Subclinical Varicocele (SCV): What the Urologists Need to Know?

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Abstract

Sub-Clinical Varicocele (SCV) is characterized by normal clinical examination and diagnosed mainly by Doppler Ultrasound imaging. About 10% to 15% of infertility cases were found to be SCV. SCV is one of the common causes of primary infertility and major cause in males with secondary infertility. Presence of sub-cutaneous varicocele in case of pediatric patients is considered a risk factor as it progresses to palpable clinical varicocele. Despite various imaging modalities being tried to diagnose SCV, color Doppler ultrasound is considered the gold standard imaging for diagnosis of SCV, having a sensitivity and specificity of nearly 100%. Diagnostic criteria parameters of SCV includes measurement of diameter of scrotal veins in supine, upright and after valsalva maneuver along with sum of venous diameter, venous blood flow volume and retrograde flow direction during valsalva. SCV exerts a significant impact on spermatogenesis. Of all the theories proposed, the most accepted one is the oxidative stress theory. In many instances, SCV is the only abnormality associated with oligospermia. Various meta-analyses have shown a significant improvement in seminal parameters following surgical intervention but pregnancy rate did not improve much when compared to the non-intervened group. Controversies in surgical management are all centered on the pregnancy rate. This leaves the treating andrologists and urologists even more confused on how to go about managing these patients with SCV. The American society of Reproductive Medicine and American Urological Association do not recommend surgical repair for SCV, if the indication for varicocelectomy is to improve the pregnancy rate.

Background

Primary infertility continues to be a daunting problem that the world faces now. Studies have shown that up to 15% of married couples are infertile and up to 20% to 50% of those are male related causes, mainly varicocele [1,2]. This number reaches 80% in those males with secondary infertility [3]. Ever since Tulloch in 1952 propagated the association of varicocele with infertility, the indications for treatment of varicocele have undergone a paradigm change [4]. Scott in 1961 studied 108 patients with varicocele and concluded that larger the size of varicocele, greater the damage caused [5]. However, despite much advances in imaging and better understanding of this condition over the next 6 decades, controversies and differences of opinions in the management of non-palpable varicocele continued to persist. Though many grading systems for varicocele are available in literature, Dublin grading system is the most widely accepted classification that takes into consideration visibility and palpability to classify varicocele into 3 different grades [6]. These include. Grade 1: Palpable during Valsalva manoeuvre; Grade 2: Palpable at rest; Grade 3: Visible and palpable at rest. Various studies have proven that all small, medium and large sized varicoceles were associated with altered semen parameters [7,8]. But the entity that every urologist needs to bear in mind is the Sub-Clinical Varicocele (SCV), which is neither seen nor palpated either during rest or on valsalva manoeuvre but only detected by Doppler ultrasound of abdomen [9]. As vast majorities of research studies are on clinically diagnosed varicoceles, the consensus on the management of SCV is controversial. This review discusses the magnitude of problem in our community, impact of SCV in infertility and various controversies in diagnosis and management of SCV.

Literature Review

The prevalence of SCV in any community may be difficult to estimate, but the overall incidence of SCV in infertile males needs to be ascertained in order to get to know the actual impact of SCV on fertility status. Zini et al. [10] in 1997 published a retrospective study in 404 infertile patients...
who presented for evaluation and found that 10% of them had left SCV. Cervellione et al. [11] conducted school screening of 2107 schoolboys aged 10 to 16 years of age and found that 16.8% had subclinical varicocele. A number of techniques have been used in the past to diagnose SCV. Ahlberg et al. [12] in 1966 introduced spermatic venography and was considered gold standard in diagnosing subclinical varicocele [13]. Comhaire et al. [14] in 1976 called this condition as SCV. He defined SCV as a reflux of blood back into the internal spermatic vein without palpable distension of pampiniform plexus of veins. Despite being highly sensitive, due to its invasive nature, high cost and associated morbidity, thermography it is not widely performed nowadays [15]. Non availability in many centers and a high degree of unreliability makes thermography being least accepted by the clinicians [16]. It was noted by thermography that a retrograde flow of blood into the non-dilated internal spermatic veins can result in venous stasis without any physical or palpatory evidence of varicocele. Though SCV is a widely accepted nomenclature these days, there are a few lesser-known terminologies that were used in the past for a similar condition. Greenberg in 1977, called it as an ‘Impulse only’ varicocele, where the testicles and the spermatic cord were normal, but a palpable cough impulse was felt on valsalva manoeuvre [17]. Borella et al. [18] in 1985 called it an ‘inconstant varicocele’, where the varicocele is clinically palpable on some but non-palpable on certain other occasions. Gonadal venogram is an invasive procedure associated with contrast allergy and side effects and may not be physiologic in all cases [19,20]. Color Doppler Ultrasound (CDU) is currently the Gold-standard investigation for making a diagnosis of SCV. It helps us to report the condition with a high degree of accuracy with a sensitivity and specificity of nearly 100% [21]. It also helps us to stage the condition thereby helping the urologists to prognosticate the condition.

