Intravascular Ultrasound-Guided Intervention for May–Thurner Syndrome

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The most common variant of ilio caval compression occurs when the left common iliac vein is compressed between the right common iliac artery and the lumbosacral spine, termed *May–Thurner Syndrome* (MTS) or Cockett's syndrome. Aside from effacement of the vein, arterial pulsations cause vascular thickening, intimal proliferation, and fibrous adhesions that can result in venous obstruction. Patients may present with nonthrombotic MTS, acute deep venous thrombosis (DVT), or chronic occlusion of the left common iliac vein. Correspondingly, clinical symptoms range from sudden onset of left lower extremity swelling with DVT to less dramatic presentations of chronic venous disease including edema, pain, varicose veins, pigment changes, ulcers, or other stigmata of postthrombotic syndrome. Endovascular approaches with pharmacologic and mechanical thrombolysis, intravascular ultrasound (IVUS), and self-expanding stents have resulted in high clinical success rates in the treatment of MTS.

Preprocedure Evaluation

Initial evaluation includes a thorough history with a focus on risk factors for DVT, prior potential DVT events, and prior therapy. Clinical assessment tools such as CEAP (Comprehensive Classification System for Chronic Venous Disorders) are recommended for standardization. Aside from routine laboratory exams, a hypercoagulable workup may be undertaken. Lower extremity ultrasonography is the first-line exam to evaluate for DVT and venous reflux. Additionally, venous-phase contrast computed tomography (CT) or magnetic resonance imaging (MRI) of the pelvis is able to show the relationship of the common iliac veins and arteries relative to the spine. Moreover, collateral venous outflow or DVT in the pelvic veins may be visualized with either cross-sectional modality.

Procedural Preparation and Approaches

Preprocedural antibiotics are not absolutely necessary, but a single dose to cover skin flora may be administered. Commonly, the procedure is performed with intravenous conscious sedation; though if a prolonged or difficult recanalization is suspected, large clot burden with considerable thrombolysis is expected; or if the patient has comorbid conditions, general anesthesia may be warranted. Positioning is supine on the angiography table, but if extensive thrombus is present, then the lower extremities may be situated frog-leg or the patient may be placed prone. Sterile preparation and draping of each potential access site is performed: most often the left groin and either the right groin or right neck. Our preferred access sites are the right internal jugular vein and the left greater saphenous vein (GSV). The benefits of GSV access are as follows: it frequently remains patent despite thrombosis of the deep venous system, minimizes damage to the deep venous system, can accommodate necessary sheaths and devices, does not compromise angioplasty or stenting of the deep venous system even into the common femoral vein, and upon completion allows for easy compression to establish hemostasis. Standard sheaths, wires, catheters, high-pressure angioplasty balloons, and self-expanding stents can be used to address the majority of cases. Adjunctive items may include a variety of thrombolysis and thrombectomy devices as well as needles, snares, and wires for sharp recanalization. IVUS is quite helpful in vascular interventions and the authors recommend having IVUS capability for use in all suspected MTS patients.

Venography and IVUS Findings

Initial left pelvic venography will reveal the flow dynamics of the deep venous system and can confirm compression of the left common iliac vein. Findings may include effacement or occlusion of the left common iliac vein, DVT (acute with

expanded veins or chronic with contracted channels), and/or the presence of cross-pelvic or lumbar collaterals draining veins. Pressure gradients across the area of suspected compression can be acquired and compared with the right common iliac vein to further support the diagnosis. If there is a discrepancy of greater than 2 to 3 mm Hg between each side, it is likely hemodynamically significant. However, because intraprocedural gradients, which are measured with the patient supine and at rest, are small and comparable to hemostatic gradients between a patent inferior vena cava (IVC) and internal/common iliac vein confluence, we do not often use manometry to guide treatment decisions.

Through the 1990s, several authors began reporting on the use of IVUS for the evaluation and treatment of MTS.^{1–4} IVUS provides intraluminal imaging (synechiae, webs, trabeculations, thrombus, etc.), direct assessment of the vascular wall and valves, proximity to expected juxtavenous arteries, and accurate dimensional relationships of compression for stent sizing and placement. Following prolonged procedures, IVUS is used to judge residual venous cross-section and presence of intramural thrombus within or outside stented segments, which can influence decision to extend stent coverage. IVUS proved to be superior to single plane venography, impacted the treatment plan in half of the MTS cases, and is presently the best available method.^{1–4} Venographic and IVUS findings in clinical scenarios of three types of MTS are presented.

