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REVIEW ARTICLE

Interventional Radiology of Male Varicocele: Current Status

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Abstract Varicocele is a fairly common condition in male individuals. Although a minor disease, it may cause infertility and testicular pain. Consequently, it has high health and social impact. Here we review the current status of interventional radiology of male varicocele. We describe the radiological anatomy of gonadal veins and the clinical aspects of male varicocele, particularly the physical examination, which includes a new clinical and ultrasound Doppler maneuver. The surgical and radiological treatment options are also described with the focus on retrograde and antegrade sclerotherapy, together with our long experience with these procedures. Last, we compare the outcomes, recurrence and persistence rates, complications, procedure time and cost-effectiveness of each method. It clearly emerges from this analysis that there is a need for randomized multicentre trials designed to compare the various surgical and percutaneous techniques, all of which are aimed at occlusion of the anterior pampiniform plexus.

Keyword Male varicocele · Retrograde sclerotherapy · Antegrade sclerotherapy · Microsurgical subinguinal varicocelectomy · Infertility · False bilateral varicocele · Subinguinal venous compression maneuver

Introduction

Varicocele was discovered nearly 2,000 years ago. It was the Roman physician Cornelius Celsus (42 BC–37 AC) who first observed a decreased testicular size with a correspondingly enlarged hemiscrotum caused by dilated scrotum veins [1]. Although the link between varicocele and male infertility was identified in the 18th century, it was only in 1889 that Bennett described a case of bilateral varicoceles (BVAs) in which semen improved after "one side had been cured" by surgery [2]. Since then, various surgical techniques and types of percutaneous treatments have been devised, but discussions about treatment of this condition continue. The most hotly debated issues are: (1) frequency and bilaterality; (2) pathophysiology; (3) clinical diagnosis; (4) correlation with infertility; (5) selection of adult and pediatric patients; and (6) outcomes, recurrence, and complication rates of each surgical and percutaneous type of varicocelectomy.

Here we report an overview of recent studies of male varicocele and compare the benefits and drawbacks of surgical varicocelectomy and radiological treatment in light of our experience.

Definition and Incidence

Varicocele is an abnormal dilation of the pampiniform plexus (PP) secondary to a defect in the venous renospermatic system. In very severe cases, it may be associated with subcutaneous or testicular varicose veins [3–5]. Varicocele may cause subfertility or infertility and testicular pain and discomfort, i.e., a feeling of heaviness in the scrotum. In the past, most cases of varicocele were diagnosed during military service. Today military conscription is no longer mandatory in many countries, and the condition is usually diagnosed later in life or in the context of competitive sports training.

The incidence of varicocele in young healthy male individuals is 8–23% [6, 7], with the left side being

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affected in 70–100% of cases and the right side in only 0–9% of cases. It is bilateral in 0–23% of cases [6, 8]. BVA is associated with inferior vena cava agenesis, long-standing inferior vena cava occlusion, and the hemodynamic Budd–Chiari syndrome. The incidence of BVA is reported to be as high as 80% based on ultrasound Doppler evaluation [9–11], whereas it is approximately 8–15% based on physical examination [12, 13]. These discrepancies may be due to the frequent misdiagnosis of right varicocele (RVA) due to false-positive results [14, 15], a condition that is identified by simply performing a "subinguinal venous compression maneuver" (see "Clinical Aspects of Male Infertility due to Varicocele").

Radiological Anatomy and Pathophysiology of Varicocele

The PP originates from the mediastinum testis. It is accompanied by numerous venous sinuses, lymphatic vessels, fat tissue, and nerve fibers. It is divided into three groups of veins that anastomose with each other:

1. The first group of veins is the anterior or internal PP, which joins the internal spermatic vein (SV) plexus through the external inguinal ring. Sometimes the anterior PP does not end at infrainguinal level but continues for a few centimeters in the pelvis before joining the internal SV.
2. The second group of veins is the medium PP, which runs parallel with the ductus deferens to the pelvis.
3. The third group of veins is the posterior PP, also called the cremasteric or external SV, which follows the posterior edge of the spermatic cord. The latter drains in the external inguinal ring and then into two branches (superficial and deep) of the pudendal vein.

The medium and posterior PP constitutes a complex vein drainage system that allows additional collateral circulation of the testicular venous drainage. Numerous anastomoses are formed between the medium and posterior PP veins and the systemic venous circulation either through the pudendal vein or through the saphenous-femoral system. The SV flow is reversed in a varicocele. As a consequence, occlusion of all venous branches of the anterior PP at the inguinal canal level does not cause irreversible testicular damage but rather results in the certain cure of the varicocele. Conversely, if surgical ligation is made on the posterior PP, which impedes systemic venous drainage, testicular damage is inevitable and irreversible. This well explains the many recurrences after surgical or percutaneous treatment. In this context, it is interesting to note that in the 1950s, in fact, some surgeons performed total PP excision, which corrected the varicocele but, in contrast, resulted in testicular atrophy and severe hydrocele.

However, the interventional radiologist is more interested in the functional phlebographic anatomy with all its many variations. Consequently, we refer the reader to the article by Porst et al. [16], which describes various types of left spermatic vein (LSV), and to the article by Siegel et al. [10] for right spermatic (RSV) phlebography (Fig. 1). It is important to consider that urogenital anomalies are frequent and obviously associated with SV variations [17]. Renal anomalies generate significant problems for renal vein and SV catheterization; therefore, renal ultrasound examination before percutaneous treatment is strongly recommended.

Varicocele may be primary (idiopathic) or secondary. Primary varicocele is considered to result from mesoaortic compression of the left renal vein (LRV) and is particularly evident when the patient is standing ("nutcracker syndrome") [18, 19]. Hematuria is sometimes found in patients with this syndrome due to the increased pressure in the LRV caused by strong mesoaortic compression associated with intrarenal varices [20, 21]. Hematuria disappears when the patient has rested for 24 h or more because of the decrease of intrarenal venous hypertension [22]. Some patients we treated complained of left renal soreness that lasted 15–30 days; this was probably due to a further increase in renal venous pressure [23, 24]. Nevertheless, increased intrarenal and spermatic venous pressure, which creates venous reflux in the spermatic plexus, could also be related to anatomical variations of the LRV, e.g., retroaortic LRV, double LRV (aortic ring), and two LRVs draining to different inferior vena cava levels. However, with the advent of multidetector computed tomography angiography (MDCT-A) it has become easy to identify mesoaortic compression, all of the other anatomical variations of the LRV, and also rare compression of the common left iliac vein.

Secondary varicocele can be due to compression of the PP draining veins in cases of pelvic, abdominal and renal tumors, lymphomas [25], and cecum cancer. In the latter case, a RVA is observed [26]. Nontumor causes of secondary varicocele can be hydronephrosis and hydroureter [27]. A pseudoaneurysm consequent to an aortic graft can produce an RVA [28]. A high-flow arteriovenous fistula caused by rupture of an aortic aneurysm in the LRV results in a secondary left varicocele (LVA) (see Fig. 2 for example) [29]. Finally, a varicocele may be caused by a splenorenal shunt due to portal hypertension. Therefore, in secondary varicocele, the PP venous ectasia never disappears when the patient is in a supine position.

