VARICOCELE: A REVIEW

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ABSTRACT

The link between varicocele and infertility was first reported by Celsius in the first century AD, but it was not widely acknowledged until Tulloch and colleagues reported the improvement of sperm parameters in 26 of 30 patients undergoing varicocelectomy. The World Health Organization also reported that varicocele was present in 25% of patients with abnormal sperm parameters and 12% of patients with normal sperm parameters. Varicocele is the most frequently encountered surgical disease causing male infertility.

Keywords: Male infertility, varicocele, varicocelectomy.

INTRODUCTION

The link between varicocele and infertility was first reported by Celsius in the first century AD.¹ A varicocele was described as a ‘bag of worms’ by Dubin and Amelar in 1970,² although a more scientific definition would be: an abnormal venous dilatation of the pampiniform plexus caused by various aetiologies. The first usage of the word ‘varicocele’ was by Curling in 1843.³ Varicocele remained out of the spotlight until Tulloch and colleagues⁴ reported the improvement of sperm parameters in 26 of 30 patients undergoing varicocelectomy. The World Health Organization reported that varicocele is present in 25% of patients with abnormal sperm parameters and 12% of patients with normal sperm parameters.⁵ The condition is commonly encountered in the left testicular side: 90% of cases are isolated in the left side and only 2% are isolated in the right side; this phenomenon can be explained by the venous anatomy.⁶

AETIOLOGY

There are three commonly accepted theories:

• Differences between left and right testicular venous drainage anatomy: The left internal spermatic vein has about 8-10 mm H₂O higher blood pressure and relatively slower blood flow compared with the right side. This is mainly caused by the drainage of the left testicular vein to the left renal vein with a perpendicular angle, whereas in the right testicular vein the drainage is to the vena cava at a steeper angle. This causes less cranial venous drainage.

• Venous reflux: Reflux to the pampiniform plexus is caused by the lack of valves in the internal spermatic vein and/or the reflux caused by venous collateral flow. The lack of valves in the junction of the left renal and internal spermatic veins was shown by Shiraishi and Naito.⁷ Braedel and colleagues⁶ demonstrated a lack of venous valves in 73% of 659 male patients with varicocele.

• Partial obstruction of testicular veins: This phenomenon, called ‘the nutcracker phenomenon,’ occurs when a specific vein is compressed by arteries. In proximal type, the left renal vein is compressed by the aorta and the superior mesenteric artery. In distal type, the left common iliac artery compresses the left common iliac vein.

PATHOPHYSIOLOGY

The underlying pathophysiology can be summarised in the following hypotheses. It is
proposed that varicocele is associated with increased testicular blood flow; Grasso Laenza and colleagues\(^8\) reported increased blood flow in patients with varicocele compared with healthy controls in colour Doppler studies. An increase in interstitial fluid was described in animal models of varicocele formation,\(^9\) with the increased number of leukocytes potentially attributable to this increase. In addition, a higher testicular temperature may inhibit spermatogenesis. In both animal models and humans, an increased intra and intertesticular temperature was shown in the presence of varicocele.\(^{10,11}\) Increased venous pressure caused by reflux may contribute to decreased testicular flow,\(^{12}\) while Tek et al.\(^{13}\) demonstrated a higher apoptotic index in patients with varicocele (0.693 versus 0.206; \(p<0.05\)). Varicocele also causes impairment of the blood—testis barrier,\(^{14}\) which leads to the formation of anti-sperm antibodies.\(^{15}\)

### DIAGNOSIS

Diagnosis is made using physical examination. Physical examination should be completed in both sitting and standing positions inside a warm and comfortable room. The scrotum should be inspected first and then palpated to evaluate spermatic cord and testes. The diagnosis is finally made by observing and/or palpating a dilated or tortuous segment.\(^{16}\) Varicocele can be classified as one of three grades:

**Grade 1:** Dilated veins are palpable only with Valsalva manoeuver.

**Grade 2:** Dilated veins are seen whilst the patient is standing but not without Valsalva manoeuver, the physician can palpate dilated veins.

**Grade 3:** Tortuous and dilated veins can be seen in scrotum skin.

Radiology can assist in diagnosis: scrotal ultrasonography (USG) is not indicated for diagnosis of varicocele, but can be helpful if the diagnosis is inconclusive, such as in patients with morbid obesity, previous scrotal surgery, or accompanying ipsilateral hydrocele. The spermatic cord and epididymis can be evaluated with conventional USG. The assessment of testicular volume can also be helpful for indicating a need for intervention. Nowadays, because of the wide usage of Doppler USG and the subjectivity of physical examination, Doppler USG has become a standard diagnostic tool. It is recommended that patients should have at least one diagnostic imaging modality combined with physical examination. Through the use of Doppler USG, blood flow to the testes and reflux can be evaluated. Hirsh et al.\(^{17}\) graded varicocele according to the reflux observed in Doppler USG:

**Grade 1:** No spontaneous venous reflux.

**Grade 2:** Intermittent spontaneous venous reflux.

**Grade 3:** Continuous spontaneous venous reflux.

However, an objective grading system is lacking and a validated Doppler grading system is needed. The most sensitive test for diagnosing varicocele is venography, but, due to its invasiveness and relatively high cost, it is no longer recommended unless a therapeutic occlusion is planned. The success rate of the occlusion procedure is as high as 85% for recurrent varicoceles.\(^{18}\) Scrotal thermography is another tool for diagnosis although it is not a widely used method, mainly due to the widespread use of Doppler USG. This method can be used to document elevated temperature of the scrotum due to varicocele.

