CLINICAL STUDY

Contralateral Deep Vein Thrombosis after Iliac Vein Stent Placement in Patients with May-Thurner Syndrome

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ABSTRACT

Purpose: To investigate the incidence and potential causes of contralateral deep vein thrombosis (DVT) after common iliac vein (CIV) stent placement in patients with May-Thurner syndrome (MTS).

Materials and Methods: Data of 111 patients (women: 73%) who had CIV stent implantation for symptomatic MTS at a single center were retrospectively analyzed. Mean patient age was 63.1 ± 15.2 years. Median follow-up was 36 months (range, 1–142 months). Stent location was determined by venogram and classified as extended to the inferior vena cava (IVC), covered the confluence, or confined to the iliac vein. Potential causes of contralateral DVT were presumed based on venographic findings. The relationship between stent location and contralateral DVT was analyzed.

Results: Ten patients (9%, men/women: 4/6) exhibited contralateral DVT at a median timing of 40 months (range, 6–98 months). Median age was 69 years (range, 42–85 years). Median follow-up was 73.5 months (range, 20–134 months). Potential causes were venous intimal hyperplasia (VIH) (n = 7), "jailing" (n = 2), and indeterminate (n = 1). All patients with VIH had previous CIV stents overextended to the IVC. Overextension of CIV stent was associated with contralateral DVT ($P < .001$). The primary patency rate of the contralateral CIV stent was 70% at 20 months.

Conclusions: Contralateral DVT after CIV stent implantation has a relatively high incidence and often occurs late during follow-up. Overextension of the CIV stent to the IVC is associated with development of contralateral DVT, and VIH should be considered a potential cause.

ABBREVIATIONS

CDT = catheter-directed thrombolysis, CIV = common iliac vein, DVT = deep vein thrombosis, MT = manual thromboaspiration, MTS = May-Thurner syndrome, PMT = percutaneous mechanical thrombectomy, PTA = percutaneous transluminal angioplasty, VIH = venous intimal hyperplasia

May-Thurner syndrome (MTS) is a main cause of deep vein thrombosis (DVT) and chronic venous insufficiency, with an observed rate ranging from 18% to 49% (1,2). Endovascular stent insertion has been recognized as a treatment of choice for venous outflow obstruction since it is safe and effective in restoring venous outflow, ensuring long-term patency, preventing DVT recurrence, and reducing risk of post-thrombotic syndrome (3–8). However, there is a lack of consensus on the ideal location of the stent, particularly in case of stenosis adjacent to the confluence, such as MTS. If the stenosis is not sufficiently covered, the stent could migrate caudally or be compressed into a tapering cone shape, facilitating restenosis (9,10). Conversely, placing a stent that overrides the stenosis and extends into the inferior vena cava (IVC) can impair the contralateral venous outflow, commonly known as "jailing," which consequently increases the risk of contralateral DVT (10–12). Moreover, persistent "insult" exercised by the stent struts on the IVC wall can trigger intimal hyperplasia (13). Contralateral DVT after common iliac vein (CIV) stent placement has a reported incidence that varies from 1% to 9.7% (9–12,14). Nonetheless, these studies included both thrombotic and nonthrombotic patients with different venous

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pathologies (9–12,14). The purpose of this study was to further investigate the incidence of contralateral DVT after CIV stent insertion in the subset population of MTS. Potential causes of contralateral DVT were also evaluated.

MATERIALS AND METHODS

Patient Demographics

This study received institutional review board approval, and informed consent was obtained from all patients. Data of 111 consecutive patients (men/women: 27%/73%) treated with stent placement for symptomatic MTS in a single institution between October 2004 and January 2017 were retrospectively analyzed. Mean patient age was 63.1 ± 15.2 years. Median follow-up duration was 36 months (range, 1–142 months). Exclusion criteria were preexisting contralateral DVT, residual IVC thrombus from initial procedure, and loss of follow-up (patients who did not undergo any imaging follow-up). MTS was diagnosed by computed tomographic venogram. All data were retrieved from the hospital database.

