

Comparison of sperm parameters and fertility rate in subclinical varicocele patients treated with varicocelectomy versus no varicocelectomy: a systematic review



Afdal^{1*}, Fakhri Zuhdian Nasher²

ABSTRACT

Introduction: Subclinical varicocele is defined as non-palpable varicocele which diagnosed solely through imaging examination, namely ultrasonography. Despite the current high prevalence of subclinical varicocele as one of the most common cause of men infertility, there is still lack of evidence regarding the need to perform varicocelectomy among these patients. This systematic review aims to evaluate and compare the sperm parameters and fertility rate of subclinical varicocele patients treated with varicocelectomy versus no treatment.

Methods: A systematic literature search was conducted on the international databases PubMed, Scopus, Cochrane, EMBASE, EBSCOHost, and Google Scholar published in the last ten years up to August 21st 2022. Risk of bias assessment was performed using the Newcastle-Ottawa Scale tools for cohort study and converted regarding the AHRQ standards.

Results: Three cohort studies were conducted in three different countries with 363 patients. The risk of bias assessment revealed that all of the three studies included in this review have good quality and low risk of bias. Varicocelectomy significantly improves sperm parameters in terms of sperm concentration ($p < 0.05$) and sperm motility ($p < 0.05$) while its effects on sperm morphology are not significant ($p > 0.05$). The effects of varicocelectomy on fertility rate are reported by one study by Cantoro et al. as significant ($p = 0.011$).

Conclusion: Varicocelectomy correction has been proved to significantly improve sperm parameters in terms of sperm concentration and motility, while its effect on fertility rate remains unclear and no conclusion can be drawn yet. Therefore, this study recommends further randomized controlled studies with larger sample size in the future to prove the effectiveness of varicocelectomy in subclinical varicocele patients before its implementation in clinical settings.

Keywords: Subclinical varicocele, varicocelectomy, sperm parameter, fertility, systematic review.

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¹Faculty of Medicine, Universitas Riau- Arifin Achmad General Hospital, Pekanbaru, Indonesia;

²Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia;

*Corresponding author:
Afdal;

Faculty of Medicine, Universitas Riau- Arifin Achmad General Hospital, Pekanbaru, Indonesia;
afdaluurologi@gmail.com

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INTRODUCTION

Varicocele remains as one of the most common causes of men infertility, affecting up to 35% of men with infertility problems around the world.¹ However, it is also found in 15% of healthy men without clinical symptoms of infertility.² By definition, varicocele is the condition when the veins within the scrotum enlarge due to defective valves in the veins. While the exact pathogenesis of how varicocele impacts one's fertility is not fully understood until today, some researchers believe that varicocele causes disruption of the testicular drainage, thus, causing increased testicular temperature and dysfunction of sperm production.³ Recently, the oxidative stress theory has

emerged as an important contributory factor due to an association between elevated reactive oxygen species and impaired sperm function in men with varicocele. Additionally, reduction of oxidative stress markers has been noted after varicocele repair.⁴

Varicoceles can be classified according to its severity based on the Dubin and Amelar system⁵, which consists of grade 1, grade 2, and grade 3. Varicoceles are visible through the scrotum and can be palpated while standing, which is classified as grade 3. If the varicoceles are not visible but still can be palpated while standing without Valsalva maneuver, they are regarded as grade 2. Meanwhile, grade 1 varicoceles refer to non-palpable varicoceles in

normal conditions and only palpable during Valsalva maneuver while standing.⁶ Furthermore, an enlargement of the venous plexus which is not palpable even with Valsalva maneuver, but is diagnosed through ultrasound imaging is regarded as a subclinical varicocele (SCV).⁷ The prevalence of subclinical varicocele among infertile men is estimated around 55-70% according to study by Yarborough et al.⁸

