Endovascular treatment and the long-term results of postpartum deep vein thrombosis in 18 patients

Orhan Saim Demirtürk, Levent Oğuzkurt, İsa Coşkun, Öner Gülcan

PURPOSE
We aimed to describe the long-term outcome of endovascular treatment of iliofemoral deep vein thrombosis in the postpartum period.

MATERIALS AND METHODS
Between 2002 and 2010, 18 consecutive female patients with acute or subacute iliofemoral deep vein thrombosis in the postpartum period who had endovascular treatment were retrospectively evaluated. Treatment consisted of manual aspiration thrombectomy with or without catheter-directed thrombolyis. Stents were placed in the iliac veins, if deemed necessary. Clot removal was graded as complete (>95%), partial (50%-95%), and poor (<50%).

RESULTS
The initial treatment was technically successful in 17 patients (94%). There was complete clot removal in 15 of 22 limbs (68%). Twenty-three stents were implanted in 15 patients (83%). The primary and secondary patencies were 58% and 82% at one year, 58% and 72% at three years, and 58% and 58% at five years, respectively. There were recurrent thromboses in 11 patients (61%), which occurred within the first month in nine of these patients (81%). Ten patients had repeated intervention, and five had successful outcomes. At a mean follow-up of 30 months, 11 patients had uninterrupted in-line flow in the affected limb, and six patients did not. Six of the patients with uninterrupted flow were asymptomatic, and five patients had minimal swelling at the ankle.

CONCLUSION
Endovascular treatment of postpartum iliofemoral deep vein thrombosis with percutaneous aspiration thrombectomy alone or combined with catheter-directed thrombolyis and iliac vein stenting is an effective therapy resulting in a high rate of thrombus removal. However, recurrences are high, particularly in the first post-intervention month. Frequent patient follow-up in the first post-intervention month is necessary.

Key words: postpartum period • deep vein thrombosis • thrombectomy • mechanical thrombolysis • May-Thurner syndrome

The incidence of venous thromboembolisms was reported to be 199.7 per 100 000 women-years. Pregnancy and the postpartum period are known risk factors for venous thromboembolisms, and the risk is highest throughout the postpartum period (1). Although the incidence of pulmonary embolism has been steadily decreasing over time, the incidence of deep vein thrombosis (DVT) has remained constant (1). Iliofemoral DVT is an extensive form of DVT in which the thrombosis involves the iliac vein and/or the common femoral vein. Patients with iliofemoral DVT have the worst clinical findings due to the extent of the thrombosis and the long-term higher frequency of post-thrombotic syndrome (2).

Standard medical therapy of DVT does not provide rapid symptom resolution or the recanalization of long venous occlusions and is associated with long-term disability due to chronic venous insufficiencies (3). Only approximately 6% of patients with acute DVT exhibit complete lysis of the thrombus within 10 days (3). The value of thrombus removal with endovascular methods for acute symptomatic relief and for the prevention of post-thrombotic syndrome has been reported (2). It has become our institutional policy to treat acute or subacute iliofemoral DVT with endovascular methods in every patient. A retrospective study of 139 consecutive patients on the outcome of endovascular treatment in our institution showed that postpartum patients had the worst prognosis (4). Although many studies have evaluated the safety and effectiveness of endovascular treatment methods in the treatment of iliofemoral DVT, only one previous study with five patients has shown the outcome of endovascular treatment in the postpartum period (5).

Postpartum DVT patients are young and will most likely suffer from post-thrombotic sequelae for a much longer time than patients in the general population with DVT. The prevalence of May-Thurner syndrome was 22%–24% in a series of cadaveric and asymptomatic patients and 37%–46% in patients with left lower extremity swelling (6–8). These features make DVT in postpartum patients quite unique.

The aim of our report is to describe the initial and long-term results of 18 consecutive postpartum patients who had iliofemoral DVT and who were treated with endovascular methods using manual aspiration thrombectomy and catheter-directed thrombolysis complemented occasionally with stent placement.

Materials and methods

Patients
All procedures performed on humans were in accordance with the ethical standards of the Declaration of Helsinki developed by World Medical Association. Between September 2002 and March 2010, 22 limbs in 18 consecutive patients in the postpartum period with acute or
subacute iliopopliteal DVT were treated by endovascular methods. The post-partum period was defined as the first 42 days (six weeks) after childbirth. All data were analyzed retrospectively. Fourteen of these patients were among 139 consecutive patients with acute or subacute iliopopliteal DVT treated by endovascular methods at our institution. All patients with iliopopliteal DVT were treated with endovascular methods per the routine protocol at our institution in the absence of contraindications.

