



Varicocele repair for infertility: what is the evidence?

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Purpose of review

Considering the persistent controversy concerning the impact of varicocele repair on fertility, we decided to perform an update of the review of the literature with the aim to evaluate whether the most recent research in this field gives us more evidence about the indications to treat or not to treat varicocele in dyspermic or infertile men.

Recent findings

Randomized controlled trials (RCTs) and prospective studies evaluating semen parameters before and after varicocelectomy clearly demonstrate that varicocele repair is associated with a significant improvement of sperm concentration, motility and normal morphology. Moreover, some recent studies highlighted the potential role of varicocelectomy in reduction of seminal oxidative stress and sperm DNA damage. One recent RCT showed a statistically significant advantage in favor of varicocelectomy in comparison with observations in terms of spontaneous pregnancy rate. Meta-analysis including this study confirmed the heterogeneity of pooled studies and showed a significant trend in favor of varicocele repair. This trend has become statistically significant when an 'as-treated' analysis is performed (odds ratio 2.69, 95% confidence interval 1.16–6.24). The advantages in favor of varicocele treatment were also observed in a recent RCT analyzing couples with first-term recurrent miscarriage.

Conclusion

Varicocele repair must be proposed in young adult men with impairment of seminal parameters and not yet interested in pregnancy. Men of infertile couples should be adequately counselled concerning the high possibility of attaining a significant improvement in seminal parameters after varicocele repair. This condition can be associated with a spontaneous pregnancy rate of 30%. The main alternative remains the use of artificial reproductive techniques.

Keywords

infertility, pregnancy rate, semen parameters, varicocele

INTRODUCTION

Varicocele is the dilatation of the pampiniform plexus due to the inversion of venous blood within the spermatic veins. The alteration of vasa vasorum of the tunica adventitia, the reduction of the longitudinal and oblique smooth muscle cells, the increase in connective tissue and decrease in the circular smooth muscle cells of the tunica media are the main histological alterations described in the wall of the spermatic plexus veins of varicocele patients [1]. Although in adult men this clinical condition can be associated with testicular pain and hypogonadism, the most relevant effects are represented by semen parameter alteration and male infertility. Indeed, varicocele is the most frequent cause of male infertility. This condition can be detected in 19–41% of patients with primary

infertility and 45–81% of those with secondary infertility [2]. Although several studies have been performed in the last decades, the exact mechanism by which varicocele can induce male factor infertility is still not well known. Simultaneously, the impact of varicocele repair on fertility is still one of the most controversial issues due to a lack of

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KEY POINTS

- Varicocele repair for infertility is mainly indicated in patients with clinically palpable varicocele and abnormal semen parameters. Evidence demonstrates that varicocele repair is clearly associated with a significant improvement in sperm concentration, motility and normal morphology.
- Some studies evaluated the impact of varicocele repair on the level of seminal reactive oxygen species and DNA Fragmentation Index, demonstrating an increase in antioxidant capacity and a decrease in oxidative stress after varicocele repair. However, more studies are needed to confirm the potential benefit of varicocele repair in reduction of seminal oxidative stress and sperm DNA damage.
- Some randomized controlled trials (RCTs) and recent nonrandomized controlled studies showed significant advantages also in terms of pregnancy rate in patients who received varicocelectomy in comparison with observation. Obviously, more data supporting the role of varicocelectomy in infertility are needed.

conclusive, well done randomized controlled trials [3]. This controversy is also present in the most recent recommendations produced by the last version of international guidelines.

In 2004, the National Institute for Health and Clinical Excellence's clinical guideline on fertility declared that varicocele repair should not be offered as a form of fertility treatment because it does not improve pregnancy rates [4]. In 2008, the Practice Committee of the American Society for Reproductive Medicine and the American Urological Association's Male Infertility Best Practice Policy Committee suggested that repair of the male partner's varicocele should be considered in patients with clinically palpable disease and abnormal semen parameters for infertile couples in which the female partner has no proven or a potentially treatable cause of infertility [5]. In 2012, the updated European Association of Urology's guidelines on male infertility recommend the treatment only in the case of a clinical varicocele, oligospermia, duration of infertility of at least 2 years and otherwise unexplained infertility in the couple. At the same time, these guidelines do not recommend the varicocele repair in infertile men who have normal semen analysis or in men with subclinical varicocele [6].