### TREATMENT INDICATIONS

Guidelines from the European Association of Urology\(^{19}\) recommend treatment in the case of clinical varicocele, oligozoospermia, infertility lasting longer than 2 years, and unexplained infertility. The American Urological Association recommends treatment when the following criteria are met: palpable varicocele on physical examination (may be validated via ultrasound), known infertility, normal female fertility potential, and abnormal semen parameters.\(^{20}\)

### TREATMENT OPTIONS

The main aim of treatment is to disrupt internal spermatic venous drainage whilst preserving arterial and lymphatic blood flow. There are several defined methods, the most widely used of which are the inguinal,\(^{21}\) subinguinal, and microscopic subinguinal approaches. Although not very commonly used, retroperitoneal,\(^{22}\) scrotal,\(^{23}\) and laparoscopic approaches\(^{24}\) have been described. Furthermore, a minimally invasive method, angiography, and embolisation for internal spermatic veins, have also been defined.\(^{25}\)
TREATMENT OUTCOMES

In 2009, a meta-analysis suggested that varicocele repair did not improve the likelihood of conception. After the meta-analysis was published, it was greatly criticised for heterogeneity among enrollment and having normal semen parameters of patients suffering from infertility. Furthermore, the study included one of the most debatable topics in urology, the subclinical varicocele, which will be discussed in more detail below. In contrast to this meta-analysis, several papers published in subsequent years advocated the use of varicocelectomy to improve sperm parameters and reported improvement of sperm parameters and paternity rates.

Subinguinal varicocelectomy can yield high improvement rates: 75.2% improvement in semen parameters and 45.5% in pregnancy rates. Abdel-Meguid et al. treated patients with varicocelectomy and followed their progress. They revealed a significant improvement in the treatment arm of the study, and a 3.04-times higher rate of spontaneous pregnancy. There is a debate as to whether varicocele repair improves pregnancy rates. Nilsson et al. reported the first comparative study of varicocele repair and did not reveal a significant difference in pregnancy rates among patients treated with varicocelectomy. Krause and colleagues conducted a study of 65 men treated with sclerotherapy and revealed no significant improvement compared with those who received no treatment. However, both studies have been criticised for low cohort size and poor follow-up.

On the other hand, Okuyama et al. compared patients treated using Palomo repair with those who received no treatment and revealed significantly higher pregnancy rates in the treatment arm (30% versus 18%; p<0.05). Schlegel wrote a review on varicocele treatment outcomes and revealed a 33% pregnancy rate in patients with varicocele repair compared with 16% in the no-treatment group. Varicocele can cause scrotal pain and some surgeons prefer surgery to treat this painful disease. In several studies pain was shown to be resolved with conservative treatment (e.g. oral anti-inflammatory medicine and limiting physical activity) in 5-15% of patients. Several studies reported success rates between 75-91%.

PROGNOSTIC FACTORS

Not all patients improve after a successful varicocelectomy. Patients with a disease history <2 years and who have high-grade varicoceles are more likely to improve following varicocelectomy. Patients with a total motile sperm count <5 million, who have genetic disorders, altered follicle-stimulating hormone (FSH)/testosterone levels, small testis volume, or concomitant metabolic syndrome have worse treatment outcomes.

Subclinical varicocele is defined as varicocele that is only diagnosed radiologically. Several investigators have conducted trials concerning treatment of subclinical varicocele and do not recommend treatment. Both the European
and American Urological Associations do not recommend treatment of subclinical varicocele.²⁰

**Paediatric and Adolescent Varicocele**

Indications for treatment are: varicocele associated with small testis, additional testicular condition affecting fertility, bilateral palpable varicocele, pathological sperm quality, and symptomatic varicocele.ª Cayan and colleagues¹⁴ compared studies of paediatric varicocelectomy and proposed that a 10% volume difference in the affected testis should be the indication for surgical repair; they reported that 53% of patients gained normal sperm volume following the operation before 14 years of age. With the subinguinal microscopic approach, recurrence rates are usually <10%.⁵⁵-⁵⁷

**KEY MESSAGES**

- The WHO reported that varicocele was present in 25% of patients with abnormal sperm parameters and 12% of patients with normal sperm parameters.
- Diagnosis is made using physical examination. Nowadays, because of the wide usage of Doppler USG and subjectivity of physical examination, Doppler USG has become a standard diagnostic tool. It is recommended that patients should have at least one diagnostic imaging modality combined with physical examination.
  - The main aim of treatment is to disrupt internal spermatic venous drainage while preserving arterial and lymphatic blood flow. There are several methods defined, with the most widely used being the inguinal, subinguinal, and microscopic subinguinal approaches.
  - Patients with a disease history <2 years and with high-grade varicoceles are more likely to improve following varicocelectomy.
  - Not all patients improve after a successful varicocelectomy. Patients with a total motile sperm count <5 million, who have genetic disorders, altered FSH/testosterone levels, small testis volume, or concomitant metabolic syndrome have worse treatment outcomes.
  - Both European and American Urological Associations do not recommend the treatment of subclinical varicocele.
  - Following the improvement of the technique with microscopy, one of the most feared complications, testicular atrophy, is encountered at a rate of only 1%.
  - Several papers advocate for varicocelectomy in improving sperm parameters, and report improvement of sperm parameters and paternity rates.

**REFERENCES**