Diagnosis of acute and chronic iliac vein thrombosis

Diagnostik des akuten und chronischen Beckenvenenverschlusses

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ABSTRACT

The clinical picture of acute iliac vein thrombosis can be dramatic. Iliac vein thrombosis is associated with a high risk of a life-threatening pulmonary embolism. It can also result in the development of phlegmasia cerulea dolens, a dangerous complication which can lead to the loss of the affected extremity. In addition to conservative treatment approaches, such as compression therapy and anticoagulation, there are a number of interventions that can limit the severity of post-thrombotic syndrome and prevent the disease from becoming fatal.

The prognosis of the disease depends to a large extent on an early and reliable diagnosis. Duplex ultrasound plays a key role both in the acute and chronic stages of the disease. It sheds light on the pathomorphology of the iliac and leg veins and provides information about the dynamics of blood flow.

In contrast to an ultrasound examination of the deep and epifascial veins in the leg, investigating the proximal vascular segments requires the use of both a linear and curved-array probe. A limited resolution deep inside the pelvis requires delicate handling of the settings on the ultrasound device.

Radiological and functional diagnostic methods can provide additional information for treating post-thrombotic changes in the iliac veins.

ZUSAMMENFASSUNG

Die akute Beckenvenenthrombose stellt ein dramatisches Krankheitsbild dar. Auf der einen Seite geht sie mit einem hohen Risiko für eine lebensbedrohliche Lungenembolie einher, auf der anderen Seite kann sie die Entwicklung einer Phlegmasia coerulea dolens bewirken, welche zum Verlust der betroffenen Extremität führen kann und ebenfalls eine vital bedrohliche Komplikation darstellt. Neben konservativen Behandlungsansätzen wie Kompressionstherapie und Antikoagulation stehen eine Reihe interventioneller Optionen zur Verfügung, welche darauf abzielen, fatale Krankheitsverläufe zu verhindern und auch die Ausprägung eines postthrombotischen Syndroms zu begrenzen.

Die Prognose der Erkrankung hängt maßgeblich von der frühzeitigen sicheren Diagnosestellung ab. Sowohl in der akuten Krankheitsphase, als auch im chronischen Stadium nimmt die Duplexsonographie die Schlüsselrolle ein. Sie gibt Aufschluss über die Pathomorphologie der Becken- und Beinvenen und liefert zusätzlich hämodynamische Informationen.

Im Gegensatz zur sonographischen Befundung der tiefen und epifaszialen Beinvenen ist zur Exploration der proximalen Gefäßabschnitte neben dem Einsatz einer Linearsonde auch die Untersuchung mittels Konvexsonde erforderlich und die eingeschränkte Auflösung in der Tiefe des kleinen Beckens macht einen subtilen Umgang mit den Einstellungen des Ultraschallgerätes nötig.

Im Rahmen der Behandlung postthrombotischer Veränderungen der Beckenvenen können radiologische und funktionsdiagnostische Methoden zusätzliche Informationen liefern.

Introduction

In addition to anticoagulation and compression therapy, the current German and international guidelines on the treatment of deep vein thrombosis (DVT) also recommend, in appropriate cases, the early use of recanalisation measures such as surgical thrombectomy, thrombolysis and pharmacomechanical thrombectomy, in order to reduce the risk of developing a post-thrombotic syndrome (PTS) [1, 2]

Technological developments in the treatment of PTS over the past twenty years have contributed to establishing recanalisation and stenting in the treatment of chronic iliac vein occlusion.

The incidence of DVT is estimated to be 1–3 cases per 1000 population per year. The risk of PTS is given as 20–50 %, with 5–10 % of cases expected to be severe [3, 4]. Various authors give figures of 1–5 % for the prevalence of PTS [5, 6].

Invasive options for treating thrombosis and PTS are aimed mainly at the treatment of the proximal pelvic and leg veins. While the ATTRACT study, which was carried out independently of the manufacturers, did not show any advantage of catheter-directed thrombolysis in the treatment of acute deep vein thrombosis (no reduction of post-thrombotic syndrome) [7], numerous studies indicate that recanalisation and stenting of chronic iliac vein occlusion relieves the symptoms in a select patient population [8, 9, 10].

The few available data on topographic manifestations of post-thrombotic changes suggest, however, that an isolated iliac vein thrombosis suitable for endoluminal recanalisation is a rare disease entity [11, 12, 13, 14].

Even though the available studies show excellent therapeutic results and a high degree of safety, it is still a procedure associated with radiation exposure and discomfort for the patient, not to mention the aspects of health economics that need to be considered. Examination of the iliac veins and the inferior vena cava is particularly important in planning treatment and has a significant effect on the prognosis.