The variability and evolution of international guidelines can be justified considering the potential impact and significance assigned to some meta-analyses of randomized and/or non-randomized controlled trials (RCTs). Briefly, several meta-analyses of RCTs highlighted that there was no available

evidence justifying surgical or radiological treatment of varicocele in males from infertile couples [7]. However, previous meta-analysis was based on poor-quality RCTs with significant bias due to patient selection, debatable clinical classification of the disease and questionable semen analysis before the treatment. Moreover, all the analyzed RCTs were underpowered considering the issues in enrollment emerging in all studies, especially regarding patients refusing to be randomized to the no-treatment group. Moreover, an 'as-treated' analysis of the three RCT studies analyzed patients with clinically palpable varicocele, and subfertile patients revealed a significantly higher pregnancy rate in the treatment group than in controls [3]. Although in 2008 Evers and Collins [7], two gynaecologists involved in the artificial reproductive techniques, repropose a further Cochrane review against the opportunity to use varicocelectomy for infertile men focused on the same previous RCTs, there are several other meta-analyses including nonrandomized comparative studies based on Potsdam criteria for meta-analysis performance and a scoring system. One of those studies including two RCTs and three observational studies showed an odds ratio of 2.87 in favor of varicocele repair in terms of pregnancy rate [7,8]. Interestingly, another meta-analysis including data from RCTs and observational studies showed that varicocele repair may result in a significant improvement in sperm concentration, motility and morphology [2]. This aspect is really important considering that the direct effect of interruption of venous reflux within the spermatic veins is the improvement in testicle function and spermatogenesis process. It is well known that pregnancy rate can also be influenced by other female factors. Indeed, in our personal experience, the majority of patients treated for varicocele were young men with dyspermia not yet interested in pregnancy [9]. Considering the persistent controversy concerning the impact of varicocele repair on fertility, we decided to perform an update of our critical review of the literature published in 2006 with the aim to evaluate whether the most recent research in this field gives us more evidence about the indications to treat or not to treat the varicocele in dyspermic or infertile men.

RECENT FINDINGS

In this section we describe the impact of varicocelectomy on semen parameters, pregnancy rate and artificial reproductive techniques.

Impact on semen parameters

In 2011, Abdel-Meguid *et al.* [10] analyzed the changes from baseline in mean semen parameters

in patients randomly allocated to receive microsurgical varicocelectomy (73 patients) or an observation protocol (72 patients) as secondary endpoint of their RCT. Semen analyses were obtained at baseline and 3, 6, 9 and 12 months after the randomization. This study clearly showed the superiority of treatment group in comparison with the observational ones in terms of improvement in all semen parameters. In detail, in the treated arm an improvement of 15% was observed in sperm concentration, 15.2% in motility and 8.03% in normal morphology. Conversely, none of the semen parameters revealed significant changes from baseline in the control group [10[■]]. The favorable effects on semen parameters were also recently reconfirmed by two meta-analyses of the literature. In 2011, Baazeem *et al.* [11[■]] published a comprehensive meta-analysis of the literature with the aim to evaluate the role of varicocele repair in male-factor infertility. The authors identified 22 prospective studies reporting on sperm concentration before and after varicocele repair. The meta-analysis of these non-homogeneous studies showed a significant increase in sperm concentration after varicocelectomy. Specifically, the random effects model combined improvement in sperm concentration was 12.32×10^6 sperm/ml (95% CI: 9.45–15.19). In a recent meta-analysis on 17 prospective studies that evaluated the percentage total sperm mobility before and after varicocelectomy, the random effects model combined improvement in sperm total motility was 10.86% (95% CI 7.07–14.65). Similarly, the meta-analysis of five prospective studies reporting on percentage progressive sperm motility before and after the treatment confirmed a significant improvement in this sperm parameter. The random effects model combined improvement in progressive sperm motility was 9.69% (95% CI 4.86–14.52). Interestingly, all the studies included in this meta-analysis evaluated men with abnormal semen parameters and palpable varicocele at diagnosis. However, data were not stratified according to the different approaches used to repair the varicocele [11[■]]. In 2012, Schauer *et al.* [12[■]] performed a further meta-analysis including 14 articles evaluating improvements in semen parameters after suprainguinal, inguinal and subinguinal varicocelectomy. Inclusion criteria for this meta-analysis were at least two semen analyses (before and 3 or more months after the procedure), patient age older than 19 years, clinical subfertility and/or abnormal semen parameters, and a clinically palpable varicocele. This meta-analysis suggests that varicocelectomy leads to significant improvements in sperm count and motility regardless of surgical technique [12[■]].

