Interventional Therapy of Pelvic Venous Disorders (PeVD)

Interventionelle Therapie des Beckenvenensyndroms

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Keywords

pelvic venous disorders (PeVD), pelvic congestion syndrome, nutcracker syndrome, may thurner syndrome, endovascular therapy

received 14.9.2023
accepted 23.11.2023
published online 19.2.2024

Bibliography

Fortschr Röntgenstr 2024; 196: 921–927
DOI 10.1055/a-2229-4100
ISSN 1438-9029

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

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ABSTRACT

Background Pelvic venous disorders (PeVD) are an underdiagnosed cause of chronic pelvic pain in women. They are caused by venous insufficiency of the pelvic or ovarian veins, leading to the development of mainly periuterine and periovarian varices. It is a progressive disease if left untreated and can cause swelling, dyspareunia, dysmenorrhea, and other symptoms, some non-specific, that affect the patient's quality of life. Interventional therapies are a central component of the treatment of PeVD, with a variety of techniques available for both diagnosis and treatment.

Method This review provides an overview of the pathophysiologic background, diagnosis, and, most importantly, interventional treatment options for PeVD.

Results There is a lack of standardized nomenclature and internationally accepted diagnostic criteria for PeVD as well as randomized controlled trials demonstrating clinical success. However, in clinical trials, endovascular therapy for PeVD has been shown to be safe and effective. This review presents the various interventional techniques for the treatment of PeVD, including embolization, stenting, and sclerotherapy.

Conclusion The importance of PeVD is receiving growing recognition. Recent advances, such as the development of the Symptoms-Varices-Pathophysiology (SVP) classification, provide an impetus to standardize nomenclature and are the first step toward systematizing disease management. Interventional therapies provide a safe and tailored minimally invasive treatment option for patients with PeVD.

Key Points

- Pelvic venous disorders are an underdiagnosed condition with frequently delayed diagnosis and debilitating symptoms.
- Until now, the PeVD nomenclature has been imprecise, with terms like May-Thurner syndrome/Nutcracker syndrome.
- Interventional approaches are effective and play a central role in PeVD treatment.

Citation Format

- Dewald CL, Becker LS, Meyer BC. Interventional Therapy of Pelvic Venous Disorders (PeVD). Fortschr Röntgenstr 2024; 196: 921–927

ZUSAMMENFASSUNG

Hintergrund Das Beckenvenensyndrom ist eine unterdiagnostizierte Ursache für chronischen Beckenschmerz bei Frauen. Ursächlich ist eine venöse Insuffizienz der Becken- oder Ovarialvenen, die zur Ausbildung von meist periuterinen und periovarialen Varizen führt. Es handelt sich um eine unbehandelt fortschreitende Erkrankung, die Schwellungen, Dyspareunie und Dysmenorrhoe und weitere, teils unspezifische Symptome verursachen kann, die die Lebensqualität der Patientinnen beeinträchtigen. Die interventionelle Therapie stellt einen zentralen Bestandteil der Behandlung des Beckenvenensyndroms dar, wobei verschiedene Techniken sowohl zur Diagnosestellung als auch zur Behandlung zur Verfügung stehen.

Methode Die folgende Arbeit gibt einen Überblick über den pathophysiologischen Hintergrund, die Diagnostik und vor allem die interventionellen Behandlungsoptionen des Beckenvenensyndroms.

Ergebnisse Bei dem Beschwerdebild des Beckenvenensyndroms mangelt es bisher an einer einheitlichen Nomenklatur und an international anerkannten Diagnosekriterien als auch an randomisierten kontrollierten Studien, die den klinischen

Erfolg belegen. In klinischen Studien hat sich die endovaskuläre Therapie des Beckenvenensyndroms jedoch als sichere und wirksame Therapie erwiesen. In dieser Übersicht werden die verschiedenen interventionellen Techniken zur Behandlung des Beckenvenensyndroms dargestellt, darunter die Embolisation, das Stenting und die Sklerotherapie.

