 20 days; while the other two filters were not removed due to old age of patients.

*Catheter-directed thrombolysis (CDT)*

For patients with PE confirmed by CT pulmonary angiography (CTA), a pigtail catheter was inserted into the pulmonary artery to the bulk of the main pulmonary artery thrombosis, 200,000-400,000 units of urokinase were injected through the catheter, and the catheter was retained in the pulmonary artery [9]. Upon returning to the Ward, thrombolytic therapy was continued to be given. Then, 100,000-200,000 units of urokinase were injected according to age, clinical symptoms and blood oxygen saturation levels of the patient. Urokinase was injected two to four times a day. At the same time, patients were subcutaneously injected with low-molecular-weight heparin (5,000 U/12 hours). Angiography (2D-3D) was performed every 2-3 days to observe the thrombus, and thrombolysis was continued until the thrombus was mostly or completely dissolved.

When the pulmonary artery thrombosis was mostly or completely dissolved, we shifted the thrombolysis catheter (5F, L6 side hole or 8 side hole) to the femoral iliac vein for DVT thrombolytic therapy. Dosage of thrombolytic agents and anticoagulants were the same with the dosage given to PE patients. IVC filters were removed when the thrombosis was dissolved. Then, patients were given warfarin for anticoagulation treatment. A retrievable IVC filter was immediately implanted in patients without PE, but had iliac vein thrombosis that spread into the IVC as confirmed by IVC angiography. Then, the thrombolytic catheter was shifted and inserted into the distal end of the ilio-femoral vein thrombosis, and drugs with doses as above were administered until the thrombosis was dissolved.

Patients with left ilio-femoral vein thrombosis and common iliac vein stenosis or occlusion did not undergo IVC filter placement. The thrombolysis catheter was directly inserted into the distal end of the left femoral vein thrombosis for thrombolytic therapy. Angiography was performed during the indwelling catheter process; the end of catheter thrombolysis was evaluated according to the final angiography result.

*Balloon dilatation and stent implantation*

After the ilio-femoral vein thrombosis was completely dissolved, patients with left common iliac vein stenosis or occlusion underwent balloon dilation or stent implantation. A balloon with a larger diameter was chosen as much as possible. Thirty-four cases underwent balloon dilation through the right jugular vein (12-16 mm diameter balloon, Cook Inc.); there was 13 cases' blood vessels were still under pressure or acute retraction after balloon dilatation, all of which were implanted with stents. Stent implantation (14 or 16 mm diameter, Cordis Corp.) was performed in them.

*Dorsal foot vein thrombolysis*

Popliteal and tibiofibular vein thrombosis was found in 10 cases. Due to catheter length limitations, a dorsal foot vein assisted thrombolysis approach was adopted to reach the distal end. An indwelling trocar was inserted through the ipsilateral dorsal foot vein, and the superficial vein above the ankle joint and below the knee joint was blocked using a tourniquet. During this blocking state of the superficial vein, urokinase (100,000 U/time, 12 hours/time) was intravenously injected; and the tourniquet was untied 10 minutes after injection.

*Auxiliary treatment and rehabilitation*

After the operation, the patient was instructed to perform appropriate foot activities to promote deep vein reflux. At the same time, anti-infection, oral warfarin and low-molecular-weight heparin were administered. Blood coagulation function was regularly monitored to control PT/INR between 2-3 [10].

*Follow-up and evaluation after discharge*

After discharge, warfarin was orally administered for one year. Bilateral iliac and lower limb deep vein color Doppler ultrasound examinations were performed to evaluate venous patency, while X-ray examinations were performed to evaluate the location of the stent (or filter) in one, three, six and 12 months after discharge.

