Endovascular treatment of iliofemoral deep vein thrombosis in pregnancy using US-guided percutaneous aspiration thrombectomy

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PURPOSE
We aimed to describe ultrasonography (US)-guided percutaneous aspiration thrombectomy in pregnant women with iliofemoral deep vein thrombosis.

METHODS
This study included nine pregnant women with acute and subacute iliofemoral deep vein thrombosis, who were severe symptomatic cases with massive swelling and pain of the leg. Patients were excluded from the study if they had only femoropopliteal deep vein thrombosis or mild symptoms of deep vein thrombosis. US-guided percutaneous aspiration thrombectomy was applied to achieve thrombus removal and uninterrupted venous flow. The treatment was considered successful if there was adequate venous patency and symptomatic relief.

RESULTS
Complete or significant thrombus removal and uninterrupted venous flow from the puncture site up to the iliac veins were achieved in all patients at first intervention. Complete relief of leg pain was achieved immediately in seven patients (77.8%). Two patients (22.2%) had a recurrence of thrombosis in the first week postintervention. One of them underwent a second intervention, where percutaneous aspiration thrombectomy was performed again with successful removal of thrombus and establishment of in line flow. Two patients were lost to follow-up after birth. None of the remaining seven patients had rethrombosis throughout the postpartum period. Symptomatic relief was detected clinically in these patients.

CONCLUSION
Endovascular treatment with US-guided percutaneous aspiration thrombectomy can be considered as a safe and effective way to remove thrombus from the deep veins in pregnant women with acute and subacute iliofemoral deep vein thrombosis.

Pregnancy is a risk factor for venous thromboembolism (VTE) and the risk is highest in the postpartum period (1, 2). Anticoagulants are very effective in the prevention of pulmonary embolism (PE) and recurrent thrombosis, but the treatment of deep vein thrombosis (DVT) remains a challenge, because lysis of the thrombus formed in the deep veins is slow and frequently inadequate as a therapy (3, 4). Complete or significant lysis occurs only in 4% of patients treated with heparin alone (3). Persistence of thrombus within deep veins leads to venous hypertension, which is ultimately the cause of post-thrombotic syndrome (PTS) and late disability in 20% to 50% of patients. PTS is a conglomerate of lifestyle-limiting symptoms that commonly includes chronic leg pain and swelling, heaviness, and/or fatigue, venous claudication, stasis dermatitis, and in advanced cases skin ulcerations due to valvular incompetence accompanied by persistent venous outflow obstruction (4–8). Pregnant women are generally younger than other women in the general population, and they likely suffer a more severe form of PTS for a much longer time.

Anticoagulants have been the standard therapy of DVT in pregnant women because of concerns related to administering contrast agent, exposing the fetus to radiation during interventional radiologic procedures, and bleeding complication associated with thrombolysis (9). Nonetheless, there are a few publications describing thrombolytic therapy of DVT with good success during pregnancy and peri- or postpartum period (10–13). In a previous study (14), a pregnant woman with DVT was treated using percutaneous mechanical thrombectomy under venographic guidance with contrast agent. Percutaneous aspiration thrombectomy (PAT) with or without fluoroscopy guidance in preg-
nant women with iliiofemoral DVT has not been reported to date. We aimed to report the technical feasibility and initial success of ultrasonography (US)-guided PAT as a thrombus removal method in pregnant women with acute and subacute iliio-

feral DVT.

Methods

Patients
Following institutional review board approval, we conducted a retrospective search of pregnant patients with symptomatic acute and/or subacute iliiofemoral DVT treated with PAT under real-time US guidance. This study was limited to nine pregnant women who had massive leg swelling similar to phlegmasia alba dolens. The exclusion criteria were asymptomatic or mild cases, femoropopliteal DVT only, any previous surgery or intervention concerning the leg veins, thrombus in the inferior vena cava, symptomatic PE, acute on top of chronic DVT, acute infection at the puncture site, and contraindication to hep-

arin treatment. Mean age of patients was 29.7±5.03 years (range, 24–36 years).

The diagnosis was confirmed by color Doppler US (CDUS). Because ionizing radiation is potentially hazardous to the fetus, we did not perform conventional venography. Iliac, femoral, popliteal, crural veins, as well as great and small saphenous veins (GSV and SSV) were examined with CDUS. Intravenous unfractionated heparin or subcutaneous low-molecular weight heparin was started as soon as a diagnosis of DVT was made. Endovascular treatment using PAT under US guidance was proposed to all patients for the best long-term outcome.

