

Safety and Efficacy of Endovascular Treatment on Pregnancy-Related Iliofemoral Deep Vein Thrombosis

Clinical and Applied
Thrombosis/Hemostasis
Volume 28: 1-8
© The Author(s) 2022
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/10760296221124903
journals.sagepub.com/home/cat



Zhao-Xuan Lu, MD¹, Heng-Le Wei, MD², Yadong Shi, MD¹,
Hao Huang, MD¹, Haobo Su, PhD¹, and Liang Chen, MD¹

Abstract

Objective: This study investigates the safety and efficacy of endovascular treatments on pregnancy-related iliofemoral deep vein thrombosis (DVT). **Methods:** We retrospectively reviewed data of 46 patients who had symptomatic pregnancy-related iliofemoral DVT and underwent endovascular treatment. The patients treated with catheter-directed thrombolysis (CDT) were classified as the CDT group. In contrast, those treated with CDT combined with pharmacomechanical thrombectomy (PMT) or angioplasty/stenting were classified as the pharmacomechanical catheter-directed thrombolysis (PCDT) group. **Results:** Based on the immediate post-operative clot burden reduction rate analysis of 46 patients: 22 cases were completely dissolved (lysis grades III), 12 were partially dissolved (lysis grades II), and 12 failed (lysis grades I). There was a statistically significant difference in the rate of clot burden reduction between the CDT group (n = 19) and the PCDT group (n = 27) ($p = 0.001$). There was no statistically significant difference in the number of bleeding events between the two groups ($p = 0.989$). At 24 months, cumulative venous patency in the CDT group was 50.0%, compared to 78.2% in the PCDT group. Furthermore, there was a statistically significant difference in Villalta score ($p = 0.001$) and venous severity scoring (VCSS score) ($p = 0.005$) between the two groups. **Conclusions:** CDT treatment combined with PMT or angioplasty/stenting is comparatively safe and effective for pregnant-related DVT patients. PCDT outperforms CDT in terms of immediate efficacy and reduces the incidence of post-thrombotic syndrome with better midterm outcomes.

Keywords

pregnancy-related, deep vein thrombosis, catheter-directed thrombolysis, pharmacomechanical thrombectomy

Date received: 23 June 2022; revised: 18 August 2022; accepted: 22 August 2022.

Introduction

The risk for venous thromboembolism (VTE) increases during pregnancy and the postpartum period. Notably, the risk of VTE increases five-fold during pregnancy, and thrombotic events are the major cause of maternal morbidity and mortality.^{1,2} Besides mortality, long-term morbidity is associated with post-thrombotic syndrome (PTS).³ As a standard medical therapy for deep vein thrombosis (DVT), anticoagulation cannot provide rapid thrombus resolution or the recanalization of extensive venous occlusion, thus increasing the risk for post-thrombotic morbidity significantly.⁴ Several randomized controlled trials have confirmed the safety and efficacy of various endovascular treatments such as catheter-directed thrombolysis (CDT) and pharmacomechanical thrombectomy (PMT) for

acute symptomatic relief and prevention of PTS in DVT patients.⁵⁻⁸ However, peripartum patients were usually

¹ Department of Vascular and Interventional Radiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, China

² Department of Radiology, The Affiliated Jiangning Hospital with Nanjing Medical University, Nanjing, China

Corresponding Authors:

Liang Chen, Department of Vascular and Interventional Radiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, China.
Email: chenliangdh@sina.com

Haobo Su, Department of Vascular and Interventional Radiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, China.
Email: doctorsuhaobo@163.com



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use,

reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access page (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

excluded from these trials. Therefore, due to the scarcity of available data and evidence, guidelines for this specific cohort often refer to non-pregnant patients.^{5,9} Thus, it remains to be determined whether an aggressive endovascular thrombus removal strategy should be considered for a better prognosis in this young group. The present study describes the initial and midterm outcomes of 46 consecutive pregnancy-related iliofemoral DVT patients treated using CDT and adjunctive PMT or angioplasty, occasionally integrated with stent placement.

Material and Methods

Patients

The local institutional review board approved this retrospective study. Patients were offered CDT or PCDT at our hospital if they had symptomatic iliofemoral DVT, had failed at least a short trial of anticoagulation therapy, and had no absolute contraindication to thrombolysis. The information system database was searched between January 2012 and February 2020 for patients meeting the inclusion criteria. The inclusion criteria were as follows: (1) pregnancy-related DVT (patients with DVT during pregnancy or within 12 weeks after abortion or delivery); (2) patients with swollen lower limbs and pain; (3) Doppler ultrasound or venography confirmed DVT of the iliofemoral venous segments in lower extremities; and (4) patients underwent endovascular treatment. Exclusion criteria included the following: (1) peripheral DVT (thrombosis below the popliteal vein); (2) patients who were contraindicated to the use of anticoagulants/thrombolytic or contrast agents; and (3) patients who refused endovascular treatment. We retrospectively reviewed 46 patients who had endovascular treatment for symptomatic pregnancy-related iliofemoral DVT between January 2012 and February 2020. All patients were treated using CDT with or without adjunctive PMT and angioplasty/stenting if necessary. The patients treated with CDT were classified as the CDT group, whereas those treated with CDT combined with other treatments were classified as the pharmacomechanical catheter-directed thrombolysis (PCDT) group. Patient information, including the clinical data, venography results, treatment plans and follow-up results was collected and retrospectively reviewed to assess the immediate efficacy, midterm outcomes and safety of endovascular treatment.

