Technical Details and Clinical Outcomes of Transpopliteal Venous Stent Placement for Postthrombotic Chronic Total Occlusion of the Iliofemoral Vein

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ABSTRACT

Purpose: To evaluate the technical aspects and early clinical results of stent placement for managing postthrombotic chronic total occlusion (CTO) of the iliofemoral vein through ipsilateral popliteal access.

Materials and Methods: A retrospective analysis of 110 patients (44 men; mean age, 51 y; 118 limbs; 102 left limbs) with postthrombotic CTO of the iliofemoral vein treated with stent placement in a single institution from January 2007–December 2011 was conducted. All occlusions were initially accessed via ipsilateral popliteal veins under the guidance of venography or ultrasonography. Technical aspects, quality of life, stent patency, and Villalta scores were recorded at follow-up evaluation. Risk factors of in-stent restenosis and early in-stent thrombosis were evaluated using Cox proportional hazards regression model.

Results: Percutaneous recanalization was successful in 112 of 118 limbs (95%). The mean duration of the procedure was 43 minutes (range, 10–120 min). The quality of life and Villalta scores were significantly improved (P < .01). The 3-year primary, assisted primary, and secondary cumulative stent patency rates were 70%, 90%, and 94%. During a median follow-up period of 25 months (range, 1–52 mo), the relief rates of severe leg pain (visual analog scale >5) and severe leg swelling (grade 3) were 72% (49 of 68) and 70% (64 of 91), respectively, and the healing of ulcers was successful in 78% (36 of 46) of the cases. After stent placement, the limbs with visible remaining collateral circulation had a higher rate of early in-stent thrombosis (22.5% vs 6.1%; P = .007). The patients with long stents extending below the inguinal ligament had a higher rate of in-stent restenosis (hazard ratio = 1.77–6.5; P = .0146).

Conclusions: Transpopliteal venous stent placement is an effective, safe, and feasible method of managing postthrombotic CTO of the iliofemoral vein. The stent extending below the inguinal ligament is the major risk factor of in-stent restenosis. The visible remaining collateral circulation after stent placement may indicate persistent hemodynamically significant stenosis.

ABBREVIATIONS

CTO = chronic total occlusion, PTS = postthrombotic syndrome

Despite the widespread usage of anticoagulants, post-thrombotic syndrome (PTS) is the most common complication encountered in deep vein thrombosis, developing in 20%–50% of patients after a proximal deep vein thrombosis, and is severe in 5%–10% of cases (1–3). Venous bypass, previously the only option for symptomatic PTS, is challenging and has a relatively low graft patency (4). Some authors have reported favorable results in treating chronic total occlusion (CTO) of the iliofemoral vein with endovascular therapy from the midthigh femoral vein or internal jugular vein access (5–7). However, the effectiveness of transpopliteal access for recanalization, as well as the reasons for early in-stent thrombosis and restenosis, is unknown. In 2002, endovascular treatment for postthrombotic CTO of the iliofemoral vein was implemented at our institution, and this alternative approach has gradually become the first-
choice treatment for these lesions. In this article, we report our experience with stent placement from the ipsilateral popliteal access for managing CTO of the iliofemoral vein, including clinical characteristics, technical details, clinical effects, early stent patency, and complications. We also analyze the risk factors of early in-stent thrombosis and restenosis.

MATERIALS AND METHODS

Patient Selection

This retrospective study comprised 110 consecutive patients (44 men) with 118 limbs (102 left limbs), who underwent attempted angioplasty and stent placement for CTO of the iliofemoral vein in a single institution from January 2007–December 2011. All patients provided written informed consent, and the approval of the Ethics Committee of the hospital was obtained. The age range of patients was 32–81 years, with an average age of 51 years. The CEAP (Clinical-Etiology-Anatomy-Pathophysiology) clinical classification of the treated limbs is shown in Table 1. The mean time from acute iliofemoral deep vein thrombosis to the procedure was 8.2 years (range, 1–40 y). Patients with mild PTS, which corresponds to Villalta scores < 10, were treated with conservative therapy, such as compression stockings or venoactive drugs (8). Data on these interventions were retrospectively collected from a dedicated database containing demographics, clinical presentation, classification, Chronic Venous Insufficiency Quality-of-Life Questionnaire, procedure duration, technical success, patency, symptomatic relief, Villalta scores, and interventional complications during follow-up period.