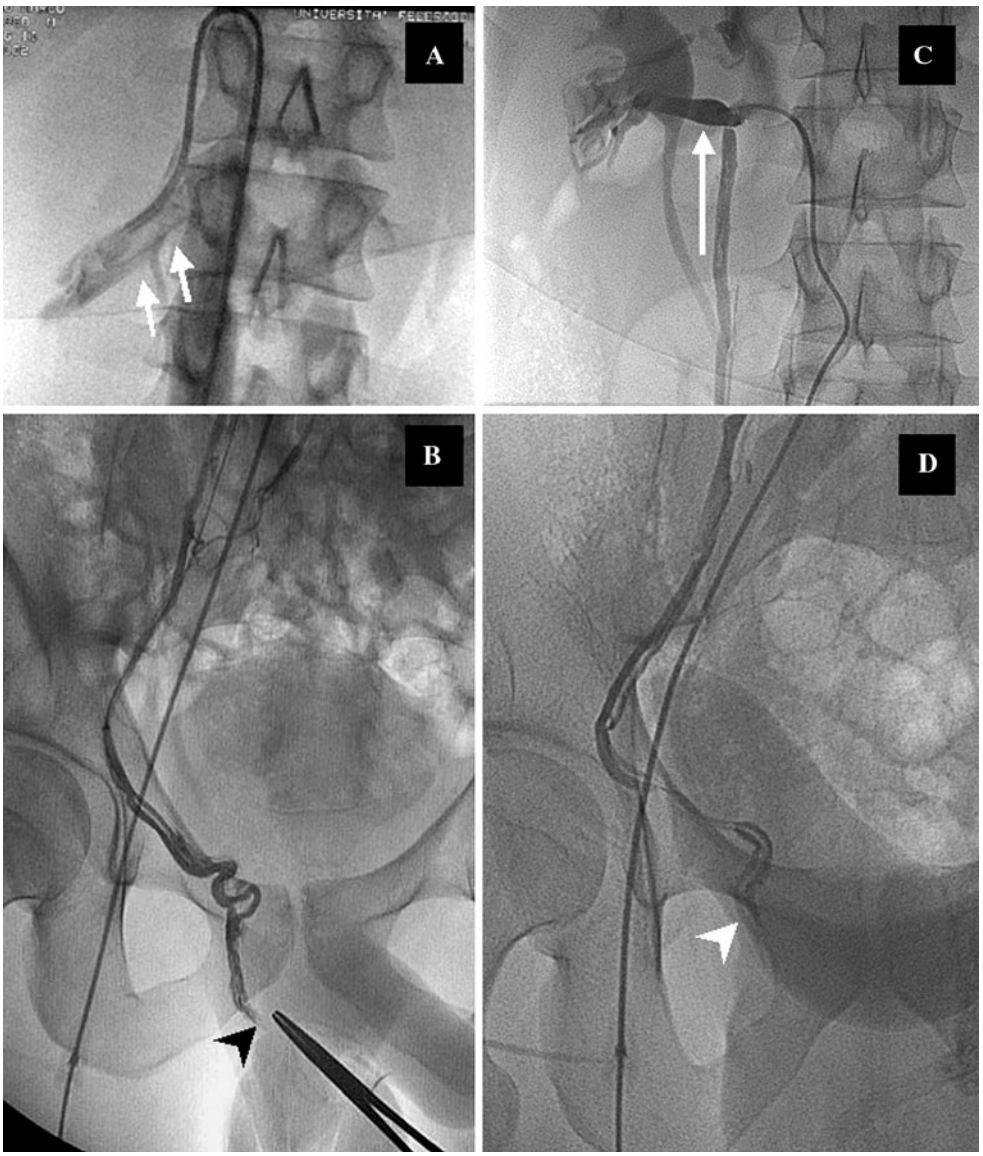

Fig. 1 Right varicocele phlebography in two patients with suspicious BVA. **A** and **B** Case no. 1 (26 years old). **A** RSV (*arrows*) drains only in the right renal vein. **B** RVA retrograde sclerotherapy with barrage (*black arrowhead*). **C** and **D** Case no. 2 (28 years old). **C** RSV drains into the right inferior renal vein (*arrow*). **D** RVA retrograde sclerotherapy (*arrowhead*). In both cases, the RSV catheterization was performed using hydrophilic Sidewinder 3, a 3F coaxial hydrophilic microcatheter, and 0.018 inch hydrophilic guidewire

Relationship Between Varicocele and Infertility

Varicocele is the most frequent as well as correctable cause of male infertility. Fertility is decreased in 21–41% of cases of varicocele [30]. Several hypotheses have been proposed to explain the link between varicocele and infertility. The most important factor is increased scrotal temperature [8, 31–34]. This well correlates with the observation that testes that descend late in the scrotum or are retained in the inguinal canal become hypotrophic when the child is >2 years old. A tense and short scrotum with testes close to the perineum is also a cause of slow testicular atrophy. An improvement in semen quality was achieved using a device to decrease scrotal temperature in infertile patients with varicocele [35]. Telethermography has also been used to identify infertile patients who would benefit from treatment to cure varicocele [36].

Subclinical varicocele is no longer considered a cause of infertility, and already in 1981, at the Third World Congress of Andrology (Varicocele Symposium) in Tel Aviv, there was unanimous consensus not to treat subclinical and small varicoceles. However, left intrarenal venous hypertension may gradually increase over the years, along with an increase in renospermatic reflux, and may cause

Fig. 2 MDCT-A in a 73-year-old man with left varicocele secondary to left aorto-renal arteriovenous fistula. **A** Three-dimensional (3D) reconstruction showing an aortic aneurysm (*asterisk*) ruptured into the LRV (*arrowhead*) and spermatic venous plexus opacification up to the inguinal level (*arrows*). **B** Axial scan with evident communication between the aortic aneurysm and the LRV (*black arrow*). **C** Oblique multiplanar reconstruction showing high-flow venous hypertension (hyper flow) signs in LRV and LSV (*arrows*)

infertility. At onset, the testicular damage induced by intrarenal venous hypertension is lowest or absent, but it may become severe. Seminology findings are always more severe in patients with LVA and contra lateral testicular atrophy (caused by trauma, postsurgery, undescended testis, etc.). Left varicocelectomy gives often satisfactory results in such patients. We assume that left high-grade varicocele associated with bilateral hemodynamic venous overload due to peripubic and transscrotum collateral circulation may lead to increased scrotal temperature and therefore to subfertility. It is difficult to identify transscrotum and peripubic collaterals as a cause of false BVA. This could explain why approximately 60% of people with a varicocele are fertile but can become infertile in the future. Figure 3 shows a computed tomography (CT) image of transscrotal venous anastomoses showing false BVA.

Clinical Aspects of Male Infertility due to Varicocele

Evaluation of patients should include a well-structured interview and questionnaire (Table 1) as well as physical examination to exclude other or concomitant causes of infertility. If a young man complains of testicular pain, one should enquire about his sexual habits because prolonged abstinence may produce pain (congestion of the epididymis) that is not related to varicoceles.

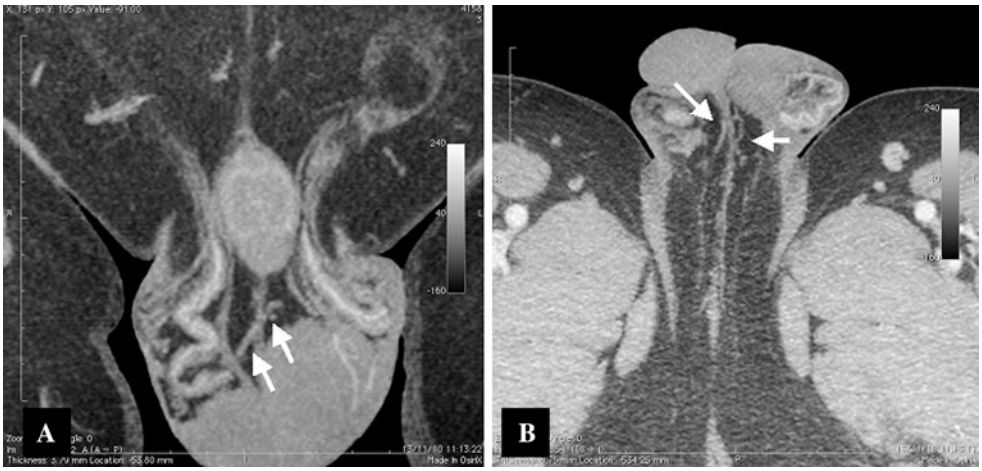

Fig. 3 Patient treated for BVA with surgical recurrence. **A** MDCT-A coronal multiplanar rendering (MPR) reconstruction of the scrotum showing transseptal venous communications that resulted in cross-circulation (*arrows*). **B** Axial CT image of the same patient with transscrotal venous anastomoses (*arrows*) showing a false BVA and persistent LVA

