

# Impact of varicocele repair on semen parameters and spontaneous pregnancy: An endless debate put to rest

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## ABSTRACT

There has been much controversy about the true value of varicocele repair for improving fertility and the chances of natural conception. This review summarizes the latest research findings, current professional societies' recommendations, and the conclusions of recent systematic reviews and meta-analyses. The current evidence suggests a positive role for varicocele repair in improving basic sperm parameters and increasing the likelihood of natural pregnancy.

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## Introduction

Varicocele is reported in varying prevalences depending on the method of diagnosis, age, and fertility status [1]. It has been reported that 15% to 18% of the general male population has a clinically significant varicocele [2], and this is more common in infertile men, with 35% of men with primary infertility and 81% of men with secondary infertility being affected [3]. The relationship between varicocele and male infertility has been widely researched in recent decades. Although the exact etiology and pathogenesis of varicocele-mediated infertility are unclear, heat stress, toxin accumulation and blood stasis, hormonal imbalance, oxidative stress, and testicular hypoperfusion have been suggested as potential mechanisms. However, none of these mechanisms alone can fully explain the damaging effects of varicocele on testicular function [4]. In a large study conducted by the World Health Organization (WHO) on 9,038 men, varicocele was detected in 25% of men whose semen analysis was abnormal [5]. Although this demonstrates the association of varicocele with defects in semen analysis, it has been puzzling that many men with varicocele can have children naturally without any treatment.

The value of varicocele repair (VR) in improving semen parameters and pregnancy rates has been controversial. On the one hand, varicocele is considered to be one of the most common causes of male infertility that can be corrected by surgery [6]. Current guidelines recommend that VR be offered to infertile men if they have a clinically palpable varicocele and semen

abnormalities [7,8]. The recommendations are based on two meta-analyses that reported improvements in sperm concentration, total and progressive sperm motility, and morphology after VR [9,10]. Recent surveys, systematic reviews, and meta-analyses also highlight the positive effect of VR on semen parameters and spontaneous pregnancy rates [9,11–13].

On the other hand, other studies have claimed contrary evidence. The study by Nieschlag et al. [14] compared VR (by ligation or embolization) with no treatment (only counseling) and found no difference in cumulative pregnancy rates between the two groups at the end of the 12 month follow-up period (29% vs 25.4%, respectively) even though sperm concentrations increased significantly only in the VR group. Similarly, early Cochrane reviews on varicocele did not find increased chances of conception after VR [15,16]. While the latest Cochrane review concluded that pregnancy rates are improved after VR, it still questions the value of VR in improving live birth rates, given the poor quality of the current evidence [17].

In this article, we summarize the latest findings from the literature on the impact of VR on conventional semen parameters and spontaneous pregnancy outcomes.

## Varicocele repair in infertile men: Results of recent systematic reviews and meta-analyses

A recent meta-analysis by the Global Andrology Forum investigated the effect of VR on semen

parameters of infertile men, as compared with a control group who were not operated [18]. This meta-analysis showed that VR was associated with a significant increase in sperm concentration (standardized mean difference (SMD) 1.739; 95% CI 1.129–2.349;  $p < 0.001$ ), total sperm count (SMD 1.894; 95% CI 0.566 to 3.222;  $p < 0.05$ ;  $I^2 = 97.8\%$ ), total sperm motility (SMD 0.887; 95% CI 0.036 to 1.738;  $p = 0.041$ ), and normal sperm morphology (SMD 1.673; 95% CI 0.876 to 2.470;  $p < 0.05$ ).

The second meta-analysis by the same group evaluated the impact of VR on semen parameters in 351 studies using a before-after approach [12]. Following VR there was a significant increase in semen volume (SMD 0.203, 95% CI: 0.129–0.278;  $p < 0.001$ ), sperm concentration (SMD 1.590, 95% CI: 1.474–1.706;  $p < 0.001$ ), total sperm count (SMD 1.824, 95% CI: 1.526–2.121;  $p < 0.001$ ), progressive sperm motility (SMD 1.845, 95% CI: 1.537–2.153,  $p < 0.001$ ), (SMD 1.613, 95% CI: 1.467–1.759;  $p < 0.001$ ), and sperm morphology (SMD 1.066, 95% CI: 0.992–1.211;  $p < 0.001$ ).

The beneficial effect of VR on basic sperm parameters has been supported by other meta-analyses [13,19,20]. Additionally, these results are consistent with current guidelines [7,8]. However, the level of evidence that VR has a positive impact on sperm parameters is limited by the heterogeneity of the included studies and the notably high risk of publication bias toward studies showing positive results since these have a greater chance of being published compared to those that do not benefit [21]. Researchers may likely avoid submitting negative results that would lead to non-response bias.

