

# Surgical management of adolescent varicocele: Systematic review of the world literature

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**Abstract** Historically, idiopathic varicocele is the most commonly diagnosed pre-pubertal andrological condition. The clinical presentation of varicocele may vary from dull and dragging unilateral or bilateral testicular pain to visible varicose veins lying over the hemiscrotum. Over the last decade, significant strides were made in managing symptomatic varicoceles, particularly minimal invasive procedures and surgeries. We sought to review the published literature in a systematic manner to gain an overview and streamline the presentations and main treatment modalities.

**Key Words:** Management, surgery, varicocele

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## INTRODUCTION

Idiopathic varicocele is the most commonly diagnosed pre-pubertal andrological condition.<sup>[1]</sup> Varicocele has first been described as early as 1<sup>st</sup> century B.C. Armelius Cornelius Celsus wrote "when the disease has spread over the testicle and its cord, the testicle sinks a little lower, and becomes smaller than its fellow, in as much as its nutrition has become defective".<sup>[1]</sup> The earliest description of varicocele in the modern literature was in 1885 when a conventional description of surgical treatment was given by Barwell.<sup>[2]</sup> However, it has only been in the last two decades that adolescent varicocele have been shown to affect testicular growth and its function.<sup>[3,4]</sup>

As early as 1970s, paediatric and adolescent varicocele were thought to be an unimportant clinical entity. This belief then

changed when Kogan *et al.*<sup>[5]</sup> published a number of clinical studies that confirmed that there was a clear-cut reduction in ipsilateral testicular volume of the varicocele, leading to change of the management of varicocele thereafter. It is now well documented that there is an increase in both ipsilateral and contralateral testicular growth in children and adolescents who have undergone varicocele treatment compared with those who had not.<sup>[6,7]</sup>

Varicocele is the most common correctable aetiology found in adult men with infertility. The main goal of all surgical methods of treating varicocele is to improve the potential for future fertility.<sup>[8-13]</sup> The aim of treatment in children is to prevent testicular injury and maintain testicular normal function, which can be achieved by surgical ligation of varicoceles.<sup>[14,15]</sup> An ideal surgical treatment for varicocele would be one where the testicular function is preserved, while the varicocele is completely eliminated with a low rate of recurrence, hydrocele formation, adjacent nerve damage or any other potential complications.<sup>[16-19]</sup> Despite the well-established natural history of the varicocele disease process, the optimal method for ligation of the varicocele is still a matter of debate as more interventional radiology as well as minimal invasive surgical procedures are ever emerging.<sup>[17-30]</sup>

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## MATERIALS AND METHODS

A detailed, comprehensive literature review was performed to identify all published peer-reviewed articles, which describe varicocele in the urological literature over last two to three decades. The search was conducted through the MEDLINE® database, the Cochrane Library® Central Search and the Web of Science. Initial search terms were varicocele and surgical management. Search results were screened for appropriate studies, with particular emphasis on clinical and experimental studies, as well as review articles. Articles referenced were screened to maximise review and inclusion of pertinent data. While English language text was not a specific search parameter, only English language publications were considered. All relevant studies collected were carefully examined to extract relevant data pertaining to varicocele and its surgical management.

## EVIDENCE SYNTHESIS FOR THIS REVIEW

### Anatomy of varicocele

Testis has a complex venous drainage network of interconnecting veins that form pampiniform plexuses, which eventually drain into the internal spermatic veins bilaterally. The testes are drained by two venous systems, which are the primary (deep venous system) and secondary venous systems (superficial venous system). These venous systems are highly anatomically variable, and had complicated venous connections through the cremasteric branches of the external spermatic and femoral veins. Such anatomical variation and complexity of the varicocele can ultimately impose challenges on the treatment of varicocele and elimination of recurrences.<sup>[17-19]</sup>

Varicocele predominately occurs on the left side. This is because on the left side the gonadal vein drains into the inferior aspect of the left renal vein at a right angle near renal the hilum. Whereas the gonadal vein enters obliquely into the inferior vena cava on the right side. Varicocele develops through insufficiency of the venous valves and results in retrograde flow into the spermatic veins, which results in dilation and tortuosity of the pampiniform plexus. Causes of varicoceles are well established in the literature, most commonly, an external compression of the renal vein by a tumour, an aberrant or obstructed renal vein. More importantly, the finding of left-sided varicocele should prompt clinicians and/or urologists to order appropriate tests and imaging, i.e. abdominal ultrasonography or other advanced radiological studies to rule out an associated abdominal mass causing compression effects on the renal veins, specifically the left renal vein.<sup>[31-35]</sup>