Puncture Process under Road Map (Subtracted Fluoroscopy) Guidance

In an upright standing position, a tourniquet was placed above the ankle to drive the contrast material into the deep venous system. A 22-gauge plastic intravenous cannula was inserted into the dorsal vein of the foot. The patient was asked to lie prone, and the contrast material was injected via the cannula. A road map was performed in the ipsilateral popliteal vein. After the administration of local anesthesia in the popliteal space, an ipsilateral popliteal vein puncture under road map guidance was successfully achieved (Fig 1a).

Stent Placement Procedure

After the ipsilateral popliteal vein puncture was successfully achieved, heparin sodium 80 IU/kg was administered to achieve an activated clotting time of 250–300 seconds in all patients. An anterograde venogram was obtained to define the existing venous anatomic features from the introducer sheath (Radilocus Introducer II; Terumo, Tokyo, Japan) (Fig 1b,c). A straight 0.018-inch hydrophilic guide wire (V-18 Control Wire; Boston Scientific Corporation, Natick, Massachusetts) was directed through the obstruction of the iliofemoral vein under the guidance of a matched multipurpose catheter or angled-tip catheter (MP A1; Cordis Corporation, Miami Lakes, Florida; TrailBlazer; ev3 Endovascular, Inc, Plymouth, Minnesota). Passage of the guide wire away from the expected direction of the iliofemoral vein with sudden ease denoted venous perforation (5), which was easily recognized by fluoroscopic projection. The guide wire could be withdrawn and redirected under the guidance of an angled-tip catheter. A 6-F, 55-cm Flexor Raabe Guiding Sheath (Cook, Inc, Bloomington, Indiana) placed in the ostium of the occluded iliofemoral vein expedited advancement through the lesions. The guide wire was removed after the catheter was advanced through the lesion. Venography was performed to ensure that the catheter tip was located within the lumen of the inferior vena cava (Fig 1d).

A balloon catheter (EverCross; ev3 Endovascular, Inc; Reckross; ClearStream Technologies, Wexford, Ireland; PowerFlex P3; Cordis Corporation) with a diameter of 4–16 mm and a length of 60–220 mm was used for dilation (Fig 1e). After balloon dilation, self-expanding stents (EverFlex; ev3 Endovascular, Inc; LIFESTENT; BARD, Tempe, Arizona; WALLSTENT; Boston Scientific Corporation) with a diameter of 10–16 mm and a length of 60–150 mm were implanted. Two stents were usually required because of the long segment of the occluded lesion. The femoral stent was deployed first, followed by the iliac stent. The femoral stent was deployed in the common femoral vein and below the inguinal ligament if needed. The iliac stent extended approximately 2.0 cm into the inferior vena cava. Coverage of the contralateral iliac vein ostium was avoided. The optimal stent diameters of the common femoral vein and iliac vein of most patients ranged from 10–12 mm (common femoral vein) and from 12–16 mm (iliac vein).

