

## Clinical and laboratory profiles of a large cohort of patients with varicocele

Sani Aminu

*Department of Urology, Colchester Hospital University Foundation Trust, Essex, United Kingdom*

The prevalence of varicocele is 7% and 10–25% in pre pubertal and post pubertal males, respectively [1]. Varicoceles are found in 21–41% of men with primary infertility and 75–81% of those with secondary infertility. Physical examination of varicocele has a sensitivity and specificity of around 70%. The Color Doppler ultrasound (7MHz) has sensitivity of 50% and specificity of 90%. A pencil probe of 9 MHz is good in detecting subclinical varicocele. This has advantage when bilateral varicoceles are suspected [2]. The effect of varicocele on the testis is due to stasis of blood, increased testicular temperature, and reflux of toxic metabolites from the kidney and adrenal gland. This leads to oxidative stress, apoptosis, a deleterious effect on DNA integrity, and the OAT syndrome [3].

The indications for varicocele treatment are pain, arrest of testicular growth, and infertility.

Varicoceles in early adolescence should be followed up and treated if there is persistent discrepancy of testicular size by >20% or >2 cm. However, this should be taken in to consideration together with the peak retrograde flow. A peak retrograde flow of 38cm/s or more may indicate that the arrest of testicular growth is likely to worsen [4]. Research by Goldstein's group in 2011 showed that men with varicoceles have lower testosterone than a comparison group (men without varicoceles presenting for reversal of vasectomy). There was a 70% improvement in testosterone levels of men who had varicocelectomy. The mean increase was 178 ng/dl [5].

Controversies have dominated research on varicocelectomy as a treatment for infertility in the last decade, but research in the last couple of years tends to favor treatment of varicoceles in the presence of abnormal semen parameters and infertility.

A prospective randomized trial by Abdel Meguid et al. in which 150 men were randomized to either observation or a microscopic subinguinal varicocelectomy revealed an overall improvement in the odds of achieving pregnancy with varicocelectomy. After 12 mos. of follow-up, 13.9% of the observation group and 32.9% of the treatment group had achieved pregnancy (odds ratio [OR]: 3.04; 95% confidence interval [CI], 1.33–6.95). The authors found a number needed to treat of 5.27 (95% CI, 1.55–8.99), which suggests

that 5.27 men need to undergo varicocelectomy to achieve one spontaneous pregnancy [6].

A meta-analysis of outcomes of varicocelectomy in the treatment of infertility in oligospermic men in 2011 by Bazeem and coexperts in the field revealed that combined odds ratio was 2.23 (95% CI, 0.86–5.78;  $p = 0.091$ ), showing varicocelectomy is moderately superior to observation, but the effect is not statistically significant. They concluded that there is no evidence that a varicocele repair improves spontaneous pregnancy rates. They had observed that varicocelectomy improves sperm parameters (count, total, and progressive motility), reduces sperm DNA damage and seminal oxidative stress, and improves sperm ultramorphology [7].

An updated Cochrane systemic review in 2012 involving 894 men from 10 studies found out that the combined fixed-effect odds ratio (OR) of the 10 studies for the outcome of pregnancy was 1.47 (95% CI 1.05 to 2.05). The number needed to treat for an additional beneficial outcome was 17. A sub analysis of five studies in which patients had normal semen analysis, but were subfertile also favored treatment with a combined OR 2.39 (95% CI 1.56 to 3.66). The number needed to treat for an additional beneficial outcome was seven. The authors concluded that treatment of varicocele in men from couples with otherwise unexplained subfertility may improve a couple's chance of pregnancy. However, the findings are inconclusive as the quality of the available evidence is very low and more research is needed with live birth or pregnancy rate as the primary outcome [8].

Analyzing the different meta-analyses, the European Association of Urology guidelines recommended varicocele repair in cases of infertility with clinical varicocele and oligospermia, as well as in adolescents with progressive failure of testicular development (Grade B). It recommended against treatment of varicocele in infertile men with normal semen parameters and subclinical varicocele (Grade A) [9].

The current popular methods of varicocele treatment are microsurgical lymphatic and arterial sparing, subinguinal varicocelectomy, and radiological embolization.

The authors, with over one thousand patients in their study, have added one of the largest series of clinical

and laboratory profiles on men with varicoceles to the literature on the subject. Their finding of slightly higher level of testosterone in men with grade 3 varicocele compared to grade 1 and 2 has defied most studies

as discussed above, but their explanation is plausible though more research is needed on it. However, it is a known fact that precision and standardization of testosterone assay is a challenge in itself [10].

## References

1. Akbay E, Çayan S, Doruk E, Duce MN, Bozlu M: The prevalence of varicocele and varicocele-related testicular atrophy in Turkish children and adolescents. *BJU Int.* 2000; 86: 490–493.
2. Miyaoka R, Esteves SC. A Critical Appraisal on the Role of Varicocele in Male Infertility. *Adv Urol.* 2012; 2012:597495. doi: 10.1155/2012/597495.
3. Reyes JG, Farias JG, Henríquez-Olavarrieta S, Madrid E, Parraga M, Zepeda AB, Moreno RD. The hypoxic testicle: physiology and pathophysiology. *Oxid Med Cell Longev.* 2012; 2012:929285. doi: 10.1155/2012/929285.
4. Waalkes R, Manea IF, Nijman JM. Varicocele in adolescents: a review and guideline for the daily practice. *Arch Esp Urol.* 2012; 65: 859–871.
5. Tanrikut C, Goldstein M, Rosoff JS, Lee RK, Nelson ChJ, Mulhal JP. Varicocele as a risk factor for androgen deficiency and effect of repair. *BJU Int.* 2011; 108: 1480–1484.
6. Abdel-Meguid TA, Al-Sayyad A, Tayib A, Farsi HM. Does Varicocele Repair Improve Male Infertility? An Evidence-Based Perspective From a Randomized, Controlled Trial. *Eur Urol.* 2011; 59: 455–461.
7. Abdulaziz Baazeem, Eric Belzile, Antonio Ciampi, Dohle G, Jarvi K, Salonia A, Weidner W, Zini A. Varicocele and Male Factor Infertility Treatment: A New Meta-analysis and Review of the Role of Varicocele Repair. *Eur Urol.* 2011; 60: 796–808.
8. Kroese AC, de Lange NM, Collins J, Evers JL. Surgery or embolization for varicoceles in sub fertile men. *Cochrane Database Syst Rev.* 2012 Oct 17;10:CD000479. doi: 10.1002/14651858.CD000479.
9. European Association of Urology guidelines 2012. Guideline on Male infertility, pp. 30–33.
10. Genna Rollins. The Trials of Testosterone Testing. *Clinical laboratory news.* 2010; 36; 8: 1–5. ■

## Correspondence

Dr. Sani Aminu  
saniaminu@doctors.org.uk