Procedure

Following diagnosis, DVT patients were subcutaneously injected with low-molecular-weight heparin (LMWH, 100 IU/kg) once every 12 h. Argatroban was administered intravenously by an infusion pump (ZNB-XD intelligent infusion pump; KellyMed Co, Ltd, Beijing, China) to patients suspected or diagnosed with heparin induces thrombocytopenia (HIT). When using argatroban, the activated partial thromboplastin time ratio (APTT-ratio) was kept between 1.5 and 2.5. After pre-operative venography, the patients select between CDT

and PCDT based on a standardized description of each procedure's benefits, risks and costs. Following local anesthesia, a temporary filter was placed in the inferior vena cava (IVC) before the subsequent treatment in patients with a potentially life-threatening thrombus in the iliofemoral vein. Alternatively, the filter could be inserted via the jugular or femoral vein of the non-affected limb. Then, a thrombus removal strategy was introduced, which included CDT, PMT or angioplasty/stenting. Regarding the location and distribution of the thrombus and the visibility of the ipsilateral popliteal vein or contralateral iliofemoral vein by venography, CDT was performed using either an antegrade approach via the ipsilateral popliteal vein or a retrograde approach via contralateral femoral vein access/right jugular vein.¹⁰ Afterward, a 4-5 French (F) infusion catheter with multiple side holes (Unifuse Infusion Catheter, AngioDynamics, USA, or Fountain Infusion Catheter, COOK, USA) was placed in the thrombus section. Overnight infusion of urokinase (Livzon Pharmaceutical Group, Inc.) using the infusion catheter was initiated at 20 000 to 30 000 U/h. Thrombolytic therapy was monitored daily with routine blood tests. After the treatment, venography examinations were performed daily to monitor the progression of thrombolysis. If necessary, the position of the perfusion catheter was adjusted to ensure that the infusion covered the thrombus. When urokinase thrombolysis was unsatisfactory, alteplase (recombinant tissue plasminogen activator, rt-PA) (Actilyse®; Boehringer Ingelheim International GmbH) was administered at 0.01 mg/kg/h. The infusion rate of thrombolytic agents was adjusted according to the fibrinogen level (FIB) and the thrombolysis effects. Thrombolysis was temporarily stopped when FIB was <1.0 g/L.¹¹ PMT was performed using an 8-F guiding catheter (Boston Scientific, USA) for manual thrombus aspiration or a 6-F AngioJet catheter (Bayer, Warrendale, Pennsylvania) for rheolytic thrombectomy, occasionally supplemented with balloon dilatation (6–12 mm). If necessary, self-expanding stents (8–14 mm) were placed in the iliac veins to relieve the May-Thurner syndrome. Stents used included smart control (Cordis, USA) and luminexx (Bard, USA). All procedures were operated by two experienced interventional physicians. According to ACCP guidelines, thrombolysis was followed by a continuous anticoagulation therapy (warfarin or new oral anticoagulants).¹² The anticoagulation with warfarin was bridged with LMWH, and the international normalized ratio (INR) was maintained between 2.0 and 3.0. Warfarin was recommended for anticoagulation therapy in lactating women. The anticoagulation therapy was required for at least 3 months and extended to at least 12 months for patients who underwent stenting. Medical elastic compression stockings (class II) were recommended after discharge.

Evaluation

The immediate efficacy of the therapy was evaluated using a total thrombus score by adding the scores of seven vein segments, including IVC, common iliac vein, external iliac vein, common femoral vein, proximal and distal segments of

femoral vein, and popliteal vein.¹³ Thrombus scores were calculated as follows: 0-vein was patent and completely thrombus-free; 1-partially occluded; and 2-completely occluded. Clot burden reduction rate was calculated as (pre-lysis thrombus score vs post-lysis thrombus score)/ pre-lysis thrombus score *100%. Then classified into three groups for analysis: grade I (<50% lysis), grade II (50%-99% lysis) and grade III (100% lysis with no residual clots). Lysis grades II and III (\geq 50% lysis) were considered successful outcomes. The clinical efficacy was evaluated by comparing the difference in limb circumference at 15 cm above and 10 cm below the knee (pre-operative limb circumference vs post-operative limb circumference).¹⁴ We included the unilateral limb with more severe symptoms or preferentially treated for statistical analysis in patients with bilateral DVT. Patients were followed up clinically and by Doppler ultrasound at 3, 6 and 12 months and then annually. Venography was recommended if the ultrasound findings indicated a potential iliac vein occlusion. Venous patency was determined using Doppler ultrasound or venography. Patients with partial or complete incompressibility of the femoral vein, no pelvic or femoral vein flow, and/or functional venous obstruction were classified as not having regained iliofemoral venous patency.^{15,16} The diagnosis and grading of PTS were performed using the Villalta score¹⁷ and venous severity scoring (VCSS score) at 12 months.¹⁸ The HAS-BLED Score¹⁹ was used to predict major bleeding risk.