However, to this day, the treatment guideline for subclinical varicocele, as proposed by the American Urological Association (AUA) and the American Society for Reproductive Medicine (ASRM) remains unclear regarding the need of surgical correction.^{9,10} These guidelines, on the contrary, recommend

surgical correction strictly for patients with clinical varicocele when the sperm parameters are abnormal. Therefore, patients with subclinical varicocele which still have normal sperm parameters, should not be treated with varicocelectomy. On the other hand, several recently conducted cohort studies revealed that surgical correction might improve sperm parameters in patients with subclinical varicocele. In addition, these studies have also found that surgical varicocelectomy may enhance the fertility rate among couples with the men having subclinical varicocele.^{9,10}

Therefore, this study aims to systematically analyze and compare the sperm parameters and fertility rate between subclinical varicocele patients treated with varicocelectomy versus no varicocelectomy. The author hopes this study may provide clear understanding of current evidence regarding the need for surgical correction in the form of varicocelectomy among patients with subclinical varicocele.

MATERIALS AND METHODS

This study was conducted according to the Cochrane Handbook 6.2 and the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).¹¹

Information sources and search strategy

The author performed a systematic literature search in databases including PubMed, Scopus, Cochrane, EMBASE, EBSCOhost, and Google Scholar, searching for studies implementing varicocelectomy procedures to improve infertility problems among patients with subclinical varicocelectomy up to August 21st 2022 with the following keywords: (varicocelectomy OR subclinical varicocelectomy) AND (subclinical varicocele) AND (sperm analysis OR spermogram OR sperm OR fertility OR paternity). The detailed keywords for each database can be seen in [Table 1](#).

Study eligibility criteria

The authors predetermined the following inclusion criteria: (1) type of study, clinical trials; (2) study population, patients with subclinical varicocele as diagnosed by physician; (3) intervention, varicocelectomy surgical procedure with control group consists of no treatment or no surgical procedure; (4) outcomes, sperm parameters (i.e., sperm motility and morphology), and fertility or paternity rate. Meanwhile, the exclusion criteria are set to: (1) unsuitable study design; (2) incomplete outcome data; (3) irretrievable full-text articles; (5) no control group; and (6) languages other than English.

Data extraction

The following data were extracted: (1) author and year of publication; (2) study characteristics, including study design and location of study; (3) study population, including sample size and mean age; (4) intervention, characteristics of each intervention and control group; and (5) study outcomes, including the assessed parameters, values with and without intervention, as well as significance (p-values) whenever applicable.

Quality assessment

The quality of each study was assessed using the Newcastle-Ottawa Scale for Cohort Studies (NOS-Ottawa). The overall quality of study is then converted based on the Agency for Healthcare Research and Quality (AHRQ) standards into good, fair, or poor quality, as shown in [Table 4](#). Independent author performed this assessment and any disagreements were resolved based on consensus.

RESULTS

Search results and study selection

The results from our initial search from PubMed, Scopus, Cochrane, EMBASE, EBSCOhost, and Google Scholar using previously mentioned strategy resulted in a total of 1,465 studies ([Figure 1](#)). Before the screening process, we excluded 451 studies either deduplicated or 852 studies

Table 1. Table of keywords for literature search.

Database	Search strategy	Findings	Included Studies
PubMed	("varicocelectomy"[MeSH Terms] OR varicocelectomy[Text Word] OR subclinical varicocelectomy) AND ("subclinical varicocele"[MeSH Terms] OR subclinical varicocele[Text Word]) AND (sperm analysis OR "spermatozoa"[MeSH Terms] OR sperm[Text Word] OR sperm analysis OR fertility rate)	24	2
Scopus	TITLE-ABS-KEY ((varicocelectomy OR subclinical varicocelectomy) AND (subclinical varicocele) AND (sperm analysis OR spermogram OR sperm OR fertility OR paternity))	55	1
EBSCOhost	(varicocelectomy OR subclinical varicocelectomy) AND (subclinical varicocele) AND (sperm analysis OR spermogram OR sperm OR fertility OR paternity)	42	0
Cochrane	("varicocelectomy"[MeSH Terms] OR varicocelectomy[Text Word] OR subclinical varicocelectomy) AND ("subclinical varicocele"[MeSH Terms] OR subclinical varicocele[Text Word]) AND (sperm analysis OR "spermatozoa"[MeSH Terms] OR sperm[Text Word] OR sperm analysis OR fertility rate)	11	0
EMBASE	(varicocelectomy OR subclinical varicocelectomy) AND (subclinical varicocele) AND (sperm analysis OR spermogram OR sperm OR fertility OR paternity)	83	0
Google Scholar	(varicocelectomy OR subclinical varicocelectomy) AND (subclinical varicocele) AND (sperm analysis OR spermogram OR sperm OR fertility OR paternity)	1,250	3

