Systematic review of endoscopic mucosal resection versus transanal endoscopic microsurgery for large rectal adenomas

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CRD summary
The review found that there was insufficient evidence to determine whether endoscopic mucosal resection or transanal endoscopic microsurgery was more effective for large rectal adenomas. The review was limited by methodological weaknesses such as a limited search, a potentially unreliable synthesis, and unclear applicability, which means that the reliability of this conclusion is unclear.

Authors' objectives
To compare the safety and effectiveness of endoscopic mucosal resection versus transanal endoscopic microsurgery for treatment of large rectal adenomas.

Searching
PubMed and EMBASE were searched for studies published in English, German or Dutch from 1980 up to January 2009. Search terms were available in a separate online appendix.

Study selection
Eligible studies were randomised or quasi-randomised trials that compared endoscopic mucosal resection versus transanal endoscopic microsurgery for treatment of large (over 2cms non-pedunculated rectal adenomas). Cases series that evaluated either treatment were also eligible. The interventions had to be performed using published methods referenced in the review. Studies were required to report effectiveness or safety. Effectiveness outcomes included early recurrence (after a single intervention), late recurrence (not counting participants successfully re-treated for residual adenoma within three months of initial intervention), operating time, length of hospital stay, and readmission rate. Safety outcomes included perioperative/postoperative complications and mortality. Where case series included data on colonic adenomas or rectal cancers, it was planned to include only the data on rectal adenomas. Studies in which over 25% of adenomas were smaller than 2cms were excluded.

The review included only observational data, as no trials comparing the two interventions were found. The mean age of all participants was 67 to 68 years; the percentage of men ranged from 55 to 61%. Weighted mean polyp size was 31mm (range 2mm to 86mm) in endoscopic mucosal resection studies and 37mm (range 3mm to 182mm) in transanal endoscopic microsurgery studies. Most studies of endoscopic mucosal resection described adenomas as colorectal and failed to report their exact location. Some transanal endoscopic microsurgery studies reported inclusion of participants with adenomas that were not endoscopically resectable. The studies varied greatly in design (such as whether participant selection was consecutive) and the specific techniques used for each type of surgery.

Two reviewers independently selected the studies

Assessment of study quality
Study quality was evaluated using sequence generation, objective definitions of outcomes, potential confounding related to diagnosis at baseline, design, cohort size, types of lesions prior to intervention, lesion size, and length of follow-up. Studies were rated as good quality, at risk of bias, or at unclear risk of bias, depending whether they met a satisfactory standard for the first three items.

The authors did not state how many reviewers performed the assessment.

Data extraction
All data were analysed as if they derived from case series due to lack of comparative data. Data for both rectal and colorectal endoscopic mucosal resection were extracted due to lack of rectal-only data. For dichotomous outcomes, the proportion of participants with an event was extracted from relevant study arms. For continuous data, means and standard deviations were extracted or estimated from reported medians and ranges, using published methods. If
necessary, standard deviations were imputed from other studies. In multi-arm studies, only the data from relevant study arms were included. Where studies compared variations of one of the interventions of interest, data from both arms were combined (the rationale being that this only occurred in a single study of endoscopic mucosal resection). Participants lost to follow-up were excluded from analysis of recurrence rates.

Two reviewers independently extracted the data.

Methods of synthesis
Data were pooled in a non-linear mixed meta-regression model to calculate estimates of pooled event rates with 95% confidence intervals (CIs). For most analyses, studies of rectal and colorectal endoscopic mucosal resection were pooled. The authors stated that they addressed any between-study variation by using a random-effects model, and within-study variation by using the exact binomial distribution. A random-effects model was also used to pool continuous data. P values were reported for comparisons between pooled effect estimates for each type of intervention.

Sensitivity analyses were used to investigate potential confounding related to mean polyp size, mean length of follow-up, and/or prospective or retrospective study design.

Results of the review
Sixty-eight studies were included with 5,887 patients (five randomised controlled trials - RCTs, 30 prospective studies, 23 retrospective studies and 10 studies of unclear design); 3,890 patients were included in analyses of recurrence and 553 patients were analysed for complication rates. Twenty-three of the studies clearly enrolled participants consecutively. Three studies clearly defined complications. Fourteen studies clearly defined recurrence. Complications and/or recurrences were considered attributable to participant diagnoses prior to the intervention in 58% to 75% of studies.

Recurrence: Endoscopic mucosal resection of rectal and colorectal adenomas was associated with an early recurrence rate of 11.2% (95% CI 6.0 to 19.9; one rectal study and 15 colorectal studies) and a late recurrence rate of 1.5% (95% CI 0.6 to 3.9; one rectal and 10 colorectal studies). In the only study of rectal adenoma, five participants underwent repeat surgery at three months, which was successful in four out of five cases. Transanal endoscopic microsurgery for rectal adenoma was associated with an early recurrence rate of 5.4% (95% CI 4.0 to 7.3; 38 studies) and a late recurrence rate of 3.0% (95% CI 1.3 to 6.9; 16 studies). These estimates did not indicate a significant difference between the interventions for early recurrence (p=0.04 for early recurrence and p=0.29 for late recurrence).

Postoperative complications: Endoscopic mucosal resection of rectal (two studies) and colorectal (15 studies) adenomas was associated with a postoperative complication rate of 3.8% (95% CI 2.8 to 5.3). Transanal resection for rectal adenoma was associated with a postoperative complication rate of 13% (95% CI 9.8 to 17; 12 studies). Rates were significantly higher in the transanal resection group (p<0.001).

Operating time and hospital stay: There was no significant difference between the interventions in duration of hospitalisation nor in readmission rate, but the pooled mean operating time was significantly shorter for endoscopic mucosal resection (43 minutes; p<0.001; number of studies not reported) compared with transanal endoscopic resection (97 minutes).

Sensitivity analyses did not change the main findings of the review. Other findings were reported in the review.

Authors’ conclusions
There was insufficient evidence to determine whether endoscopic mucosal resection or transanal endoscopic microsurgery was more effective for large rectal adenomas.

CRD commentary
The objectives and inclusion criteria of the review were clear. Due to shortage of relevant data, the authors did not adhere to their inclusion criteria and included data on both rectal and colorectal adenomas, which made it difficult to determine the applicability of the review findings. The search was limited to two databases and restricted by language and (apparently) publication status, so the review was at potential risk of language and publication biases. The risk of publication bias was not assessed. Steps were taken to minimise the risk of reviewer bias and error in the processes of study selection and data extraction, but it was unclear whether this also applied to quality assessment.
The methods used to combine the data and (indirectly) compare the groups did not appear reliable, even though the authors attempted to adjust for potential confounding. Also, the authors noted that complications associated with re-interventions in the endoscopic mucosal resection group were missing from the analysis as they were not reported in the primary studies. There was marked clinical and methodological heterogeneity within and between the two sets of studies. It did not appear that statistical heterogeneity was assessed; the use of a random-effects model did not appear to be a reliable method of addressing between-study variability. As the authors noted, the review was limited by potential confounding related to differences between participants in the two sets of studies, with a likelihood of more favourable tumour characteristics in one group.

The review was limited by methodological weaknesses such as a limited search, a potentially unreliable synthesis, and unclear generalisability, which means that the reliability of the conclusion is unclear.

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

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

**Research:** The authors stated that an RCT was needed before recommendations could be made on the comparative safety and effectiveness of endoscopic mucosal resection versus transanal endoscopic microsurgery for treatment of large rectal adenomas.

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