Chapter

Venous Interventions: From Lower-Limb Deep Vein Thrombosis to May-Thurner Syndrome and Budd-Chiari Syndrome

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Abstract

Over the past decade, there have been great innovations in the diagnosis of venous disorder since the introduction of dual-source computed tomography (DSCT) in 2006. It provides fast and reliable diagnosis of deep vein thrombosis (DVT) with the capability of full leveling of thrombus burden and allows early endovascular interventions with pharmacomechanical aspiration thrombectomy (PMAT) being performed aiming to reduce the post-thrombotic syndrome (PTS) and improve quality of life. The newly introduced ultrafast clot removal system, in patients who failed with PMAT, AngioJet, and EKOS, aids in rapid restoration of venous flow and decline of venous hypertension to mitigate the valve damage. Percutaneous transluminal angioplasty (PTA) and stenting yield high technical success rate of 93–96% and a promising short-term 1-year and 2-year patency of around 93% and 75–79%, respectively, for symptomatic May-Thurner syndrome (MTS). Based on the cumulative endovascular treatment experience in over 2000 cases in Xizou, China, some relevant precipitating factors are addressed, and a new classification of subtypes have been proposed to guide the proper selection of endovascular management of Budd-Chiari syndrome (BCS).

Keywords: deep vein thrombosis, computed tomographic venography, magnetic resonance venography, digital subtraction angiography, May-Thurner syndrome, Budd-Chiari syndrome, catheter-directed thrombolysis, pharmacomechanical aspiration thrombectomy, percutaneous transluminal angioplasty, stenting

1. Lower-limb deep vein thrombosis (DVT)

1.1 Introduction and background

It has been estimated that approximately 200,000 to 250,000 cases of lower-limb DVT occurred annually in the USA [1, 2]. Dated back as early as in 1860, German pathologist Rudolf Virchow initially depicted the gold rules of pathophysiology involved in DVT: the triad of (1) venous stasis, (2) endothelial damage, and (3) hypercoagulability. Venous stasis can be resulted from external compression,

traumatized venous wall injury as a consequence of indwelling catheters and devices, and infusion of chemotherapeutic agent and lipid substance as prescribed in hyperalimentation, as well as in lower cardiac output state and prolonged immobilization. Hypercoagulability is generally linked to hematological and genetic disorders, i.e., polycythemia rubra vera, antithrombin III deficiency, protein S/C deficiency, hyperhomocysteinemia, and cancerous disease, oral contraceptive and tobacco use, as well as pregnancy and postpartum state [3, 4].

2. Clinical presentations

The most common symptoms and signs in acute DVT (<2w) are a tender and swollen lower limb along with local heat on palpation. In subacute (2w–6 m) and chronic (>6 m) DVT, patients usually presented with chronic lower-limb swelling, pigmentation, and ulceration in lower calf and ankle. Among the complications resulted from lower-limb DVT, the most serious one is acute pulmonary embolism, which can precipitate acute pleuritic chest pain, tachycardia, hypotension, hypoxia, and death from acute decompensated right heart failure in those patients presented with massive pulmonary embolism. Despite adequate medication used, post-thrombotic syndrome occurs in approximately 20–40% of patients with subacute and chronic lower-limb DVT [2–4].

3. Diagnostic imaging modalities

A diversity of imaging tools, i.e., ultrasonography with color-flow mapping, CT venography, MR venography, radionuclide venography, and contrast venography, have been implicated in the diagnosis of lower-limb DVT.

3.1 Ultrasonography (US)

Grayscale ultrasonography is the first-line tool, which can delineate low echogenicity or nearly anechoic thrombi and a non-compressible vein in acute DVT, with a sensitivity and specificity of 90–100%, respectively. In chronic DVT, diagnosis can be made on the basis of detecting (1) a thickened vein wall with hyperechoic intraluminal projections, (2) a non-compressible vein, (3) little or no change of vein caliber with flow augmentation, and (4) the presence of collateral vessels. Color-flow Doppler ultrasound can assist in the detection of a patent versus non-patent venous lumen [5, 6]. The limitations of US are the inconsistency in the depiction of below-knee venous thrombi in terms of anatomical variants and small caliber as well as potential difficulty in assessing iliac veins [7].

3.1.1 Contrast venography

Prior to the invention of US, contrast venography, done with cannulation of a sizable pedal vein and a tourniquet compressing at the ankle, on a remote control unit with tilting facility, had been the diagnostic gold standard of lower-limb DVT. However, the foot back tends to be congestive and swollen, and a sizable vein for cannulation may not be available. A couple of methods have been raised to enhance the detectability including limb elevation and Ace wrap, digital compression, nitroglycerin paste, Doppler US localization with a pencil probe, and surgical cutdown. Technical difficulty does exist. In addition, there are certain diagnostic pitfalls and tricks that may result in false-positive and false-negative consequences,

mainly incomplete contrast opacification of the deep venous system and a variety of artifacts that may mimic intraluminal clots [8–10].

In acute DVT, the hallmark features are the detection of filling defects (thrombi) with simulated "tram-tracking sign" appreciated between the venous lumen and the venous wall and the acute venous cutoff identified not at the valve region. The affected veins tend to get distended along with the increased thrombi burdens [3, 9, 10]. In chronic DVT, the hallmark features are (1) clot retraction, (2) clot recanalization, (3) valve destructions, and (4) loss of normal venous pathway. In selective minor case, the affected veins may recanalize completely and appear essentially normal [10].

3.2 Magnetic resonance venography (MRV)

Over the past decade, there have been remarkable advances in the magnetic resonance (MR) imaging technology of deep venous system that prompt both non-contrast-enhanced and contrast-enhanced MRVs nearly as comparable as contrast venography in the diagnostic accuracy of DVT [11–13]. As shown in 2007, one meta-analysis evaluated the diagnostic sensitivity and specificity of MRV in lower-limb DVT to be 92 and 95%, respectively [14]. Aside from claustrophobia, the limitations of MRV include a lengthy procedure time, pregnancy, and patient with renal failure and with implanted metallic devices.

3.3 Computed tomographic venography (CTV)

CTV had been used for diagnosis of DVT at the single-slice CT era [14, 15]. Over the past decade with the emergence of dual-source computed tomography (DSCT) in 2006 by Siemens, tremendous advances in fundamental technology and clinical utility of CTV have been brought about. In our institution, since the availability of the second-generation DSCT (Somatom Definition Flash, Siemens) in September 2009, we were able to develop our own scanning protocol in CTV with superb imaging quality in the majority of the patients around 2013 (**Table 1** and **Figure 1**). Proper opacification of deep venous system of lower limb, starting from the lower inferior vena cava (IVC) down to the mid-level of tibioperoneal veins, can be acquired as a routine (**Figure 2**). Except in some selective patients with idiopathic increase in below-knee peripheral vascular resistance (PVR) and in patients with advanced

1. Anatomic collimation: Aortic bifurcation at L3–L4 level to toes
2. Contrast bolus injection: 120–140 ml of Ultravist 370 mg I/ml BMI: <23.9 120 ml, 24–27.9 130 ml, > 28 140 ml Flow rate: 4 ml/s, followed by a 40 ml saline chasing
3. Scan initiation: 3 min after contrast bolus
4. Scan mode: Flash
5. Scan parameters Acquisition: 128 × 0.6 mm Slice thickness: 5 mm Pitch: 2.5
6. Dose modulation: Care dose 4D
7. Effective radiation dose: 4–5 msv

Table 1.
Dual-source CT venography protocol.

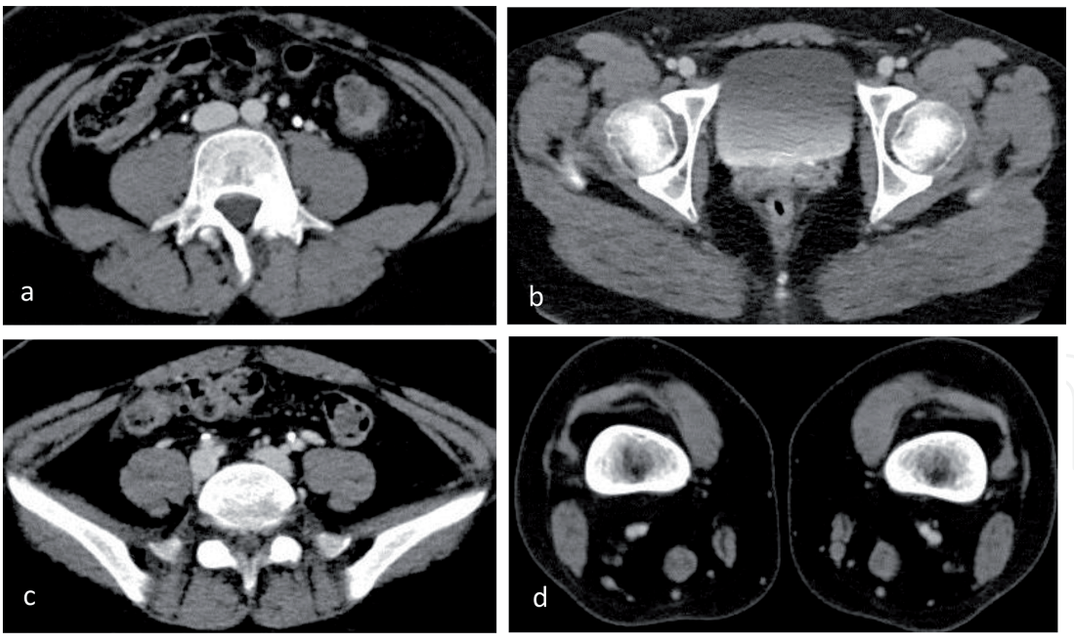

Figure 1.
(a-d) CTV depicted optimal opacification of venous structure from bifurcation of IVC to the lower level of popliteal veins.

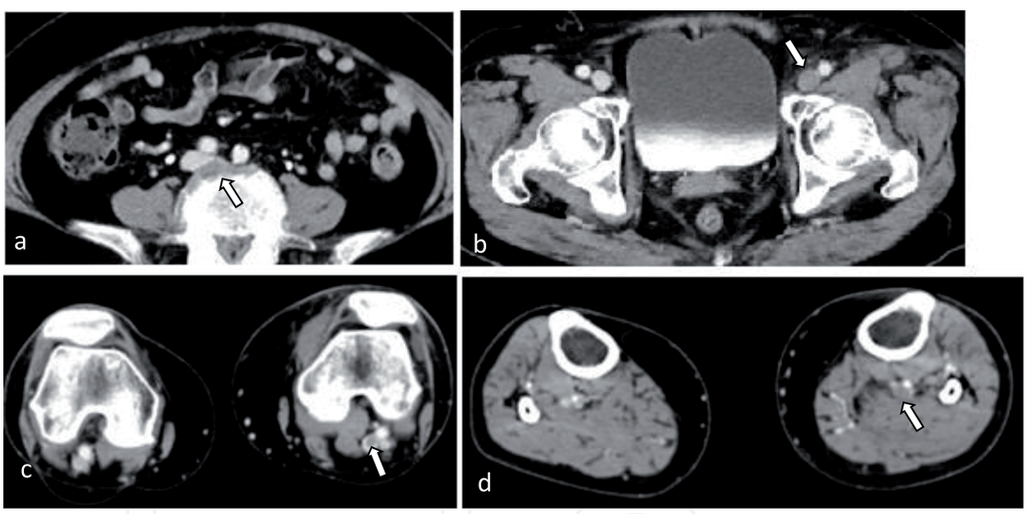

Figure 2.
(a–e) CTV depicted extensive DVT from the LCIV to tibioperoneal veins (arrows).

peripheral arterial obstructive disease (PAOD), both of which result in sluggish input arterial flow and thus suboptimal venous opacification at CTV. In patients suspected of coexisting PAOD, a CT arteriography can be performed in one set prior to proceeding of CTV (**Figure 3**). Approximately 80 ml of 370 mgI contrast medium is injected at rate of 4 ml/s, and the collimation is made at 64 × 0.6 mm to cover shortly above the aortic bifurcation down to the toes. The CTA is displayed in maximum intensity projection (MIP) and bone removal to facilitate visual reading. The tibioperoneal artery greater than 1.5 mm can be well delineated; however, in the lower calf where close alignment of the artery is adjacent to the bone cortex, loss of artery outline may be encountered due to equalization of post-processing threshold.

In a recent meta-analysis focused on the diagnosis of lower-limb DVT, the cumulative sensitivity and specificity are 96 and 95%, respectively [16]. The limitations of CTV are patients with significant renal failure, with idiopathic increase in below-knee PVR, and with severe PAOD.

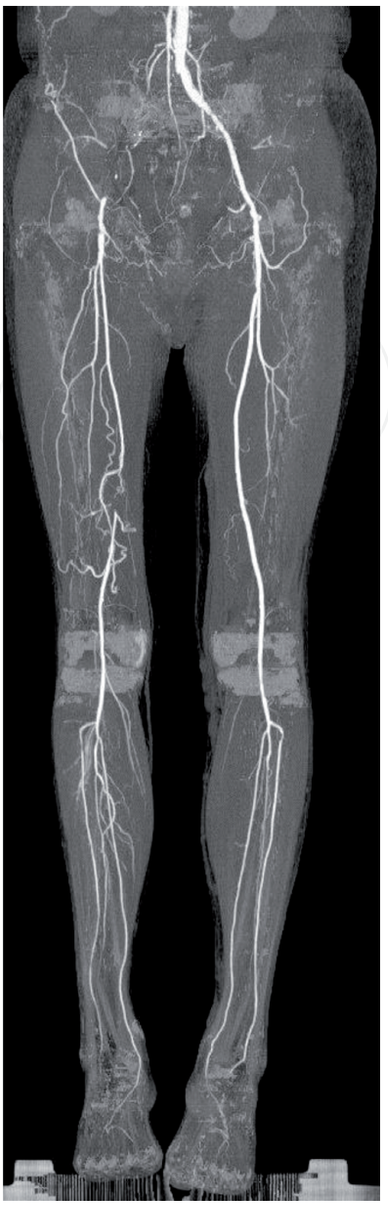

Figure 3.
CT arteriography at the same set as CTV showed high-grade imaging quality as well as identification of two discrete obstructions in the right iliac and superficial femoral arteries. Collateral arteries were also clearly depicted.

