Image-Guided Treatment of Varicoceles: A Brief Literature Review and Technical Note

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Varicoceles have been associated with orchialgia, subfertility, hypogonadism, and testicular hypotrophy. Testicular hypotrophy (particularly in adolescents), ipsilateral testicular pain, and male factor infertility with abnormal sperm analysis and clinical varicocele are indication to treat varicoceles patients. We have reviewed the literature on pathogenesis, patient selection, vascular anatomy, treatment techniques, and outcomes. Treatment options include surgical and image-guided approaches. Varicocele embolization is a safe and durable technique which provides pain relief and improved fertility in a well-chosen patient population. In our experience, a combination of coil embolization and sclerotherapy provides favorable clinical outcomes.

A varicocele is the abnormal dilatation of the pampiniform venous plexus which is typically caused by reflux or less commonly by obstruction. It is a common condition present in approximately 15% of the adolescent and adult male population, affecting 35% of men with primary infertility, and up to 80% of men with secondary infertility.¹ The incidence increases as the prepubertal male enters adulthood, from around 1% at 10 years of age to a plateau of nearly 14% in late adolescence.¹ Varicoceles are more frequent and larger on the left; however, some series have placed the percentage of bilateral varicoceles up to 50%.² A unilateral right-sided varicocele is rare (0.4%)^{3,4} and as such deserves clinical workup for underlying pathologic etiology. However, the most common cause of a right-sided varicocele is variant anatomy, with right spermatic vein entering the right renal vein similar to usual anatomy of the left side.^{1,5}

Presentations of varicocele include decreased testosterone levels, subfertility/infertility, testicular atrophy, and scrotal pain.⁶ The complex pathogenesis of varicocele-induced testicular dysfunction is incompletely understood, involving multiple factors such as altered blood flow, increased temperature, oxidative stress, and reflux of gonadotoxic metabolites leading to a progressive toxic effect that results in low testosterone levels and impaired spermatogenesis.⁶

Despite the association between varicoceles and testicular dysfunction, the cause and effect relationship between this condition and male infertility has not been established with 85% of males who have varicoceles remaining fertile. In cases of male factor infertility, varicocele remains the most common, correctable diagnosis. Varicocele repair is proven effective to improve sperm parameters and pregnancy rates.^{6,7} There is also a growing understanding of the relationship between varicocele and hypogonadism, demonstrated by beneficial molecular effects of varicocele repair on spermatogenesis and testicular microenvironment.⁵

Patient Selection/Indications

Indications for treatment of varicocele are an area of ongoing debate. Some indications have gained wide clinical acceptance, while others remain controversial. There is clear evidence that a patient with orchialgia and an associated ipsilateral varicocele will benefit from varicocele treatment including percutaneous embolotherapy. Treatment of varicoceles is indicated in cases of aesthetic concerns,³ infertility, testicular pain, and testicular volume loss in the pediatric population.^{8,9} In their recent review of literature, Halpern et al concluded that orchialgia is an indication for percutaneous embolization of the varicocele.⁹ Percutaneous embolization is a viable option for this group of patients, particularly given the inflammation and pain associated with surgery.¹⁰ A retrospective review of 154 patients demonstrated that 86.9% of patients were pain free at 39 months after percutaneous retrograde embolization.¹¹

Management considerations for couples with male infertility in the presence of varicocele include assisted reproductive techniques such as intrauterine insemination and in vitro fertilization/intracytoplasmic sperm injection along with varicocele treatment. Treatment of varicocele should be considered when the female partner has normal or correctable fertility status and sperm analysis reveals an abnormality.¹²

Varicocele repair carries the potential benefit of correcting the underlying pathology of infertility in a cost-effective way for well-selected patients.^{13,14} Other factors that should be considered in deciding whether to offer varicocele treatment versus assisted reproductive techniques include age and time available for conception, as it may take 3 to 6 months after varicocele correction for sperm parameters to improve. Predictors of improvement after varicocele treatment such as varicocele size, follicle-stimulating hormone level, preoperative total motile sperm count should be taken into account.¹²