Diagnostic investigation of acute iliac vein occlusion

Acute thrombosis of the common iliac vein and/or the external iliac vein with a relevant haemodynamic impact on the venous return and the associated pressure increase in the deep veins of the ipsilateral leg usually causes a marked, painful venous leg oedema, often accompanied by venous cyanosis (▶ **Fig. 1**).

With complete thrombosis and a poor collateral circulation, the severe and potentially limb- and life-threatening condition of phlegmasia cerulea dolens (blue painful leg) may develop due to the arterial blood supply being compromised. The resultant amputation rate is between 25 % and 50 % [15].

In bedridden patients, however, there may be no swelling at all.

Ultrasound exploration of acute pelvic and leg vein thrombosis

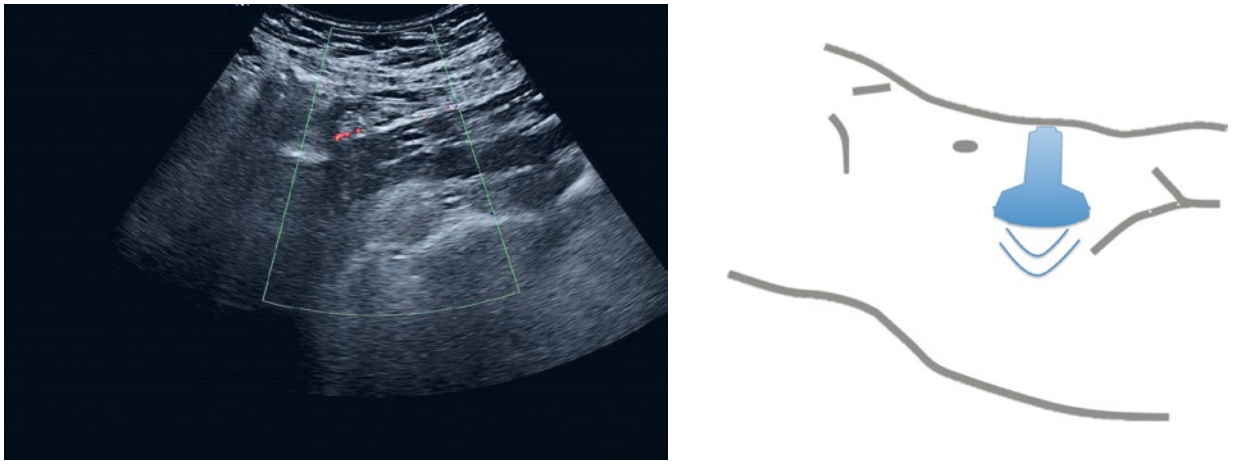
As with all thromboembolic disease, the clinical probability of acute iliac vein thrombosis should be estimated at the start of the diagnostic process [1]. A D-dimer test is only worthwhile when the clinical probability is low, as only then can a negative result rule out thrombosis with sufficient certainty. With a moderate or high clinical probability, the first diagnostic step is an ultrasound scan of the pelvic and leg veins.

▶ **Fig. 1** **a** Acute thrombosis of the left external and common iliac veins as well as partial thrombotic occlusion of the inferior vena cava: painful oedema of the left leg from the medial malleolus to the thigh, livid discolouration, a difference in the circumference of the thighs, with the left thigh + 4 cm larger, venous claudication. **b** Ultrasound findings: fresh inhomogeneous echogenic thrombus in the dilated common femoral vein. Flow signal ceases directly at the bifurcation.

Despite the high sensitivity of continuous wave Doppler ultrasonography for proximal DVTs, this method has become obsolete due to its lack of accuracy in the distal leg veins and failure to identify incomplete thromboses. The standard examination to confirm or rule out a DVT is now continuous B-mode compression ultrasound of the deep veins from the common femoral vein to the distal leg veins, including the calf muscle veins, and continuing as far as the plantar region, if there is a specific clinical indication. In our opinion, the examination should start proximally. It should also include the saphenous trunks, as the thrombus often grows from these vessels into the deep veins of the leg.

Compression ultrasound is not suitable for assessing the veins in the pelvis, as only the distal external iliac veins can be compressed sufficiently. Therefore, before carrying out a compression ultrasound of the leg veins, the clearly visible distal segments of the external iliac veins should first be examined by colour-coded duplex ultrasound, even with unprepared and/or obese patients, in order to record the respiratory variation in the flow signals.

By using different acoustic windows, it is also possible to examine the proximal external iliac veins and common iliac veins adequately in some patients. It is often not possible to detect any flow,



▶ **Fig. 2** No flow can be seen in the iliac vein due to overlying intestinal gas (left) and an unfavourable Doppler angle (middle and right).

