

Management of pelvic venous disorders

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ABSTRACT

Patients with pelvic congestion syndrome, which is the part of pelvic venous disorders (PeVDs), present with unexplained chronic pelvic pain greater than six months, and anatomical findings including pelvic venous insufficiency and pelvic varicosities. Venography is usually necessary to confirm ovarian vein reflux and should be the first step of embolization. Endovascular therapy has been validated by several large patient series with long-term follow-up and should be the first-line therapy. Embolization has been shown to be significantly more effective than surgical therapy in improving symptoms in patients who fail hormonal therapy. Briefly, the goal is to eliminate the ovarian vein reflux with direct sclerosis or embolization of enlarged pelvic varicosities. Symptom improvement is seen in 70 to 90% of the treated patients, despite technical variation. Different embolic agents can be used for this purpose. Therefore, in this review, we discuss the different types of treatment available, with focus on embolic materials.

Keywords: Embolization, female varicocele, interventional radiology, pelvic congestion syndrome, venous reflux.

Pelvic congestion syndrome (PCS), which is the part of pelvic venous disorders (PeVD), is defined as chronic pelvic pain for more than six months combined with pelvic varicose veins, resulting from reflux or obstruction of the gonadal, gluteal, or parauterine veins.^[1,2] Interest in this condition has increased over the last five years due to its frequent association with lower limb venous insufficiency. Although it is prevalent, PCS is still underdiagnosed. Despite diagnostic challenges, large-scale studies have shown promising results of percutaneous treatment of PCS.^[3] In this review, we discuss the techniques and outcomes of the several different types of percutaneous treatment available.

Indications

Pelvic varices are very frequent, but are asymptomatic in most of cases. It is important to consider treatment only for symptomatic pelvic varices evocative of

PCS.^[3] The only indication to treat asymptomatic pelvic varices is before lower limb varices treatment, whatever the treatment, to avoid recurrence, or in case of recurrence of leg varices after surgery or ablative technique due to leak points communicating pelvic varices with leg varices.^[2]

Selective venography

Retrograde catheter-directed venography is the gold-standard examination for diagnosis of PCS.^[1] A four-vessel phlebography (both ovarian veins and both hypogastric veins) should be performed under Valsalva maneuver. A tilting table may be helpful, but is not essential while performing venography. If the choice is between a non-tilting angiographic table and a tilting table without rapid-sequence image acquisition, the latter is recommended. It is important to look for findings suggesting PCS such as dilation of the ovarian vein (diameter >6 mm), ovarian vein

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reflux, uterine vein engorgement, congestion of the ovarian venous plexus, filling of pelvic veins across midline, and potential filling of vulvovaginal or thigh varicosities (Figure 1).^[1,4] Venography should look for pelvic leakage sites from internal iliac veins and afferents (inferior gluteal veins, uterine veins, internal pudendal veins and obturator veins) (Figure 2). Finally, left renal vein and left iliofemoral return studies should be part of the venography to look for Nutcracker syndrome and May-Thurner syndrome, respectively. Since it is an invasive examination, venography should preferably be reserved for patients who require intervention or when diagnostic doubts remain.^[4] It is usually the first step of endovascular treatment which is performed during the same single session.

Therapeutic options

Medical treatment

The goal of drug-based treatment is to suppress ovarian function and induce vasoconstriction of the dilated veins. Medroxyprogesterone acetate, gonadotropin-releasing hormone (GnRH) analogs, and venotonic agents for six months provoke partial relief from symptoms.^[5] However, long-term pharmacological therapy is not recommended for the treatment of PCS due to the adverse symptoms and limited efficacy.