Furthermore, improvement in semen quality after VR may not lead to a proportionate increase in pregnancy or live birth rates, as these outcomes depend on a variety of factors in both men and women. A recent meta-analysis that included only prospective trials whose primary outcome was pregnancy rate, found that VR resulted in significant increase in pregnancy rates (odds ratio 1.29, 95% CI 1.00–1.65,  $p = 0.047$ ) which was paralleled by significant improvement in sperm concentration ( $p = 0.006$ ) [22]. Interestingly, in this study, the authors could find only 12 randomized controlled trials to analyze out of the 557 articles that they reviewed. This highlights the difficulty of finding high-level evidence to comment on the utility of VR. The beneficial effect of VR was evident only in patients with abnormal semen parameters. Likewise, an earlier meta-analysis showed an approximately two-fold increase in the odds of pregnancy rate, irrespective of the pattern of sperm abnormalities ( $p < 0.001$ ), as well as improvement in the live birth rate (odds ratio: 2.8;  $p < 0.001$ ) [13]. On the contrary, a previous meta-analysis including 349 patients in 4 studies found no significant difference in pregnancy rates [23]. However, the small number of studies included in the latter study precludes the ability to draw a firm conclusion regarding the lack of positive outcomes.

Table 1 summarizes the findings of recent meta-analyses investigating the effect of VR on basic semen parameters and spontaneous pregnancy rates.

### Current recommendations of professional societies

According to the AUA/ASRM guidelines [7], VR is recommended when there is a palpable varicocele in

**Table 1.** Summary of recent meta-analyses on the effect of varicocele repair on basic semen parameters and spontaneous pregnancy rates.

Study	Sperm concentration	Total sperm motility	Progressive sperm motility	Sperm morphology	Pregnancy rate
Cannarella [12]	Improved (SMD 1.590, 95%CI: 1.474–1.706; $p < 0.001$ )	Improved (SMD 1.613, 95%CI 1.467%-1.759%; $p < 0.001$ )	Improved (SMD 1.845, 95%CI: 1.537%-2.153%; $p < 0.001$ )	Improved (SMD 1.066, 95%CI 0.992%-1.211%; $p < 0.001$ )	-
Agarwal [18]	Improved (SMD: 1.739; 95%CI 1.129 to 2.349; $p < 0.001$ )	Improved (SMD 0.887; 95%CI 0.036 to 1.738; $p = 0.04$ )	Improved (SMD 3.301; 95%CI 2.164 to 4.437; $p < 0.01$ )	Improved (SMD 1.673; 95% CI 0.876 to 2.470; $p < 0.05$ )	-
Fallara [22]	Improved (MD: 12.34, 95%CI 3.49–21.18; $p = 0.006$ )	-	NS	NS	Improved (OR = 1.29; 95%CI 1.00–1.65; $p = 0.047$ )
Soetandar [20]	Improved by + 8.23%	Improved by + 7.17%	Improved by + 2.77%	Improved by + 0.64%	-
Persad [17]	-	-	-	-	Improved (RR = 1.94; 95%CI 1.23–3.05; $p = 0.004$ )
Wang [23]	-	-	-	-	NS (RR = 1.05; 95%CI: 0.72, 1.54; $p = 0.43$ )
Birowo [13]	-	-	-	-	Improved (OR = 1.82; 95%CI: 1.37–2.41; $p < 0.0001$ )
Birowo [24]	Improved (MD 9.59; 95%CI: 7.80, 11.38; $p < 0.00001$ )	-	Improved (MD 8.66; 95% CI: 6.96, 10.36; $p < 0.00001$ )	Improved (MD 2.73; 95% CI: 0.65, 4.80; $p = 0.01$ )	-

CI: Confidence interval; MD: Mean difference; NS: not significant; OR: Odds ratio; RR: Risk ratio; SMD: Standardized mean difference.

an infertile man with abnormal semen parameters, except in the case of azoospermia. The EAU guidelines [8] note that VR may significantly improve semen parameters and recommend VR in men with oligoasthenoteratozoospermia (OAT). They also suggested that VR may benefit some men with non-obstructive azoospermia and some couples with unexplained infertility. By analysing factors that may predict natural pregnancy after VR, the AUA/ASRM guidelines state that 'maternal age is the strongest predictor of fertility outcome' but they do not specify varicocele-related factors that would suggest a greater chance of benefit from VR [7]. EAU guidelines correlate a higher grade of varicocele with greater chances of recovery [8]. According to GAF experts, the greatest success after VR can be expected in cases where the female partner is young, the patient has initial mild to moderate OAT, bilateral and large varicoceles, normal testicular volume and follicle-stimulating hormone levels, and secondary infertility [11].