Statistical Analysis

Continuous variables were presented as mean \pm standard deviation (SD), while non-normally distributed data were presented as median (P25, P75). A t-test was used for independent samples to establish the differences between the groups, while a Mann-Whitney test was used for normally and non-normally distributed continuous variables. A Chi-square test was used to analyze the baseline differences in categorical data, whereas Fisher's exact test was used when Chi-square test conditions were not met. Kaplan-Meier survival analysis was used to assess the degree of venous patency. Correlation analysis was applied to assess the correlation between immediate lysis grade and midterm venous patency. Statistically significant was determined at $p < 0.05$ (two-tailed). The statistical analyses were performed using the IBM SPSS version 24.0.

Results

Baseline Characteristics of Patients

Between January 2012 and February 2020, 46 symptomatic pregnancy-related iliofemoral DVT patients who underwent endovascular treatment were reviewed retrospectively. All patients were followed up for at least 24 months. 5 patients continued follow-up at other local hospitals. The CDT group had 19 patients, whereas the PCDT group had 27. Table 1 summarizes the baseline clinical characteristics of all patients.

Table 1. Baseline Clinical Characteristics of Patients.

Parameters	CDT Group (n = 19)	PCDT Group (n = 27)	P Value
Age (years, mean \pm SD)	27.9 \pm 4.9	29.6 \pm 5.4	0.298
Pregnancy-related status, n (%)			0.967
pregnant	3 (15.8)	2 (7.4)	
Abortion	0	3 (11.1)	
Vaginal delivery	2 (10.5)	4 (14.8)	
Cesarean delivery	14 (73.7)	18 (66.7)	
Previous pregnancy history, n (%)			0.685
Abortion	4 (21.1)	4 (14.8)	
Vaginal delivery	3 (15.8)	6 (22.2)	
Cesarean delivery	1 (5.3)	3 (11.1)	
Duration of symptoms, n (%)			0.982
\leq 14 days	15 (78.9)	22 (81.5)	
>14 days	4 (21.1)	5 (18.5)	
Side of DVT, n (%)			0.888
Left side	14 (73.7)	19 (70.4)	
Right side	2 (10.5)	3 (11.1)	
Bilateral	3 (15.8)	5 (18.5)	
May-Thurner Syndrome, n (%)	11 (57.9)	16 (59.3)	0.926
Pulmonary embolism (PE), n (%)	2 (10.5)	4 (14.8)	1.000
IVC involvement, n (%)	6 (31.6)	15 (55.6)	0.162
Pre-operative thrombus score (median (P25, P75))	9 (7.11)	11 (10.13)	0.227

Abbreviations: CDT, catheter-directed thrombolysis; DVT, deep vein thrombosis; IVC, inferior vena cava; PCDT, pharmacomechanical catheter-directed thrombolysis.

The majority of baseline clinical characteristics were equally distributed between the two groups. There was no statistically significant difference between the two groups in age, pregnancy-related status, previous pregnancy history, duration of symptoms, positive VTE history, side of DVT, positive of May-Thurner Syndrome and pulmonary embolism (PE). 2 patients in the CDT group and 3 in the PCDT group had a VTE history but no other evidence of thrombophilia. Moreover, 3 patients in each group had a HIT diagnosis or were suspected of HIT. All these 6 patients experienced severe thrombotic progression after anticoagulation with LMWH, with or without adjunctive thrombolytic therapy, while blood tests showed a significant reduction in platelets of at least 50%.

Approximately 70% of these patients had a cesarean delivery, and 46% had a pregnancy history. The median time between delivery and hospitalization for 38 postpartum DVT patients was 22.5 days (14–60 days). 5 pregnant patients were in their first trimester agreed to endovascular treatment followed by pregnancy termination. Notably, 80% of these patients were diagnosed in the acute stage (\leq 14 days). DVT was bilateral in 8 patients (17%), right-sided in 5 patients (10%), and left-sided in remaining patients. 4 out of 8 bilateral DVT patients had HIT or suspected HIT, while 7 had IVC involvement. Although the differences were not statistically significant, the incidence of IVC involvement and pre-operative

thrombus score was higher in the PCDT group than in the CDT group. Furthermore, these individuals were frequently associated with May-Thurner Syndrome (59%).

Short-Term Outcomes

There were 22 cases of thrombus that were completely dissolved (lysis grade III), 12 that were partially dissolved (lysis grade II), and 12 that failed (lysis grade I). The pre-operative and post-operative venography of a 36-year-old postpartum patient with acute IVC and iliofemoral vein thrombosis are illustrated in Figure 1. The clot burden reduction rate revealed that PCDT group had better thrombolytic efficacy than the CDT group, with a statistically significant difference ($p=0.001$). The difference in the limb circumference between the PCDT and CDT groups was slightly superior but not statistically significant at 15 cm above the knee ($p=0.086$) and 10 cm below the knee ($p=0.253$). In the present study, an AngioJet catheter for rheolytic thrombectomy was performed in 11 patients of the PCDT group. There were 27 patients with iliac vein stenosis, 9 of them had iliac balloon dilatation, while 7 underwent iliac vein stenting. Except for 5 patients who had an IVC filter placed because their VTE history was irretrievable, the rest had successful filter removal. There were no statistically significant differences in filter removal intervals and hospital stay. Table 2 presents the details of the treatment procedure and the immediate outcomes.

