

Varicoceles: Overview of Treatment from a Radiologic and Surgical Perspective

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Abstract

A testicular varicocele is the result of the expansion of the venous pampiniform plexus of the scrotum. Often painless, a significant number of patients experience orchialgia, swelling, testicular atrophy, and abnormalities in spermatogenic parameters. Treatment of symptomatic varicocele involves a radiologic or surgical intervention to obstruct the reflux of venous drainage. Testicular anatomy, diagnostic evaluation and imaging, options for surgical intervention, and a step-by-step description of retrograde embolization and antegrade scrotal sclerotherapy are discussed. Furthermore, included is an overview of postprocedural management and patient outcomes for radiological interventions, and the most up-to-date evidence on the efficacy of varicocele treatments as well as how they compare to each other.

Keywords

- ▶ varicocele
- ▶ varicocelectomy
- ▶ embolization
- ▶ sclerotherapy
- ▶ male fertility

A varicocele is an abnormal dilation and subsequent expansion of the venous pampiniform plexus of the scrotum, which drains blood from the testicles.¹ It is typically characterized as a “bag of worms” on physical examination. Often painless, severe cases present with a history of dull, aching pain that is worse with increased activity, standing, and straining.² Symptomatic patients may also present with scrotal swelling or testicular atrophy.

Varicoceles are classified as primary or secondary. Primary varicoceles make up the majority of cases and are defined by incompetent gonadal venous valves with resulting reflux; secondary varicoceles are much less common and are the result of increased pressure in the vein from either compression or obstruction.³ Causes include compression from extrinsic masses or lymphadenopathy as well as obstruction from renal vein thrombosis. The left testis is more commonly involved making up approximately 90% of cases, while approximately 9% of cases are bilateral. Unilateral right-sided varicoceles are very rare comprising approximately 1% of cases. If an isolated right-sided varicocele is encountered, additional workup for secondary causes should be performed.¹

In addition to being a cause of orchialgia, varicoceles are the most common cause of abnormal sperm morphology, abnormal semen analysis, decreased sperm motility, and low sperm count.^{1,4} The significant morbidity caused by varicocele affects 15 to 20% of adult men and nearly 40% of infertile men.^{1,2} This prevalence increases with age, as varicoceles affect over 40% of the elderly population.⁵ The exact cause of infertility in patients with varicocele is unclear; however, the most important factor is likely increased scrotal temperature. Additional factors may include reflux of toxic metabolites as well as hypoxia related to venous stasis.^{6–8}

The treatment of varicocele involves surgical or procedural interventions, as pharmacological therapies do not provide a definitive solution to this anatomical problem.⁹ Surgical intervention to treat varicocele varies in approach and shares the goal of obstructing the reflux of venous drainage while avoiding the vas deferens and the testicular artery.^{10–13} Meanwhile, radiological treatment can occur via embolization or sclerotherapy.¹⁴

Treatment for varicoceles should be reserved for symptomatic patients with pain, mass effect, bothersome appearance, or infertility, as treatment has been shown to efficiently

improve the pain and decrease the size of large varicoceles.^{14–16} Analgesics and scrotal support are alternatives to relieve pain or discomfort experienced by patients.¹ When intervention is warranted, varicocele can be treated via surgery or radiological intervention. Due to a lack of consensus on how varicoceles should be graded, it should be at the physician's discretion to decide when to intervene based on history, physical exam, and imaging findings.¹⁷

In this article, an outline of the current evidence and practice of radiological interventions for varicocele and a brief overview of the diagnosis and management of this disease will be discussed. With images and step-by-step explanations, the authors focus on describing both retrograde embolization and antegrade sclerotherapy, comparing these treatments with other available interventions based on recent evidence.

Anatomy

A varicocele is a dilated tortuous vein of the pampiniform plexus, the venous drainage of the testicles. The pampiniform plexus is divided into three groups of veins that anastomose with each other. These include the anterior pampiniform plexus that joins the gonadal vein near the external inguinal ring, the medium pampiniform plexus that runs parallel to the ductus deferens, and the posterior pampiniform plexus that follows the posterior edge of the spermatic cord. The posterior pampiniform plexus drains into the external inguinal ring as well as into two branches of the pudendal vein.¹⁴ There are numerous collaterals between the medium and posterior pampiniform plexuses and the systemic venous circulation through the saphenous-femoral system and the pudendal venous system. These collateral pathways explain why embolization of the anterior pampiniform plexus at the level of the inguinal canal does not infarct the testicle.