### Current practices

Recently, a large survey on worldwide practice patterns of varicocele management in infertile men was reported by the Global Andrology Forum [11]. A total of 574 urologists and andrologists from 59 countries submitted responses. The most common indication for VR, reported by 91.6%, was clinical varicocele associated with infertility, abnormal semen parameters, and a female partner <35 years old. For infertile men with clinical varicocele and isolated asthenozoospermia or teratozoospermia, VR was recommended by 63% and 41.1% of respondents respectively. In addition, for couples planning for IVF, 62.7% of clinicians recommended VR before ART. Finally, the most commonly used indicator to measure successful outcomes was an improvement in semen parameters, reported by 58.7%, rather than an increase in pregnancy rates (16.3%) or live birth rates (9.8%).

### Expert comment

Recent systematic reviews and meta-analyses provide sufficient evidence suggesting that VR in infertile men significantly enhances semen quality and men's fertility potential. The conclusions of these new studies indicate that VR improves most of the conventional semen parameters, including sperm concentration, semen volume, total sperm count, motility, progressive motility, and sperm morphology. Additionally, recent evidence indicates a positive impact of VR in infertile men on sperm DNA fragmentation [24] and the chances of spontaneous pregnancy. Therefore, VR can be recommended for infertile men with a clinical varicocele and abnormal semen parameters. Future research should assess the significance of VR in special

cases like clinical varicocele associated with isolated sperm defects, azoospermia, or unexplained infertility. Additionally, new studies are needed to investigate the impact of VR on live birth rates.

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### References

- [1] Alsaikhan B, Alrabeeh K, Delouya G, et al. Epidemiology of varicocele. *Asian J Androl.* 2016;18(2):179–181. doi: [10.4103/1008-682X.172640](https://doi.org/10.4103/1008-682X.172640)
- [2] Meacham RB, Townsend RR, Rademacher D, et al. The incidence of varicoceles in the general population when evaluated by physical examination, gray scale sonography and color Doppler sonography. *J Urol.* 1994;151(6):1535–1538. doi: [10.1016/S0022-5347\(17\)35295-3](https://doi.org/10.1016/S0022-5347(17)35295-3)
- [3] Gorelick JJ, Goldstein M. Loss of fertility in men with varicocele. *Fertil Steril.* 1993;59(3):613–616. doi: [10.1016/S0015-0282\(16\)55809-9](https://doi.org/10.1016/S0015-0282(16)55809-9)
- [4] Clavijo RI, Carrasquillo R, Ramasamy R. Varicoceles: prevalence and pathogenesis in adult men. *Fertil Steril.* 2017;108(3):364–369. doi: [10.1016/j.fertnstert.2017.06.036](https://doi.org/10.1016/j.fertnstert.2017.06.036)
- [5] World Health Organization. The influence of varicocele on parameters of fertility in a large group of men presenting to infertility clinics. *Fertil Steril.* 1992;57(6):1289–1293. doi: [10.1016/S0015-0282\(16\)55089-4](https://doi.org/10.1016/S0015-0282(16)55089-4)
- [6] Jensen CFS, Ostergren P, Dupree JM, et al. Varicocele and male infertility. *Nat Rev Urol.* 2017;14(9):523–533. doi: [10.1038/nrurol.2017.98](https://doi.org/10.1038/nrurol.2017.98)
- [7] Schlegel PN, Sigman M, Collura B, et al. Diagnosis and treatment of infertility in men: AUA/ASRM guideline part I. *J Urol.* 2021;205(1):36–43. doi: [10.1097/JU.0000000000001521](https://doi.org/10.1097/JU.0000000000001521)
- [8] Minhas S, Bettocchi C, Boeri L, et al. European association of urology guidelines on male sexual and reproductive health: 2021 update on male infertility. *Eur Urol.* 2021;80(5):603–620. doi: [10.1016/j.eururo.2021.08.014](https://doi.org/10.1016/j.eururo.2021.08.014)
- [9] Baazeem A, Belzile E, Ciampi A, et al. Varicocele and male factor infertility treatment: a new meta-analysis and review of the role of varicocele repair. *Eur Urol.* 2011;60(4):796–808. doi: [10.1016/j.eururo.2011.06.018](https://doi.org/10.1016/j.eururo.2011.06.018)