Although many studies demonstrated an improvement in semen quality, the appropriate length of time required following varicocelectomy for semen quality evaluation is not well established. This aspect was recently considered by Al Bakri *et al.* [13[■]] in a retrospective study analyzing 304 patients who underwent varicocele repair for subfertility. All men were tested with semen analysis 3 and 6 months after varicocelectomy. Considering only the 100 cases (50 receiving an embolization of spermatic veins and 50 a microsurgical repair) who met the study inclusion criteria, the authors concluded that the best semen quality recovery occurs after 3 months from surgery and then does not improve further. Such a result was not affected by the different approaches used to repair the varicocele. Specifically, sperm counts increased by 53 and 38%, 3 and 6 months after the treatment, respectively. Simultaneously, 3 and 6 months later, the authors observed a mean of 2.5-fold and 1.5-fold higher total motile count compared to the preoperative values, respectively [13[■]]. This study supports the 3-month follow-up as a key moment to evaluate the effectiveness of varicocele repair in terms of seminal changes allowing the physicians (and infertile couples) a good parameter for the following decision-making.

Furthermore, new parameters of assessing varicocele treatment outcomes, such as seminal reactive oxygen species and DNA Fragmentation Index measurement, may prove useful. In 2006, Agarwal *et al.* [14] published a meta-analysis demonstrating that infertile men with varicocele had significantly higher semen reactive oxygen species levels than fertile men with no clinical varicocele and normal semen parameters. Few prospective studies evaluated the impact of varicocele repair on the level of oxidative stress [11[■]]. In particular, Chen *et al.* [15] in 2008 reported an increase in antioxidant capacity and a decrease in oxidative stress after varicocele repair.

Several studies showed that damaged sperm DNA is also present in men with poor sperm motility and morphology. In 2011, Zini *et al.* [16] analyzed the percentage of sperm DNA damage before and after subinguinal microsurgical varicocelectomy in 25 patients with clinical varicocele. The authors reported a significant decrease in the percentage of DNA Fragmentation Index after microsurgical treatment. In 2011, Sadek *et al.* [17] evaluated sperm chromatin condensation in infertile men after varicocele repair. Ninety-two men were recruited prospectively: 72 infertile men with varicocele and 20 normozoospermic individuals as control group. The authors found that there was a significant increase in abnormal sperm chromatin condensation in men with varicocele. Moreover, sperm chromatin

condensation was markedly improved following treatment of varicocele [17].