Table 1 Causes of infertility questionnaire

Alcohol abuse
Iatrogenic (prolonged drug-therapy with antiepileptics or neuroleptics, antibiotics, steroids)
Exposure to toxic substances (heavy metals, pesticides, paint fumes, or hazardous substances) [113]
Metabolic and hereditary diseases (cystic fibrosis or Klinefelter syndrome), previous obesity, scrotal dermatoses
Previous surgically corrected hypospadia, cryptorchidism, hydrocele and hematocele
Infective prostate-urethritis (*Chlamydia trachomatis*, postpuberal mumps, or orchi-epididymitis)

Physical examination should be performed with the patient in a supine position and then in a standing position. Scrotum palpation when the patient is supine serves to determine the presence of the ductus deferentes and to exclude intrascrotal masses: testicular cancer, epididymal cysts, hemangioma, vascular malformations, and hydrocele. Inguinal hernia must also be excluded. Varicocele is secondary when it remains evident when the patient is lying down.

Patients are asked to stand up quickly facing the physician to determine the time required for the varicocele to be completely filled. A slow appearance of the varices (after $\geq$30 s) is often due to a continent spermatic valve at renal entry. The physician must check the position of the testes to see if one or both testicles are close to the perineum and if they tend to rise in the inguinal canal. The scrotal skin should be inspected to exclude cutaneous and/or intrascrotal hemangioma and cutaneous varices secondary to a large varicocele. In rare cases, the skin can be as thick as "leather'' due to scratch dermatitis, which may be another cause of infertility, or due to scrotal skin ichthyosis, which responds to local steroid therapy. However, the latter treatment does not improve fertility. In fact, in cases of scratch dermatitis and scrotal skin ichthyosis, there is an increased testicular temperature due to altered transscrotum thermal exchange caused by cutaneous thickening.

The clinical examination includes evaluation of the volume and size of the testicles and the varicocele grade, which is assessed with the patient standing up. The classification is as follows [37]: grade I (small [only palpable during a Valsalva maneuver]); grade II (medium [easily palpable]); and grade III (large [visible without palpation]). We suggest that the following grade be added to the classification: grade IV (very large [varicocele becomes visible immediately the patient stands up, the varicosities are hypertensive, and subcutaneous varices are present, often associated with a false RVA]).

In case of BVA, especially of a grade III or IV LVA, we suggest the physician perform a subinguinal venous compression maneuver to exclude a false RVA consequent to transscrotal hemodynamic overload. The procedure is conducted as follows:

1. The patient rests in a supine position for a few minutes.
2. A soft clamp is placed around the highest part of the left PP.
3. With the patient standing and the clamp in place, the right PP is palpated for at least 1 min and also palpated while the patient performs a Valsalva maneuver. If the right PP becomes dilated, BVA is really present, and the subinguinal venous compression maneuver is ended. In contrast, in case of a false RVA, there is no palpable ectasia of the right PP.
4. When the patient has been standing for as long as 2 min without right PP ectasia, remove the clamp on left side and observe how quickly the swelling of the right PP begins (in false RVA it should start within 20–30 s). This maneuver must be repeated under ultrasound Doppler, and we recommend using Sarteschi's varicocele classification [38, 39].

Finally, bilateral testicular ultrasound volume (TUV) evaluation is useful in adult and mandatory in children. An adult testis is considered small when TUV is <10–12 ml [40]. Moreover, ultrasound evaluation of the testicular parenchyma can exclude changes that cause infertility and sometimes predispose to neoplastic degeneration, such as testicular microlithiasis [41].

Laboratory Diagnosis of Infertility

Infertility should be considered when a couple fails to conceive after attempting unprotected sex for at least 1 year [42–46]. It is noteworthy that infertility is attributed to female causes in 58% of cases, to male causes in 25% of cases, and to unknown causes in the remaining 17% of cases [47]. A patient who has already fathered a child and who wants to be treated for testicular pain or discomfort does not need special laboratory tests. Our oldest patient (82 years old) who had the largest persistent LVA after surgery in our series, was treated, notwithstanding his age, because of discomfort during sexual activity (Fig. 4). In contrast, infertile patients with varicocele should undergo the following hormonal tests: luteinizing hormone, follicle-stimulating hormone, prolactin, inhibin B, and testosterone [48, 49].

Screening and evaluation of oligo-azoospermia is essential for differential diagnosis [50–55]. Microscope analysis of semen is subjective, not useful for follow-up and does not detect all possible sperm abnormalities. Therefore, semen should be analyzed with the computer-assisted sperm analysis method as indicated in the World Health Organization guidelines [46]. In case of suspected

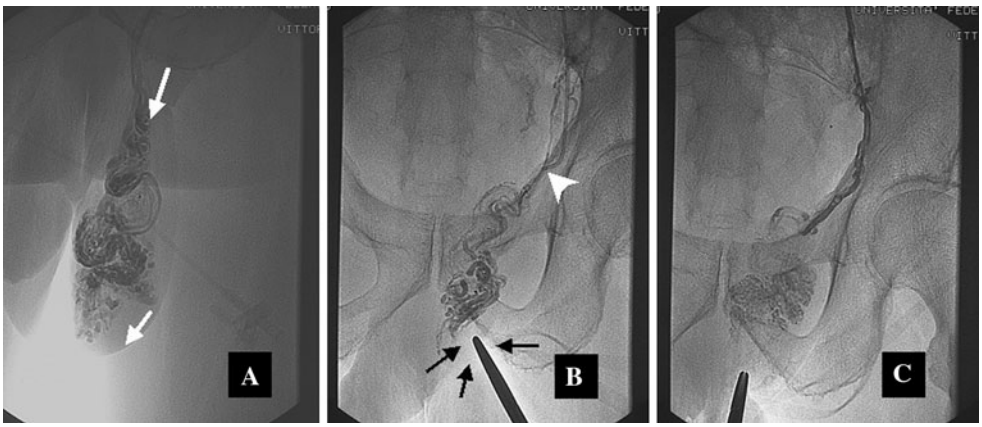

Fig. 4 Retrograde sclerotherapy of a grade IV LVA in an 82-year-old man with persistent postsurgical LVA after 10 years. **A** Retrograde phlebography shows a large anterior PP secondary to an obvious long-standing venous spermatic plexus insufficiency (*arrows*). **B** External elastic barrage application (*black arrows*) with catheter tip at the iliopubic level (*arrowhead*) for sclerotherapy. **C** Satisfactory occlusion of the large anterior PP. There is absence of percutaneous recurrence at 12 month follow-up

excretory azoospermia, a transrectal ultrasound examination should be performed [56, 57].

Selecting Patients for Treatment

Varicocele treatment is indicated in the following cases: (1) painful varicocele; (2) large varicoceles that create aesthetic problems; (3) varicocele with moderate oligospermia (although varicocele treatment may not improve fertility, some of these patients may in the future benefit from assisted reproduction); and (4) young men with abnormal semen and a desire for fertility.

In case of suspected BVA, treatment of only the left or the larger side is recommended. Treatment is not recommended for patients with a small or subclinical varicocele, namely grade I to II of Sarteschi's classification [39], because it does not improve fertility or symptoms. However, such patients should undergo yearly semen examination and ultrasound-Doppler with TUV evaluation. Only adolescents with 10% decreased TUV in one testis versus the contralateral one should be treated. If TUV evaluation is normal in these patients, it must be repeated yearly together with semen examination, when possible, after puberty [58, 59].