Nonthrombotic: Patients present with complaints similar to those of chronic postthrombotic syndrome, most commonly leg heaviness and swelling, pelvic pain, and prominent superficial veins in the vicinity of the left groin. Many patients may have subtle symptoms and may favor the right leg over the left; notice a difference in how pants, socks, or shoes fit between the right and left legs; or may avoid exercise to minimize lower extremity discomfort. Additionally, it is important to discern the underlying cause from alternative etiologies and CT or MRI may be particularly useful to exclude pelvic congestion syndrome or other etiologies of their pain (**Fig. 1a, b**). Venography may reveal a flattened vein with decreased contrast density from the overlying impression of the right common iliac artery (**Fig. 1c**). IVUS will reveal the characteristics of the lumen, identify if a compressive lesion is present, and quantify if the lumen is less than 50% of the expected diameter (**Fig. 1d**). Increasingly, stenting is advocated to prevent venous scarring as intraluminal changes, when they occur, are irreversible.

Acute deep venous thrombosis: Sudden onset of symptoms is common with severity directly related to the extent of DVT, which may be focal or extend from the point of left common iliac vein compression to below the knee. Redness, warmth, pain or tenderness, and engorgement of superficial veins may be present. Chest pain or tightness, dyspnea, and tachycardia may reflect concomitant pulmonary embolus. Doppler ultrasonography will reveal acute DVT, which may be focal or involve multiple stations. If possible, access should be gained below the most distal level of thrombus to facilitate complete clearance and maximize future antegrade venous flow. Venography will reveal acute thrombus, which

is identified as a filling defect in the center of an occluded vein or may be outlined by peripheral contrast. Additionally, acutely thrombosed veins appear expanded, as opposed to contracted in chronic venous occlusions. Diversion of contrast into perforating veins and engorgement of the superficial venous outflow may be noted. Recanalization of the deep venous system can usually be performed across the “soft” clot with a hydrophilic guidewire and catheter (**Fig. 2a**). IVUS helps localize the guidewire by identifying adjacent anatomy and may help confirm the acuity of the thrombus (**Fig. 2b**). Subsequently, thrombectomy or thrombolysis may be performed in the same session or overnight (**Fig. 2c–e**). After clearing the thrombus, venography can reveal the flow dynamics, unmask an underlying lesion, and evaluate for septations, webs, or stenosis reflecting sequela of prior venous thrombosis. Repeat IVUS is used to characterize the degree of compression and evaluate for intraluminal thickening or formation of venous “spurs.”

Chronic left iliac vein occlusion: Asymmetric leg swelling or heaviness may have been ongoing for years and may have served as a nidus for recurrent DVT. Additional symptoms may include pelvic pain or the presence of prominent upper thigh, peri-pelvic, or lower abdominal superficial veins. Doppler ultrasonography of the left lower extremity may be normal. CT or MRI will reveal compression of the left common iliac vein by the right common iliac artery and prominent cross-pelvic and lumbar collateral veins (**Fig. 3a, b**). Venography reveals little direct flow to the IVC, enlarged and well-developed collateral venous drainage to the central circulation in addition to contracted venous channels (**Fig. 3c**). Crossing this long-standing occlusion may be challenging and may require advanced techniques including sharp recanalization. IVUS findings may include obliteration of the venous lumen, thickening of the venous wall, and the length of overlying compression (**Fig. 3d, e**).

Stent Technique

After the MTS lesion is crossed, the thrombus has been addressed, and stenting is planned, we use self-expanding stents. Most often, we use Wallstents (Boston Scientific, Marlborough, MA) ranging in size from 14 to 18 mm in diameter and 6 to 8 mm in length. Because the left common iliac vein may be flattened by the overlying artery, IVUS is particularly helpful to accurately determine stent diameter, length, and position.⁴ We estimate the optimal stent size by calculating the diameter of normal-appearing segments of the left common iliac vein, both immediately proximal and distal to the point of compression, and then selecting a stent diameter that is the next larger in size (e.g., for a 12–14 mm diameter, we choose a 16-mm diameter stent; **Fig. 3i**). Our most common choices for self-expanding stents are 16 mm diameter for the common iliac vein and 14 mm for the external iliac and common femoral veins, with postdilation balloons of 16, 14, and 12 mm for the common, external iliac, and common femoral veins, respectively. Moreover, IVUS allows for accurate stent length selection by evaluating the length of the compressed areas. The length of the stent

