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INPLASY

Effect of varicocele surgical repair on antisperm antibody positivity rate in patients with clinical varicocele: a systematic review and meta-analysis protocol

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 8 May 2026 and was last updated on 8 May 2026.

INTRODUCTION

Review question / Objective To assess the effect of varicocele surgical repair on the antisperm antibody (ASA) positivity rate in infertile men with clinical varicocele, and to compare the efficacy of different surgical techniques (microsurgical, laparoscopic, and high ligation) for this immunological outcome.

Condition being studied Varicocele is defined as abnormal dilation and tortuosity of the pampiniform plexus veins within the spermatic cord. It is one of the most common correctable causes of male infertility, affecting approximately 15% of the general male population and up to 35% of men with primary infertility. Varicocele can impair spermatogenesis through multiple mechanisms, including testicular hyperthermia, venous stasis, oxidative stress, and reflux of renal and adrenal metabolites. In addition, varicocele may disrupt the blood–testis barrier, leading to exposure of sperm antigens to the immune system and subsequent production of antisperm antibodies (ASA). ASA can bind to sperm surface antigens, impair sperm motility, hinder cervical mucus penetration, interfere with acrosome reaction, and reduce fertilization capacity. Therefore, ASA positivity is considered an important immunological cause of male infertility. Although varicocele repair is widely performed to improve semen parameters and pregnancy rates, its effect on ASA status is not well established. This systematic review and meta-analysis focuses on the relationship between varicocele repair and ASA positivity in men with clinical varicocele.

METHODS

Participant or population Adult men (aged ≥18 years) with clinically palpable varicocele (diagnosed by physical examination and/or Doppler ultrasound), with or without abnormal semen parameters. Patients with subclinical varicocele (diagnosed only by ultrasound without palpable findings) or adolescent varicocele (age <18 years) were excluded.

Intervention Varicocele surgical repair (varicocelectomy), including microsurgical varicocelectomy, laparoscopic varicocelectomy, open high ligation (retroperitoneal or inguinal approach), and other surgical techniques (e.g., subinguinal, embolization, or sclerotherapy where applicable). No restriction on surgical approach.

Comparator Preoperative baseline status (before-after comparison). No untreated concurrent control group was used because all included studies were self-controlled (pre- and post-surgery). For studies that reported both treated and untreated groups, the untreated observation group was also considered as a comparator when available.

Study designs to be included We will include before-after (pre-post) studies, including case series, prospective or retrospective cohort studies, and randomized controlled trials (RCTs) from which preoperative and postoperative antisperm antibody (ASA) data can be extracted (i.e., using the study as a self-controlled analysis).

Eligibility criteria Inclusion criteria: (1) Before-after (pre-post) studies of varicocele surgical repair in men with clinical (palpable) varicocele; (2) reporting antisperm antibody (ASA) positivity rate (or ASA levels) before and after surgery; (3) providing extractable data (number of ASA-positive cases/ total patients, or mean ± SD); (4) full-text available.
Exclusion criteria: (1) Subclinical varicocele or adolescent patients (age <18 years); (2) no preoperative ASA data; (3) studies not reporting extractable data (e.g., only p-values or directional statements); (4) case reports (n<10), reviews, conference abstracts without full text, animal studies, or in vitro studies; (5) duplicate publications.

Information sources Electronic databases searched: PubMed, Web of Science, EMbase, Cochrane Library, CNKI (China National Knowledge Infrastructure), VIP (Chinese Scientific Journals Database), Wanfang Data, and SinoMed (Chinese Biomedical Literature Database). The search will be performed from database inception to April 2026. No language restrictions will be applied. Reference lists of included studies and relevant reviews will be manually screened for additional eligible studies. Grey literature and trial registries will not be searched.

Main outcome(s) Outcome: Antisperm antibody (ASA) positivity rate.
Timing: Measured before surgery (baseline) and after surgery (postoperative follow-up). The primary time point for analysis is the first postoperative measurement (3 months in most studies, range 3–12 months).
Effect measure: Risk ratio (RR) with 95% confidence interval (CI). A random-effects model will be used due to anticipated heterogeneity. RR < 1 indicates a reduction in ASA positivity after surgery.

Quality assessment / Risk of bias analysis The methodological quality of included studies will be assessed independently by two reviewers using the JBI Critical Appraisal Checklist for Case Series (10 items). Each item is rated as "yes," "no," "unclear," or "not applicable." Studies are categorized as high quality (≥8 "yes"), moderate quality (6–7 "yes"), or low quality (≤5 "yes"). Disagreements will be resolved by discussion or a third reviewer. Results will be ented in a summary table. No studies will be excluded solely based on quality; however, sensitivity analysis will be performed excluding moderate-quality studies to test robustness.

Strategy of data synthesis Meta-analysis will be performed using RevMan 5.4. For the primary outcome (ASA positivity rate, dichotomous), the risk ratio (RR) with 95% confidence interval (CI) will be calculated. For continuous outcomes (ASA level), the standardized mean difference (SMD) with 95% CI will be calculated if heterogeneity is acceptable; otherwise, results will be described narratively. A random-effects model (DerSimonian-Laird) will be used regardless of heterogeneity, given anticipated clinical and methodological diversity. Heterogeneity will be assessed using the I^2 statistic (I^2 < 50%: low-to-moderate; ≥50%: substantial; ≥75%: considerable). Statistical significance will be set at $P < 0.05$. All analyses are two-tailed.

Subgroup analysis Subgroup analysis will be performed for the primary outcome (RR) according to surgical technique, categorized as: (1) microsurgical varicocelectomy; (2) laparoscopic varicocelectomy; (3) high ligation / open conventional repair. Subgroup differences will be tested using the Chi^2 test, and I^2 will be reported for subgroup differences.

Sensitivity analysis Sensitivity analysis will be conducted by: (1) excluding studies with moderate methodological quality (JBI score < 8) and re-pooling the effect estimate; (2) using a fixed-effects model instead of the random-effects model to assess the impact of model choice. If sufficient studies are available, a leave-one-out analysis will also be performed by sequentially

excluding each study to evaluate its influence on the pooled result.

Country(ies) involved China.

Keywords varicocele; antisperm antibody; varicocelectomy; male infertility; meta-analysis.

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