The WALLSTENT delivery catheter sometimes was not long enough for the deployment of the stent into the inferior vena cava from the sheath of the ipsilateral popliteal vein. The entire delivery catheter was advanced further cephalad after partial unsheathing of the

| Table 1. CEAP Clinical Classification before and after Procedure |
|-----------------|-----------------|-----------------|
| Classifications | Before Procedure | After Procedure |
| | (118 Limbs), No. (%) | (105 Limbs), No. (%) |
| 0–1 | 0 (0%) | 19 (18.1%) |
| 2 | 2 (1.7%) | 2 (1.9%) |
| 3 | 38 (32.2%) | 14 (13.3%) |
| 4 | 30 (25.4%) | 27 (25.7%) |
| 5 | 2 (1.7%) | 33 (31.4%) |
| 6 | 46 (39%) | 10 (9.5%) |

CEAP = Clinical-Etiology-Anatomy-Pathophysiology.
stent. After the deployment of all stents, balloon dilation was necessary because of the common occurrence of severe recoil. At the end of the procedure, venography was performed to examine the sheath to assess the success of the procedure and to exclude recoil, stenosis, and thromboembolic complications (Fig 1f,g). After the

Figure 1. A 59-year-old woman with an 11-year history of deep venous thrombosis and an inferior vena cava filter (Vena Tech LP Vena Cava Filter, B Braun, Bethlehem, Pennsylvania) developed severe venous claudication and swelling in the left lower extremity. (a) Popliteal vein puncture (arrow) was easy to perform under road map guidance. (b) Anterograde venogram shows CTO of the common femoral vein with numerous collateral veins (arrow). (c) CTO of the iliac vein with numerous collateral veins (arrow). (d) Venogram was obtained from the catheter to ensure that the catheter tip was located within the lumen of the inferior vena cava (arrow). (e) A long balloon catheter (EverCross), 7 mm in diameter and 200 mm in length (arrows), was used to inflate the occluded iliofemoral vein. (f) Anterograde venogram shows a channel with a stent and adequate lumen without residual stenosis and the absence of previously visualized collaterals (arrows). (g) Venogram shows the uninterrupted venous outflow and the stent placed cephalad into the inferior vena cava (arrow).
procedure, all access sites were compressed with a bandage without using a sealing device, even when large sheaths (10-F) were used.

All patients received 4,000 IU of low-molecular-weight heparin every 12 hours after stent placement and a therapeutic dosage of warfarin (international normalized ratio 2–3) for at least 6 months after discharge from the hospital. Long-term warfarin was indicated for patients with thrombophilia according to current guidelines (9).

Follow-up

Technical success was defined as recanalization with anterograde flow and <30% residual stenosis after stent placement (10). In-stent restenosis was defined as occlusion or >50% stenosis, as demonstrated on computed tomography (CT) or venography. Complications were classified as major and minor based on Society of Interventional Radiology (SIR) standards (11). Early in-stent thrombosis was defined as thrombosis within 1 month after stent placement. Preoperative local ulcer care methods were continued after intervention until healing. Ulcer healing was defined as complete epithelialization. All patients were scheduled to return every 3 months after treatment for follow-up consultations including physical examination of the treated lesions. Follow-up imaging was primarily performed with duplex ultrasound scanning, but 23 patients underwent CT or venography because obtaining adequate imaging of the stents was difficult with ultrasound alone. If the patient showed recurring symptoms, CT or venography was performed to assess the patency of the venous outflow tract. Preoperative and postoperative evaluations were performed using the Villalta scale (8) and the CEAP clinical classification (12). Patients also were asked to complete a quality-of-life questionnaire assessing objective edema, subjective pain, sleep disturbance, morale, social activities, and physical activities (13). The same evaluation was performed postoperatively during each follow-up visit. The evaluations were performed after 3 and 6 months and then every 12 months. The most recent completed questionnaire for each patient was used to assess the outcome.

Data Collection and Statistical Analyses

At each patient visit, all clinical data and clinical outcomes were entered into a time-stamped database for subsequent analysis. Individual data are presented as median with range, mean ± SD, and proportions. Primary, primary-assisted, and secondary patency rates were estimated using the Kaplan-Meier method with a log-rank test. The risk factors of in-stent reocclusion and early in-stent thrombosis were evaluated through univariate and multivariate analyses using Cox proportional hazards regression model. SPSS version 21.0 (SPSS, Inc, Chicago, Illinois) was used for statistical analyses. A $\chi^2$ test was used to compare the outcomes of symptom relief. Differences with $P < .05$ were considered significant.

