Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract

CRD summary
The authors concluded that endoscopic submucosal dissection improved en bloc, curative resection and local recurrence rates for gastrointestinal tract tumours compared with endoscopic mucosal resection, but was more time-consuming and had higher complication rates. These conclusions appeared to reflect the evidence, but lack of reporting of review methods and concerns about exclusion of some studies from analyses undermined their reliability.

Authors' objectives
To compare endoscopic submucosal dissection with endoscopic mucosal resection for the treatment of premalignant and malignant lesions of the gastrointestinal tract.

Searching
PubMed, EMBASE, the Cochrane Library and Web of Science were searched for studies published in any language between 1966 and October 2008. Search terms were reported. In addition, reference lists of identified studies were handsearched and abstracts from meetings of three specified relevant societies were screened (2005 to 2008).

Study selection
Studies that compared endoscopic submucosal dissection with endoscopic mucosal resection for the treatment of premalignant and malignant lesions of the gastrointestinal tract were eligible for inclusion. Primary review outcomes were rates of en bloc and curative resections. Secondary outcomes were operating time, bleeding, perforation rates and local recurrence. Definitions for these outcomes were reported.

Most of the studies were set in Japan; others were set in Korea; one study did not report the location. Most studies were in patients with early gastric cancer; other patients had early oesophageal cancer or colorectal tumours. Where reported, the mean age of patients ranged from 61 to 71 years and the tumour size ranged from 5 to 60mm.

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

Assessment of study quality
Validity was assessed using the following criteria for non-randomised studies: sample size (more or less than 10 patients); follow-up (more than six months); comparable (yes or no); comparison of operating procedures, endoscopic submucosal dissection versus endoscopic mucosal resection (yes or no); consecutive (yes or no); and clear description of outcome measures. The maximum quality score was 6 points.

The authors did not state how many reviewers assessed validity.

Data extraction
Numbers of events were extracted for each group and used to calculate odds ratios (ORs) with 95% confidence intervals (CIs). Mean differences were calculated for continuous data.

Two reviewers abstracted data independently and reached consensus on all items.

Methods of synthesis
Analyses appeared to be based on lesions data for dichotomous outcomes. Pooled odds ratios and 95% confidence intervals were calculated for dichotomous data, and pooled weighted mean difference (WMD) and 95% confidence intervals were calculated for continuous data. Statistical heterogeneity was assessed using the I^2 statistic. Fixed-effect
models were used in the absence of statistical heterogeneity. Potential sources of heterogeneity were explored using subgroup analyses. Studies that were potentially responsible for the heterogeneity were excluded and random-effects models used where appropriate. The possibility of publication bias was explored using Egger’s test.

**Results of the review**

Fifteen non-randomised comparative studies were included; n=2,758 patients in 12 studies (the number of patients was not reported in the other three studies), with an estimated 4,791 lesions from all studies. These included seven full publications and eight abstracts. All of the studies met at least four of the six quality criteria.

**En bloc resection rate** (12 studies, 3,445 lesions): Significant heterogeneity was found ($I^2=68.4\%$). After excluding two studies responsible for the heterogeneity, endoscopic submucosal dissection was associated with a statistically significant increase in the en bloc resection rate compared with endoscopic mucosal resection (OR 13.87, 95% CI 10.12 to 18.99; 10 studies).

**Curative resection rate** (12 studies, 4,660 lesions): Significant heterogeneity was found ($I^2=93.2\%$). After excluding five studies responsible for the heterogeneity, endoscopic submucosal dissection was associated with a statistically significant increase in the en bloc resection rate compared with endoscopic mucosal resection (OR 3.53, 95% CI 2.57 to 4.84; seven studies).

Results for both the above outcomes were similar for lesions smaller than 10 mm, 10 to 20mm, and more than 20mm.

**Secondary outcomes:** Endoscopic submucosal dissection was associated with a significantly lower local recurrence rate (OR 0.09, 95% CI 0.04 to 0.18; ten studies, 3738 lesions), but a statistically significant increase in the operating time (WMD 1.76, 95% CI 0.60 to 2.92; four studies; the units of analysis were not reported) and significantly higher procedure-related bleeding rates (OR 2.20, 95% CI 1.58 to 3.07; nine studies, 2,464 lesions) and perforation rates (OR 4.09, 95% CI 2.47 to 6.80; eleven studies, 3,237 lesions). Significant heterogeneity was found for the analysis of operating time, but not for any of the other analyses.

There was no evidence of publication bias.

**Authors’ conclusions**

Endoscopic submucosal dissection improved en bloc, curative resection and local recurrence rates compared with endoscopic mucosal resection, but it was more time-consuming and had higher rates of bleeding and perforation complications.

**CRD commentary**

The review question was clearly stated and inclusion criteria were appropriately defined. Several relevant sources were searched and attempts were made to minimise publication and language bias; Egger's test showed no evidence of publication bias. Methods used to select studies, assess validity and extract data were not described, so it was not known whether efforts were made to reduce reviewer errors and bias.

Study validity was assessed using criteria appropriate for non-randomised studies, but only aggregate scores were reported, so it was to evaluate the of the quality of the evidence. Appropriate methods were used for the meta-analyses; heterogeneity was assessed and various subgroup and sensitivity analyses conducted. Studies responsible for heterogeneity were excluded from analysis without discussion about potential reasons for the heterogeneity and this weakened the strength of the evidence.

The authors’ conclusions appeared to reflect the evidence, but lack of reporting of review methods and concerns about exclusion of some studies from analyses, make it difficult to confirm their reliability.

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

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

**Research:** The authors stated that there is need for high-quality randomised controlled trials to verify the findings of
this review and to evaluate endoscopic submucosal dissection and endoscopic mucosal resection in Western populations. There is also a need to improve endoscopic submucosal dissection techniques.

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