Midterm Outcomes

According to Villalta score at 12 months, 1 case developed mild PTS (Villalta score 5) and 2 cases with severe PTS (Villalta score 15), all from the CDT group and classified as lysis grade I. The Villalta score of other patients ranged from 0 to 2. There was a statistically significant difference in the Villalta score ($p=0.001$) and VCSS score ($p=0.005$) between the two groups (Figure 2). The cumulative venous patency at 3, 6, 12 and 24 months in the CDT group was 70.0%, 70.0%, 50.0% and 50% respectively. Meanwhile, in the PCDT group, it was 91.3%, 82.6%, 78.2% and 78.2% respectively (Figure 3). Furthermore, we found that the lysis grade positively correlates with midterm venous patency ($p<0.001$). Under adequate anticoagulation, follow-up results at 6 months or 12 months of 5 patients improved slightly. The stents remained patent at the last annual follow-up in 6 out of 7 patients with iliac vein stenting. One stenting case occluded at 6 months follow-up, whereas Villalta scored 0 and VCSS scored 1 at 12-month follow-up, and the patient refused further endovascular treatment. After discharge, 23 patients continued warfarin anticoagulation therapy (target INR of 2-3), and 24 patients continued rivaroxaban anticoagulation therapy. Symptomatic patients were compliant with the use of elastic compression stockings.

Complications

We found no significant procedure-related complications. There were no reports of death or recurrent PE during

hospitalization. The HAS-BLED score for bleeding risk assessment was 0 for most patients, 3 patients scored 1, and only one had a score of 2. A total of 15 patients experienced minor bleeding events, including puncture site bleeding ($n=5$), gingival bleeding ($n=4$), vaginal bleeding ($n=3$), hematuria ($n=5$), haematochezia ($n=1$), hemoptysis ($n=1$), and nasal bleeding ($n=1$). In addition, we observed a case of pelvic hematoma (HAS-BLED score 0) with hemoglobin levels reduced to 3 g/dL. Except for the pelvic hematoma, an insignificant decrease in hemoglobin was observed in the other bleeding patients between admission and discharge. All these complications were alleviated by slowing or stopping thrombolysis, and no patient required a blood transfusion. Table 2 illustrates the details of the complications.

Discussion

The risk of pregnancy-related VTE increased due to a prothrombotic state in pregnant, blood flow stagnation, and vascular traumas during delivery, particularly with assistive devices and cesarean section.¹ Moreover, thrombophilia and a history of VTE are significant risk factors. The high prevalence of May-Thurner syndrome also contributes to DVT.^{20,21} In the present study, nearly 70% of these patients had cesarean delivery with a 59% incidence of May-Thurner syndrome. As a result, the prevention of VTE in peripartum patients with the above-mentioned risk factors should be emphasized.

Anticoagulation therapy is an important standard treatment for DVT because it prevents new clot formation and reduces the risk of recurrent venous thromboembolism, but it cannot lyse the thrombus.^{9,22-25} Even with long-term anticoagulation therapy, 20%-50% of patients developed PTS after DVT, with 5%-10% developing severe PTS.^{3,26} The incidence of PTS is relatively high in pregnancy-related DVT. According to a study of long-term outcomes of pregnancy-related VTE, 42% of patients with DVT had PTS (mean time since first VTE was 9.1 years), which was severe in 7% of the patients.²⁷ This high rate could be attributed to the high proportion of proximal DVT (83%) and only a few patients had systemic thrombolysis or endovascular therapy. The patients with pregnancy-related DVT are relatively young and likely to suffer from PTS for a longer period. Therefore, more active therapy is preferred to achieve early thrombus removal, prevent PTS and improve quality of life.

CDT and PMT are minimally invasive techniques often used to treat acute iliofemoral DVT. Several comparative studies support the potential of CDT to prevent PTS. Additionally, when compared to systemic thrombolysis, CDT is associated with a lower rate of major bleeding.^{8,28} PMT may help to prevent PTS by promoting early symptom resolution, preventing valvular dysfunction and preserving limb function.^{6,8} Nevertheless, pregnancy, obstetric delivery and lactation are usually considered relative contraindications to thrombolysis and advanced endovascular treatment. In trials that included peripartum patients, no specific comprehensive analysis was reported concerning this cohort.^{6, 8 29} A retrospective study of