*Observation of curative effect*

Based on the expert consensus on deep vein thrombosis interventional treatment standards

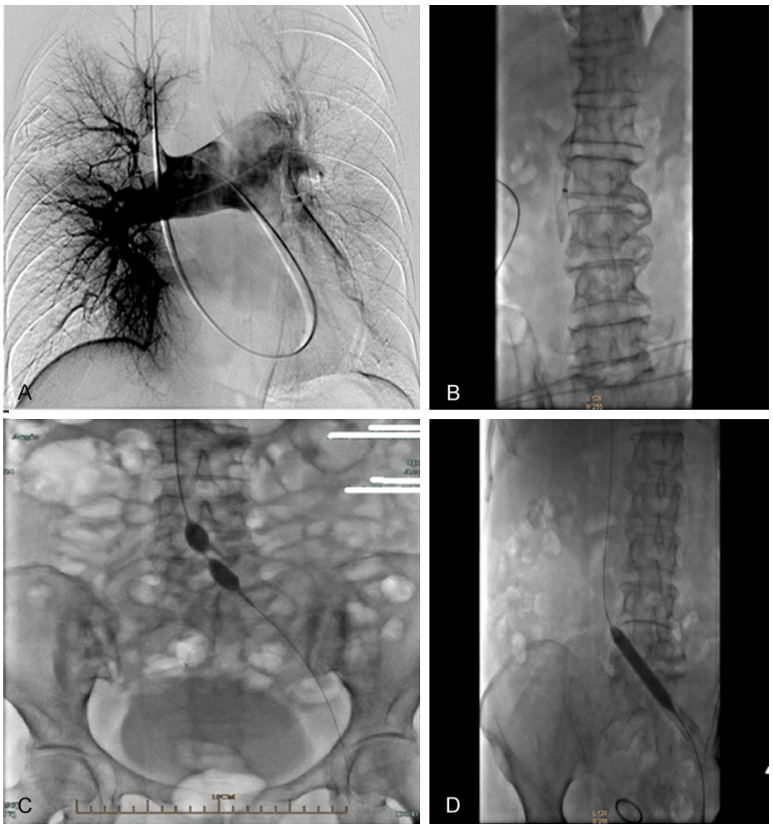


**Figure 1.** A. A female, 65-year-old lower limb deep venous thrombosis patient underwent CT pulmonary angiography via jugular vein, which revealed a right pulmonary embolism. The pigtail catheter was retained for thrombolysis. B. Inferior vena cava filter implantation and recovery via jugular vein approach. C. The Cockett syndrome by balloon dilatation. D. Cockett syndrome patients undergoing stent implantation.

of the Chinese Society of Interventional Radiology, curative effect was evaluated prior to discharge according to limb circumference, tension, activity, and angiography blood flow recovery results. Curative effects were classified into four grades: excellent, good, medium, and poor [10].

Excellent: Compared with the healthy side, limb circumference, tension, and lesion-limb activity are normal after treatment. Difference in limb circumference is ≤1.0 cm. Angiography shows blood flow recovery, no abnormal collateral vessels, no contrast agent retention, and smooth vascular walls.

Good: Compared with the healthy side, limb circumference, tension, and lesion-limb activity are almost normal after treatment. Difference in limb circumference is between 1-1.5 cm. Angiography shows blood flow mostly recovered, small amounts of collateral vessels, no obvious contrast agent retention, and almost smooth vascular walls.

Medium: Compared with the healthy side, limb circumference, tension, and lesion-limb activity significantly improved after treatment. Difference in limb circumference is within 1.5-2 cm. Angiography showed blood flow recovered, various collateral vessels, mild contrast retention, and slightly smooth vascular walls.

Poor: Compared with the healthy side, limb circumference, tension, and lesion-limb activity did not show any significant improvement after treatment. Difference in limb circumference is more than 2.0 cm. Angiography shows no blood flow recovery, a large number of collateral vessels, contrast agent retention, and rough vessel walls.

*Statistical analysis*

SPSS18.0 software was used to analyze data, data results were expressed as mean ± standard deviation (mean ± s), and data was compared using *t*-test and chi-square test. $P<0.05$ means that the difference was statistically significant.

## Results

*Angiography and IVC filter placement*

Among the 58 patients, 17 patients had PE confirmed by CTA with an incidence rate of 29.3%, while 34 cases had Cockett syndrome with an incidence rate of 58.6%. A total of 24 IVC filters were implanted, and 22 filters were recovered. Average retrieval time was two minutes, filter bounce rate was <2 mm, and a filter tilt of approximately 20° occurred in one case during the retrieval process (**Figure 1A-D**).

