Scrotal ultrasonography as a predictive tool for the severity of varicocele

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Abstract

Varicocele is a common finding in male population with a documented association with impaired spermatogenesis and subfertility. However, the majority of individuals with varicocele are not affected and thus, recognition of patients at high risk is mandatory before deciding surgical correction. Scrotal ultrasound is a noninvasive and low-cost tool for the evaluation of varicocele, which facilitates the diagnosis and adds useful information regarding its harmful potential. In this review, we discuss the significance of specific parameters of scrotal ultrasound as predictive markers in the severity of varicocele.

1. Introduction

Varicocele is defined as the abnormal enlargement of the veins of the pampiniform plexus and is associated with the disturbance of normal testicular growth and reduced fertility [1]. The entry of left testicular vein via right angle to the renal vein is account for the dominance of left-sided varicocele, whereas absence of valves in the testicular vein and the nutcracker phenomenon are also implicated as possible causative factors [2]. The condition is found in up to 15% of general male population and shows a rising of 10% for each decade of life; moreover, in men with primary infertility, varicocele is found in up to 35% and surges impressively up to 80% in men with secondary infertility [3]. The hypothesis that varicocele is a dynamic phenomenon is supported by evidence that up to 20% of normal subjects will eventually develop a subclinical varicocele [4], whereas this form rarely resolves and up to 28% will eventually progress to a clinical varicocele [5]. The deterioration of semen parameters is a well-documented finding in varicocele but theories such as scrotal hyperthermia and backflow within the veins do not conclusively explain the harmful potential of the condition; sperm count, concentration and morphology are mostly affected and fertility may be reduced [6]. Hopefully, the

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correction of varicoceles is associated with improvement in semen characteristics and increase in pregnancy rate; nevertheless, the latter conclusion is controversial [7], [8]. The condition may also cause chronic orchialgia, worsened by increased physical activity and may require surgery [9]. In clinical practice, the diagnosis of varicoceles is based on clinical examination, according to the classification of Dubin and Amelar, which divides the condition in three distinct groups accordingly to findings of palpation and observation [10]. However, this system cannot assess the severity of varicocele, as far as improvement in semen parameters after correction appears to be similar for all groups [10]. On the contrary, scrotal ultrasound and especially Color Doppler Ultrasound (CDU) is a promising tool for the evaluation of varicocele, as it may establish and stratify the condition and unmask the subclinical form [2]. In this paper, we review of the potential correlation between specific scrotal ultrasound characteristics and varicocele severity.

2. The role of ultrasound

2.1 The role of venous size

The measurement of maximal venous size is considered an objective tool for the diagnosis of the condition, although bibliography lacks an optimal cutoff [2]. Some authors propose a cutoff point of 2.6 mm in the supine position during the Valsava maneuver as the optimal cutoff for the detection of varicocele [11]. In another study, a cutoff of 2.95 mm during the Valsava maneuver in the supine position detected most varicoceles with high accuracy, albeit being unsuitable for distinguishing between varicocele grades [12]. Regarding the palpability of the condition and the identification of clinical form, an approximate cutoff of 3-3.5 mm may be used as Hoekstra et al observed that most varicoceles were found palpable above that range; however, setting this limit, smaller, significant varicoceles could be missed [13]. Regarding the prognostic role of vein diameter, Schiff et al mentioned that varicoceles with a largest vein diameter larger than 3 mm showed a significant improvement after varicocelectomy [14], whereas Hussein also observed that patients with a testicular vein diameter greater than 2.5 mm at the inferior pole of the left testis have a significant improvement in semen parameters after correction [15]. However, in another study, authors concluded that varicocele size was not correlated with the outcome as varicoceles both markedly dilated (>4 mm in diameter) and less dilated (less than 4 mm in diameter) all exhibit similar postoperative paternity rates [16]. The latter findings are compatible with the observations by some authors that varicocele size is not a reliable prognostic tool for the outcome of varicocelectomy, with the exception of grade 3 varicoceles [17].

2.2 The role of testicular volume

Testicular volume is determined automatically by the ultrasound unit, based on the three dimensions of the testicles, according to the formula Volume (ml) = 0.523 x Length x Width x Height. In general terms, the varicocele may affect negatively the testicular growth; asymmetry between left and right testis is a usual finding, irrespectively of the fertility potential [18]. However, grade cannot certainly predict the asymmetry [19]. The role of testicular volume differential is significant in adolescents, since no determined criteria exist for the prediction of future fertility in this subgroup of patients; discrepancy is an indication for surgery, carrying though the risk of overtreatment [1]. The main concern about overtreatment, renders to the fact that varicocelectomy may improve testicular volume, but improvement in semen parameters does not go hand in hand with rebound growth [20]. Therefore, some studies have evaluated the amount of discrepancy of volume between left and right testicles to stratify patients in high risk group. Diamond et al observed that a differential larger than 20% is associated with worsened sperm parameters, regarding concentration and motility and these patients should be at least tracked closely [21]. Further to the previous study, Kurtz et al observed that adolescents with a differential greater than 20% [calculated as (volumeright-volumeleft) / volumeright x 100] carry a significant risk for low counts of motile sperm and moreover, a total testicular volume less than 30 cc quadruples the odds [22]. Moreover, adolescents with asymmetry greater than 20% will likely progress to greater asymmetry and observation may not be an option for this subgroup [19]. In adults and regarding the outcome of varicocelectomy, Alshehri et al observed that patients with normal-sized testes enjoy better paternity rates compared to patients with small volume tests [16]. Finally, in the special subgroup of subclinical varicocele, asymmetry between the testicles may also be observed, although controversy exists among studies [18], [23]. In a study trying to determine useful predictive factors for infertility, Chen et al observed that patients with subclinical varicocele and total testicular volume less than 27 cc may suffer from subfertility, regardless of age [24].
2.3 The role of reflux

