

# Radiation- and contrast medium-free catheter-directed thrombolysis for early pregnancy-related massive ilio caval deep venous thrombosis



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## ABSTRACT

Catheter-directed thrombolysis for iliofemoral deep venous thrombosis (DVT) aims to reduce acute leg symptoms and to prevent the post-thrombotic syndrome. There are no data from controlled trials in pregnant patients. Reports of thrombolysis for treatment of DVT during pregnancy are scarce. Pregnancy is considered a relative contraindication to thrombolytic therapy because of the risk of bleeding and concerns about the effects of radiation exposure on the fetus. We report on a catheter-directed thrombolysis procedure without radiation and contrast medium exposure in a first-trimester pregnant patient with massive iliofemoral DVT and free-floating thrombus extending to the suprarenal inferior vena cava. (*J Vasc Surg: Venous and Lym Dis* 2019;7:122-5.)

**Keywords:** Radiation-free; Catheter-directed thrombolysis; Pregnancy; Deep venous thrombosis

Deep venous thrombosis (DVT) is a major complication that occurs in 1.36 per 1000 pregnancies, with pulmonary embolism being a leading cause of maternal morbidity in developing countries.<sup>1</sup> Anticoagulation therapy, the current standard of care for DVT, inhibits thrombus propagation and provides prophylaxis against pulmonary embolism.<sup>2</sup>

Iliofemoral DVT is associated with a high risk of post-thrombotic syndrome (PTS).<sup>3,4</sup> Treatment of DVT in pregnancy with anticoagulation alone results in a high rate of post-thrombotic morbidity and impaired quality of life in this group of young and otherwise healthy patients. In a study of 104 women with pregnancy-related thrombosis, only 22% reported freedom from post-thrombotic symptoms after a median follow-up of 11 years.<sup>5</sup>

Because of the bleeding risk of systemic lysis and the high risk of rethrombosis after surgical procedures, catheter-directed thrombolysis (CDT) for iliofemoral DVT has been established for selected patients with good functional status and a low risk of bleeding.<sup>6</sup> Administration of recombinant tissue-type plasminogen activator directly into the venous clot allows a significant dose reduction compared with systemic thrombolysis.<sup>7</sup>

In one randomized trial, CDT improved clinically relevant long-term outcome after iliofemoral DVT by reducing PTS compared with conventional treatment with anticoagulation and compression stockings alone.<sup>7</sup> In another trial, Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT), the incidence of PTS was not reduced by CDT, most likely because almost half of the patients had proximal DVT without involvement of the iliac veins.<sup>8</sup>

There are concerns about the effects of radiation exposure on proliferating maternal breast tissue and on the fetus during pregnancy, particularly during organogenesis in the first trimester. We report on a CDT procedure without radiation and contrast medium exposure in a first-trimester pregnant patient with massive thrombus extending from the proximal part of the left common femoral vein to the suprarenal inferior vena cava (IVC) without involvement of the renal veins.

The patient provided written informed consent to the publication.

## CASE REPORT

A 29-year-old woman at 11 2/7 weeks of gestation was referred to our clinic because of sudden massive, painful swelling of the left lower extremity with inability to walk. Ultrasound revealed a complete obstruction of the left common femoral and iliac veins with extension of a free-floating thrombus into the suprarenal IVC (Fig 1).

On admission, an intravenous bolus of 5000 IU of unfractionated heparin was given, followed by continuous intravenous infusion of unfractionated heparin, adjusted to maintain an activated partial thromboplastin time between 46 and 70 seconds. The hypercoagulability evaluation was negative for antiphospholipid antibody syndrome, factor V Leiden mutation, and prothrombin gene variant. Protein C, protein S, and antithrombin III levels were normal.