Procedure

All thrombus removal procedures were carried out using PAT under US guidance. Before initiation of PAT, potential risks and benefits were explained in detail, and a writ-

ten consent was obtained from all patients. The patients were positioned prone or semi-prone on the operating table and monitored with blood pressure measurement and pulse oximetry throughout the procedure. Skin and subcutaneous tissue were infiltrated with 1–2 mL of 1% lidoca-

caine using a 25G needle. After puncture of the ipsilateral popliteal vein under US guidance (Antares, Siemens) with a 21G or 18G needle, a 9 F or 10 F vascular sheath was placed (Fig. 1a, 1b). GSV and SSV were also accessed, when the thrombus extend-

ed to this vein. The procedure was carried out with local anesthesia in all patients. Propofol (0.5 mg/kg) was administered as intermittent intravenous bolus to achieve procedural sedation, if required. Heparin was administered intravenously as an initial bolus of 5000 U followed by 2500 U every 45 minutes throughout the procedure. PAT was performed cautiously using large bore (7 F to 9 F) guiding catheters (Fig. 1c) con-

nected to a 20 mL syringe under real-time US guidance (Figs. 2 and 3). A straight guiding catheter was used to remove thrombus in regular straight veins whereas a guiding catheter with angled tip was preferred in a convoluted vein.

The distance from the puncture site to the estimated proximal common iliac vein was measured and the guiding catheter was intended to aspirate thrombus up to the level of common iliac vein. The guiding catheter was gently advanced without a guidewire. During the advancement of the guiding catheter, negative pressure was applied to aspirate the thrombus. If there was a resistance to the advancement of guiding catheter in a convoluted vein, the catheter was advanced over a hydrophilic guidewire or an angled guiding catheter was rotated for safe advancement to prevent dissec-

tion. Aspiration was performed from the caudal to cranial ends of thrombosed veins. The most cranial part was aspirated last to prevent or decrease the risk of PE. The pro-
cedure was repeated several times until complete or significant thrombus removal was achieved and uninterrupted venous flow was observed on CDUS. The veins in the thigh could be visualized on CDUS, but it was not possible to visualize the iliac veins from a posterior approach when the patient was lying prone.

The patients were admitted for one day of anticoagulation after the procedure and discharged the next day. Subcutaneous heparin and graduated elastic compression stockings were recommended to all pa-


tients until the end of the postpartum pe-

riod. Patients were called for follow-up visits at three months after delivery. Patency was assessed by physical examination and CDUS. Venography was obtained if there was any clinical doubt regarding the paten-

ty of the iliac veins.
Statistical analysis
Statistical analyses were performed using SPSS v. 17 (SPSS Inc.). Numeric data are expressed as mean ± standard deviation or percentage.

Results
Six patients with only femoropopliteal DVT or mild symptoms of DVT were excluded from the study. All nine patients were severe symptomatic cases with massive swelling and pain of the leg. Five patients were in the first trimester of pregnancy, two were in the second trimester, and two in the last trimester. None of the patients had a previous history of DVT or major PE symptoms. The lesion was on the left side in seven patients (77.8%) and on the right side in two patients (22.2%). All patients had anticoagulation therapy with heparin until diagnostic evaluation or potential consequent endovascular therapy. DVT was acute (1–14 days) in four patients (44.4%), acute and subacute (15–28 days) in five patients (55.6%). Seven patients had involvement of the iliac, femoral, popliteal, and crural veins. The popliteal and crural veins were patent in two patients with thrombosis of femoral and iliac veins. Thrombus was also present in the proximal GSV in three patients and in the proximal SSV in a patient because of descending DVT, probably due to May-Thurner syndrome. Initial access to the venous system was through the popliteal vein in all patients. Two patients had additional GSV access and one patient had an additional SSV access to remove thrombus and improve blood flow to the femoral and iliac veins.

Complete or significant thrombus removal and uninterrupted venous flow from the puncture site up to the iliac veins were achieved in all patients at first intervention. Complete relief of leg pain was achieved immediately in seven patients (77.8%), but minimal swelling remained around the ankle. Two patients (22.2%) had a recurrence of thrombosis in the first week postintervention. One of the two underwent a second intervention and PAT was performed again with successful removal of thrombus and establishment of in line flow. The other patient refused a second intervention. None of the patients required blood transfusion because of blood loss during thrombus extraction. The average volume of blood aspirated as thrombus ranged 200–400 mL for each patient.

