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Varicocele in Children and Adolescents: A Challenge for Diagnosis and Treatment Indications

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Abstract

Varicocele, fertility, and paternity are terms that are frequently used in a common topic of clinical and pathologic conditions; however, any form of direct relationship has not been found. Is the high incidence and presence of a varicocele in boys, adolescents, and adults a normal variant? The hypotheses for a possible association between varicocele and fertility are based on issues such as temperature, volume, and growth of the testis, and sperm count, and indirect evidence indicating improved semen parameters after varicocele repair. However, what it comes down to, is the chance to father a child—to introduce pregnancy rather than a sperm count difference. This article highlights evidence-based findings and recent observations for a better understanding of which boys and adolescents would benefit from treatment or reassurance.

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1. Etiology and epidemiology of varicocele

The approximate incidence of varicocele in young adolescents and adults is around 16%; however, this incidence may be underestimated, as they might not be detected during "regular clinical exams" [1]. The sudden higher incidence during puberty, compared with childhood, is most probably due to puberty-associated testicular growth and increased blood flow [2].

Anatomical differences between left and right venous drainage of the testis at the level of the testicular vein are used to explain the presence of dilated veins of the plexus pampiniformis, mainly on the left side. On the right side, the testicular vein drains into the vena cava in a sharp angle. On the left side, however, the testicular vein drains into the left renal vein in an almost 90° angle. The *nutcracker effect* is thought to occur when the left renal vein is compressed between the superior mesenteric artery and aorta, proximal of the point where the left testicular vein runs in it, which is thought to increase the hydrostatic pressure resulting in varicocele formation [3].

2. Prevalence of varicocele in men from couples with fertility problems

The prevalence of varicocele is 20–40% in men who request investigation of fertility problems [4]. Another observation is the fact that patients with a varicocele have a higher incidence of an ipsilateral smaller testis and poorer sperm quality compared with patients without a varicocele [5]. In conclusion, there is a definite association between the presence of a varicocele and male fertility; however, the cause and relationship between the varicocele and fertility is unknown [6].

Depending on how one looks at numbers and incidence, only 15–20% of men with a varicocele require treatment for

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infertility, suggesting that most men with a varicocele have no fertility problems [7].

Controversial data exist on the effect of varicocele grade on semen quality. Recently, Al-Ali et al [8] showed that oligozoospermia was present twice as much in patients with a grade III varicocele compared with patients with a grade I or II varicocele. They also stated that sperm density significantly decreased with increasing grade of varicocele. These results correlate with the previously published results of Steckel et al [9] who stated that men with a grade 3 varicocele had lower sperm counts and poorer fertility indexes compared with men with grades 1 and 2 varicocele. Krishna Reddy et al showed total sperm motility of 30%, 29%, and 21% (World Health Organization lower reference limit [range]: 40 [38–42]) and mean sperm concentrations of 16.8 million/ml, 14.7 million/ml, and 9.75 million/ml (World Health Organization lower reference limit [range]: 15 [12–16]) in men presenting with infertility with grade 1, 2, and 3 varicocoele, respectively [10].

However, Shiraishi et al [11] and Diamond et al [12] reported no significant difference between varicocele grade and semen quality.

It has also been realized that azoospermia and severe oligoasthenospermia are extremely rare in *pure varicocele* patients [3]. In contrast, it is even estimated that almost 15% of men with azoospermia carry microdeletions of the long arm of chromosome Y [13]. Patients with azoospermia or severe oligoasthenospermia and a varicocele will probably not benefit from surgical treatment of the varicocele. Those patients would rather benefit from genetic counseling.

3. The importance of testis growth and volume

Testicular growth impairments associated with the presence of a varicocele have been variably reported; some studies have found growth arrest while others have not [14–16].

The volume of the testis is strongly related to fertility and sperm count. Although the American Society for Reproductive Medicine Practice Committee recommends obtaining a semen analysis in pediatric patients presenting with a varicocele, even in the absence of significant testicular atrophy. Semen parameters do not belong in routine assessment of a varicocele in an adolescent. In addition, there are significant barriers to performing semen analysis in an adolescent, more specifically from the view of the adolescent himself, the parents, and the practitioner [17]. There is also a lack of representative normal semen values in the adolescent age group and in addition, this may be influenced by the difference in Tanner stage and development.

It is known from previous studies that a 10% size variance between testes without associated abnormalities such as presence of a varicocele is considered as normal [18].

Diamond et al [12] showed that ultrasonographically derived volume differentials greater than 10% between normal and affected testes in Tanner V adolescents correlate with a significantly decreased sperm concentration and total motile sperm count.

Sigman and Jarow [19] showed a statistically higher incidence of hypotrophy in grade 3 varicoceles (73%) compared with grade 1 and 2 varicoceles (49% and 55%, respectively). These authors also found a significant difference in total motile sperm count between men with or without testicular hypotrophy; however, there seemed to be a trend of decreasing sperm count with increasing difference in testicular size, although this was not statistically significant.

Haans et al [20] and Laven et al [21] found in their studies that left testicular growth failure in patients with varicocele relative to controls correlated with lower total sperm number but they did not find a correlation with sperm concentration. In contrast, Guarino et al [22] found no predictive value of testicular volume measurement with regard to semen analysis in Tanner V adolescents and no statistical difference in testicular volume difference in patients with versus without varicocele.

Skoog et al [7] have pointed out an important issue in the difficult interpretation and the contradictory results of previous studies: the growth of the testis rather than the volume itself. They explained that a volume difference between the two testes becomes clear in adolescents with a varicocele during the rapid growth of the testes during puberty. They also stated that the loss of testicular volume is accompanied by a decrease in sperm count and advocate the early diagnosis of the disease as this is important for the prevention of sperm impairment and infertility.

A recent study that has investigated the relationship between testicular volume differential, total testis volume, and total motile sperm count in adolescents with a varicocele have found that a testicular volume differential of greater than 20% doubles the odd of a lower total motile sperm count; however, if the total volume of both testis equals 30 ml or more, the total motile sperm count is found to be normal [23].

4. Paracrine and endocrine regulation of the spermatogenesis

The testis has an endocrine and exocrine function, where exocrine function is mainly controlled by Sertoli cells, under the influence of follicle stimulating hormones, and they regulate the spermatogenesis by activin, androgen binding protein, and direct interactions with spermatogonia and spermatids [3]. The endocrine function is then mainly controlled by the Leydig cells and they regulate in turn by achieving a high intratesticular testosterone concentration. The Leydig cells also produce the epidermal growth factor and this controls the mitotic division of the germinal epithelium and stimulates the division of peritubular myoid cells, that in return produce another paracrine hormone, peritubular myoid substance. The list of paracrine substances involved in the molecular mechanisms controlling spermatogenesis is steadily increasing due to the continuous efforts of research. The understanding of endocrine, paracrine, and even neurotropins on spermatogenesis, together with the eventual ability to measure these