for other reasons. Furthermore, 81 and 57 studies were excluded after title and abstract screening, respectively. Studies that are not related to our main topics are excluded in this phase. In addition, 21 studies were further excluded since 8 studies only measured qualitative outcomes, 6 studies used other language than English, and 7 studies were not available in full-text versions. The final search yielded in a total of 3 studies, consisting of mostly prospective cohort studies to be included in further analysis.

Study characteristics

All three studies included are cohort studies conducted in three different countries with different socioeconomic backgrounds, namely Spain, Italy, and Iraq. These studies were conducted in a range of years between 2012-2022. Among the included studies, participants were adult patients with subclinical varicocele as diagnosed by their physicians. Subclinical varicocele was defined as a finding from ultrasonography (USG). Patients included in these studies are not related to other infertility problems. Moreover, the patients' partners were normal without infertility problems as clinically checked by gynecologists. On the other hand, the control group is patients not given any surgical intervention. Outcomes measured via sperm parameters (including sperm concentration, sperm motility, and sperm morphology) and fertility or paternity rates. The detailed characteristics of included studies are shown in Table 2, while the detailed study outcomes are presented in Table 3.

Risk of bias assessment

The results from bias assessment were shown in Table 4 with the details shown in Appendix 1. In summary, we found that all studies included in this review have good quality in terms of AHRQ standards. Therefore, we found that all studies included in this review were of low risk of bias.

Improvement of sperm parameters after varicocelectomy

Sperm concentration

Studies by Cantoro et al. and Hammadi et al. reported the effect of varicocelectomy

in terms of sperm parameters. The first indicator of sperm is concentration. These two studies consistently reported similar findings: the statistically significant differences of improvement regarding sperm concentration of individuals treated with varicocelectomy compared to no treatment ($p < 0.05$).

Sperm motility

Second observed sperm parameter is sperm motility. The study by Cantoro et al. and Hammadi et al. reported similar superiority of the group of patients treated with varicocelectomy versus no treatment. These studies have shown that the percentage of motile sperms increases significantly after varicocelectomy procedure ($p < 0.05$).

Sperm morphology

For the third parameter, namely sperm morphology, study by Cantoro et al. and Hammadi et al. again reported similar superiority of intervention group when compared to control group. In this case, these studies examined the percentage sperm with normal morphology compared to the total sperm. However, the differences are not statistically significant ($p > 0.05$).

Sperm DNA fragmentation

Study by Garcia-Peiro et al. examined the sperm samples using DNA fragmentation technique. This examination technique results in several indicators, such as the terminal transferase dUTP nick-end labeling (TUNEL), sperm chromatin structure assay (SCSA), sperm chromatin