Two patients were lost to follow-up after birth. Two patients were followed with only CDUS and five patients underwent venography after birth. None of these patients had rethrombosis throughout the postpartum period. Symptomatic relief was detected clinically in these seven patients. Venous patency was demonstrated with CDUS and venography (Fig. 4). Venography also revealed left common iliac vein compression syndrome (May-Thurner syndrome) in three patients (33.3%).

Discussion
This study showed that PAT can be performed safely under US guidance as a thrombus removal method in pregnant women with acute or subacute iliofemoral DVT. We achieved complete or near complete thrombus removal and rapid symptomatic relief in seven of nine patients.
The risk of VTE increases 4- to 5-fold during pregnancy and 20-fold or more in the postpartum period. The main reason for increased risk of VTE is the hypercoagulable state of pregnancy which protects women from bleeding during miscarriage or child-birth. Other underlying factors include venous stasis and vascular damage. DVT and PE are two different manifestations of VTE. PE is the leading cause of maternal deaths (1, 2, 9). Anticoagulation with heparin reduces the risk of PE and is currently considered the standard of care for the prevention of PE. However, the management of DVT remains a major clinical problem because this form of therapy does not adequately protect the patient from the development of PTS. Resolution of the present thrombus formed in the deep veins is slow and frequently inadequate in this form of therapy (3, 4). In a previous study, 4% of patients treated with heparin had significant or complete lysis, whereas 14% of patients had partial lysis (3). Lysis did not occur in 82% of patients who either failed to improve or worsened. Persistence of thrombus in the deep veins leads to venous outflow obstruction and valvular incompetence, which is ultimately the cause of PTS in most patients (4–8). Data from the National Venous Thrombolysis Registry, strongly point to a relationship between the degree of lysis and venous valvular function; 62% of patients with <50% lysis had valvular incompetence, whereas 72% of patients who had complete lysis had normal valve function (15). Patients who progress to PTS could have a poor quality of life and disability due to clinical features of post-thrombotic sequelae including lifestyle-limiting chronic leg pain and edema, heaviness, and/or fatigue, and in severely affected patients venous claudication, varicosities, stasis dermatitis, hyperpigmentation and subsequently venous stasis ulcers (4–8).

A preponderance of the evidence in patients with lower extremity DVT suggests a strategy of early thrombus elimination for fast symptom relief and restoration of venous patency to protect valve function and prevent development of the PTS (4–8, 15–24). Alternative treatment options have been used to remove thrombus from deep veins because of the disappointing results with anticoagulation therapy (16–18). Published evidence indicates that thrombolytic agents, even when administered systemically, are superior to anticoagulation therapy for achieving early lysis of thrombus. Comerota and Aldridge (3) stated that 45% of patients treated with systemic thrombolysis had significant or complete lysis compared with 4% of patients treated with heparin. Among those receiving systemic thrombolysis, 18% had partial lysis, while 37% failed to improve or worsened. Despite its potential benefits, thrombolysis is associated with a greater risk of minor or major bleeding complication than anticoagulation therapy. Catheter-directed thrombolysis (CDT) was recommended in selected patients with extensive acute proximal DVT (e.g., iliofemoral DVT, symptoms lasting <14 days, good functional status, life expectancy of >1 year) who have a low risk of bleeding (25). It may be used to reduce acute symptoms and post-thrombotic morbidity if appropriate expertise and resources are available. CDT offers distinct advantages compared with systemic thrombolysis, and anticoagulation alone. Catheter-directed infusion allows higher concentrations of the thrombolytic agent to be delivered directly into the thrombus with a reduced systemic effect (15–19, 24). A recent comparative study (18) provides support for the potential of adjunctive CDT to prevent PTS. In this study, patients with iliofemoral DVT treated with CDT had a significantly decreased the frequency of PTS compared with patients treated with anticoagulation alone. A study of systemic thrombolysis use versus CDT in treating iliofemoral DVT demonstrated that CDT may be superior to systemic thrombolysis in preserving venous valvar function (19). They also found that in CDT group, the needed dose of thrombolytic agents was lower and the duration of treatment was shorter. On the other hand, CDT has some potential disadvantages that include the long infusion times required to lyse extensive DVT, lengthy hospital stays, greater bleeding risk and high medication and hospitalization costs (15,16). Recently, percutaneous thrombectomy methods alone or combined with CDT have been widely used as an effective endovascular method for thrombus removal. Compared with CDT, percutaneous thrombectomy methods are able to remove the thrombus more rapidly without the risk of bleeding complication (17, 20–24, 26–29). Vedantham et al. (20) found that the use of adjunctive percutaneous mechanical thrombectomy to augment CDT provides comparable procedural success and may reduce thrombolytic dose requirements and infusion times. PAT has been successfully used alone or in combination with local thrombolytic infusion to remove thromboembolic material from limb arteries (27, 28). PAT is a cheap and simple method. It proposes a rapid and effective way to remove thrombus. Moreover, it can be used in almost every patient who is unresponsive to anticoagulation therapy or has a contraindication to thrombolysis (22, 27–29).
PAT has also been effectively used alone or in combination with thrombolysis to treat lower extremity DVT (22, 29). The efficacy of PAT as the primary method of thrombus removal has been previously shown in 139 patients with acute and subacute iliofemoral DVT (22). In that study, successful recanalization without the use of CDT was achieved in the majority of patients. CDT was required in only one-fourth of the patients as an adjunctive treatment following PAT. In other patients who required CDT, the dose of the thrombotic agent was quite low.