An American Society for Reproductive Medicine practice committee recommended treatment of palpable varicoceles in an infertile couple when the female partner has normal or correctable fertility and semen analysis is abnormal.¹² They do not recommend treatment of subclinical varicoceles.^{12,15} Treatment may be considered in a man with similar presentation who has a desire to maintain future fertility options but has no immediate plans.^{8,12} Significant atrophy of the testicle ipsilateral to a varicocele with abnormal sperm analysis in a Tanner stage V adolescent may indicate testis at risk and varicocele treatment should be considered.^{8,16} If the patient elects observation with annual exam/ultrasound, follow-up with an adult urologist should be recommended, given the progressive nature of the condition.⁸

Unilateral left-sided varicoceles are most suited for endovascular treatment, while patients with bilateral, unilateral right varicoceles or very large varicoceles may benefit more from surgical referral.^{3,17} Postsurgical recurrence of varicocele is also an indication for percutaneous embolotherapy, given the difficulty of the postoperative field for lymphatic/arterial sparing surgery, and possibility of collateral formation/variant anatomy (gonadal vein duplication). Results in this patient cohort have been very favorable with technical success rates approaching 100%.^{18,19}

The debate whether or not to treat subclinical varicocele continues. Cantoro et al in their prospective study of 337 patients (218 patients intervention and 119 patients control) demonstrated retrograde percutaneous embolotherapy of subclinical small varicoceles in infertile men with impaired sperm quality significantly improves the spontaneous pregnancy rate to 46.3% (11.8% in control group).²⁰ On the other hand, Baazeem et al in a large meta-analysis concluded that studies are not sufficient to recommend in favor or against subclinical varicocele repair.⁷

Choice of Treatment

Treatment options for varicoceles (and resultant infertility) include surgery and percutaneous embolization/sclerotherapy. Surgical options for varicocelectomy include the open inguinal (Ivanissevich), high retroperitoneal (Palomo ligation of testicular veins and artery), and subinguinal microsurgical approaches, as well as laparoscopic repair (Palomo type mass ligation or artery sparing).⁸

Microsurgical varicocelectomy is the most effective and least morbid method among the surgical techniques for treating varicocele in infertile men.^{21,22} Open microsurgical inguinal or subinguinal varicocelectomy techniques have

been shown to result in higher spontaneous pregnancy rates and fewer recurrences and postoperative complications (particularly hydrocele) than conventional varicocelectomy techniques in infertile men.²³ In a meta-analysis from 2009, Cayan et al compared 3,319 surgically repaired patients with 314 percutaneous embolization patients, all of who had clinical palpable varicoceles and male factor infertility.²³ Failure rate and spontaneous pregnancy rates for surgery were 3.25 and 41.97%, respectively, and 13.05 and 33.2%, respectively, for the embolization group, differences of which were statistically significant. These findings and reported advantages of the microscopic surgical approach over percutaneous embolization are largely based on indirect comparisons. After this meta-analysis, Cassidy et al¹⁷ published a large series of varicocele embolization patients (158) from a single center and demonstrated that the reported 13% technical failure is largely related to failure to occlude the right gonadal vein. They revealed a 19.3% failure rate when treating the right with only a 2.3% failure rate when treating the left due to significantly more challenging catheterization of the right internal spermatic (gonadal) vein (ISV).¹⁷ Possible other contributing factors to the divergent results of technical success and recanalization rates of embolization include increasing experience, improved angiography techniques, and thrombogenic/embolic materials.¹¹ In 2009, Gandini et al reported a retrospective series of percutaneous sclerotherapy with sodium tetradecyl sulfate (STS) foam for varicocele treatment and demonstrated a technical success rate of 97.1%, pain resolution in 96.5% of patients, and recurrence rate of 3.6% with a mean follow-up time of 40.3 months. They also demonstrated spontaneous pregnancy rate of 39%.²⁴

