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Pelvic Congestion Syndrome

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Pelvic congestion syndrome (PCS) is often an underdiagnosed cause of chronic pelvic pain in female patients with radiology detection of gonadal vein dilatation and parauterine varices. It may occur either alone or in combination with vulvar varicosities and/or lower extremity venous insufficiency. Although transcatheter venography represent the gold standard for PCS diagnosis, it is performed after inconclusive noninvasive imaging such as Doppler Ultrasound, CT scan, and MRI. Once diagnosis has been confirmed, management of PCS include medical, surgical, and endovascular therapy. Medical and surgical treatments have been shown to be less effective than transcatheter pelvic vein embolization. This latter has been proven to be a safe, effective, and durable therapy for the treatment of PCS. Numerous studies have shown their results in PCS endovascular treatment, but neither of them has been subjected to an adequate randomized controlled trial. A well-designed randomized controlled trial is urgently needed to assess transcatheter embolization clinical success.
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Introduction

Pelvic congestion syndrome (PCS) is one of the underdiagnosed cause of chronic pelvic pain in female patients.[1,2] PCS is often described in literature also as "pelvic pain syndrome," "female varicocele," "pelvic vascular congestion," and pelvic venous insufficiency (PVI).[3] PCS is defined as the presence of ovarian and pelvic varicose veins associated with chronic pelvic pain persisting for more than 6 months that increases with prolonged standing, coitus, and menstruation.[4] PCS may typically affects young multiparous women between 20 and 30 years and may be suspected after exclusion of other causes of chronic pelvic pain such as endometriosis, adenomyosis, urologic disorders, and gastrointestinal disorders.[3-5]

Pathophisiology and Clinical features

PCS consists in gonadal vein reflux and venous engorgement causing chronic pelvic pain of at least 6 months duration.[4] The presence of gonadal vein dilatation and parauterine varices alone are not enough to make diagnosis of PCS.[1] It may also manifest with lower back pain and pelvic heaviness (sometimes unilateral) exacerbated with menses, pregnancy or coitus.[1,6,7]

PCS may occur either alone or in combination with atypical vulval varicose veins and/or lower extremity venous insufficiency.[5-8] This latter may results from transmission of venous reflux to the saphenofemoral-junction through the external pudendal collateral veins.[8]

PCS caused by incompetent or absent vein valves is known as PVI.[6] Valves are absent from ovarian veins in 15% of women and incompetent on the left and right in 40% and 35%, respectively.[9]

PVI is anatomically analogous to the male varicocele, with more difficult diagnosis due to the not external view or palpation.[6] The gonadal veins originating from the ovarian venous plexus drain into either the infrarenal Inferior Vena Cava (IVC) on the right side or the left renal vein on the left side (Fig. 1).[10] Some external compression and obstruction at suprapelvic drainage (infrarenal IVC or left renal vein) or at pelvic drainage (internal iliac veins) may cause PVI of gonadal or uterine venous system providing an alternate route for blood flow between the IVC and the internal iliac veins.[10,11] PVI may be a consequence of extrinsic compression of left common iliac veins between the overlying right common iliac artery and the fifth lumbar vertebra, in a condition known as May-Thurner Syndrome[12] (Fig. 2). As varicocele in men, PVI closely involves

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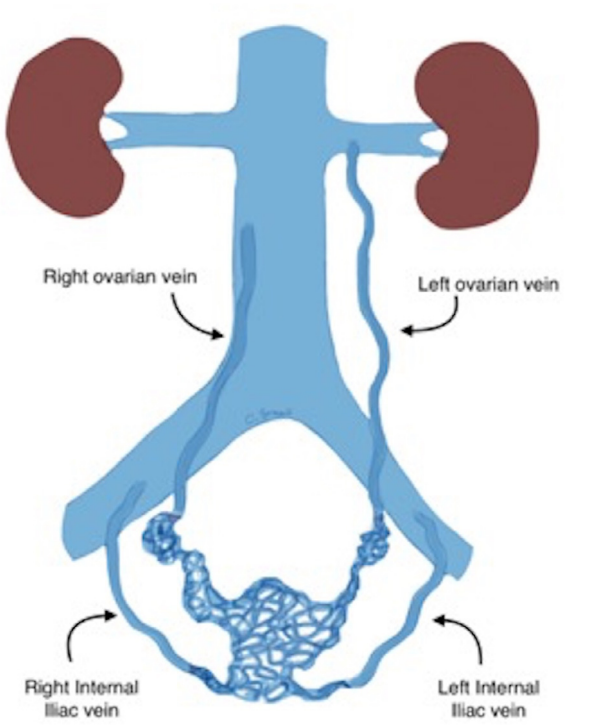