4. Indication for endovascular interventions in DVT

4.1 Introduction and background

Anticoagulation therapy has long been the first-line management in patients presented with acute DVT. In the 1980s, systemic thrombolysis using streptokinase demonstrated better resolution of thrombus than heparinization alone but carried an unacceptable risk of bleeding complication [17]. It was until the late 1990s when intraluminal catheter-directed thrombolysis (CDT) was initiated as an adjuvant to treat those patients in whom heparin worked slowly and patient could not tolerate intractable swelling of the affected lower limb. The treatment safety and the clinical efficacy of CDT were validated in iliofemoral DVT by Bjarnason et al. in 1997 [18]. Within the following years, after conducting a nationwide multicenter study, Mewissen et al. proposed that CDT was safe and effective and to be preferentially carried out in proximal iliofemoral and femoropopliteal DVT in patients presented

with symptomatic venous obstruction [19]. In 2006, the Society of Interventional Radiology published the guidelines for the treatment of lower extremity deep vein thrombosis [20]. (1) In a clinical subset of patients objectively documented with iliofemoral DVT, early debulking of thrombus burden can help mitigate post-thrombotic syndrome (PTS). (2) In patients presented with severe symptoms of massive swelling and intractable pain, early intervention helps reduce mobility and prevent progression to venous gangrene (**Table 2**). As the thrombus ages, approximately 10 to 14 days after acute onset, CDT becomes less effective in terms of thrombus debulking. As indicated in the CaVenT study, the incidence of PTS reduced to 14.4%, and the 6-m venous patency rate was 65.9% in CDT vs. 47.4% in control, respectively ($p = 0.012$) [21]. The long-term outcome of the ATTRACT study, a multicenter randomized controlled trial, was published in *The New England Journal of Medicine* in December 2017. The result showed no reduction of overall PTS at 2 years (48.0% vs. 47.4%), but a noteworthy difference of 6% declines in moderate-severe degree of PTS (24% vs. 18%, $p = 0.04$) [22]. Given that primary endpoint was not achieved, however, in selective patients presented with profound DVT symptoms and lower risk of bleeding, the benefit of CDT in reducing moderate-severe PTS and earlier symptomatic relief [23, 24] may gain reappraisal by clinicians and interventional radiologists. In addition, patients presented with significant venous steno-occlusive disease after CDT can be managed concomitantly with percutaneous transluminal angioplasty (PTA) or stent deployment to prevent recurrence of DVT [25].

4.2 Current technology in endovascular managements of DVT

4.2.1 Patient selection

In our institution, patients suspected of having DVT routinely received color-flow mapping and Doppler US and CTV. In advanced symptomatic patients presented with CT documentation of high-level (femoroiliac veins) or extensive involvement beyond popliteal and tibioperoneal veins but with lower risk of bleeding, CDT is conducted with pharmacomechanical thrombolysis with continued infusion of urokinase for 48–96 hours with an aim for early thrombus debulking and rapid symptomatic relief. While those presented with mild to moderate symptom and CTV documented popliteal and/or tibioperoneal DVTs, conventional anticoagulation is justified.

4.2.2 Access site of CDT

Typically, with the patient in prone position, the popliteal vein of the affected limb is accessed with US guidance. A 3-F micropuncture set (Cook Corporation, Indiana, USA) is used for a safe puncture and access into the popliteal vein as well as to prevent subsequent focal bleeding. The cannula is replaced with a 9-F introducing sheath for easy venous access.

1. Percutaneous aspiration thrombectomy
2. Percutaneous pharmacomechanical thrombectomy
3. AngioJet (rheolysis)
4. Device-assisted thrombolysis Balloon-assisted system Ultrasound-assisted system (EKOS)

Table 2.
Methods of endovascular interventions for deep vein thrombosis.

4.2.3 CDT with pharmacomechanical aspiration thrombectomy (PMAT)

A 5-F pigtail catheter was inserted through the sheath, which is moved up and down a couple of times through the thrombosed segment in popliteofemoroiliac veins, accompanied with simultaneous infusion of 100,000–250,000 IU of urokinase, to assist macerating the thrombus burden for 15 min. An 8-F 60-cm-long multipurpose guiding catheter, attached with a 50-ml syringe, is used to aspirate the macerated thrombi (**Figure 4**). In the case presented with significant residual thrombi, a multi-slit infusion catheter of suitable length (Fountain infusion catheter, Merit, USA) was embedded into the distal-most segment and spared the proximal-most segment for sustained continual infusion of 500,000–1,000,000 IU of urokinase per 24 hours for up to 48–96 hours. The patient is kept in a ACU/ICU for close monitoring of general condition and bleeding. Concomitant intravenous infusion of heparin 20,000 IU per 24 hours to prevent new thrombus formation around the infusion catheter was also deemed necessary. Daily check of aPTT (<1.5 time of control level) and fibrinogen and platelet count was mandatory. The patient is sent back to DSA suite every 8–12 hours to check for the resolution of thrombi and repositioning of infusion catheter to facilitate further thrombus resolution toward the proximal end until satisfactory results are achieved. The infusion dose of urokinase can be adjusted depending on the bulk of residual thrombi. After successful CDT, the patient is put on anticoagulation with warfarin for at least 6–12 months.

4.2.4 CDT with new devices by using pharmacomechanical catheter-directed thrombolysis

The consensus that the earlier the thrombi lysed, the less severe the PTS will be paves the way for a better quality of life and less daily limitation of physical activity. Speedy thrombus resolution to salvage valve damage and venous insufficiency sounds reasonable and practical. In recent years, an ultrasound-emitting thrombolytic infusion catheter (EKOS Corporation, Bothell, WA) and the AngioJet Rheolytic Catheter System (MEDRAD Interventional, Minneapolis, MN) have become available in our institution (**Table 2**). In terms of being high-cost treatment modalities, they both are reserved for those patients who failed to respond well with PMAT (**Figures 5** and **6**).

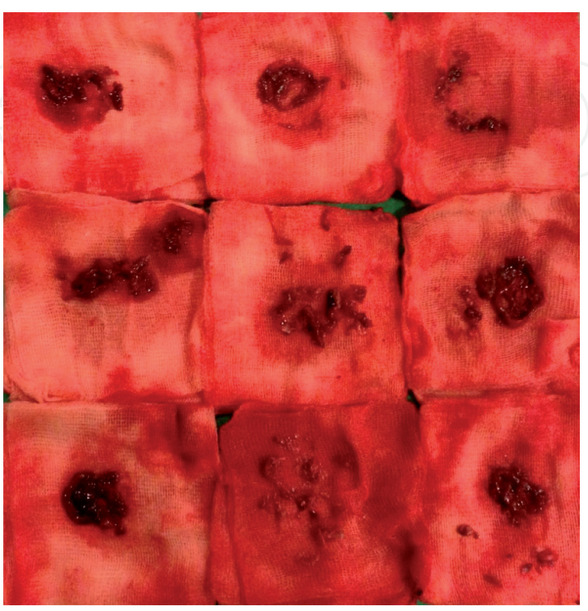

Figure 4.
Relatively fresh and subacute thrombi were aspirated by PMAT from the left iliofemoral veins in a 32-year-old female taking oral contraceptive pills for dysmenorrhea.

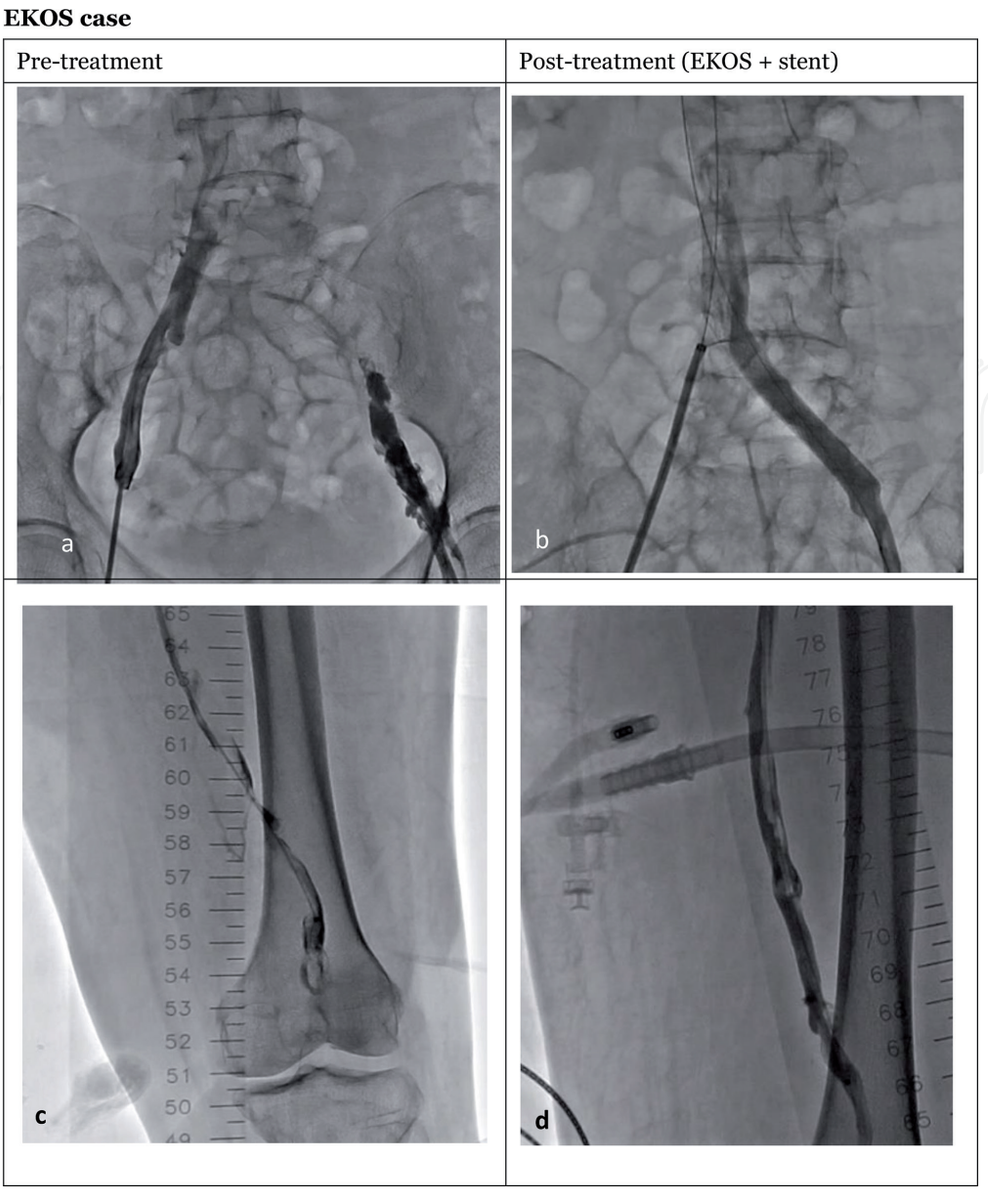

Figure 5.
An 81-year-old female with lower third esophagus adenocarcinoma, cT3N0Mb, Stage III under palliative chemotherapy, suffered from left leg swelling, and CTV documented massive DVT in iliofemoropopliteal veins. (a and c) Nearly complete obstruction of left iliofemoropopliteal veins by DVT. (b and d) s/p EKOS catheter for enhanced CDT treatment and s/p PTA and Wallstent deployment in left common and external iliac vein restored good blood flow.

4.2.5 Percutaneous transluminal angioplasty and stenting

After successful PMAT is achieved, the whole affected proximal venous pathway should be documented with DSA for any residual steno-occlusive disorder. A 0.035″ hydrophilic guide wire (Terumo, Tokyo Japan) is negotiated, and a 4-F Teflon-coated catheter (Terumo, Tokyo Japan) is advanced through the lesion. A 0.035″ stiff hydrophilic guide wire (Terumo, Tokyo Japan) is exchanged. Sequential ballooning was conducted, with 3-mm, 5-mm, and 8-mm balloons until the balloon waist was completely gone, to accommodate a self-expandable stent of sufficient size and length, mainly the Wallstent (Boston Scientific, Massachusetts, USA). Postdeployment dilation is carried out with a balloon catheter of appropriate size to scaffold the venous fibrosis that frequently comes across with significant venous stenosis. Follow-up DSA is performed to document the technical success, which is graded as a residual stenosis of <30% [26, 27] (**Figure 7**). Aspirin 100 mg and clopidogrel 75 mg are recommended for at least 3 months after stenting.

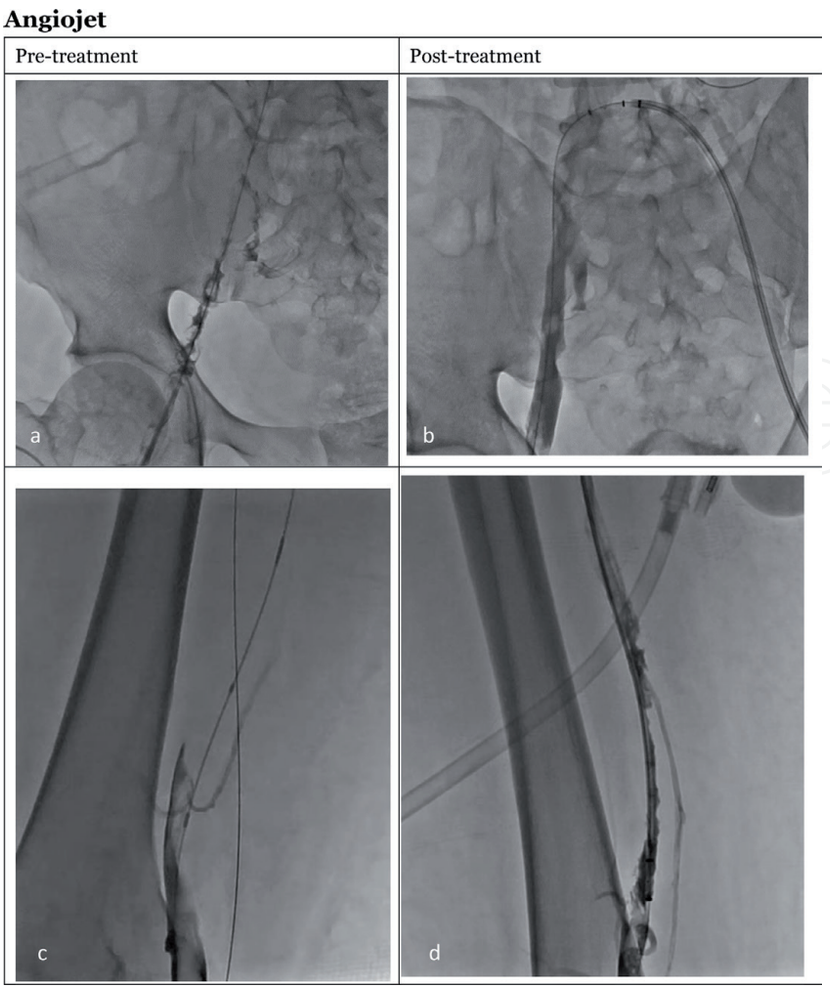

Figure 6.
A 31-year-old obese male with hypertension suffered from gunshot wound over the abdomen and complicated with diffuse right leg iliofemoral DVT. (a and c) Diffuse DVT in the right iliofemoropopliteal veins due to immobilization. (b and d) After AngioJet, good blood flow regained.

