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Research Article

# A Retrospective Study Comparing Pharmacomechanical Thrombectomy with Catheter-Directed Thrombolysis for Acute Deep Venous Thrombosis

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**Abstract**

**Purpose:** To compare the clinical efficacy and safety of pharmacomechanical thrombectomy (PMT) with catheter-directed thrombolysis (CDT) for acute lower-extremity deep venous thrombosis (LEDVT).

**Materials and Methods:** Database of patients with acute LEDVT at our institution from February 2011 to December 2019 were analysed. The patients were divided into two groups on the basis of the thrombolytic procedures: PMT group (particularly referred to PMT with Angio Jet in our study), and CDT group. Patients' demographics, risk factors, procedural factors, thrombolysis grade and complications were collected, and post-thrombotic syndrome (PTS) and quality of life (QOL) were followed up at 1 year after treatment.

**Results:** 348 patients were identified (mean age, 50.12 ± 15.87 years; 194 female). 200 patients in the early stage (during 2011 to 2017) received CDT, and 148 patients from 2017 to 2019 received Angio Jet PMT. Baseline data of the two groups were of no statistical difference. thrombus score was significantly decreased in both groups after therapy (each $p<0.001$). Patients who underwent a PMT procedure had higher thrombolysis rates (77.35±9.44% vs 50.85±6.72%), less administered amounts of thrombolytic agent urokinase [20(20-20) vs 350(263-416), $p<0.001$], larger limb circumference difference (above the knee: 6.03±1.76cm vs 4.51±1.82cm, $p<0.001$; below the knee: 2.90±1.16cm vs 2.51±0.90cm, $p<0.001$), and shorter length of stay(7.19±3.11 days vs 12.33±4.77 days, $p<0.001$), but got higher hemoglobin decline (13.41±10.59 g/L vs 10.88±11.41 g/L, $p=0.038$) and creatinine increase [9.58(2.32-15.82) umol/L vs 4.53(2.87-6.08) umol/L, $p<0.001$] compared with the CDT group. There was no difference in numbers of balloon angioplasty, stents implantation (each $p>0.050$) and minor and major complications between the two groups. At the 1-year follow-up, post-thrombotic syndrome (PTS) was observed in 13.51% of the PMT group compared to26% of the CDT group ($p=0.025$), and moderate-severe PTS were more in CDT group (8% vs 2.7%, $p=0.036$).

**Conclusion:** PMT and CDT were effective and safe treating methods for acute LEDVT. PMT offered favorable resolution of thrombosis, and lower risk of post-thrombotic syndrome.

**Keywords:** deep venous thrombosis; catheter-directed thrombolysis; pharmacomechanical thrombectomy; angiojet

## 1.Introduction

Venous thromboembolism is a major global burden with about 10 million cases occurring every year, representing the third leading vascular disease after acute myocardial infarction and stroke [1]. Anticoagulation has been established as the standard therapy for the treatment of acute Deep Venous Thrombosis (DVT), aimed at preventing thrombus propagation and pulmonary embolism (PE), and disease recurrence [2]. Despite standard anticoagulant therapy, up to 25-50% of lower limb DVT patients will develop some degree of post-thrombotic syndrome (PTS), resulting in physical limitations and impaired quality of life [3]. More aggressive interventional approaches using catheter-directed thrombolysis (CDT) or CDT in combination with pharmacomechanical thrombectomy (PMT) [4, 5] have emerged, with expectation to rapidly restore venous patency, preserve venous valvular function, and prohibit the progression of PTS.

However, there is little information on whether there are advantages of efficacy or reduced complications by PMT compared with CDT. Accordingly, we reviewed the clinical data of patients admitted to our hospital with acute lower-extremity DVT, who were treated by CDT or PMT to compare the efficacy and safety of the two approaches.