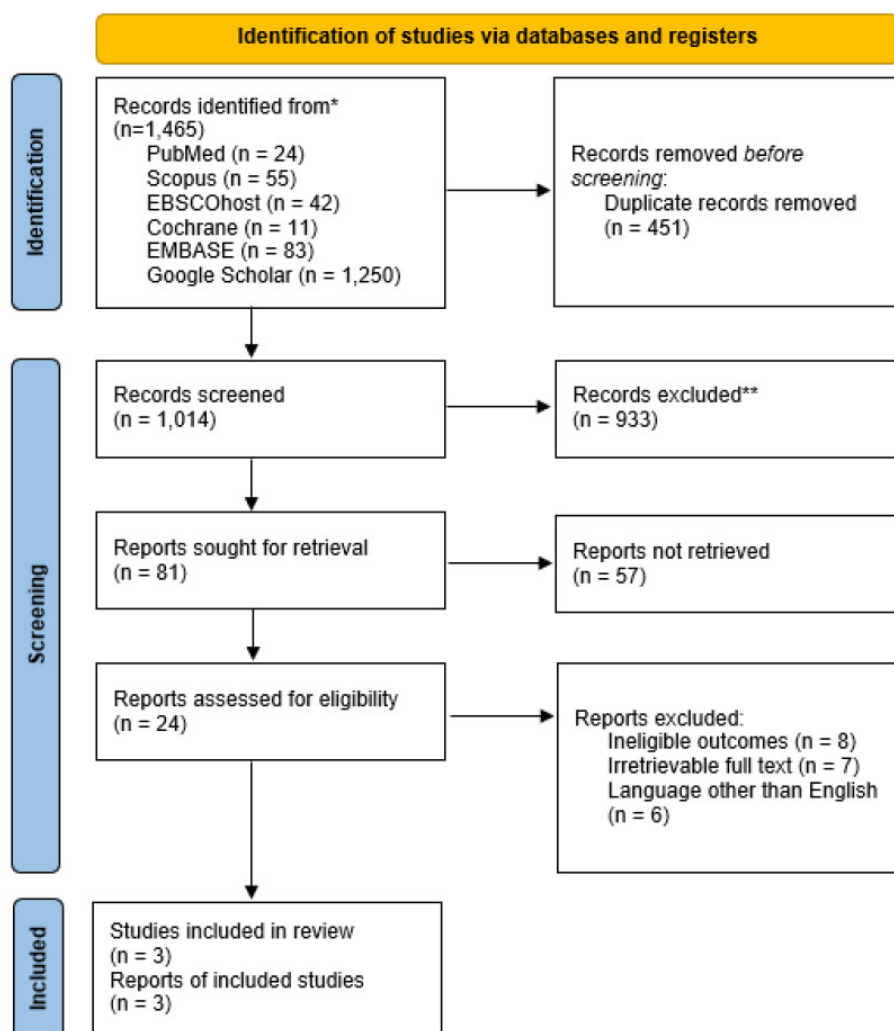


Figure 1. Diagram flow of literature search strategy.

dispersion (SCD), and DNA degraded sperm (DDS). However, for each parameter, Garcia-Peiro et al reported no significant effect of varicocelectomy on subclinical varicocele patients regarding sperm's DNA fragment quality.

Increased pregnancy rates after varicocelectomy

Another parameter which needs to be assessed when determining the benefits of varicocelectomy is pregnancy rates. Study by Cantoro et al. reported the pregnancy rate of the patient's partners after approximately 39 months following the procedure. This resulted in a statistically significant differences of pregnancy rates between the intervention group and control group, 46.3% and 11.8% respectively (p=.011). Furthermore, annual pregnancy rate in the group of patients treated with varicocelectomy equals to 11%, compared to 4% in those without treatment.

DISCUSSION

Current guidelines on subclinical varicocele treatment

The primary choice of treatment for varicoceles is surgical procedures. However, current guidelines proposed by the American Urological Association (AUA) and the American Society of Reproductive Medicine (ASRM) suggest that surgery is not indicated for subclinical varicocele with unpalpable varicocele, where the sperm parameters are actually normal. These recommendations were proposed due to previous systematic review of varicocelectomy for subclinical varicocele patients by Kim et al.¹⁵ which demonstrates no significant benefits of varicocele repair in a non-clinical varicocele patients in terms of pregnancy rates and seminal parameters. Therefore, the current AUA/ASRM guideline recommends that clinicians should not perform varicocelectomy if patients present with non-palpable varicoceles which are detected solely by imaging. This is a strong recommendation with grade C level of evidence.⁹

Mechanisms of varicocelectomy

Theoretically, varicocelectomy is defined as a surgical procedure to remove the swollen veins in scrotal area or also called

Table 2. Study characteristics.

