

Endovascular Treatment of Male Varicocele

An overview of recent evidence-based literature.

BY GLORIA M. SALAZAR, MD, AND T. GREGORY WALKER, MD

Varicocele is defined as the dilatation of the veins of the pampiniform plexus. It is a well-known clinical entity that may result in mass-effect, pain, testicular atrophy, and infertility. It is estimated to be present in 40% of males with fertility issues¹ and in up to 16% of male adolescents.² The pathophysiology of varicocele is related to venous insufficiency and reflux involving the veins that drain the testis. The left internal spermatic vein (ISV) is involved more often than the right, and a bilateral presentation is seen in up to 10% of clinical varicoceles.³ Although varicocele may be first noticed as a palpable abnormality, the more important pathology associated with varicocele is that it is a known etiology for abnormal spermatogenic parameters leading to infertility. Fortunately, there are numerous treatment options, including endovascular, open, and laparoscopic surgical approaches.

ANATOMY AND PHYSIOPATHOLOGY

The veins of the pampiniform plexus that drain the testis and the epididymis into the internal spermatic vein are usually very small in diameter (up to 2 mm) and are therefore typically difficult to visualize by ultrasound.⁴ Varicoceles usually result from venous reflux in the ISV, which may be caused by the congenital absence of valves and/or the presence of variant collateral veins entering the ISV and bypassing competent valves. This abnormal venous anatomy eventually results in venous hypertension, with enlarged and distended veins seen along the course of the spermatic cord and epididymis.



Figure 1. Venography of the left ISV via transfemoral approach demonstrating varicocele. Selective catheterization of the left ISV demonstrating a type 1 Bährén varicocele (A). Distal venography of the ISV with dilated plexus pampiniform plexus (B).

Other causes of internal spermatic vein dilatation and/or elevated venous pressure include extrinsic venous compression by lymphadenopathy or other masses and certain anatomic circumstances such as the Nutcracker syndrome in which the left renal vein is compressed between the aorta and the superior mesenteric artery. Anatomic differences between the drainage of the left and right internal spermatic veins predispose to a higher incidence of left-sided varicoceles, because the left ISV drains into the left renal vein, while the right

drains directly into the inferior vena cava. It has been hypothesized that the hyperemia induced by a varicocele produces a persistent increase in testicular temperature, and that this is the reason for impaired fertility and testicular atrophy. The decrease in testicular temperature that has been observed in patients after varicocele treatment further suggests that hyperthermia caused by venous reflux into the pampiniform plexus may contribute to the pathology that is associated with varicocele.⁵ However, there is still controversy regarding the exact clinical effects of a varicocele. Some investigators have suggested that testicular hypoxia, rather than hyperemia, is the main mechanism leading to male infertility and have noted restoration of spermatogenesis after varicocele treatment.⁶ Elevated hydrostatic pressure causing a reversed pressure gradient between the venular and arteriolar systems in the testicle would result in hypoxia at the level of the seminiferous tubules.⁷ Therefore, by eliminating the persistently elevated venous pressure in the testis, ligation and/or embolotherapy are able to reverse abnormal semen parameters (low sperm counts, decreased motility, and abnormal sperm morphology). This has been demonstrated in previous investigational studies.^{6,8,9} However, some investigators have challenged the impact of this improvement in semen parameters upon fertility and achieving successful pregnancy.¹⁰

CLINICAL FINDINGS AND INDICATIONS FOR TREATMENT

The diagnosis of varicocele is made in the majority of patients during a clinical evaluation in which the physical examination demonstrates a palpable testicular cord. These physical findings can be categorized as follows: grade I (palpable only during Valsalva maneuver), grade II (palpable in standing position), and grade III (visible through the scrotal skin).¹¹ Adult patients may present with infertility, testicular atrophy, and scrotal pain, while others may be asymptomatic. In adolescents, asymmetry in testicular size has been used as a criterion for intervention.¹² However, normalization of testicular volumes can occur over time, and therefore, treatment is typically indicated only in cases in which

there is persistent or worsening testicular asymmetry present on an ultrasound examination at 1-year follow-up after diagnosis.¹³ Noninvasive imaging techniques may be used to supplement the abnormal physical examination findings in a patient in whom a varicocele is suspected in order to confirm the diagnosis or if there is a suspicion of malignancy. These imaging modalities include Doppler ultrasound, computed tomography, and magnetic resonance imaging. Doppler ultrasound typically demonstrates numerous dilated veins as well as increased color Doppler flow when reflux is elicited by the Valsalva maneuver. Computed tomography and magnetic resonance imaging are less frequently used for varicocele evaluation unless a malignant condition is suspected. For example, an isolated right-sided varicocele may be more worrisome for malignancy than if present on the left and may be further evaluated with cross-sectional imaging.