## 2. Design and Methods

Study Design The study was approved by the ethics committee of the Second Affiliated Hospital of Nanchang University. All acute lower extremity DVT

patients diagnosed by clinical manifestation, ultrasound and serum D-dimer were evaluated by the same operation team to confirm the feasibility and safety of the interventional therapy. The operation indications were as follows: (1) acute lower-extremity DVT that duration of disease≤14 days, (2) patients in good physical condition, (3) expected survival time longer than 1 year and (4) low risk of bleeding. The contraindications were as follows: (1) contraindications to the use of anticoagulant drugs, thrombolytic drugs and intravenous contrast media, (2) history of serious trauma or major operation in the preceding 4 weeks, (3) pregnancy, (4) younger than 16 or older than 75 years of age, (5) poorly controlled high blood pressure (systolic blood pressure>180 mmHg, diastolic blood pressure>110 mmHg), (6) history of intracranial hemorrhage in the previous 3 months and (7) expected survival time less than 1 year. Consecutive patients who underwent endovascular intervention of CDT and PMT between 2011 and 2019 were identified, and bilateral DVT, inferior vena cava affected DVT and distal DVT were excluded in this study. The patients' data were analyzed and detailed in Table 1.

**Thrombolysis technique**

Each Patient got routine admission examinations, and when the consent forms were finished, patients were transferred to interventional operating room, and given 1000-2000ml saline infusion and venous indwelling catheterization. The anterograde venography of lower extremity deep veins was performed to confirm that the LEDVT was in the acute stage (Figure 1. b, d: Double track sign). The retrievable IVC filter (opt Ease filter, Cordis, Miami Lakes, USA; Aegisy filter, Lifetech Scientific, Shenzhen, China; Celect filter, Cook, USA) was implanted prior to thrombolysis, and removed within two weeks after thrombolysis. The approaches for catheterization procedures in the early stage include the popliteal vein, contralateral femoral vein, and the great and small saphenous veins. Currently, the anterior or posterior tibial vein (ATV or PTV) or peroneal vein (PV) was used mostly, under the real-time guidance of X-ray with contrast agent (Figure 1. a, c).

In the CDT group, A multiple side-hole infusion catheter (Angio dynamics, NY, USA; infusion length: 30–50 cm) was placed inside the thrombosed segment. Urokinase (Tianjin Biochemical Pharmaceutical, China) was infused into thrombolysis catheter from an external micropump 500,000-1 million IU/d, and low molecular weight heparin (hepatunn, Chengdu, China) was pumped through the sheath tube 6250 IU/d to avoid block pipe. The thrombolytic catheter and sheath tube were fixed and patients were sent back to the ward for continuous thrombolytic therapy. The coagulation function was tested every 4 hrs. to adjust the urokinase pump speed; when fibrinogen level dropped to 1.5 g/L, the urokinase dosage was halved, and when it decreased to 1.0 g/L, urokinase was suspended. The venography was checked every 24-48 h to monitor thrombolysis, and reset catheter position in vain if necessary. The maximum time of lysis therapy was 1 week, during which the thrombolysis therapy was stopped if there was complete thrombolysis, deep venous patency, or no change upon two successive examinations.

In the PMT group, AngioJet thrombectomy catheter (6F, 120 cm) was implanted into the thrombosed vein segment in an anterograde fashion. Power pulse lytic mode was used to administer urokinase (0.4 million units in 250 ml of saline) via the catheter. 20 mins was waited for urokinase exerted its thrombolytic effect. Next, the AngioJet catheter was changed to standard rhyolitic thrombectomy mode with a 2 mm/s speed back and forth in the residual thrombus segments (Figure 1. g). The maximum approved suction liquid volume was 500ml for this study. In this one-stage PMT group, the retrievable IVC filter was not totally detached in IVC, and it was retrieved before the operation was over. If the residual thrombus still existed when the maximum suction liquid volume reached 500ml, adjunctive CDT therapy with urokinase was performed as described as above.

Residual iliac vein stenosis was treated with balloon dilation, or stent implantation if residual iliac-vein lesion stenosis was more than 50% in the vein diameter. The stent diameter was 20% larger and 2 cm - 4 cm longer than the stenotic segment, and the proximal position of the stent was 0.5 cm - 1 cm in IVC. The procedure-related information of 2 groups is detailed in Table 2.

**Perioperative management and follow-up**

Hydration treatment of 1000-2000ml normal saline or properly basification of urine was executed 6 hrs. preoperatively to 24 hrs. postoperatively in the PMT group. Blood routine and renal function were re-tested. The anticoagulant drugs were prescribed and used according to the ACCP guidelines, and all the patients were prescribed knee-high elastic compression stockings (class II, 30 mm Hg) as a standard adjunct treatment for at least half a year. A Doppler scan was performed to assess patency and valve function as a routine part of follow-up. Patients' follow-up visits were scheduled at 1, 6, and 12 months after the operation.