Impact on pregnancy rate

In 2011, Abdel-Meguid *et al.* [10[■]] published the results of an RCT comparing the effect of varicocele repair with observation in terms of spontaneous pregnancy rate in men of infertile couples. According to the most shared indications for the treatment of varicocele in infertile patients, inclusion criteria of the study comprised married men 20–39 years old who had experienced infertility for at least 1 year, had palpable varicocele and at least one impaired semen parameter (sperm concentration <20 million/ml, progressive motility <50% or normal morphology <30%). According to the sample size analysis, 73 patients were randomly allocated to subinguinal microsurgical varicocelectomy and 72 to observation. Notably, starting from the 251 patients assessed for eligibility, 48 (19%) cases did not meet inclusion criteria and 53 (21%) declined to participate. Any pregnancy that might occur during the 12-month period of study was documented. Spontaneous pregnancy was achieved in 32.9% in the treatment group vs. 13.9% in the control group with an odds ratio (OR) of 3.04 [95% confidence interval (CI), 1.33–6.95] and a number needed to treat 5.27 patients (95% CI, 1.55–8.99) [10[■]]. The most critical aspect of this RCT is represented by the low number of pregnancies reported in the control group, considering the short duration of infertility and the young age of the female partners. Indeed, the 14% pregnancy rate reported in the control group is significantly lower in comparison with the values of 16–20% reported in other studies [3,8]. Probably, the publication of the previous RCT pushed Baazeem *et al.* [11[■]] to perform a new meta-analysis of literature in 2011. This meta-analysis was focused on four RCTs reporting on pregnancy outcome after repair of palpable varicocele in dyspermic patients. Using the intention-to-treat (ITT) analysis, 192 cases were randomized to varicocele repair and 188 to observation. Conversely, using the ‘as-treated’ analysis 180 couples were really treated and 192 represented a real control group. Considering the ITT analysis, the fixed-effects model combined OR was 2.10 (95% CI, 1.31–3.38; $P=0.002$), suggesting that the effect of varicocelectomy is statistically superior to observation. However, the significant nonhomogeneity of the included study and consequently using the random effects model, the combined OR was 2.23 (95% CI, 0.86–5.78; $P=0.091$) indicating only a relevant but no statistically significant advantages in favor of varicocelectomy compared to observation. Obviously, the ‘as-treated’ analysis showed

statistically significant advantages in favor of varicocele repair with an OR of 2.69 (95% CI 1.16–6.24). Although the ITT analysis should be considered as the most appropriate method to minimize bias in the context of RCTs, we believe that in the context of nonblinded trials evaluating the results of a surgical therapy considering and comparing the results between the treatments really performed could be more realistic. One pregnancy obtained in a couple initially allocated to the control group but receiving a varicocele repair during the study period cannot be considered as a success of the observational protocol.

After the publication of this last meta-analysis of RCTs, Mansour Ghanaie *et al.* [18[■]] performed an RCT to evaluate the effects of varicocelectomy on pregnancy rate and live birth in couples with first-term recurrent miscarriage. All the husbands had normal semen parameters but clinically palpable varicocele. The couples were randomly assigned to a group in which the male partners underwent varicocele repair (68 cases) and another that underwent expectant protocol (68 cases). Within a 12-month period, the pregnancy rate was 44.1% in the first group and 19% in the second one ($P=0.003$) [18[■]].

In a nonrandomized study comparing 137 patients who received varicocele treatment and 185 who did not receive any varicocele correction, Giagulli and Carbone [19] showed that the overall pregnancy rate in corrected and uncorrected varicocele groups did not differ significantly. However, when the analysis was restricted to the individuals with infertility beyond 2 years, couples receiving a varicocele repair had a significantly higher pregnancy rate than patients with uncorrected varicocele (26 vs. 13.4%, $P=0.02$). According to the results of this study, the correction of varicocele aimed at restoring fertility could be more appropriate for men of couples with infertility longer than 2 years [19]. In a retrospective study analyzing 183 infertile patients with varicocele, Al-Ghazo *et al.* [20] reported a spontaneous pregnancy rate higher in patients with an infertility duration shorter than 3 years (37.3%) in comparison with patients with longer infertility duration (34.9% for the infertility period ranging between 3 and 6 years; 26.3% for infertility longer than 6 years).

Table 1 [10[■],18[■],19,21–23] summarizes pregnancy rates and seminal parameters improvement in the most recent studies published in the literature.