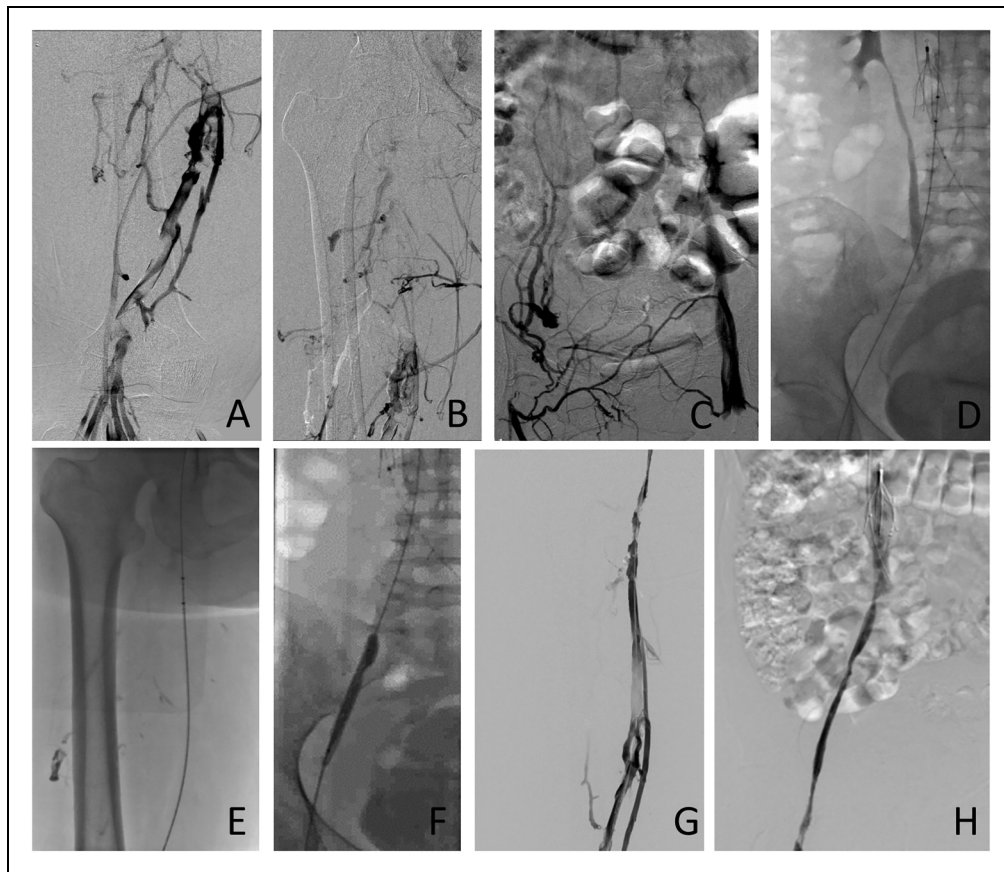


Figure 1. Venography of a 36-year-old postpartum patient with acute inferior vena cava (IVC) and iliofemoral vein thrombosis. (A-C) Pre-operative venography demonstrates the thrombosis of IVC and the right iliofemoral vein. The patient underwent IVC filter placement, AngioJet mechanical thrombus removal (D-E), angioplasty (F) and catheter-directed thrombolysis. (G-H) Post-operative venography shows the patency of IVC and the right iliofemoral vein (lysis grade III).

endovascular treatment outcomes even revealed that postpartum patients had the worst prognosis.³⁰ Although a few retrospective studies and case reports that included pregnancy-related DVT patients have shown that endovascular treatment during pregnancy and postpartum is effective (80%-100%), almost no studies compared the safety and efficacy of different endovascular methods in this specific cohort.³¹⁻³⁶ This work focused on the safety and efficacy of different endovascular treatments, and it found that 57.9% of the CDT group and 85.2% of the PCDT group had successful outcomes. We found that the PCDT group had more IVC involvement and a higher pre-operative thrombus score; only 11 patients of the PCDT group underwent AngioJet rheolytic thrombectomy, which may indicate that the PCDT group did not show a significant advantage in reducing the dosage and duration of thrombolysis, thereby reducing the length of filter removal interval and hospitalization.

Patients with iliofemoral DVT had a high rate of IVC involvement and a high incidence of May-Thurner syndrome. This was more likely in pregnant-related DVT patients with left common iliac vein obstruction exacerbated by an enlarged uterus.²⁰ In the present study, 27 patients had May-Thurner Syndrome, but only 7 underwent stent placement. Although

iliocaval stenting is not contraindicated in women of reproductive age,³⁷ it is a difficult decision among the younger cohort due to the risk of long-term stent complications. However, insufficient stenting for residual stenosis of the left common iliac vein may reduce the long-term venous patency. The cumulative venous patency we observed was comparable to the patency rate reported in the present study.^{32,33,36} Furthermore, follow-up results at 6 or 12 months for a few patients depicted a slight improvement of venous patency with adequate anticoagulation. The benefit of regular anticoagulation for patients should not be underestimated. Previous studies reported that PTS rates from 0% to 18% of peripartum women underwent CDT and stenting.^{29,32,34,35} At the 12 months follow-up, we found a 6.5% PTS rate, and severe PTS occurred at 4.3%, consistent with previous studies.

Furthermore, there are particular concerns about bleeding complications and radiation exposure. A literature review discovered a 14.75% rate of maternal complication and a 5.2% rate of fetal demise in patients who underwent CDT. However, no such complications were reported after mechanical thrombectomy.²⁸ In the current study, we found that one-third of patients had minor bleeding and a 2.2% rate of major

Table 2. Details of Treatment Outcomes and Complications.

