

Invited Review**Pelvic venous disease; knowledge gap**ID Marie Josee E van Rijn¹, ID Clark J Zeebregts²¹Erasmus University Medical Center, Department of Surgery, Division of Vascular Surgery, Rotterdam, The Netherlands²University Medical Center Groningen, Department of Surgery, Division of Vascular Surgery, Groningen, The Netherlands

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**Abstract**

Good quality data is lacking for pelvic venous disease (PeVD) and there are knowledge gaps in several topics. While we know that multiple pregnancies, hormonal factors and compression syndromes are risk factors, less is known about environmental and lifestyle factors. Most studies investigated the effect of coil embolization in relation to pain, but outcomes missing are quality of life (QOL), recurrence, complications, cost-effectiveness and predictors of a good response. There are no studies comparing different embolization techniques and hardly any studies on alternative treatment modalities or pharmacological treatment. It is important to distinguish different symptoms PeVD can cause when reporting patient related outcomes. Most studies use VAS scores, however, there is more to PeVD than pain. Concomitant diseases are common and may impact QoL by itself and must be taken into consideration as well. Finally, there are gaps in patient education and awareness. A scoring system would help in identifying patients. Recently, such a screening score was proposed. In conclusion, research in the field of PeVD is still in its infancy creating gaps in knowledge and awareness. Closing these gaps is essential for PeVD diagnosis and treatment.

Keywords: Knowledge gap, patient outcome, quality of life, awareness**INTRODUCTION**

Pelvic venous disease (PeVD), previously referred to as pelvic congestion syndrome, is now widely recognized as a serious entity, affecting women (and to a lesser extent men) all over the world. Guidelines and consensus documents have included PeVD and aimed to formulate recommendations on diagnosis and treatment. [1-3] Recently, the Symptoms-Varices-Pathophysiology (SVP) classification was developed to improve clinical decision making and develop disease-specific outcome measures [4]. These are very important steps forward for both patients and physicians, as well as for industry partners and all others that are aiming to provide optimal PeVD care. From a search through PubMed®, it becomes clear that there is increasing interest and awareness for PeVD. Between 1949 and 1999, a total of 106 hits appear when searched for MESH terms “pelvic congestion”. This has increased to 388 hits for the years 2000-2023, mainly increasing from the year 2014 onwards. However, only a handful of these

studies were randomized controlled trials (RCT), indicating a lack of good quality data. This is represented in the fact that the 6 recommendations on PeVD in the ESVS guidelines on chronic venous disease, are all level of evidence B or C [2]. In the knowledge gap chapter of the ESVS guidelines, the lack of well-defined clinical criteria for the diagnosis, the absence of a scoring tool or imaging criteria to select patients who would benefit the most from intervention, and the lack of RCTs proving the efficacy of intervention and comparing different treatment modalities, are mentioned. In this paper, we will discuss several PeVD related topics with an ongoing knowledge gap, that should be prioritized first as issues to focus on in future studies.

Etiology and Risk Factors

While there are numerous population based studies that have investigated risk factors for chronic venous disease (CVD) of the lower extremities, there are hardly any studies performed

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aiming to identify etiologic causes or risk factors for PeVD. So far, multiple pregnancies and hormonal factors have been identified as risk factors, as well as compression syndromes such as nutcracker syndrome (compression of the left renal vein by the superior mesenteric artery) and May-Thurner syndrome (compression of the left common iliac vein by the right common iliac artery) [4]. Data on environmental and lifestyle factors are scarce. While a higher body mass index (BMI) has been associated with CVD [5], a reversed association was found for PeVD. A group of 100 women with PeVD was categorized into 59 women with normal BMI, 23 overweight women, and 18 obese women. Patients with ovarian vein dilation had significantly lower BMI, although no differences were identified for pelvic varices or reflux. Leg varicosities on the other hand were significantly more prevalent in obese patients [6]. Increasing our knowledge of PeVD etiology and risk factors is specifically important in light of prevention and screening tools, for which high risk individuals should be selected.

Treatment Modalities

Which treatment modality is best suited for which patient starts with understanding the etiology of the pelvic problems. Hemodynamically, there can be obstruction, reflux, or both, resulting from a thrombotic, non-thrombotic or congenital cause [4]. Most studies investigated the effect of coil embolization of refluxing pelvic veins, mainly in zone 2 of the SVP classification [4], i.e. the gonadal and internal iliac veins and associated pelvic venous plexuses. A systematic review of 970 patients, all female, who underwent isolated ovarian vein or mixed veins coil embolization from 20 studies were included. Pooled analysis revealed mean improvements of 5.47 points (95% CI, 4.77-6.16) on the visual analogue scale (VAS), with reported improvements of urinary urgency (78-100%) and dyspareunia (60-89.5%). However, the review included only 2 RCTs. One compared coils with plugs, and one compared coils with hysterectomy [7-9]. Follow-up ranged from 6 weeks to 90 months, and most were retrospective studies. The main outcome studied was pain using the VAS score and only 4 studies reported symptoms specific for PeVD. Quality of life (QOL), recurrence, complications, cost-effectiveness or predictors of a good response to embolization have not been included in the majority of studies so far [10].