The mean age of patients was 28±5.6 years (range, 20–42 years) (Table). All patients had iliopopliteal DVT diagnosed with color Doppler ultrasonography (CDUS) and confirmed with venography at the time of the intervention. The exclusion criteria were distal (femoropopliteal) DVT, contraindications to iodinated contrast media, and malignancy with short survival expectancy. No patients met these criteria during the study period. The DVT risk factor for all of the included patients was being in the post-partum period. The additional risk factors involved were a documented thrombophilic disorder in five patients (28%) and femoral vein catheterization in one patient (5.6%).

Table. Patient demographics

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>21–42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of symptoms, n</td>
<td></td>
</tr>
<tr>
<td>&lt;14 days</td>
<td>13</td>
</tr>
<tr>
<td>&gt;14 days</td>
<td>3</td>
</tr>
<tr>
<td>Recurrent</td>
<td>2</td>
</tr>
<tr>
<td>Location of DVT, n (%)</td>
<td></td>
</tr>
<tr>
<td>Left sided</td>
<td>12 (72)</td>
</tr>
<tr>
<td>Right sided</td>
<td>2 (12)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>4 (24)</td>
</tr>
<tr>
<td>May-Thurner Syndrome, n (%)</td>
<td></td>
</tr>
<tr>
<td>11 (61)</td>
<td></td>
</tr>
<tr>
<td>Type of DVT, n (%)</td>
<td></td>
</tr>
<tr>
<td>Ascending type</td>
<td>11 (61)</td>
</tr>
<tr>
<td>Descending type</td>
<td>7 (39)</td>
</tr>
<tr>
<td>IVC involvement, n (%)</td>
<td></td>
</tr>
<tr>
<td>5 (28)</td>
<td></td>
</tr>
<tr>
<td>MAT, n</td>
<td>17</td>
</tr>
<tr>
<td>CDT, n</td>
<td>6</td>
</tr>
<tr>
<td>Endovenous stents, n</td>
<td>23 (to 15 patients)</td>
</tr>
<tr>
<td>Estimated percentage of clot removed, %</td>
<td></td>
</tr>
<tr>
<td>&gt;95%</td>
<td>68</td>
</tr>
<tr>
<td>50–90%</td>
<td>27</td>
</tr>
<tr>
<td>&lt;50%</td>
<td>5</td>
</tr>
</tbody>
</table>

DVT, deep vein thrombosis; IVC, inferior vena cava; MAT, manual aspiration thrombectomy; CDT, catheter-directed thrombolysis.

In the early period of the study, catheter-directed thrombolysis (CDT) was the first-line of treatment, whereas manual aspiration thrombectomy (MAT) became the first-line of treatment later on. Two patients underwent CDT as the first-line thrombus removal method, and four patients who had a residual thrombus after MAT required CDT. The total treatment time ranged from 1 to 5 days (mean, 1.5 days). The MAT became the first-line treatment method after the first two patients. Patients were placed prone on the angiography table (Innova IQ3100, GE Healthcare, Waukesha, Wisconsin, USA). Endovascular access was established using ultrasonography-guided puncture of the ipsilateral popliteal vein with a 21 G or 18 G needle in all patients. The posterior tibial vein was additionally accessed in two patients. A 4 F plastic dilator was introduced into the vein initially, and ascending venography was performed. A 9 F or 10 F vascular sheath (Avanti, Cordis Europa NV, Roden, The Netherlands) was then placed after the removal of the dilator over a guide wire. Thrombus removal was performed by MAT using 8 F or 9 F guiding catheters (Cordis Europa NV) connected to a 20 mL syringe or CDT. CDT was usually adjunctively used to treat the residual thrombus or to treat crural vein thrombosis. Tissue plasminogen activator (tPA) (Actilyse, Boehringer Ingelheim, Rhein, Germany) was administered through a multi-sidehole infusion catheter (Ev3, Irvine, California, USA) at a dose of 1 mg/hour. Venography was repeated every 8–12 hours during thrombolysis until the entire thrombus was resolved or there was no more lysis with CDT. After thrombus removal with MAT or CDT, additional pelvic venograms were obtained for a detailed evaluation of the iliac veins during the procedure. One or more self-expanding stents were placed in the iliac veins if there was May-Thurner (iliac vein compression) syndrome, irregularity due to a residual thrombus, or severe stenosis of the iliac vein limiting blood flow. Twenty-one stents were self-expanding Wallstents (Boston Scientific, Natick, Massachusetts, USA), and two were self-expanding nitinol stents (Protege, Ev3, Plymouth, Minnesota, USA). If there was chronic occlusion due to iliac vein compression, a hydrophilic guide wire was...
passed through the occlusion (Terumo Europe, Leuven, Belgium), and one or more self-expanding stents were placed. The stent was always dilated with a balloon catheter of the same diameter as the stent (Ultrathin, Boston Scientific, Galway, Ireland).