*Complications*

Hemorrhage was the most common complication during indwelling catheter-directed throm-

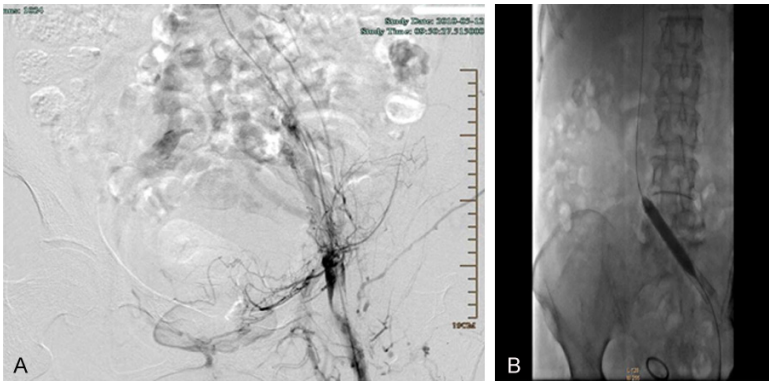

**Figure 2.** A male, 56-years-old patient: (A) angiography reveals the left iliac femoral vein thrombosis in the subacute period, (B) the thrombosis was completely dissolved after one week of thrombolysis treatment.

**Table 1.** Comparison of leg circumferences before and after treatment

| | *n* | Circumference difference of thigh | Circumference difference of calf |
|---|---|---|---|
| Before treatment | 58 | 7.8 ± 4.0 | 5.5 ± 2.6 |
| After treatment | 58 | 4.5 ± 2.3 | 3.1 ± 1.5 |
| | *P* | <0.05 | <0.05 |

bolysis. Three days after thrombolysis, bleeding occurred in five patients including catheter sheath hemorrhage, gingival bleeding, and skin scattered bleeding. Hematuria occurred in three patients during the treatment process, but symptoms disappeared 2-5 days after discontinuing urokinase administration. A filter shifted to the right atrium in one patient, and was taken out using a catcher. No other complications or fatal PEs occurred during treatment.

*Effects of thrombolysis and limb-circumference changes after treatment*

Among the 17 PE patients, PEs were completely dissolved in six cases (35.3%) and >80% of PEs were dissolved in 11 cases (64.7%). Blood flow imaging revealed that the lower limb recovered or basically recovered in 34 patients (58.6%), and no abnormal collateral vessels were observed. Angiography revealed that blood flow recovered in 21 patients (36.2%) and small amounts of collateral vessels were observed (**Figure 2A**, **2B**).

All symptoms of patients significantly improved, and lower limb swelling subsided one week after operation. As one of swelling indicator, the outer peripheral of the thigh (15 cm upper patella inferior margin) and outer peripheral of the calf (15 cm lower superior border of patella) in the lesion side were measured. At the same time, the outer peripheral in the healthy side was also measured. Differences were statistically significant before and after treatment ($P<0.05$) (**Table 1**).

*Effect of grading*

Curative effect was evaluated before discharge based on standards [10]. Results were classified into four grades; and among these patients, 34 cases (58.6%) were evaluated as excellent, 21 cases (36.2%) were evaluated as good, and three cases (5.2%) were evaluated as medium.

*Follow-up*

After hospital discharge, all 58 patients were followed up in three, six and 12 months. Color Doppler ultrasound of bilateral iliac veins and deep veins were performed to evaluate venous patency. Abdominal X-ray was performed to evaluate the shape of the sent (or filter). Results have shown that thrombosis recurred in one case and a stent occluded in one case. A total of 13 stents and two IVC filters were implanted and placed well. No severe limb superficial varicose veins and venous nutrition disorders were observed in patients.

## Discussion

CDT has become an important technique for the clinical treatment of DVT. CDT is generally classified into the following types: I, femoral vein catheter method; II, jugular vein catheter method; III, popliteal venous catheter method; IV, arterial thrombolysis method; V, special equipment for use in thrombolytic method [11, 12]. These methods have advantages and disadvantages. In this study, we adopted the jugular vein approach to treat DVT and PE at the same time.