Surgical Repair of Varicocele

Since 1800, various surgical procedures have been proposed for the treatment of varicocele, but surgical repair remains the best known and most widely applied treatment [60]. The most frequently used surgical procedures in this field are open, laparoscopic, and microsurgical varicocelectomy. The recurrence rate of traditional surgical procedures ranges between 0 and 37% [61, 62]. It is evident that the recurrence rate is greater after surgical varicocelectomy than after a percutaneous procedure. In fact, urologists tend to apply radiological therapy only after surgical failure [63, 64]. However, traditional surgery of varicocele began >150 years ago, although percutaneous therapy was one of the innovations of the pioneering era of interventional radiology. In fact, percutaneous treatment of varicoceles started approximately four decades ago [65–67]. Figure 5 shows a patient treated in 1975. However, despite the most sophisticated and modern surgical means, recurrence is always possible after open and laparoscopic surgery. The striking difference among surgical recurrences rates is reflected in the wide spectrum of percentages of reported improved semen cases (from 0 to 92%) and improved conception rates (from 0 to 63%) [61, 68–70].

Open Varicocelectomy

Open varicocelectomy can be performed through three abdominal sites of incision: (1) high retroperitoneal ligation of spermatic vessels, also known as the "Palomo technique" [60]; (2) inguinal in which the incision is performed at the external inguinal ring; and (3) subinguinal. Obviously, all types open varicocelectomy require that the patient be under general or spinal anesthesia. Moreover, a wide range of recurrences (3.9–17%) and a high overall complication rate (5–30%) have been reported [71, 72]. Common complications are hydrocele, inadvertent arterial ligation, testicular atrophy, vas deference occlusion, and epidymitis.

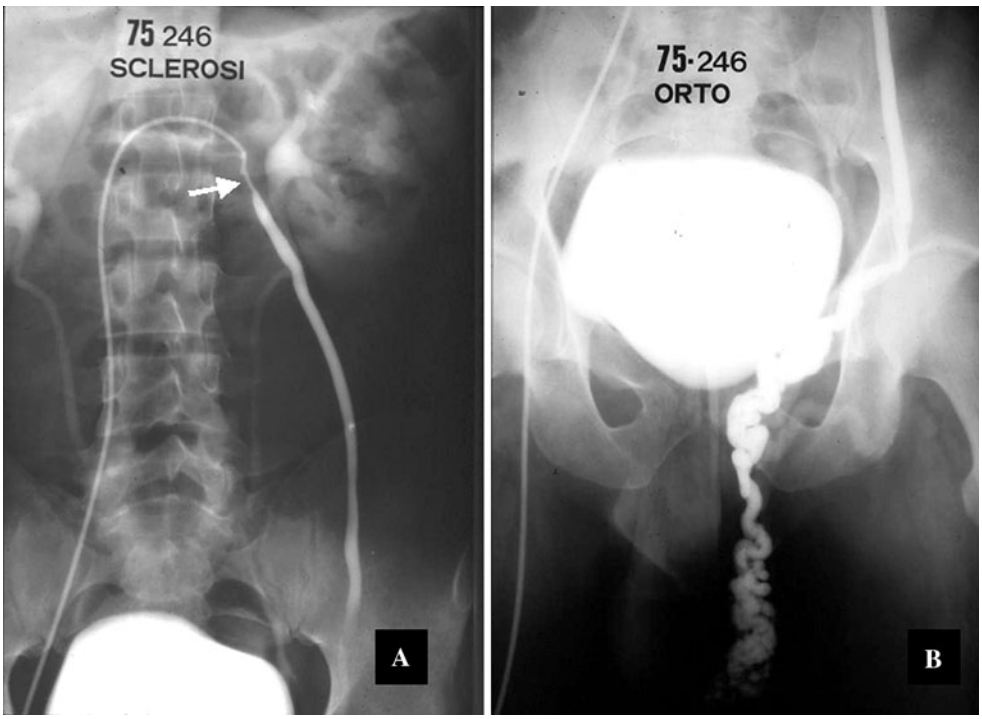

Fig. 5 Patient treated in 1975 (image obtained from the original slides) using a 7.5F PTE Cook catheter (Cook Medical, Bloomington, IN, USA). **A** The catheter tip is positioned in the proximal LSV with evident spasm (*arrow*) and opacification of the large LSV. **B** Intense left anterior PP opacification followed by sclerotherapy with 3% polidocanol (Aethoxysklerol; Kreussler Pharma, Wiesbaden, Germany). Note that sclerotherapy was performed without scrotal barrage and without inguinal LSV catheterization. The varicocele disappeared after 24 h with no recurrence

Laparoscopic Varicocelectomy

Laparoscopic varicocelectomy is generally performed transperitoneally. Complications occur in 8–12% of cases [73–75] and include hydrocele, embolism, genitofemoral nerve injury, intestinal injury, and peritonitis. Hydrocele is the most frequent complication. Recurrence rate is approximately 6–15% [75]. General anesthesia is always needed. The disadvantages of laparoscopic varicocelectomy include need for a highly skilled experienced laparoscopic surgeon, high cost, and an operating time of 20–80 min/side.

Microsurgical Subinguinal Varicocelectomy

Microsurgical subinguinal varicocelectomy (MSV) has many advantages: (1) the incision avoids abdominal fascia and muscle exposure; (2) good identification of dilated PP veins and their small collaterals and consequently a significant decrease in recurrence; (3) good identification of lymphatic vessels with a low risk of their accidental ligation; (4) excellent identification of arteries through the use of intraoperative microvascular Doppler and papaverine irrigation; and (5) an operating time of 25–60 min/side when performed by an experienced surgeon. These advantages account largely for the low complication rate of this procedure (0–2%). However, unintentional testicular artery ligation was reported in 1% and testicular atrophy in 5% of 2102 cases treated microsurgically [76]. Treatment of large varicoceles with MSV increases sperm count and pregnancy rate (47%) [77, 78]. An additional advantage of the procedure is that it can be performed in the outpatient clinic because local anesthesia is normally used.

Interventional Radiology

Retrograde Sclerotherapy: Standard Procedure

Patients with congenital or acquired hemostatic disorders can undergo retrograde sclerotherapy only after prophylactic measures. In cases of patients with severe contrast-medium reactions, carbon dioxide digital subtraction angiography (CO_2 DSA) can be used.

The optimal equipment for retrograde sclerotherapy is the multipurpose wide-angle Trendeleburg X-ray unit with digital flat-panel angiography because of the low radiation doses and better quality of the road map. Patients must be monitored and instructed how to perform the Valsalva maneuver. Retrograde sclerotherapy is usually performed in the outpatient clinic with the patient under local anesthesia, and if necessary, mild sedation. The use of 4–5 F hydrophilic catheters and hydrophilic guidewires that do not

cause venous spasms are recommended. In cases of difficult SV catheterization e.g., of a continent subrenal valve, it is preferable to use a braided superior torque control catheter with appropriate tip configuration. The percutaneous vascular access is normally through the right common femoral vein; if SV catheterization is not possible, proximal brachial access is preferred, especially for RSV [79].

Before retrograde sclerotherapy, diagnostic phlebography study of the SV is performed. Subsequently, hydrophilic guidewire are used to ensure that the catheter tip reaches the more distal part of the SV. Generally, the catheter tip must reach the lower edge of the ischiopubic ramus (see Fig. 6). In more complex cases, a road map must be obtained, and a microcatheter with a 0.018 inch hydrophilic guidewire is used. Once distal catheterization is obtained, a rubber band must be applied at the highest level of the scrotum and contrast media is immediately injected during a Valsalva maneuver to check that there is no reflux in the PP below the rubber band. Depending on the size of veins, it is recommended that 2–6 ml of 3% Na-tetradecyl-sulphate be injected in the anterior PP during the Valsalva maneuver and with the patient in the reverse Trendeleburg position. Scrotum elastic compression continues to be applied for 1 min and then is released with the patient in the Trendeleburg position to prevent posterior PP phlebitis. If sclerosant remains in the anterior PP, the procedure ends. Otherwise, sclerotherapy is repeated 10 min later, as described previously.