The impact of compression on the symptoms of PCS has been investigated, with no clinical improvement or improved venous drainage of the pelvic organs associated with wearing elastic stockings.^[6]

Surgical treatment

Surgery is a last resort option for patients who are refractory to other treatment techniques and with symptoms that compromise daily activities. The most often used method is laparoscopic transperitoneal ligation of the ovarian vein.^[1] However, limiting factors include higher rate of surgical mortality and morbidity, such as deep venous thrombosis, retroperitoneal hematoma, and ileus.^[7]

Endovascular treatment

Access for percutaneous embolization can be obtained via the femoral vein or via the jugular or basilic veins. If the approach is via the inferior vena cava, Cobra 2 or Simmons 1 catheters can be used to reach the left renal vein or the right ovarian vein, respectively. If the approach is the superior vena cava, MPA 2 catheters are more often used. After left renal phlebography to identify reflux in the gonadal vein and eliminate stenosis of the renal vein, the ovarian vein is catheterized. Phlebography of the gonadal vein should initially be performed at rest, to assess reflux along its entire length, and then during the Valsalva

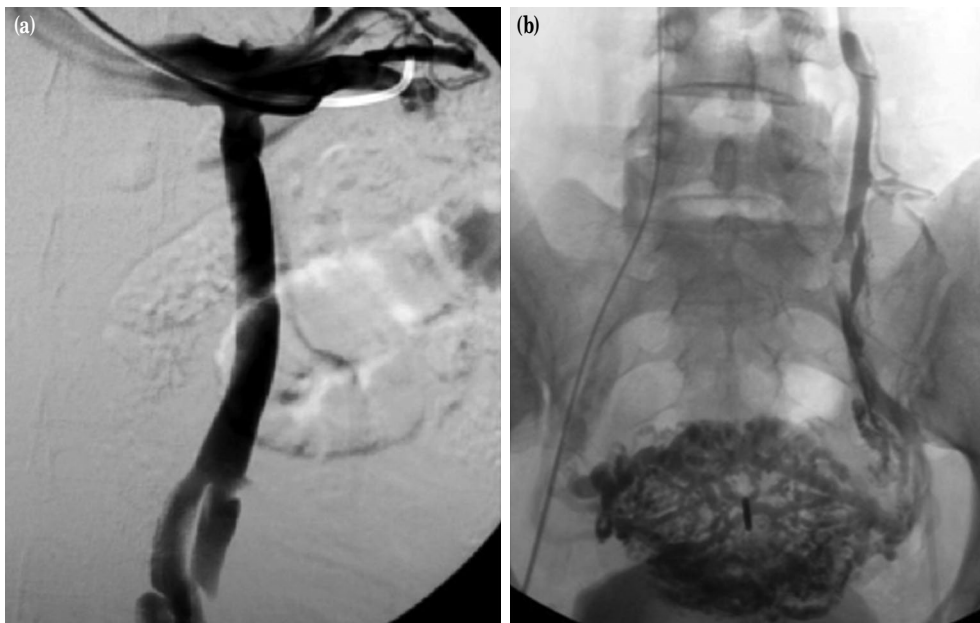


Figure 1. Venographic findings suggesting PCS. (a) Dilation of the left ovarian vein greater than 6 mm with ovarian vein reflux. (b) Uterine vein engorgement with congestion of the pelvic venous plexus (reservoir) and filling of pelvic veins across midline.

PCS: Pelvic congestion syndrome.



Figure 2. Typical leakage sites to look for during phlebography for PCS. (a) Inferior gluteal vein. (b) Uterine vein. (c) Internal pudendal vein. (d) Obturator vein.
PCS: Pelvic congestion syndrome.

maneuver, to assess contralateral venous reflux and reflux to the lower limbs. Embolization is facilitated by the use of a microcatheter and detachable microcoils, but 0.035" coils or plugs may also be used, depending on the experience of the operator and the availability of materials.^[8,9] No standard technique exists for embolization of the pelvic varices and ovarian veins.