▶ **Fig. 3** The right external iliac artery (red) and the right external iliac vein (blue) seen through a suprainguinal acoustic window in the same patient.

if the transducer is placed vertically over the centre of the iliac vein axis, because of overlying intestinal gas and an almost 90° angle of incidence (▶ **Fig. 2**); however, by tilting the probe in the direction of the course of the vein, the external iliac vein can be visualised through a suprainguinal acoustic window (▶ **Fig. 3**) and the common iliac vein through a paraumbilical window (▶ **Fig. 4**). Alternatively, the Doppler angle can be optimised by placing a curved array probe that does not allow tilting of the colour window at the lateral edge of the image. A low pulse repetition frequency (PRF), i. e. a lower speed range in the colour presentation, improves the sensitivity of the flow imaging.

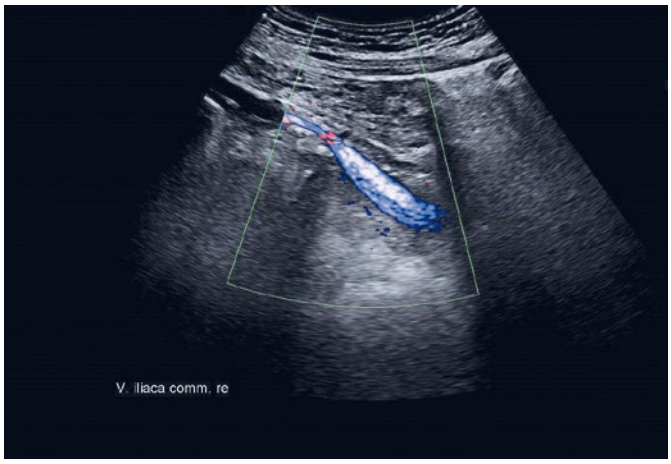
Besides direct imaging of the pelvic veins, bilateral measurements comparing the flow in the left and right distal external iliac veins, which are almost always accessible, and common femoral veins are carried out, in order to gain information on the presence or absence of a haemodynamically relevant downstream obstruction to vascular flow.

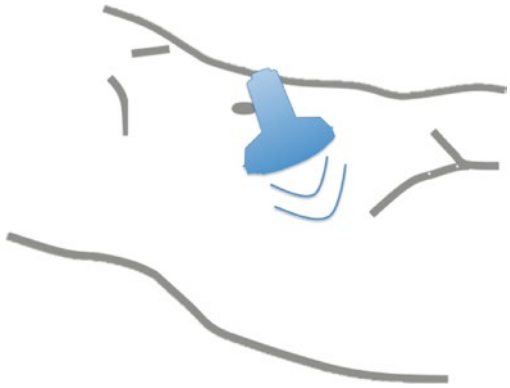
Ultrasound findings in acute iliac vein thrombosis

Direct signs in the immediate vicinity of the thrombosis are reduced internal echogenicity in comparison with a patent vessel widening of the vein and a partial or complete lack of flow (▶ **Fig. 5**).

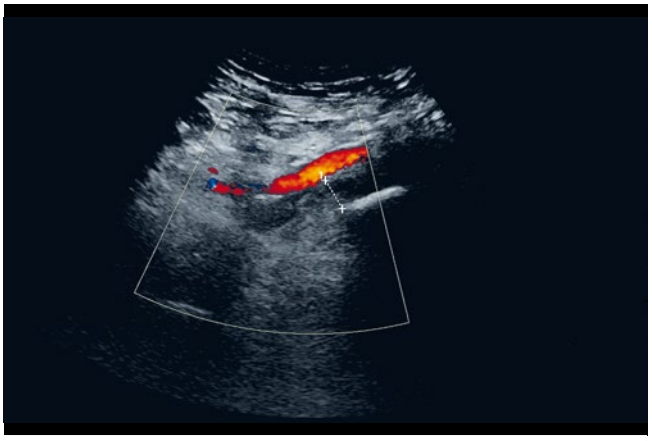
Indirect signs include a detectable widening of the ipsilateral common femoral vein (and possibly also the external iliac vein) in comparison with the contralateral side, with attenuation or loss of cardiac and respiratory variation in the pulsed wave (PW) Doppler signal (▶ **Fig. 6**), more difficult compressibility of the leg veins and evidence of spontaneous flow in collateral veins draining the iliac and pudendal regions, sometimes with a reversal of flow.

The inferior vena cava should also be examined whenever thrombosis is found in the iliac veins or if a pulmonary embolus occurs without any thrombosis identified in the pelvic or leg veins [16].