Schlussfolgerung Die Bedeutung des Beckenvenensyndroms erlangt zunehmend Aufmerksamkeit. Rezente Fortschritte, wie die Entwicklung der Symptome-Varizen-Pathophysiologie (SVP)-Konsensusklassifikation geben einen Anstoß zur Vereinheitlichung der Nomenklatur und sind der erste Schritt zur Systematisierung des Krankheitsmanagements. Interventionelle Therapien bieten eine sichere und maßgeschneiderte minimalinvasive Therapieoption für Patientinnen mit Beckenvenensyndrom.

Kernaussagen

- Beckenvenensyndrom ist ein unterdiagnostiziertes Erkrankungsbild mit oft verzögerter Diagnosestellung und lähmenden Symptomen.
- Bisher war die Nomenklatur des Beckenvenensyndroms durch Begriffe wie May-Thurner-Syndrom/Nussknacker-Syndrom ungenau.
- Interventionelle Ansätze sind wirksame Techniken mit zentralem Stellenwert in der Beckenvenensyndrom-Therapie.

Introduction

Pelvic venous disorders (PeVD) are common but are underdiagnosed and typically diagnosed with a delay. They are associated with chronic pain and symptoms in the region of the genitals and pelvis. The prevalence of pelvic venous disorders is difficult to determine since the clinical picture is not well known and there is no consensus about the definition and diagnostic criteria. However, studies indicate that pelvic venous disorders are the cause of chronic pelvic pain in up to 30 % of patients [1].

The spectrum of symptoms in this disease relates to the pelvic veins and their primary drainage pathways. The underlying pathology is pelvic venous insufficiency characterized by varicose dilation and venous dysfunction with slow flow and reflux [1, 2]. Various terms have been used in the past to describe the various diseases in this disease spectrum, including pelvic congestion syndrome as well as syndromes describing the individual underlying pathology, namely May-Thurner syndrome and Nutcracker syndrome. Since this nomenclature provides only an imprecise description of the partially complex overlapping of these diseases and does not sufficiently take the underlying pathomechanism into consideration, these terms should no longer be used [3]. This article provides an overview of pelvic venous disorders in women.

Anatomy of the pelvic veins

The blood from the uterus drains via the uterine venous plexus. The lower part of the uterine venous plexus drains via the uterine vein into the internal iliac vein. The upper part is connected to the ovarian venous plexus via the broad ligament of the uterus and drains into the ovarian vein. While the right ovarian vein usually drains directly into the anterolateral inferior vena cava below the right renal vein at an acute angle, the left ovarian vein opens into the left renal vein. There are typically multiple collateral connections between the pelvic veins [1, 3, 4].

Pathophysiology

Pelvic venous disorders can be caused by various mechanisms. One of the most common causes is primary acquired ovarian vein insufficiency. Venous valves are seen in the ovarian veins in approx. 80 % of patients. However, they are incompetent in 35–40 % of all women. An additional strain on the venous system can result in increasing insufficiency of the venous valves. Therefore, pregnancy is considered a main risk [1, 3–5]. In particular, the up to 60 times greater uterine blood flow during pregnancy and hormonal influences result in a chronic volume load and consecutive ectasia of the ovarian veins, which can cause valve incompetence [1, 5–7]. As a consequence of the increasing insufficiency of the ovarian veins, venous stasis develops and central drainage stops or a reversal of flow occurs. The congestion and reflux result in the formation of varices of the periuterine and periovarian venous plexus and a volume load of the internal iliac vein. The increased venous pressure can also manifest as superficial varices of the vulva, clitoris, perineum, or the inguinal region via various pelvic escape points [7]. For example, the prevalence of vulva varices in pelvic venous disorders is 24–40 % [1, 8].

Pelvic venous disorders can also occur on a secondary basis. There are two anatomical locations at which venous congestion can occur due to an obstruction: (a) in the case of compression of the left common iliac vein due to crossing of the right iliac artery (previously known as May-Thurner syndrome) and (b) in the case of compression of the left renal vein when constricted either between the superior mesenteric artery and the abdominal aorta (anterior type) or between the abdominal aorta and the spinal column (posterior type). This anatomy is also known as Nutcracker syndrome. The result is elevated venous pressure in the left renal vein, which is relieved by perirenal collateral veins and the left ovarian vein. The reflux results in secondary ovarian vein insufficiency with consecutive formation of periuterine and periovarian varices.