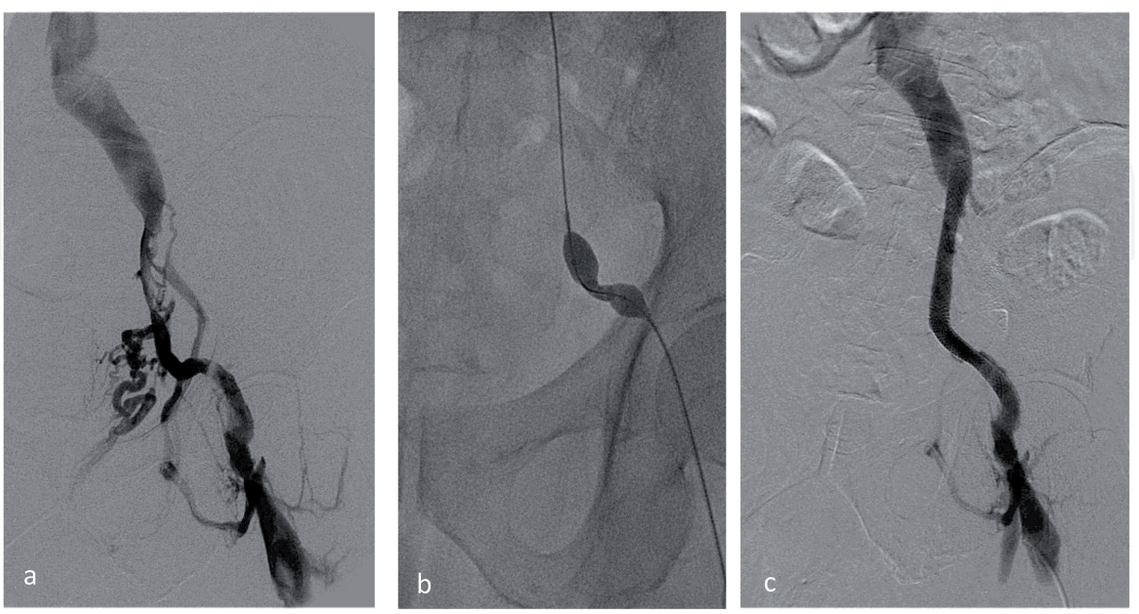

Figure 7.
A 48-year-old male developed chronic DVT in the left iliofemoral veins as a complication of dwelling perm catheter and successfully managed with PTA and two overlapping 8 m and 10 cm Wallstents. At 8-year follow-up, the stents remained patent. (a) Contrast venography revealed long-segment stenosis of the left iliofemoral veins and venous collaterals. (b) Balloon waist at predilation with an 8-mm balloon catheter. (c) Immediately after stenting, good flow is restored and minimal venous collaterals visualized.

5. Endovascular management of May-Thurner syndrome (MTS)

5.1 Introduction and anatomical background

MTS has two synonyms: Cockett syndrome and iliac vein compression syndrome. In 1983, Dr. Ernest Ferris for the first time proposed May-Thurner syndrome in memory of Dr. May and Dr. Thurner for their relevant contributions [28]. The first description of a septum-like structure in the left common iliac vein (LCIV) was made in 32% (10 out of 32) of cadavers, in 1906 by an anatomist McMurrich, with which a congenital remnant was implicated as such [29]. In 1943, Ehrich and Krumbhaar through anatomic dissection in 412 cadavers found that obstructive lesion in the left common iliac vein (LCIV) in 23.8 and 33.8% of the lesion occurred after the first decade. The lesions were regarded as acquired and not congenital. In 1957, May and Thurner, through autopsy in 430 cadavers, demonstrated that among 19% of cadavers, the overriding right common iliac artery (RCIA) compressed the LCIV against the spine [30]. Other investigators also presented different incidence of spurs in the LCIV by different imaging tools: 14% by Negus et al. [31], 50% by Vollman et al. with vascular endoscopy [32], and 62% by Juhan et al. with contrast venography [33], respectively.

5.2 Pathophysiology of MTS

Long-lasting pulsatile injury elaborated by the overlying RCIA prompted projectile fibrotic spurs into the lumen of the LCIV, which in turn resulted in accumulation of elastin and collagen over the spurs and extensive intimal proliferation of venous wall. Three varieties of classic venous spurs had been addressed, especially associated with a lower bifurcation position of the abdominal aorta [29]. Other theories had been implicated as possible causative factors, namely, compression by pregnant uterus [34] and by sigmoid colon associated with constipation [35]. Currently, with availability of modernized cross-sectional imaging modalities, like intravascular ultrasound and optic coherence tomography, the venous spurs can be well depicted and precisely documented the severity of venous obstruction than contrast venography [36–38]. Regardless of spur-forming mechanism [36], congenital or acquired, in case predisposed to hypercoagulability, thrombosis of the LCIV then issues initially at the stenosed segment and propagates in antegrade and retrograde fashions. However, in chronic MTS, the patient may be asymptomatic for quite a certain period of time if sufficient venous collaterals have developed [39].

5.3 Clinical manifestation and staging

MTS has a strong tendency to affect young and middle-aged woman (mean age, 42 y/o), although it does affect man [40]. In acute stage, the majority of patients frequently presented with sudden onset of pain and swelling of the left lower extremity due to the accompanying DVT. In chronic stage, the symptoms may be more or less vague to define but generally comprised of persistent edema, heaviness, lower calf and ankle skin pigmentation, venous claudication, and ulcer as well as varicose veins [41, 42]. Rarely, in some selective patients affected with phlegmasia alba dolens and phlegmasia rubra dolens, limb salvage may provide an extremely difficult challenge for the multidisciplinary team physicians. Based on the clinical and imaging findings, MTS is classified into three stages: Stage I, asymptomatic LCIV compression; Stage II, presence of intraluminal venous spurs; and Stage III, occurrence of DVT in the LCIV (**Figure 8**) [43, 44]. Failure to correct

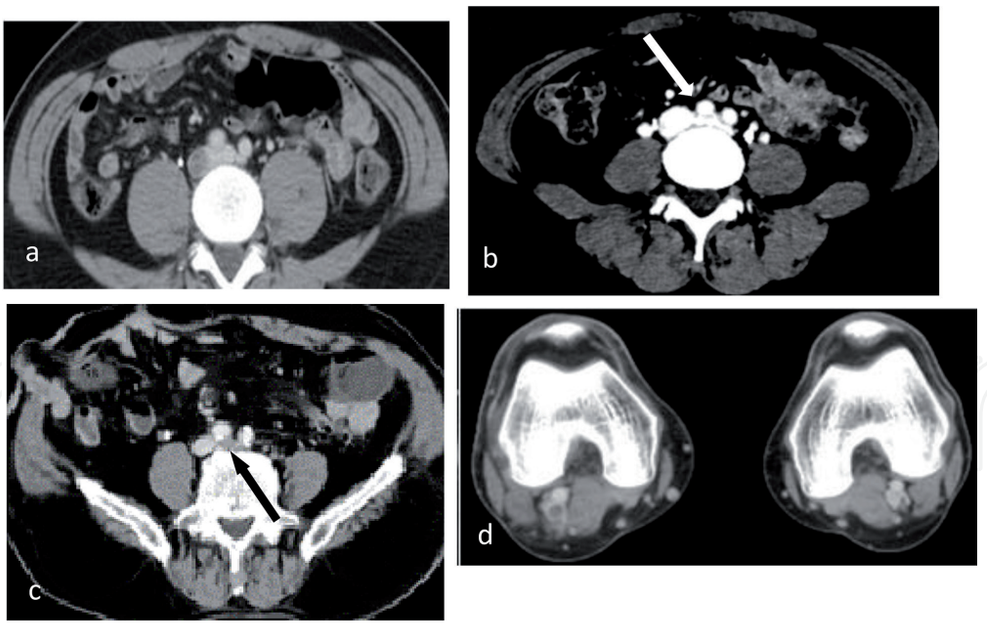

Figure 8.
Classification of MTS into three clinical stages. (a) CTV showed Stage I MTS 9 (arrow) incidentally while imaging of DVT. (b) CTV showed Stage II MTS presented with venous spur. (c and d) CTV showed Stage III MTS presented with DVT (black arrow).

the underlying anatomic substrate of the LCIV, complication of MTS can include pulmonary embolism, chronic venous stasis, PTS, and iliac vein rupture [39].

5.4 Diagnostic imaging modalities of MTS

As mentioned in the imaging diagnosis of DVT, a variety of imaging tools can offer a figure of diagnostic sensitivity and specificity. Each has its own advantages, disadvantages, and limitations. Among them, US is the first-line followed by CTV, MRV, and contrast venography to objectively document the level of DVT and grade the severity of iliac vein obstruction. A stenosis of >50% in the LCIV is considered as hemodynamically significant. As the stenosis percentage of the LCIV may be periodically altered with the circulating blood volume and the body position [38, 39], in suspicious case, a pressure gradient across the RCIV and LCIV of >2 mmHg at rest and > 3 mmHg with exercise aids in making a definite diagnosis. Over the past decade with the availability of second generation of DSCT scanner (Somatom Definition Flash, Siemens) in our institution, CTV has nearly replaced others and become the first-line imaging modality for MTS in terms of rapid dataset acquisition and precise leveling of steno-occlusion of the LCIV and the associated DVT [45–47]. In conjunction with 3-D volume rendering technique at CTA, the compressed segment of the LCIV by the overlying RCIA can be appreciated more precisely than contrast venography. Of paramount importance is the precise depiction of floating thrombi in the lower segment of the IVC with CTV, which may prompt the strategy to implant a temporary IVC filter to prevent pulmonary embolism during endovascular procedure.

5.5 Endovascular treatment of MTS

The endovascular treatment of MTS by PTA and stenting has been reported in the literature to be minimally invasive, technically feasible, and safe and clinically effective. Isolated PTA is not effective, similar to the result in other large central veins. The access site is from the left popliteal or common femoral veins.

5.5.1 Percutaneous CDT in the treatment of MTS with extensive DVT

Pharmacomechanical aspiration thrombectomy (PMAT), as described in the treatment of isolated DVT, is well suited for MTS in acute stage presented with extensive thrombi, which is thoroughly dictated in Subsection 4.2.3.

5.5.2 Percutaneous transluminal angioplasty (PTA) and stenting for MTS

In patients with isolated stenosis but free of DVT, PTA and stenting are a straightforward procedure. In 1995, Berger et al. reported the first successfully

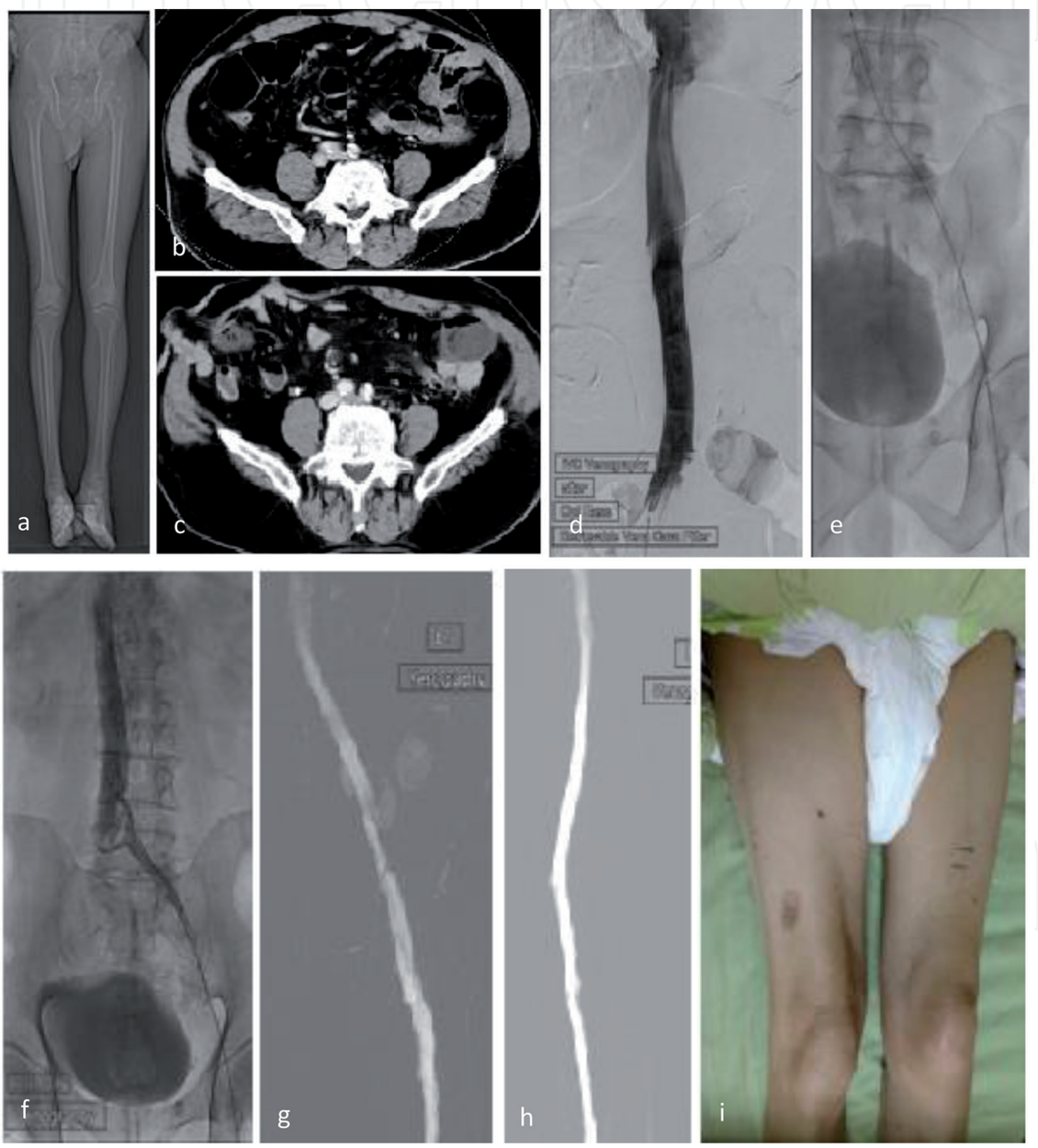

Figure 9.
A 70-year-old male with Stage III MTS successfully treated with PTA and stenting. (a) CT topography showed remarkable swelling of the entire left lower extremity. (b) CTV incidentally showed Stage II MTS half year age at workup for colon cancer. (c) CTV showed Stage III MTS with diffuse DVT from the upper left tibioperoneal vein to the common iliac vein. (d) Contrast venography showed minimal floating thrombin into the IVC (arrow). (e) A Teflon-coated 4-F catheter successfully navigated through the tight stenosis in the common iliac vein (arrow). (f) After sequential PTAs, a minimal channel was reanalyzed in the LCIV. (g and h) After a 14 mm x 80 mm Wallstent deployment and thrombolysis with a multi-slit infusion catheter for 48 hours, successful recanalization was achieved. (i) At discharge (8 days after admission), the left leg limb was even smaller than the right leg.