Spasms and/or lacerations occur more frequently in children than in adults. In such cases, 1 ml aliquots of nitroglycerin (100 μg/ml) can be injected or the physician can wait several minutes before continuing the procedure. For cases of severe venous laceration, a microcatheter can be placed further downstream. In case of persistent contrast extravasations, the procedure should be postponed for 1 month.

In case of a large SV, or in patients with bidirectional flow because of increased cardiac output in addition to distal barrage, a temporary proximal compliant balloon catheter of suitable diameter is also recommended to obtain a closed venous system with the double barrage. To ensure the sclerosant is always visible, 20% of contrast media can be added to avoid occlusion of dangerous collateral anastomoses with mesenteric or splenic veins, which can open during double barrage. Another trick is this: After inguinal barrage, inject 10–20 ml of CO_2 followed by sclerosant through a three-way stopcock (see Fig. 7). This procedure results in much more effective and faster sclerosis.

We have used Na-tetradecyl-sulphate as sclerosant for almost 30 years. It has proven to be effective, and it is not painful. Moreover, we have never encountered allergic reactions or adverse effects with this sclerosant, even when using it for other procedures. A more distal catheterization should be used with an appropriate volume of sclerosant one or more times. This procedure results in occlusion of all collateral veins, even those not visible at phlebography; but with time these veins may increase in size and generate recurrences. In contrast, recurrences will not occur when all of the anterior PP is occluded. Indeed, mechanical occlusion means or gluing agents can be considered equivalent to surgical vascular ligation. Moderate hemoglobinuria occurred in a few cases in which the sclerosant exceeded 15 ml. This can happen with all sclerosant agents and subsides after adequate hydration. Patients are usually discharged 2 h later with the following recommendations: resume normal activity after 48 h; avoid heavy physical activity for 7 days; assume a liquid diet for 3 days to prevent constipation; clinical check-up after 1 month; ultrasound Doppler examination after 3 months; and semen analysis after 4–6 months.

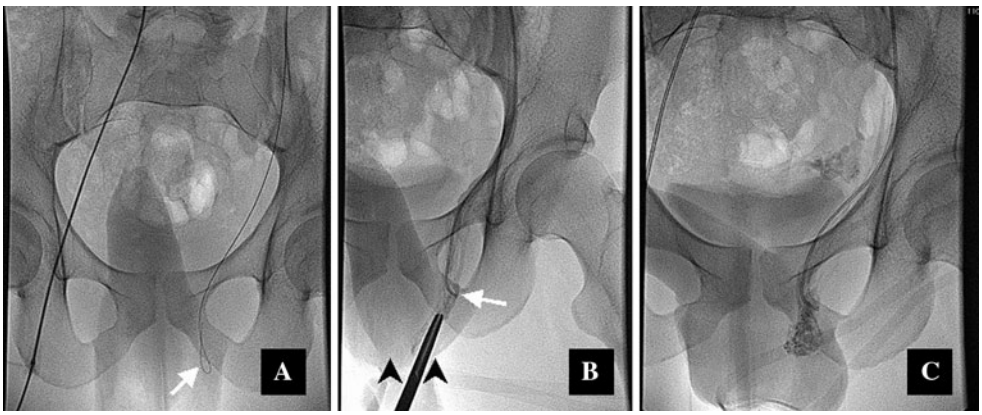

Fig. 6 Optimal distal catheterization for LVA sclerotherapy. **A** The 0.035 inch hydrophilic stiff guidewire reached the left ischiopubic level (*arrow*). **B** The catheter tip is positioned at the left ischiopubic level (*arrow*) and the barrage correctly placed before sclerotherapy (*black arrowheads*). **C** Postsclerotherapy control shows stasis of the sclerosant at the level of the subinguinal anterior PP (the barrage was removed)

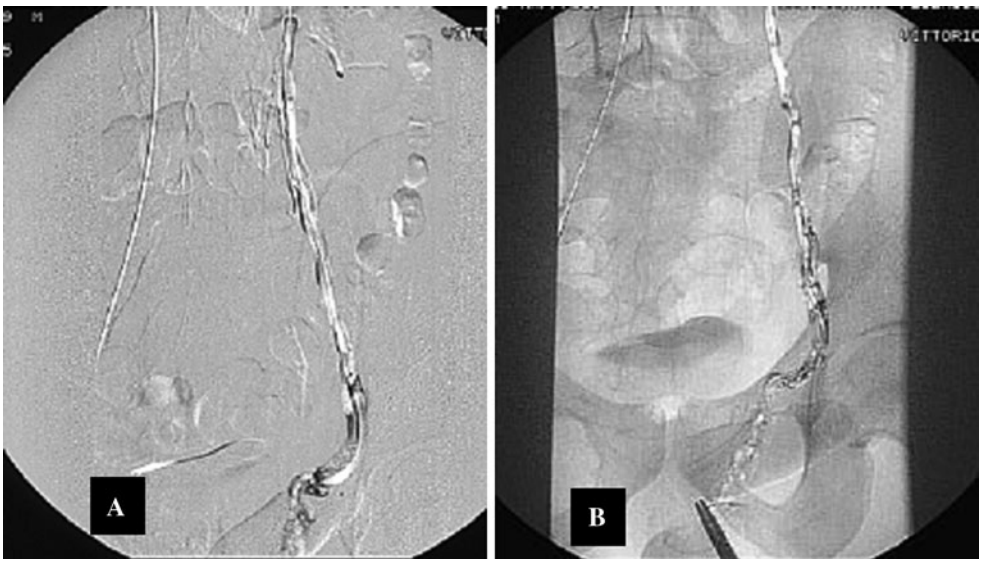

Fig. 7 CO_2 DSA of a large LSV with a large collateral venous plexus. **A** The catheter tip at iliopubic level and negative visualization of the entire left spermatic plexus. **B** The barrage was positioned at the ischiopubic level without visualization of CO_2 and sclerosant below the clamp. Sclerotherapy was performed immediately after the injection of 20 ml CO_2

Retrograde Embolization

Coil Embolization

Several groups still use stainless coils [80, 81], whereas other groups have started using detachable coils [82]. All coils are now magnetic resonance imaging (MRI)-compatible. Jackson detachable coils (Cook Medical, Bloomington, IN, USA) are available in 0.035- and 0.038-inch sizes and in various lengths and diameters (3–12 mm). They have fibers to promote thrombosis. Venous embolization is safer and more accurate with these coils; moreover, they allow distal occlusion. A coil can be safely removed from the catheter before its detachment in case of inappropriate size or position [82]. Detachable microcoils (Terumo Medical Corporation, Tokyo, Japan) are available for cases of more distal occlusion in the inguinal canal. These low-profile systems are equipped with a 0.014 inch guidewire, which allows more precise embolization. Selective catheterization of the left SV can be performed with the Left Vena Spermatica Coaxial Infusion Set AQ Hydrophilic Coating (Cook Medical) and the microcatheter directed, if possible, up to inguinal canal [83].

Another advantage of detachable microcoils is their hydrogel coating, which enables the coil to expand up to six times its original volume [84]. They are much more expensive than traditional coils. However, it is noteworthy that sclerosis can be achieved after release of the detachable coil [82]. In fact, standard coils were often used instead of the much cheaper external inguinal barrage to prevent sclerosant reflux in the PP, and many investigators still use them for scleroembolization.