Impact on artificial reproductive techniques

The varicocelectomy does not seem to offer any significant advantages in terms of pregnancy rate in couples who underwent intracytoplasmic sperm injection (ICSI). Data from a retrospective analysis

Table 1. Summary of most important studies present in literature on impact of varicocelectomy on pregnancy rate and semen parameters

Authors	Study design	Semen parameters improvement		Pregnancy rate	
		Treated	Control	Treated	Control
Madgar <i>et al.</i> [21]	RCT	Yes	No	15/25	2/20
Nieschlag <i>et al.</i> [22]	RCT	Yes	No	18/62	16/63
Krause <i>et al.</i> [23]	RCT	No	No	5/33	6/34
Abdel-Meguid <i>et al.</i> [10 [¶]]	RCT	Yes	No	24/73	10/72
Mansour Ghanaie <i>et al.</i> [¶] [18 [¶]]	RCT	Yes	No	30/68	13/68
Giagulli and Carbone [19]	Not randomized prospective controlled study	No	No	40/185	35/137

[¶]The author evaluates the effects of varicocelectomy on pregnancy rate and live birth in couples with first-term recurrent miscarriage.

of 248 patients receiving ICSI showed that the 169 cases having varicocelectomy before ICSI had no differences in pregnancy rate (31.1 vs. 30.9%), implantation rates (22.1 vs. 17.3%) and miscarriage rates (21.7 vs. 23.9%) in comparison with the 79 cases receiving ICSI without prior varicocele repair [24[¶]]. However, in a recent randomized study comparing couples in which male partners underwent varicocele repair versus couples who underwent expectant therapy, the authors showed a significant lower percentage of spontaneous first trimester miscarriage (13.3 vs. 69.2%) in the first group [18[¶]]. However, it is possible that the improvement in semen parameters achieved after varicocele correction could offer a significant advantage also in terms of downstaging or shift of the level of artificial reproductive techniques needed to bypass male factor infertility [25]. More data on this important goal should be reported in the future.

CONCLUSION

Varicocele repair for infertility is mainly indicated in patients with clinical palpable varicocele and abnormal semen parameters. Evidence demonstrates that varicocele repair is clearly associated with a significant improvement in sperm concentration, motility and normal morphology. These data must be strongly considered to recommend varicocelectomy in dyspermic young adults not yet interested in pregnancy. Although preliminary data are promising, more studies are needed to confirm the potential benefit of varicocele repair in reduction of seminal oxidative stress and sperm DNA damage.

Concerning the impact of varicocelectomy on pregnancy rate of infertile couples, available meta-analyses continue to be influenced by previous heterogeneous and methodologically poor RCTs. However, recent RCTs and nonrandomized

controlled studies showed significant advantages also in terms of pregnancy rate in patients who received varicocelectomy in comparison with observation. Obviously, more data supporting the role of varicocelectomy in infertility are needed.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 525–526).

1. lafrate M, Galfano A, Macchi V, *et al.* Varicocele is associated with an increase of connective tissue of the pampiniform plexus vein wall. *World J Urol* 2009; 27:363–369.
2. Agarwal A, Deepinder F, Cocuzza M, *et al.* Efficacy of varicocelectomy in improving semen parameters: new meta-analytical approach. *Urology* 2007; 70:532–538.
3. Ficarra V, Cerruto MA, Liguori G, *et al.* Treatment of varicocele in subfertile men: the Cochrane Review – a contrary opinion. *Eur Urol* 2006; 49:258–263.
4. National Collaborating Centre for Women's and Children's Health (UK). Fertility: assessment and treatment for people with fertility problems – clinical guideline February 2004. <http://www.nice.org.uk/80/nicemedia/pdf/CG011fullguideline.pdf>. [Accessed on 6 June 2012].
5. Practice Committee of American Society for Reproductive Medicine. Report on varicocele and infertility. *Fertil Steril* 2008; 90(Suppl 5):S247–S249.
6. A Jungwirth, T Diemer, GR Dohle, *et al.* EAU Guidelines on male infertility. ■ Update February 2012. <http://www.uroweb.org>. [Accessed on 6 June 2012]. The guidelines recommended varicocele repair in case of a clinical varicocele, oligospermia, duration of infertility of at least 2 years and otherwise unexplained infertility in the couple.
7. Evers JL, Collins JA. Surgery or embolisation for varicocele in subfertile men. *Cochrane Database Syst Rev* 2008. CD000479.
8. Marmar JL, Agarwal A, Prabakaran S, *et al.* Reassessing the value of varicocelectomy as a treatment for male subfertility with a new meta-analysis. *Fertil Steril* 2007; 88:639–648.
9. Galfano A, Novara G, lafrate M, *et al.* Improvement of seminal parameters and pregnancy rates after antegradesclerotherapy of internal spermatic veins. *Fertil Steril* 2009; 91:1085–1089.