Invasive diagnostic imaging is performed for varicocele evaluation only when there is a clinical indication for treatment. Internal spermatic venography should be performed, with initial retrograde selective catheterization of the left renal vein from either a jugular, femoral,

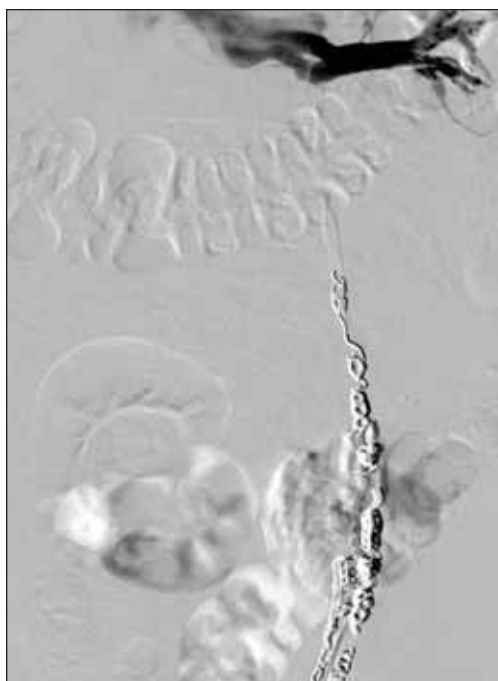


Figure 2. Postembolization venography via jugular approach in a left-sided varicocele demonstrating occlusion of the ISV.



Figure 3. Retrograde venography of left-sided ISV with microcatheter positioned at the parallel duplicated channel demonstrating distal collateral branches and venous duplication. Previous coil embolization of the lateral duplicated ISV is seen.

TABLE 1. CLASSIFICATION OF LEFT-SIDED VARICOCELES^a

Type 0	No evidence of venous reflux in ISV
Type 1	Single ISV with insufficient or absent valve
Type 2 Single ISV with communication to IVC/accessory gonadal/ ascending lumbar/iliac veins	A: Insufficient confluence valve function B: Sufficient confluence valve function
Type 3	Single incompetent ISV at renal vein junction, with caudal duplication
Type 4 Collaterals between ISV and segmental renal/retroperitoneal veins	A: Insufficient confluence valve function B: Sufficient confluence valve function
Type 5	Inferior vena cava or renal vein anomaly, ISV may drain into inferior vena cava, renal, and ascending lumbar veins
Abbreviation: IVC, inferior vena cava. ^a Adapted from Bühren W et al. <i>Rofo</i> . 1983;138:172–179 ¹⁴ and from Sigmund G et al. <i>Radiology</i> . 1987;164:161–168. ¹⁵	

or upper extremity transvenous approach. Contrast should be injected and images obtained with the patient performing a Valsalva maneuver and breath hold. Following left renal venography, the internal spermatic vein may be selectively catheterized and imaged with a retrograde contrast injection. Gonadal shielding and avoidance of direct gonadal radiation should be routine components of internal spermatic venography. If available, the examination may be performed on a tilted fluoroscopic table in the Trendelenburg position (Figure 1). The venographic findings may then be categorized according to either of two different currently accepted classification systems that have been described.

Bühren and colleagues¹⁴ described the anatomical findings of left-sided varicoceles based on valvular incompetence of the ISV, the presence of collateral venous channels, and anatomic variant anatomy (Table 1). This classification was subsequently used for sclerotherapy of left-sided varicoceles with the addition of subtypes demonstrating competent ISV orifice valves associated with insufficient venous collaterals bypassing the origin of the ISV.¹⁵ Duplicated gonadal (ISV) veins can also occur lower in the inguinal canal region. Murray and colleagues described this in a system, based on the location of varicocele, as renal, scrotal, and parallel duplications of the ISV. Duplications of the ISV are then subdivided into three levels: high (above the iliac crest), middle (between the iliac crest and pubic ramus), and low (below the inguinal canal).¹⁶ Although there is no evidence of any apparent correlation between the angiographic appearance of a varicocele and the clinical outcome after embolization treatment, pretreatment

classification of a varicocele may be useful for procedural planning, in order to determine the best means of eliminating retrograde flow in the ISV. Moreover, venographic evaluation demonstrates the presence of collateral pathways or abnormal venous anatomy, which if unrecognized may lead to failure of either endovascular or surgical varicocele treatment.¹⁷