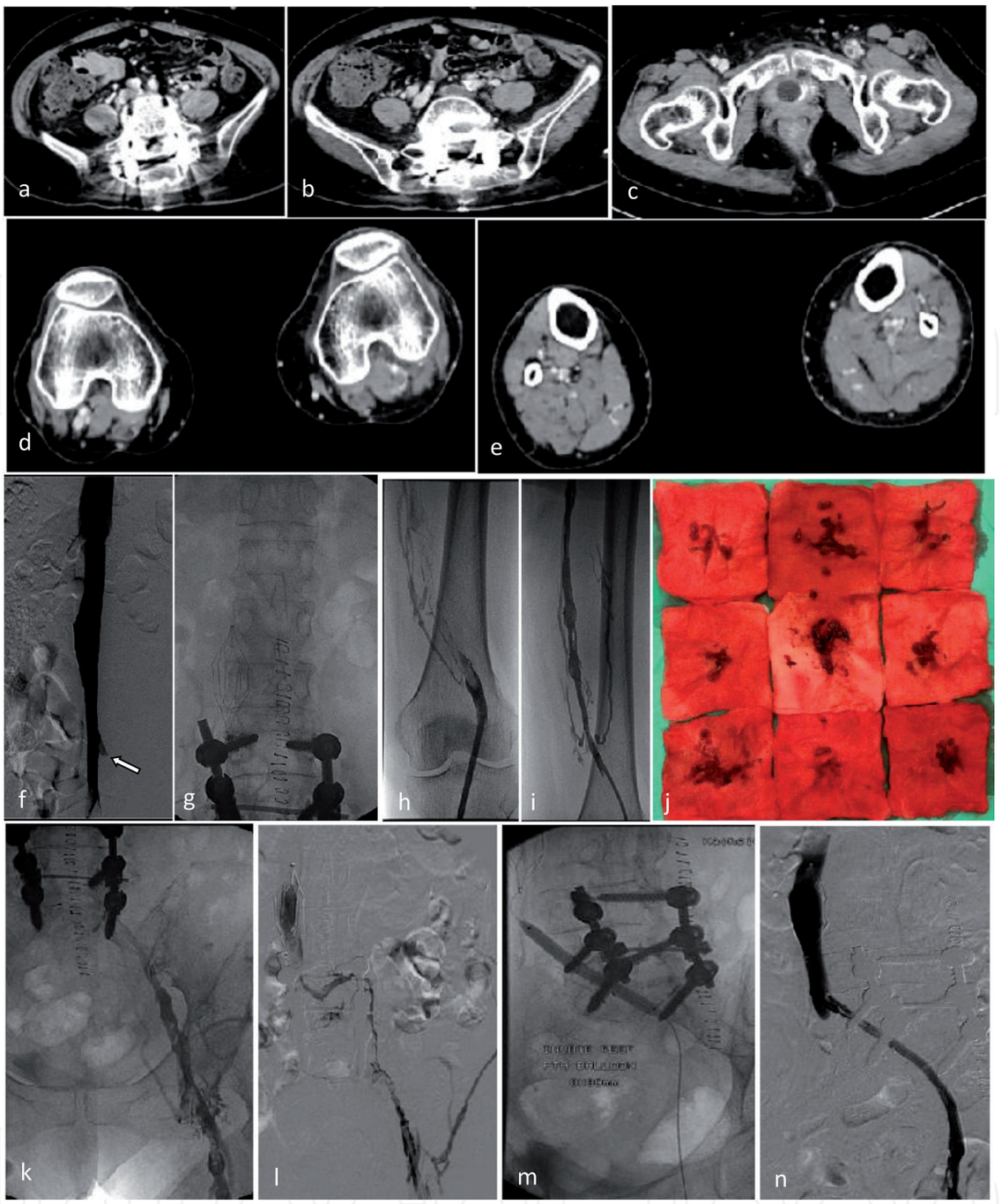

Figure 10.
A 65-year-old schizophrenic female suffered from subacute Stage III MTS, successfully recanalized with PMAT and Wallstent deployment. (a–e) CTV showed excellent depiction of massive DVT spanning from the lower IVC down to the left tibioperoneal vein. (f and g) Venography demonstrated floating thrombi in the lower IVC (arrow), and an Optease caval filter was implanted to prevent pulmonary embolism. (h–j) Subacute thrombi were removed with aspiration thrombectomy. (k and l) After aspiration thrombectomy, venography revealed minimal residual thrombi and long-segment tight steno-occlusion of left iliofemoral veins and venous collateral. (m and n) After sequential PTAs and Wallstent deployment, the venous flow was restored, and at 2.5-year follow-up, the stent remained patent.

deployed stent to decompress left iliac vein obstruction. After successful PMAT is achieved, as done exactly in the treatment of DVT section, a 0.035″ hydrophilic guide wire (Terumo, Tokyo Japan) is vigorously negotiated through the steno-occlusion in the LCIV, and a 4-F Teflon-coated catheter (Terumo, Tokyo Japan) is advanced in to the lower IVC. A 0.035″ stiff hydrophilic guide wire (Terumo, Tokyo Japan) is exchanged. Sequential ballooning was conducted, with 3-mm, 5-mm, and 8-mm balloons until the balloon waist is completely gone, to accommodate a self-expandable stent of sufficient size and length. Wallstents (Boston

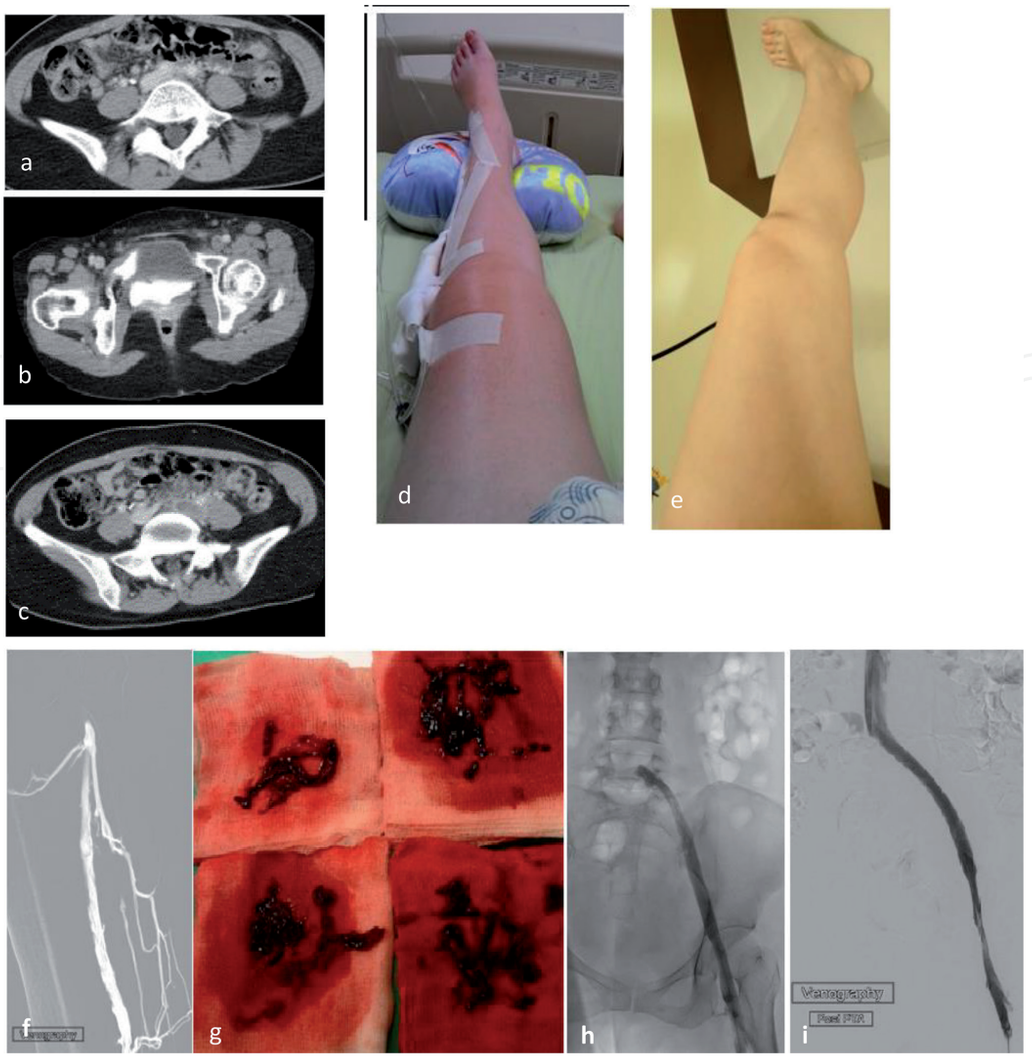

Figure 11.
A 41-year-old with MTS Stage III presented in acute stage was successfully managed with PMAT, PTA, and stenting. (a–c) CTV depicted extensive DVT in the left femoroiliac veins. (b) Pre-treatment photo showed swelling of the left leg and cellulitis. (e) Posttreatment photo showed disappearance of swelling and healing of cellulitis at 1-month follow-up. (f and g) Venography showed extensive DVT above the left femoral vein and relatively fresh thrombi obtained by PMAT. (h and i) After PTA and stenting in the LCIV, good patency was depicted, and minimal residual thrombi were treated with warfarin.

Scientific, Massachusetts, USA) of 12–14 mm in diameter and 80–120 mm in length are used to span the lesion. During the deployment, the Wallstent is initially deployed in the lower IVC, after which the whole unit is pulled down to retain a distal landing zone in IVC of approximately 1–1.5 cm and spans over the entire steno-occlusive segment with a proximal landing zone of >2 cm. Postdeployment dilation is carried out with a balloon catheter of appropriate size to scaffold the venous spurs and fibrosis that frequently accompany MTS. Follow-up DSA is performed to document the technical success, which is graded as a residual stenosis of <30% (**Figures 9–11**) [26, 27]. Aspirin 100 mg and clopidogrel 75 mg are recommended for at least 3 months after stenting. Kaplan-Meier life table analysis is used to calculate the primary and secondary patency rate in the follow-up periods. Repeat PTA/stenting as indicated is relevant to maintain the long-term patency.

5.5.3 Technical success and treatment outcome of MTS

As reported in the literature, the technical success rates ranged between 93 and 96% [42–44, 47]. With repeat PTA/stenting, the midterm patency rates were

promising and ranged between 95 and 100% [47, 48]. Although the prevalence of overall PTS did not decline with the adjunct use of PMAT, however, the reduction of moderate to severe degree of PTS was noteworthy. As to the long-term patency, it reserves meticulous monitoring.

6. Budd-Chiari syndrome

Budd-Chiari syndrome (BCS) occurs when obstruction of the hepatic venules anywhere along the inferior vena cava (IVC) to the right atrium junction can lead to portal hypertension. BCS can be life-threatening. The prevalence of BCS has different geographic variances. In Western countries, the prevalence of BCS is rare, occurring in about 1 in every 2.5 million people, whereas in some Asian countries, such as China, India, and Nepal, BCS is a common disease. For instance, in China's Yellow River and Huaihe River region, 6.8–12 people per 100,000 people suffer from BCS; and more than 20,000 BCS have been documented in China [49]. Differences in obstruction sites can also be seen between Western and Asian populations. In the West, hepatic vein occlusion is more common, and venous congestion involving the IVC is less documented. However, in Asia, the diaphragm-type Budd-Chiari syndrome accounts for as high as 70% of all cases. Geographical variance, obstruction location, and pathological and anatomical differences have led to significant differences in clinical symptoms, treatments, and prognosis of BCS in the East and West. The development of modern imaging has enabled observing the hepatic vein, portal vein, inferior vena cava, and azygous vein in vivo, which revealed discordances in comparison to traditional liver biopsy and autopsy findings as described in the previous literature. Therefore, it is necessary to revisit BCS.

6.1 Etiology

BCS is considered primary or secondary based on the origin of the hepatic venous outflow obstruction. When the hepatic vein outflow tract is compressed or infiltrated, it is regarded as secondary BCS. Some examples include a primary or metastatic tumor of the liver, leiomyomas of the inferior vena cava, and tumor thrombus. So far, the most common etiology of primary BCS in Western countries is thrombosis, and 25–46% of patients are in prethrombotic or hypercoagulable states. Therefore, primary BCS is predisposed by prethrombotic conditions [50]. However, in China, the etiology of BCS is different. The current research shows that in China, the primary thrombotic disease is not a common cause of BCS. Studies have demonstrated that (1) patients with inferior vena cava obstruction have elevated blood vascular endothelial growth factor (VEGF) [51], (2) there is higher groundwater iodine concentration in high-prevalence areas [52], (3) BCS patients have higher blood and urine iodine concentrations [53], (4) people living in rural areas have a higher prevalence, (5) restenosis can occur despite balloon venoplasty of the hepatic vein and inferior vena cava [54], and (6) membranous reformation can occur despite surgery.

Statistical analysis of 2406 patients found that the proportion of hepatic vein occlusion in adolescents under 30 years of age was significantly higher than in patients over 30 years of age [55, 56]. The proportion of inferior vena cava obstruction increases with increasing age in patients aged 30–79 years old. In 256 BCS patients in the 60–69 age group, 222 cases have inferior vena cava obstruction, and 34 cases have hepatic vein obstruction (7.2%); only 1 case of 34 cases of BCS in 70–79 years old was hepatic vein obstruction type (2.9%).

6.1.1 Iodine and vascular endothelial proliferation

Guo et al. found that in the groundwater iodine concentration of drinking water in 128 patients with inferior vena cava obstruction in Heze, Shandong Province, 98.44% of the 128 patients had iodine content of 150 μg/l or more, of which 150–300 μg/l accounted for 27.35% and 300 μg/l accounted for 71.09%. This result indicates that an area with high groundwater iodine concentration is at high risk of developing BCS [52]. Further studies by Zhuang et al. found that blood iodine levels in 233 BCS patients were also higher than that in the healthy population [53] (see **Table 3**).

The results showed that the serum iodine concentration of BCS patients was more than five times higher than that of the control group. On this basis, we tested the urine iodine of BCS patients and found that the urinary iodine of BCS patients was also higher than the average population. Li et al. carried out in vitro research on the culture of umbilical vein endothelial cells and fibroblasts using different concentrations of iodide culture medium. It was found that at iodine concentration of 300–500 μg/l, the proliferation of vascular endothelial cells and hyperplasia of fibroblasts can be induced. It is speculated that high iodine concentration can lead to vascular endothelial cell proliferation [57, 58]. Our study of the inferior vena cava septum revealed that the vascular endothelium of the inferior vena cava gradually thickened and merged into a septum. The structure of the septum was fibrous connective tissue in the middle, and the upper and lower layers were vascular endothelium (**Figure 12**). However, the mechanism of how vascular endothelial cells migrate to form inferior vena cava septum is still unclear.