In the case of significant compression of the left common iliac vein, reflux into the left internal iliac vein results in the formation of rectal and periuterine varices [7]. The increased volume load of the ovarian vein can also result in secondary ovarian vein insufficiency. While the described mechanisms have various etiologies, the effect is comparable with that of primary ovarian vein insufficiency.

Symptoms

The clinical spectrum of pelvic venous disorders ranges from mild symptoms like a feeling of fullness and discomfort in the pelvis to chronic debilitating dull pelvic pain, dyspareunia, and dysmenorrhea, which impact quality of life [9]. Dysuria or desire to urinate can also be caused by perivesical varices. However, the relationship between pathological venous changes and symptoms is complex and not yet fully understood: Similar pathologies can cause different symptoms in different patients and identical symptoms can have different underlying pathophysiologies.

Diagnosis

Reliable detection of pelvic venous disorders is not always simple due to their complexity, particularly since the presence of the often nonspecific symptoms and insufficient pelvic veins does not necessarily have a causal relationship: Reflux into the ovarian vein is seen in 100 % of patients with symptomatic pelvic varices as well as approx. 25 % of asymptomatic patients [3].

In the case of suspicion of pelvic venous disorders, a transabdominal or transvaginal ultrasound (US) examination of the pelvic veins is performed first. In the case of transabdominal duplex US, an ovarian vein with a diameter of greater than 5 mm and retrograde flow in the ovarian vein are important signs of a pelvic venous disorder [10]. Moreover, transabdominal US allows direct visualization and evaluation of the renal and pelvic veins [11]. In contrast, transvaginal US decreases the distance between the probe and the pelvic structures. As a result, better resolution and image quality than in transabdominal US can be achieved at higher frequencies [10]. Particularly in an upright position, periuterine and periovarian varices that are seen as dilated tubular structures can be identified. A hemodynamic evaluation of reflux can be performed using the Valsalva maneuver [10, 11]. Three sonographic criteria are important for confirming the suspected diagnosis of a pelvic venous disorder: Dilated tortuous pelvic veins with a diameter of more than 6 mm, slow blood flow (≤ 3 cm/s), and a dilated arcuate vein in the myometrium that is connected to the pelvic varices [12, 13].

Together with abdominal US, transvaginal US is the first step in the diagnosis of pelvic venous disorders. However, US is readily available but is highly examiner-dependent. In addition, US can only be used on a conditional basis for surgical planning.

A suitable dynamic examination modality for evaluating pelvic veins as well as for surgical planning is time-resolved MR angiography, which can provide exact information about the direction of flow in the veins. Dilated ovarian veins and pelvic veins can be best visualized in the venous phase on contrast-enhanced T1-weighted images. In a comparison between time-resolved MR angiography and venography, the specificity, sensitivity, and exactness were 61–75 %, 100 %, and 79–84 %, respectively [14]. Subtracted images with maximum intensity projection are used for 3 D imaging of the course of the dilated veins (▶ **Fig. 1**). The pelvic varices appear as multiple dilated tubular structures around the uterus, ovaries, and pelvic side wall. They are hypointense on T1-weighted images and hyperintense on T2-weighted images [7]. With its high spatial resolution and excellent soft-tissue contrast, MRI has the added advantage that other pathologies like endometriosis and gastrointestinal or musculoskeletal pathologies that can also cause chronic pelvic pain, can be ruled out [1, 7].

▶ **Fig. 1** Time-resolved MR-angiography of a 45-year-old female patient with chronic lower abdominal pain for approx. 5 years. **a–d** Subtracted T1-weighted images in maximum intensity projection in coronal orientation with a 5-second time delay between images. The contrast agent flows in a retrograde direction through the insufficient, dilated left ovarian vein (**a**) and the varicose left periuterine venous plexus (**b**) to the contralateral vein plexus (**c**) and then in an anterograde direction through the right ovarian vein (**d**).