RESULTS

Procedural Success

The overall recanalization success rate was 95% (112 of 118 limbs). Of 112 limbs, 54 were accessed under the guidance of road map and 58 were accessed under ultrasound. The mean duration of the procedure was 43 minutes (range, 10–120 min). The cause of technical failure in six patients (six limbs) with failed angioplasty was the inability to cross the occluded iliofemoral vein. All six patients were treated with graduated compression stockings (23–32 mm Hg). Bilateral occlusions were present in eight patients, and recanalization was successful in the bilateral limbs of these eight patients (recanalization performed simultaneously in seven patients and as a staged procedure in one patient). The mean number of balloons was 2.33 (range, 2–5), and the mean number of stents was 2.06 (range, 1–3). Two stents were needed in 90.2% (101 of 112) of the treated lesions; only one stent was needed in 2 limbs and three stents were needed in nine limbs.
Stent Patency
The cumulative primary, assisted primary, and secondary patency rates over 3 years were 70%, 90%, and 94% (Fig 2). After angioplasty and stent deployment, 13 patients (13 limbs) had no follow-up visits. Restenosis of the treated lesions occurred in 20 patients (21 lesions). The symptoms of five patients (five lesions) with occluded stents were treated with graduated compression stockings without clinical impairment during the follow-up period. Repeat endovascular angioplasty was successfully performed in the remaining 15 patients (16 lesions).

Several factors that potentially influence the development of early in-stent thrombosis and restenosis were analyzed with cumulative survival. Sex, age, duration of thrombosis, thrombophilia, number of stents, stent diameter, length of the stent, procedure duration, early in-stent thrombosis, and side of lower extremities did not affect the outcome (Table 2). Stents extending below the inguinal ligament exhibited a higher risk of in-stent restenosis within the first 12 months (hazard ratio = 1.77–6.5; P = .0146). Early in-stent thrombosis was observed in 9 of 40 limbs with visible remaining collateral circulation after stent placement (22.5%) and in 5 of the other 82 limbs with no visible collateral circulation (6.1%). Patients with visible remaining collateral circulation after stent placement showed a high rate of early in-stent thrombosis (22.5% vs 6.1%; P = .007).

Therapeutic Effects
In follow-up sessions conducted at a median period of 25 months (range, 1–52 mo), quality-of-life questionnaires were completed by 74 patients, and a significant improvement was observed in all six categories (P < .01 in all categories) (Table 3). The Villalta scale was used to analyze 87 patients; the total Villalta PTS score decreased from 22.0 before the procedure to 9.3 after the procedure (P = .001) (Table 4). Active ulcers were present in 46 limbs, and the cumulative recurrence-free ulcer-healing rate was 78% at follow-up evaluation. Severe swelling (grade 3) was present in 91 limbs, and

Table 2. Risk Factors of In-Stent Restenosis Analyzed Using Cox Proportional Hazards Regression Model

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P Value</td>
<td>HR (95%)</td>
</tr>
<tr>
<td>Male</td>
<td>.0834</td>
<td>1.39 (0.53–2.1)</td>
</tr>
<tr>
<td>Age</td>
<td>.2722</td>
<td>0.81 (0.37–4.3)</td>
</tr>
<tr>
<td>Duration of thrombosis</td>
<td>.1643</td>
<td>0.43 (0.12–1.9)</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>.0618</td>
<td>1.35 (0.46–2.7)</td>
</tr>
<tr>
<td>Side of limbs</td>
<td>.4152</td>
<td>0.56 (0.16–3.2)</td>
</tr>
<tr>
<td>Number of stents</td>
<td>.0612</td>
<td>0.51 (0.14–1.8)</td>
</tr>
<tr>
<td>Early in-stent thrombosis</td>
<td>.0738</td>
<td>1.15 (0.36–2.2)</td>
</tr>
<tr>
<td>Diameter of stents</td>
<td>.1574</td>
<td>0.46 (0.26–2.3)</td>
</tr>
<tr>
<td>Length of stents*</td>
<td>.0246</td>
<td>3.14 (1.77–6.5)</td>
</tr>
<tr>
<td>Duration of procedure</td>
<td>.0731</td>
<td>0.46 (0.26–2.5)</td>
</tr>
<tr>
<td>Visible collateral post stents</td>
<td>.0633</td>
<td>1.79 (0.15–2.8)</td>
</tr>
</tbody>
</table>

HR = hazard ratio.
*P < .05.