Group	n	Serum iodine (μg/l)	Ranges (min-max)
IVC-type BCS	144	347 ± 272.3[a]	4.3–1095.1
HV-type BSS	71	237 ± 231.1[a]	12.3–937.2
MIX-type BCS	18	307 ± 134.4[a]	72.1–512.7
Control group	60	76.3 ± 25.7	30.2–97.4

Values are given as means±SD.
[a]Versus control group ($p < 0.05$)

Table 3.
Serum iodine levels in patients with BCS in different types and in the control group.

6.1.2 Vascular endothelial growth factor (VEGF)

In studies using enzyme-linked immunosorbent essay of 40 patients with inferior vena cava obstruction, Han et al. revealed that patients with inferior vena

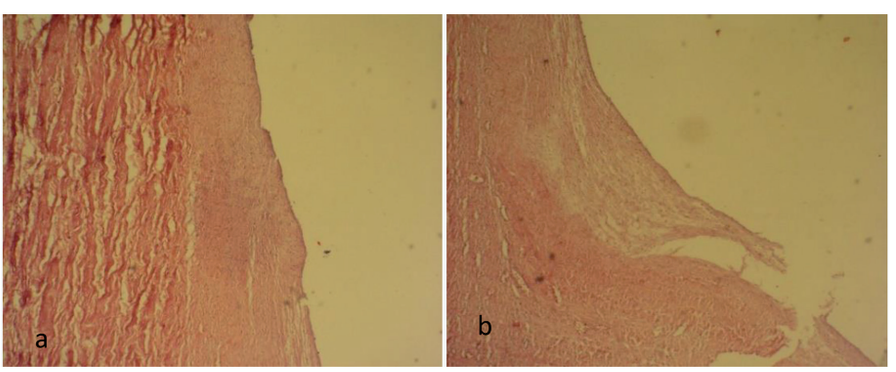

Figure 12.
Thickening of the vascular endothelium above the inferior vena cava septum (a). Lateral migration of thickened vascular endothelium cells and fibrous connective tissue forming the septum (b).

cava obstruction have serum VEGF concentration four times higher than that of the control group. These findings hint that the formation of the IVC septum may be related to inferior vena cava endothelial damage and repair [51] (see **Table 4**).

6.1.3 Abnormal bone marrow hyperplasia and gene mutation

A significant advance in myeloproliferative neoplasm research was the discovery of the Janus kinase 2 (JAK2) V617F mutation in 2005. This mutation was detected in 90% of patients with polycythemia vera and 50% of patients with essential thrombocytopenia and primary myelofibrosis. JAK2 is a member of the Janus family of tyrosine kinases. A retrospective analysis by Kiladjian showed that the detection of the JAK2 V617F mutation was the first diagnostic step in the diagnosis of BCS basic research [59].

In China, Wang collected 65 cases of BCS blood samples from October 2009 to July 2010. EDTA-K2 anticoagulation treatment, DNA extraction, primer design, the establishment of allele-specific polymerase chain reaction system, and comparison of point mutations at nine sites between the study group and control group were performed. After allele-specific PCR, there were nine positive mutations in the study group JAK2 V617F with a mutation rate of 13.85% (9/65). The control group did not have this point mutation. The mutation rate of JAK2 V617F was significantly lower than that of BCS patients in Western countries. The results show that differences exist in the pathogenesis of Chinese BCS compared with that of Western countries [60].

6.1.4 Acquired condition

Many acquired conditions can provoke the occurrence of BCS. Acquired prethrombotic lesions such as Behcet's disease, antiphospholipid syndrome, hyperhomocysteinemia, and paroxysmal nocturnal hemoglobinuria (PNH) promote BCS development. Behcet's disease, paroxysmal nocturnal hemoglobinuria, and oral contraceptives accounted for less than 1% of the study population.

6.2 Clinical manifestation and diagnosis

The clinical manifestations of portal hypertension caused by venous obstruction and posthepatitic cirrhosis and drug-induced (*Gynura segetum*) hepatitis are very similar, which often lead to misdiagnosis. For patients developing abdominal distension, hepatosplenomegaly, massive and refractory ascites, gastrointestinal bleeding, and hypersplenism leading to symptoms of white blood cells and thrombocytopenia, but without past medical history of hepatitis, chronic alcoholism, nor a history of taking *Gynura segetum*, hepatic venous occlusion should be considered. The clinical manifestations of inferior vena cava occlusion have characteristic signs including swelling, hyperpigmentation, varicose veins, and long-term unhealed ulcers of bilateral lower extremities. In addition, bulging varicose veins above the skins of the chest and abdomen wall, longitudinal varicose veins, and the lower back varicose veins are also indicative of inferior vena cava occlusion (**Figure 13a–f**). Non-specific clinical

Group	Number	Average VEGF concentration (ng/ml)	Standard error	t-value	p-value
Control group	40	23.15	19.27	5.273	$p < 0.001$
Study group	40	5.63	8.38		

Table 4.
VEGF concentration value t-test result.

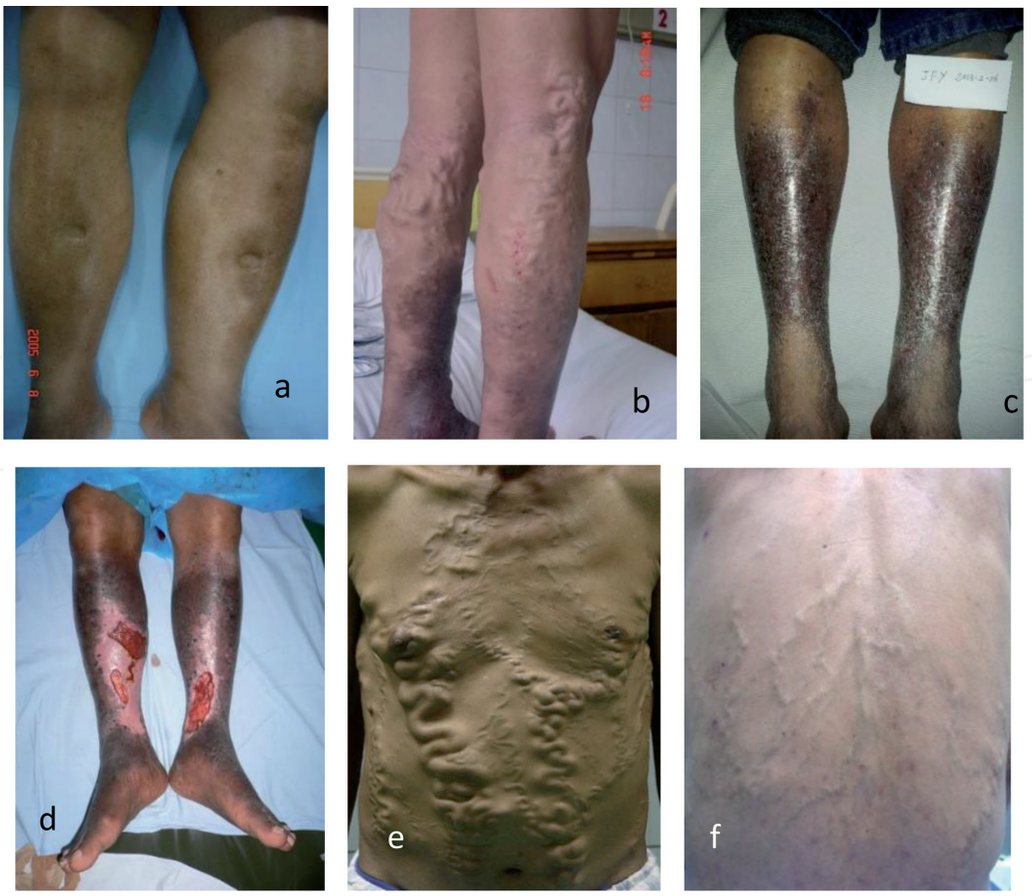

Figure 13.
Clinical manifestations. (a) Swelling of the lower extremities. (b) Varicose veins of the lower extremities. (c) Pigmentation of the lower extremities. (d) Ulcers of bilateral lower extremities. (e) Thoracic and abdominal wall varices. (f) Lumbar dorsal varices.

manifestations of inferior vena cava obstruction include fatigue, exercise-induced asthma, irregular menstruation in women, habitual abortion, and primary infertility.

6.3 Imaging diagnosis

The diagnosis of BCS is based on the manifestations of hepatic venous outflow obstruction. This obstruction can be accurately displayed by noninvasive imaging such as Doppler ultrasound, CT, or magnetic resonance imaging (MRI). Doppler ultrasound is considered to be the preferred initial technique, with the ability to directly show the obstruction and reverse blood flow of the hepatic vein and inferior vena cava. The formation of collateral branches between hepatic veins is an indirect sign of hepatic vein obstruction. Ultrasound has a high sensitivity and specificity for the diagnosis of BCS.

CT scan and MRI are effective methods for diagnosing obstruction of the hepatic vein outflow tract. MR angiography is superior to CT, ultrasound, and angiography in demonstrating anatomic structures of the hepatic veins, accessory hepatic veins (AHV), inferior vena cava, azygous veins, and superficial veins of the abdominal wall (**Figure 14a**). Magnetic resonance angiography can directly display the hepatic veins, the inferior vena cava septum and its thickness, length of segmental occlusion of the inferior vena cava and hepatic vein, location and size of thrombus, as well as the location, orientation, thickness, and number of collateral circulations. Although it is not as effective as Doppler ultrasound in recording the intrahepatic collateral branches, it is unique in showing the extrahepatic collateral and collateral circulations in the abdominal cavity and the abdominal wall (**Figure 14b**). MRI and CT

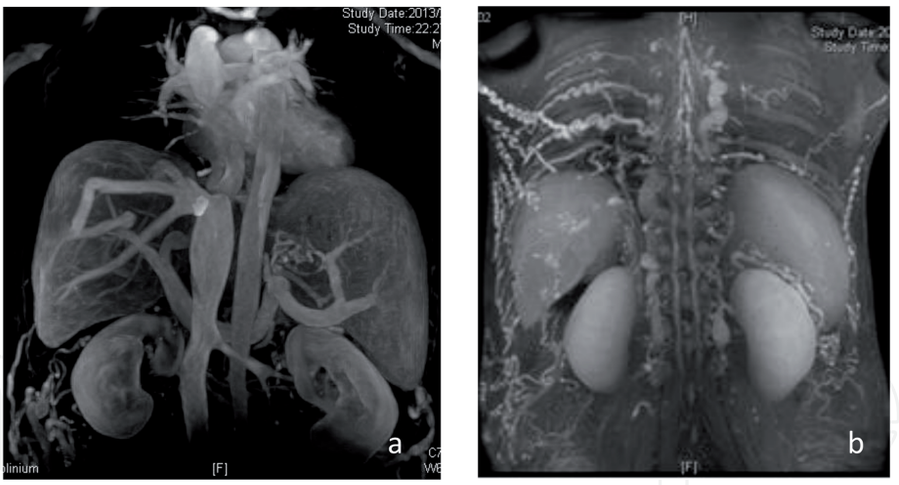

Figure 14.
MRV images. (a) MRV directly shows the hepatic vein, inferior vena cava, and portal vein. (b) MRV shows extensive extrahepatic collateral circulations after inferior vena cava obstruction.

can effectively show areas of liver parenchyma with reduced perfusion or necrosis. Magnetic resonance angiography not only makes the diagnosis of BCS more reliable but also facilitates the planning of treatment strategies. BCS can be precisely diagnosed by magnetic resonance angiography alone [61]; traditional percutaneous biopsy diagnosis of BCS may no longer be necessary [50].

Angiography is still the golden standard for the diagnosis of BCS. It complements ultrasound, CT, and MRI to provide comprehensive imaging diagnosis of BCS. At present, angiography is no longer used exclusively for diagnosis but also as a means of evaluating the efficacy of interventional therapy.

6.4 Definition of a membrane and segmental obstruction

Inferior vena cava and hepatic venous septum formation is a unique pathological feature of BCS. Segmental obstruction can coexist in the inferior vena cava and hepatic vein in some circumstances, making pathological differentiation of the septum and segmentation difficult sometimes. Thus, proper differentiation of the septum and segmentation not only contribute to unified diagnostic criteria and straightforward description of multiple imaging inspection techniques but also promote subtyping BCS. Furthermore, it has significant clinical value for interventional therapy. Therefore, it is necessary to define the inferior vena cava and hepatic venous septum and segmental obstruction.

In January 2016, we organized interventional radiology, pathology, and imaging diagnostic experts to analyze and discuss ultrasound, CT, MRI, and DSA images of more than 1000 patients with BCS and proposed the following viewpoints: inferior vena cava and hepatic vein "septum" and "segmentation" are defined by its thickness, 5 mm or less as a membrane, 10 mm or more as a segment, and 6–9 mm as a transitional zone where the two differentiations can coexist [62].

6.5 Classification and subtype

Because the method of interventional therapy is utterly different from surgical treatment, the classification used for surgery is not suitable for interventional therapy. Imaging diagnosis of hepatic vein and inferior vena cava obstruction has become a routine. After summarizing and reviewing the clinical experience of 10,000 cases of interventional therapy in China, the conditions for the

establishment of BCS interventional classification have matured. Interventional classification will promote and standardize the behavior and procedures of BCS imaging diagnosis and interventional therapy. It has an objective, realistic, and long-term clinical significance.

In 2010, more than 10 experts in the Chinese Interventional Radiology Group engaged in developing an expert consensus guideline on interventional therapy of BCS. BCS is classified into three main types, namely, hepatic vein obstruction type, inferior vena cava obstruction type, and mixed type [63, 64], which are still widely used today. Because of the vast differences in the extent, number, and thrombosis of hepatic veins and the inferior vena cava between individuals, it is necessary to subtype BCS.

In January 2016, experts from the Intracavitary Catheterization Committee of the Chinese Medical Association and experts of interventional radiology, vascular surgery, pathology, and imaging diagnostics discussed to further divide the 3 major types of BCS into 10 subtypes (**Table 5**, **Figures 15–24**). For the first time, the hepatic vein and inferior vena cava obstruction combined with thrombosis were included in the subtype, before which none of the previous classifications have done so.