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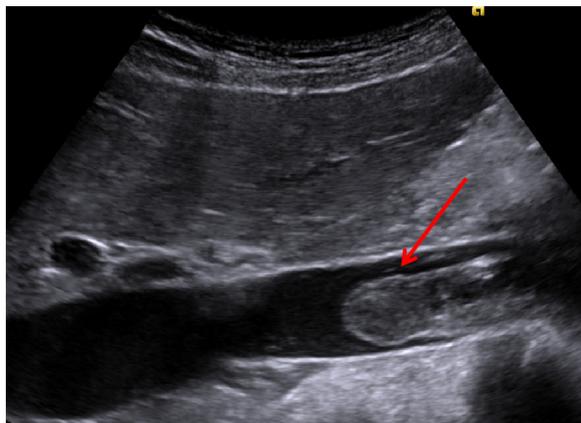
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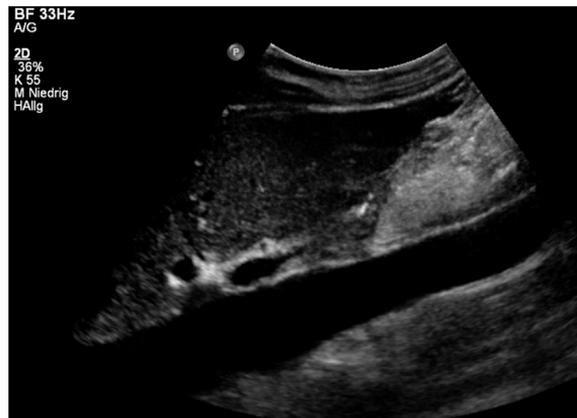
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**Fig 1.** Free-floating thrombus in the supracaval inferior vena cava (IVC; *arrow*, longitudinal view).



**Fig 3.** Supracaval inferior vena cava (IVC) after catheter-directed thrombolysis (CDT) with complete thrombolysis success (longitudinal view).

After 24 hours of heparin treatment, no improvement of the clinical status was seen. Serial ultrasound examination revealed persistence of the free-floating supracaval IVC thrombus. Implantation of an IVC filter was deemed technically not feasible because of the proximity of the thrombus to the right atrium. To avoid a fatal pulmonary embolism and to reduce acute leg symptoms, we decided to perform CDT, inserting the thrombolysis catheter under ultrasound guidance to avoid radiation and contrast medium exposure. We preferred CDT over pharmacomechanical thrombectomy to minimize the risk of embolization of the free-floating IVC thrombus with mechanical maneuvers.

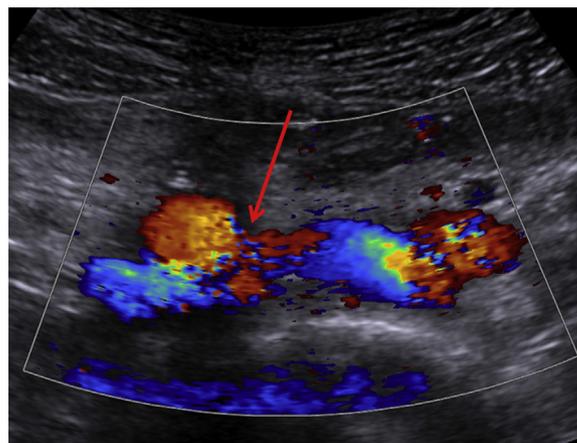
The insertion of the thrombolysis catheter was performed with heart surgery standby. Venous access was obtained in the nonobstructed femoral vein at the proximal thigh by ultrasound guidance with the patient in supine position. After insertion of a 6F sheath, a 0.035-inch hydrophilic guidewire (Terumo Corporation, Tokyo, Japan) and a standard angiographic 4F diagnostic catheter (Berenstein; Cordis, Milpitas, Calif) were used to pass the thrombus. Ultrasound guidance was performed with

B-mode ultrasound using a 6 MHz sector ultrasound probe tracking the inserted catheter material in the iliofemoral veins and IVC in longitudinal and transverse views (Fig 2). The angiographic catheter was then exchanged for the drug delivery catheter with a 30-cm treatment zone corresponding to the length of the thrombotic occlusion (EKOS Corporation, Bothell, Wash). Finally, the guidewire was replaced by the MicroSonic Device (EKOS Corporation) that contains multiple small, radiopaque ultrasound transducers distributed along the treatment zone to deliver high-frequency (2.2 MHz) and low-power (0.5 W per transducer) ultrasound.

After introduction of the thrombolysis catheter, the patient was transferred to the intermediate care unit. The thrombolysis infusion was started with recombinant tissue-type plasminogen activator (Actilyse; Boehringer Ingelheim, Ingelheim, Germany) at a rate of 2 mg/h for the first 5 hours, then reduced to 1 mg/h during 10 hours. Unfractionated heparin infusion was administered and adjusted every 6 hours to achieve and to maintain an activated partial thromboplastin time corresponding to therapeutic heparin levels.