Figure 1 Drawing shows suprapelvic and pelvic venous drainage.

above all the left ovarian vein due to the predisposing anatomic abnormalities such as more frequent lack of venous valves and left renal vein compression in Nutcraker syndrome[7,13] (Figs. 3 and 4). The latter can be distinguished in the "anterior" type, when the compression involves the left renal vein between the aorta and the superior mesenteric artery, and posterior type between the aorta and a vertebral body.[14,15] When the right ovarian vein is affected, its junction with the IVC is usually anomalous.[16]

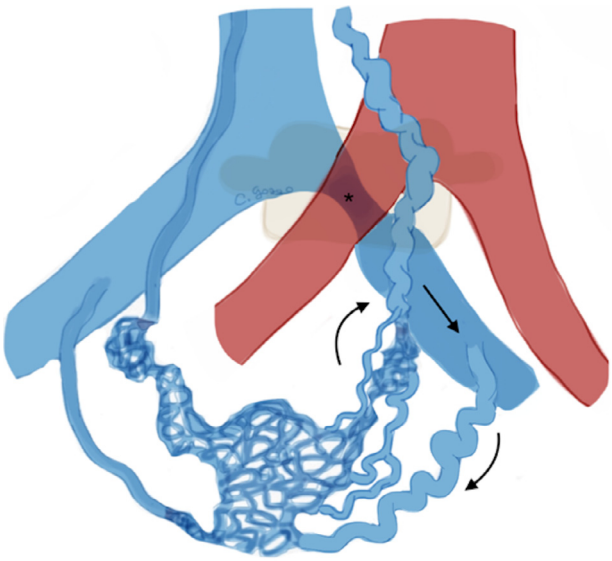


Figure 2 Drawing shows May-Thurner Syndrome: extrinsic compression (*) of left common iliac veins between the overlying right common iliac artery and the fifth lumbar vertebra. Arrows show the alternate route for blood flow between the internal iliac veins and IVC.

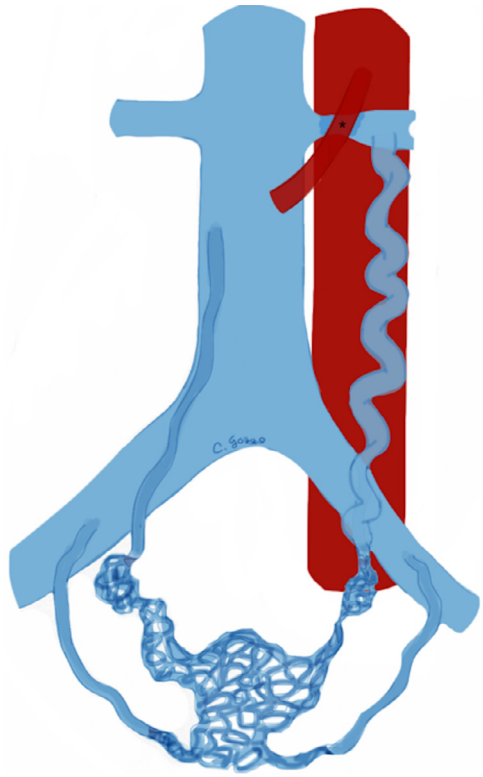


Figure 3 Drawing shows anterior Nutcraker syndrome: compression (*) of left renal vein between the aorta and the superior mesenteric artery.

Diagnosis

Among the noninvasive imaging, doppler ultrasound is considered the first imaging approach which allows real-time dynamic imaging and flow evaluation.[1] Transvaginal US and doppler ultrasound criteria for PCS diagnosis include a

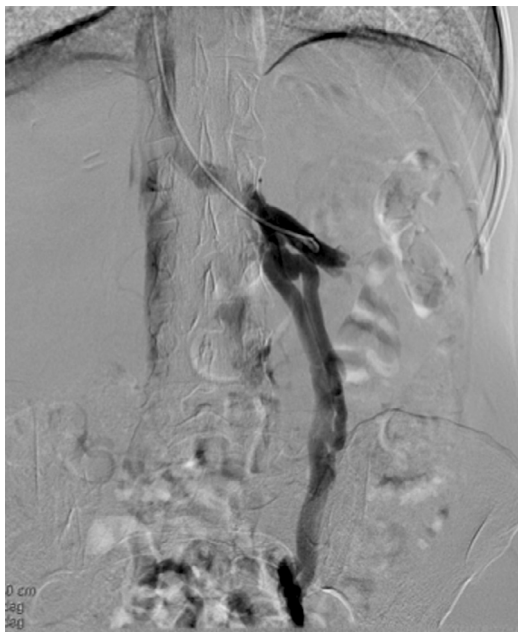


Figure 4 Venographic image showings late stage of anterior Nutcraker syndrome with left ovarian vein dilation.