The left gonadal vein drains into the left renal vein at a perpendicular angle and is approximately 8 to 10 cm longer than the right gonadal vein. In contrast, the right gonadal vein drains into the inferior vena cava at an oblique angle.¹⁸ The perpendicular insertion of the left gonadal vein into the renal vein exposes the left gonadal vein to increased pressure changes in the left renal vein. A common cause of increased left renal vein is nutcracker syndrome where the renal vein is compressed between the aorta and superior mesenteric artery.¹⁹ The right gonadal vein is protected from pressure changes in the inferior vena cava by its oblique insertion.²⁰ These anatomic differences result in higher hydrostatic pressures within the left gonadal vein and predispose it to varicocele formation.²¹

Evaluation and Diagnostic Imaging

Examination of a patient for varicocele should be performed in a warm room with the patient both supine and standing. Having the patient perform a Valsalva maneuver while standing increases venous pressure and subsequently varicocele size with the typical “bag of worms” finding. Additional pathologies that should be considered include

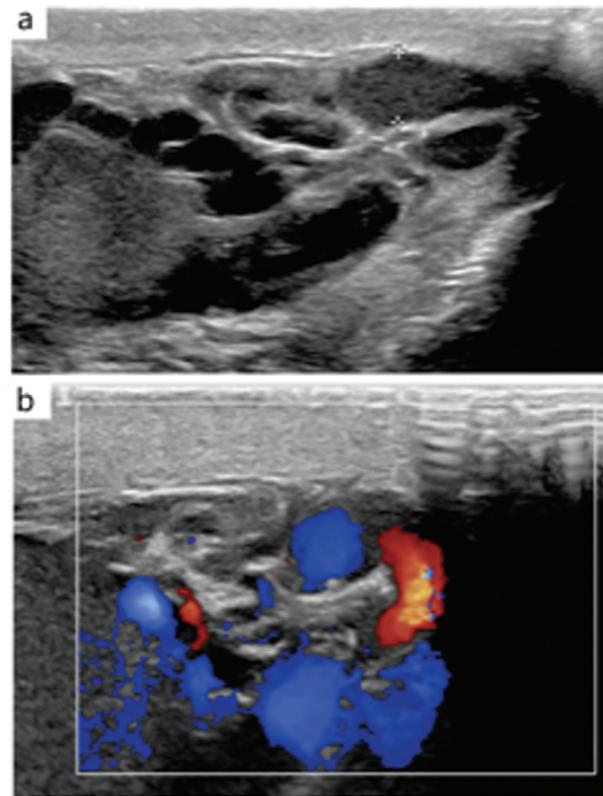


Fig. 1 A 21-year-old male being evaluated for left varicocele. (a) Multiple serpiginous hypoechoic and anechoic vessels measuring up to 6 mm in diameter (calipers). (b) Color Doppler ultrasound demonstrating patent flow through the anechoic vessels.

hydrocele, epididymal cysts, spermatocele, testicular cancer, and chronic epididymitis. Diagnostic imaging is useful for differentiating varicocele from these conditions. On physical exam, it is reassuring if the palpable area reduces in size or resolves with the patient supine and increases in size with the Valsalva maneuver.¹⁸

High-resolution color flow Doppler ultrasound is the imaging modality of choice for the evaluation of varicocele when there is high clinical suspicion.^{17,22} Typical findings confirming the diagnosis include dilatation of the pampiniform plexus veins >3 mm in diameter with a characteristic serpiginous appearance (**► Fig. 1**). Additional findings include flow reversal with the Valsalva maneuver (**► Fig. 2**).²³ Thermal imaging and testicular strain elastography are also being evaluated for their use in varicocele diagnosis.^{24–26}

Guidelines on how to perform the sonographic examination and how to classify the sonographic findings have been published only recently by the Scrotal and Penile Imaging Working Group of the European Society of Urogenital Radiology (ESUR-SPIWG).^{17,27} Bilateral color, gray-scale, and spectral Doppler analysis should be performed with the patient both supine and standing, and both during spontaneous breathing and the Valsalva maneuver.²⁷

Surgical Interventions

Surgical intervention of varicocele involves obstructing the reflux of venous drainage to the testes. Varicocelectomy is