6.6 Subtyping of BCS as a guideline for endovascular therapy

Endovascular therapies for BCS include percutaneous balloon dilatation, stent implantation, thrombolysis, transjugular intrahepatic portosystemic shunt (TIPS), and hepatic vein reconstruction [65]. Approximately 98% of BCS patients benefit from interventional therapy. The difficulty of BCS intervention varies individually, depending on the procedures performed. Interventional treatment of inferior vena cava septum with a small opening is fairly simple. After completion of inferior vena cava angiography, dilation with a balloon of suitable diameter and length can be done straightforward. However, interventions involving inferior vena cava segmental occlusion, thrombosis formation, occlusion end with the formation of collateral branches, or diffuse hepatic vein occlusion can take the operators hours or even days to complete the procedure. The new subtyping system provides a clear guideline for the preparation of preoperative treatment plannings and selection of equipment including medications and tools for thrombolysis, as well as the proper selection of percutaneous puncture routes and endovascular treatment methods (**Table 6**).

Hepatic vein obstruction subtypes	**Inferior vena cava obstructive subtypes**	**Mixed-type occlusions**
Hepatic vein/hepatic venous membranous obstruction (**Figure 15**)	Inferior vena cava membranous perforation (**Figure 19**)	Hepatic vein and inferior vena cava occlusion (**Figure 23**)
Hepatic venous segmental obstruction (**Figure 16**)	Inferior vena cava membranous obstruction (**Figure 20**)	Hepatic vein and inferior vena cava occlusion with thrombosis (**Figure 24**)
Extensive hepatic vein occlusion (**Figure 17**)	Inferior vena cava segmental obstruction (**Figure 21**)	
Hepatic vein occlusion combined with thrombosis (**Figure 18**)	Inferior vena cava obstruction with thrombosis (**Figure 22**)	

Table 5.
Ten subtypes of Budd-Chiari syndrome.

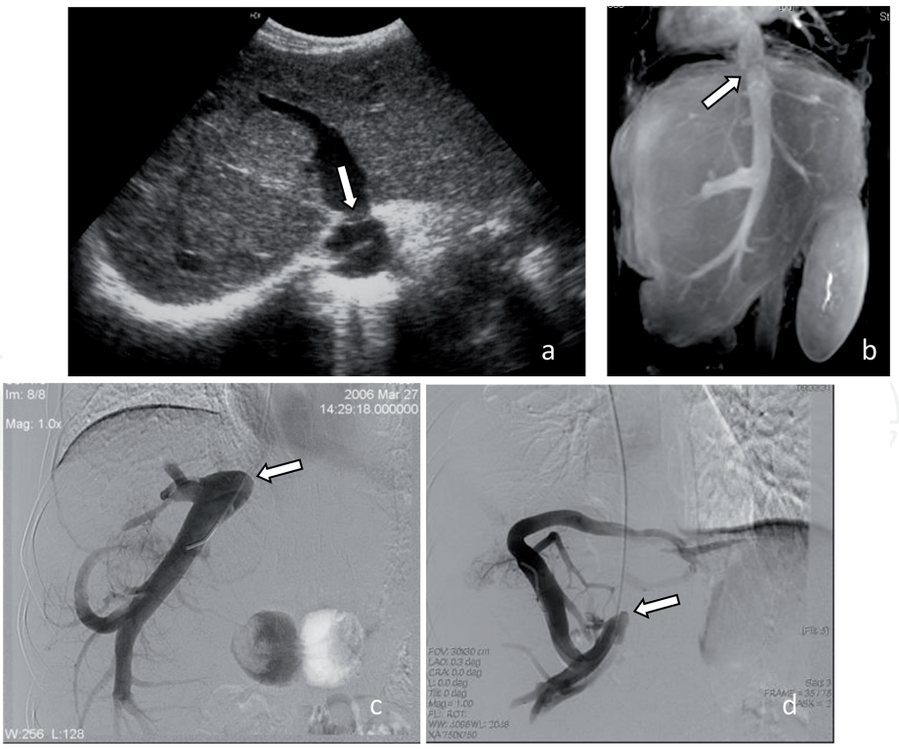

Figure 15.
Hepatic vein/hepatic venous membranous obstruction. (a) An ultrasound showing the septum at the left hepatic vein opening (arrow). (b) MRV showing the venous septum in the IVC (arrow). (c) DSA showing membranous venous occlusion in the right hepatic vein (arrow). (d) DSA showing membranous obstruction of the accessory hepatic vein (arrow).

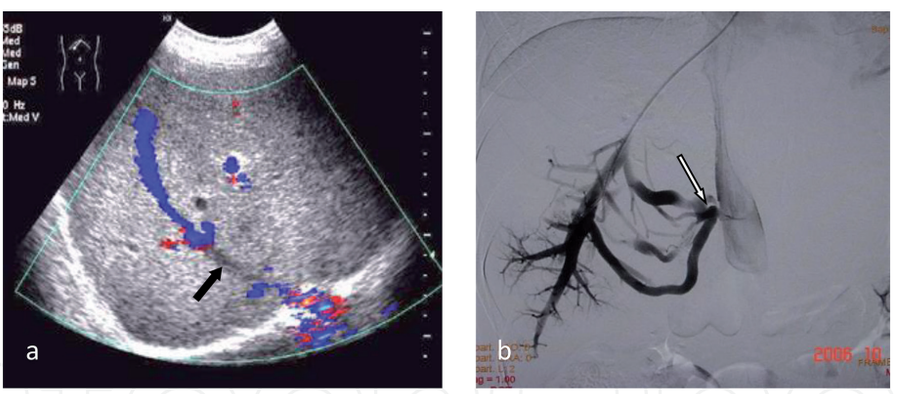

Figure 16.
Hepatic venous segmental obstruction. (a) An ultrasound showing the segmental obstruction (black arrow) of the right hepatic vein. (b) DSA showing segmental occlusion of the middle hepatic vein along with membranous obstruction (white arrow) of parahepatic venous structures.

6.7 New perspectives

6.7.1 Anatomical occlusion versus functional occlusion

According to our data analysis of more than 2400 cases, the incidence of obstruction of the left hepatic vein in patients with BCS is higher than 95%. Due to the small volume and smaller venous return of the left hepatic lobe, the outcome of occlusion of the left hepatic vein is minimal since collateral branches can form between the left hepatic vein, right hepatic vein, and left inferior diaphragmatic vein. Due to the presence of the collateral branches, even if the left hepatic vein and the middle hepatic vein are occluded, venous return can be entirely compensated by the venous return of the right hepatic vein or accessory hepatic vein. Therefore, we

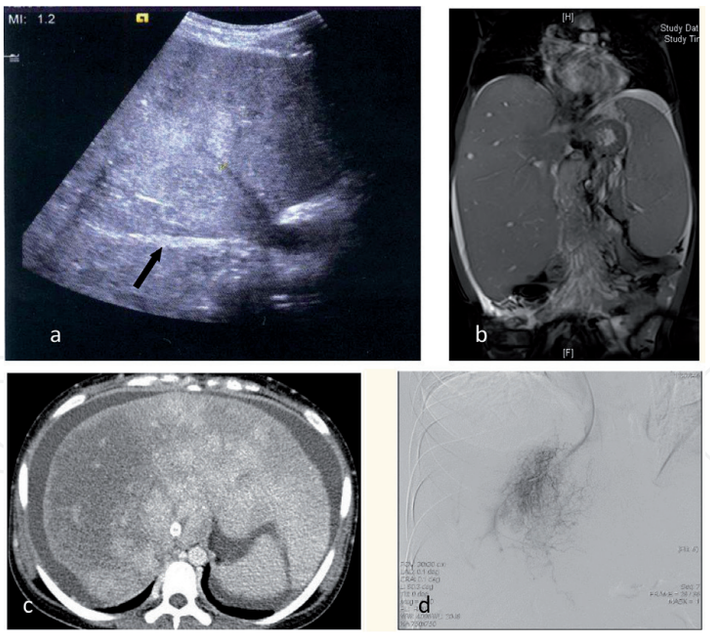

Figure 17.
Extensive hepatic vein occlusion. (a) An ultrasound showing the right hepatic venous occlusion of the liver with hyperechoic texture. The right hepatic vein is faintly depicted (black arrow), and the left hepatic vein is small in caliber. (b) MR showing hepatosplenomegaly. Hepatic veins are few and small in calibers. (c) Enhanced CT showing hepatomegaly and heterogeneous parenchymal enhancements. (d) DSA showing the disappearance of the main trunk of the hepatic vein and small reticular-shaped collateral vessels.

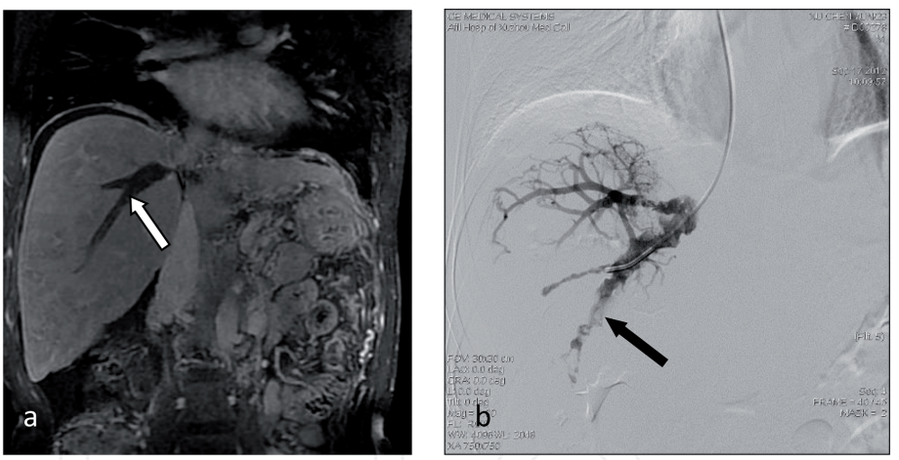

Figure 18.
Hepatic vein occlusion combined with thrombosis. (a) MRI showing the right hepatic vein occlusion with thrombosis (white arrow). (b) DSA showing hepatic venous occlusion with thrombosis (black arrow).

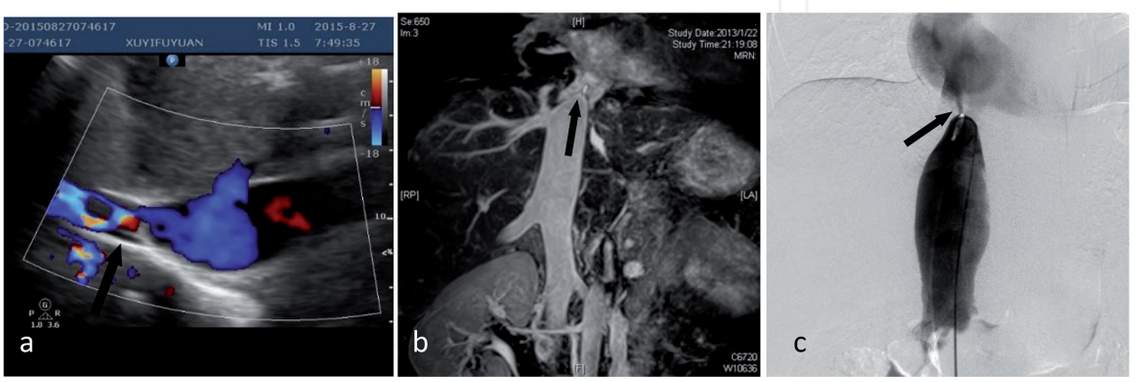

Figure 19.
Inferior vena cava membranous obstruction with a tiny perforation. (a) Color-flow mapping showing membranous obstruction (black arrow) of the inferior vena cava. (b) MRI showing membranous obstruction (black arrow) of the inferior vena cava. (c) DSA showing membranous obstruction of the inferior vena cava with a tiny perforation (black arrow).

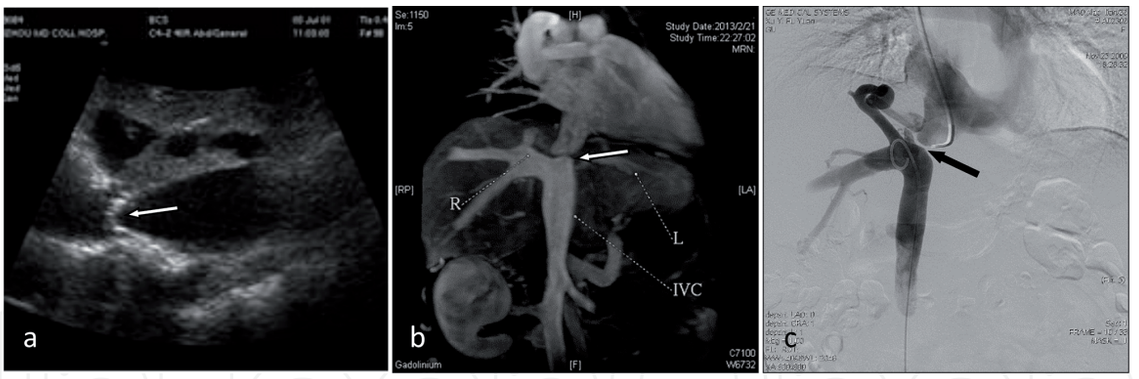

Figure 20.
Inferior vena cava membranous obstruction. (a) An ultrasound showing the vena cava septum as an echoic texture (white arrow). (b) MRV showing hypointense inferior vena cava septum (white arrow) right above the hepatic vein opening. (c) DSA showing membranous occlusion (black arrow) of the inferior vena cava.

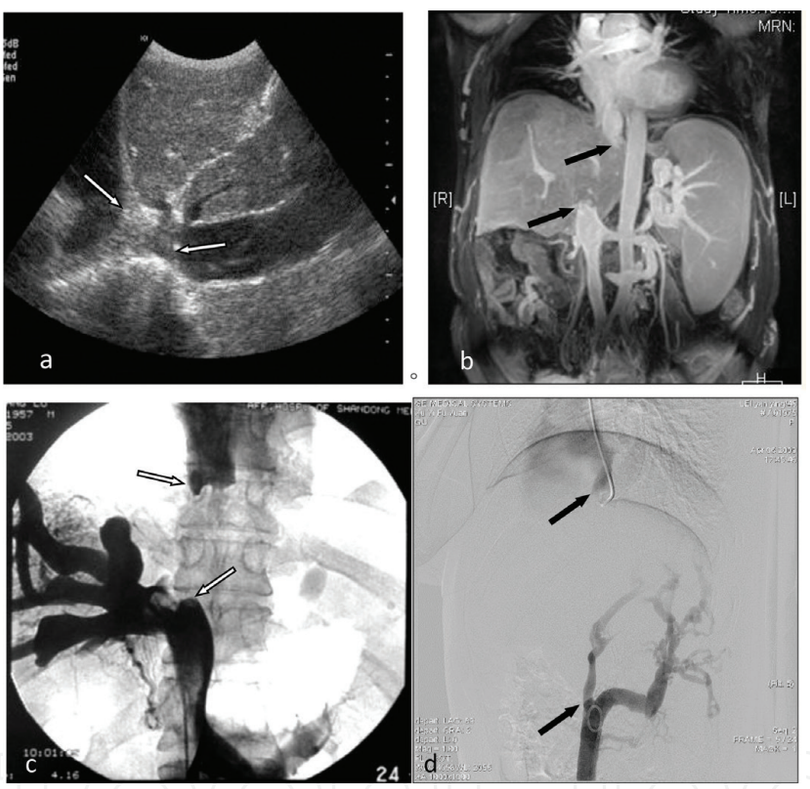

Figure 21.
Inferior vena cava segmental obstruction. (a) An ultrasound showing segmental occlusion (white arrows) of the inferior vena cava. (b) MRV showing a long segmental occlusion (black arrows) of the inferior vena cava. (c) DSA showing a long segmental occlusion (black arrows) of the inferior vena cava. (d) DSA projected in a lateral view showing an ultra-long segmental occlusion (black arrows) of the inferior vena cava.

still subtype cases with obstruction of the left hepatic vein and middle hepatic vein as isolated inferior vena cava obstruction type.