OVERVIEW OF ENDOVASCULAR TECHNIQUES

Since the first reports of endovascular embolization to eliminate retrograde flow within the ISV, several techniques have been developed. Currently, there is no universally accepted regimen for the transcatheter endovascular treatment of a varicocele. There have been refinements to embolization techniques in recent years, including the use of microcatheters and the availability and use of various embolic materials. Several embolic agents have been used for transcatheter embolization, including hot contrast medium, isobutyl-2-cyanoacrylate (glue), coils, detachable balloons, and sclerosant agents.^{3,9,17-20} The choice of embolic material may reflect operator preference, product availability in the market, cost, ISV anatomy, and safety of use. For example, liquid/sclerosant agents may distribute better than solid embolic agents (eg, coils) in the presence of venous collaterals; they can also be used alone or in combination with solid agents. Given the heterogeneity of materials employed for varicocele embolization, there are no studies to date that demonstrate the superiority of any one particular embolic agent. Furthermore, despite the use of different embolic agents, technical success ranges from 95% to 100% in series published in the past 10 years.^{3,9,17-19} Lower rates of success are mostly due to

failure to catheterize the ISV. Additionally, there are several described embolotherapy techniques, with recent modifications tailored for the pediatric population, allowing for preservation of the more proximal levels of the ISV at the vessel origin. This may be important in the event of a recurrent varicocele that might require future intervention.¹⁸ Despite technical procedural differences, there is consensus regarding the optimal embolization endpoint: complete obliteration of the ISV and venous collateral channels, starting above the pubic symphysis or at the sacroiliac joint levels, until reflux is no longer seen in the ISV (Figure 2).^{3,9,17-19}

Standardization of the embolotherapy technique is evolving, particularly in the setting of duplicated gonadal veins and the presence of venous collaterals.¹⁷ High technical success rates and good clinical outcomes with retrograde sclerotherapy are well established in the literature. More recently, an antegrade approach for sclerotherapy by means of direct puncture of the plexus vein has been described in the urology literature. With antegrade sclerotherapy (Tauber procedure), a 2-cm longitudinal incision is made at the base of the scrotum in order to expose the funiculum. Subsequently, the most enlarged vein is punctured, and sclerosant material is infused under fluoroscopic guidance while a Valsalva maneuver is performed.²¹ This technique has been compared to the open surgical approach and has similar outcomes and complication rates.

IMPACT OF COLLATERAL VENOUS SUPPLY IN THE VARICOCELE TREATMENT

The venous drainage of the testis is via both superficial and deep venous systems. These two systems communicate at the level of the cremasteric branches. Anatomical variations at this level may result in collateral venous drainage of a varicocele in the presence of a normal ISV with competent valves.²² Therefore, diagnosing the presence or absence of any abnormal venous drainage of a varicocele has an important implication on treatment outcomes. The incidence of venous collaterals in the presence of a varicocele, as noted during retrograde venography for treatment, was described to be 19% on the left and 17% on the right side.²² Undiagnosed collateral veins are associated with treatment failures and persistent or recurrent varicoceles.^{15,17,23} Moreover, there is an increased risk of technical inability to selectively catheterize the ISV in this setting due to the presence of competent orificial valves in the ISV.¹⁵

Various investigators have suggested technical refinements in the evaluation and treatment of varicoceles in order to address the issues related to the presence of collateral venous channels and their potential impact

upon both endovascular and surgical treatment outcomes. Collateral veins have been reported in 19% of patients undergoing laparoscopic varicocele treatment; this study further demonstrated that recognition and subsequent ligation of these vessels resulted in a very low 1% recurrence rate.²² Other investigators have recommended that the venographic evaluation of a varicocele include renal venography, with opacification of intrarenal branches in order to identify any abnormal collateral pathways or anatomical variants.²³ The venogram should further delineate the entire ISV so as to identify any duplication, other collateral channels, or connecting branches (Figure 3).