Reflux within the veins of pampiniform plexus can be detected easily via Color Doppler Ultrasound and may provide useful information. Nevertheless, there is no consensus about the optimal framework for the diagnosis or stratification of varicocele according to reflux. A recent stratification system by Patil correlates the clinical grading of Dubin and Amelar in 3 grades based on the duration of reflux in milliseconds; this grading offers the additional benefit of detecting rare intratesticular varicoceles [25]. Complicated classification systems like those by Sariteschi and Chiou either lack of reproducibility or are limited to the diagnostic process [2], [26]. A simplified grading system proposed by Hirsch is a serviceable tool which divides varicoceles into 3 groups depending on the spontaneity of the reflux and seems that has a role in the assessment of the severity of the condition [2]. For example, spontaneous venous reflux associated with any grade of varicocele may result in testicular growth arrest and a strict follow-up is mandatory, as it has been observed by Zampieri et al [27]. In another study by Verim et al, increasing reflux grade by Hirsch had a negative impact on sperm concentration, motility and morphology; interestingly, total motile sperm count was constantly affected by any grade of reflux [28]. Regarding the progression, a continuous pattern of reflux during Valsava maneuver according to Hirsch classification, is associated with higher rate of progression of a subclinical varicocele to a clinical form in the next 4 years [5]. According to a more simplified grading system, varicoceles may be divided into two types according to characteristics of reflux; stop-type varicoceles bear a decrescendo bruit appeared at the beginning of a Valsava maneuver, whereas shunt-type varicoceles exhibit a steady flow caused by retrograde and orthograde flow; the latter type is associated with higher incidence of testicular asymmetry and may predict the necessity of surgery in adolescents [29]. In adults, patients with continuous reflux enjoyed a significantly higher paternity rate after correction compared to those with stop-type reflux [16]. Of note, these types of reflux may explain the pathophysiological pathway, as reflux may be associated with increasing impotence of valves and consequent dramatic changes in testicular function [26]. Duration of reflux in milliseconds can also be used for the assessment of spermatogenesis, as varicoceles with reflux of longer than 1 second had significantly worse semen parameters [11]. Moreover, a duration of venous reflux longer than 4.5 seconds is associated with better outcomes after correction [17]. Regarding post-operatively findings, reversal of flow after varicocelectomy is strongly associated with significant improvements in sperm parameters [14]. No retrograde venous flow after surgical correction results also more likely in catch-up growth of the testicle, according to Batavia et al [30], while reflux on the first postoperative day was found to be pivotal in predicting recurrence [31]. Finally, regarding location of the reflux, Hussein concluded that reflux of any grade detected in the lower pole of the testis is associated with important improvement in sperm concentration, motility and morphology [15].

2.4 The role of venous hemodynamics

Peak retrograde flow (PRF) is defined as the velocity measured at the vein of varicocele with the maximal diameter, during Valsava maneuver; this parameter seems to carry prognostic value in selecting patients at risk of future subfertility [2]. Kozakowski et al have observed that when PRF is greater than 38 cm/s and testicular asymmetry > 20% spontaneous catch-up growth is unlikely and adolescents with such characteristics should be advised for surgical correction [19]. Moreover, PRF may be used as a prognostic tool for recurrence after varicocelectomy; postoperative PRF > 20 cm/s at 1 year follow-up is associated with a lower incidence of catch-up growth and higher need for re-operation [30]. In adults, Chen et al have also observed that higher PRF values (mean values of 32.4 cm/s) are combined with greater risk of deterioration of semen parameters within 5 years; this observation was common in patients with both initial normal and abnormal semen parameters [32]. Verim et al also concluded that PRF > 30 cm/s may be an indicator of progression as it is strongly associated with worsened semen parameters [28]. Similarly, patients with subclinical varicocele and a PRF > 29 cm/s may suffer from subfertility [24]. Finally, one study did not demonstrate the predictive role of PRF due to low values; however, the authors admit that the differences may be related to the technique, as standing position may impede flow within the veins [29].