Several embolic agents, alone or in combination, can be used, with different advantages and drawbacks. Our preferred technique is to combine distal embolization of what we call the « pelvic reservoir » with liquid embolic agents with proximal embolization of the gonadal vein with mechanical embolic agents such as microcoils (Figure 3).^[8-12]

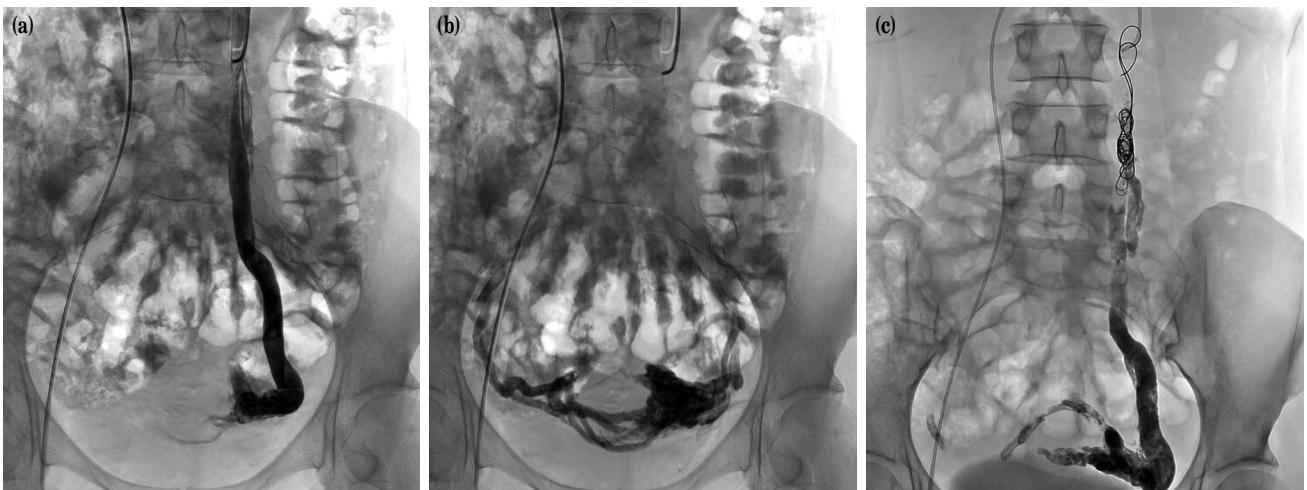


Figure 3. Typical glue embolization of the left ovarian vein for PCS. (a) Phlebography of the left ovarian vein after catheterization with a Cobra 2 catheter showing dilation and reflux. (b) Periuterine engorgement with opacification of the pelvic reservoir crossing the midline. (c) Result after coiling of the proximal gonadal vein, passing through the coils with a microcatheter and embolization of the reservoir and gonadal vein with a glue/lipiodol mixture in a 1:1 ratio up to the coils.

PCS: Pelvic congestion syndrome.

Embolization is, then, initiated in the proximal part of the gonadal vein, about 5 cm below the renal vein level, with the use coils or plugs which are released into the gonadal vein. Next, a microcatheter is positioned in the pelvic veins (reservoir) after passing through the microcoils, as distally as possible, and liquids are injected under Valsalva maneuver while removing slowly the microcatheter. Embolization is, then, performed up to the microcoils.^[12] The same procedure can be repeated on the right side, if involved. Then, it is mandatory to check during angiography both internal iliac veins and afferents to complete embolization of collaterals and to close potential leakage sites. After embolization, the patient may suffer mild to moderate discomfort, which typically responds to non-steroidal anti-inflammatory drugs.^[8]

Few comparative studies have been reported regarding embolic materials. One randomized trial of endovascular embolization treatment in PCS compared fibered platinum coils versus vascular plugs with one-year clinical outcomes.^[13] Embolization resulted in pain relief in 90% of patients. Clinical success was not affected by embolic device (89.7% for coils *vs.* 90.6% for plugs, $p=0.760$). However, plugs were associated with decreased fluoroscopy time and radiation dose. The use of coils alone has some limitations. First, it needs a lot of coils. Second, recanalization is frequent. Last, veins with caliber greater than 12 mm increase the risk of coils migrating to the pulmonary artery, which is one of the main complications of the procedure.^[14] Procedural cost and radiation time

appear to be favorable with sclerosant-only approach. Foam of polidocanol and air is, then, used.^[10] The volume of sclerosant required typically ranges from 2.5 to 12.5 mL per ovarian vein. However, the main limitations are the risk of allergy, transient stroke, unpredictable diffusion space, limited total amount to inject, and the risk of recurrence in case of large varices.^[15] This is why combining sclerosing agents with coils is probably preferable.