In a more recent review of randomized clinical trials, Ding et al did not perform a meta-analysis to compare embolization with surgical techniques because of lack of good-quality studies comparing surgical approaches with embolization.²¹

The latest Cochrane systematic review on varicocele treatment in 2012 concluded that surgical or radiological treatment of varicocele in subfertile men with clinical varicocele and abnormal semen analysis may be of benefit, but the evidence is not conclusive. The value of surgical or radiological treatment in subfertile men with subclinical varicocele and normal semen analysis is disputable based on this systematic review. They did not differentiate between surgical and endovascular treatment.¹⁵

Detection/Grading

A good physical examination is key in the diagnosis of varicoceles and should be conducted in both the supine and standing positions. Dubin and Amelar suggested a varicocele grading system: Grade 0 is subclinical and not detectable by physical exam; Grade 1 (< 1 cm) is only palpable with Valsalva maneuver; Grade 2 (1–2 cm) is easily palpable; and Grade 3 (> 2 cm) is detectable on visual inspection.²⁵ Bilateral varicoceles with a high-grade left-sided varicoceles can be confirmed by performance of a subinguinal venous compression maneuver, to exclude a false right-sided varicocele (related to transscrotal venous stasis) rather than a true

bilateral varicocele.³ Testicular size can be measured by orchidometer, particularly in an adolescent patient.

Ultrasonography is a useful adjunct study, particularly in adolescent patients and subclinical cases.²⁶ However, other than patients who undergo varicocele treatment for testicular pain, a Grade 0 varicocele in an infertile man with abnormal sperm analysis that can only be detected with ultrasonography is an area of debate for treatment.^{12,15,20} Per American Society of Reproductive Medicine guideline, additional tests (including ultrasonography) are not recommended routinely and should be reserved for cases where clinical examination is nonconclusive.¹²

Vascular Anatomy

The pampiniform plexus or spermatic venous plexus is the network of small veins receiving venous blood from each testicle. They coalesce near the femoral head and drain into ISV on each side. The left ISV joins the left renal vein and the right ISV joins the IVC directly. This classic anatomy is seen only in 79% on the left and 78% on the right. Common variations from this anatomy can cause recurrence of varicocele due to inadequate treatment. These include a right ISV which drains into the right renal vein (8%) and multiple veins draining into the IVC and right renal vein (16%). The most common anatomic variation on the left is multiple veins draining into the left renal vein (20%) or less frequently the IVC.²⁷ The route of venous drainage of the testes also includes the external pudendal vein with the cremasteric and vasal veins representing smaller collaterals. The external pudendal vein forms at the level of superior pubic ramus and drains into the great saphenous vein. The vasal vein drains into the vesicular veins (superior or inferior) to eventually join the internal iliac system. The cremasteric vein drains into inferior epigastric and eventually external iliac vein.

Typically, there is no cross-communication between the right and left spermatic venous systems in the scrotal, retro-pubic, or pelvic areas. In men with a varicocele, the spermatic venous plexus is formed of numerous venous sinuses and large dilated veins.²⁸ The typical collateral pathway between the right and left ISVs forms near their central drainage. Bilateral ISVs commonly divide into medial and lateral divisions near the L4 vertebral level. The medial divisions create interconnections between the two networks and drain into renal capsular branches or colonic branches. The lateral divisions drain into the renal vein on the left and IVC on the right.^{9,28–30} In 50% of men, the only cross-communication is at the level of the L3 vertebral body.³⁰ Understanding the anatomy is crucial to provide adequate treatment and identify possible causes for clinical failure and/or recurrence.²⁶ Examples may include identification of significant collaterals for additional selective embolization during retrograde embolization or venography in the evaluation of recurrence after surgery.

Technique

Percutaneous retrograde varicocele embolotherapy is generally an outpatient procedure, performed under moderate

sedation. Given patients are usually young healthy adult males, limiting radiation exposure is paramount. We recommend aggressive collimation, minimizing use of digital subtraction angiography, use of low-dose/low-pulse fluoroscopy if possible, and use of gonadal/buttock shielding to minimize gonadal radiation.

