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CLINICAL AND LABORATORY PARAMETERS INFLUENCING VARICOCELECTOMY SUCCESS IN THE TREATMENT OF SUBFERTILE MEN

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ABSTRACT

Varicocele, a condition in which the veins within the scrotum become enlarged, has been studied for over a thousand years. However, there are still many debates surrounding its treatment, particularly with regard to its limited efficacy in improving fertility in men from infertile couples. There are various clinical and laboratory factors that may impact the success of varicocele repair. Recent analysis suggests that evidence on the predictors of varicocele repair efficacy remains controversial. However, initial semen parameters such as sperm concentration and/or TMSC may be relatively important in predicting the success of varicocelectomy in treating male infertility.

INTRODUCTION

Varicocele is one of the most frequently identified correctable causes of male subfertility.(Bozhedomov et al., 2021; Machen & Sandlow, 2019; Salonia et al., 2022). According to the recent literature data, among men suffering from primary infertility, the ratio of people with varicocele is 50%, and among those suffering from secondary infertility, it can reach 69%(Witt & Lipshultz, 1993). Although the exact mechanisms affecting male fertility by varicocele are still widely debated, overall, the study results demonstrate that varicocele have a negative impact on spermatogenesis.(Akilov et al., 2023; Bozhedomov et al., 2021; Bryniarski et al., 2017; Redmon et al., 2019; A. B. Shomarufov, 2024; A. B. Shomarufov & Mirkhamidov, 2023).

Recent evidence suggests that the effects of varicocelectomy are not limited to changes in traditional semen parameters, but also include improved sperm DNA fragmentation and increased rates of spontaneous and assisted reproductive technology (ART) pregnancies.(Cho et al., 2016; Jensen et al., 2017). The European Association of Urology (EAU), the American Urological Association (AUA), and the American Society for Reproductive Medicine (ASRM) recommend surgical correction of varicocele in men with clinical varicocele and abnormalities in at least one semen parameter.(AUA | ASRM, 2020; Salonia et al., 2022; Samplaski & Jarvi, 2016).

H. Ding et al.(Ding et al., 2012), E. Persad et al.(Persad et al., 2021) citing a large number of studies indicated that microsurgical spermatic veins ligation is the most acceptable surgical treatment option for the treatment of clinical varicocele in infertile men in comparison with traditional open (without the use of microscopic equipment), laparoscopic methods, endovascular occlusion of veins. Simultaneously, varicocelectomy does not always lead to improved semen quality and fertility restoration: semen improvement after surgery usually occurs in 60-70% of cases, and natural pregnancies occur in 30-40% of couples (Abdel-Meguid et al., 2011; Almekaty et al., 2019; Cantoro et al., 2015; A. B. Shomarufov et al., 2021, 2023).

To date, there are insufficient studies on predicting the effectiveness of varicocelectomy based on a combination of clinical and laboratory characteristics of patients. For example, the results of a study conducted by M. Samplaski et al.(Samplaski et al., 2014), indicate the possibility of predicting the effectiveness of varicocelectomy in practice using special nomograms developed based on the study of clinical and laboratory parameters of subfertile men with varicocele. According to the authors, such information can help both the physician and the patient when deciding on the advisability of varicocele surgical treatment for the treatment of infertility in a married couple(Jang et al., 2020; Liu et al., 2023; Samplaski et al., 2014).

In this review we tried to analyze the recent evidence concerning factors affecting varicocelectomy efficacy in male infertility treatment.

Semen parameters and other laboratory predictors

According to the results of most studies assessing the prognostic criteria for the effectiveness of varicocelectomy, initial semen parameters, such as sperm concentration and motility, can be reliable predictors of the effectiveness of surgical correction of varicocele in male infertility (Madhusoodanan et al., 2020; Masterson et al., 2019; Ren et al., 2020; Zhang et al., 2017). According to Shomarufov et al. total progressively motile sperm count (TMSC) can be the most reliable predictor for semen improvement and also for natural pregnancies after varicocele repair (A. Shomarufov et al., n.d.; A. B. Shomarufov et al., 2021, 2023). They also showed in their critical evidence analysis that TMSC is accepted as a predictor of varicocelectomy fertility outcomes in many other studies (A. B. Shomarufov et al., 2023). Here we should note that they analyzed the data concerning only microsurgical varicocelectomy outcomes separately for semen improvement and pregnancy.