In recent years, scholars have suggested that DVT and PE are two stages of the same kind of

disease [13]. In this study, the incidence of PE was 29.3%. A large-sample study carried out by Zu *et al.* [14] reported that the incidence of PE was 29.77% among 645 cases of DVT, which was consistent with our results. Diagnosis in PE patients was confirmed by CTA before operation. After puncture, IVC angiography was performed; then, IVC filters were directly implanted via the jugular vein. Other patients initially underwent CTA, followed by IVC angiography and ipsilateral iliac-femoral angiography. This is the first time that direct risk levels of PE were clearly assessed in PE patients, and sequential interventions of thrombolytic therapy were determined. Among these cases, IVC filter implantation was not performed in 34 patients with Cockett syndrome; while for patients with PE or patients with right and left lower limb DVT, IVC filter was placed.

The advantage of an indwelling thrombolysis catheter in PE treatment is that angiography can be repeated during thrombolytic treatment. After a contrast material is directly administered into the catheter to the iliac vein thrombosis, the scope and nature of the thrombus could be comprehensively and objectively observed such as fresh thrombus, orientation of the thrombus, or mixed thrombus. This advantage could provide a means for objectively determining the left common iliac vein compression status, and a basis for balloon dilation and stent implantation. Thrombolytic effects on the PE can be dynamically observed until clinical results were satisfactory [15-17]. Our study, 34 patients have short disease-duration, angiography showed catheter thrombolysis results achieved satisfying; the other 21 patients have longer disease-duration, their thrombus was old, catheter thrombolysis cannot completely removed these old blood vessels, however, the patients' limb function recovered good. It is difficult for the catheter to reach the popliteal and tibiofibular veins in some patients with venous thrombosis due to catheter length and patient height factors. Thus, we adopted the dorsal foot vein approach to infuse thrombolytic drugs, and compensate for this limitation of jugular vein indwelling catheter thrombolysis [18-20].

By applying the urokinase method in high local serum concentrations, systemic blood concentration was reduced compared with systemic thrombolysis. Among the patients, thrombus was mostly or completely dissolved in 15 patients with venous thrombosis after 10 days of thrombolytic catheter treatment. The position of the catheter should be adjusted to the large saphenous vein or internal iliac vein openings when chronic thrombosis or thrombolytic effects were not satisfactory. Main collateral vessel openings can provide better clinical results [21, 22]. In this study, two cases had lower limb DVT over a long period of time. Although CDT infusion therapy on both sides of the iliac vein collateral vessel opened more, thrombosis in patients with lower limb DVT was dissolved.

Bleeding complications were difficult to avoid during the course of anticoagulant and thrombolytic drug treatments. In this study, puncture point bleeding, hematuria, and skin scattered bleeding occurred in patients with jugular vein indwelling catheters.

Five patients had bleeding gums and skin scattered bleeding within the first three days of CDT therapy, while three patients had hematuria during thrombolysis therapy. These symptoms disappeared after 2-5 days of discontinuing urokinase administration. Thrombolytic and anticoagulant drug treatments were first discontinued once bleeding and other symptoms presented in patients, then corresponding treatments were provided. In addition, IVC filters were retrieved in order to prevent the filters from permanently shifting in the thrombosis and occlusion of the IVC [6, 23, 24]. The filter shifted to the right atrium in one patient, and a capture extractor was used to retrieve the filter. IVC filter recovery rate reached 91.67%.

According to reported literatures, the incidence rate of DVT was 56/10,000-122/10 million, and this rate has been continuously increasing annually [24]. Thrombolytic therapy by internal jugular vein catheter for lower limb DVT is an effective treatment, which provides rapid relief of symptoms and shortened hospitalization time. In addition, balloon dilatation or stent implantation can improve long-term efficacy and reduce DVT recurrence. IVC filters can effectively prevent the occurrence of fatal PE. However, IVC filter placement should strictly have a firm grasp of its indications [25, 26].

In summary, the authors believe that interventional treatment via the jugular vein for lower

limb DVT is a simple and safe approach that provides a high success rate and reliable curative effect. At the same time, with nursing and rehabilitation guidance, it can effectively improve the quality of life and prognosis of patients.

## Disclosure of conflict of interest

None.

**Address correspondence to:** Jianmin Shen, Department of Medical Imaging, Taizhou Municipal Hospital, Taizhou University School of Medicine, No. 381 East Zhongshan Road, Taizhou 318000, Zhejiang, China. Tel: +8657688858000; Fax: +8657-688823052; E-mail: jianmshen@163.com

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