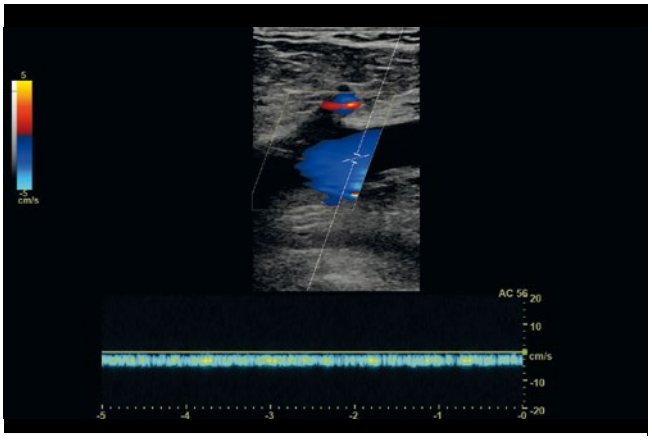




▶ **Fig. 4** The right common iliac vein (blue) seen through a paraumbilical acoustic window in the same patient.



▶ **Fig. 5** Longitudinal section showing the left external iliac artery and dilated left external iliac vein with a lack of flow due to acute thrombosis (direct sign).



▶ **Fig. 6** Blood flow in the left common femoral vein with loss of cardiac and respiratory variation in a patient with acute thrombosis of the left external iliac and common iliac veins.

In addition to imaging of the pelvic and leg veins and demonstration of the venous and arterial blood flow, B-mode ultrasound allows the visualisation of perivascular soft tissue structures and can be used to clarify conditions such as neoplastic processes that affect the vessels externally, e. g. conglomerate lymph node masses.

The value of radiological procedures

Indirect magnetic resonance imaging (MRI) and computed tomography (CT) venography visualise the vena cava and the iliac veins well; they are the diagnostic methods of choice in the case of suspected iliocaval thrombosis when the results of colour-coded duplex ultrasound are inconclusive. The disadvantage of MR venography is that it is more time-consuming, while CT venography involves radiation exposure.

With the use of ultrasound procedures and cross-sectional imaging techniques (CT and MRI) becoming more widespread, classical direct invasive intravenous venography has become less important for primary diagnostic investigations and is now principally used in the context of interventional radiology. [17].

Diagnostic investigation of chronic iliac vein occlusion

While iliac vein thrombosis is usually associated with acute pain and characterised by oedema and a livid discolouration that often involves the entire affected limb, patients with a chronic occlusion, post-thrombotic stenosis or non-thrombotic stenosis in the region of the iliac veins experience a feeling of heaviness and pain in the proximal leg as well as in the lower abdomen and sometimes exercise-induced venous claudication. Women may complain of dysmenorrhoea and dyspareunia and varicose veins may occasionally develop in the vulva and pudendum. Following post-thrombotic occlusion, epifascial collateralisation via a spontaneous Palma shunt (named after the venous bypass procedure developed by Eduardo Palma) can often be seen (▶ **Fig. 7**). Typical skin chang-

▶ **Fig. 7** Post-thrombotic occlusion of the iliac vein with epifascial collateral vessels in the pudendal region and a tributary with a larger diameter and corkscrew-like appearance above the symphysis ('spontaneous Palma shunt') draining to the iliac vein on the contralateral side. Additional collateral supply via tributaries from areas drained by the anterior and lateral accessory saphenous veins.

es of chronic venous insufficiency (CVI) equivalent to CEAP clinical class C4-C6 may also occur.

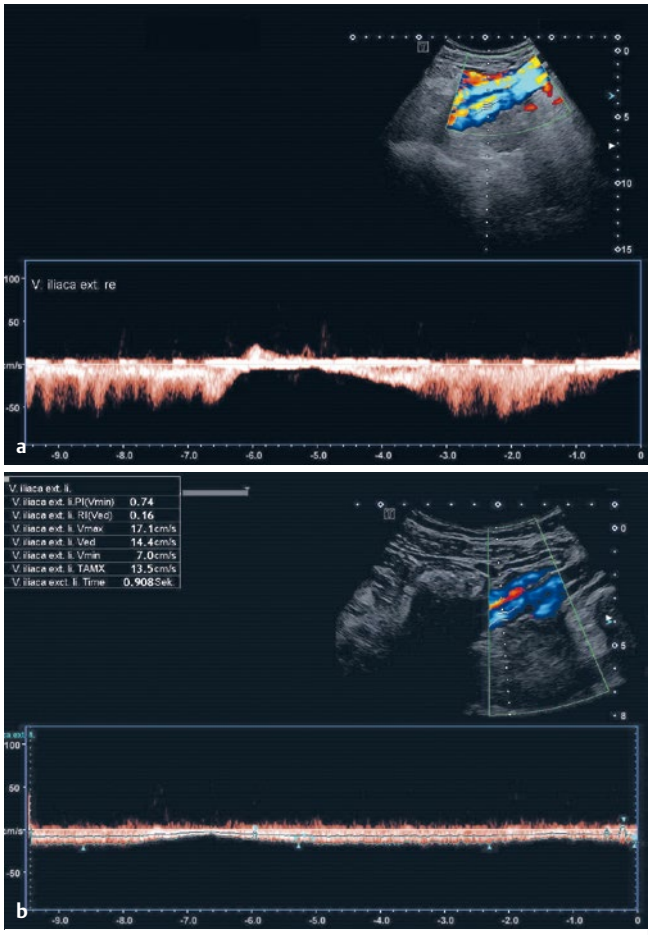
Ultrasound exploration of chronic iliac vein occlusion