The use of cyanoacrylate glue in such a setting leads to less radiation exposure, less pain, and lower recurrence rates compared to other embolic materials (Figure 3).^[15] As n-butyl cyanoacrylate (NBCA) and other liquid embolic agents have the advantage of penetrating into collateral pathways, they can be associated with greater effectiveness and a lower risk of recurrence. A deep learning curve is needed with the use of glue. It can be very challenging, as the occlusion is permanent and almost instantaneous. Therefore, cyanoacrylate embolization should be reserved for specialized centers.^[16-19] Few cyanoacrylates are officially available on the market worldwide for endovascular purpose: Glubran®2 (GEM, Viareggio, Italy) and Trufill® (Cordis, Miami Lakes, FL, USA) have the CE mark and United States Food and Drug Administration (FDA) approval, respectively.^[3] Histoacryl® (B-Braun, Tuttlingen, Germany) has neither the CE mark nor FDA approval for endovascular interventions, for which it is widely used off label. Its faster polymerization rate compared to other glues makes Histoacryl® more challenging

to use. Glubran® 2 has the advantages of being very inexpensive compared to Trufill® (about 100 € vs. 2000 \$ per 1-mL vial) and available worldwide, whereas Trufill® is used only in the United States. A new α -hexil-cyanoacrylate glue (MagicGlue®, Balt Extrusion, Montmorency, France), known as Purefill® (Peters Surgical, Bobigny, France), has been recently developed and has exhibited short- and long-term occlusive efficacy and histopathological responses similar to those seen with Histoacryl® and Glubran®2.^[17] However, α -hexil-cyanoacrylate seems to have less adhesive strength compared to Histoacryl® and Glubran®2. Glue must be mixed with ultra-fluid ethiodized alcohol (Lipiodol® Ultra Fluid; Guerbet, Aulnay-sous-Bois, France) to be radiopaque. A 1:1 ratio is used for PCS embolization to produce a fast polymerization and prevent from any risk of migration in case of reflux.^[17] The mixture of cyanoacrylate, Lipiodol®, and tantalum must be prepared just before the injection. The NBCA comes in small, sterile, 1-mL containers. Our preferred method to prepare the glue/Lipiodol® mixture is aspiration of the glue out of its sealed container using a 5-mL syringe followed by glue injection into the desired volume of Lipiodol in a 5-mL syringe, shot glass, or medicine cup. The two components are, then, thoroughly mixed. The catheter is flushed thoroughly with dextrose 5% solution to completely clear ionic solutions from its lumen. This should be done just before the glue injection.^[17]

Among liquid embolic agents, copolymers such as Onyx® (Ev3 Irvine, CA, USA) or Squid® (Balt Extrusion, Montmorency, France), can be used for safer embolization with controlled release (Figure 4). It allows less inflammation post-procedure with no risk of migration.^[20] As a cohesive agent, it does not stick to the catheter as glue does. A specific 6-mL vial exists for peripheral applications. It needs the injection of a solvent which is called dimethyl sulfoxide (DMSO) before injection of the ethylene vinyl alcohol (EVOH) copolymer, which can be painful. It provides complete filling and distal penetration.^[20,21] The main limitation is the cost which is higher than that of other embolic agents.

