Fibroids and infertility: an updated systematic review of the evidence
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CRD summary
This review assessed the effect of myomectomy in improving fertility outcomes in women with uterine fibroids. The authors concluded that myomectomy could improve clinical pregnancy rates in women with submucosal fibroids, but that there was insufficient evidence for those with intramural fibroids. Given potential methodological weaknesses in the review process, the extent to which this conclusion is reliable is unclear.

Authors' objectives
To assess the effect of myomectomy in improving fertility outcomes in women with uterine fibroids. The authors also investigated the effect of fibroids on fertility outcomes; this aspect does not form part of this abstract.

Searching
PubMed and the Cochrane Library were searched without date or language restrictions for relevant studies. Search terms were reported. Bibliographies were cross-checked, and hand searches of the following conference proceedings were carried out for the years 1998 to 2004: Society for Gynecologic Investigation, the American Society for Reproductive Medicine, the American Association of Gynecologic Laparoscopists, and the Pacific Coast Fertility Society.

Study selection
The inclusion criteria appeared to be controlled studies of women with uterine fibroids undergoing myomectomy to improve outcomes relating to clinical pregnancy, spontaneous abortion, ongoing pregnancy/live birth rate, implantation rate, and pre-term delivery.

The included control groups were women with or without fibroids, some of whom had undergone treatment with in vitro fertilisation, intracytoplasmic sperm injection, or were oocyte donor recipients. The mean age of participants (where reported) ranged from 34 to 41 years, and their fibroids were classified as intramural (lesions residing within myometrium without distortion of the endometrial cavity), submucosal (lesions causing distortion of the endometrial cavity), and subserosal (those extending predominantly outside the myometrium).

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

Assessment of study quality
Study quality was independently assessed by two reviewers using a checklist, with an apparent maximum score of 18. A mean score was calculated on the basis of study design, loss to follow-up, the methods used, and uniformity of evaluation across the included studies.

Data extraction
Data were extracted to calculate risk ratios (RR), odds ratios (OR), log (OR), and corresponding 95% confidence intervals (CI). Study authors were contacted for missing data, or to verify existing data, where necessary.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Summary estimates were pooled in a random-effects meta-analysis. In the analysis, women with both submucosal and intramural fibroids were classified as submucosal; and those with intramural and subserosal fibroids were classified as intramural. Statistical heterogeneity was assessed using the Cochran Q test, and explored further in meta-regression analysis using the study quality score as the independent variable and the log (OR) as the dependent variable.
Publication bias was explored using a funnel plot, and tested using the Begg and Mazumdar rank correlation test. The Duval and Tweedie trim and fill method was used to estimate the number of missing studies. The Rosenthal fail-safe N
method was used to calculate the number of negative studies required to nullify the intervention effect.

**Results of the review**

Seven studies (n=536 women) were included in the meta-analysis. There was one RCT (n=170 women); two prospective studies (n=112 women); and four retrospective studies (n=254 women). Summary quality scores were not reported for each study, but the RCT appeared to be well-conducted. The remaining studies did not fulfil all criteria. Publication bias was not reported to impact on the authors’ conclusion.

Women with submucosal fibroids who underwent myomectomy were reported to have a statistically significant higher clinical pregnancy rate when compared to women with fibroids in place (RR 2.03, 95% CI 1.08 to 3.83; two studies). There were no other statistically significant differences in this group in terms of ongoing pregnancy/live birth rate or spontaneous abortion rate; for any outcome in women with intramural fibroids (based on four studies); or when women undergoing myomectomy were compared with infertile women with no fibroids.

Study quality was not a significant contributory factor to the reported heterogeneity amongst the included studies (results were not reported).

**Authors' conclusions**

Myomectomy appeared to improve fertility outcomes in women with submucosal fibroids. There was insufficient evidence to support this intervention in women with intramural fibroids.

**CRD commentary**

The review question was clear, but the inclusion criteria were not sufficiently well-specified to allow replication. The search strategy appeared to be limited in its reference to electronic sources, but there were adequate attempts to minimise the effects of potential language and publication biases. The review process was poorly reported, which made it difficult to assess whether attempts had been made to minimise error and bias in the processes of study selection and validity assessment. Quality assessment results were not summarised for each study, although a basic interpretation of the components was possible in relation to the subset of intervention studies. Study details were provided, and the method of synthesis appeared to be appropriate in the presence of heterogeneity (although statistical heterogeneity was not reported). The authors' conclusion reflects the limited evidence presented, but the extent to which this is reliable is unclear given some of the potential methodological weaknesses identified above.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that future high quality research should concentrate on the treatment of intramural fibroids, with focus on accurate evaluation of size, number and proximity to the endometrium.

**Funding**

Not stated.

**Bibliographic details**


**PubMedID**

18339376

**DOI**

10.1016/j.fertnstert.2008.01.051

**Original Paper URL**

http://www.fertstert.org/article/S0015-0282(08)00146-5/abstract
Additional Data URL

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Female; Fertility /physiology; Gynecologic Surgical Procedures /adverse effects /rehabilitation; Humans; Infertility, Female /etiology; Leiomyoma /complications /physiopathology /surgery; Postoperative Complications /etiology /physiopathology; Pregnancy; Pregnancy Rate

AccessionNumber
12009104301

Date bibliographic record published
02/09/2009

Date abstract record published
10/02/2010

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.