- [10] Agarwal A, Deepinder F, Cocuzza M, et al. Efficacy of varicocelectomy in improving semen parameters: new meta-analytical approach. *Urology*. 2007;70(3):532–538. doi: [10.1016/j.urology.2007.04.011](https://doi.org/10.1016/j.urology.2007.04.011)
- [11] Shah R, Agarwal A, Kavoussi P, et al. Consensus and diversity in the management of varicocele for male infertility: results of a global practice survey and comparison with guidelines and recommendations. *World J Men's Health*. 2023;41(1):164–197. doi: [10.5534/wjmh.220048](https://doi.org/10.5534/wjmh.220048)
- [12] Cannarella R, Shah R, Hamoda TA-M, et al. Does varicocele repair improve conventional semen parameters? A meta-analytic study of before-after data. *World J Men's Health*. 2024;42(1):92–132. doi: [10.5534/wjmh.230034](https://doi.org/10.5534/wjmh.230034)
- [13] Birowo P, Tendi W, Widyahening IS, et al. The benefits of varicocele repair for achieving pregnancy in male infertility: a systematic review and meta-analysis. *Heliyon*. 2020;6(11):e05439. doi: [10.1016/j.heliyon.2020.e05439](https://doi.org/10.1016/j.heliyon.2020.e05439)
- [14] Nieschlag E, Hertle L, Fishedick A, et al. Update on treatment of varicocele: counselling as effective as occlusion of the vena spermatica. *Hum Reprod*. 1998;13(8):2147–2150. doi: [10.1093/humrep/13.8.2147](https://doi.org/10.1093/humrep/13.8.2147)
- [15] Evers JL, Collins JA. Surgery or embolisation for varicocele in subfertile men. *Cochrane Database Syst Rev*. 2004;3:CD000479. Update in: *Cochrane Database Syst Rev*. 2008;(3):CD000479.
- [16] Kroese AC, de Lange NM, Collins J, et al. Surgery or embolization for varicoceles in subfertile men. *Cochrane Database Syst Rev*. 2012;10:CD000479. doi: [10.1002/14651858.CD000479.pub5](https://doi.org/10.1002/14651858.CD000479.pub5)
- [17] Persad E, O'Loughlin CA, Kaur S, et al. Surgical or radiological treatment for varicoceles in subfertile men. *Cochrane Database Syst Rev*. 2021;2021(4):CD000479. doi: [10.1002/14651858.CD000479.pub6](https://doi.org/10.1002/14651858.CD000479.pub6)
- [18] Agarwal A, Cannarella R, Saleh R, et al. Impact of varicocele repair on semen parameters in infertile men: a systematic review and meta-analysis. *World J Men's Health*. 2023;41(2):289–310. doi: [10.5534/wjmh.220142](https://doi.org/10.5534/wjmh.220142)
- [19] Majzoub A, ElBardisi H, Covarrubias S, et al. Effect of microsurgical varicocelectomy on fertility outcome and treatment plans of patients with severe oligozoospermia: an original report and meta-analysis. *Andrologia*. 2021;53(6):e14059. doi: [10.1111/and.14059](https://doi.org/10.1111/and.14059)
- [20] Soetandar A, Noegroho BS, Siregar S, et al. Microsurgical varicocelectomy effects on sperm DNA fragmentation and sperm parameters in infertile male patients: a systematic review and meta-analysis of more recent evidence. *Arch Ital Urol Androl*. 2022;94(3):360–365. doi: [10.4081/aiua.2022.3.360](https://doi.org/10.4081/aiua.2022.3.360)
- [21] Easterbrook PJ, Berlin JA, Gopalan R, et al. Publication bias in clinical research. *Lancet*. 1991;337(8746):867–872. doi: [10.1016/0140-6736\(91\)90201-Y](https://doi.org/10.1016/0140-6736(91)90201-Y)
- [22] Fallara G, Capogrosso P, Pozzi E, et al. The effect of varicocele treatment on fertility in adults: a systematic review and meta-analysis of published prospective trials. *Eur Urol Focus*. 2023;9(1):154–161. doi: [10.1016/j.euf.2022.08.014](https://doi.org/10.1016/j.euf.2022.08.014)
- [23] Wang X, Chen T, Qiu J, et al. Effects of primary varicocele and related surgery in male infertility: a meta-analysis. *Front Surg*. 2020;7:586153. doi: [10.3389/fsurg.2020.586153](https://doi.org/10.3389/fsurg.2020.586153)
- [24] Birowo P, Rahendra Wijaya J, Atmoko W, et al. The effects of varicocelectomy on the DNA fragmentation index and other sperm parameters: a meta-analysis. *Basic Clin Androl*. 2020;30(1):15. doi: [10.1186/s12610-020-00112-6](https://doi.org/10.1186/s12610-020-00112-6)