Other embolization techniques like Onyx® [11] and foam [12] have shown promising results too. There are however no studies comparing these different embolization techniques, so it is unknown which technique is preferred. Data on alternative treatment modalities, specifically in comparison to embolization, are also lacking. Lifestyle changes, psychological support or pain consultation might all be beneficial too, but without studies providing evidence for the effectiveness of these non-invasive measures, they will not be incorporated into daily practice. That is why, embolization is the number one treatment choice to date, however, there is no real evidence to support this.

An additional knowledge gap is the fact that there are no studies describing the percentage of pelvic veins that need to be embolized to reach good clinical results. Clinical success in relation to a multidisciplinary approach, or centralizing embolization procedures in specialized (high volume) centers, is also not studied so far. Lastly, patient related outcome measures (PROMS), designed and validated for PeVD, are not available. Scoring the effect of invasive treatment using only VAS scores, or PeVD symptoms, just isn't good enough (see also paragraph patient outcomes).

Data on pharmacological treatment (for pain relief, hormonal therapy or veno active drugs) is scarce. Due to the limited drug administration period, low quality studies, insufficient follow-up (during administration and after cessation) and small patient numbers, the authors of a review on pharmacological treatment of PeVD concluded that there is insufficient data to make any recommendations [13].

In case obstruction is the cause of PeVD, treatment should be aimed on elevating the obstruction. This may be done using dedicated venous stents, or by means of transposing the compressed vein. In case of nutcracker syndrome, another option is transposing the superior mesenteric artery. The goal is to eliminate venous hypertension by facilitating venous drainage from the pelvic reservoir. Stenting iliac vein compression, in the presence of ovarian vein reflux, as the sole treatment of pelvic symptoms achieved complete symptom resolution in 76% of 82 patients in one study [14]. In another study however, 10 out of the 12 stented patients needed embolization during follow-up due to persisting symptoms [15].

When the pelvic veins are collaterals, draining the leg and the pelvis when the deep veins are obstructed after deep venous thrombosis (DVT), stenting should be the first choice because occluding the collaterals would instantly cause more problems. When the ovarian vein is the primary draining vein of the left kidney, in case of a nutcracker configuration, embolizing the ovarian vein might trigger an acute nutcracker syndrome. However, since there are no RCTs randomizing between embolization and treating the obstruction, we cannot make recommendations or treatment pathways for these specific patients.

Patient Outcomes

It is important to distinguish different symptoms PeVD can cause when reporting PROMs. So far, most studies have used VAS scores as their primary outcome, however, there is more to PeVD than just pain. Besides chronic pelvic pain, perineal heaviness, urgency, postcoital pain as well as vulvar, perineal, and lower limb varicose veins, all impact QOL. Pain relief is an important treatment goal, but therapy should improve other symptoms as well. In addition, recurrence rates, specifically during long-term follow-up, are unknown.

PeVD is not typically associated with female infertility, but it can be challenging to diagnose and manage in women of childbearing age. Fertility outcomes related to PeVD (with or without treatment) are not available for women. For men on the other hand, a large meta-analysis including 351 studies showed that conventional semen parameters improved significantly following varicocele repair in infertile patients [16].

Patient outcomes can vary widely, and what works best for one person may not be as effective for another. One study found that different PeVD symptoms vary according to age. Venous stenting progressively increased with each decile of age whereas the prevalence of ovarian vein embolization was similar between the age groups. The authors also found that women in their twenties, did not respond as well to intervention as women in other age groups [17]. An online survey for members of a pelvic venous disease support group found a very high prevalence of self-reported comorbid syndromes; irritable bowel syndrome (29%), fibromyalgia (13%), spinal nerve problems (18%), interstitial cystitis (10%), postural tachycardia syndrome (9%), hypertension (11%), chronic fatigue syndrome (10%), and Ehlers-Danlos syndrome (6%) [18]. Concomitant diseases may very well impact QoL by itself and must be taken into consideration as well. As mentioned previously, VAS scores alone do not cover all the aspects PeVD entails. Quality of life is related to all of the above and should be incorporated as outcomes in future studies.

Finally, there are still gaps in patient education and awareness of PeVD. Efforts to increase awareness among both healthcare providers and patients can lead to earlier diagnosis and treatment. Pelvic venous disease is not as well-known among the general public as some other medical conditions. Many individuals experiencing pelvic pain may not be aware that PeVD is a potential cause of their symptoms. Raising public awareness about PeVD and its symptoms is crucial to help individuals seek timely diagnosis and treatment. A scoring system would help in identifying patients. Recently, such a screening score was proposed, including symptoms like chronic pelvic pain for more than 3 months, vulva varicosities and aggravation of pain during upright position, sexual intercourse or menstruation. For each symptom a certain amount of points are awarded with ≥ 3 points indicating the PeVD is possible or likely [19].

CONCLUSION

In conclusion, research in the field of PeVD is still in its infancy creating enormous gaps in knowledge and awareness. Closing these gaps through research, collaboration, and advancements in diagnostic techniques is essential for improving the accuracy and effectiveness of PeVD diagnosis, ultimately leading to better patient care and outcomes.

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