One study of the endovascular treatment of recurrent postsurgical varicoceles demonstrated a high incidence of duplicated gonadal veins in the pelvic or inguinal region, leading to incomplete surgical varicocele resection/ligation.¹⁷ In initial publications, in which retrograde sclerotherapy was used for treatment of left-sided varicoceles, recurrence rates of up to 9.8% were noted.¹⁵ In more recent series, however, recurrence rates range between 1.6% and 10%.^{3,19} The technical success rate of coil embolization in abnormally drained varicoceles is 73% on the left and 57% on the right. These success rates are lower than in varicoceles with normal anatomical venous drainage patterns (97%).²³ These results likely reflect either additional venous collaterals that were unrecognized and untreated at the time of the procedure, or collaterals that were incompletely treated by coil embolization. Success rates ranging from 80% to 85% have been described with the use of sclerosant agents, likely as a result of the ready distribution of the agent into the collateral channels.^{3,15} However, the major drawback of sclerotherapy is the potential for uncontrolled sclerosant distribution into various pelvic, renal, or lumbar venous collaterals. If extensive collaterals such as these are demonstrated, embolization with a sclerosant should probably not be performed. In order to address this issue, a modified technique combining coil embolization with sclerotherapy using sodium tetradecyl sulfate has been described to obtain retrograde filling of parallel and collateral vessels. This has achieved a technical success rate of 94% in the treatment of adolescent varicoceles.¹⁸

COMPLICATIONS

Transcatheter venous embolization using a retrograde approach is a relatively safe procedure for varicocele treatment. Procedural complications include nontarget embolization, vessel perforation, vasospasm, flank or scrotal pain, phlebitis, and localized numbness. Vein perforation may result from manipulation of guidewires

and catheters through the vein valve, particularly in the presence of competent valves and is typically self-limited.³ Nontarget embolization can be minimized by using occlusion balloon catheters during sclerotherapy. Pampiniform plexus phlebitis occurs in up to 5% of patients and is caused by passage of sclerosant material into the peritesticular venous structures. This complication may be avoided by external compression of the inguinal canal during embolization. If phlebitis occurs, treatment includes antibiotics and nonsteroidal anti-inflammatory drugs. Postembolization recurrence of varicoceles is reported to range from 1.6% to 10% in more recent series.^{3,9,19}

COMPARATIVE STUDIES WITH THE SURGICAL APPROACH

To date, there are no randomized trials in the literature comparing endovascular and surgical techniques for the treatment of varicocele. However, retrospective comparative data from 1997 demonstrated that both approaches resulted in similar rates of improvement in semen parameters and successful pregnancy outcomes in infertile men.²⁴ The major advantage of transcatheter versus surgical treatment is the absence of postprocedural complications such as hydrocele and arterial injury.^{25,26}

CONCLUSION

Endovascular transcatheter embolization techniques may be used as a minimally invasive, safe, and effective alternative for treatment of varicocele in the adolescent and adult population; however, to date, there are no randomized comparative studies with surgical techniques. ■

The authors thank Drs. Suhny Abbbara, John H. Brannen, and Florian J. Fintelmann for their assistance with this article.

Gloria M. Salazar, MD, is an assistant radiologist and instructor in radiology in the Division of Vascular Imaging & Intervention at the Massachusetts General Hospital, Harvard Medical School in Boston, Massachusetts. She has disclosed that she holds no financial interest in any product or manufacturer mentioned herein. Dr. Salazar may be reached at (617) 726-8314; gmsalazar@partners.org.

T. Gregory Walker, MD, is an associate radiologist and the Associate Director of the Fellowship in the Division of Vascular Imaging & Intervention at the Massachusetts General Hospital, and an instructor in radiology, Harvard Medical School in Boston, Massachusetts. He has disclosed that he is a paid consultant to Medtronic Endovascular,

Inc., but holds no financial interest in any product or manufacturer mentioned herein. Dr. Walker may be reached at (617) 726-8314; tgwalker@partners.org.