Items	CDT Group (n = 19)	PCDT Group (n = 27)	P Value
Total urokinase dose (U, mean \pm SD)	222.1 \pm 138.9	169.6 \pm 153.3	0.241
Total rt-PA dose (mg, median (P25, P75))	0 (0.40)	40 (0.60)	0.091
Infusion time (hours, mean \pm SD)	142.8 \pm 70.4	156.9 \pm 91.9	0.576
Puncture access, n (%)			0.843
Popliteal vein	3 (15.8)	8 (29.6)	
Femoral vein	13 (68.4)	12 (44.4)	
Jugular vein	3 (15.8)	7 (25.9)	
Complication, n (%)	8 (42.1)	13 (48.1)	0.989
Puncture site bleeding	2 (10.5)	3 (11.1)	
Gingival bleeding	1 (5.3)	3 (11.1)	
Vaginal bleeding	2 (10.5)	1 (3.7)	
Hematuria	2 (10.5)	3 (11.1)	
Haematochezia	0	1 (3.7)	
Hemoptysis	1 (5.3)	0	
Nasal bleeding	0	1 (3.7)	
Pelvic hematoma	0	1 (3.7)	
Clot burden reduction rate (%, median (P25, P75))	60.5 (43.0.88.0)	100.0 (92.0.100.0)	0.001
Lysis grade, n (%)			0.001
Grade I	8 (42.1)	4 (14.8)	
Grade II	8 (42.1)	4 (14.8)	
Grade III	3 (15.8)	19 (70.4)	
Limb circumference difference (cm, median (P25, P75))			
15 cm above the knee	1.3 (1.0.2.0)	3.0 (1.0.5.0)	0.086
10 cm below the knee	1.0 (0.5.2.0)	2.0 (1.0.3.0)	0.253
Filter removal interval (days, median (P25, P75))	11.0 (8.0.14.0)	10.0 (6.0.11.0)	0.032
Hospital stay(days, median (P25, P75))	14.0 (10.0.16.0)	15.0 (13.0.16.0)	0.638

Abbreviations: CDT, catheter-directed thrombolysis; PCDT, pharmacomechanical catheter-directed thrombolysis; rt-PA, recombinant tissue plasminogen activator.

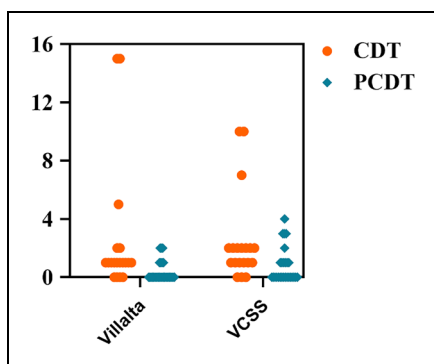


Figure 2. Comparison of the Villalta score and VCSS score at 12 months follow-up. CDT, catheter-directed thrombolysis; PCDT, pharmacomechanical catheter-directed thrombolysis; VCSS, venous severity scoring.

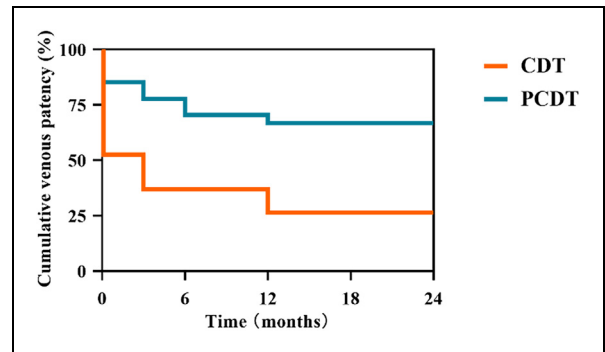


Figure 3. Kaplan-Meier analysis for cumulative venous patency during follow-up. CDT, catheter-directed thrombolysis; PCDT, pharmacomechanical catheter-directed thrombolysis.

maternal bleeding without other significant complications. Our high rate of minor bleeding could be associated with using CDT for longer, and we included all minimal bleeding. Besides, HAS-BLED risk score may underestimate the risk of bleeding in patients with thrombolysis therapy and anticoagulation. Additional concerns for women with VTE during pregnancy include radiation exposure and its effects on proliferating breast tissue and the fetus.^{12,23,38,39} Ultrasound guidance is a better approach to this concern.⁴⁰ Appropriate radiation protection precautions should be considered in regulating fetal exposure under the maximal accepted limit for major organ malformation.⁴¹ We also noted a successful delivery after minimized radiation in pregnant patients in all three trimesters at different case series.^{35,42,43} Herein, 5 pregnant patients were determined to abort their pregnancies after treatment. Lactating women were recommended warfarin for anticoagulation therapy, whereas lactation was not recommended for postpartum patients taking new oral anticoagulants.^{22,23}

According to several guidelines, the IVC filter placement is recommended under restricted conditions such as anticoagulation contraindications, recurrent VTE under adequate anticoagulation, and PE or thrombus involving iliac vein evaluated as potentially life-threatening. Moreover, IVC filter should be retrieved later to avoid filter complications including migration, deformation, fracture, failed retrieval and filter occlusion.^{9,22–25,44} In the present study, except for 5 patients with IVC filters placed due to a history of VTE, filter retrieval was successful in the other patients. The filter removal interval was slightly lower in the PCDT group but not statistically significant.