Fig. 1 An 18-year-old female with asymmetric left lower extremity swelling without history of deep venous thrombosis. (a) Axial image from CT venography (CTV) reveals left common iliac vein (LCIV) compression (black arrow) between the anterior right common iliac artery (RCIA) (white arrow) and the spine posteriorly. (b) Axial image from same CTV two slices caudal confirming LCIV compression (black arrow) by the RCIA (white arrow). No tissue plane is present between the LCIV and the RCIA. Moreover, the AP diameter of the LCIV is narrowed by greater than 50% at this point compared with the adjacent venous segments. (c) Pelvic venography re-demonstrates compression of the left common iliac vein by the overlying right common iliac artery. Collateral venous drainage is present via the ascending lumbar vein (black arrowhead). A paucity of contrast is present in the left common iliac vein subjacent at the site of maximal compression from the right common iliac artery (white arrowhead). (d) Intravascular ultrasound (IVUS) image highlights compression of the LCIV (white arrow) by the RCIA (white arrowhead). (e) Fluoroscopic image obtained during stenting. The IVUS catheter is in position from a right internal jugular access (black arrow) and is monitoring the deployment of a Wallstent from the left groin access. (f) IVUS image postintervention with a widely patent LCIV (white arrow), which is no longer collapsed by compression from the RCIA (white arrowhead). (g) Completion pelvic venography with a widely patent stent and LCIV. Collateral draining veins no longer fill with contrast.

Fig. 2 A 34-year-old woman with factor V Leiden mutation presents with left lower extremity swelling and pain after a cross country flight. (a) Pelvic venography revealing occlusion of the left external iliac vein. The guidewire extends rostral to the occlusion (white arrow). (b) Fluoroscopic image after crossing the venous obstruction. The intravascular ultrasound (IVUS) catheter is positioned at the point of venous compression. The tip of the catheter is noted with the white arrow, and corresponds to the IVUS in ►Fig. 2c. (c) IVUS image highlighting compression of the LCIV (white arrow) by the RCIA (white arrowhead) at the same point as ►Fig. 2b. (d) Fluoroscopic image illustrating course of ultrasound-assisted thrombolysis catheter. White arrowheads denote the rostral and caudal margins of infusion sideholes in the catheter. (e) Fluoroscopic image showing an IVC filter in place (white arrow) and rheolytic thrombectomy catheter (white arrowhead). (f) Fluoroscopic image demonstrating a “waist” in the venoplasty balloon at the site of LCIV compression. (g) Pelvic venography poststenting reveals brisk antegrade flow through the previously thrombosed left common and left external iliac veins (white arrowheads). (h) Venography of the IVC showing patency of the right common iliac vein and IVC after LCIV recanalization and stenting. (i) Completion IVUS image confirming a widely patent LCIV (white arrow) and crossing RCIA (white arrowhead) at the same level as ►Fig. 2c.

Fig. 3 A 29-year-old man with a 12-year history of left lower extremity pain, swelling, and varicose veins with worsening pelvic and subcutaneous varicosities. (a) Axial image from CT venography (CTV) revealing left common iliac vein (LCIV) compression (black arrow) by the right common iliac artery (RCIA) (black arrowhead). Note the subcutaneous collateral vessel (white arrowhead). (b) Axial image from the same CTV delineating the extensive cross-pelvic venous collateralization (white arrowheads). (c) Pelvic venography from the left GSV access revealing a chronically narrowed left common iliac vein (black arrowhead), extensive cross-pelvic collateralization (white arrowheads), and washout via the right common iliac vein (white arrow). (d) Fluoroscopic image after crossing the occlusion with an intravascular ultrasound (IVUS) catheter positioned at the point of occlusion. The tip of the catheter is noted by the black arrow, corresponding to the IVUS in ►Fig. 3e. (e) IVUS image highlighting compression of the LCIV (white arrow) by the RCIA (white arrowhead) at the same point as ►Fig. 3d. (f) Fluoroscopic image demonstrating a “waist” in the venoplasty balloon at the site of LCIV compression. This can confirm site of compression prior to stenting. (g) Fluoroscopic image from IVUS-guided stent deployment highlighting position of IVUS at the ilio caval confluence (white arrow), rostral aspect of a partially deployed Wallstent (black arrow), and the constrained portion of the stent (black arrowhead). The stent can be adjusted as needed based on overlap of the right common iliac vein at the ilio caval confluence. (h) Fluoroscopic image after initial stent deployment showing IVUS position (black arrow) with subsequent evaluation prior to additional stenting. (i) IVUS image corresponding to catheter position of ►Fig. 3h and measurement example. (j) Completion IVUS image confirming a widely patent LCIV (white arrow) and crossing RCIA (white arrowhead). Note the echogenicity of the stent. (k) Completion venography with widely patent left common and left external iliac veins. Robust anterograde flow is present. Cross-pelvic collateralization is no longer visualized.