In our experience, traditional coils can be associated with several complications, which can be serious: coil migration, venous dissection, and venous perforation. In contrast, few technical complications have been associated with detachable coils, and these have been due to entangled fibers in the treated venous segments [85]. The overall complication rate with detachable coils is 9.7%, and the recurrence rate is 4.8% [83]. However, because an average of five coils is used, the cost of each detachable microcoil procedure is estimated at <$7000 in the United States, which is similar to the cost of laparoscopic treatment.

The following precautions should be taken when performing coil embolization:

- Use detachable coils because they are easily removed in case of venous perforation.
- Do not use tungsten coils because some resorption can occur [86–88].
- Before releasing coils, measure, by a digital process, venous diameter to ensure coil migration cannot occur; coil diameter must have expanded at least 2 mm greater than the venous diameter.
- Occlusion should be performed as distal as possible to avoid recurrence [89].

Acrylic Glue Embolization

Acrylic glue embolization was introduced in the 1980s. The technique is similar to coil embolization performed with a coaxial microcatheter to try to reach the inguinal canal. *N*-butyl cyanoacrylate (NBCA) glue (Trufill, Cordis,

Miami, FL, USA) is normally mixed at a ratio of 1:3–4 per volume with Ethiodol (Savage Labs, Melville, NY, USA) or Lipiodol (Guerbet, Roissy, France) and slowly injected through the microcatheter. This kind of embolization is frequently used in cases of persistent and recurrent post-surgical varicoceles [64].

Possible complications are glue migration into the pulmonary circulation, glued catheter, severe SV, or PP phlebitis. To prevent oil and glue migration, it is advisable to prepare oil and glue emulsion and apply it through a three-way stopcock. The emulsion is best prepared by passing it alternately through two syringes for as long as necessary. The glue should be injected through a three-way stopcock. The use of a three-way stopcock also allows the injection of 10% dextrose before, during, and after the glue injection to avoid a glued-catheter and occlusion of the catheter and microcatheter. Applying silicone oil on the tip of the catheter and the microcatheter will decrease the risk of their adhesion to the glue. NBCA glue modified with the addition of monomer synthesized by the manufacturer (Glubran 2; GEM, Viareggio, Italy) should be preferred because its polymerization is slower and therefore the thermal reaction is lower (<45°C); consequently, the procedure is safer and painless.

Considerations About Retrograde Embolization

We started retrograde sclerotherapy for male varicocele in 1975 and we used this technique up to 1980. From 1980 to 1985, we used various kinds of occlusion techniques. However, with mechanical occlusion we had a high recurrence rate (20–30%) and various complications: pulmonary migration of coil (1 case); pulmonary embolization of fibrin and collagen sponge (1 case); Lipiodol pneumonia (1 case); temporary phlebitis of PP (5 cases); glued catheter (1 case); "prisoner" catheters (15 cases); and SV ruptures with evident contrast extravasation (12 cases). We have also successfully used with hot contrast medium [90, 91] but only in few cases because it is too painful. Therefore, since 1985 we have used only sclerotherapy, which is inexpensive, safe, without evident complications, and without recurrence, in a total of approximately 4,000 patients.

Antegrade Sclerotherapy

During the first 10 years of percutaneous treatment of varicocele, we encountered difficulties in SV catheterization in complex anatomical cases with the technical aids available at that time. Furthermore, the percutaneous procedure was impossible in some surgical recurrences. In such cases, we realized that antegrade phlebography and sclerotherapy (AS) could be the solution. We started performing AS in the early 1980s and reported our findings in the Work in Progress Session at the 1990 Annual Meeting and Postgraduate Course of Cardiovascular and Interventional Radiological Society of Europe (Brussels, Belgium) Figure 8 illustrates the procedure of LVA ascending sclerotherapy in a patient in whom retrograde catheterization of the LSV was not possible. In 1994, Tauber and Johnsen were the first to publish an article devoted to antegrade scrotal sclerotherapy [92]. They subsequently reported a success rate of 91% [93]. However, an even better success rate can be obtained with a more accurate technique (see later text). The surgical access can be inguinal or subinguinal.

Groin Access

After skin disinfection, with the middle finger as a guide, the external inguinal orifice is reached, and local skin up to the fascia is anesthetized preferably with ropivacaine (Naropin 10 mg/ml; AstraZeneca, London, UK), which

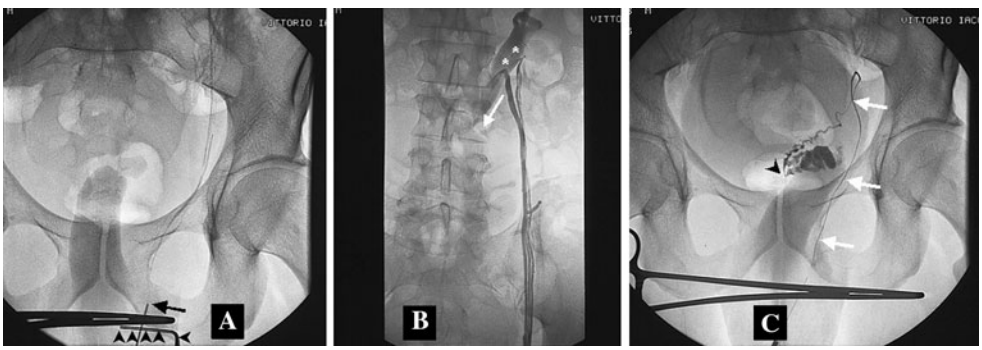

Fig. 8 LVA antegrade sclerotherapy in a patient in whom retrograde catheterization of the LSV was not possible. **A** Ascending phlebography by the subinguinal access of a surgically isolated vein of left anterior PP. Note the soft titanium angiostat (*black arrowheads*) positioned below the plastic cannula (*black arrow*). **B** Ascending phlebography shows 2 LSVs (*double asterisk*) draining into the ectopic LRV. The LRV drains in a marked oblique caudal direction at the L3 level (*white arrow*). **C** Simultaneous left vasography (*white arrows*) performed after sclerotherapy. Note the dilation of the left seminal vesicle secondary to ipsilateral ejaculatory duct stenosis (*black arrowhead*)

lasts 6–8 h. The incision is performed using the middle finger as a guide, and the fascia is cut after hemostasis. Once isolated, the PP is soaked in anesthetic for a few minutes. The spermatic cord is kept external with a right-angled clamp, and a small PP vein is isolated and cannulated with a 22–25 G needle. The needle is securely tied to the vein to prevent leakage of contrast media or sclerosant. It is also fastened to the edges of the skin to prevent its accidental removal. A diluted contrast solution is injected into the vein to check its integrity. Antegrade phlebography is performed after placing a soft vascular angiostat immediately below the cannulation site around the PP to prevent contrast reflux. Phlebography is repeated while the patient carries out a standard Valsalva maneuver and again while in a 45° reverse Trendeleburg position. It is important to (1) inject the contrast medium in a branch of the anterior PP and not the posterior PP; (2) confirm the absence of contrast reflux in the posterior PP below the angiostat; (3) exclude opacification of collateral veins, such as the mesenteric venous branches; and (4) inject an appropriate volume of sclerosant together with 20% contrast media during the Valsalva maneuver and reverse Trendeleburg maneuvers while taking care to keep the angiostat in position. The surgical field must be completely irrigated with saline during sclerotherapy. Finally, the needle is removed and the two venous edges ligated. Hemostasis must be checked and the wounds sutured in two layers.

Groin access has the advantage of facilitating venous isolation and cannulation because veins are larger at this level. However, the wound is always fibrous and hard, and for 2 months the patient often complains of discomfort. This discomfort can be relieved in a few days with the application of local ultrasound therapy. However, groin access is impossible if the patient has undergone any type of inguinal surgical procedure.