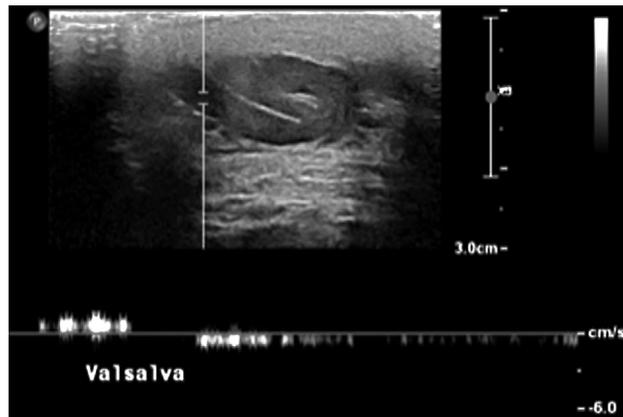


Fig. 2 A 21-year-old male being evaluated for a left varicocele. Spectral Doppler waveform of the varicocele demonstrates reversal of flow with Valsalva.

the most performed surgical intervention for varicocele, with multiple approaches described in the literature. Varicocelectomy can be performed laparoscopically, open retroperitoneally, or open macroscopically or microscopically. An open macroscopic or microscopic surgical approach can be done at the inguinal or subinguinal level.¹⁰ While the surgical approach may vary, the overarching goal is to ligate the internal and external spermatic veins with sutures or surgical clips to deviate testicular venous return to the internal pudendal system, which usually contains competent valves while avoiding injury to the testicular artery and other vital structures.²⁸

There is controversy in the literature as to which surgical approach is best. As with most surgical interventions, the correct approach usually involves a combination of surgeon comfort, patient goals, and safety. The open microsurgical approach has the strongest evidence for the lowest recurrence rates, fewer complications, and highest improvement in pregnancy rates and sperm parameters when compared to laparoscopic or retroperitoneal approaches.^{29–34} Historically, a laparoscopic approach has led to higher rates of vasal injury, genitofemoral nerve injury, and injury to visceral organs; however, recent studies suggest that laparoscopic surgery is comparable to microscopic approaches.³⁵ In addition, a laparoscopic approach has the benefit of ease of treating bilateral varicocele. In a meta-analysis comparing recurrence rates of various techniques, the retroperitoneal high ligation approach was found to have the highest rate of varicocele recurrence at nearly 15%, compared to 4.3% laparoscopically and 1.05% microsurgically, finding a significant difference between techniques.³⁶ Although there is a lack of randomized, prospective clinical trials with strong enough evidence to suggest the best surgical intervention for varicocele treatment, the open microsurgical approach has the most evidence behind its efficacy and safety.

Retrograde Embolization

Percutaneous retrograde varicocele embolization is an outpatient procedure performed under moderate sedation with

patients in the supine position. The procedure has three main components which include venous access, renal and subsequent gonadal venography and catheterization, and embolization.

Multiple venous access sites can be utilized for retrograde treatment, including femoral, internal jugular, or antecubital venous approaches. The right internal jugular vein allows the most direct approach to both the right and left gonadal veins and is the preferred approach at the authors' institution. Once venous access is obtained, a 7-Fr sheath is placed to coaxially introduce a 4- or 5-Fr hydrophilic catheter. A microcatheter system may be required for navigating tortuous vessels. If the femoral approach is used, a C1 or C2 catheter (Cook Medical, Bloomington, IN) can be used for accessing the left renal vein. From this approach, a reverse curve catheter is useful for accessing the right gonadal vein. A benefit of the internal jugular approach is that the same catheter can be used for accessing both the left and right gonadal veins.

When treating the left gonadal vein, once the left renal vein has been catheterized, having the patient perform a Valsalva maneuver while gently injecting contrast is helpful to ensure the catheter is seating in the gonadal vein ostium (→ Fig. 3). If the patient is unable to perform a Valsalva maneuver, they can be placed in reverse Trendelenburg for a similar effect. If the



Fig. 3 Sclerotherapy and coil embolization of a left gonadal vein varicocele. (a) Selective digital subtraction venogram of the left renal vein accessed with a C2 catheter with opacification of the left gonadal vein. (b) Left gonadal venogram demonstrating reflux of contrast inferiorly to the pelvis with poor visualization of the more distal varicocele outflow veins. (c) Venography after distal coil embolization of the dominant gonadal vein demonstrates improved visualization of varicocele outflow veins. (d) Completion of left gonadal venogram after sclerotherapy with sodium tetradecyl sulfate slurry and proximal stepwise coil embolization to the proximal left gonadal vein.

gonadal vein has incompetent valves, the contrast will move in a retrograde fashion opacifying the gonadal vein and collaterals. It is important to identify possible capsular, hilar, or colic collaterals that may affect treatment efficacy.