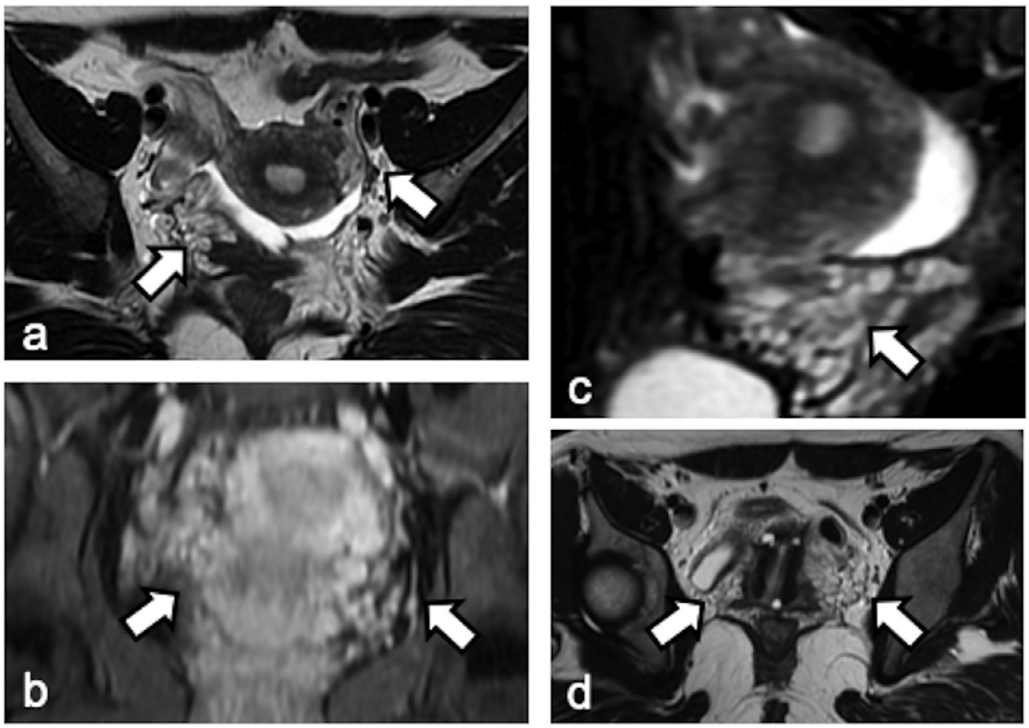


Figure 5 MRI imaging. Axial (a) and oblique (d) T2-weighted SSFSE, T1-weighted LAVA after contrast media administration (b) and T2 sagittal MRI (c) sequences showing pelvic venous congestion (arrows).

dilated tortuous parauterine and paraovaric vein with a diameter larger than 4 mm, slow blood flow (≤3 cm/s) or retrograde flow, and a dilated arcuate vein in the myometrium communicating with pelvic varicosities.[17,18] Unlike CT and MRI, US evaluation allows also dynamic study with provocative Valsalva maneuvers in order to accentuate venous reflux for visualization.[1] Cross-sectional imaging, such as CT and MRI (Fig. 5) have limited role for PCS workup, due to the supine position assumed during image acquisition which reduces the sensitivity of detecting subtle pelvic vein dilation.[1,19]

Conversely, CT venography or even standard contrast-enhanced CT allows detection of extra pelvic pathology such as abnormal uterine or venous anatomy that may influence management.[19] According to Hiromura et al.,[13] CT also allows identification of left ovarian vein reflux defined as its early opacification occurring simultaneously with opacification of the renal veins. At CT venography we can quantify the degree of reflux by dividing it into: grade I (limited to the left ovarian vein); grade II (it involves the ipsilateral parauterine veins and no farther); grade III (it crosses the midline passing through the uterus from the left into the right parauterine plexus)[13] (Fig. 6-8).

Multiplanar pelvic MRI may reveal evidence of other causes of chronic pelvic pain, such as endometriosis, or other uterine, adnexal, urologic, gastrointestinal, or musculoskeletal pathology.[18] Both for CT and MRI, imaging criteria of PCS diagnosis include the presence of at least 4 ipsilateral tortuous parauterine veins (at least one >4 mm in diameter) or an ovarian vein diameter greater than 8 mm.[20]

Although transcatheter venography represents the gold standard for PCS diagnosis, it is performed after inconclusive noninvasive imaging or when interventional treatment is planned.[18] Transcatheter venography can confirm dilated ovarian veins (diameter of at least 5 mm), retrograde ovarian vein reflux (Fig. 9), uterine venous engorgement and reflux of contrast material across the midline with filling of vulvovaginal or thigh varicosities[1,7,18] (Fig. 10).