Note. Quality-of-life assessment values are mean ± SD.
Table 4. Villalta PTS Score before and after Procedure

<table>
<thead>
<tr>
<th></th>
<th>Before Stent</th>
<th>After Stent</th>
<th>Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms component</td>
<td>11.4 (3.1)</td>
<td>5.1 (1.7)</td>
<td>−6.3 (2.5)</td>
<td>.002</td>
</tr>
<tr>
<td>Signs component</td>
<td>10.6 (2.4)</td>
<td>4.2 (1.4)</td>
<td>−6.4 (2.8)</td>
<td>.002</td>
</tr>
<tr>
<td>Total Villalta score</td>
<td>22.0 (4.3)</td>
<td>9.3 (2.6)</td>
<td>−12.7 (3.5)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Note. Values are Villalta PTS score (SD). PTS = postthrombotic syndrome.

Severe leg pain (visual analog scale > 5) was present in 68 limbs, for which the relief rates were 70% (for severe swelling) and 72% (severe leg pain).

Complications
All patients tolerated the procedure well, and no major complications were encountered. Specifically, no perioperative deaths or pulmonary embolism occurred. No clinically apparent procedure-related bleeding was observed, and no access complications requiring intervention occurred. Minor complications (SIR grade A) occurred in 72 patients (65.5%), including back pain after the procedure in 57 patients (51.8%), venous perforation in 31 patients (28.2%), and both in 16 patients. Back pain occurred after stent placement, but the symptoms were self-limiting, and no patients required hospitalization or medical therapy. Venous perforation disappeared in all cases without sequelae after balloon angioplasty and stent placement for the occluded iliofemoral veins (Fig 3a–d).

DISCUSSION
This retrospective study investigates the technical success and effectiveness of trans-popliteal venous stent placement for managing CTO of the iliofemoral vein. Stent placement from the ipsilateral popliteal vein was effective in treating CTO of the iliofemoral vein, with high levels of technical success, clinical symptom improvement, and acceptable short-term patency rate. The effectiveness of stent placement for CTO of the iliofemoral vein has been evaluated elsewhere (5–7,14–17). Rosales et al (14) reported 2-year primary, primary-assisted, and secondary patency rates of 67%, 76%, and 90% in 32 patients. Similarly, Raju et al (15) reported a 5-year secondary patency rate of 82% in 285 limbs. In the present study, the primary, assisted primary, and secondary cumulative stent patency rates after 2 years were 70%, 90%, and 94%, which are comparable to patency rates in other studies. The results of this retrospective study confirm results of previous studies on the short-term outcomes of stent placement for CTO of the iliofemoral vein and indicate the efficacy and high technical success rate of the trans-popliteal approach.

Most authors have reported success in using internal jugular vein cannulation, mid-thigh femoral vein access, multiple accesses, and snaring techniques in most cases (5–7,14–17). By contrast, we initially accessed CTO of the iliofemoral vein through the ipsilateral popliteal vein under the guidance of a road map or ultrasonography. Similar to the findings of Neglén (18), recanalization from retrograde was exceedingly difficult when the common iliac vein was occluded, especially in patients with an occluded inferior vena cava. The results of this study clearly illustrated the feasibility of trans-popliteal venous stent placement in patients with CTO of the iliofemoral vein, achieving technical success in 95% of all patients who underwent endovascular interventions. Also, no procedure was terminated because of the patient’s intolerance of the operation. The mean duration of the procedure was 43 minutes, which was comparable to other studies. Raju and Neglén (5) reported that most occluded iliofemoral veins could be recanalized within 30–40 minutes through mid-thigh femoral vein access.