The management of DVT in pregnancy is still challenging for several reasons. DVT is generally treated with intravenous or subcutaneous heparin during pregnancy and the postpartum period, but the subsequent risk of post-thrombotic compication development in this young patient population is a concern. Many interventional radiologic treatment modalities that are extensively used in nonpregnant patients, have not been appropriately validated in pregnancy. Image-guided interventional thrombus removal procedures are potentially hazardous to the fetus in terms of adverse effects of ionizing radiation and contrast agent. Pregnancy and the peripartum period are generally considered as a contraindication for thrombolytic therapy because of the risk of uncontrolled bleeding complication (9). However, a few case reports have been published describing thrombolytic therapy of DVT during pregnancy and in the peri- or postpartum period (10–13, 30). Henrich et al. (10) performed systemic streptokinase lysis without complications in a pregnant woman at 29 weeks of gestation who had acute iliac DVT. They concluded that thrombolytic therapy during pregnancy is possible and may help to prevent serious long-term sequelae of DVT in these young patients. They also stated that the risk of bleeding must be considered and thrombolytic therapy should only be administered under close observation. In a study by Krishnamurthy et al. (11), a pregnant woman with PE, seriously ill, and two pregnant women with iliofemoral DVT who failed to respond to treatment with intravenous heparin were treated with catheter-directed urokinase. All three patients had fast symptom relief and successful pregnancy outcomes. They suggested that CDT offered a reasonably safe alternative therapy for these young women and may prevent PTS in the long-term. Patterson et al. (12) treated a patient with iliac vein thrombosis 48 hours after delivery with catheter-directed urokinase because there was no clinical improvement despite heparin infusion. Acharya et al. (13) used CDT to treat four women with acute postpartum iliofemoral DVT (within 42 days of childbirth) and achieved a successful result and symptom relief in all four patients. Demirturk et al. (30) reported that endovascular treatment of postpartum iliofemoral DVT (within 42 days of childbirth) with PAT alone or combined with CDT was rapid, very safe and resulted in a very high rate of thrombus removal in 18 patients. In a previous study (14), a pregnant woman with DVT underwent percutaneous mechanical thrombectomy with the use of venograms because pregnancy was considered a contraindication to thrombolysis. Thrombus removal using PAT with or without fluoroscopy guidance has not been used to date in pregnant women with iliofemoral DVT. Our institution prefers a strategy of early thrombus elimination as quickly as possible, particularly in young patients, to relieve symptoms and minimize the development of long-term sequelae. For this purpose, we performed PAT under US guidance to treat our pregnant patients with iliofemoral DVT. Full systemic anticoagulation remains an essential element of our treatment to prevent PE and recurrent thrombosis.

Our study is limited by its retrospective nature. Technical success and short-term patency were good, but the mid- and long-term results are not known in our patients. Thus, our results must be considered preliminary. Use of PAT may require experience. Our center has been using this method for the last 15 years and is quite experienced in using PAT for thrombus removal. Therefore it may not be easily recommended to those who have less experience in using this method. Nonetheless, the use of PAT in pregnant women is justifiable because of the absence of other viable treatment options.

In conclusion, endovascular treatment with US-guided PAT can be considered as a safe and effective way to remove thrombus from the deep veins in pregnant women with acute and subacute iliofemoral deep vein thrombosis.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References


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