Access is obtained either via the right internal jugular or right common femoral veins. The right jugular access may provide a more favorable angle for catheterization of the right ISV from the IVC (using a hockey stick catheter), while the left renal vein and subsequently left ISV catheterization are commonly performed via either a right common femoral vein or right internal jugular vein approach (using a cobra or hockey stick catheter). Catheterization of the right ISV can be challenging from a right common femoral vein approach (with the use of a cobra or reversed hook catheter). One should keep in mind that origin of ISV from IVC can be more anterior than expected. On the left, a renal venogram (while patient performing a Valsalva maneuver) can demonstrate the possible reflux into the left gonadal vein. If advancement is difficult due to small size of the vein (such as pediatric cases) or the presence of a proximal-competent venous valve, microcatheters can be used. After engaging the ISV orifice, spermatic venography is performed during a Valsalva maneuver. Demonstration of the venous anatomy and reflux/retrograde flow in the ISV is important before delivery of embolic/sclerosing agent.

Choice of embolic agents includes vascular coils, plugs, and liquid embolization agents such as n-butyl cyanoacrylate. Sclerotherapy is another option and sclerosing agents include 3% STS, hot contrast media, hypertonic glucose (70–80%), and absolute alcohol.

We perform a combination of coil embolization and additional 3% STS foam sclerotherapy. This includes three levels of coil embolization. For the first coil nest, we use 0.035-in. pushable coils just above the level of inguinal ligament where the ISV courses medially. A second coil stack is made at the level of mid-ISV using 0.035-in. pushable coils. Subsequently, catheter is advanced between the two coil nests and approximately 5 mL of sclerosing foam (mixture of 3% STS and CO₂) is administered slowly. Eventually, a nest of detachable coils is formed just below the renal vein confluence. Any predominant collateral should also be catheterized and selectively embolized. Completion venography is performed to confirm adequacy of treatment. Successful embolization of the ISV using only coils as well as retrograde and antegrade sclerotherapy have been described and shown effective.^{3,20,26,31}

Postprocedure Care/Results

Patients are typically observed for 1 to 2 hours until they meet routine discharge criteria, such as independent ambulation and oral intake tolerance. They may return to regular daily activities the next day and are encouraged to avoid strenuous activities and heavy lifting for 2 weeks. Expected postembolization systemic symptoms include testicular and back pain, nausea, and low-grade fevers usually responding to over-the-counter non-steroidal anti-inflammatory drugs. A 1- and 6-follow-up visit with scrotal ultrasound is recommended. Patients who undergo

the procedure usually have improved semen analysis in 2 to 3 months with spontaneous pregnancy rates being reported to be as high as 46.3%.^{20,23,24,31} Pain relief from percutaneous treatment is typically durable, with 86.9% of patients having pain relief during a mean follow-up of 39 months.¹¹

Complications

Complications of this procedure include venous injury/extravasation, which usually is not persistent and does not preclude successful treatment. If extravasation is persistent, the procedure may require postponement with reattempt at a later session. Technical failure to cannulate the spermatic vein has been reported and is more frequently encountered on the right, most frequently due to an unfavorable origin from the IVC or a competent valve. Adjusting the base catheter, and/or use of microcatheters, can be helpful in these challenging cases. Recurrence rates have been reported at 18.9% on the right versus 3.2% on the left in a large retrospective review.¹⁷ Recanalization/recurrence was reported between 0 and 24% in older studies, but it has decreased with more modern techniques, being reported at 2.3 to 3.6%.^{20,24} Pampiniform plexus thrombophlebitis presents with scrotal pain and swelling in 1 to 4% of patients.²⁶ To prevent this complication, coiling of the distal ISV is performed.

Conclusion

In conclusion, varicocele embolization is a safe and durable technique which provides pain relief and improved fertility in a well-chosen patient population.

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