The venographic study allows the calculation of scoring system proposed by Beard et al.[21] and based on 3 components: maximum diameter of the ovarian vein, time to disappearance of contrast material, and degree of congestion. Each component is scored from 1 to 3 and a score of 5 or more is an objective measure of pelvic congestion. Ovarian vein diameter was considered normal between 1 and 4 mm; moderate, 5-8 mm; and severe, greater than 8 mm. Time to disappearance of contrast medium was scored on the basis of a time of 0, 20, or 40 seconds. Degree of congestion was considered normal if veins were small, straight, and easily seen; moderate when veins were tortuous with variable caliber; and severe if veins were highly tortuous, wide with great variation in caliber.[21]

Therapy

Management of PCS include medical, surgical and endovascular therapy. Medical and surgical therapies have been shown to be less effective than transcatheter pelvic vein embolization in case of PVI.[22] According to the theory for which estrogen is a venous dilator, medical treatment of PVI

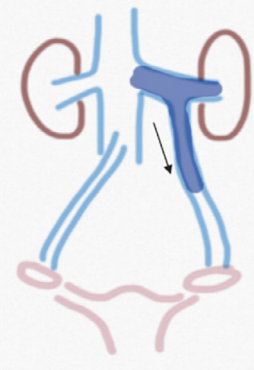
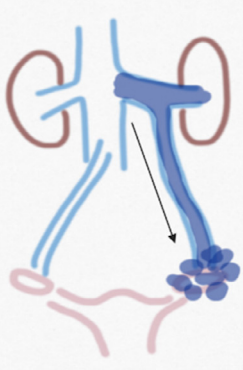
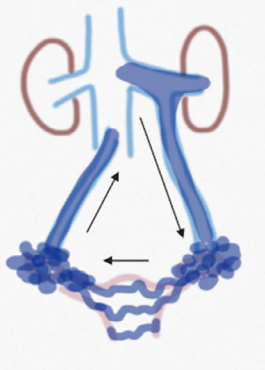
Grade	I	II	III
CT findings	Retrograde flow remained in the left ovarian vein (not reaching the parauterine veins)	The retrograde flow advanced into the ipsilateral parauterine veins and no farther	Retrograde flow crossed the midline passing through the uterus (from the left to the right parauterine plexus)
Illustration			

Figure 6 Table summarizes CT findings of the three grades of reflux according to Hiromura Classification.

Figure 7 CT imaging shows a left ovarian vein Grade II reflux: (a) left parauterine veins dilation (arrow); (b) left ovarian vein dilation (arrow); (c) MIP reconstruction showing left ovarian vein dilation (arrow).

consists in pharmacologic ovarian suppression and estrogen levels reduction through medroxy-progesterone acetate (MPA) and gosereline.[18] Before 1993, the PCS management was mainly surgical.[23] Surgical approach, consisting in hysterectomy with bilateral salpingo-oophorectomy in the past and ovarian vein ligation (either via a retroperitoneal and laparoscopic approach) now, is rarely performed and reserved for patients refractory to other less invasive treatment.[1,18,23] Surgical treatment may be burdened by intraoperative damage to nearby pelvic nerves and the development of collateral