**Outcome Assessments**

The thrombus score was evaluated for seven venous segments using a venogram: the popliteal vein, the distal and proximal superficial femoral vein, the common femoral vein, the external iliac vein, the common iliac vein and the inferior vena cava. The thrombus score was 0 if the vein was completely free of thrombus, 1 for partial occlusion, and 2 for complete occlusion by the thrombus [6]. The rate of thrombolysis was calculated as the difference between the prelysis and postlysis scores compared to the prelysis scores.

PTS was diagnosis by the Villalta scale, and a total score of <5 indicated no PTS, a score of 5-9 indicated mild PTS, a score of 10-14 indicated moderate PTS, a score of >15 or leg ulcer indicated severe PTS [7].

Patient-reported health-related quality of life at baseline and 24 months was assessed with the use of the generic medical outcomes study 36-Item Short Form Health Survey (SF-36). For the SF-36, an established computer scoring algorithm was used to generate scores for the physical component summary (PCS) and mental component summary (MCS) scales (which reflect physical and mental health status, respectively) [8].

## Statistical analysis

All data were analyzed with SPSS 23.0 software (Chicago, IL, USA). Continuous data were expressed as the mean ± standard deviation or medians (interquartile ranges) compared with the t-test or Mann-Whitney U test, and categorical variables were analyzed with the Chi-square test or Fisher exact test. Ranked data were compared using a two-sided Mann-Whitney test. The level of significance was determined as $p < 0.05$.

## Results

From Feb 2011 to Dec 2019, a total of 348 consecutive eligible patients were included, mean age 50.12 ± 15.87 years, 194 females. 200 patients received CDT in the early stage during 2011 to 2017, and 148 patients got PMT from 2017 to 2019, as AngioJet was available and adopted as a first-line treatment of LEDVT at our institution since 2017, followed by CDT when the treating physician thought that thrombus clearance was inadequate. Among the 148 patients, only 5 need adjunctive CDT treatment. Baseline data about the risk factors, comorbidity, thrombosis extent etc. of the two groups were listed in Table 1. and of no statistical difference.

Successful lysis was (50.85±6.72) % in CDT and (77.35±9.44) % in PMT group respectively (Table 2). Thrombus score. PMT group required significantly less UK per patient [20(20-20) vs 350(263-416); $P < 0.001$] and average length of stay (7.46±3.47 days vs 12.33±4.75 days; $P < 0.001$). The rate of Balloon angioplasty for residual stenosis and stent implantation for persistent stenosis was similar between the two groups (PMT 60.13% vs CDT 56%, P = 0.44; PMT 22.30% vs CDT 25.5%, P = 0.49). A total of 9 bleeding complications (7 vs 2, p= 0.032) occurred all within the first 2 days in CDT versus PMT patients, and none of which were classified as major. There was no occurrence of death, pulmonary embolisms, or cerebral hemorrhage related to CDT and PMT. The incidence of acute kidney injury was 7 vs 4 in PMT vs CDT patients, and preoperative and postoperative hemoglobin decline was significant between groups (13.41±10.59 g/L vs 10.88±11.41 g/L in PMT vs CDT group, P =0.038). There were also significant differences of creatinine increase between the two groups [9.58(2.32-15.82) umol/L in PMT vs 4.53(2.87-6.08) umol/L in CDT group, $P < 0.001$].

During the 12-month follow-up, the total follow-up rate was 95.11% (93.5% in CDT group vs 97.3% in PMT group, $P > 0.05$). 8 patients in CDT group vs 3 patient in PMT group got the recurrent DVT, due to failure to take oral anticoagulant or insufficient anticoagulant drugs. Villalta Scale for the assessment of PTS showed that in PMT group, 13.51% got PTS and 26% in CDT group, P = 0.004. And 2.7% got moderate-severe PTS in PMT group, while 8% in CDT group, P=0.001. Preoperative and postoperative D-value of SF-36 PCS and SF-36 MCS had no between-group difference.