Author; year of publication	Study design	Location	Subject characteristics		
			Sample characteristics	Sample number; Mean age (SD)	Follow-up duration
Garcia-Peiro et al. ¹² (2014)	Cohort study	Bellaterra, Spain	Infertile male patients with subclinical varicocele were diagnosed by scrotal Doppler ultrasonography (ScV). Patients were surgically treated with varicocelectomy. Patients with genitourinary inflammation, leukocytospermia, or altered hormonal profiles were excluded from the study.	Intervention: 10 patients; 25-35 y Control: 16 patients; 25-35 y	6-12 months
Cantoro et al. ¹³ (2015)	Cohort study	Ancona, Italy	Patients diagnosed with subclinical left-sided varicocele, primary infertility persisting >1 year despite regular unprotected intercourse, one or more abnormal semen parameters, and without other male infertility factor. The partners of these patients were normal without infertility problems as evaluated by gynecologist	Intervention: 218 patients; 29.4 ± 5.1 y Control: 119 patients; 31.3 ± 4.2 y	39.4 ± 6.5 months
Hammadi et al. ¹⁴ (2015)	Cohort study	Baghdad, Iraq	Patients with subclinical varicocele diagnosed by Doppler ultrasound studies presented to Al- Yarmuok teaching Hospitals seeking advice for infertility treatments. Exclusion criteria include recurrent varicocele, azoospermic (zero sperms in ejaculate) or have cause of infertility other than varicocele.	Intervention: N/A Control: N/A	3-6 months

varicoceles. Varicocelectomy mainly consists of two different techniques, namely microscopic varicocelectomy and laparoscopic varicocelectomy.¹⁶ Both techniques are performed under general anesthesia and usually do not need any inpatient care.¹⁷ Firstly, microscopic varicocelectomy is the procedure performed through a small incision in the subinguinal or inguinal region. This procedure uses a powerful microscope to help the surgeon identify small veins that need to be ligated. Microscopic varicocelectomy usually lasted for only 2-3 hours and recommended as the gold-standard approach, however this applies for clinical varicocele patients only. The superiority of microscopic varicocelectomy was based on its high success rates without significant complications.¹⁸

On the other hand, other technique is also available, called laparoscopic varicocelectomy. In this technique, the surgeon will perform varicocelectomy using a video camera and surgical equipment, passing through an incision in the lower abdomen area. The downside of this technique is that there will be fewer veins to ligate because of the characteristic of vein networks in that area. However, this procedure is relatively fast compared to microscopic varicocelectomy, usually only last 30-40 minutes.^{17,19}

Efficacy of varicocelectomy on subclinical varicocele

In this study, the author examines the efficacy of the varicocelectomy procedure on subclinical varicocele cases by determining sperm parameters and fertility rate. Sperm parameters assessed include sperm concentration, sperm motility, and sperm morphology. Sperm concentration was defined as the sperm count per milliliter (mL). The normal range of sperm concentration in adult men is 15-200 million per mL. Meanwhile, sperm motility is defined as sperm with progressive forward motions of at least 25 micrometers every second. The normal range of sperm motility is 32-75 percent. Lastly, sperm morphology, while consisting of various types, is indicated abnormal if the morphology of the sperm unable it to have progressive motility. The normal range of sperm morphology is

Table 3. Study outcomes.