**Diagnosis of SCV**

Though Comhaire coined the term SCV, the clinical diagnosis many a time may be confusing or misleading. The contraction of Cremaster muscle or the Dartos may mimic distended veins leading to false-positive clinical diagnosis [22,23]. In such instances, a physical examination of SCV would be sub-optimal and the diagnosis would be mainly based on imaging techniques. As the most common presentation of sub-clinical varicocele is infertility, patients presenting with male infertility should undergo a standard evaluation protocol that includes basic hormonal evaluation and a detailed semen analysis. CDU is the widely accepted imaging modality of choice in evaluating such conditions. A widespread availability, low cost, high specificity, and sensitivity make it the investigation of choice in diagnosing SCV [24]. Pilatz suggested certain parameters to diagnose sub-clinical varicocele that included measurement of diameter of scrotal vein in supine, upright and after a valsalva manoeuvre, sum of venous diameter, venous blood flow volume and a retrograde flow direction & change of flow during inspiration [25]. As the ipsilateral testicular volume and the intra-testicular arterial resistance remain largely unaffected in SCV, venous diameter, retrograde flow during valsalva manoeuvre and venous tangle remain the diagnostic criteria to define a SCV [26]. Figure 1 illustrates the Doppler features of right and left sided SCV at rest and during Valsalva manoeuvre.

**Impact on Fertility**

Extensive studies have been carried out to assess the impact of SCV on male fertility. A variety of explanations are proposed to correlate SCV and male infertility [27]. Some of these include an elevated temperature in the scrotum resulting in sperm damage, venous stagnation, and retention of waste products within the pampiniform plexus of veins, an elevated serum testosterone levels in these vessels, damage to sperm DNA and oxidative stress causing sperm damage [28]. About 50% of infertile men without clinical varicocele may have subclinical varicocele, suggesting that subclinical varicocele contributes to infertility [29]. Men with ipsilateral clinical varicocele may have synchronous contralateral SCV in one-fourth of the cases [30]. An increased sperm DNA fragmentation was observed in men with SCV [31]. Zini et al. [31] in 2005 stated that in infertile patients with sub-clinical varicocele was found to have increased sperm DNA fragmentation. Abo El-Khair et al. [32] observed an increased level of fractalkine to be an indicator of DNA fragmentation. He also observed an evidence of oxidative stress & increased leucocytes in semen in patients with SCV. In andrology practice, the SCV may sometimes be the only identifiable abnormality in couples presenting with primary infertility and oligospermia, where despite recent advances in technology, the cause of male infertility is unknown [33]. In their study, Hammadi et al. [33] observed that the SCVs are associated with abnormal hormones and seminal fluid parameters that affect the spermatogenesis process.

**Treatment Options**

With advances in medical imaging, those SCV that could not be assessed on clinical examination are being increasingly diagnosed these days. Kursh reported in 1987 that subclinical varicocele was diagnosed in 44% of fertile men and had no major role to play in male infertility [34]. This study raised many controversies on whether one really needs treatment for SCV. In one of the prospective randomized study done on 42 infertile males, Unal et al. [35] randomized those 42 men with subclinical varicocelectomy and 50 mg/day of Clomiphene citrate in each arm. The authors objectively documented an improvement in sperm motility and density after varicocelectomy, but there were no differences in the pregnancy outcome and seminal parameters. Zampieri et al. [36], in their retrospective study on 168 men with left SCV who were treated with bioflavonoids noted a lesser progression to palpable varicocele, higher stability in venous reflux and a better resolution rate. Cantoro et al. [37] studied 337 men with infertility and successfully performed percutaneous embolization in 218 men and observed a fourfold increase in pregnancy rates in comparison to the control group. Another randomized study by Yamamoto et al. on 85 men with SCV noted improvements in seminal parameters following varicocelectomy but no increase in pregnancy rates [38].

**Controversies in Management**

With advancements in imaging techniques, with increase in numbers of incidentally detected SCVs and with ambiguities and controversies in the guidelines for management of SCV, the magnitude of problems in patients with SCV also increases multifold. The evidence supporting treatment of SCV largely remains equivocal. In a randomized study on 42 patients with surgery and medical management as two arms with 21 patients of SCV each, Tiseo et al. [39] found a significant increase in sperm density and motility in the operated group and noted that the cumulative pregnancy rates in operated group were twice that of what was observed in the medically treated group. In a study on 150 patients presenting with primary male infertility, McClure observed that patients with SCV showed a significant increase in sperm motility after varicocelectomy than in those with clinical varicocele [40]. This reiterates that size of
varicocele does not have a significant impact on the ultimate surgical outcome. In a systematic review and meta-analysis, Kinn et al. [41] in 2016 analyzed seven trials in 548 patients and stated that there is an improvement in motility and sperm density but no significant increase in pregnancy rate. Dhabuwala, in his study on 54 men with varicocele identified that about 50% of those with SCV showed improvement in semen analysis post varicocelectomy [42]. In yet another a systematic review and one of the largest meta-analysis done from 13 studies on 1,357 males by Kohn et al. [43] in 2018 concluded that the bias and heterogeneity between various studies are so high that little overall clinical benefit was derived from surgical correction of SCV. This leaves the treating andrologists and urologists even more confused on how to go about managing these patients with SCV. However, the American Society of Reproductive Medicine and American Urologic Association do not recommend surgical repair for sub-clinical varicocele [44,45].

Take Home Points

1. Subclinical varicocele refers to presence of impalpable varicocele that is imaging techniques like CDU, Scrotal thermography and venography.
2. The ideal investigation of choice in case of sub-clinical varicocele is Scrotal CDU.
3. In pediatric age group left subclinical varicocele is considered risk factor for clinical left varicocele progression.
4. Dilated veins of size more than 3 mm in DUS is the widely accepted criteria.
5. There is no firm evidence supporting the therapeutic role of varicocele repair in infertile men with subclinical varicocele.

Conclusion

Subclinical varicocele is a common cause of male infertility in the era of technological advances and modern imaging. Management of SCV continues to be a great challenge to the treating urologists and andrologists. Various studies that assess the clinical utility of subclinical varicocelectomy are associated with a high risk of inherent bias. Recent meta-analyses have conclusively demonstrated that surgical management of SCV offers little benefit in the ultimate pregnancy rates.

References