## Discussion

With the development of interventional techniques, several therapies complementary to CDT have been developed, like PMT and ultrasound-assisted CDT (USCDT). PMT seem to improve the efficacy of thrombus clearance [9]. Some scholars reported AngioJet PMT vs catheter-directed thrombolysis, demonstrating that PMT was a safe, effective, and cost-effective technique in the resolution of acute DVT [10, 11]. But there was a lack of major randomized controlled trials to support the routine use of PMT over CDT alone.

A systematic review by the Cochrane Collaboration group [12], concluded that there was insufficient evidence to draw any conclusions about the effectiveness and the safety of PMT versus anticoagulation alone in the management of people with acute iliofemoral DVT. According to this lack of evidence, recommendations provided by current guidelines about the use of CDT and/or PMT as adjunctive therapy to standard anticoagulation for the treatment of lower limb DVT are weak. Current guidelines recommend early thrombus removal using percutaneous catheter-based techniques mainly in patients with symptomatic proximal DVT with good life expectancy and low bleeding risk [2].

Increasing reports recommendate complete DVT lysis and stent placement within a single procedure if resources are available. However, catheter-directed therapy is limited, as it requires a multistage process including prolonged urokinase infusion times and monitoring in the intensive care unit [13].

Our study showed benefits of PMT compared to CDT, for it allowed immediate thrombus extraction and simultaneous lytic infusion. It had been associated with more complete resolution of thrombus, lower dosage of thrombolytic drug administered with lower systemic side effects, shorter monitor and hospital stays, and fewer venograms. Thus, the current recommendation in our department is too complete DVT lysis, stent placement and filter implantation and withdraw within a single operation procedure, and PMT became a first-line treatment in our practice.

The AngioJet device works by forceful injection of solvent (saline or thrombolytic) retrograde with powerful suction at the more proximal portion of the catheter applied through the exhaust port. The powerful Venturi effect created in the region surrounding these ports is able to fragments and extracts thrombus, but also give a destruction to the red blood cells, with an evident hemoglobin decline, creatinine increases and acute kidney injury [14, 15]. But in our experience, transient hemoglobin decrease and creatinine increase would back to normal within 1month follow-up. And the acute kidney injury rate was low and not serious, no one needed hemodialysis.

There are several reasons why PMT resulted in less post-thrombotic morbidity for patients. First of all, almost all the PMT access vessels were calf veins in our department, especially the anterior tibial vein. Thus, thrombi in the popliteal vein and below the knees can be effectively dissolved. What's more, since the anterograde catheterization from below the knee, the function of the valve is better preserved. The occlusion and destruction of the popliteal vein valve are often the cause of PTS; thus, this approach can lower the incidence of PTS by dissolving the popliteal vein thrombus while avoiding mechanical injury from the sheath to the vein valve [16-18]. Besides, improved physician experience has contributed to improved outcomes overtime. Patients are treated today more efficiently, have shorter treatment times, receive lower doses of thrombolytic agent, resulting to better overall outcomes than patients treated years earlier.

The limitations of our study include the inherent bias of retrospective data collection, nonrandomized nature, the small study population and short follow-ups.

## Conclusion

Both CDT and AngioJet PMT appears to be a safe, efficacious approach in restoring iliofemoral venous outflow in the presence of acute LEDVT. AngioJet PMT could resulted in more efficient thrombus removal with shorter treatment times and lower doses of Urokinase, and lower risk of post-thrombotic syndrome.

## Abbreviations:

| Abbreviations | extensions |
|---|---|
| PMT | pharmacomechanical thrombectomy |
| CDT | catheter-directed thrombolysis |
| LEDVT | lower-extremity deep venous thrombosis |
| PTS | post-thrombotic syndrome |
| QOL | quality of life |
| DVT | deep venous thrombosis |
| PE | pulmonary embolism |
| IVC filter | inferior vena cava filter |
| ATV or PTV | anterior or posterior tibial vein |
| PV | peroneal vein |
| SF-36 | 36-Item Short Form Health Survey |
| PCS | physical component summary |
| MCS | mental component summary |
| USCDT | ultrasound-assisted catheter-directed thrombolysis |

## Author contributions

XiXi Min. Wei Chen wrote the main manuscript text and Jiehua Qiu. Xiande Zeng. Xiong Zeng Kang Hui Dai. Zhi Nan Ju prepared figures of manuscript. All authors reviewed the manuscript.

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## Data availability

The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

## Competing interests

The authors declare no competing interests.

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