Bähren *et al.*<sup>[36]</sup> and Murray *et al.*<sup>[37]</sup> have previously highlighted the anatomical classifications of varicoceles. According to Bähren's classification system,<sup>[36]</sup> type 0 anatomy shows no

evidence of venous reflux on venography; type 1 anatomy shows reflux into a single gonadal vein without duplication; type 2 anatomy shows reflux into a single gonadal vein that communicates with accessory gonadal, lumbar and/or iliac veins, or the vena cava; and type 3 anatomy shows reflux into a gonadal vein duplicated caudally, coalescing into a single trunk at the renal vein junction. Type 4 anatomy shows a competent valve at the renal/gonadal junction, but reflux into a renal hilar or capsular collateral vessel that communicates with the gonadal vein. Type 5 shows reflux into a gonadal vein that drains into a circumaortic renal vein. Furthermore, according to Murray's classification system,<sup>[37]</sup> type R is renal, encompassing types 2 and 4 in the report of Bähren *et al.*<sup>[36]</sup>; type S is scrotal, showing cross-scrotal collateral vessels; type P is parallel; and sub-type A shows duplication superior to the iliac crest; sub-type B shows midretroperitoneal duplication between the iliac crest and pubic ramus; and sub-type C shows duplication at or below the inguinal canal.

### Cause of varicocele

Varicocele is a very common finding in young men and boys. It can affect up to 15% of men in the general population. In men, it usually constitutes up to 35% of primary infertility and up to 80% of secondary infertility.<sup>[11]</sup> Diagnosing varicocele can be challenging for clinicians and/or urologists as it may cause no symptoms, complaints and/or clinical signs. As a result, it may often be diagnosed late.<sup>[11]</sup>

An idiopathic varicocele is caused by an abnormal degree of venous distension of the pampiniform plexus due to incompetent venous valves along the spermatic cord. The retrograde flow of blood from the dilated or distended veins drains into the pampiniform plexus causing an increase pressure within.<sup>[11]</sup> Varicocele is a relatively common condition and may clinically present as scrotal pain and/or swelling. The patient may complain of a dragging like, or aching, pain within the scrotum, a feeling of heaviness in the ipsilateral testicle, atrophic testicle or visible enlarged veins, which can be palpable occasionally.<sup>[11,38]</sup> Or if asymptomatic, it may not present until during investigation of male sub-fertility.<sup>[39,40]</sup> With the recent advancement of imaging technology, most of the varicoceles are diagnosed nowadays incidentally while undergoing scrotal ultrasonography for testicular related pain or other symptoms.<sup>[41,42]</sup>

A secondary varicocele can occur due to compression on the venous drainage of the testicle by pelvic or abdominal malignancy. Urgent referral to clinician or urologist should be immediately sought to carefully examine the patient and order the appropriate imaging tests to rule out any underlying abdominal or pelvic mass, or malignancies such as renal cell carcinoma.<sup>[35]</sup> A non-malignant cause of a secondary varicocele

is the nutcracker syndrome. This is where the superior mesenteric artery compresses the left renal vein causing an increase in pressure, which will be transmitted backwards into the left pampiniform plexus.<sup>[43]</sup>

### Clinical diagnosis

Whereas in adult males most varicoceles are identified during investigation for infertility,<sup>[39,40]</sup> in the paediatric and adolescent populations they are commonly diagnosed after referral to a paediatric urologist as a result of an asymptomatic swollen left hemiscrotum. Most of these cases are discovered during a routine examination by a primary care physician.<sup>[44,45]</sup> Careful examination of the scrotum usually yields correct diagnosis of varicocele in most cases. Valsalva manoeuvre can also be helpful in examining varicocele. It often causes distension of the pampiniform plexus, which allows greater visualisation and palpation of the varicocele.<sup>[46,47]</sup> Varicocele diameter greater than 4 mm is usually clinically apparent.<sup>[47]</sup> However, numerous large varicoceles are often described as a bag of worms in the scrotum on palpation. In 1970, Dubin and Amelar<sup>[3]</sup> devised a clinical grading system for palpable varicocele, which is classified as follows: Grade 1 consists of only palpable varicocele while the patient is performing the valsalva manoeuvre; Grade 2 consists of palpable varicocele without the need to perform the valsalva manoeuvre; and Grade 3 consists of visible varicocele on examination before palpation.<sup>[3,4]</sup>