Author; year of publication	Study outcomes		
	Parameters	Intervention group	Control group
Garcia-Peiro et al. ¹² (2014)	TUNEL (%)	28.95 (11.06–53.65)	31.38 (17.99–74.10)
	SCSA (%)	26.12 (8.99–68.77)	21.30 (12.94–74.48)
	SCD (%)	29.00 (24.00–70.00)	37.75 (19.50–78.00)
	DDS (by SCD) (%)	17.25 (10.00–30.00)	19.50 (11.50–37.00)
Cantoro et al. ¹³ (2015)	Sperm concentration (million/mL)	Baseline: 16.5 ± 4.6 Postintervention: 37.4 ± 10.7	Baseline: 18.4 ± 6.1 Postintervention: 17.5 ± 5.6
	Sperm total motility (%)	Baseline: 32.4 ± 10.6 Postintervention: 46.6 ± 9.4	Baseline: 30.7 ± 11.7 Postintervention: 31.5 ± 9.1
Hammadi et al. ¹⁴ (2015)	Sperm normal morphology (%)	Baseline: 27.6 ± 5.2 Postintervention: 24.3 ± 6.1	Baseline: 26.9 ± 4.4 Postintervention: 24.0 ± 5.6
	Pregnancy rate (%)	46.3	11.8
Hammadi et al. ¹⁴ (2015)	Annual pregnancy rate (%)	14	N/A
	Sperm concentration (million/mL)	62.7 ± 13.6	40.4 ± 14.7
Hammadi et al. ¹⁴ (2015)	Percentage of motile sperms	61.85 ± 21.07	64.75 ± 23.85
	Percent of sperm with normal morphology	42.6 ± 16.9	39.2 ± 22.4

*Significant results. Abbreviations: TUNEL: Terminal transferase dUTP nick-end labeling; SCSA: sperm chromatin structure assay; SCD: sperm chromatin dispersion (SCD); DDS: DNA degraded sperm; NS: non-significant.

4-48 percent.²⁰ On the other hand, fertility rate is the number of children born alive from the mother, in this case, the partner of the patients.²¹

From this systematic review, the author found different findings from a previous study by Kohn et al which concluded that varicolectomy only improves the clinical aspect of sperm parameters without significant effects on fertility rate when done on subclinical varicocele patients.³ This study by Kohn et al. concluded that correction is only needed in men with already impaired semen parameters; while in this study, it is not clear about the inclusion or exclusion of the patients based on their semen parameters. In this study, it is proposed that varicolectomy improves sperm parameters, in terms of its concentration and motility, as well as the pregnancy rate (p=.011). However, with these findings only found in one study by Cantoro et al¹³, the author concludes that no strong conclusion can be drawn from current best evidence. Therefore, more studies should be conducted to prove the effectiveness of varicolectomy on subclinical varicocele patients.

Future recommendation

Our findings from this conducting this systematic review proved that although theoretically varicolectomy holds a potential impact to improve sperm parameters and fertility rate among subclinical varicocele patients, no strong conclusion can be drawn from current best evidences. Therefore, to conclude the final recommendation, we still need to conduct randomized controlled trials in adult patients with subclinical varicocele to confirm the effect of varicolectomy in improving sperm parameters and fertility rate.

Strengths and limitations

This systematic review study has several strengths and limitations. Firstly, this study is the most updated systematic review, to our knowledge, assessing the effectiveness of varicolectomy in subclinical varicocele patients in terms of sperm parameters and fertility rate. Secondly, the outcomes from included studies are pretty similar, so they can be compared parallelly. However, the author also identified several important

Table 4. Quality assessment of selected studies (AHRQ grading calculation).

Study	Selection			Comparability		Outcome			Total quality score	AHRQ Standard
	Representativeness of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Design or analysis controlled for confounders	Assessment of outcome	Follow-up length	Loss to follow-up rate		
Garcia-Peiro et al. ¹² (2014)	a(*)	a(*)	a(*)	a(*)	b(*)	b(*)	a(*)	a(*)	8	Good
Cantoro et al. ¹³ (2015)	a(*)	a(*)	a(*)	a(*)	b(*)	b(*)	a(*)	a(*)	8	Good
Hammadi et al. ¹⁴ (2015)	a(*)	a(*)	a(*)	a(*)	b(*)	b(*)	a(*)	b(*)	8	Good

The study is considered:

- Good: 3 or 4 stars in selection domain AND 1 star in comparability domain AND 2 or 3 stars in outcome domain.
 - Fair: 2 stars in selection domain AND 1 star in comparability domain AND 2 or 3 stars in outcome domain.
 - Poor: 0 or 1 stars in selection domain AND 0 star in comparability domain AND 0 or 1 stars in outcome domain.
- (*) Stars are given for each of the study aspects.