6.7.2 Accessory hepatic veins

In addition to the three hepatic veins, there are scattered small hepatic veins, collectively called the accessory hepatic vein (AHV) or the short hepatic veins, that drain directly into the IVC. After conducting anatomic researches, Liu et al. find that there are two primary sources of AHV: one is from the caudate lobar vein and the other from the right posterior hepatic vein. However, since most of the AHV are too small and are not the central draining vein of the liver, they are often neglected [65]. However, in patients with BCS, when hepatic vein occlusion occurs, AHV is

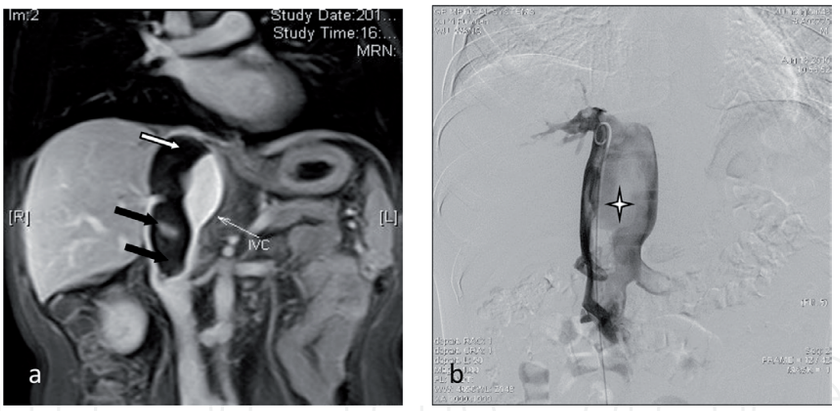

Figure 22.
Inferior vena cava obstruction with massive thrombosis. (a) Gadolinium-enhanced MRI demonstrating massive thrombi of various ages (black arrows and white arrow) in the IVC below the level of obstruction. (b) DSA showing membranous obstruction in the IVC along with bulky thrombi (asterisk).

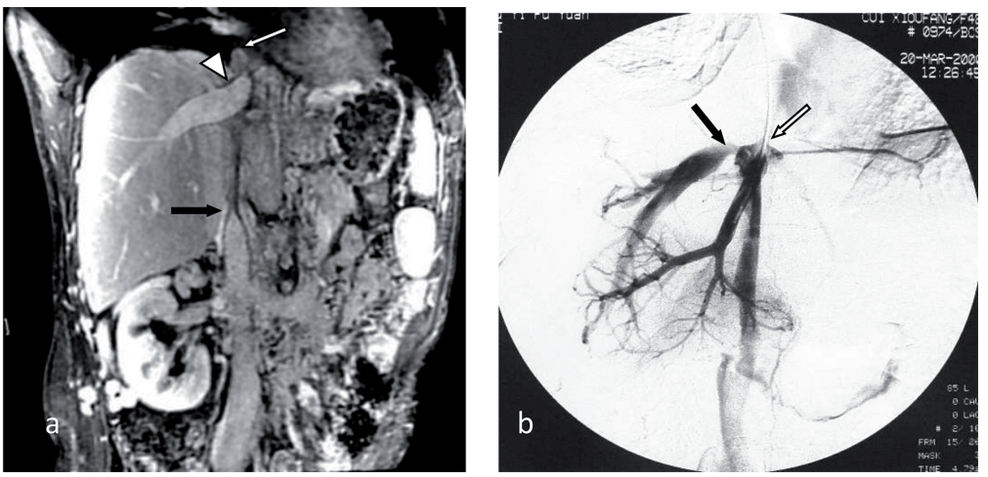

Figure 23.
Hepatic vein and inferior vena cava occlusion. (a) MRI showing right hepatic venous membranous obstruction (white arrowhead) with segmental occlusion (black and white arrows) of the inferior vena cava. (b) DSA showing membranous occlusions of the right hepatic vein (black arrow) and inferior vena cava (white arrow).

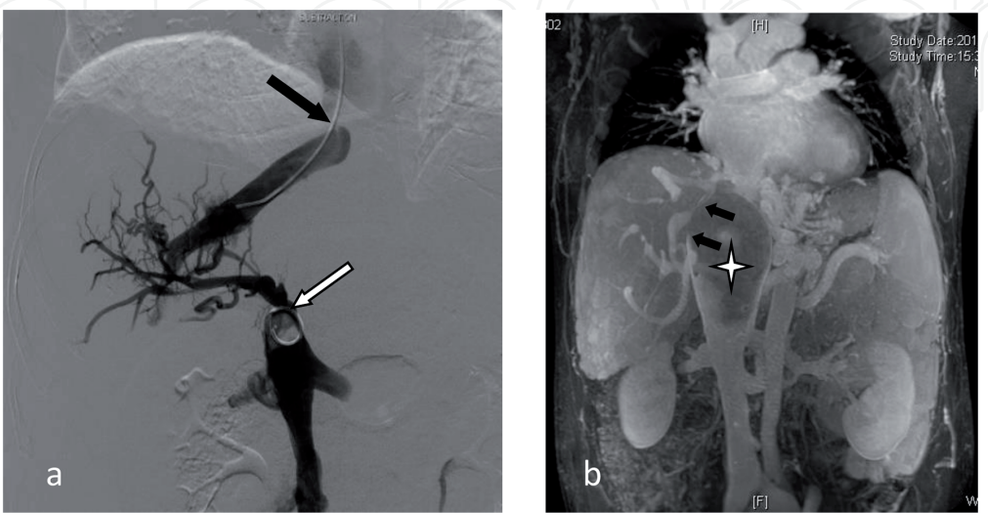

Figure 24.
Hepatic vein and inferior vena cava occlusions with thrombosis. (a) DSA showing right hepatic vein occlusion (black arrow) and IVC segmental occlusion with massive thrombosis (white arrow). (b) MRI showing occlusions of the hepatic vein (black arrows) and IVC with massive thrombi of various ages (asterisk).

Subtype	Endovascular therapy
Hepatic vein with membranous obstruction	Balloon dilatation
Hepatic vein segmental obstruction	Balloon dilatation + stent
Hepatic vein extensive obstruction	TIPS, hepatic vein reconstruction
Hepatic vein occlusion with thrombosis	Thrombolysis and balloon dilatation
Inferior vena cava membranous axonal	Balloon dilatation
Inferior vena cava membranous obstruction	Balloon dilatation
Inferior vena cava segmental obstruction	Balloon dilatation + stent
Inferior vena cava obstruction with thrombosis	Thrombolysis + balloon dilation/stent
Inferior vena cava and hepatic vein obstruction	Balloon dilation/stent
Inferior vena cava and hepatic vein obstruction with thrombosis	Thrombolysis + balloon dilation/stent

Table 6.
Selection of endovascular treatment methods based on the subtypes of BCS.

the main channel for venous return. Gai performed an ultrasound investigation on 244 BCS patients and found 191 (78.3%) cases presented with AHV. Among the 244 BCS patients, 209 had hepatic caudate lobar veins with an average diameter of (7.88 ± 2.78) mm, and 147 had a right inferior hepatic vein with an average diameter of (9.50 ± 3.11) mm [66]. During expansion of the AHV lumen, collateral branches between the hepatic vein and the accessory hepatic vein can fully compensate the hepatic venous return (see **Figure 21c**). In cases accompanied with IVC obstruction, the degree of IVC obstruction aggravates the expansion of AHV lumen. The accessory hepatic vein can also get obstructed. When the diameter of the AHV reaches 6 mm, it has sufficient compensatory capacity. Therefore, the interventional treatment of the obstructed accessory hepatic vein above 6 mm is equivalent to the treatment of the hepatic vein. In short, the accessory hepatic vein is of equal value to the hepatic vein in the diagnosis and treatment of BCS [67].

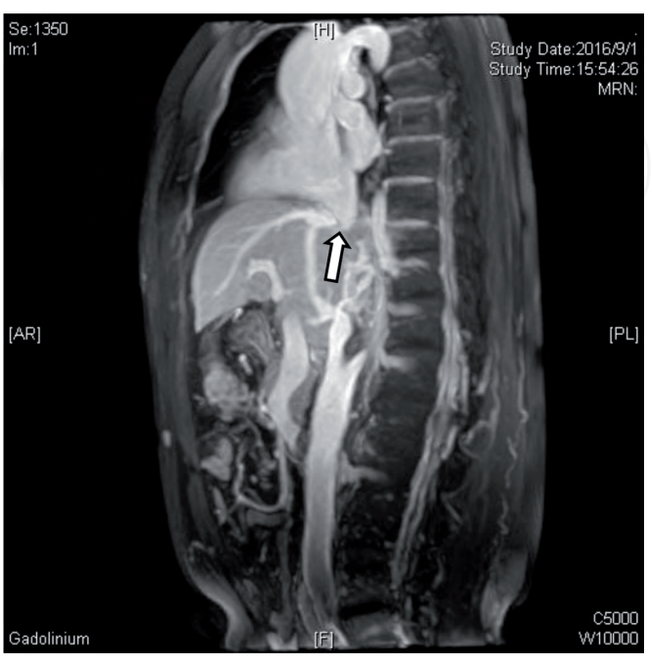

Figure 25.
MRV showing that the middle hepatic venous opening (hatched arrow) is above the inferior vena cava obstruction.

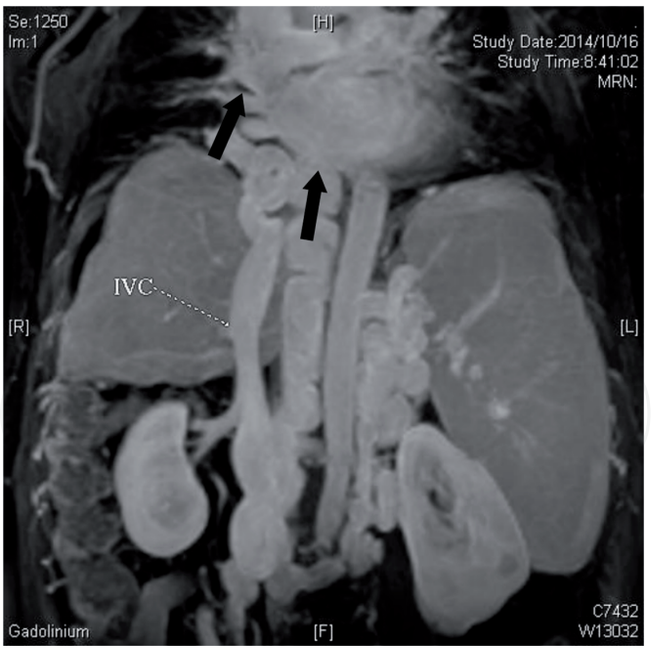

Figure 26.
MRV showing inferior vena cava obstruction with substantial azygos vein (black arrows) compensation.

6.7.3 Inferior vena cava septum and position of hepatic vein opening

The location of the inferior vena cava septum is generally above the hepatic vein opening, often causing hepatic venous blood flow obstruction. As the number of BCS cases increases, we find cases with the left hepatic vein and middle hepatic vein locating above the inferior vena cava septum. Dr. Zhang of the Chinese Department of Vascular Surgery also found a case (**Figure 25**) with the hepatic vein opening directly above the inferior vena cava septum while providing surgical resection of inferior vena cava septum. Although the numbers of this kind of cases are exceptionally few, the consideration on redefining BCS may be raised.

6.7.4 Azygos veins and its collateral branches

When hepatic vein becomes obstructed, the establishment of collateral branches between the intrahepatic veins is simple, but it is difficult for collateral branches to develop outside of the liver. This can result in portal hypertension with poor prognosis. In contrast, the establishment of the collateral branches after the inferior vena cava obstruction is relatively easy and extensive (see **Figure 26**). The azygous vein is the most crucial collateral branch when inferior vena cava obstruction occurs. The azygous vein can expand to a diameter of 2 cm (**Figure 21**) and compensate for the venous return of the inferior vena cava, and the patient usually can survive longer. Therefore, the severity of clinical symptoms of BCS is closely related to the compensatory capacity of the collateral circulation.

6.7.5 Closed collateral branch

After significant obstruction of the inferior vena cava, the superficial and deep vein begins to form collateral and communicating branches. In some cases, one or more collateral branches can appear above the site of inferior vena cava obstruction, with the diameter of reaching 2–3 mm. It can appear as single or multiple saclike structures, which are difficult to detect on preoperative ultrasound, CT, and MRV. However, DSA can easily show the obstruction and collateral branches

which play a vital blood flow compensation. During endovascular treatment, the existence of this collateral branch poses a potential risk. Since the collateral branches cannot be wholly identified under fluoroscopy, they may be ruptured during balloon dilatation, resulting in fatal intra-abdominal or intrathoracic bleeding. Thus, it is essential to be aware of this situation to ensure the safety of endovascular therapy.

7. Conclusion

With the adjunct use of PMAT incorporated in percutaneous CDT technology dedicated to the sophisticated endovascular management of DVT and DVT-related syndrome, the prevalence of PTS of moderate to severe degree and the intractable pain associated with advanced venous hypertension can be improved substantially. However, a randomized controlled study, comparing the adjunct use of PMAT or not, is demanded to offer convincing evidence. In conjunction with PTA and stenting after successful PMAT, symptomatic MTS can be well managed in terms of high technical success rate and midterm patency rate with acceptable minor complications. Along with the appreciations of newly identified pathophysiology and the creation of a new classification of subtypes, the selection of optimal mode of endovascular interventions in BCS may be solidly anticipated.

Literature search methods

The key references used in this manuscript are primary obtained using PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) and the textbooks "Abrams' Angiography: Interventional Radiology Third Edition" and "Venous Interventional Radiology With Clinical Perspectives 2nd Edition," as listed in References section. Some co-authors' references and new concepts are acquired from the recent Chinese radiology professional committee discussions.