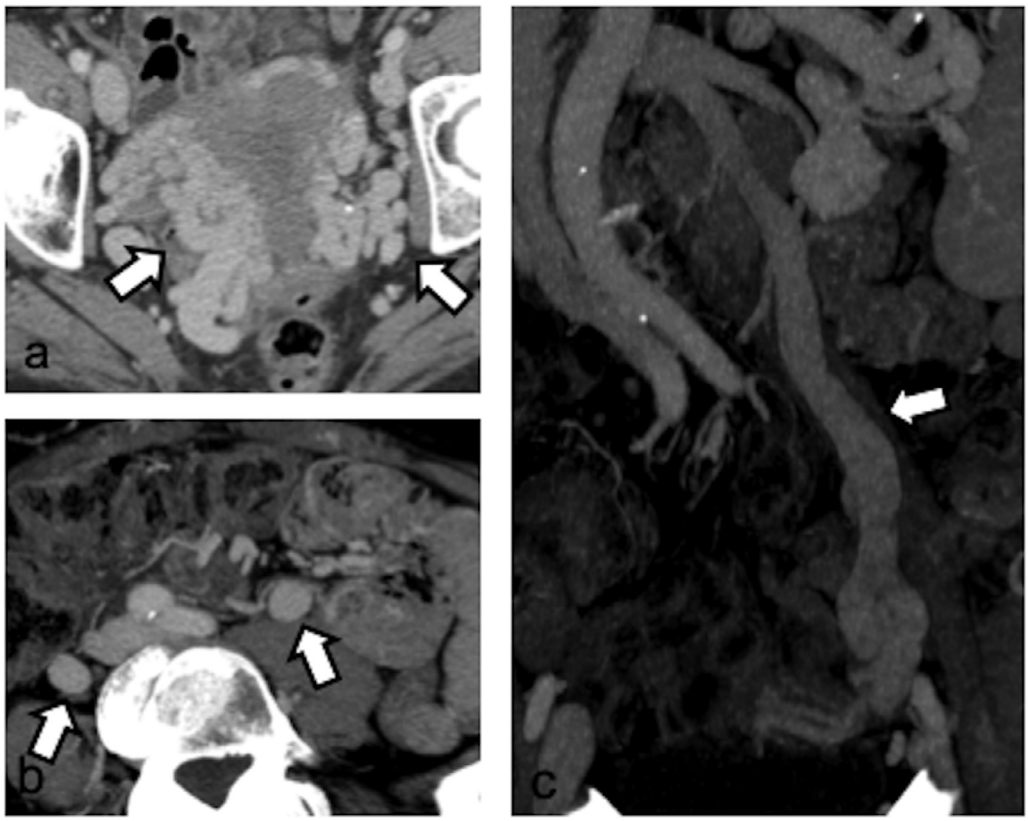


Figure 8 CT imaging shows bilateral ovarian veins Grade III reflux: (a) bilateral parauterine veins dilation (arrows); (b) right and left ovarian veins dilation (arrows); (c) MIP reconstruction showing left ovarian vein dilation (arrow).

channels.[23,24] Surgical procedures do not perform better than endovascular treatment in terms of postoperative results as it is associated with more common recurrence.[23-25]

Unlike surgical techniques, endovascular techniques are minimally invasive and may be performed in a day-hospital setting, with consequently lower costs and patient discomfort.[23-26]

The purpose of transcatheter embolization is the occlusion of insufficient venous axes as close as possible to the origin of the reflux.[23] Transcatheter embolization of ovarian and pelvic veins has been proven to be safe, effective and durable therapy for PCS and it is recommended with a 2B level of evidence.[27-29]

Figure 9 Venography image showing venous reflux and dilation of the left ovarian vein with uterine vein engorgement.

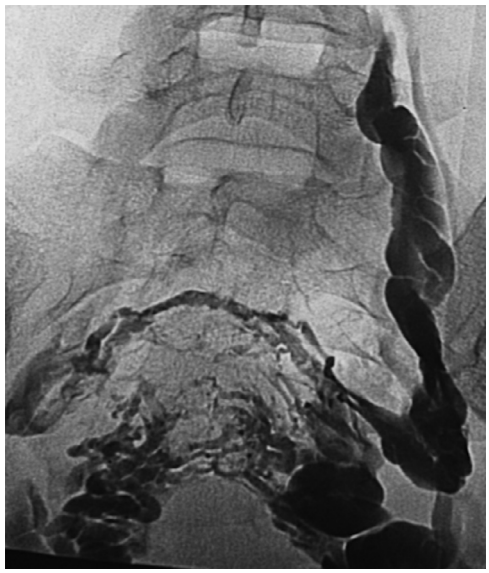


Figure 10 Venographic features of uterine plexus engorgement with filling of contralateral vein and vulvar varicosities.