There are multiple methods of embolization that can be used including mechanical embolization (plugs, metallic coils), liquid embolic agents, sclerosants, as well as different combinations of the three. There is no preferred standardized approach and there is similar efficacy between the different techniques.³⁷ Liquid embolic agents with metallic coils have become the most commonly used in practice.

When using metallic coils, it is important to have accurate measurements of the spermatic vessel from venography for appropriate sizing, deploying coils approximately 20% larger than the vessel diameter to avoid migration. In general, two to three coils are required to achieve vessel occlusion. The initial coil should be placed distally near the level of the inguinal ring: 0.035- and 0.038-inch coils are compatible with 4- or 5-Fr hydrophilic catheters. For smaller vessels, 0.025- and 0.018-inch coils are available that can be placed through microcatheter systems. Post coil venography is necessary to evaluate venous flow with either sluggish flow or complete occlusion expected (► **Fig. 3**). The increased venous pressure may also reveal new small collateral vessels that will limit treatment efficacy. If these vessels are large enough, they can be directly accessed with a catheter and occluded with additional coils. For smaller vessels, a sclerosing agent or glue may be required. The final coil should be placed near the gonadal vein ostium while taking care not to involve the renal vein. If the coil pulls back into the renal vein, it can migrate into the systemic venous circulation and eventually into the pulmonary artery. A plug can also be used in the proximal gonadal vein, although use is limited by cost.

Sodium tetradecyl sulfate (STS) sclerosant in either foam or liquid form can be used alone or in addition to coils. For STS foam, a 2:1 mixture of 3% STS to sterile saline is aggressively mixed with an equal volume of air to create a foam. This foam mixture is injected into the catheter until contrast is displaced followed by an immediate 1 mL sterile saline flush to prevent catheter clogging. While injecting STS, it is helpful to have the patient hold Valsalva ideally for 1 to 2 minutes. It is important to avoid embolizing the scrotum itself. This can be accomplished with a distal coil or by having an assistant hold pressure to occlude the vein at the inguinal ring. After injection, the catheter should be pulled back to the mid/upper gonadal vein where a repeat venogram is performed to assess flow and evaluate for new collaterals. STS should be injected while the patient holds Valsalva to the iliac crest if a proximal coil is used or 1 to 2 cm distal the gonadal vein ostium if not. Care must be taken not to reflux sclerosant into the renal vein where it can spread into the systemic circulation and eventually the pulmonary vessels. In addition to foam, STS liquid made by mixing 2 mL 3% STS with 1 mL contrast can be used. This is placed similar to STS foam with a volume of 2.5 to 5 mL generally being adequate.

Glue can also be used and has been shown to have equal efficacy to coils and sclerosing agents.³⁷ It is made by mixing cyanoacrylate and lipiodol in ratios between 1:1 and 1:6. When using glue, it is important to inject D5W dextrose

solution into the catheter initially and to flush the catheter with D5W immediately after injection to avoid catheter clogging. With glue, the ideal vessel territory to cover is similar to other embolic methods and extends from just distal to the inguinal ring to 1 to 2 cm from the gonadal vein ostium proximally and covering collateral vessels over this territory. With glue, it is important to be purposeful with injections to avoid off-target embolization either distally affecting the scrotum or proximally with glue migrating into the renal vein and IVC. Some proceduralists will place a distal coil to avoid off-target embolization, otherwise manual compression is necessary. There are two methods to inject glue. The less technically difficult method involves starting with the catheter inserted distally and pulling back while slowly injecting. However, this is not always possible if the catheter cannot be maneuvered distally. The second method of glue injection involves refluxing glue from a more proximal position while the patient holds Valsalva.

Minor complications include postprocedure back pain and testicular swelling, which is reported in approximately 10% of patients.³⁸ This is likely secondary to thrombophlebitis of the pampiniform plexus and responds well to conservative therapy with nonsteroidal anti-inflammatory medications. More severe complications include coil migration to the heart and pulmonary vessels, vessel perforation, and off-target embolization resulting in testicular venous infarcts.³⁹

Antegrade Scrotal Sclerotherapy

An alternative to radiological embolization is antegrade scrotal sclerotherapy, a technique first presented by Tauber and Johnsen in 1994, with technical improvements and alternatives presented by Iaccarino and Venetucci, Ficarra et al, and Crestani et al.^{14,40–42} As opposed to retrograde sclerotherapy, this approach is feasible in almost all patients, given the lower risk of complications. However, an alternative treatment might be preferred when the patient has undergone previous scrotal operations, as the procedure becomes more challenging.⁴³