10. 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.
- The study demonstrated that varicocelectomy in infertile men with palpable varicoceles and impaired semen quality, increased odds of spontaneous pregnancy and improved semen characteristics.
11. 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; 60:796–808.
- The study demonstrated that varicocelectomy improved sperm parameters, reduced sperm DNA damage and seminal oxidative stress, and improved sperm ultra-morphology. Microsurgical repair seems to be associated with better outcomes.
12. Schauer I, Madersbacher S, Jost R, *et al*. The impact of varicocelectomy on sperm parameters: a meta-analysis. *J Urol* 2012; 187:1540–1547.
- The meta-analysis demonstrated that varicocelectomy leads to significant improvements in sperm count and motility regardless of surgical technique, with the inguinal approach offering the highest pregnancy rate.
13. Al Bakri A, Lo K, Grober E, *et al*. Time for improvement in semen parameters after varicocelectomy. *J Urol* 2012; 187:227–231.
- The study demonstrated that sperm parameters following varicocelectomy improved within 3 months from surgery and that no further improvement was seen thereafter.
14. Agarwal A, Prabakaran S, Allamaneni SS. Relationship between oxidative stress, varicocele and infertility: a meta-analysis. *Reprod Biomed Online* 2006; 12:630–633.
15. Chen SS, Huang WJ, Chang LS, Wei YH. Attenuation of oxidative stress after varicocelectomy in subfertile patients with varicocele. *J Urol* 2008; 179:639–642.
16. Zini A, Azhar R, Baazeem A, Gabriel MS. Effect of microsurgical varicocelectomy on human sperm chromatin and DNA integrity: a prospective trial. *Int J Androl* 2011; 34:14–19.
17. Sadek A, Almohamdy AS, Zaki A, *et al*. Sperm chromatin condensation in infertile men with varicocele before and after surgical repair. *Fertil Steril* 2011; 95:1705–1708.
18. Mansour Ghanaie M, Asgari SA, Dadrass N, *et al*. Effects of varicocele repair on spontaneous first trimester miscarriage: a randomized clinical trial. *Urol J* 2012; 9:505–513.
- The trial demonstrated that varicocelectomy improved semen quality, increases pregnancy rate, and decreases miscarriage rate significantly.
19. Giagulli VA, Carbone MD. Varicocele correction for infertility: which patients to treat? *Int J Androl* 2011; 34:236–241.
20. Al-Ghazo MA, Ghalayini IF, al-Azab RS, *et al*. Does the duration of infertility affect semen parameters and pregnancy rate after varicocelectomy? A retrospective study. *Int Braz J Urol* 2011; 37:745–750.
21. Madgar I, Weissenberg R, Lunenfeld B, *et al*. Controlled trial of high spermatic vein ligation for varicocele in infertile men. *Fertil Steril* 1995; 63:120–124.
22. 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; 13:2147–2150.
23. Krause W, Muller H, Schafer H, Weidner W. Does treatment of varicocele improve male fertility? *Andrologia* 2002; 34:164–171.
24. Pasqualotto FF, Braga DP, Figueira RC, *et al*. Varicocelectomy does not impact pregnancy outcomes following intracytoplasmic sperm injection procedures. *J Androl* 2012; 33:239–243.
- The study demonstrated that varicocele repair did not increase pregnancy rates nor decrease miscarriage rates following ICSI.
25. Cayan S, Erdemir F, Ozbey I, *et al*. Can varicocelectomy significantly change the way couples use assisted reproductive technologies? *J Urol* 2002; 167:1749–1752.