Although the valsalva manoeuvre is simple and easy to perform in the clinical evaluation of varicocele, previous clinical studies have demonstrated high subjectivity.<sup>[46,47]</sup> The World Health Organization (WHO)-based study of 141 men with sub-fertility showed that scrotal contact thermography using flexible strips was found to be the most accurate when compared with retrograde venography of the internal spermatic vein for a final diagnosis of varicocele. In addition, Doppler sonography had a higher false-positive rate, whereas radionuclide angiography with static imaging had a higher false-negative rate. However, the combination of Doppler sonography and contact thermography resulted in the highest diagnostic accuracy, with only 1% false-negative results and 44% false-positive findings.<sup>[32]</sup>

### Clinical imaging

Retrograde venography is considered the gold standard test for diagnosing testicular varicocele. However, this test is both time-consuming and invasive; hence, it is not performed as a first-line testing modality.<sup>[32,33]</sup> If a varicocele is present, the internal spermatic vein will be enlarged and there will be reflux into the abdominal, inguinal, scrotal or pelvic portions of the spermatic vein. There will also be venous collateralisation and anastomotic channels. Retrograde venography is usually performed in the assessment of uncertain cases or prior to

definitive treatment by venous embolisation. It is important to cover the gonads during venography and treatment procedures to reduce exposure to unnecessary radiation.<sup>[41]</sup>

Scrotal ultrasonography is now the most frequently used method of detecting varicoceles. The features on greyscale ultrasound include a prominence of two to three veins, one of which should have a diameter greater than 2-3 mm in a supine position. A valsalva manoeuvre is an important part of this examination and may be performed in some cases as this causes an increase in vessel size. Patients are advised to stand up for a few minutes as this allows some varicocele to fill up while waiting for their scrotal ultrasonography to be performed. This improves diagnostic ability by detection of reverse flow in the incompetent vein. Scrotal ultrasound has a sensitivity of 98% and a specificity of 100% compared with venography.<sup>[22,23,33]</sup> On the other hand, colour Doppler ultrasonography is routinely used as an integral part of the examination as this has been shown to improve diagnostic ability.<sup>[33,34]</sup> Whereas scrotal scintigraphy is not routinely used nowadays as this technique is time-consuming and has low sensitivity, preoperative sequential scrotal scintigraphy can be a more useful technique for assessing the prognosis for post-operative improvement of seminal findings, particularly sperm concentrations.<sup>[48]</sup>

Imaging with other techniques, such as magnetic resonance imaging (MRI) or computed tomography (CT), is only occasionally required, for example, to evaluate the presence of obstructing masses particularly on the right side. When conventional venography is contraindicated (history of anaphylaxis, etc), magnetic resonance venography (MRV) is a suitable alternative. Magnetic resonance angiography has been used for assessment of recurrent varicoceles.<sup>[49,50]</sup>

There has been some recently reported evidence that suggests that varicocele could be a bilateral disease (2.5%). This should prompt careful examination of the right testis in all patients with left-sided varicoceles. Supporting this, it is proposed that a bilateral colour Doppler ultrasonography should be performed on all patients diagnosed with a left-sided varicocele to rule out any underlying malignancy or abnormal pathology.<sup>[32-34]</sup>

### Effect on testicular function

The exact mechanism of impaired testicular function in patients with varicocele is not well understood yet. The most widely currently accepted concept is that varicocele can result in increased intra-testicular temperature, leading to destruction of viable sperms. Normally speaking, the difference between the intra-abdominal and scrotal temperature is approximately 2.2°C. Varicoceles can cause an increase in scrotal temperature by 2.6°C, neutralising the required temperature gradient. The varicocele-associated pathology mainly includes changes

in testicular size, histology, function of Leydig cells, sperm characteristics and testicular steroidogenesis. The WHO study reported that varicoceles (mainly left sided) were associated with relative left testicular atrophy compared with the contralateral testis. By contrast, right and left testicular size were not significantly different in men without varicocele. Decrease of testicular volume was associated with increasing varicocele grade.<sup>[32]</sup> Although testicular histological findings associated with varicocele are variable, the most common histological findings are hypo-spermatogenesis and premature sloughing of germ cells.<sup>[51,52]</sup> Leydig cell dysfunction has been documented in men with varicocele. It was suggested that hyperplasia of Leydig cells is the poor prognostic factor for fertility.<sup>[40]</sup> Additionally, the mean testosterone concentration of men with varicocele older than 30 years was found to be significantly lower than that of younger patients with varicocele, whereas this trend was not observed in men without varicocele. Conversely, significant increase in mean testosterone levels was documented after varicocelectomy without concomitant increase in the serum levels of leutinising hormone (LH) and follicle-stimulating hormone (FSH).<sup>[53]</sup> These findings suggest a detrimental time-dependent effect of varicocele on Leydig cell function.<sup>[40,53]</sup>