- Amelar RD, Dubin L. Therapeutic implications of left, right, and bilateral varicocelectomy. *Urology*. 1987;30:53-59.
- Skoog S, Roberts K, Goldstein M, Pryor J. The adolescent varicocele: what's new with an old problem in young patients? *Pediatrics*. 1997;100:112.
- Wunsch R, Efinger K. The interventional therapy of varicocele amongst children, adolescents and young men. *Eur J Radiol*. 2005;53:46-56.
- Zwiebel WJ, Benson CB, Doubilet PM. Duplex ultrasound of the male genitalia. In: Zwiebel WJ and Pellerito, eds. *Introduction to Vascular Ultrasonography*. 5th edition. Philadelphia, PA: Elsevier Saunders; 2005. Page 668.
- Wright EJ, Young GP, Goldstein M. Reduction in testicular temperature after varicocelectomy in infertile men. *Urology*. 1997;50:257-259.
- Gat Y, Gornish M, Chakraborty J, et al. Azoospermia and maturation arrest: malfunction of valves in erect poster of humans leads to hypoxia in sperm production site. *Andrologia*. 2010;42:389-394.
- Gat Y, Gornish M, Chakraborty J, et al. Right varicocele and hypoxia, crucial factor in male infertility: fluid mechanics analysis of the impaired testicular venous drainage system. *Reprod Biomed Online*. 2006 Oct;13:510-515.
- Galfano A, Novara G, Iafrate M, et al. Improvement of seminal parameters and pregnancy rates after antegrade sclerotherapy of internal spermatic veins. *Fertil Steril*. 2009;91:1085-1089.
- Flacke S, Schuster M, Kovacs A, et al. Embolization of varicoceles: pretreatment sperm motility predicts later pregnancy in partners of infertile men. *Radiology*. 2008;248:540-549.
- Evers JH, Collins J, Clarke J. Surgery or embolisation for varicoceles in subfertile men. *Cochrane Database Syst Rev*. 2008 Jul 16;(3):CD000479. Review. Update in: *Cochrane Database Syst Rev*. 2009;(1):CD000479. PubMed PMID: 18646066.
- Dubin L, Amelar RD. Varicocele size and results of varicocelectomy in selected subfertile men with varicocele. *Fertil Steril*. 1970;21:606-609.
- Decastro GJ, Shabsigh A, Poon SA, et al. Adolescent varicocelectomy—is the potential for catch-up growth related to age and/or Tanner stage? *J Urol*. 2009;181:322-327.
- Spinelli C, Di Giacomo M, Lo Piccolo, et al. The role of testicular volume in adolescents with varicocele: the better way and time of surgical treatment. *J Urol*. 2010;184:1722-1726.
- Bähren W, Lenz M, Porst H, et al. Side-effects, complications and contraindications of percutaneous sclerotherapy of the internal spermatic vein for the treatment of idiopathic varicoceles. *Fortschr Röntgenstr (Rofo)*. 1983;138:172-179.
- Sigmund G, Bähren W, Gall H, et al. Idiopathic varicoceles: feasibility of percutaneous sclerotherapy. *Radiology*. 1987;164:161-168.
- Murray RR Jr, Mitchell SE, Kadir S, et al. Comparison of recurrent varicocele anatomy following surgery and percutaneous balloon occlusion. *J Urol*. 1986;135:286-288.
- Sze DY, Kao JS, Frisoli JK, et al. Persistent and recurrent postsurgical varicoceles: venographic anatomy and treatment with N-butyl cyanoacrylate embolization. *J Vasc Interv Radiol*. 2008;19:539-545.
- Reiner E, Pollak JS, Henderson KJ et al. Initial experience with 3% sodium tetradecyl sulfate foam and fibered coils for management of adolescent varicocele. *J Vasc Interv Radiol*. 2008;19:207-210.
- Heye S, Maleus G, Wilms G. Pain experience during spermatic vein embolization for varicocele: comparison of two cyanoacrylate glues. *Eur Radiol*. 2006;16:132-136.
- Hunter DW, King NJ, Aeppli DM, et al. Spermatic vein occlusion with hot contrast material: angiographic results. *J Vasc Interv Radiol*. 1991;2:507-515.
- Zuchi A, Mearini L, Mearini E, et al. Treatment of varicocele: randomized prospective study on open surgery versus Tauber antegrade sclerotherapy. *J Androl*. 2005;26:328-332.
- Nyirady P, Kiss A, Píró L, et al. Evaluation of 100 laparoscopic varicocele operations with preservation of testicular artery and ligation of collateral vein in children and adolescents. *Eur Urol*. 2002;42:594-597.
- Marsman JWP. The aberrantly fed varicocele: frequency, venographic appearance, and results of transcatheter embolization. *AJR*. 1995;164:649-657.
- Shlansky-Goldberg RD, VanArsdalen KN, Rutter CM, et al. Embolization versus surgical ligation for the treatment of infertility: changes in seminal parameters and pregnancy outcomes. *J Vasc Interv Radiol*. 1997;8:759-767.
- Cuda SP, Musser JE, Belnap CM, Thibault GP. Incidence and clinical significance of arterial injury in varicocele repair. *BJU Int*. 2010. In press.
- Storm DW, Hogan MJ, Jayanthi VR. Initial experience with percutaneous selective embolization: a truly minimally invasive treatment of the adolescent varicocele with no risk of hydrocele formation. *J Pediatr Urol*. 2010;6:567-571.