Duplex ultrasound is also the first-line diagnostic investigation for assessing chronic iliac vein occlusion. The examination should provide information on the anatomical, pathological and functional aspects. Ultrasound exploration aims to visualise morphological changes in the iliac veins (stenosis or occlusion; extent of the obstruction or occlusion). In addition, the question of whether or not the vena cava is involved must be clarified and the extent of collateralisation estimated.

Ultrasound findings in chronic iliac vein occlusion

Comparison of the flow signals on the two sides is used to assess post-thrombotic changes in the pelvic veins. In contrast to acute DVT, respiratory variation in the post-thrombotic iliac vein is often not completely absent but may be significantly attenuated and delayed (▶ **Fig. 8a**, ▶ **Fig. 8b**). This can be attributed to the large-diameter collateral vessels that have developed in the venous plexus of the lesser pelvis as part of the post-thrombotic syndrome.

It must be emphasised that assessment of the venous return on the contralateral side of the affected pelvic vein is particularly important, as it provides us with information on the involvement of the inferior vena cava, the distal segment of which can be seen to only a very limited extent. While, as in the leg veins, the flow signals in the downstream external iliac veins can be recorded optimally with an 8–12 MHz linear probe, a curved array probe ('abdominal probe') is preferable for examining the collaterals in the lesser pelvis.



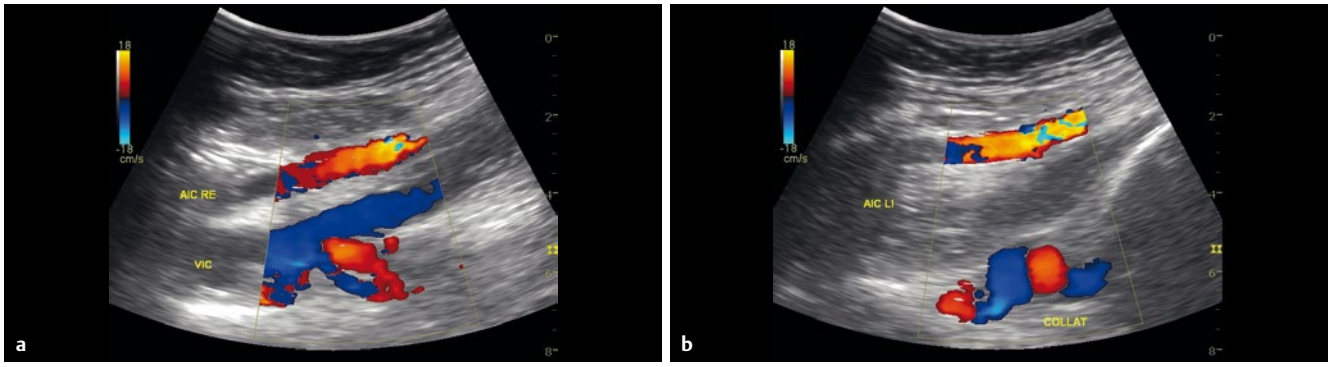
▶ **Fig. 8** **a** Respiratory variation of the signal from the intact right external iliac vein. **b** Clearly reduced respiratory variation in the left iliac vein, distal to a post-thrombotic occlusion.

As a rule, the common iliac vein with post-thrombotic changes can be demonstrated only schematically with the colour Doppler, due to the limited resolution. The accompanying artery is therefore identified as the main structure. In the event of complete occlusion, it is not possible to visualise the vein at all. The collaterals are, however, dilated to compensate and have a marked corkscrew-like appearance with high frequency flow signals (▶ **Fig. 9a**, ▶ **Fig. 9b**).