The detrimental effect of varicocele on spermatogenesis in the sub-fertile male is manifested by low sperm count, decreased sperm motility and low percentage of normal sperm morphology together or in different combinations. This 'stress pattern', described by Macleod in 1969, is also characterised by an increased number of tapered forms and immature cells.<sup>[54]</sup> However, the characteristic stress pattern is not a sensitive marker for varicocele and is not specific for this pathology. The LH and FSH serum levels may be determined and used as a marker for post-operative recovery of testicular function.<sup>[40,53]</sup>

Surgical repair of varicocele should be aiming to restore testicular function and improve fertility in the setting of varicocele-associated infertility. Furthermore, there have been numerous studies that have shown an increase in sperm quality and concentration in adult males who underwent varicocelectomy.<sup>[39,40,53,54]</sup>

### **Surgical treatment**

Large varicocele in adolescents, childhood varicocele with testicular atrophy, varicoceles with elevated FSH levels, low testosterone levels, varicoceles with scrotal pain, cosmose and male infertility with pathological semen analysis are all indications for surgical intervention. There has been success in the treatment of varicocele with diverse surgical procedures such as the Palomo retroperitoneal technique; the Ivanissevich inguinal approach; and the more recent antegrade sclerotherapy, retrograde embolisation, microsurgery, retroperitoneoscopic

and laparoscopic procedures.<sup>[8,14,20,21,24-30]</sup> Since its description in 1988, the laparoscopic varicocele ligation procedure has become the most popular surgical method for treating this condition in children.<sup>[14,28]</sup>

Lima and co-workers<sup>[55]</sup> have recently pioneered natural orifice transluminal endoscopic surgical procedures (NOTES) to perform varicocelectomy as an important minimally invasive approach.<sup>[55,56]</sup> In addition, various studies have thoroughly described the safety and efficacy of laparoendoscopic single-site (LESS) surgical repair of varicoceles.<sup>[31,57]</sup> Essentially, both NOTES and LESS are hybrid modification of the laparoscopic technique. In the case of LESS, it usually utilises a single port to provide a surgical approach for varicocele repair. In a study by Barone *et al.*,<sup>[29]</sup> 11 adolescent patients underwent LESS varicocele repair. There were no intra-operative complications, and there were no conversions to open surgery or traditional laparoscopy. Estimated blood loss was minimal and mean operative time was 66.9 min (range 48-91 min). The varicocele was corrected in all cases. At 14 month follow-up, there was no recurrence, testis atrophy or hernia in any patient. However, in only one patient sub-clinical hydrocele developed post-operatively. This study concluded that the LESS varicocele repair is a safe and effective method for varicocele repair in adolescents.<sup>[29]</sup>

Although NOTES and LESS are considered very attractive surgical options, being minimally invasive, with less post-operative pain requirement, its role needs to be validated in large randomised, clinical trials where patient's safety, surgical outcomes and instrumental technicality should be served as end points. Adding to this, future innovative research, particularly biomedical engineering, should be directed to improve the technicality and mechanistic application, hence, better safety and efficacy, of NOTES and LESS.

Ideally, successful surgical repair of varicocele is often measured by the radical elimination of the varicocele and has low rates of varicocele recurrences and hydrocele formation, as well as a low rate of testicular compromise. The classic Palomo technique includes mass ligation of the testicular artery, testicular vein and lymphatics. This technique is associated with a high level of post-operative complications, including high rate of hydrocele, recurrence of varicocele and discomfort.<sup>[24]</sup> As a result of these complications the Palomo technique was modified. Varicocelectomy by the Palomo technique remains an often used procedure because of the low rates of recurrence, low cost, low rates of testicular atrophy and easy performance.<sup>[24]</sup> A modified Palomo procedure was developed, which used an inguinal approach with ligation of the vascular pedicle above the vas deferens. This is performed with preservation of the testicular artery and ligation of the testicular vein and

lymphatics.<sup>[24]</sup> A sub-inguinal approach can also be utilised.<sup>[30]</sup> The Ivanissevich technique is one where the testicular vein is tied at the inguinal ring and the testicular artery and lymphatic vessels are spared, hence a lower rate of hydrocele formation post-operatively.<sup>[58]</sup> The use of microsurgical techniques has been examined in the ligation of spermatic veins at inguinal or sub-inguinal level compared with the outcomes of open surgical techniques.<sup>[30]</sup> In this study, there was no significant difference in operative time, complications, relapse rates, Doppler flow and semen parameters.<sup>[30]</sup> The presence of high protein level in the hydrocele fluid identified in these patients confirms that lymphatic obstruction is an important cause of hydrocele formations.<sup>[59,60]</sup> One possible way of avoiding a post-operative hydrocele has been suggested previously by performing simultaneous scrotal incision with fenestration of the tunica vaginalis at the time of varicocelectomy.<sup>[19]</sup>