The diagnostic gold standard for pelvic venous disorders is direct venography. However, due to the invasiveness, this method should be reserved for patients with significant suspicion of a pelvic venous disorder after noninvasive imaging [1, 10]. In addition to visualization of the etiological venous compression, detection of reflux after selective probing of the ovarian vein and internal iliac vein can help to determine the diagnosis. Reflux manifests as retrograde flow in the examined vascular region that is spontaneous or stimulated by the Valsalva maneuver [15]

Since strict definitions and randomized prospective studies have been lacking in the past, the existence of pelvic venous disorders has been regularly questioned [3]. Recognizing the need to

improve the nomenclature in order to support clinical communication, decision making, and the quality of future research, the American Vein and Lymphatic Society published the first consensus classification in 2021 [15]. This new Symptoms-Varices-Pathophysiology (SVP) classification includes three categories: symptoms (S), varices (V), and pathophysiology (P). Pathophysiology includes further anatomical (A), hemodynamic (H), and etiological (E) aspects of the disease, which are mentioned as a subscript after pathophysiology (P). The symptoms of each patient are thus classified as $SVP_{A,H,E}$. Symptoms (S) and varices (V) are divided into 4 anatomical zones ((1) left renal vein, (2) gonadal veins, internal iliac veins, and pelvic veins, (3) veins originating in the pelvis that run via escape points to the genitals or the lower extremities, and (4) veins of the lower extremities). The fourth zone is assigned to the CEAP (clinical, etiologic, anatomic, physiologic) system, which is already established for the classification of venous diseases of the lower extremities. In spite of its complexity, the classification allows standardization of the nomenclature and is the first step in systematizing management of the disease. Thanks to this new classification, it is now possible to create homogeneous patient groups in studies. However, generally used, internationally accepted diagnostic algorithms allowing objective diagnosis and differentiation of diseases with similar symptoms are still lacking.

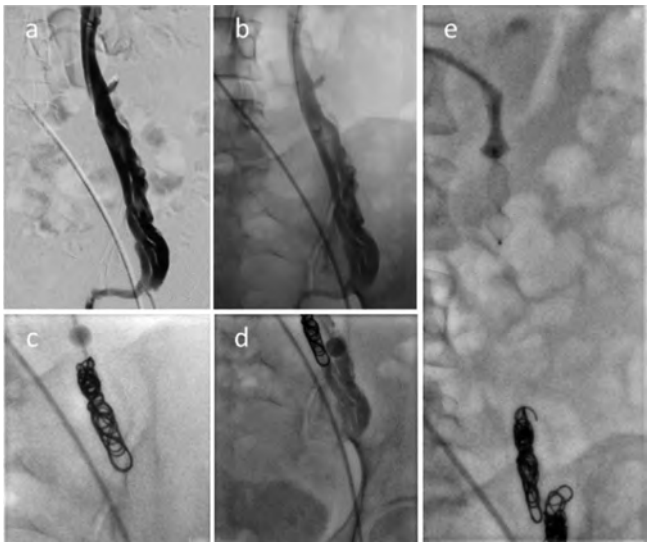
Interventional treatment options

Endovascular treatment options include treatment of incompetent ovarian and pelvic veins with embolization and sclerotherapy and the treatment of venous obstructions. The treatment approach depends on the underlying pathology. Diagnostic imaging of the pelvic veins on both sides and the two ovarian veins is performed first.

Embolization of the ovarian veins

At our institute, a short 6F sheath is initially inserted into the left common femoral vein to examine the iliac veins regarding compression of the left common iliac vein. The sheath is then changed to a long 6.5F sheath and the left ovarian vein which drains into the left renal vein is then probed with a diagnostic catheter. Imaging is subsequently performed possibly using the Valsalva maneuver. The presence of reflux confirms the pelvic venous disorder. The ovarian vein is embolized from distal (near the uterus) to proximal [3]. In the literature, various combinations of embolization agents are described including liquid embolization agents like n-butyl cyanoacrylate, ethylene-vinyl alcohol, and sclerosants. Today, coils and vascular plugs are usually used as solid embolic agents that allow mechanical embolization. Detachable balloons are rarely used anymore [16].