This procedure is performed with the patient supine in a slight reverse Trendelenburg position, while the scrotum is elevated, and the area of the incision shaved. Patients should be invited to close their thighs to allow for the scrotum to be in a more accessible superficial position.⁴¹ The area of the incision is shaved, and the operative field is disinfected and prepared. Before administering local anesthesia, palpate the vas deferens to separate it from other spermatic cord structures at the scrotal root level, reducing vagal stimulation during spermatic cord traction.⁴²

When the patient is well-positioned, and the sterile field is ready, local anesthesia is administered, avoiding deep infiltration of the spermatic cord, which could lead to edema and bleeding. Once the area is anesthetized, a 2-cm vertical incision is created at the scrotal root level. After the incision, the spermatic cord is exposed and suspended. The vaginal fascia of the spermatic cord is opened exposing dark yellow fat tissue that covers the anterior portion of the pampiniform plexus. A (preferably large and straight) vein of the anterior

pampiniform plexus is dissected, distally ligated, and cannulated in an antegrade fashion toward the internal spermatic vein with a 24- or 25-gauge venous catheter. The spermatic cord is ligated to prevent the reflux of sclerosant agent or contrast medium into the vein, and, consequently, potential unintended testicular damage.

It is helpful to have a venous catheter with a two-way Y-adapter in the proximal portion, a 7-cm-long flexible and transparent intermediate portion, and a butterfly thin-walled cannula in the 4-cm-long distal portion. The intermediate flexible portion allows the assistant surgeon to maneuver the catheter without interfering with the movements of the primary surgeon. One port is used to infuse contrast medium or a sclerosant agent, while the other is used to remove the fine mandrel. The needle is then inserted a few millimeters into the vein, then the mandrel is immediately removed, and the soft segment of the catheter is advanced into the lumen of the vein. The needle is then tied to the vein to prevent leakage and fastened to the skin to prevent unintended removal.

Before the delivery of the sclerosant agent, antegrade phlebography should be performed. Three to 5 mL of contrast medium is injected to verify the correct positioning of the cannula into the pampiniform plexus by fluoroscopy. The flow of the contrast medium allows the tracing of the spermatic vein toward the renal vein on the right and toward the inferior vena cava on the left. The patient should be invited to perform a Valsalva maneuver, as this facilitates the visualization of the involved structures.

If the internal spermatic veins are not visualized through phlebography, the procedure should be immediately halted to avoid potential complications.⁴⁴ Paravascular application of the sclerosant must be treated immediately with abundant and meticulous lavage with normal saline. If an arterial branch is incised, the vessel should be immediately ligated; it should not be sclerosed as the latter affects all branches.⁴³

The sclerosant agent is then injected in 4 to 5 seconds while the patient performs a Valsalva maneuver using the air-block technique, in which 1 mL of air is introduced followed by 4 mL of the sclerosant agent. By slowing down the flow of the sclerosant agent into the veins, the air-block technique reduces the risk of passage of the sclerosant agent into the renal vein and increases the time of contact with the endothelium of the spermatic veins. Only one injection of the sclerosant agent is administered.

Radiological monitoring is not needed during the injection of the sclerosant agent, but the spermatic cord should remain clamped for 5 minutes after the sclerosing phase of the procedure. After that, the cannula is removed and the vein is ligated both below and above the point of injection. Finally, hemostasis is checked and the wound is sutured in two layers, spermatic cord fascia and skin.

Postprocedural Follow-up for Radiological Interventions

The patient is reassessed 2 hours after the procedure and discharged home if no complications are suspected. During

the first week, patients should refrain from sexual intercourse and intense physical activity, and perform daily wound care. During postoperative week 2, the patient should still refrain from intense physical activity. Bed rest is unnecessary.

Follow-up appointments are scheduled: at 1 week, to assess for recovery and complications; at 3 months, to assess for the persistence of varicocele with Doppler ultrasound; and at 6 months, to perform a semen analysis.