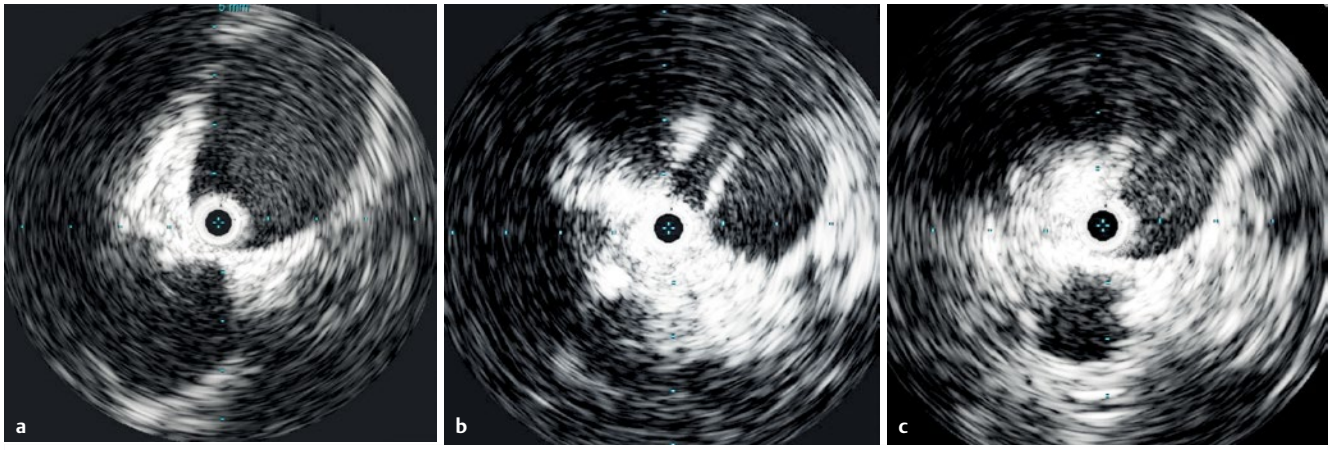
Limitations of colour-coded duplex ultrasonography

It is usually possible to detect iliac vein thrombosis with colour-coded duplex ultrasound. Murphy et. al. published a study, in which the sensitivity did not differ from that of MR venography [18]. However, the diagnostic accuracy of colour-coded duplex ultrasound is limited by the frequently poor sound propagation in the abdomen and depends on the examiner's experience and the anatomical conditions pertaining to the patient.

In a single-centre study involving a routine ultrasound examination of the venous system, the examiners detected only 10 of the 36 isolated iliac vein thromboses demonstrated on cross-sec-



▶ **Fig. 9** **a** Right common iliac artery (red) and vein (blue) with normal signals. **b** Close to the transdducer lies the left common iliac artery (red), further from the transducer is the corkscrew-like distorted collateral vessel. In between lies the post-thrombotic occluded and dilated vein.



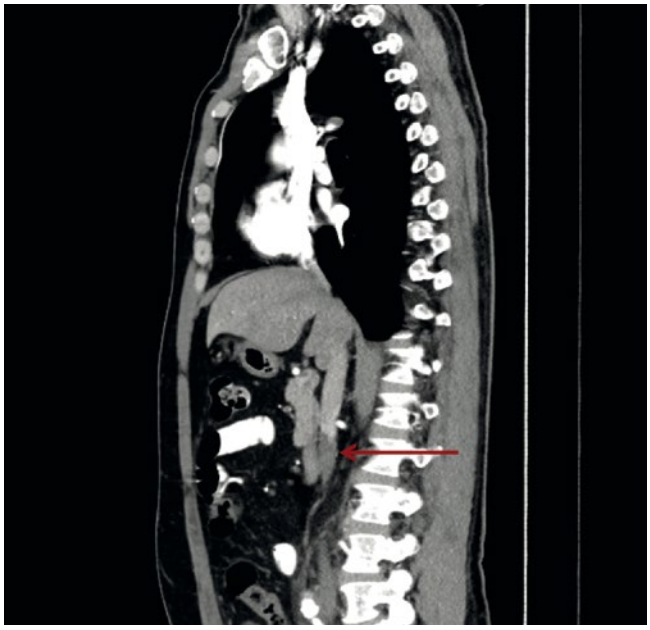
▶ **Fig. 10** **a** IVUS probe in the proximal iliac vein (the artery can be seen below left). **b** IVUS probe in the stenosis (at 1 o'clock) in a patient with May-Thurner syndrome. **c** IVUS probe distal to the stenosis.

tional imaging, corresponding to a sensitivity of only 27.8 %. Standardised differentiated examination protocols could possibly improve the results [19,20].

