The effect of antireflux surgery on esophageal carcinogenesis in patients with Barrett esophagus: a systematic review

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CRD summary
The authors concluded that for patients with Barrett oesophagus, anti-reflux surgery appeared to be associated with significantly higher rates of regression than medical treatment, but controlled evidence showed no significant difference in rates of adenocarcinoma. The conclusions may need to be interpreted cautiously due to the limited search, failure to assess study quality and lack of information about review methods.

Authors' objectives
To determine whether antireflux surgery was associated with a lower incidence of oesophageal cancer in patients with Barrett oesophagus than medical therapy alone.

Searching
MEDLINE was searched from 1966 to October 2005. Search terms were reported. The reference lists of articles retrieved were checked and experts in the field were consulted. The search was limited to published studies in English.

Study selection
Studies were eligible if they described medical and/or surgical therapy for histologically confirmed Barrett oesophagus and reported data from which rates of oesophageal adenocarcinoma per patient year could be calculated for the two groups. Barrett oesophagus was defined as intestinal metaplasia (of any length) in the distal oesophagus. Studies of surgical therapy were required to use predominantly standard procedures (fundoplication). All participants were required to have undergone surveillance endoscopy within a year of starting therapy. The primary outcome in the review was oesophageal adenocarcinoma. Other outcomes of interest were progression and regression of disease, defined as a change in stage of disease between non-dysplastic Barrett oesophagus, low grade dysplasia, high grade dysplasia and adenocarcinoma. Randomised controlled trials, cohort studies and case series were eligible for inclusion, as were subsets of relevant data from studies designed for other purposes that were included as case series. Studies predominantly of paediatric patients were excluded.

Nissen fundoplication was the most common surgical procedure used in the review. Proton pump inhibitors and type II histamine receptor antagonists were the most common medical treatments. The mean age of patients in the surgical group was 53.8 years and in the medical group was 59.4 years. The prevalence of high grade dysplasia/low grade dysplasia in the two groups was 0.3 per cent/15.5 per cent in the surgical group and 2 per cent/8 per cent in the medical group.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

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

Data extraction
The number of events in each treatment group of each study was extracted, using initial and final biopsy results to calculate incidence rates of adenocarcinoma and regression and progression of disease. Patients who underwent both surgical and medical therapy were included in the surgical group.

The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction. They did not contact authors of primary studies for additional data.
Methods of synthesis
Data were pooled using a Bayesian modelling framework to calculate pooled incidence rates of adenocarcinoma and rates of progression and regression in each treatment group, with 95% credible intervals. The effect of study design on outcomes was explored in random-effects meta-regression. The Byar approximation to the Poisson was used to calculate cumulative estimates with 95% confidence intervals, adding each study in chronological order and stratified by study design.

Results of the review
Twenty-five studies were included (n=1,696): one randomised controlled trial (n=101); four cohort studies (n=496); and 20 uncontrolled studies (case series or subsets of data from larger studies, n=1,099).

Adenocarcinoma incidence (25 studies): When data from controlled studies only were pooled, there was no statistically significant difference between the median rate of cancer in the two groups in cases per 1,000 patient years (4.8, 95% confidence interval: 1.7, 11.1 versus 6.5, 95% confidence interval: 2.6, 13; p=0.32, five studies, n=597). When data from all studies were pooled, the median incidence of adenocarcinoma was significantly higher in the medically treated group (2.8 versus 6.3 per 1,000 patient years, p=0.034).

Regression and progression of Barrett oesophagus (21 studies): There was a statistically significant difference in regression rates favouring the surgical group for controlled studies (6.4 per cent versus 0.5 per cent, p=0.024) and for all studies combined (15.4 per cent versus 1.9 per cent, p=0.004). When all studies were combined, significant heterogeneity was detected between controlled studies and case series for medically treated patients. There was no statistically significant difference in progression rates to low grade dysplasia or high grade dysplasia among controlled studies (3.6 per cent versus 9.5 per cent, p=0.088), or among all studies combined (2.9 per cent versus 6.8 per cent, p=0.054).

Authors’ conclusions
For patients with Barrett oesophagus, anti-reflux surgery appeared to be associated with significantly higher rates of regression than medical treatment, but controlled evidence shows no significant difference in rates of adenocarcinoma.

CRD commentary
The review objectives and inclusion criteria were clear. Only one database was searched, which meant that studies may have been missed. The restriction to published English-language studies meant that the review was prone to publication and language biases. It was unclear whether steps were taken to minimise potential error and bias during the review process (such as study selection and data extraction being undertaken by two reviewers independently). Moreover, it did not appear that study quality was systematically assessed. Lack of detailed information about review methods or study quality (for example, blinding and follow-up rates) made it difficult to evaluate the reliability of the evidence presented. However, suitable methods appeared to have been used to pool the data and investigate the effects of study design, and potential sources of heterogeneity and bias were well addressed in the text. The controlled evidence was appropriately given priority over case-series evidence. The authors’ conclusions appeared to be supported by the evidence presented, but may need to be interpreted cautiously due to the limited search and lack of information about study quality or review methods.

Implications of the review for practice and research
Practice: The authors stated that anti-reflux surgery could not be recommended as a technique to reduce the risk of neoplasm.

Research: The authors stated that as an adequately powered randomised controlled trial was infeasible, a registry to follow up patients with Barrett oesophagus would be a suitable way of determining whether antireflux surgery reduced the risk of adenocarcinoma compared to medical therapy.

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