In our clinic, we use a combination of coil and plug embolization in connection with polidocanol foam as a sclerosant (▶ **Fig. 2**). To apply the sclerosant, a 5.5F balloon catheter is first inserted via a 0.035-in guide wire into the distal ovarian vein and is inflated. By filling the pelvic varices with contrast agent until the contrast flows into the competent deep pelvic veins, the volume for sclerotherapy can be determined. This volume can vary but is often between 5 and 15 ml. The contrast agent is then immediately expelled by injecting the sclerosant foam. By leaving the inflated balloon catheter in the distal ovarian vein for approximately 10 minutes, early washout of the sclerosant can be avoided. Coil embolization of the distal ovarian vein and sclerotherapy of the ovarian veins according to the described technique are then performed. Below the opening into the renal veins, the sclerosed ovarian vein is then sealed with a vascular plug. If the right ovarian vein is also insufficient, the procedure is performed here again using the same technique. Patients with pelvic varices originating from the internal iliac vein can also benefit from embolization. Due to the increased risk of migration at this anatomical location, coil embolization is usually avoided here [3].



▶ **Fig. 2** Embolization of the ovarian vein in a 36-year-old female patient with chronic lower abdominal pain. **a** and **b** Images of the left ovarian vein after selective probing with a 4F diagnostic catheter. A dilated vessel diameter of the vein, which is split into two branches in the distal portion, and retrograde flow are seen. The diagnosis of a pelvic venous disorder can thus be made. Balloon occlusion of the medial branch (**c**) and then the lateral branch (**d**) of the distal ovarian vein is performed. Both branches are filled with contrast agent to determine the amount of polidocanol foam needed for the subsequent sclerotherapy of the periovarian/periuterine varices and are then embolized with multiple coils of varying size and configuration. Sclerotherapy of the ovarian vein and plug embolization of the proximal ovarian vein are then performed. Final imaging shows sufficient embolization of the ovarian vein (**e**).

The administration of NSAIDs can partially alleviate postinterventional symptoms due to the induced phlebitis [12]. More serious complications like deep vein thrombosis, pulmonary embolisms, and coil migration are rare [3]. Embolization has a very high technical success rate of 97–100 % [3, 17]. The clinical result is also described as very good with success rates of 70–100 % [18], and the published recurrence rates are approximately 10–40 % [3, 12, 19]. However, long-term clinical success can only be measured on a limited basis or cannot be measured due to the current lack of standardization of data regarding treatment results in published studies. As long as randomized controlled studies are not available, structured analyses of available data can be used. For

example, a meta-analysis recently conducted by de Carvalho et al. shows an efficient reduction of symptoms [20].

Venous stent implantation

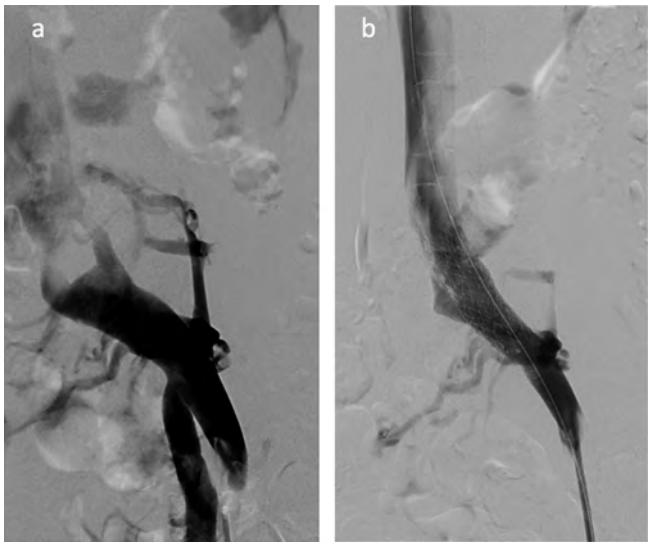
When an obstruction of the internal iliac vein or left renal vein is assumed to be the cause of a pelvic venous disorder, stent implantation can be performed.

However, the indication for decompression of the left renal vein is still controversial [21, 22]. In the case of mild hematuria and mild symptoms, conservative treatment is primarily preferred. Treatment should last for a minimum of 6 months in adults and for at least 24 months in growing patients [23, 24]. Low-dose acetylsalicylic acid (ASS) can be prescribed to improve renal perfusion but its routine use is controversial. Moreover, angiotensin-converting enzyme inhibitors can help to alleviate orthostatic proteinuria [21, 23, 25]. Since the presence of an obstruction of the left renal vein is associated with a low body mass index, weight gain can be helpful [26]. Stent implantation should only be discussed in patients who do not respond to conservative therapy and in the case of advanced effects of the obstruction [21]. However, even if stent implantation is not performed, the secondary pelvic insufficiency can be treated with embolization of the ovarian vein. It must first be confirmed on angiography that venous drainage of the kidneys is not dependent on the ovarian vein [25].

