The safety and effectiveness of endoscopic and non-endoscopic approaches to the management of early esophageal cancer: a systematic review

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CRD summary
This review compared endoscopic with non-endoscopic treatment of early oesophageal cancer and concluded that the results encouraged development of early oesophageal cancer treatment algorithms that, following pre-treatment assessment of disease stage and multidisciplinary discussion, took into account patient characteristics. This was generally a well-conducted review, but the paucity and poor quality of data precluded firm conclusions.

Authors' objectives
To assess the safety and effectiveness of endoscopic versus non-endoscopic treatment of early oesophageal cancer.

Searching
PubMed, EMBASE, CINAHL, The Cochrane Library, DARE, HTA database, NHS EED, Web of Science and EconLit databases were searched for published and unpublished studies and abstracts that provided sufficient information on participants and outcomes. The search was restricted to studies in English. Search dates appeared to be 1988 to July 2008. Update searches of PubMed were performed to January 2009. Search terms were reported. Sources of grey literature were searched (meetings abstracts of the American Society of Clinical Oncology and Digestive Disease Week, cancer organisation websites, clinical practice guidelines and clinical trials). Reference lists of retrieved papers, technology assessments, clinical practice guidelines and systematic reviews were handsearched for relevant papers.

Study selection
Controlled trials, cohort studies (retrospective, prospective or concurrent) and case or clinical series that investigated use of photodynamic therapy, oesophagectomy, radiotherapy, chemoradiotherapy, chemotherapy and other ablative treatments and the non-ablative technique endoscopic mucosal resection in patients diagnosed with early oesophageal cancer were eligible for inclusion. Eligible comparators were the same as the interventions. Included studies had to report response (tumour eradication or regression), recurrence or cause-specific, disease-specific survival or overall survival. Early oesophageal cancer was defined as stages 0 to IIA without spread to lymph nodes.

The included studies were mostly of male patients with squamous cell carcinoma (SCC) and adenocarcinoma. Patient age ranged from 38 to 91 years. The studies investigated the endoscopic ablative techniques of argon plasma coagulation, cryoablation, radiofrequency ablation and photodynamic therapy. Endoscopic mucosal resection was investigated. Non-endoscopic treatments were predominantly oesophagectomies (various surgical approaches). Other studies used chemotheraphy and/or radiotherapy with or without surgery. Some patients received additional interventions and some had received previous interventions. Adverse events were reported in addition to the eligible outcomes.

Two reviewers independently selected studies for inclusion. Disagreements were resolved through discussion.

Assessment of study quality
Study quality was assessed in terms of type of study design independently by two reviewers using the Oxford Levels of Evidence to produce a score out of 5 (5 indicated the poorest level, expert opinion). It appeared that the methodological quality of individual studies was not assessed. Disagreements were resolved through consensus.

Data extraction
Data were extracted independently by two reviewers for the outcomes: complete/partial/no response (the extent to which cancerous tissue could be removed), recurrence (whether, after removal, cancerous tissue re-appeared), cause-specific survival (patients who did not die from oesophageal cancer during study follow-up), overall survival (patients who did not die during follow-up) and adverse events. Mean values and ranges were extracted for each study using intention-to-treat principles. Disagreements were resolved by consensus. Authors of the primary studies were contacted for missing data where necessary.
Methods of synthesis
Means were pooled to obtain weighted mean values for each outcome. Subgroup analyses were performed for treatment type, cell type and stage of disease.

Results of the review
Seventy-five studies were included in the review (3,124 participants; half of the studies included <20 patients). One study was a non-randomised controlled trial, fourteen studies were comparative cohort studies and the others were non-comparative case series. The authors stated that most of the studies were low quality (scored 4). Where reported, follow-up was up to 145 months.

Endoscopic techniques: A complete response was achieved in 54% of patients with ACC and 71% of patients with SCC using photodynamic therapy (24/26 photodynamic therapy studies). In the one argon plasma coagulation study, ACC was eradicated in all three patients; similarly, complete eradication was achieved in all 16 ACC and SCC patients in the only study of radiofrequency ablation. In the one study of cryotherapy, 75% of 23 patients with ACC or SCC achieved complete response. Endoscopic mucosal resection was associated with complete response in 98% of ACC and 88% of SCC patients (seven studies).

Non-endoscopic techniques: In four out of six chemoradiotherapy studies, 86% of patients with SCC reported complete response; similar results were reported in the one study of both SCC and ACC patients (77%). In three of the radiotherapy studies that assessed complete response in patients with SCC only, the response rate was 81%. One study compared oesophagectomy study to photodynamic therapy and found no significant difference between groups in terms of complete response.

Survival: None of the studies of patients who received endoscopic versus non-endoscopic treatments reported overall or cause-specific survival. Other survival results were reported in the review.

Results were reported for recurrence and adverse events (details available in the full paper).

Authors’ conclusions
There is no single best-practice approach to the treatment of early oesophageal cancer.

CRD commentary
The research question was supported by well-defined inclusion criteria. Grey literature was sought specifically, which reduced the possibility of publication bias. Only studies in English were included and so language bias was possible. Although aspects of study quality were not examined, the included study designs were prone to bias and the poor quality of the studies was taken into account in the analysis. Review processes were performed in duplicate, which reduced risks of error and bias. There was evidence of clinical and methodological heterogeneity. Some findings were from only one study. The analyses used appeared reasonable considering the paucity and poor quality of data available for each treatment. The authors acknowledged that some studies pooled information across patients with stage I to IV disease (so some patients had advanced disease). It was acknowledged that it was difficult to evaluate the long-term clinical benefit attributable to a particular treatment as some studies included other treatments.

This was generally a well-conducted review, but the paucity and poor quality of data available precluded any firm conclusions.

Implications of the review for practice and research
Practice: The authors stated that there appeared to be consensus on the use of multimodality (therefore multidisciplinary) approaches.

Research: The authors stated that this review encouraged the development of early oesophageal cancer treatment algorithms that, following a thorough pre-treatment assessment of disease stage and discussion with a multidisciplinary team (oncologists, thoracic surgeons and gastroenterologists), took into account patient characteristics (patient preference included), local expertise and available technology.

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