There is still no evidence whether unilateral or bilateral embolization produces better outcomes. The treatment decision should, therefore, depend on the severity of symptoms, on the anatomy of the pelvic varicose veins, and on the degree of reflux.^[8]

Post-procedural care and follow-up

Most of procedures are performed on an ambulatory basis. Patients are discharged the same day and they

are instructed to avoid heavy lifting or exercise for one week after discharge. Per os anti-inflammatory medication is systematically given for 10 days to avoid or to control post-procedural pain. Patients should be re-evaluated at three months for clinical response, with both clinical and radiological examination.^[11] If the presentation was chronic pelvic pain, questioning can reveal that symptoms have only partially improved. It is important to temper patient expectations, as many patients would have less frequent and severe pain rather than complete symptom elimination as their ultimate outcome. If the presentation was vulvar or leg varicosities, in most cases there would be only minimal change at follow-up. The main role of ovarian vein embolization is eradication of the highest point of reflux. Sclerosis, ablation or resection of vulvoperineal or lower limb varicosities that have not resolved may be performed with lesser chance of recurrence.^[11]

Outcomes

Safety of percutaneous treatment

Procedural complications of embolization for PCS are minor and rare.^[22,23] No additional treatment-related sequelae were identified in a recent systematic review.^[10] To date, no studies specifically address attempted conception following embolization for PCS. Galkin et al.^[24] reported a series of ovarian varix embolization to treat infertility, with improvement of clinical symptoms, laboratory tests, and 14 of 19 patients conceiving. Capasso et al.^[25] reported no significant change in menstrual cycle after treatment.^[25] Kim et al.^[23] reported no change in pre- and post-embolization levels of follicle-stimulating hormone, luteinizing hormone, or estradiol.^[23]

Efficacy of percutaneous treatment

Percutaneous endovascular embolization for PCS is an effective technique of treatment having a high rate of symptom improvement. Studies using a visual analog scale as a quantitative measure of pelvic pain report statistically significant symptom improvement comparing post- and pre-treatment values with an average decrease of 5.7 within 0 to 10 scale in the published series.^[10,22]

Many studies have reported greater than 80% reductions in pelvic varicose veins and symptoms after embolization.^[26] In a review covering 520 patients with an average follow-up time of 15 months, 46% reported significant relief and 40.6% reported moderate relief from symptoms after embolization. The review compared the number of patients for whom treatment resulted in relief with the number who did

