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Perspective

Indications for Varicocele Repair in Male Infertility: Semen Parameters

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DESCRIPTION

We analyzed the current status of varicocele in men from infertile couple. There are still a lot of unresolved issues that require clarification. It is still unclear the exact mechanism of spermatogenesis failure in men with varicocele. All world-recognized guidelines recommend varicocelectomy in men from infertile couples with "abnormal" semen values. However, it is not clear the reference values of normal semen and abnormal semen according to the 6th edition of World Health Organization (WHO) laboratory manual for the examination and processing of human semen. Moreover, the real role of such a parameter as Total Motile Sperm Count (TMSC) is not completely clear, despite numerous studies confirming its value for assessing of male fertility status. All above-mentioned issues indicate the necessity of organizing further large-scale multicenter (international) randomized clinical trials.

Varicocele has been identified as the most prevalent and correctable cause of male infertility [1]. They are common in the general male population being present in 15% of healthy young adolescents and men [2]. Additionally, 35% of men with primary infertility and up to 81% of men with secondary infertility have a varicocele [3].

It is still unclear the exact connection between damage of spermatogenesis and varicocele. In a study conducted by the WHO, it was shown that men with varicocele had lower sperm concentration and motility than men without varicocele [4]. Another study conducted in healthy European men identified deteriorations in semen parameters even in men with a Grade-I varicocele [5]. Simultaneously, the study with total 3908 patients (3632 sub fertile and 276 fertile) demonstrated almost the similar prevalence of varicocele between fertile and sub fertile male groups (29,5% and 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, the AUA does not define the term "abnormal semen parameters". In addition, it is decided to refuse the terms that define different kinds of semen abnormalities in recent 6th edition of WHO manual for human semen analysis [8].

Meta-analysis demonstrated that surgical techniques with an inguinal and sub inguinal approach had the greatest improvement in sperm concentration and sperm motility parameters (compared with the retroperitoneal technique) [9]. 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 [10]. Again, the term "abnormal semen parameters" is not defined.

Hence, although according to the EAU and AUA/ASRM guidelines varicocelectomy is recommended in infertile men with a clinical varicocele and abnormal semen parameters, the sperm parameters used to determine the indication for VR and to assess its efficacy are not detailed.

Surely, the recent meta-analyses and Randomized Controlled Clinical Trials (RCCT) indicated the efficacy of varicocele treatment in terms of semen quality improvement and reproductive function recovery [9-11]. But, there is a still question why VR improves semen quality only in 60%-70% of treated men, and real fertility only in 30% of cases [12-15].

The results of our evidence critical analysis have shown that the Total Motile Sperm Count (TMSC) with sperm concentration can be the significant predictors of semen improvement and pregnancy after varicocele repair. For semen improvement alone, scrotal Distinctness, Uniformity and Stability (DUS) parameters, sperm DNA Fragmentation Index (DFI) and bilateral varicocelectomy are reliable predictors of microsurgical varicocelectomy success. They also concluded that despite microsurgical varicocelectomy is the "gold standard" option for varicocele repair, there is still insufficient evidence on predictors of this technique efficacy in terms of pregnancy and live birth occurrence [16].

So, how should we assign sub-fertile men to surgery group or observation group according to semen quality? According to some recent data TMSC is the better indicator of male fertility status than other traditional semen parameters [17,18]. But, where is that "magic" border line between normal TMSC and

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other semen parameters when VR is not indicated and abnormal TMSC.

Interestingly, according to our data in patients with initial high TMSC the semen quality may even worsen after VR. In our study with 93 included sub-fertile 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, $p<0.001$). At the same time the great improvement of semen and PR (46%) were revealed in 48 (52%) patients with relatively low TMSC (that changed from median of 15 million to 105 million, $p<0.001$) [19].

From the above, it becomes clear that with the introduction of the new (6th edition) WHO Manual for Human Semen Analysis, the recent recommendations of the EAU and AUA seem to be "vague" and require further clarification. We can no longer fully rely on these guidelines, which in turn require 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, as well as the true role and implementation TMSC into everyday practice.

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