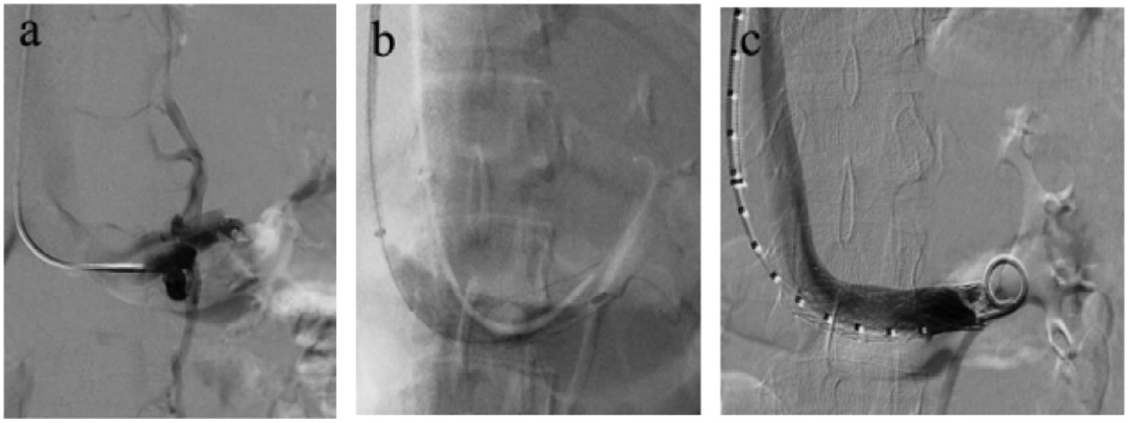


Figure 11 Fluoroscopic digital subtraction angiography images: a) first venography documenting Nutcraker syndrome with some perimedullary collateral veins and (b, c) subsequent stent placement in left renal vein.

When the cause of PCS lies in obstruction of suprapelvic drainage (ie, Nutcraker syndrome) or pelvic drainage (May-Thurner syndrome), interventional radiology plays also a role in their management through endovascular recanalization.[30,31]

In detail, endovascular left renal vein stenting may be considered for the treatment of late stage Nutcraker syndrome associated with PCS (Fig. 11).[32] LVR placement was followed by up to 8% of stent migration.[33]

In case of PCS caused by May-Thurner syndrome, the left common iliac vein obstruction can be solved with intravascular thrombolysis with the possibility of stent placement.[30,31]

Endovascular technique

Transcatheter embolization consists in endovascular occlusion of uterine and pelvic refluxing veins with embolizing material.[18]

First transcatheter pelvic vein embolization was described in 1993 by Edwards et al.[34] performed with coils as embolic agent. Endovascular procedure can be performed via femoral or jugular vein catheterization under local anesthetic or sedation.[29,35]

There are divergent opinions as to whether limited or complete embolization should be performed.[35] The first planning includes the choice of vessels to be embolized: only refluxing veins (usually the left), both ovarian veins and both ovarian veins and internal iliac veins.[8,11,36]

There is no statistically significant difference comparing unilateral and bilateral embolization.[35] PCS embolization, in case of persisting symptoms over a period of 3/6 months or if communication with Internal Iliac Vein (IIV) is seen, can be followed by IIV embolization.[8]

Laborda et al.[28] presented their experience in both PCS and IIV treatment through embolization of all four venous axes of the pelvis (both OVs and IIVs) with coils. Their hypothesis was based on the possibility of hypertrophy of the remaining vessels after treatment of 1 or 2 of them might due to their close connection.[28]

Embolization can be made with various type of embolizing agents from liquid (ie, sclerosant, glue) to solid (i.e., coils and plugs). Embolization techniques include coil or plugs placement[22,28,37] (Fig. 12), with or without the adding of sclerosant,[36-38] glue,[39] and lipiodized oil injection[40] and sclerotherapy with 3% sodium tetradecyl sulfate.[26,41] As a completion of pelvic varicocele embolization with residual low-outflow collaterals tributy to the hypogastric vein, a balloon-occluded retrograde transvenous embolization from the hypogastric veins has been proposed.[26,36] This balloon-occluded technique allows to determine when the pelvic varices are completely filled by the sclerosing agent, thus optimizing the quantity of the agent used and avoiding its systemic dispersion[26] (Figs. 13 and 14).

In all of these techniques of embolization, the technical success defined as completely occluding a vein that previously showed reflux, was high in all the studies (98%-100%) with few and minor complications.[29]

Our group also described the first reported case of ovarian vein embolization with Amplatzer Vascular Plug in place of coils[42] (Fig. 15).

Complications

Conventional surgical treatment options are followed by several complications such as high rate of residual (33%) or recurrent (20%) pelvic pain, damage to nearby pelvic nerves, and postprocedural loss of gonadal function which require hormonal replacement.[25]

Endovascular treatment complications are rare (0.85%-10% rate) and include immediate (i.e. haematoma to the puncture site, perforations or injuries to the target vein, non target embolization, stroke) and delayed one (coil migration).[29,35,43]

Clinical outcome

There was no agreement on how and when to measure clinical success.[29]

One study used a pain evaluation through pain questionnaire or visual analogue score (VAS).[38]