limitations in this study. First, the included studies have relatively high heterogeneity in terms of included subjects, with no clear inclusion and exclusion criteria, so we do not know whether the included patients have previously normal or abnormal sperm parameters before the treatment. This is highly important as previous study shows that varicocelectomy is actually beneficial if the patient has abnormal sperm parameters before the treatment. The second limitation of this review study is that the author could not perform meta-analysis due to limited amount of data from recent studies. Therefore, as a recommendation for the future, the author recommends further studies in the form of a randomized controlled trials (RCT) with bigger sample size to conclude a solid recommendation for clinical settings.

CONCLUSION

In conclusion, varicocelectomy correction in subclinical varicocele patients has been clinically significant in improving sperm parameters, namely sperm concentration and sperm motility rate. However, it is still unclear whether varicocelectomy in subclinical varicocele patients can improve the fertility rates among couples. Due to limited number of data and no available data from randomized controlled trials from recent studies, this study recommends the need to perform randomized studies in the future regarding this issue to conclude a solid recommendation for clinical settings finally.

CONFLICT OF INTEREST

Author declares there is no conflict of interest regarding publication of this study.

ETHICAL CONSIDERATION

Ethical clearance in systematic review is not mandatory.

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REFERENCES

1. Alsaikhan B, Alrabeeh K, Delouya G, Zini A. Epidemiology of varicocele. *Asian J Androl* [Internet]. 2016;18(2):179–81. Available from: <https://pubmed.ncbi.nlm.nih.gov/26763551>
2. Kroese ACJ, de Lange NM, Collins J, Evers JLH. Surgery or embolization for varicoceles in subfertile men. *Cochrane Database Syst Rev* [Internet]. 2012; Available from: <http://dx.doi.org/10.1002/14651858.cd000479.pub5>
3. Kohn TP, Kohn JR, Pastuszak AW. Varicocelectomy before assisted reproductive technology: are outcomes improved? *Fertil Steril* [Internet]. 2017;108(3):385–91. Available from: <http://dx.doi.org/10.1016/j.fertnstert.2017.06.033>
4. Tiseo BC, Esteves SC, Cocuzza MS. Summary evidence on the effects of varicocele treatment to improve natural fertility in subfertile men. *Asian J Androl* [Internet]. 2016;18(2):239–45. Available from: <https://pubmed.ncbi.nlm.nih.gov/26806080>
5. Dubin L, Amelar RD. Varicocele Size And Results of Varicocelectomy in Selected Subfertile Men with Varicocele*. *Fertil Steril* [Internet]. 1970;21(8):606–9. Available from: [http://dx.doi.org/10.1016/s0015-0282\(16\)37684-1](http://dx.doi.org/10.1016/s0015-0282(16)37684-1)
6. Patil V, Shetty SMC, Das SK. Redefining the Criteria for Grading Varicoceles Based on Reflux Times. *Ultrasound Q* [Internet]. 2016;32(1):82–5. Available from: <http://dx.doi.org/10.1097/ruq.0000000000000168>
7. Belay RE, Huang GO, Shen JKC, Ko EYK. Diagnosis of clinical and subclinical varicocele: how has it evolved? *Asian J Androl* [Internet]. 2016;18(2):182–5. Available from: <https://pubmed.ncbi.nlm.nih.gov/26780869>
8. Yarborough MA, Burns JR, Keller FS. Incidence and Clinical Significance of Subclinical Scrotal Varicoceles. *J Urol* [Internet]. 1989;141(6):1372–4. Available from: [http://dx.doi.org/10.1016/s0022-5347\(17\)41311-5](http://dx.doi.org/10.1016/s0022-5347(17)41311-5)