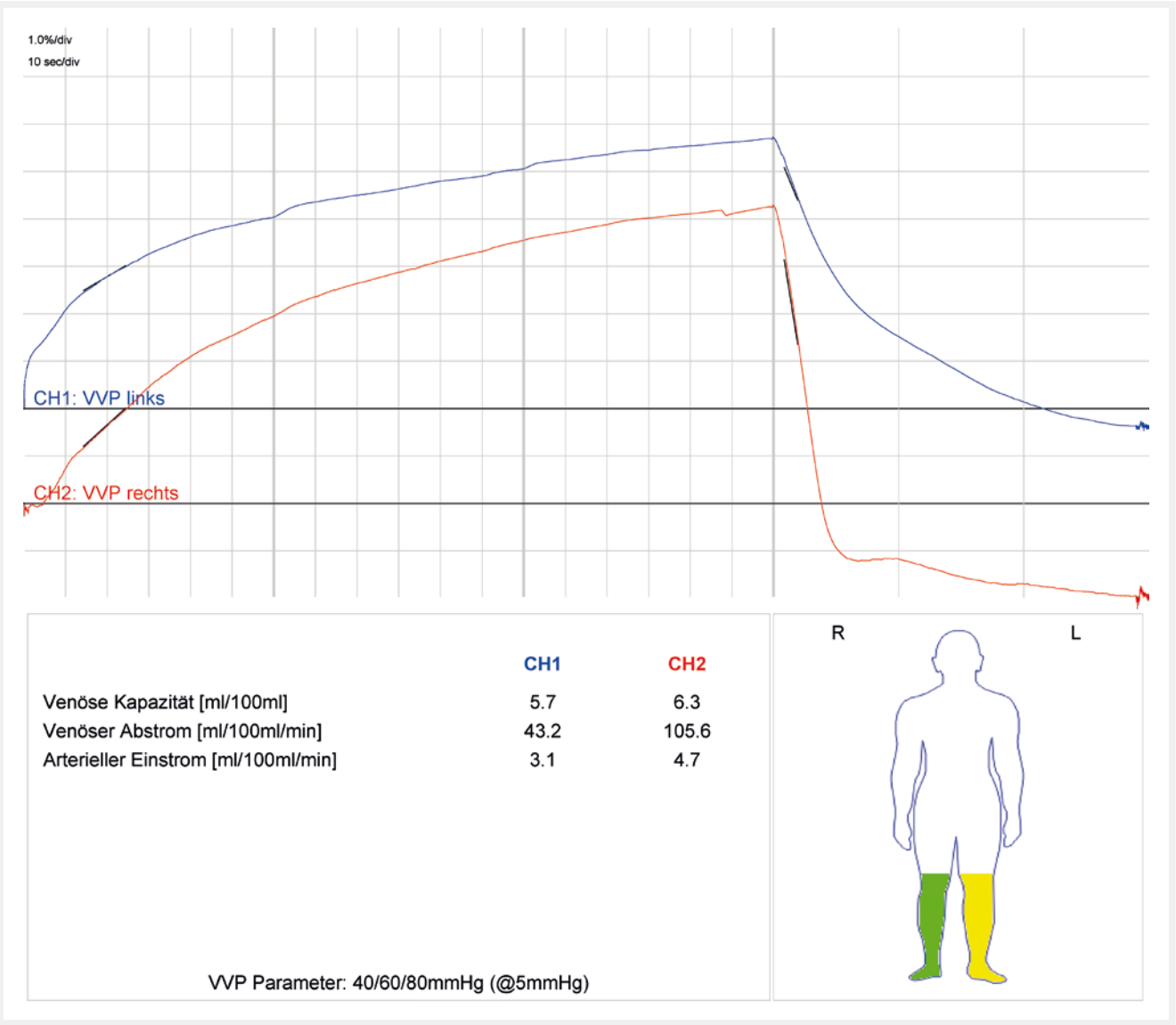
Radiological procedures and intravascular ultrasound (IVUS)

Thromboses of the iliac veins are eight times more common on the left than on the right, a finding that can be attributed to the topographical relationship between the right iliac artery and the spine. Looking at post-mortem specimens, the Austrian pathologists May and Thurner demonstrated local endothelial proliferation and intimal hyperplasia with the formation of a 'spur-like' structure as the result of chronic mechanical changes in 15–22 % of the individuals investigated [21, 22, 23].

Even though numerous case reports and small-scale case studies have been published over the past sixty years, there are not many epidemiological data on the incidence of this 'pelvic venous spur' [24, 25, 26]. In addition, the clinical and prognostic relevance remains unclear at the present time [27]. It is therefore necessary to obtain more information on the functional importance of a confirmed chronic iliac vein occlusion before any recanalisation procedure is carried out.



▶ **Fig. 11** The proximal segment of the inferior vena cava (patient from ▶ **Fig. 1**) eludes the ultrasound. The CT shows a thrombus (arrow) with subtotal narrowing of the lumen in the distal segment of the vessel.



▶ **Fig. 12** Venous occlusion plethysmography (VOP). Comparing the two sides, there is a clear reduction in the venous flow on the left after iliac vein occlusion (43 ml/min vs 106 ml/min). It is not possible to draw any conclusions about the level of the occlusion, its length or the prognosis for patency.