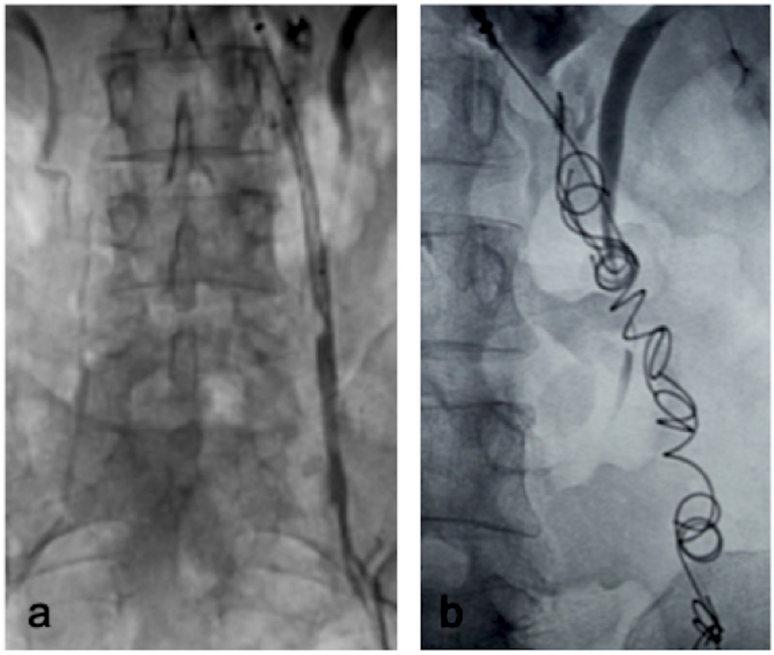


Figure 12 Fluoroscopic image showing left ovarian vein dilation (a) followed by coil embolization (b) for PCS.

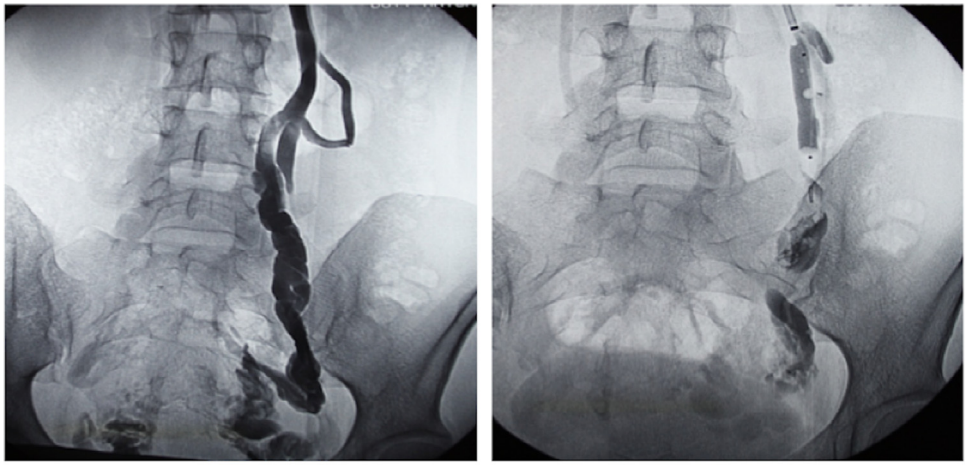


Figure 13 Venography images showing Balloon-occluded technique in ovarian vein treatment: (a) dilation of ovarian vein with reflux; (b) balloon from the same ovarian vein.

Other studies measured the change on menstrual cycle intervals and length and hormone levels.[36-38]

About the time to assess clinical success, some studies reported symptom improvement in the early post-procedural period ranging from 1 day to 3 months, other in 6 months.[35]

Surgical treatment such as hysterectomy with bilateral oophorectomy or ligation shows lowest clinical success rate (respectively 66% and 73 %).[21-24] Chung et al.[22] made a comparison between endovascular treatment (unilateral ovarian vein embolization) and surgical one (hysterectomy with bilateral/unilateral oophorectomy) in 118 patients with PCS. This study showing the hysterectomy with unilateral oophorectomy as the least effective treatment, has the limit to exclude patients with bilateral PCS.[22]

Several groups have reported their experience in endovascular treatment of ovarian veins alone or in combination with internal iliac veins. The largest published series to date are reported by Kim et al.[36] (131 patients treated with combined ovarian and internal iliac vein embolization), by Laborda et al.[28] (202 patients treated with both PCS and Internal Iliac Vein through embolization of all four venous axes of the pelvis with coils), and by Monedero et al.[44] (215 patients treated with recurrent varices after surgery).