This study has limitations. First, this is a single-center retrospective study with a small number of participants. Second, we only focused on patients undergoing endovascular treatment for iliofemoral vein thrombosis. Therefore, further investigation is necessary to identify the differences in outcomes between patients treated with endovascular therapy and those treated with anticoagulation alone. Furthermore, we did not compare the efficacy of different oral anticoagulants used to continue anticoagulation therapy after discharge. Finally, more comprehensive studies and extended follow-up are required to provide evidence for treating pregnant-related VTE patients.

Conclusions

The risk of VTE increased during peripartum period, and there are particular concerns about the safety of endovascular treatment. However, few studies have compared different endovascular treatments in the peripartum group. This study found that the treatment of pregnant-related DVT patients with CDT combined with PMT or angioplasty/stenting is comparatively safe and effective. PCDT outperforms CDT in terms of immediate efficacy and reduces the incidence of PTS with improved midterm outcomes. Thus, it convinces us that an aggressive endovascular thrombus removal strategy could be considered in this specific cohort. However, more comprehensive studies and extended follow-up are required to provide further evidence.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors


Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article

ORCID iD

Liang Chen  <https://orcid.org/0000-0003-1271-8602>

References

- Nichols KM, Henkin S, Creager MA. Venous thromboembolism associated with pregnancy: JACC focus seminar. *J Am Coll Cardiol.* 2020;76(18):2128-2141.
- Parunov LA, Soshitova NP, Ovanesov MV, et al. Epidemiology of venous thromboembolism (VTE) associated with pregnancy. *Birth Defects Res, Part C.* 2015;105(3):167-184.
- Kahn SR. Determinants and time course of the postthrombotic syndrome after acute deep venous thrombosis. *Ann Intern Med.* 2008;149(10):698.
- Aburahma AF, Perkins SE, Wulu JT, et al. Iliofemoral deep vein thrombosis: Conventional therapy versus lysis and percutaneous transluminal angioplasty and stenting. *Ann Surg.* 2001;233(6):752-760.
- Watson L, Broderick C, Armon MP. Thrombolysis for acute deep vein thrombosis. *Cochrane Db Syst Rev.* 2016;11(11):CD002783.
- Garcia MJ, Lookstein R, Malhotra R, et al. Endovascular management of deep vein thrombosis with rheolytic thrombectomy: Final report of the prospective multicenter PEARL (peripheral use of AngioJet rheolytic thrombectomy with a variety of catheter lengths) registry. *J Vasc Interv Radiol.* 2015;26(6):777-785.
- Zhang X, Ren Q, Jiang X, et al. A prospective randomized trial of catheter-directed thrombolysis with additional balloon dilatation for iliofemoral deep venous thrombosis: A single-center experience. *Cardiovasc Inter Rad.* 2014;37(4):958-968.
- Enden T, Haig Y, Kløw N, et al. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): A randomised controlled trial. *The Lancet.* 2012;379(9810):31-38.
- Linnemann B, Scholz U, Rott H, et al. Treatment of pregnancy-associated venous thromboembolism - position paper from the working group in women's health of the society of thrombosis and haemostasis (GTH). *Vasa.* 2016;45(2):103-118.
- Qian C, Chen G, Lou W, et al. The perplexity of catheter-directed thrombolysis for deep venous thrombosis: The approaches play an important role. *J Thromb Thrombolysis.* 2021;51(3):757-766.
- Gong M, He X, Song J, et al. Catheter-Directed thrombolysis with a continuous infusion of low-dose alteplase for subacute proximal venous thrombosis: Efficacy and safety compared to urokinase. *Clin Appl Thromb Hemost.* 2018;24(8):1333-1339.
- Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *Chest.* 2016;149(2):315-352.
- Mewissen MW, Seabrook GR, Meissner MH, et al. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: Report of a national multicenter registry. *Radiology.* 1999;211(1):39-49.
- Chen GP, Gu JP, He X, et al. Efficacy comparison of interventional treatment by antegrade or retrograde catheterization for acute lower extremity deep venous thrombosis. *Zhonghua Yi Xue Za Zhi.* 2017;97(5):353-358.
- Enden T, Kløw NE, Sandvik L, et al. Catheter-directed thrombolysis vs. Anticoagulant therapy alone in deep vein thrombosis: Results of an open randomized, controlled trial reporting on short-term patency. *J Thromb Haemost.* 2009;7(8):1268-1275.
- Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: Revised version. *J Vasc Surg.* 1997;26(3):517-538.
- Kahn SR, Partsch H, Vedantham S, et al. Definition of post-thrombotic syndrome of the leg for use in clinical investigations: A recommendation for standardization. *J Thromb Haemost.* 2009;7(5):879-883.
- Rutherford RB, Padberg FT, Comerota AJ, et al. Venous severity scoring: An adjunct to venous outcome assessment. *J Vasc Surg.* 2000;31(6):1307-1312.
- Pisters R, Lane DA, Nieuwlaet R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation. *Chest.* 2010;138(5):1093-1100.
- Chan WS, Spencer FA, Ginsbergm JS. Anatomic distribution of deep vein thrombosis in pregnancy. *Can Med Assoc J.* 2010;182(7):657-660.
- Jeon YS, Yoon YH, Cho JY, et al. Catheter-Directed thrombolysis with conventional aspiration thrombectomy for lower extremity deep vein thrombosis. *Yonsei Med J.* 2010;51(2):197.
- And ACOG, Committee G. ACOG Practice bulletin No. 196: Thromboembolism in pregnancy: Correction. *Obstet Gynecol.* 2018;132(4):1068.
- Kalaitzopoulos DR, Panagopoulos A, Samant S, et al. Management of venous thromboembolism in pregnancy. *Thromb Res.* 2022;211:106-113.