9. Schlegel PN, Sigman M, Collura B, De Jonge CJ, Eisenberg ML, Lamb DJ, et al. Diagnosis and Treatment of Infertility in Men: AUA/ASRM Guideline Part I. *J Urol* [Internet]. 2021;205(1):36–43. Available from: <http://dx.doi.org/10.1097/ju.0000000000001521>
10. Choksi A, Harnisch B, Honig S. What Every Provider Should Know About the 2020–2021 Updated AUA/ASRM Guidelines on Male Factor Infertility. *Curr Sex Heal Reports* [Internet]. 2022;14(2):31–8. Available from: <http://dx.doi.org/10.1007/s11930-022-00325-y>
11. *Cochrane Handbook for Systematic Reviews of Interventions* [Internet]. John Wiley & Sons, Ltd; 2008. Available from: <http://dx.doi.org/10.1002/9780470712184>
12. García-Peiró A, Ribas-Maynou J, Oliver-Bonet M, Navarro J, Checa MA, Nikolaou A, et al. Multiple determinations of sperm DNA fragmentation show that varicocelectomy is not indicated for infertile patients with subclinical varicocele. *Biomed Res Int* [Internet]. 2014/05/20. 2014;2014:181396. Available from: <https://pubmed.ncbi.nlm.nih.gov/24967335>
13. Cantoro U, Polito M, Muzzonigro G. Reassessing the Role of Subclinical Varicocele in Infertile Men With Impaired Semen Quality: A Prospective Study. *Urology* [Internet]. 2015;85(4):826–30. Available from: <http://dx.doi.org/10.1016/j.urology.2015.01.015>
14. J. Hammadi I, Th. Saeed G, How. Abed Tawney R. Evaluation of the Effects of Surgical Varicocelectomy on the Seminal Fluid Parameters in Patients with Clinical and Subclinical Varicocele. *J Fac Med* [Internet]. 2015;57(1):40–4. Available from: <http://dx.doi.org/10.32007/med.1936/jfacmedbagdad.v5711.10>
15. Kim HJ, Seo JT, Kim KJ, Ahn H, Jeong JY, Kim JH, et al. Clinical significance of subclinical varicocelectomy in male infertility: systematic review and meta-analysis. *Andrologia* [Internet]. 2015;48(6):654–61. Available from: <http://dx.doi.org/10.1111/and.12495>
16. Hai-ling J, Li-fu Z, Hang Y, Xiao-ping C, Shu-dong W, Xue-ke L, et al. Comparison of accuracy and stability of estimating winter wheat chlorophyll content based on spectral indices [Internet]. 2014 IEEE Geoscience and Remote Sensing Symposium. IEEE; 2014. Available from: <http://dx.doi.org/10.1109/igarss.2014.6947104>
17. Wang Q, Liu Y, Wang L. Open, Laparoscopic, and Microsurgical Varicocelectomy for Male Infertility: a Systematic Review and Meta-analysis. *Indian J Surg* [Internet]. 2019;82(4):478–85. Available from: <http://dx.doi.org/10.1007/s12262-019-02011-1>
18. Mehta A, Goldstein M. Microsurgical varicocelectomy: a review. *Asian J Androl* [Internet]. 2012/11/12. 2013 Jan;15(1):56–60. Available from: <https://pubmed.ncbi.nlm.nih.gov/23147467>
19. Tan SM, Ng FC, Ravintharan T, Lim PHC, Chng HC. Laparoscopic varicocelectomy: technique and results. *Br J Urol* [Internet]. 1995;75(4):523–8. Available from: <http://dx.doi.org/10.1111/j.1464-410x.1995.tb07276.x>
20. Tang Q, Pan F, Wu X, Nichols CE, Wang X, Xia Y, et al. Semen quality and cigarette smoking in a cohort of healthy fertile men. *Environ Epidemiol (Philadelphia, Pa)* [Internet]. 2019 Aug 13;3(4):e055–e055. Available from: <https://pubmed.ncbi.nlm.nih.gov/31538136>
21. Vander Borgh M, Wyns C. Fertility and infertility: Definition and epidemiology. *Clin Biochem* [Internet]. 2018;62:2–10. Available from: <http://dx.doi.org/10.1016/j.clinbiochem.2018.03.012>



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