The patients were discharged on the same day or the first post-procedural day. Patients were put on oral warfarin sodium therapy and maintained on an international normalized ratio in the range of 2.0–3.0 for at least six months after the procedure. The administration of anticoagulation was bridged with low molecular weight heparin when switching from intravenous heparin to oral warfarin. Graduated compressive stockings were recommended to all patients.

**Data collection**

Data concerning the demographics, past medical histories, and laboratory findings were evaluated retrospectively. Venography findings were analyzed using images stored on digital media. Real-time examinations and the interpretation of venography findings were performed by the same interventional radiologist (L.O.).

**Definition of criteria, outcomes, and follow-up**

May-Thurner syndrome was defined as severe compression causing intimal changes in the lumen of the left common iliac vein by the overlying artery (9). Mild compression of the vein that did not cause significant narrowing of the lumen with normal venous intima was not regarded as the syndrome but as mild compression.

Definitions of criteria were based on the guidelines concerning lower extremity DVT defined by the Society of Interventional Radiology (10). Technical success was defined as the successful restoration of antegrade in-line flow in the treated vein with the elimination of any underlying obstruc- tive lesion and was assessed on the final procedural venogram. Clot removal was regarded as complete (grade III) if clot removal was >95%, partial (grade II) if clot removal was between 50%–95%, and poor (grade I) if clot removal was <50% in the popliteal femoroiliac axis, including the inferior vena cava (IVC).

Each patient was followed during regular outpatient visits at 1, 3, 6, and 12 months and then annually for five years. At each clinical visit, a clinical examination for symptoms and CEAP (Clinical-Etiology-Anatomic-Pathophysiologic) score and CDUS for venous patency and insufficiency were performed. Venography was recommended at one or three years of follow-up or if the clinical or CDUS findings indicated potential occlusion of the iliac vein. The patients were recalled after the study ended, their latest CEAP scores were obtained, and the presence of the iliac, femoral, popliteal, and greater saphenous veins was examined using CDUS.

**Statistical analysis**

Data are expressed as the mean±standard deviation for continuous variables and percentages for categorical variables. Patency at the end of the follow-up was analyzed using a Kaplan-Meier analysis. Statistical analyses were performed using a computer software (Statistical Package for Social Sciences version 11.0, SPSS Inc., Chicago, Illinois, USA).

**Results**

**Short-term results**

All patients were symptomatic and had leg swelling; nine patients (50%) had pain, three patients (17%) had phlebitis, and none had phlebitis. DVT was acute (1–14 days) in 13 patients (72%), subacute (15–28 days) in three patients (17%) and acute with underlying chronic DVT in two patients. DVT was bilateral in four patients, left sided in 12 patients (72%), and right sided in two patients (12%). The popliteal and crural veins were patent in seven patients (39%) with thrombosis of the proximal femoral vein, common femoral vein and iliac veins. The popliteal vein and its distal tributaries were patent in the latter group. Therefore, six patients had involvement of the iliac and femoral veins, and 12 patients had involvement of the iliac, femoral, popliteal, and crural veins. Five of these 12 patients also had IVC involvement. Three patients had pulmonary thromboembolism at the time of diagnosis (17%). None of the patients had a pulmonary embolism during or after the intervention at a mean of 30 months of follow-up. Eleven of 18 patients (61%) had iliac vein compression syndrome (May-Thurner syndrome).

Three patients (17%) had mild compression of the iliac vein by the overlying artery. Eleven of 12 left-sided DVT patients (92%) had May-Thurner syndrome.