In some authors' data, peripheral blood parameters may also be predictors of the outcome of varicocele repair (Ates et al., 2019; Erdogan et al., 2021). E. Ates et al. based on the results of their study concluded that the ratio of neutrophils to lymphocytes (neutrophil-lymphocyte ratio or NLR) can be an independent predictor of the varicocelectomy success. According to their data, the optimal NLR indicator is 1.98, while the borderline indicator is 0.89. (Ates et al., 2019)

There is also data confirming the influence of immune factors on the effectiveness of varicocele treatment. According to Bozhedomov et al., the presence of anti-sperm antibodies (ASAB) in sperm is a predictor of low effectiveness of varicocele repair (Bozhedomov et al., 2014). Several studies have found that the initial sperm DNA fragmentation (SDF) level may also play a predictive role in the assessment of varicocelectomy success (Abdelbaki et al., 2017; Kadioglu et al., 2014; Ni et al., 2016; Telli et al., 2015). Also, according to other authors data ASAB and SDF do not affect varicocelectomy efficacy in male subfertility treatment (Al-Adl et al., 2014; Baker et al., 2013).

Clinical and anamnestic parameters

In the literature there are some studies which evaluated initial clinical and anamnestic parameters of men as the predictors of varicocelectomy fertility outcomes (Abbosov et al., 2023, 2024; Akilov et al., 2023; B Shomarufov, 2023; FA Akilov, AB Shomarufov, Shavakhabov Sh Sh, UA Xudoybergenov, SS Kasimov, 2023; Giyasov et al., 2024; Kamalov et al., 2023; A. Shomarufov et al., 2023; A. B. Shomarufov et al., 2020; A. B. Shomarufov, 2024; A. B. Shomarufov et al., 2024; U.A.Xudaybergenov, S.S.Kasimov, Sh.A.Abbosov, A.B.Shomarufov,

2023). According to some studies, a male age (Cantoro et al., 2015; Kimura et al., 2017; Samplaski et al., 2014; A. B. Shomarufov et al., 2021), varicocele grade (Samplaski et al., 2014; Shabana et al., 2015), serum gonadotropins and testosterone level (Abbosov et al., 2024; Al-Adl et al., 2014; Cantoro et al., 2015; Chen, 2014; Khudaybergenov et al., 2017; A. Shomarufov et al., 2023; A. B. Shomarufov, 2024; A. B. Shomarufov et al., 2020, 2024; A. B. Shomarufov & Mirkhamidov, 2023), infertility duration (Abdelbaki et al., 2017; Ren et al., 2020; A. B. Shomarufov et al., 2021), body mass index (BMI) (Cantoro et al., 2015) and testicular volume (Al-Adl et al., 2014; Chen, 2014) may be the predictors of varicocele treatment efficacy. At the same time it should be noted that there are studies that decline the prognostic value of the above criteria such as varicocele grade (Cantoro et al., 2015; A. B. Shomarufov et al., 2023; Wang et al., 2015), testicular volume (Cantoro et al., 2015), and a male age (A. B. Shomarufov et al., 2023; Yazdani et al., 2015).

Systematic reviews and meta-analyses

Recent meta-analyses provided by Y. Niu et al. and N. Ou et al. compared unilateral versus bilateral varicocelectomy (Niu et al., 2018; Ou et al., 2019). The authors agreed that performing bilateral varicocelectomy significantly improved sperm quality and the chances of conception in infertile couples.

The results of other systematic review provided by Asafu-Adjei et al., where they analyzed the literature on the effect of the varicocele grade on varicocelectomy efficacy in subfertile men, demonstrated that the varicocele grade had a direct impact on varicocelectomy success. However, given that the studies included in the review were heterogeneous, the validity of this conclusion may be debatable (Asafu-Adjei et al., 2020).

CONCLUSIONS

It is seen from the above despite the numerous studies on varicocelectomy effectiveness in men from infertile couples, as well as predictors that determine its success, the question of ineffectiveness (or lack of effectiveness) of varicocele repair in certain groups of men remains open. According to most studies, only some initial semen parameters (sperm concentration, TMSC etc.) may be the reliable predictors of varicocelectomy efficacy. Further large-scale and good-quality randomized clinical trials and meta-analyses are required to clarify those debatable issues.

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