Fig. 3 (Continued)

optimally covers the extent of the intravascular irregularity, and extends beyond the margin by approximately 1 cm on each side. This may entail stent extension into the IVC, which is generally well tolerated without compromising contralateral venous drainage, although we prefer to have no more than 50% coverage of the cross-sectional diameter of the IVC as seen by IVUS.⁵ Predilation of the vein, up to the nominal size of the stent, is helpful and suggested to facilitate stent placement and establish flow prior to deployment (►Fig. 2f). The authors commonly deploy Wallstents from the left groin access while observing the rostral end of the stent via IVUS, adjusting the partially deployed stent caudally as needed to minimize coverage of the right common iliac vein and IVC (►Fig. 1e; ►Fig. 3f–i). After stent deployment and angioplasty, repeat venography is performed to confirm prompt antegrade venous flow, improvement in the degree of venous compression, and collapse of collateral venous drainage (►Fig. 1f, g; ►Fig. 2g–i; ►Fig. 3j, k). Completion IVUS is used to document any intraluminal thrombus and potentially for sizing of additional stents, as needed.

Postprocedural Management

After completion of the procedure, patients are observed overnight and discharged the next day. Therapeutic anticoagulation and dual antiplatelet therapy are initiated with 1 mg/kg enoxaparin twice daily, clopidogrel 75 mg daily for 2 months, and aspirin 81 mg daily indefinitely. Patients are counseled on the importance of venous hygiene, smoking cessation, and the use of compression stockings. Initial clinic follow-up is scheduled 2 weeks postprocedure where patients are transitioned to oral anticoagulation, usually warfarin, and may have a concomitant lower extremity ultrasound examination. Subsequently, our patients return for follow-up venography at 6-, 12-, and 24-month intervals. We evaluate for in-stent stenosis and biopsy any such areas to evaluate the chronicity of thrombus formation. In the absence of a long-term indication for anticoagulation and if stent patency is maintained, we obtain a D-dimer 5 months

post stenting, and if negative we repeat the D-dimer 2 weeks after discontinuing anticoagulation. If venography reveals no in-stent stenosis and the D-dimer remains negative, we do not resume anticoagulation. If in-stent stenosis reveals acute thrombus or if the D-dimer is positive, we recommend patients to resume anticoagulation and reassess the patient in the next visit, with potential changes to their anticoagulation regimen as needed.

Discussion

In 1851, Virchow observed that left iliofemoral DVT was five times more likely than right iliofemoral DVT.⁶ Successive publications in the 1900s by McMurrich, Ehrich and Krumbharr, and May and Thurner revealed that 22 to 30% of studied cadavers had venous obstructions, termed “spurs” in the left common iliac vein, which was attributable to the overlying right common iliac artery.^{7–9} Cockett and Thomas subsequently defined the anatomic compression and noted that patients who developed left common iliac vein “spurs” could be asymptomatic due to venous collateral formation, though the “spurs” were irreversible and predisposed to venous thrombosis and lower extremity venous disease.¹⁰ Although the true incidence is not known, a review of all patients undergoing emergency department imaging found that 24% of patients had at least 50% compression of the left common iliac vein, which is in keeping with the historical cadaveric studies.¹¹ Three stages of MTS are recognized: stage I, asymptomatic left common iliac vein compression; stage II, the formation of an intraluminal spur; and stage III, left iliac vein DVT, distal to the compression. MTS afflicts younger and middle-aged females, particularly during pregnancy or after immobilization, and males of the same age groups.¹²

Historically, treatment consisted of anticoagulation and surgical thrombectomy with vein patch or bypass graft.^{3,13} Berger et al treated MTS with venous stenting in 1995.¹⁴ Additional series subsequently described combinations of pharmacologic thrombolysis and mechanical thrombectomy with angioplasty and stent placement through the late 1990s

and early 2000s.^{1,3,15–17} IVUS findings of MTS and its utility in the treatment were described in the early 2000s.^{1–3} Collectively, the technical success of venous stenting for nonthrombotic MTS and acute DVT approaches 100%, while chronic iliac occlusion approaches 90%. Clinical improvement with partial or complete relief of symptoms is expected in more than 80% of patients and in some reports exceeds 90%.^{5,17–19} Primary and secondary stent patency exceeded 80% in long-term studies with patients followed up for 72 months.^{5,17–19}

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