In our experience, puncturing the mid-thigh femoral vein was highly operator-dependent even under ultrasound guidance, and the routine use of a sealing device was necessary (5). The femoral vein was frequently occluded or stenotic. By contrast, puncturing the popliteal vein under the guidance of a road map or ultrasonography was simple, and the puncture wound was easily compressed with a bandage (19). None of the complications that required intervention, such as hematomas, arteriovenous fistulas, and bleeding, occurred in the popliteal veins, even without the use of a sealing device. The only limitation of the procedure was the length of the WALLSTENT delivery catheter, which was occasionally insufficient for the deployment of the stent into the inferior vena cava from the sheath of the ipsilateral popliteal vein. This disadvantage can be managed by placing the entire delivery catheter cephalad after the partial unsheathing of the stent. The results of the present study demonstrate that popliteal vein access is an optional method of treating postthrombotic CTO of the iliofemoral vein.

As previously reported, stents extending below the inguinal ligament are a risk factor of in-stent restenosis (20,21). This finding is consistent with the present results. Early in-stent thrombosis is a major cause of endovascular failure. A high rate of early in-stent thrombosis was found in patients with visible remaining collateral circulation after stent placement. This finding may indicate that persistent flow via collateral vessels compromises sufficient inflow through the stents. These patients could be treated successfully via catheter-directed thrombolysis followed by balloon angioplasty and additional stent placement. They had comparable stent patency rates during follow-up sessions.

Back pain was the most frequent complication encountered in stent placement for postthrombotic CTO of the iliofemoral vein. In this study, approximately half of the patients (51.8%; 57 of 110) had back
A 52-year-old man with a 6-year history of previous deep venous thrombosis developed severe PTS with a nonhealing ulcer on the left lower extremity. (a) Venography performed before stent placement shows CTO of the iliofemoral vein and the collateral circulation of the pelvis. (b) Venogram obtained from the catheter shows the perforation (arrows) of the iliac vein during the procedure. (c) Final venogram shows unimpeded flow in the vein segment with stent placement without stenosis. (d) Venogram shows the disappearance of perforation (arrows) and collateral circulation of the pelvis.
pain after the procedure or during balloon angioplasty and stent placement. A previous study from our institution (22) found the prevalence of back pain in patients with postthrombotic iliofemoral veins to be higher than in patients with nonthrombotic iliac vein lesions. We conjectured that the prevalence was based on the severity of the occluded lesions of the iliac vein. The prevalence was also higher than the prevalence reported by other authors (5). The reason might be that the procedures were performed under local anesthesia in this study but under general anesthesia in other studies. No patient required hospitalization or medical therapy for back pain. Venous perforations at the treated lesions during the procedure, in contrast to arterial perforation, were less dangerous and disappeared without sequelae after balloon angioplasty and stent placement for the occluded iliofemoral vein.

This study has several limitations. First, it investigated a small number of patients and was retrospective in nature. Second, the follow-up period was short, and a control group of patients treated via femoral or internal jugular vein access was lacking. Third, the different types and sizes of stents used in this study may have affected the results. Fourth, the data did not clarify whether or not in-stent reocclusion progressed over time. Fifth, no objective test was used to evaluate the effectiveness of stent placement for postthrombotic CTO of the iliofemoral vein.

In conclusion, transpontaneous venous stent placement is an effective, safe, and feasible method of managing CTO of the iliofemoral vein. This method alleviates the symptoms in the short-term and results in high stent patency rates. The major risk factor of developing in-stent stenosis is stent placement below the inguinal ligament. Early in-stent thrombosis occurs more frequently in limbs with visible remaining collateral circulation after stent placement.

ACKNOWLEDGMENT

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