Efficacy of varicocelectomy in improving semen parameters: new meta-analytical approach

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CRD summary
This review found that semen parameters in infertile men with palpable varicocele are improved by the use of surgical varicocelectomy. The review suffers from severe limitations in terms of the application of inclusion criteria, limited literature search, lack of study details and inappropriate analysis, so the findings are unlikely to be reliable.

Authors' objectives
To investigate the effects of varicocelectomy on semen parameters.

Searching
MEDLINE, EMBASE and BIOSIS Previews were searched from 1985 (end date unclear); the keywords were reported. Reference lists were handsearched. No language restrictions were applied.

Study selection
Randomised controlled trials and observational studies of varicocelectomy (high ligation or inguinal microsurgery) that provided at least three semen analyses (sperm count, motility and morphology) per patient before and after the intervention, in infertile men with unilateral or bilateral palpable varicocele with at least one abnormal semen parameter, were eligible for inclusion. Studies that assessed embolisation or selective catheterisation of the internal spermatic vein were excluded. Studies of men with subclinical varicoceles were excluded, as were studies conducted in adolescents. Additional post hoc inclusion criteria appear to have been applied: for example, for techniques only evaluated in a small number of studies. Details of the included studies were not reported. The outcomes reported in the review were changes in sperm concentration, motility and morphology before and after the intervention.

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The methodological quality of the studies was assessed, based on a new scoring method the authors had developed. Features assessed were:

- selection/follow-up (cohort derivation, participant recruitment, restricted sample);
- confounding (duration of follow-up, evaluation of confounders, analyses before and after intervention the same);
- information/detection bias (follow-up same before and after treatment, objective outcome assessment, ascertainment of outcome performed at same location before and after treatment); and
- other features (combination of outcomes across heterogeneous groups, use of established guidelines for semen analysis, evaluation of severity of varicocele).

The studies were assigned a methodological quality score for each of the four categories assessed. A minimum score was assigned for each category; studies which failed to reach the minimum score on at least two areas were excluded. If studies failed to reach the minimum score for only one category, then it was re-examined and included in the review if thought likely to be unbiased.

Two reviewers independently assessed the quality of the studies.

Data extraction
It appears that data were only extracted for the intervention groups, and that differences in semen analyses before and after the intervention were calculated.
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

**Methods of synthesis**

Weighted mean differences were calculated using a random-effects model, separately for each semen measure and type of surgical procedure. The authors did not state that they assessed heterogeneity, but the results of χ² tests were included in the figures.

**Results of the review**

Seventeen studies were included (number of participants unclear).

- **Microsurgery** (10 studies): sperm concentration increased by 9.71 x 10⁶/mL (95% confidence interval, CI: 7.34, 12.08, p<0.001). Average motility increased by 9.92% (95% CI: 4.90, 14.95, p<0.001).

- **High ligation** (8 studies): sperm concentration increased by 12.03 x 10⁶/mL (95% CI: 5.71, 18.35, p<0.001). Average motility increased by 11.72% (95% CI: 4.33, 19.12, p=0.002; based on 7 studies).

Both types of surgery combined (7 studies): World Health Organization sperm morphology improved by 3.16% (95% CI: 0.72, 5.60, p=0.01).

There was strong evidence of heterogeneity for all reported meta-analyses (p<0.0001).

**Authors’ conclusions**

Semen parameters in infertile men with palpable varicocele are improved by the use of surgical varicocelectomy.

**CRD commentary**

The review addressed a focused question and inclusion criteria were defined. However, 68 studies fulfilled these initial criteria and only 17 were included in the review: 26 studies were excluded as they did not attain the required quality scores and an additional 25 were excluded for other, unspecified reasons. The literature search was limited to three electronic databases with no additional attempts to locate studies, especially unpublished studies. The review may therefore be subject to publication bias. A detailed methodological quality assessment was carried out, but the results of this were neither presented nor considered in the results. Studies that did not fulfil a certain quality score were excluded. Given the problems associated with the use of quality scores this approach is questionable. It would have been preferable to have included all studies and then investigated the effects of different sources of bias on the study results. Appropriate steps were taken to minimise bias and errors in the quality assessment, but it is unclear whether such steps were also taken when assessing studies for inclusion and extracting the data.

No details of the included studies were reported, so it is not possible to comment on the likely reliability of the results or the generalisability of the review findings. A meta-analysis may have been appropriate, but there was considerable heterogeneity between the studies which was not investigated. Details on the methods of analysis were lacking, but it appears that data from control groups were ignored and only within-patient comparisons were used to calculated mean differences. Such an approach can be extremely misleading and is not appropriate, especially as it appears that some randomised controlled trials were included in the review. Given the severe limitations of this review in terms of the application of inclusion criteria, limited literature search, lack of study details and inappropriate analysis, the review findings are unlikely to be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that couples should be informed that varicocelectomy can improve semen parameters.

**Research:** The authors did not state any implications for further research.

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