Even in the case of stenosis of the pelvic veins, stent implantation should only be performed when the symptoms can be directly attributed to the stenosis since the prevalence of stenosis of the common iliac vein is also high in asymptomatic patients [3]. The degree of stenosis that is clinically relevant and the point at which symptom alleviation can be expected after treatment cannot be definitively determined. Venography is highly suited for evaluating collateral veins, flow rate, and flow direction but is less sensitive and accurate regarding the identification of gradual stenosis [27, 28]. In addition to venography, intravascular ultrasound can be used here with a > 50 % lumen reduction being considered significant [3, 15]. Alternatively, a moderately filled (< 1 atm) 14-mm balloon catheter can be guided through the suspected stenosis of the common iliac vein. If the balloon does not get caught or blocked, significant stenosis is unlikely [27].

If an obstruction is confirmed, stent implantation is performed after angioplasty. The stent should stretch from healthy vessel to healthy vessel, i. e., to areas with a normal vessel diameter [27, 29]. The stent is positioned so that it covers the stenosis but ideally leaves the opening of the right common iliac vein open [30]. The goal is to achieve fast, uniform contrast flow through the treated segment and to reduce collateral filling (▶ **Fig. 3**). Post-procedural anticoagulation and thrombocyte aggregation inhibition is still a topic of discussion [11]. The lack of consensus regarding this topic is reflected both in the different anticoagulant therapies specified in the literature and in the small number of recommendations in international guidelines [31, 32].

In many cases, patients have a combination of compression of the common iliac vein and reflux (into the internal iliac vein or ovarian vein). The literature contains contradictory data as to whether decompression of the common iliac vein alone or treatment of the reflux alone is sufficient for significant clinical improvement or whether both pathologies should be treated. While some authors have described clinical success after stent implantation alone, other work groups have reported a significant reduction of symptoms after pelvic vein embolization alone [27, 33–35]. Other authors recommend first treating the venous stenosis followed by reflux embolization if symptoms persist. However, patients with a large pelvic reservoir should receive simultaneous treatment [36].



▶ **Fig. 3** Venography of a 38-year-old female patient with compression of the left common iliac vein by the common iliac artery (May-Thurner syndrome). **a** After insertion of a 5F sheath into the left common femoral vein, significant stenosis of the left common iliac vein just before the confluence to the inferior vena cava is seen on initial angiography. Consecutive collateral filling and retrograde flow in the dilated internal iliac vein as a manifestation of the hemodynamic relevance. **b** After stent implantation, drainage through the left common iliac vein and the inferior vena cava has been restored.

It appears that both stenting of the common iliac vein and pelvic vein embolization as individual treatments do not have a negative effect on the postinterventional conception rate [37, 38]. To date, there are no corresponding studies regarding combination therapy. On the whole, complications after stent implantation are minor. Stent-associated lower back pain that lasts for a variable amount of time is one of the more common complaints [39]. Severe complications include heavy bleeding (up to 1 %), pulmonary embolism (< 1 %), and early restenosis or occlusion of the treated lesion (1–7 %) [21]. The periprocedural mortality rate is less than 1 %.

Outlook

In light of the increasing recognition of pelvic venous disorders as an underdiagnosed cause of chronic pelvic pain in women, both gynecology and radiology play an important role in the detection and proper treatment of the disease. While the pathomechanisms of pelvic venous disorders are increasingly understood, primary diagnosis remains challenging [1]. In the future, the development

of internationally accepted diagnostic algorithms allowing an objective diagnosis and differentiation between diseases with similar symptoms would be desirable.

The effectiveness of the interventional treatment of pelvic venous disorders can only be conditionally determined due to the variations in the diagnostic algorithms, treatment approaches, and follow-up intervals used in studies, but the clinical results of the currently available studies are promising. The new SVP consensus classification should make it easier in the future to categorize patient cohorts and to examine the treatment results of different embolization materials and techniques in randomized studies.

Conflict of Interest

The authors declare that they have no conflict of interest.

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