Outcomes

Radiological embolization is an overall safe and effective procedure that is technically successful in nearly 95% of cases.^{45,46} In patients treated for pain, treatment with embolization is estimated to resolve more than 90% of cases; whereas, in patients treated because of mass effect or aesthetic concerns, the success rate varies between 76 and 98% in the literature.^{5,16,47} The success rates following surgical and radiological treatments of varicocele are comparable. Despite similar efficacy, radiological approaches are preferred after failed surgical intervention, as it prevents repeated surgery at the same site and allows the physician to better visualize and evaluate the relevant anatomy.⁴⁸ Radiological treatment of varicocele resolved or improved symptoms in nearly 90% of patients who have recurrent varicocele after varicocelectomy.⁴⁸

It is noteworthy that outcomes and efficacy of varicocele treatment may differ based on what is being evaluated. After reviewing systematic reviews and meta-analyses published between 2020 and 2022, it is shown that varicocele treatment improves DNA integrity and total motile sperm count.⁴⁹⁻⁵¹ However, there are mixed results regarding chances of pregnancy and live births.⁵²⁻⁵⁴ A systematic review published in 2021 in the Cochrane Library by Persad et al concluded that varicocele treatment improves the chances of pregnancy, but it is uncertain about whether or not it improves live birth rates.⁵² By contrast, another systematic review and meta-analysis published in 2020 by Birowo et al found that varicocele repair increases the chances of pregnancy and live birth rates, along with sperm retrieval success in azoospermic men.⁵³ In sum, although there is still a need for more prospective randomized controlled trials to strengthen the evidence of the efficacy in the treatment of varicocele to increase fertility, recent meta-analyses and systematic reviews have confirmed the benefits and efficacy of varicocele repair to improve male fertility.⁴⁹⁻⁵⁶

Radiological versus Surgical Interventions

Both radiological and surgical treatments of varicoceles benefit patients by improving symptoms, spermatic parameters, and the chance of pregnancy. Presently, there are no studies that directly compare surgical and radiologic outcomes in a prospective, randomized control study. Single or bi-institutional retrospective studies have shown no difference in success rates, complications, sperm quality,

pregnancy rate, or overall satisfaction rates between surgical ligation and percutaneous embolization.^{57–60} A review in 2012 comparing various surgical and radiologic techniques found antegrade sclerotherapy and a subinguinal approach to have the most efficacy when looking at outcomes, complication rate, and cost-effectiveness.¹⁴ Most recent systematic reviews published between 2021 and 2022 reveal that radiologic and surgical treatments for varicocele show low certainty evidence of similar rates in recurrence and pregnancy outcomes, with radiologic treatment showing lower complication rates compared to surgical treatment.^{52,61} Current evidence suggests that radiological treatment of varicocele offers a lower risk of varicocele recurrence and hydrocele formation; yet, given the paucity of head-to-head comparative randomized controlled trials, the choice of treatment for varicoceles should remain under the discretion of the surgeon, based on a combination of surgeons' comfort and patient goals.

When considering which approach would be best for the patient, several factors may influence procedural selection. Radiologic approaches offer the advantage of forgoing general anesthesia and the other invasive placements necessary for surgery. Although a surgical microscopic approach can be done without general anesthesia, it may not be the correct approach if avoiding general anesthesia for a patient is necessary. In addition, radiological interventions have the advantage of faster recovery time and less postoperative pain when compared to surgical intervention, which may be important for patients who are poor surgical candidates and have a higher chance of suffering morbidity postoperatively.^{45,59} Radiological approaches may also be advantageous if a patient had previous surgical interventions in the operative area, to avoid possible alterations in anatomy from a prior operation, or due to body habitus. In a patient with recurrent varicocele, a radiologic approach can be an asset to better visualize and assess testicular vein anatomy, along with possible collateral pathways.⁴⁸ Surgical techniques should be considered for patients who wish to avoid radiation exposure, and a radiologic approach is contraindicated in those with allergies to contrast. While there is a lack of a golden standard in the intervention of varicocele, patient history and preference play a large role in the choice of interventional technique.

Conclusion

Procedural intervention for symptomatic testicular varicocele has been shown to improve pain and spermatic parameters, and increases the chance of pregnancy. Current evidence suggests that radiologic treatment offers a lower risk of complications and a quicker postoperative recovery compared to surgical intervention. Overall success rates, spermatic parameters, and pregnancy rates between radiologic and surgical techniques are comparable. Radiologic and surgical techniques are both efficacious and safe; thus treatment course should be determined by the physician to best fit their patient's needs.

Authors' Contributions

All authors contributed to the study's conception and design. All authors read and approved the final manuscript.

Ethics Approval

This review was deemed IRB exempt.

Conflicts of Interest

P.J.R. is a speaker for Penumbra, Inc. and advisory board for Medtronic. All other authors have no financial or nonfinancial interests to disclose. The authors also declare that no funds, grants, or other support were received during the preparation of this manuscript.

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