Endovascular Procedure

After the diagnosis of DVT, hypercoagulable workup is routinely indicated, including levels of protein C and protein S, factor V, factor II, lupus anticoagulant, anti-cardiolipin immunoglobulin, homocysteine, and anti-thrombin III. The treatment strategy of MTS was based on a multidisciplinary discussion between vascular surgeons and the interventional radiologist. Low-molecular-weight heparin and enoxaparin sodium (Clexane 1 mg/kg, Sanofi-Aventis, Paris, France) were administered. Vascular access was obtained via ultrasound-guided puncture of the popliteal vein using a micropuncture set (Cook, Bloomington, Indiana). IVC filters were inserted in 77 patients (69.4%), mainly via the unaffected common femoral vein approach. All patients with acute iliofemoral DVT underwent catheter-directed thrombolysis (CDT) with urokinase (2000 units/kg/h). Systemic anticoagulation was ceased during the procedure. Unfractionated heparin 400 IU/h was infused through the sheath during venographic follow-up. Pharmacomechanical thrombectomy (PMT) using a Trerotola device (Arrow International, Reading, Pennsylvania) was applied in case of mixed stage of acute, subacute, and chronic thrombus. The endpoints of thrombolytic therapy were thrombus dissolution and lytic stagnation. Finally, the stenotic site was treated by balloon angioplasty and stent placement within the primary intervention. Wallstents (Boston Scientific, Natick, Massachusetts) were implanted in 54 patients (48.6%), and nitinol stents (SMART, Cordis, Bridgewater, New Jersey) were implanted in 57 patients (51.4%). Stent diameter was oversized 10%–20% compared to the normal patent CIV. All implanted stents were 11–14 mm in diameter and 60–100 mm in length.

Categorization of Stent Location

Left CIV stent location was determined by venogram and classified into 3 categories: (*i*) extended to the IVC (if the cranial tip of the stent was placed ≥ 10 mm beyond the confluence, contacting the contralateral wall of the IVC); (*ii*) covered the confluence (if the stent completely or partially covered the opening of the contralateral CIV without "touching" the contralateral IVC wall); and (*iii*) confined to the CIV (without confluence involvement) (Fig 1).

Post-procedural Care and Follow-up

After discharge, all patients were prescribed vitamin K antagonist (warfarin) for 6 months according to a target international normalized ratio of 2:3. Since 2015, rivaroxaban (Xarelto, Bayer Pharma AG, Berlin, Germany) 15 mg twice a day for the first 3 weeks then 20 mg/day for 6 months has been used as an alternative. After 6 months, lifelong antiplatelet agent (aspirin 100 mg/day or clopidogrel 75 mg/day) was substituted. Imaging follow-ups were scheduled at 6 months, 1 year, and annually thereafter. IVC filters were removed according to the manufacturer's instructions for use. All procedures were performed by 1 interventional radiologist with 15 years of experience.

Statistical Analysis

Continuous data are presented as mean ± standard deviation if the variables were normally distributed or as median and range if the variables were not normally distributed. Categorical data are given as count and percentage. The Mann-Whitney U-test was used to compare medians of 2 continuous variables, whereas Pearson's chi-squared test was used to compare percentages of categorical variables. A multivariate logistic regression was run to predict the development of contralateral DVT from age, sex, stent location, rates of malignancy, and preexisting IVC filters. All analyses were performed using R version 3.1.2 software (R Core Team, R Foundation for Statistical Computing, Vienna, Austria). *P* values less than .05 indicated statistical significance for all comparisons.

RESULTS

Of 111 cases of CIV stenting, 10 patients (9.0%, men/women: 4/6) developed contralateral DVT at a median timing of 40 months (range, 6–98 months). Median patient age was 69 years (range, 42–85 years). Median follow-up duration was 73.5 months (range, 20–134 months). Of these, 3 patients received Wallstents and 7 patients received nitinol stents. All implanted stents were 14 mm in diameter and 80–90 mm in length. No patients with contralateral DVT had an abnormal thrombophilia profile. Patient characteristics are summarized in Figure 2.

The location of contralateral DVT was iliac vein (1/10), iliofemoral vein (5/10), and extensive to calf veins (4/10). Of 10 patients with contralateral DVT, 8 (80%) had the initial CIV stents extended to the IVC (category 1), and 2 (20%) had the stents covered the confluence (category 2). Venous intimal hyperplasia (VIH) was presumed as the underlying cause of contralateral DVT in 7/10 (70%)