Subinguinal Access

After skin disinfection, the spermatic cord is held with the thumb and the index and middle fingers, and local anesthesia is administered. The skin is incised while the spermatic cord is held with the fingers, and the cord is isolated in the most proximal site of the scrotum and then kept external. The spermatic cord is soaked in local anesthetic for a few minutes and, to obtain better venous dilation, the cord is wet with 6 ml of papaverine hydrochloride. A vein is isolated and the procedure is the same as described for groin access. Sclerosis must be performed and repeated if necessary, always with the angiostat below the needle. Before stitching, a tubular drain must be placed in the scrotum and fastened with one stitch to the skin to avoid severe hematocele. This drainage is removed 48 h later, and the patient is discharged the same day. Scrotal access is preferred even although venous isolation is more difficult and hemostasis takes more time. If required by the andrologist, testicular biopsy can be performed after sclerotherapy.

Throughout the 1980s, we performed >200 AS procedures. Today, we rarely use AS except in cases of recurrent surgical or percutaneous embolization when we cannot perform the catheterization until anterior PP. When we first started using this procedure, we had a few recurrences and complications (hematocele and phlebitis of the PP). Last, it is important to note that AS has been performed without phlebography [94]; we strongly discourage this because it can cause a devastating sigmoid infarction, which happened once in our hospital.

Treatment of Recurrent and Persistent Varicocele

Recurrent and persistent varicocele can occur after surgical and percutaneous treatment. Many groups use retrograde renocaval venography to determine whether duplication and collateral veins are the cause of recurrence and at the same time to occlude the veins with NBCA embolization [64, 95]. Others perform intraoperative phlebography to identify the cause of recurrent and persistent varicocele [96].

Before selecting the treatment option for recurrent postsurgical or postpercutaneous varicoceles, it is important to ascertain if the previous venous ligation, coil, or acrylic glue embolization could impede the percutaneous approach and hence spare the patient phlebography and SV catheterization. Today, MDCT-A [97, 98] or MRI-A [99, 100] are strongly recommended to identify the exact site of venous occlusion and the cause of previous treatment failure. In fact, it is easier to identify the site of venous occlusion and even small vessels up to the inguinal canal by MDCT-A than by intraoperative procedures or phlebography (Fig. 9). Distal sclerotherapy is advisable in cases in which surgical ligation or percutaneous occlusion does not impede catheterization of the anterior PP. In some difficult cases, a double-barrage balloon catheter inflated in the SV proximal position can be used. When the latter options are impracticable, the alternatives are AS or MSV (Fig 10). With increasing experience in using the AS procedure, we identified the causes of surgical recurrences and, especially, of percutaneous recurrences. To avoid them, when using the percutaneous technique, we (1) aim for the most distal retrograde catheterization; (2) apply scrotal barrage; and (3) use only sclerosant. These three measures ensure the success of retrograde sclerotherapy. In fact, only complete occlusion of the anterior PP allows a complete cure, as in AVM, in which only total

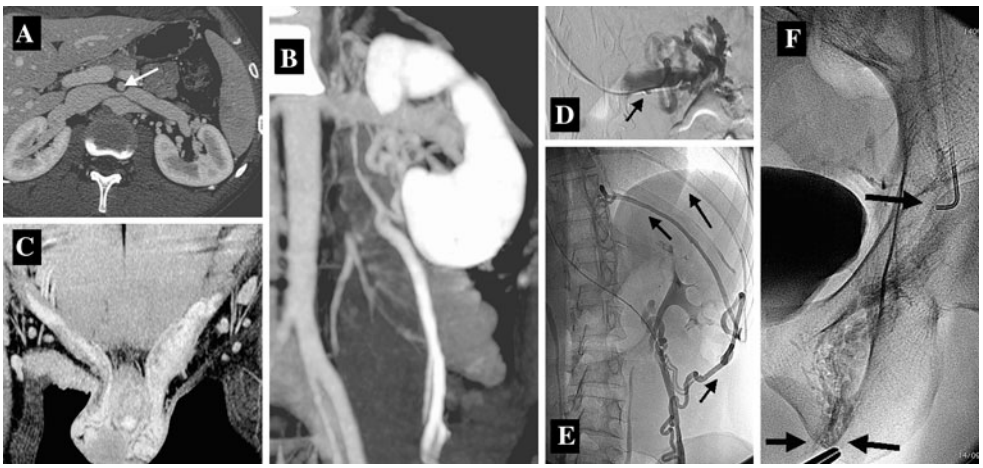

Fig. 9 MDCT-A evaluation of persistent postsurgical (inguinal ligation) grade IV LVA and its percutaneous treatment. **A** Axial CTA shows severe aorto-mesenteric compression of the LRV (*white arrow*). **B** 3D maximum-intensity projection showing large perirenal varices and dilated LSV. **C** 3D-maximum intensity projection (MIP) showing large left inguinal and scrotal PP. Note that the right PP is also dilated because of hemodynamic transscrotal overload. **D** Left renal phlebography by the right brachial approach was performed based on MDCT-A imaging: Note the small subrenal spermatic continent valve (*black arrow*). **E** Difficult selective LSV phlebography, with superior torque 5F catheter, shows multiple venous anastomoses with intercostal veins due to high venous renal hypertension (*black arrows*). **F** Successful retrograde sclerotherapy performed on a large anterior PP between scrotal external barrage up to the tip of the catheter (*black arrows*) to avoid worsening of venous-renal hypertension

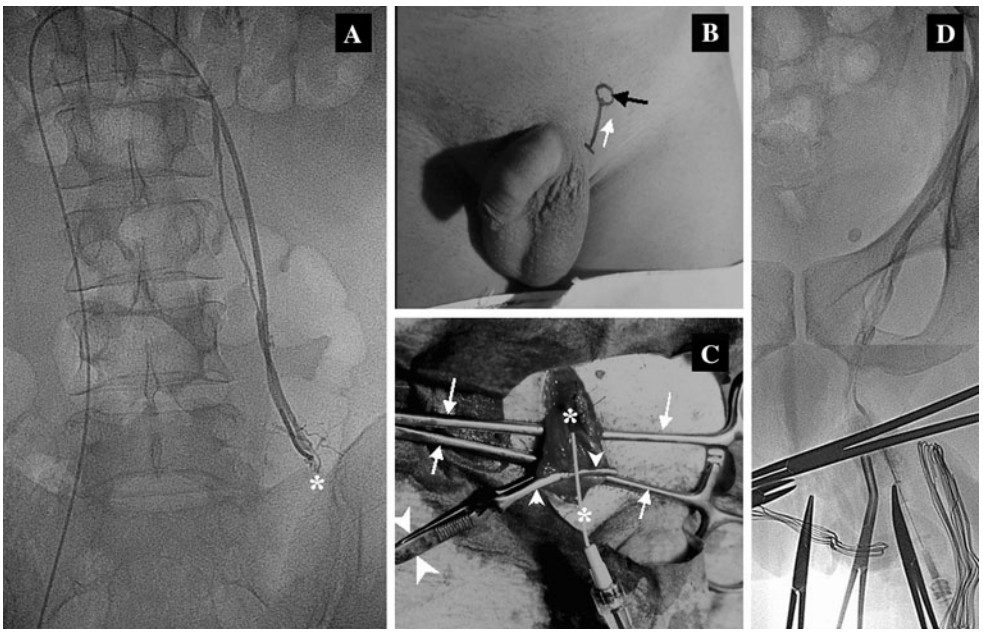

Fig. 10 LVA antegrade sclerotherapy for surgical recurrence. **A** LSV catheterization up to the sacroiliac level (surgical ligation blocking progression of the catheter) (*asterisk*). **B** Surface drawing of the anatomical site showing the direction (*white arrow*) of the surgical incision extending to the external inguinal ring (*black arrow* [groin access]). **C** Visualization of the anterior PP surgically isolated and kept external to the field by a large clamp (*arrows*). Note the plastic cannula (*double asterisk*) fixed in a single vein lumen of the anterior PP. A vascular angiostat was placed immediately below the venous access (*arrowheads*). **D** Control after sclerotherapy of the left anterior PP and of the distal segment of LSV after removal of the vascular angiostat

embolization of its nidus or radical surgical exeresis ensures the success of the procedure. We treated, finally with success, one patient by AS after he had undergone three surgical recurrences and one percutaneous recurrence—*Errare humanum est*, *perseverare diabolicum est*.