Catheter-directed thrombolytic therapy was used in only six patients. The mean dose of tPA was 30±27.4 mg (range, 10–70 mg). The mean fluoroscopy time was 14±8.6 min (range, 4–25 min). One patient had prophylactic retrievable IVC filter placement because of a large, free-floating thrombus in the IVC. The filter was removed on the second day. After removal of the thrombus using MAT or CDT (Fig. 1), a total of 23 stents were implanted in 15 patients (83%), with an average of 1.5 stents per extremity (Fig. 2). Stents were implanted in the common iliac vein (n=8), the common and external iliac veins (n=7), and from the external iliac vein to the femoral vein (n=8). The stent diameters ranged from 12 to 16 mm. None of our patients had pulmonary thromboemboli during the procedure. There were three complications during the initial treatment procedures. Two were minor dissections in the vein that did not interrupt flow. The third complication was an in-stent thrombosis that was successfully treated during the same session.

The initial treatment was technically successful in 17 patients, with a technical success rate of 94% (21 of 22 extremities). There was complete clot removal in 15 of 22 limbs (68%), partial clot removal in six limbs (27%) and poor clot removal (technical failure) in one limb. Immediate venous patency with normal in-line flow was achieved in 17 of 18 patients and 21 of 22 limbs.

**Long-term results**

The mean follow-up was 30±27 months (range, 3–96 months). One patient was lost to follow-up. All of the patients underwent a CDUS examination, and 11 patients underwent venography during the follow-up. Three patients were followed for longer than five years. A Kaplan-Meier analysis revealed that primary limb patency was 58% at one year, three years, and five years. The secondary limb patencies were 82% at one year, 72% at three years, and 58% at five years.

Eleven patients (61%) had a recurrence of thrombosis (Fig. 3). However, the two patients who had acute DVT...
Diagnostic and Interventional Radiology

with underlying chronic DVT did not experience a recurrence. Recurrences occurred in the first month in nine patients (50%), in the second month in one patient, and in the 34th month in one patient; 70% of the recurrent thromboses occurred within the first 10 days. There were no other recurrences after a mean follow-up of 30 months. One patient had very mild symptoms, and a second intervention was not needed. Ten patients underwent a second intervention. Repeated intervention established in-line venous flow in five patients but was unsuccessful in the remaining five patients. The reasons for treatment failure included immediate recurrent thrombosis despite successful endovascular recanalization in two patients, recurrent thrombosis 15 days after successful endovascular recanalization in one patient, and an inability to recanalize the occluded stent in two patients. All patients were maintained at international normalized ratio (INR) of 2.0 to 3.0 immediately after the intervention. The same techniques used for primary intervention were applied in the repeated interventions. Six patients (33%) who required repeated intervention had a grade III removal with more than 95% clearance (complete removal) in

Figure 1. a, b. Angiograms of a 28-year-old patient in a prone position. The thrombus filling the lumen of the femoral vein (a) was almost completely removed after aspiration thrombectomy (b).

Figure 2. a, b. Prone image shows a chronic occlusion, consistent with May-Thurner syndrome, after the removal of all acute thrombi in the iliac vein (a). The occlusion was first dilated, and a 12×60 mm Wallstent was then placed (b).

Figure 2. a, b. Prone image shows a chronic occlusion, consistent with May-Thurner syndrome, after the removal of all acute thrombi in the iliac vein (a). The occlusion was first dilated, and a 12×60 mm Wallstent was then placed (b).
Figure 3. Kaplan-Meier curve for primary and secondary patencies.

the primary intervention. Four (22%) of the patients who required repeated intervention had a grade II removal with less than a 95% clearance rate in the primary intervention. In the postpartum group, we encountered no contralateral DVT in patients who had stent implantation in the ipsilateral common iliac vein.

At the mean follow-up of 30 months, 11 patients had uninterrupted flow in the limb, and six patients did not. Six of the patients with uninterrupted flow were asymptomatic, and five had minimal swelling at the ankle at a mean follow-up of 30 months. The six patients with occluded veins at the end of the follow-up had mild to moderate symptoms consistent with post-thrombotic syndrome including swelling around the ankle and pigmentation of the medial malleolar region (CEAP 3 and 4). None of the patients developed ulceration (CEAP 5 and 6) during follow-up.

Results after reappraisal

All patients were recalled for a repeat examination to determine their latest CEAP scores and evaluate the presence of the iliac, femoral, popliteal, and greater saphenous veins using CDUS.