**Fig 2.** Ultrasound guidance while advancing the catheter material through the thrombotic occlusion of the iliofemoral veins (*arrow*; tip of 5F EKOS catheter in supracaval inferior vena cava [IVC], longitudinal view).



**Fig 4.** Compression of the left common iliac vein by the right common iliac artery (*arrow*).

Intermittent pneumatic compression of the whole left leg was used to enhance the thrombolysis. After 15 hours of treatment, ultrasound confirmed complete thrombus resolution in the left iliofemoral vein as well as in the IVC (Fig 3). After restoration of blood flow in the iliac veins, presence of May-Thurner syndrome was confirmed (Fig 4). Anticoagulation with intravenous heparin was switched to low-molecular-weight heparin subcutaneously. An obstetric examination with ultrasound confirmed normal vital gestation, and the patient was discharged the same day.

At 37 5/7 weeks of gestation, the patient delivered a healthy boy by cesarean section. Three months after delivery, the patient was scheduled for the stent placement procedure. Venography and intravascular ultrasound confirmed the presence of a compressed left common iliac vein, which was treated by placing an oblique hybrid stent (sinus-Obliquus 16 × 100 mm; OptiMed, Ettlingen, Germany).

## DISCUSSION

We report on a CDT procedure without radiation and contrast medium exposure in a first-trimester pregnant patient with massive iliofemoral DVT and free-floating thrombus extending to the suprarenal IVC. Our patient had no evidence of thrombophilia, and the reason for her extensive DVT was most likely ascending and descending thrombus propagation from the compressed left common iliac vein (May-Thurner syndrome). The main reason for the chosen treatment was to prevent fatal pulmonary embolism of the large IVC thrombus. Placement of an IVC filter would have been an option if the suprarenal IVC were free of thrombus. After successful thrombolysis, we postponed stent placement to completion of the postpartum period to avoid radiation and contrast medium exposure. We believe that percutaneous B-mode ultrasound guidance is not precise enough to accurately detect stent landing zones in the iliac veins.

The second principal reason for our invasive approach was the prevention of post-thrombotic morbidity. DVT is a common pregnancy-related complication, with significant morbidity and risk of PTS in patients with iliofemoral DVT. Most cases occur in the second and third trimesters. Iliofemoral DVT in the first trimester is unusual. Most physicians and guidelines recommend treating pregnancy-related iliofemoral DVT with anticoagulation alone.<sup>6</sup> In treating iliofemoral thrombosis, CDT techniques have demonstrated good results in the nonpregnant population.<sup>7,9-12</sup> The main advantage of a catheter-based approach is to increase venous patency and to preserve venous valve function, with minimal risk of bleeding complications, and to provide endovascular access for adjunctive therapeutic techniques, such as balloon angioplasty and stent placement.<sup>13</sup>

The first report of successful use of CDT in pregnancy was published in 1999, describing three midgestation patients, one with massive pulmonary embolism and

two patients with extensive proximal DVT. Thrombolytic therapy provided rapid resolution of symptoms, and no adverse fetal outcomes were observed.<sup>14</sup>

A report of 11 pregnant patients undergoing CDT or pharmacomechanical CDT is the largest series to date.<sup>15</sup> This study suggested a good safety profile with excellent short-term and midterm results. However, the authors did not address the potential risks to the fetus associated with the radiation exposure. Radiation exposure in the first trimester may cause fetal death.<sup>16,17</sup> The fetal radiation dose resulting from CDT in the first trimester can be calculated in the range of 175 to 245 mGy, which is associated with a childhood cancer risk of 1.3% to 2%. This value is 6 to 10 times higher than the risk associated with environmental/background radiation exposure.<sup>18</sup>

Because of the potential risks of the fetal radiation exposure, another case report described elective termination of pregnancies after CDT in the first trimester.<sup>18</sup> This approach, however, was not acceptable to our patient.

## CONCLUSIONS

Iliofemoral DVT in pregnant women raises a unique therapeutic challenge. In our case, we performed a successful CDT procedure in a pregnant woman in the first trimester without complications. To prevent radiation exposure, the placement of the lysis catheter was realized with ultrasound guidance. Further trial or registry experience is needed to demonstrate the efficacy and safety of this therapeutic approach.

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