Discussion

The main controversy in the current literature on the treatment of varicocele concerns the effect of varicocelectomy on infertility in patients with a palpable varicocele

and the ensuing pregnancy rate. In a Cochrane review, Evers et al. evaluated the outcome of surgery and embolization for varicocele in subfertile men [101]. They concluded that there is no evidence showing that treatment of varicoceles in men from couples with otherwise unexplained subfertility improves spontaneous pregnancy rates. However, they noted that their conclusion could reflect the scarce number of studies and their clinical and statistical heterogeneity. Other investigators [102], in contrast, found that varicocelectomy for palpable varicocele improved fertility; in fact, there was a significant increase in the pregnancy rate (36.4%) compared with nontreated patients. Similar results were reported by Marmar et al. [103]: a 33% pregnancy rate in patients treated with surgical varicocelectomy versus 15.5% in an untreated group.

In a meta-analysis conducted to identify the most effective treatment for palpable varicocele in infertile men, MSV was found to have a very low complication rate (1.05%) [75]. Similarly, in a comparison between MSV and retroperitoneal varicocelectomy in infertile men, Ghanem et al. [104] reported recurrence rates of 1.6 and 6.4% and hydrocele rates of 0 and 7%, respectively. Watanabe [105] reported a recurrence rate of 0% with MSV versus 6.1% with laparoscopic surgery and 12% with the Palomo technique.

The meta-analysis by Cayan et al. [75] showed low recurrences rate with MSV, which appears to be reflected in the high overall spontaneous pregnancy rate: 41% with MSV, 37% with the Palomo technique, 36% with macroscopic inguinal varicocelectomy, 33.2% with radiologic embolization, and 30.1% with laparoscopic varicocelectomy. However, the spontaneous pregnancy rate was closely related to female age and reproductive health condition. Moreover, it is important to note that in this meta-analysis, recurrence and hydrocele formation were evaluated in 2,094 patients treated with MSV, 608 treated with macroscopic inguinal varicocelectomy, 434 treated with the Palomo technique, 176 treated laparoscopically, and only 122 treated with radiologic embolization. A radiologic embolization failure rate of 13% occurred in a total of 314 patients treated between 1980 and 2008. In fact, Cayan et al. make a call for randomized, controlled, prospective studies that compare all of these techniques to identify the best treatment of varicocele in infertile men. The need for randomized, controlled, prospective studies was echoed in a study on management options of varicoceles conducted in 2011 [106], in which all percutaneous varicocele occlusions and all kinds of surgical repair of varicoceles were well described: The investigators concluded that is impossible to give exact information about the best treatment choice for patients with varicocele.

A comparison of the radiological and surgical treatment options in terms of spontaneous pregnancy, unperformable rate, recurrence and persistence rate, procedure time, and procedure cost is listed in Table 2. The overall complication and hydrocele rate is reported in Table 3. From these two tables, the following points emerge:

- The unperformable rate of percutaneous occlusion is unacceptably high given the sophisticated means now available.
- The recurrence and persistence rate of AS (subinguinal access) is still high ($\leq$11%) compared with a similar surgical technique such, as MSV.
- The recurrence and persistence rate of percutaneous occlusion is mainly associated with the technique used, such as sclerotherapy, coils, or acrylic glue.
- Postsurgical hydrocele is the main and most severe complication after high and inguinal ligation [107]; it is very low after MSV, and it never occurs after percutaneous occlusion or AS. Moreover, postoperative hydrocele is underestimated because it can occur many years after surgery [108]. It can be resolved in approximately 48% of patients by simple aspiration (one to three times), and long-term monitoring is justified in these patients. In the remaining cases, tunica

Table 2 Comparison between surgical and percutaneous varicocelectomy

Factor	High ligation	Inguinal ligation	Laparoscopic surgery	MSV	Percutaneous occlusion[a]	AS
Spontaneous pregnancy rate (%)	28–55	34–39	14–27	33–56	20–30	42
Unperformable rate	+	+	0–11	+	8–30	+
Recurrence/ persistence	9–45	+++	3–15	0–2	3–11	5–11
Procedure time (min)	20–50	20–46	20–80	25–62	30–60	10–33
Cost	+	+	+++	+	+/+++[b]	+
References	[71–74, 114–119]		[71, 73, 109, 114, 120–125]	[71, 77, 116, 126–128]	[16, 82, 89, 114, 129–138]	[92, 93, 112, 139–144]

+ Low, ++ medium, +++ high

[a] Retrograde sclerotherapy, personal experience: unperformable rate = 2–3%; recurrence rate = 0; procedure time = 15–45 min; cost = +

[b] Depending on the tools used

Table 3 Comparison of the complication rate between surgical and percutaneous varicocelectomy

	High ligation	Inguinal ligation	Laparoscopic surgery	MSV	Percutaneous occlusion[a]	AS
Overall complication rate (%)	5–30	+	8–12	1–5	9–30[b]	0–8
Hydrocele (%)	6–14	7	2–3[c]	0.3–1.6	0	0
References	[71–74, 114, 116, 145, 146]		[71, 73, 109, 114, 124, 142, 147]	[71, 77, 116, 127, 128]	[16, 114, 129, 132–135]	[92, 140, 142–144, 148, 149]

+ Low

[a] Retrograde sclerotherapy, personal experience: hydrocele = 0; overall complication rate as side effect = low (only chemical phlebitis of the anterior PP depending on its size)

[b] Depending on the tools used

[c] With arterial and lymphatic sparing

vaginalis eversion or resection with accurate hemostasis is needed [107, 109, 110]. A significant increase of antisperm antibodies and a significant decrease of sperm motility have been found in patients who have undergone surgery for hydrocele [111].

- A large number of patients have been treated with MSV and AS. For example, Chan et al. [76] reported 2012 patients who underwent MSV from 1984 to 2002 and had a complication rate of only 0.9%, whereas Galfano et al. [112] treated 700 patients with AS and had a complication rate of 5% and a persistent adult varicocele rate of 9.4%.
- A comparison between the number of patients treated with percutaneous occlusion and surgical varicocelectomy weighs heavily in favor of the latter approach.

Conclusion

Because of its high incidence and because it is a frequent cause of subfertility or infertility, varicocele involves a large number of specialists: urologists, andrologists, surgeons, gynecologists, assisted-reproduction technologists, and, finally, interventional radiologists. Each specialist brings grist to their own mill. Everyone has the right to their opinion, but this attitude negatively impacts on the patient suffering from varicocele. In contrast, each specialist should make every effort to decrease the complication rate, associated risks, and cost and to improve the tools now available.

Few randomized trials have been conducted to compare the best treatments for varicoceles in terms of outcome, complications, recurrence rate, and cost-effectiveness. From this overview it emerges that retrograde sclerotherapy, AS, preferably by the subinguinal access, and MSV have similar beneficial effects in terms of outcomes, complication rate, and cost-effectiveness. Considering the large number of patients affected by varicocele, multicenter randomized controlled trials should compare at least these three procedures because they all result in anterior PP occlusion.

Finally, it is important that future trials be performed in homogenous groups of patients, by skilled and experienced surgeons and radiologists in collaboration, especially for AS when needed, and hopefully under the aegis of the Cardiovascular Interventional Radiology Society of Europe.

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Conflict of interest None.

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