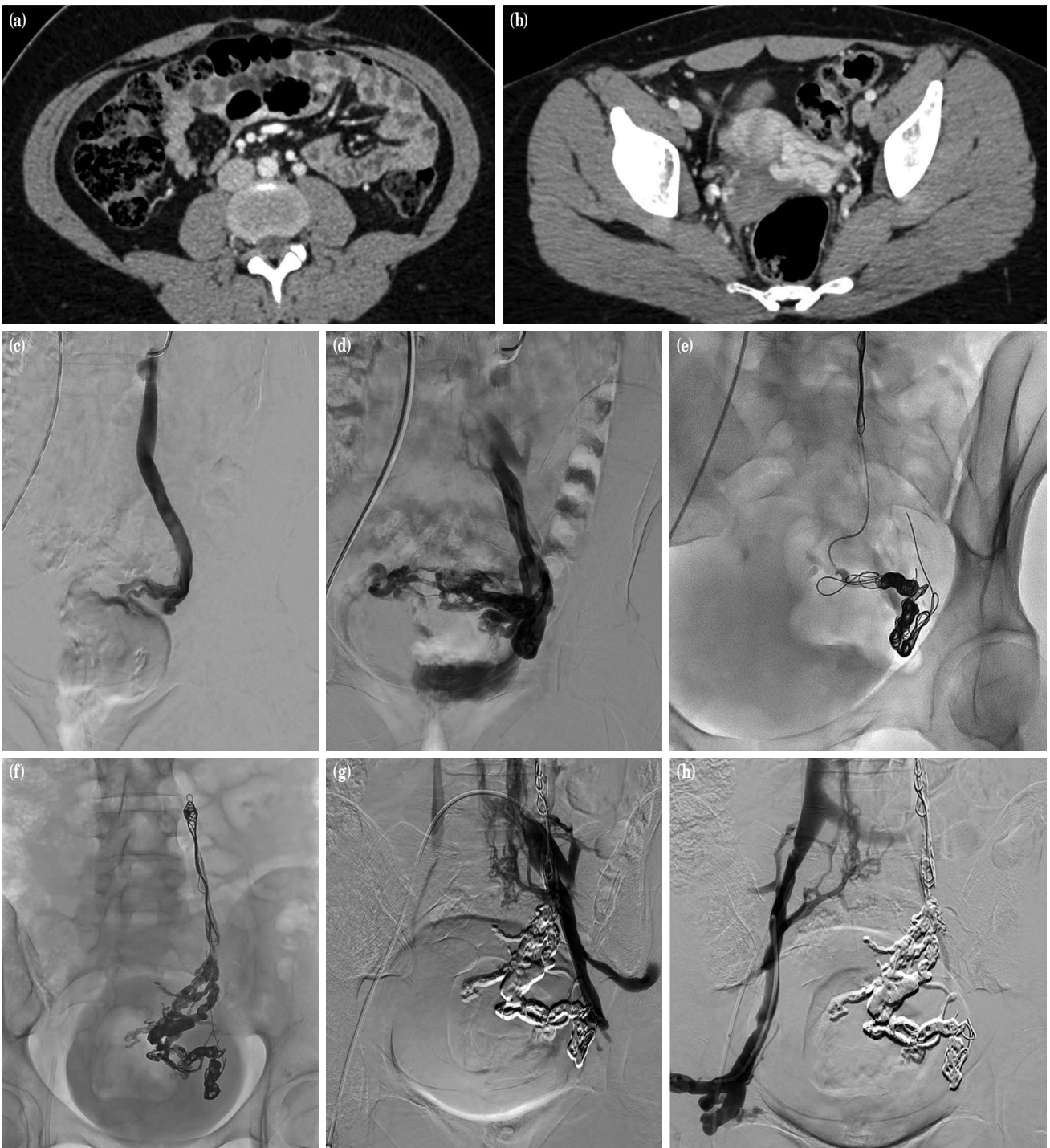


Figure 4. Embolization for PCS with a combination of copolymers and coils. (a, b) CT scan showing left ovarian vein incontinence with vein dilation and left pelvic varices. (c, d) Selective phlebography of the left gonadal vein confirming incompetence and pelvic varices with opacification of the left internal iliac vein via direct anastomosis. (e, f) Results after first coiling of the pelvic connexion for closure, coiling of the proximal gonadal vein, and then embolization of the reservoir with Onyx® through a microcatheter. (g, h) Phlebography of the left and right internal iliac veins, respectively, showing no pelvic leakage sites and no more pelvic varices. PCS: Pelvic congestion syndrome, CT: Computed tomography.

not benefit, finding that 86.6% improved and 13.4% reported little or no relief.^[27] Embolization can result in improvement of PCS in 91% of the patients and

of lower limb varicose veins in 51%.^[10] A systematic review conducted by Daniels et al.^[3] evaluated efficacy in 1,308 patients in 22 cohorts, with no randomized

clinical trials, finding a 75% mean rate of improvement of symptoms in the first three months. However, there was also improvement lasting for up to 45 months after the procedure.

In conclusion, PCS is a prevalent and easily treatable disease for which minimally invasive percutaneous treatment is safe and effective. Learned societies have endorsed with a 2B recommendation the endovascular treatment of PCS in their practice guidelines for treatment of chronic PeVDs. When ovarian venous primary insufficiency is the cause of chronic pelvic pain secondary to pelvic varices, endovascular therapy is indicated to eliminate ovarian reflux. If the cause is secondary to upstream obstruction, then that obstruction needs to be treated by stenting. Catheter-directed phlebography demonstrates improved sensitivity in detecting venous insufficiency compared to non-invasive imaging, as well as the benefit of simultaneous diagnosis and treatment. Improvement in pain symptoms should be expected in 80 to 90% of the patients, with durable results at five-year follow-up. There is still a considerable variation in the endovascular approach, and the optimal embolic material to be used remains unclear.

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