2.5 The role of testicular artery hemodynamics

The testicular artery arises from the aorta and provides the main blood supply to the organ. In the supratesticular region, the artery can be easily visualized, exhibiting tortuosity and flow toward and away from the transducer, representing different planes of the same vessel [33]. Using
real-time images analysis via CDU, the ultrasound unit can calculate measurements of peak systolic velocity (PSV), end-diastolic velocity (EDV), resistive index (RI) and pulsatility index (PI) [33]. Measurement of testicular arterial blood flow (TABF = Vm * A, where Vm is the mean velocity and A is the cross-sectional area of the artery) may also be used for the assessment of spermatogenesis [34]. In case of varicocele, Biagiotti et al observed that varicoceles carry high PSV and RI values, irrespectively of fertility status and therefore, cannot differentiate between affected and unaffected individuals [35]. The same conclusion was made by Tarhan et al, but the authors also found a positive correlation of TABF and sperm count and testicular volume; this observation may reflect a defective energy metabolism within the organ [34]. However, in the post-operative period, significant increase in PSV of left testicular artery may be seen in patients with improved both sperm count and motility [36]. A similar conclusion was made by Akand et al, as increase of PSV in 6 months in the corrected side could predict both improvement in sperm concentration and relief of pain after varicocelectomy [37].

2.6 The role of intratesticular and capsular artery hemodynamics
Capsular arteries are branches of the testicular artery, as the latter enters the posteroinferior aspect of the organ and run along the periphery as a structure named tunica vasculosa. The centriceptual or intratesticular arteries are terminal branches arising from the capsular branches and are visualized relatively straight within the testicular parenchyma. Subcapsular and intratesticular arteries exhibit similar waveforms and comparable mean values of PSV, EDV, RI and PI; thus, these parameters can be combined for the assessment of blood flow within the parenchyma [33]. Among the above parameters, RI seems to be a reliable indicator of subfertility; a mean RI > 0.6 is considered suggestive of pathological sperm count in male patients [38]. A positive correlation between RI greater than 0.6 and decreased total motile sperm, testicular hyprotrophy and increased values of FSH has been observed by Hillelsohn et al, highlighting the role of the parameter as a reliable tool for the assessment of testicular function [39]. In patients with left clinical varicocele, higher values of RI and PI in capsular and intratesticular arteries of the affected side may also imply impaired testicular microcirculation [40]. The hemodynamic parameters might also be used as indicators for the restoration of microcirculation, as Ener et al observed a significant increase in PSV and EDV and a significant decrease in resistance parameters RI and PI, 3 months after the procedure [41]. Balci et al demonstrated similar findings as mean intratesticular RI decreased 6 months after the procedure, although no correlation could be made between improvement in semen parameters and values of RI [42]. On the other hand, other authors conclude that improvement on semen analysis was correlated with decrease in intratesticular and capsular RI and capsular PI in left testicles and thus, these parameters could be used for the assessment of the outcome of the procedure regarding fertility [36]. The same conclusion was made by Akand et al, as PSV of capsular arteries at 3 and 6 months had positive predictive value [37]. Finally, a study from Tanriverdi et al did not show any significant changes in RI after varicocelectomy; nevertheless, the authors admitted that the measurement 7 days after the procedure might be a too short interval and restoration of microcirculation may be a late phenomenon [43]. In case of subclinical forms, as opposed to clinical varicocele, RI values do not differ significantly among left and right sides [44]. However, patients with subclinical varicocele and mean RI > 0.55 and PI > 0.99 may be at risk of subfertility, regardless of age [24].

2.7 Bilaterality of the disease
The bilaterality of varicocele is not uncommon as up to 50% of men with varicocele have bilateral varicoceles [3]. If varicoceles are both clinical, then repair of both sides is advisable as positive impact on semen parameters is significant in bilateral varicocelectomy [8]. However, no clear consensus exists about the management of left clinical varicocele accompanied with a right subclinical form. Correction of isolated subclinical varicocele, defined as a varicocele non-palpable but unmasked via ultrasound, is debatable, as improvement in sperm motility does not come along with increase in pregnancy rates [45]. However, some studies have highlighted the positive impact of bilateral varicocelectomy in the setting of a clinical left-subclinical right varicocele; Pasqualotto et al concluded that correction of both left clinical and right subclinical varicocele resulted in increase in testicular size and in significant improvement in sperm concentration [46]. Improvement in all semen parameters and increase in pregnancy rates have also been found by another study, when bilateral varicocelectomy was performed [47]. In addition, the authors highlighted the necessity of scrotal ultrasound in cases of infertile patients with clinical left varicocele, as the
disclosure of a subclinical right form may alter beneficially the management of the disease [47].

3. Conclusion

To sum up, scrotal ultrasound is a versatile tool for the evaluation of varicocele. Although the measurement of venous diameter is limited mainly to diagnostic purposes, other ultrasonographic parameters can assess the severity of the condition reliably. Specifically, the accurate measurement of testicular volume can assist the management in young boys and adolescents. Furthermore, the quantitative and qualitative evaluation of reflux may add useful information about the impact of varicocele on spermatogenesis and appraise the outcome of varicocelectomy. Finally, vein and arterial hemodynamics parameters are delicate tools which can predict the fertility status and the progression rate; of note, these tools may also act as prognostic markers for the final outcome after surgical correction, regarding the improvement of semen characteristics and risk of recurrence.

Conflicts of interest

The author declared no conflict of interest.