Assessment of the severity of post-thrombotic stenosis or a non-thrombotic May-Thurner syndrome with the curved array probe is possible to only a limited extent. Venography, as part of the preinterventional work-up, is performed with the patient lying supine and limbs extended, but this also does not allow a definite assessment of non-thrombotic obstruction. For this reason, some authors argue in favour of making it compulsory to carry out an intravenous ultrasound (IVUS) examination. In the VIDIO study published in 2017, Gagne et al. compared the results of venography in three views with IVUS in 100 subjects (CVI, CEAP class C4 to C6, with suspected iliofemoral vein obstruction). In 26.3 % of the cases, IVUS showed significant (≥ 50 %) stenosis that was not detected by venography. In addition, stenosis in the radiological imaging was underestimated by an average of 11 % [28] (▶ **Fig. 10a**, ▶ **Fig. 10b**, ▶ **Fig. 10c**).

The research group of Jalaie et al. favoured pre-procedural MR or CT venography, as these methods yield information about possible external compression and collateral vessels in addition to demonstrating stenosis, occlusion and atresia [29] (▶ **Fig. 11**). The Dutch group of Arnoldussen, Tonder and Wittens developed a score to standardise assessment of the iliac veins and of the inferior vena cava (LOVE score), in which MR venography and duplex ultrasonography were shown to be equivalent [30].

Venous functional diagnostics

The primary patency rate after pelvic interventions is given in the literature as 70 %, which corresponds to our experience with our own patient population [14]. This shows the necessity of haemodynamic investigations to identify suitable patients and estimate the chances of success. This is important, not least because a consider-

able number of the target group consists of young fertile women, in whom radiation exposure of the genital organs is not be taken lightly. To date, there are only very few studies on the prognostic significance of haemodynamic factors. Out of 7562 publications on iliac vein stenting and bypass surgery, Kurstjens et al. found only four papers, in which predictions based on the results from haemodynamic studies were required prior to carrying out an intervention [31]. In routine practice, phlebodynamometry (PDM) and venous occlusion plethysmography (VOP) (▶ **Fig. 12**) offer very little additional information. While PDM merely shows a slightly lower to normal pressure reduction with activity in cases of isolated iliac vein obstruction, plethysmography does not allow us to draw any conclusions on the location of a post-thrombotic lesion. Modified VOP and air plethysmography test set-ups are approaches that could offer a different perspective, as various studies have shown [32,33]. Lattimer and Mendoza conducted pioneering experiments with air plethysmography. They were able to identify the venous drainage index (VDI < 11 ml/s) as a parameter that is significantly reduced in cases of iliofemoral obstruction and may be suitable to predict the effects of recanalisation of the iliac veins. Examinations can be carried out with the legs being raised and lowered by an assistant or ideally on a tilt table. However, it should be noted that the necessary equipment is not available in Germany at present and such an examination is not feasible in routine practice [34].

Conclusions

Despite further development of interventional technology in the treatment of thrombosis and despite ever-safer anticoagulant therapy, deep vein thrombosis, pulmonary embolism and post-thrombotic syndrome have not become any less relevant. This can be attributed not least to timing being a key factor, especially in cases of acute disease.

Iliac vein thrombosis is associated with a particularly high risk of a massive pulmonary embolism, which can be explained by the large vessel diameter and the associated higher thrombus burden. Treatment must be initiated as soon as possible to prevent this complication. Colour-coded duplex ultrasound is the medium of choice to confirm the diagnosis and in the investigation proximal to the inguinal ligament. It is cost-effective, widely available and today provides an extremely good visualisation of the vessels. The examiner must be aware of the need to use a curved array probe because of the topography of the lesser pelvis and the depth of the abdomen. In individual cases, MRI and CT may be useful to confirm the diagnosis.

MR and CT venography may provide additional useful information especially in the assessment of chronic iliac vein occlusion and of the disease processes occurring in the vena cava. It must be remembered, however, that these examination techniques are restricted to specialised centres and are not available in all radiology facilities. Invasive methods such as venography and IVUS are reserved for cases involving interventional or surgical treatment, for which particular data, such as the length and cross-section of an obstruction, are required for the planning of the procedure.

SUMMARY

1. The diagnostic investigation of acute and chronic iliac vein occlusion should primarily consist of colour-coded duplex ultrasound using a curved array probe. A linear probe applied distal to the inguinal ligament provides additional indirect haemodynamic information.
2. MR or CT venography is the next diagnostic step, if the ultrasound findings are inconclusive and in cases where thrombectomy or recanalisation is planned.
3. Intravascular ultrasound can be used, if interventional treatment of non-thrombotic vascular obstruction is being considered.
4. Classical direct venography is only required in the context of interventional radiology. It is now obsolete as an isolated diagnostic method.

Conflict of interest

The authors declare that they have no conflict of interest.

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