The effect of surgical treatment for endometrioma on in vitro fertilization outcomes: a systematic review and meta-analysis

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CRD summary
The authors concluded that surgical management of endometrioma had no significant effect on in vitro fertilisation pregnancy rate and ovarian response to stimulation compared to no treatment. The conclusion reflected the evidence presented. However, due to a small number of studies included in the analysis and the presence of statistical heterogeneity, it may not be reliable.

Authors' objectives
To evaluate the effect of surgical treatment of endometrioma on in vitro fertilisation (IVF) outcomes.

Searching
MEDLINE, EMBASE, SCISEARCH, The Cochrane Library and Science Citation Index were searched up to November 2007. The Intercollegiate Study Institute Proceedings were searched for conference abstracts and International Standard Randomised Controlled Number Register and Meta-register for Randomised Controlled Trials were searched for archived and ongoing trials. There was no language restriction. Search terms were reported. References of retrieved articles and conference proceedings were searched.

Study selection
All controlled retrospective and prospective studies that evaluated the effect of surgery (ovarian stripping or cystectomy) on IVF outcome and on ovarian response to gonadotrophin stimulation eligible for inclusion in the review. Studies in which women received any medical therapy for endometriosis before or after surgery and where the study group was treated by either aspiration of the endometriotic cyst or by oophorectomy were excluded from the review.

The primary outcome of interest was clinical pregnancy rate per cycle. Clinical pregnancy was defined as visualisation of foetal heart activity on transvaginal ultrasound at six weeks or more gestation. Ovarian response to gonadotrophin stimulation was a secondary outcome of interest and was measured by: total number of gonadotrophin ampoules required for ovarian stimulation; number of follicles greater than 14mm in diameter on day 10 of ovarian stimulation; peak oestradiol levels on the day of human chorionic gonadotropin (HCG) administration; and total number of oocytes retrieved. Other outcomes of interest included: fertilisation rate; number of embryos available for transfer; implantation rate; and live birth rate per cycle.

Surgical approaches for endometrioma greater than 3cm were ovarian cystectomy or draining and stripping of the cyst wall. Most procedures were performed laparoscopically. Ovarian stimulation was induced by either recombinant follicle-stimulating hormone (FSH) or human menopausal gonadotrophin (hMG) using various protocols (long, short or ultra short).

Control groups varied and included non-treated endometrioma, tubal factor infertility, aspirated endometrioma, laparoscopically treated peritoneal endometriosis, idiopathic infertility, non-endometriotic benign ovarian cyst and normal non-operated contralateral ovary. Diagnosis of endometrioma was confirmed histologically in the surgery group and/or measurement of CA-125 levels in the control group.

Two reviewers independently performed study selection. Any disagreement resolved by a third reviewer.

Assessment of study quality
The authors stated that study quality was assessed according to study design, inclusion and exclusion criteria, type of interventions, characteristics of the study and control groups and presentation of outcomes.

Two reviewers independently assessed study quality. Any disagreements were resolved by a third reviewer.
Data extraction
Data were extracted in order to calculate odds ratios (OR) and 95% confidence intervals (CI) for dichotomous outcomes; means and standard deviations were extracted for continuous outcomes.

Two reviewers independently performed data extraction. Any disagreements were resolved by a third reviewer.

Methods of synthesis
Statistical heterogeneity was assessed using the Cochrane Q test. Pooled odds ratios and weighted mean differences (WMD) and their associated 95% CI were calculated using a random-effects model when there was evidence of statistically significant heterogeneity (p<0.05); otherwise a fixed-effects model was used.

Results of the review
Twenty studies were included in the review. Due to clinical heterogeneity, only five studies, (three retrospective case-control studies, one retrospective cohort and one prospective cohort study, n=560 participants) in which women who had surgical treatment for endometrioma were compared to women with untreated endometrioma, were included in the meta-analysis.

There was no statistically significant difference between surgical treated or untreated women for pregnancy (four studies), clinical pregnancy rate per cycle (three studies), number of embryos available for transfer per cycle (two studies), number of oocytes retrieved per cycle (two studies), number of gonadotrophin ampoules required for ovarian stimulation per cycle (two studies) and oestradiol peak (three studies). Evidence of statistically significant heterogeneity was present, but not commented on by the authors, for outcomes of number of embryos available for transfer ($I^2=64.5\%$), gonadotrophin ampoules ($I^2=86.9\%$) and oestradiol peak ($I^2=75.1\%$).

Authors’ conclusions
Surgical management of endometrioma had no significant effect on IVF pregnancy rates and ovarian response to stimulation compared to no treatment.

CRD commentary
The review addressed a clear research question. Inclusion criteria were adequate, but comparator groups were ill defined. The search strategy was good: attempts were made to locate unpublished material and there were no language restrictions, which reduced risk of language and publication biases. Study quality was stated to be assessed, but the assessment findings were neither reported nor used in the synthesis. Restricting the meta-analysis to five studies based on clinical heterogeneity was appropriate. However, there was no exploration or consideration of the statistical heterogeneity that was present in the meta-analysis. Review processes were carried out with sufficient attempts to minimise reviewer error and bias. The authors’ conclusion reflected the evidence presented. However, due to a small number of studies included in the analysis and presence of statistical heterogeneity, the authors’ conclusion may not be reliable.

Implications of the review for practice and research
Practice: The authors stated that in situations where endometriomas are found prior to IVF and the patient had previous surgery or the patient did not have previous surgery but had a cyst 3cm to 5cm they should receive GnRH for three consecutive months and then receive IVF. If a patient had no previous surgery and a cyst less than 3cm they should receive IVF. Patients with a cyst greater than 5cm should undergo a ovarian cystectomy and then begin IVF.

Research: The authors stated that a large well-designed adequately powered multicentre RCT that compared the effects of surgical removal with expectant management was required.

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