Percutaneous sclerotherapy of the internal spermatic vein is another well-described technique in the management of varicocele. Although it usually has shorter convalescence with a rapid return to daily activities, it may lead to testicular necrosis in up to 15% of patients. Additionally, it does not require general anaesthesia, not generally well tolerated by children, and requires specialised radiological equipment and settings.<sup>[27,58]</sup> In another study by Fayad *et al.*,<sup>[27]</sup> percutaneous retrograde endovascular occlusion (PREVO) has been utilised in the treatment of paediatric varicoceles. A total of 71 children with left-sided varicocele were included in this study. The proportion of varicocele-free patients 6 months after PREVO was 93% (66/71) overall and 97% (66/68) in patients whose PREVO procedure was feasible. No clinical recurrence was observed during the mean follow-up of 17.5 months. Fayad's study concluded that PREVO can be safely performed on an outpatient basis under local anaesthesia.<sup>[27]</sup>

Testicular hypotrophy secondary to varicocele is considered an indication of surgical repair of varicocele. Previous clinical studies correlated testicular size before and after varicocele repair.<sup>[10,40]</sup> The increase in testicular volume post-operatively may well be as a result of testicular function recovery. However, clinicians and urologist should be vigilant that post-operative testicular oedema and lymphstasis can ensue following interruption of lymphatic drainage channels. Thus, it is strongly recommended to measure bilateral testicular size after a period of time in which the oedema and swelling have gradually subsided.<sup>[10,40]</sup>

Recurrence of varicocele (1%) and hydrocele formation (5%) are the most commonly reported complications following varicocele repair.<sup>[59,60]</sup> Re-occurrence of varicocele is often attributed to failure of proper identification of the collaterals or perhaps persistence of collaterals between the spermatic and

the external iliac veins.<sup>[59,60]</sup> Other post-operative complications include pneumoscrotum, subcutaneous emphysema, as well as post-operative pain in the right shoulder. Other complications described are local nerve injuries to either the ilioinguinal, genitofemoral or obturator nerves, which can be accidentally injured during surgical repair, including laparoscopic approaches. Potential causes of nerve damage are cauterisation heat, direct compression by a surgical clip or micro-trauma during dissection. The symptoms of nerve injury include transient numbness of the ipsilateral anterior thigh, which is usually resolved within 8-12 months.<sup>[24]</sup>

In a recent meta-analysis study conducted by Borruto *et al.*,<sup>[61]</sup> surgical approaches and post-operative complications were compared between the classic open surgical techniques and minimally invasive surgical approaches. This meta-analysis showed that there was no statistical difference between laparoscopic surgery and open surgery regarding recurrence rate and post-operative hydrocele rate. In the laparoscopic group, the incidence of recurrence was higher in patients undergoing artery ligation compared with patients undergoing artery and venous ligation. Furthermore, a lower rate of post-operative hydrocele was recorded in patients undergoing dye injections before laparoscopic ligation. In conclusion, Borruto's study<sup>[61]</sup> showed that the results after laparoscopic varicocelectomy are comparable to other surgical procedures. Moreover, the laparoscopic approach has the advantage to treat simultaneously bilateral varicocele.

## CONCLUSION

Varicocele is a common finding that affects adolescent the population. Its clinical presentation can be widely variable and often asymptomatic or silent. If left untreated, varicocele can cause testicular damage leading to infertility. Thus, urgent clinical attention should be sought to correct and repair varicocele. Various surgical and radiological procedures have been proposed previously. More recently, significant strides were made in managing symptomatic varicoceles, particularly minimal invasive procedures and surgeries, i.e., NOTES and LESS. Interestingly, the preliminary results of NOTES and LESS in varicocele repair appear promising, yet further research using animal survival and human cadaveric models is requisite prior to human applications, especially for complicated varicocele surgeries. Future innovative research, particularly biomedical engineering, should be directed to improve the technicality and mechanistic application, hence, better safety and efficacy, of NOTES and LESS.

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