

Mini Review
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Varicocelectomy in Male Subfertility Treatment: “Updated” Indications for Surgery

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ABSTRACT

We analyzed the recent literature data on varicocelectomy in treatment men from infertile couples. There are still a lot of unresolved issues that require clarification. It is still unclear the exact pathogenesis of testicular malfunction in some men with varicocele. Recent European and American urological guidelines recommend varicocele repair in men from infertile couples with “abnormal” semen parameters. Although, according to the 6th ed. of WHO laboratory manual for the examination and processing of human semen it is not clear the cut-off values between normal and abnormal semen parameters. Also, still unclear why approximately third part of patients do not experience any improvement after varicocele repair. According to the recent data analysis, total progressively motile sperm count (TMSC) and sperm concentration can be the significant predictors of semen improvement and pregnancy after varicocele repair. However, it should be remarked that the mean quality of existed data from low to moderate. All mentioned issues indicate the necessity of further large-scale multicenter randomized clinical trials.

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Main Body

Varicocele is considered the most common and treatable cause of male subfertility [1]. Varicocele is common in the general healthy male population (present in 15% of healthy men) [2]. Additionally, 35% of men with primary infertility and up to 81% of men with secondary infertility may have a varicocele [3]. Although despite the numerous studies, it is still unclear the exact mechanism of spermatogenesis failure and varicocele. In recent large-scale studies it was shown that men with varicocele had lower sperm concentration and motility than men without varicocele [4,5]. At the same time, the study conducted by Bozhedomov et al. with total 3908 patients (3632 subfertile and 276 fertile) demonstrated almost the similar prevalence of varicocele between fertile and subfertile male groups (29,5% vs 27,2%, OR 1.13) [6].

The American Urological Association (AUA)/American Society of Reproductive Medicine (ASRM) recommend varicocele repair (VR) in case of palpable varicocele in non-azoospermic infertile men with “abnormal” semen parameters [7]. Unfortunately, they do not describe the term “abnormal semen parameters”. The European Association of Urology (EAU) also recommends VR in infertile men with a clinical varicocele, abnormal semen parameters, and without other male causes of infertility [1]. Again, the term “abnormal semen” is not defined. Considering the fact that in recent 6th edition of WHO Manual for Human Semen Analysis it is decided to refuse the terms that define different kinds of semen abnormalities, those kind of ambiguities in guidelines become crucial [8]. In addition, as a separate paragraph, EAU recommends not to treat varicocele in infertile men with normal semen parameters [1]. Again, a reasonable question arises: which is a normal sperm, and which is abnormal one?

The recent meta-analyses and RCTs indicated the efficacy of varicocele treatment in terms of semen quality improvement and reproductive function recovery [9-11]. According to E. Persad et al. meta-analysis microsurgical varicocelectomy can be considered the preferred treatment method of clinical varicocele in men with compromised reproductive function [12]. But, there is still questions why VR improves semen quality only in 60-70% of treated men, and real fertility only in 30% of cases [9,13,14].

The results of evidence critical analysis conducted by Shomarufov et al. have shown that the total progressively motile sperm count (TMSC) and sperm concentration are the significant predictors of semen improvement and pregnancy after varicocele repair. For semen improvement alone, scrotal DUS parameters, sperm DFI and bilateral varicocelectomy are reliable predictors of microsurgical varicocelectomy success. They also concluded that despite microsurgical varicocelectomy is the preferred option for varicocele surgical repair, there is still insufficient evidence on predictors of this technique efficacy in terms of pregnancy and live birth rates [15].

So, how should we select which of the patients is recommended to be operated for varicocele and who is not according to semen quality? Moreover, how could we predict which patient will experience improvement after VR and which will not? Maybe we should use other (not routine) semen parameters such as TMSC as a novel indicator of male fertility status and the best predictor of VR efficacy. According to some recent data TMSC is the better indicator of male fertility status than other traditional semen parameters [16,17]. However, where is that “magic” cut-off line

between normal TMSC (or other semen parameters) when VR is not indicated and abnormal TMSC.

Interestingly, according to data of Shomarufov et al. in patients with initial high TMSC the semen quality may even worsen after VR. In their study with 93 included subfertile men with clinical varicocele, semen worsening in 3 months after VR and low pregnancy rates (PR, 12%) were observed in 25 (27%) patients with initially high TMSC (that changed from median of 54 million to 16 million, $p < 0.001$). Simultaneously, the greater improvement of semen quality and PR (46%) were revealed in 48 (52%) patients with relatively low TMSC (that changed from median of 15 million to 105 million, $p < 0.001$) [18].

According to this analysis of recent data, it becomes clear that with the introduction of the new (6th ed.) WHO Manual for Human Semen Analysis, the recent AUA and EAU recommendations seem to be unclear and should be updated. We can no longer fully rely on these guidelines. Such kind of unresolved challenges requires us to take decisive action in organizing large-scale multicenter (international) randomized clinical trials to determine the threshold values of semen or other clinical parameters when varicocelectomy should be performed. And, until new guidelines are issued clarifying the indications for the treatment of varicocele in subfertile men, we may only be guided by the 2010 WHO Manual for the Study of Human Semen.

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