In the last years, two important literature reviews were published about PCS treatment. Brown et al.[35] have analyzed 14 studies of percutaneous treatment for PCS including a total of 828 women and 994 percutaneous interventions (15 of which repeated). Hansrani et al.[29] have analyzed 13 studies of trans-venous occlusion of ovarian and internal iliac

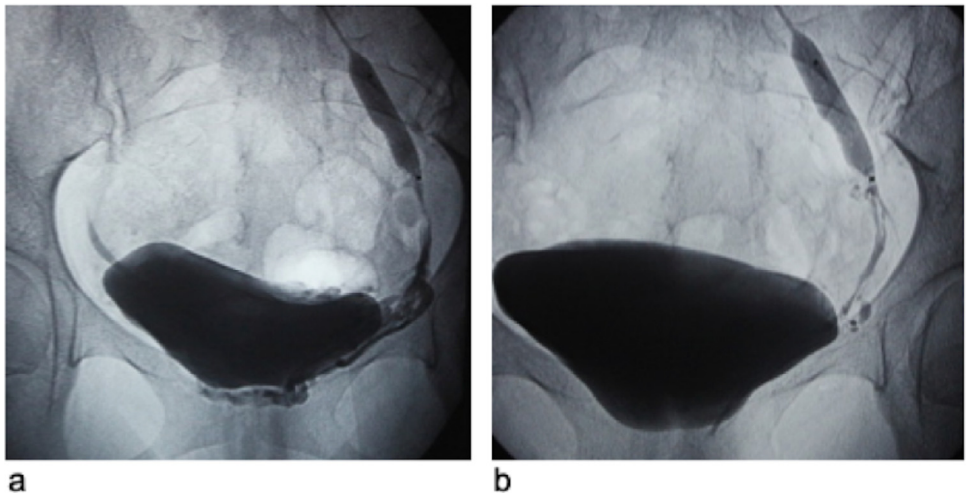


Figure 14 Venography images showing balloon-occluded technique in internal iliac vein treatment: (a) dilation of internal iliac vein with contrast media stasis after balloon catheter inflation in the same vessel; (b) final postprocedural check after sclerosant agent administration.

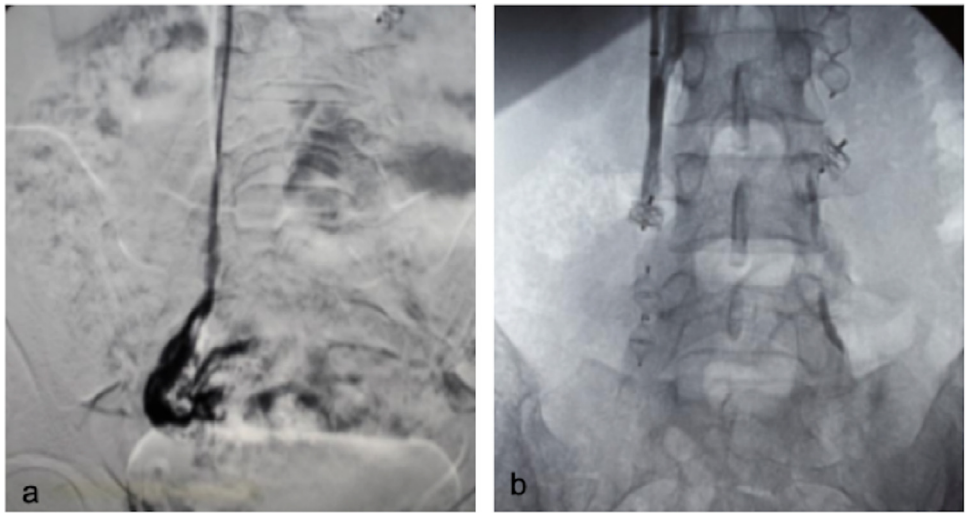


Figure 15 Venography images showing Amplatzer Vascular Plug placement in ovarian vein treatment: (a) dilation of right parauterine plexus; (b) final postprocedural check after placement of plugs in left and right ovarian veins.

veins including a total of 866 women. In neither of them, the procedure impact on health-related quality of life was reported.[29,35]

Numerous studies have shown clinical success rates ranging from 60 % to 100% variable according to the type of endovascular technique.[18,29,45]

Clinical improvement is similar between coil embolization, sclerosant, and combined use of agents, whereas that of glue and lipiodized oil is relatively lower.[35]

In detail, the clinical success rate of 80%-100% was achieved with embolization with coil and/or Gelfoam.[28,36-38] Lower clinical improvement rate with glue and lipiodized oil ranges from 68.3% to 73.7%.[40]

Combination of ovarian, internal iliac, and additional variceal intervention has a range of clinical success lower than that of ovarian and iliac interventions.[11,36]

Conclusion

In view of the highly heterogeneous results, inclusion criteria and type of technique, pooled success estimates through the scientific literature couldn't be conclusive. A well-designed randomized controlled trial is needed to assess trans-venous occlusion in an unbiased fashion to definitively determine the clinical success. However, despite the absence of any adequate scientific evidence, transcatheter embolotherapy has been proven to be a safe and may be the most effective and durable therapy for the treatment of PCS.

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