Six patients (33%) were asymptomatic, and 12 patients (67%) were symptomatic. Six patients had swelling and heaviness, five patients (28%) had swelling, one patient (8%) had pruritus, and one (8%) had pain and fatigue upon walking. The patients were classified as CEAP 0 (n=5), CEAP 1 (n=3), CEAP 2 (n=5), CEAP 3 (n=3), and CEAP 4 (n=2) in the reappraisal. Therefore, 13 of the 18 patients (72%) were CEAP 0–2.

Venous insufficiency was present in nine patients; five of six patients (80%) with occluded veins had venous insufficiency, whereas five of 12 patients (42%) with patent veins had venous insufficiency.

Discussion

The current study showed that, in patients with iliofemoral DVT, there was frequent involvement of the IVC and a high incidence of May-Thurner syndrome (92% in left-sided DVT patients). The distal veins were patent in a high number of patients (39% of patients), indicating that DVT started proximally and extended distally. This is a rare occurrence in patients with DVT in the general population (11). Complete or near-complete thrombus removal was achieved in all but one patient. Although the technical success was very high, recurrences were also high. Most recurrences occurred in the first month following the intervention while the patient was receiving therapeutic-level anticoagulation. There was no clear explanation for the recurrences. There was little problem with residual thrombi because most patients had nearly all of the thrombus removed by the endovascular methods. Hormonal factors alone and hormone-induced thrombophilia might play a role in the early recurrence of iliofemoral DVT after endovascular intervention as the hypercoagulable state of pregnancy continues in the postpartum period and does not return to normal until more than eight weeks postpartum (12). A high rate of early recurrent thrombosis can be managed by rigorous anticoagulant administration and the frequent CDUS examination of all patients in the first postprocedural month. If recurrences can be detected very early in the immediate postprocedural period, repeated interventions might be effective at preventing further thromboses. If early recurrent thromboses can be prevented in the first month after the initial procedure, good long-term results can be expected.

DVT commonly causes morbidity and mortality with serious short- and long-term medical, social, and economic consequences for patients (2). The primary aims of treatment for postpartum DVT are to restore vessel patency by removing the thrombus and alleviating the acute symptoms to prevent recurrent thrombosis and pulmonary embolism and to preserve venous valve function and thereby prevent post-thrombotic syndrome (13). Systemic anticoagulation therapy is the standard treatment for acute or subacute DVT (14). Anticoagulation does not cause lysis of the present thrombus but prevents new clot formation. It has proven to be efficient for the prevention of pulmonary embolism and recurrent thrombosis but has not been associated with fast symptom relief or recanalization of the thrombotic vessel. Akesson (15) showed that 95% of patients with iliofemoral DVT treated with anticoagulation alone had ambulatory venous hypertension at five years and 90% of patients had chronic venous insufficiency. Plate et al. (13) reported that 71% of medically treated patients developed leg swelling and 17% developed leg ulcers within a 10-year follow-up period. Plate et al. (13) also reported that 59% of medically
Laiho et al. (18) reported that valvular backs of CDT are the lengthy infusion method. The most important draw-endovascular thrombus treatment. Catheter-directed thrombolysis following standard anticoagulation therapy. Although the number of patients in this study was limited, these findings confirm our belief that MTA combined with CDT and stent placement is a safe procedure.

There are limitations of the study. The retrospective nature of this study is one of these limitations. We did not obtain data on quality of life, which is an important long-term factor. Additionally, measuring the levels of hormonal factors or inflammatory markers would have added to the study but could not be performed because this was a retrospective study, and we were unaware of the high recurrence rate among postpartum patients at the outset of the study. All patients were maintained at INR levels of 2.0 to 3.0 immediately after the intervention as explained in the methods section. However, despite frequent INR testing, some patients’ INR levels might have remained lower than planned, causing thrombosis recurrence. Unfortunately, we cannot determine whether this occurred due to the intermittent nature of INR testing, which is an inherent limitation of this study.

In conclusion, postpartum iliofemoral DVT has a massive thrombus burden with a high rate of IVC involvement and a high incidence of May-Thurner syndrome. Endovascular treatment methods with percutaneous aspiration thrombectomy alone or combined with CDT and iliac vein stenting were rapid and very safe and resulted in a very high rate of thrombus removal and clinical improvement in most patients. However, recurrences, particularly in the first post-intervention month, were very high. The postpartum hormonal state may have been instrumental in this condition. However, if no recurrences occurred in the first post-intervention month, the recurrence rate was low, and there was very good long-term patency of the involved vein. The frequent follow-up of patients in the first post-intervention month is necessary.

Conflict of interest disclosure
The authors declared no conflicts of interest.