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References

[1] U.S. Department of Health and Human Service. The Surgeon General's Call to Action to Prevent Deep Thrombosis and Pulmonary Embolism. Washington, DC: Author; 2008

[2] Salzman EW, Hirsh J. The epidemiology, pathogenesis and natural history of venoas thrombosis. In: Columan RW, Hirsh J, Marder VJ, Salzman EW, editors. Hemostasis and Thrombosis: Basic Principles and Clinical Practice. Philadelphia, PA: JB Lippincott; 1994. pp. 1275-1296

[3] Dähnert W. Deep vein thrombosis. In: Radiology Review Manual. 3rd ed. Baltimore: Williams & Wilkins; 1996. pp. 464-463

[4] White RH, Related Articles, et al. The epidemiology of venous thromboembolism. Circulation. 2003;**107**(23 supply 1):14-18

[5] Foley WD, Middleton WD, Lawson TL, Erickson S, Quiroz FA, Macrander S. Color Doppler ultrasound imaging of lower-extremity venous disease. American Journal of Roentgenology. 1989;**152**:371-376

[6] Rose SC, Zwiebel WJ, Nelson BD, Priest DL, Knighton RA, Brown JW, et al. Symptomatic lower extremity deep venous thrombosis: Accuracy, limitations, and role of color duplex flow imaging in diagnosis. Radiology. 1990;**175**:639-644

[7] Rose SC, Zwiebel WJ, Murdock LE, Hofmann AA, Priest DL, Knighton RA, et al. Insensitivity of color Doppler flow imaging for detection of acute calf deep venous thrombosis in asymptomatic postoperative patients. Radiology. 1993;**4**:111-117

[8] Haines ST, Bussey HI. Diagnosis of deep vein thrombosis. American Journal of Health-System Pharmacy. 1997;**54**:66-74

[9] Wille-Jørgensen P, Borris L, Jørgensen LN, Hauch O, Lassen MR, Nehen AM, et al. Phlebography as the gold standard in thromboprophylactic studies? A multicenter interobserver variation study. Acta Radiologica. 1992;**33**(1):24-28

[10] Savader SJ, Trerotola SO. Venous Interventional Radiology with Clinical Perspective. 2nd ed. Thieme; 2000. pp. 445-454

[11] Moody AR, Pollock JG, O'Connor AR, Bagnall M. Lower-limb deep venous thrombosis: Direct MR imaging of the thrombus. Radiology. 1998;**209**(2):349-355

[12] Fraser DG, Moody AR, Morgan PS, Martel AL, Davidson I. Diagnosis of lower-limb deep venous thrombosis: A prospective blinded study of magnetic resonance direct thrombus imaging. Annals of Internal Medicine. 2002;**136**(2):89-98

[13] Westerbeek RE, Van Rooden CJ, Tan M, Van Gils AP, Kok S, De Bats MJ, et al. Magnetic resonance direct thrombus imaging of the evolution of acute deep vein thrombosis of the leg. Journal of Thrombosis and Haemostasis. 2008;**6**(7):1087-1092

[14] Garg K, Kemp JL, Wojcik D, Hoehn S, Johnston RJ, Macey LC, et al. Thromboembolic disease: Comparison of combined CT pulmonary angiography and venography with bilateral leg sonography in 70 patients. American Journal of Roentgenology. 2000;**175**(4):997-1001

[15] Garg K, Mao J. Deep venous thrombosis: Spectrum of findings and pitfalls in interpretation on CT venography. American Journal of Roentgenology. 2001;**177**(2):319-323

[16] Thomas SM, Goodacre SW, Sampson FC, van Beek EJ. Diagnostic

value of CT for deep vein thrombosis: Results of a systematic review and meta-analysis. Clinical Radiology. 2008;**63**(3):299-304

[17] Goldhaber SZ, Buring JE, Lipnick RJ, Hennekens CH. Pooled analyses of randomized trials of streptokinase and heparin in phlebographically documented acute deep venous thrombosis. The American Journal of Medicine. 1984;**76**(3):393-397

[18] Bjarnason H, Kruse JR, Asinger DA, Nazarian GK, Dietz CA Jr, Caldwell MD, et al. Iliofemoral deep venous thrombosis: Safety and efficacy outcome during 5 years of catheter-directed thrombolytic therapy. Journal of Vascular and Interventional Radiology. 1997;**8**(3):405-418

[19] Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labropoulos N, Haughton SH. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: Report of a national multicenter registry. Radiology. 1999;**211**(1):39-49

[20] Gloviczki P. Handbook of Venous Disorder Guidelines of the American Venous Forum. 3rd ed. London, England: Edward Arnold Publishers; 2009

[21] Enden T, Haig Y, Kløw NE, Slagsvold CE, Sandvik L, Ghanima W, et al. CaVenT study group. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): A randomised controlled trial. Lancet. 2012;**379**:31-38

[22] Vedantham S, Goldhaber SZ, Julian JA, Kahn SR, Jaff MR, et al. Pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis. The New England Journal of Medicine. 2017;**377**:2240-2252

[23] Comerota AJ, Throm RC, Mathias SD, Haughton S, Mewissen M. Catheter-directed thrombolysis for iliofemoral deep venous thrombosis improves health-related quality of life. Journal of Vascular Surgery. 2000;**32**:130-137

[24] Elsharawy M, Elzayat E. Early results of thrombolysis vs anticoagulation in iliofemoral venous thrombosis. A randomised clinical trial. European Journal of Vascular Surgery. 2002;**24**:209-214

[25] AbuRahma AF, Perkins SE, Wulu JT, Ng HK. Iliofemoral deep vein thrombosis: Conventional therapy versus lysis and percutaneous transluminal angioplasty and stenting. Annals of Surgery. 2001;**233**:752-760

[26] Semba CP, Dake MD. Iliofemoral deep venous thrombosis: Aggressive therapy with catheter-directed thrombolysis. Radiology. 1994;**191**(2):487-494

[27] Vedantham S, Grassi CJ, Ferral H, et al. Reporting standards for endovascular treatment of lower extremity deep vein thrombosis. Journal of Vascular and Interventional Radiology. 2006;**17**(3):417-434

[28] Ferris EJ, Lim WN, Smith PL, Casali R. May-Thurner syndrome. Radiology. 1983;**147**(1):29-31

[29] Mc Murrich JP. The valves of the iliac vein. British Medical Journal. 1906;**2**:1699-1700

[30] May R, Thurner J. The cause of the predominantly sinistral occurrence of thrombosis of the pelvic veins. Angiology. 1957;**8**(5):419-427

[31] Negus D, Fletcher EW, Cockett FB, Thomas ML. Compression and band formation at the mouth of the left common iliac vein. The British Journal of Surgery. 1968;**55**(5):369-374

[32] Vollman JF, Hutschenreiter S. Vascular endoscopy for venous thrombectomy. In: Moore WB, Alin SS, editors. Endovascular Surgery.

Philadelphia: WB Saunders; 1989. pp. 65-73

[33] Juhan CM, Alimi YS, Barthelemy PJ, Fabre DF, Riviere CS. Late results of iliofemoral venous thrombectomy. Journal of Vascular Surgery. 1997;**25**(3): 417-422

[34] Nagayo M, Nakayama O. Ueber die Stenose bzw. Obliteration der linken V. iliaca an der Einmundungsstelle in die Hohlvene. Deutsche Medizinische Wochenschrift. 1912;**38**:749-751

[35] Akaneema J et al. Stricture of opening in the left common iliac vein in Korean people. Proceedings of The Japanese Society of Pathology. 1932;**2**:595-598

[36] Mitsuoka H, Ohta T, Hayashi S, Yokoi T, Arima T, Asamoto K, et al. Histological study on the left common iliac vein spur. Annals of Vascular Diseases. 2014;**7**(3):261-265

[37] Forauer AR, Gemmete JJ, Dasika NL, Cho KJ, Williams DM. Intravascular ultrasound in the diagnosis and treatment of iliac vein compression (May-Thurner) syndrome. Journal of Vascular and Interventional Radiology. 2002;**13**(5):523-527

[38] Brinegar KN, Sheth RA, Khademhosseini A, Bautista J, Oklu R. Iliac vein compression syndrome: Clinical, imaging and pathologic findings. World Journal of Radiology. 2015;**7**(11):375-381

[39] Cockett FB, Thomas ML, Negus D. Iliac vein compression. Its relation to iliofemoral thrombosis and the post-thrombotic syndrome. British Medical Journal. 1967;**2**(5543):14-19

[40] Hurst DR, Forauer AR, Bloom JR, Greenfield LJ, Wakefield TW, Williams DM. Diagnosis and endovascular treatment of iliocaval compression syndrome. Journal of Vascular Surgery. 2001;**34**(1):106-113

[41] Shebel ND, Whalen CC. Diagnosis and management of iliac vein compression syndrome. Journal of Vascular Nursing. 2005;**23**(1):10-17; quiz 18-9

[42] Brazeau NF, Harvey HB, Pinto EG, Deipolyi A, Hesketh RL, Oklu R. May-Thurner syndrome: Diagnosis and management. VASA. 2013;**42**(2):96-105

[43] Ibrahim W, Al Safran Z, Hasan H, Zeid WA. Endovascular management of May-Thurner syndrome. Annals of Vascular Diseases. 2012;**5**(2):217-221

[44] Kim JY, Choi D, Ko YG, Park S, Jang Y, Lee DY. Treatment of May-Thurner syndrome with catheter-guided local thrombolysis and stent insertion. Korean Circulation Journal. 2004;**34**:655-659

[45] Chung JW, Yoon CJ, Jung SI, Kim HC, Lee W, Kim YI, et al. Acute iliofemoral deep vein thrombosis: Evaluation of underlying anatomic abnormalities by spiral CT venography. Journal of Vascular and Interventional Radiology. 2004;**15**(3):249-256

[46] Oguzkurt L, Tercan F, Pourbagher MA, Kizilkilic O, Turkoz R, Boyvat F. Computed tomography findings in 10 cases of iliac vein compression (May-Thurner) syndrome. European Journal of Radiology. 2005;**55**(3):421-425

[47] Liu Z, Gao N, Shen L, Yang J, Zhu Y, Li Z, et al. Endovascular treatment for symptomatic iliac vein compression syndrome: A prospective consecutive series of 48 patients. Annals of Vascular Surgery. 2014;**28**(3):695-704

[48] Hölper P, Kotelis D, Attigah N, Hyhlik-Dürr A, Böckler D. Longterm results after surgical thrombectomy and simultaneous stenting for symptomatic iliofemoral venous thrombosis. European Journal of Vascular and Endovascular Surgery. 2010;**39**:349-355

[49] Zhang W, Qi X, Zhang X, et al. Budd-Chiari syndrome in China: A systematic analysis of epidemiological features based on the Chinese literature survey. Gastroenterology Research and Practice. 2015;**2015**:738548

[50] Martens P, Nevens F. Budd-Chiari syndrome. United European Gastroenterology Journal. 2015;**3**(6):489-500

[51] Han X, Zu M. Study the significance of VEGF abnormal expression in membranous obstruction with Budd-Chiari syndrome. Contemporary Medicine. 2010;**16**(35):672-674

[52] Guo C, Bian J, Wang Y. Effects of multiple elements in drinking water on inferior vena cava membranous obstruction type of the Budd-Chiari syndrome in Heze area of Shandong province. Chinese Journal of Endemiology. 2005;**2**:207-209

[53] Zhuang Y, Zu M, Li J, et al. Serum iodine is increased in subjects having Budd-Chiari syndrome. Biological Trace Element Research. 2015;**168**:21-24

[54] Zu M, Xu H, Gu Y, et al. Treatments to deal with difficult cases and complications during interventional therapy for Budd-Chiari syndrome: Report of 1859 cases. Chinese Journal of Bases and Clinics in General Surgery. 2014;**12**:1487-1494

[55] Wang L, Zu M, Teng F, et al. Budd-Chiari syndrome in youth: Clinical features and interventional therapy. Chinese Journal of General Surgery. 2013;**28**(9):686-689

[56] Teng F, Zu MH, Hua QJ. Correlations of iodide ions with vascular endothelial growth factor and its receptors during the proliferation of vascular endothelial cells. Genetics and Molecular Research. 2014;**13**(3):6439-6447. DOI: 10.4238/2014.August.25.7

[57] Hua Q J, Zu MH, Teng F, et al. Research on the relationship between bFGF, FGFR2 and the fibroblast proliferation promoted by high density iodine. Journal of Interventional Radiology. 2013;**22**(12):1016-1020

[58] Teng F, Zu MH, Hua Q, et al. The relationship between iodide ion and vascular endothelial growth factor together with its receptor in vascular endothelial cell proliferation. Journal of Interventional Radiology. 2013;**22**(6):486-489

[59] Kiladjian J, Cervantes F, Leebeek FW, et al. The impact of JAK2 and MPL mutations on diagnosis and prognosis of splanchnic vein thrombosis: A report on 241 cases. Blood. 2008;**111**:4922-4929

[60] Wang H, Sun G, Zhang PJ, et al. JAK2 V617F mutation and 46/1 haplotype in Chinese Budd-Chiari syndrome patients. Journal of Gastroenterology and Hepatology. 2014;**29**:208-214

[61] Xu K, Li L. Budd-Chiari syndrome: CT and MR findings. Journal of Interventional Radiology. 2008;**17**(4):294-298

[62] Expert Committee on Vena Cava Obstruction Specialized Committee of Endovasculogy, Chinese Medical Doctor Association, Maoheng Z. Expert consensus on the definition of "membranous obstruction" and "segmental obstruction" of the inferior vena cava and hepatic vein in Budd-Chiari syndrome. Journal of Interventional Radiology. 2016;**25**(7):559-561

[63] Specialized Committee of Intervention, Chinese Radiology Professional Committee, Maoheng Z. Expert consensus on interventional diagnosis and treatment of Budd-Chiari syndrome. Chinese Journal of Radiology. 2010;**44**(4):345-249

[64] Expert Committee on Vena Cava Obstruction Specialized Committee of Endovasculogy, Chinese Medical Doctor Association, Maoheng Z. Expert consensus on the classification of subtype in Budd-Chiari syndrome. Journal of Interventional Radiology. 2017;**26**(3):195-200

[65] Liu S, Xu W, Luan M. Applied anatomy of vascular architecture in caudate lobe of liver. Chinese Journal of Clinical Anatomy. 1991;**9**(3):138-142

[66] Gai Y. Ultrasonic diagnosis of accessory hepatic vein and its lesion in Budd-Chiari syndrome. Chinese Journal of Ultrasound Imaging. 2010;**26**(7):641-644

[67] Zu MH, Xu H, Gu Y, et al. The value of accessory hepatic vein in Budd-Chiari syndrome. Chinese Journal of Radiology. 1998;**32**(9):616-619