Threefold increased risk of infertility: a meta-analysis of infertility after ileal pouch anal anastomosis in ulcerative colitis

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CRD summary
This review concluded that ileal pouch anal anastomosis increases the risk of infertility in women with ulcerative colitis. The conclusions were based on retrospective studies, which are at risk of bias, and would therefore need to be confirmed using more robust studies. The authors' recommendation for further studies of modifiable risk factors for infertility appears appropriate given the lack of evidence found.

Authors' objectives
To estimate the relative risk of infertility in women who have undergone ileal pouch-anal anastomosis (IPAA) in comparison with medical management; to estimate the absolute rate of infertility following IPAA; and to identify patient or procedure characteristics associated with increased infertility rates.

Searching
MEDLINE, EMBASE and Current Contents were searched from 1966 to 31 December 2005; the search terms were reported. Manual searches of reference lists were also carried out. Only studies published in full were eligible.

Study selection
To be eligible, studies needed to provide data on participants undergoing IPAA and those medically treated for ulcerative colitis (UC), and make data available on infertility. Infertility was defined as lack of conception despite trying to conceive. Inclusion criteria for the study design were not reported.

Two reviewers independently assessed studies for inclusion in the review, with any disagreements resolved by consensus.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two reviewers appear to have extracted the data, with any disagreements resolved by consensus.

Methods of synthesis
A fixed-effect meta-analysis was conducted. If heterogeneity was identified, studies having outlying values were excluded one at a time to assess whether they contributed to the heterogeneity observed. A meta-analysis using a random-effects model was also performed to assess the effect on outcome. Publication bias was assessed using a funnel plot and a sensitivity analysis was performed to determine whether a single study unduly influenced the results. Studies where pre-operative diagnosis was not reported were excluded in a sensitivity analysis, to check that the data were representative of patients with UC. Weighted average fertility rates for treatment groups were calculated from raw data for the studies (infertility rate equals the total participants reporting infertility divided by the total participants attempting conception).

Results of the review
Eight retrospective studies (n=528) were included.

The initial fixed-effect meta-analysis showed statistically significant heterogeneity. One study was found in a sensitivity analysis to be an outlier, owing to the high infertility rate in medically treated patients. After omission of this study, the meta-analysis was more homogeneous and the fixed-effect meta-analysis was repeated. The relative risk of infertility after IPAA was 3.17 (95% confidence interval, CI: 2.41, 4.18). Using a random-effects model, the relative risk was 2.91 (95% CI: 2.11, 4.02). No evidence of publication bias was found. Further sensitivity analyses only slightly reduced
the effect sizes. Using the same studies, a weighted average infertility rate for each treatment group was calculated. Overall infertility was 14.6% after medical management and 48% after IPAA. Patient and procedural risk factors could not be identified.

Authors’ conclusions
IPAA increases the risk of infertility in women with UC and patients should be counselled to this effect. Further studies of modifiable risk factors are needed.

CRD commentary
The aims of the study were clearly stated, but inclusion criteria were not defined for study design. A range of databases were searched, supplemented by reference checking. Unpublished articles were not eligible but the authors found no evidence of publication bias. It is unclear whether foreign language studies were eligible for inclusion. Two reviewers appear to have been involved in selecting studies for the review and extracting the data, which helps to minimise bias. However, study quality was not formally assessed and it is likely that the types of study included in the review had greater risks of bias. The meta-analysis methods appeared appropriate, and the authors made efforts to examine heterogeneity and conduct sensitivity analyses to examine the role of individual studies on the summary estimate. The authors acknowledged the limitations of the included retrospective studies (including the possibilities of selection bias, response bias and recall bias). Their conclusions on increase in infertility and weighted average fertility rates would need to be confirmed in further more robust studies, but their call for research on risk factors for infertility appears appropriate.

Implications of the review for practice and research
Practice: The authors advised presenting women with all medical and surgical options available and highlighting infertility risks.

Research: The authors advised the collection of potential risk factors for infertility in future studies in this field to identify those at highest risk and to highlight any potentially modifiable risk factors.

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