24. Royal College of Obstetricians and Gynaecologists. Thromboembolic disease in pregnancy and the puerperium acute management. *Green-top Guideline No. 37b*. 2015:1-32.
25. Chan WS, Rey E, Kent NE, et al. Venous thromboembolism and antithrombotic therapy in pregnancy. *J Obstet Gynaecol Can*. 2014;36(6):527-553.
26. Tick LW, Kramer MH, Rosendaal FR, et al. Risk factors for post-thrombotic syndrome in patients with a first deep venous thrombosis. *J Thromb Haemost*. 2008;6(12):2075-2081.
27. Wik HS, Jacobsen AF, Sandvik L, et al. Prevalence and predictors for post-thrombotic syndrome 3 to 16 years after pregnancy-related venous thrombosis: A population-based, cross-sectional, case-control study. *J Thromb Haemost*. 2012;10(5):840-847.
28. Ho VT, Dua A, Lavingia K, et al. Thrombolysis for venous thromboembolism during pregnancy: A literature review. *Vasc Endovasc Surg*. 2018;52(7):527-534.
29. Vedantham S, Goldhaber SZ, Julian JA, et al. Pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis. *New Engl J Med*. 2017;377(23):2240-2252.
30. Oguzkurt L, Ozkan U, Gulcan O, et al. Endovascular treatment of acute and subacute iliofemoral deep venous thrombosis using manual aspiration thrombectomy: Long-term result of 139 patients from a single center. *Diagn Interv Radiol*. 2011;18(4):410-416.
31. Paz T, Bloom A, Roth B, et al. Pharmacomechanical catheter thrombolysis for pregnancy-related proximal deep venous thrombosis: Prevention of post-thrombotic syndrome. *J Matern Fetal Neonatal Med*. 2021;34(9):1441-1447.
32. Lestak K, Pouncey AL, Gwozdz A, et al. Midterm outcomes in postpartum women following endovenous treatment for acute iliofemoral deep vein thrombosis. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*. 2020;8(2):167-173.
33. Du X, Zhuang H, Hong L, et al. Long-Term outcome of catheter-directed thrombolysis in pregnancy-related venous thrombosis. *Med Sci Monit*. 2019;25:3771-3777.
34. Bloom AI, Farkas A, Kalish Y, et al. Pharmacomechanical catheter-directed thrombolysis for pregnancy-related iliofemoral deep vein thrombosis. *J Vasc Interv Radiol*. 2015;26(7):992-1000.
35. Herrera S, Comerota AJ, Thakur S, et al. Managing iliofemoral deep venous thrombosis of pregnancy with a strategy of thrombus removal is safe and avoids post-thrombotic morbidity. *J Vasc Surg*. 2014;59(2):456-464.
36. Demirturk OS, Oguzkurt L, Coskun I, et al. Endovascular treatment and long-term results of postpartum deep vein thrombosis in 18 patients. *Diagn Interv Radiol*. 2012;18(6):587-593.
37. Dasari M, Avgerinos E, Raju S, et al. Outcomes of iliac vein stents after pregnancy. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*. 2017;5(3):353-357.
38. Meissner MH, Gloviczki P, Comerota AJ, et al. Early thrombus removal strategies for acute deep venous thrombosis: Clinical practice guidelines of the society for vascular surgery and the American venous forum. *J Vasc Surg*. 2012;55(5):1449-1462.
39. Jaff MR, McMurtry MS, Archer SL, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: A scientific statement from the American heart association. *Circulation*. 2011;123(16):1788-1830.
40. Gedikoglu M, Oguzkurt L. Endovascular treatment of iliofemoral deep vein thrombosis in pregnancy using US-guided percutaneous aspiration thrombectomy. *Diagn Interv Radiol*. 2017;23(1):71-76.
41. Devis P, Knuttinen MG. Deep venous thrombosis in pregnancy: Incidence, pathogenesis and endovascular management. *Cardiovasc Diagn Ther*. 2017;7(S3):S309-S319.
42. Siah TH, Chapman A. Should catheter-directed thrombolysis be the standard of care for pregnancy-related iliofemoral deep vein thrombosis? *BMJ Case Rep*. 2018;2018:bcr2017223105.
43. Holly BP, Werner E, Destephano C, et al. Single-Session, pharmacomechanical thrombectomy of deep venous thrombosis in the pregnant patient. *J Vasc Interv Radiol*. 2014;25(8):1308-1311.
44. Harris SA, Velineni R, Davies AH. Inferior vena cava filters in pregnancy: A systematic review. *J Vasc Interv Radiol*. 2016;27(3):354-360.