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Meta-analysis and systematic review of colorectal endoscopic mucosal resection

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Abstract

AIM: To evaluate the proportion of successful complete cure *en-bloc* resections of large colorectal polyps achieved by endoscopic mucosal resection (EMR).

METHODS: Studies using the EMR technique to resect large colorectal polyps were selected. Successful complete cure *en-bloc* resection was defined as one piece margin-free polyp resection. Articles were searched for in Medline, Pubmed, and the Cochrane Control Trial Registry, among other sources.

RESULTS: An initial search identified 2620 reference articles, from which 429 relevant articles were selected and reviewed. Data was extracted from 25 studies (n = 5221) which met the inclusion criteria. All the studies used snares to perform EMR. Pooled proportion of *en-bloc* resections using a random effect model was 62.85% (95% CI: 51.50-73.52). The pooled proportion for complete cure *en-bloc* resections using a random effect model was 58.66% (95% CI: 47.14-69.71). With higher patient load (> 200 patients), this complete cure *en-bloc* resection rate improves from 44.19% (95% CI: 24.31-65.09) to 69.17% (95% CI: 51.11-84.61).

CONCLUSION: EMR is an effective technique for the resection of large colorectal polyps and offers an alternative to surgery.

Key words: Meta-analysis; Systematic review; Polyps; Endoscopic mucosal resection; *En-bloc* resection

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INTRODUCTION

The use of endoscopic mucosal resection (EMR), pioneered in Japan for the treatment of early gastric cancer, has expanded to include therapy of other early gastrointestinal malignancies and pre-cancerous lesions such as adenomas. At the same time, this technique has gained acceptance in Europe and in the US, especially for the treatment of Barrett's esophagus with high grade dysplasia[1-3]. Several variations of the EMR technique have been devised such as inject-lift-cut, strip biopsy, suction cup (EMRC), and EMR with a ligating device.

Throughout the world, adenomas of the colorectum represent the single most important premalignant lesion of the GI tract. Large (> 2 cm) colorectal polyps have been found in 0.8%-5.2% of patients undergoing colonoscopies for different indications[4].

Large sessile and flat polyps represent a major technical challenge to conventional snare resection. Additional procedures and therapies such as Argon plasma coagulation are frequently needed to destroy remnant tissue after resection[5]. When these techniques are not used or possible, patients are frequently referred for surgical resection[6].

EMR has been shown to be useful in the removal of large colorectal sessile and flat lesions[7]. However, there are limits to the size of lesions which can be removed *en-bloc* with the various EMR techniques, with 1.5-2 cm generally being the upper limit[8].

En-bloc removal of large polyps is desirable as it facilitates thorough histological evaluation related to the

completeness of resection, and is associated with a lower recurrence rate as compared to piecemeal removal[9-14].

MATERIALS AND METHODS

Study selection criteria

Studies using EMR technique to resect large (> 2 cm) colorectal polyps were selected. Successful cure *en-bloc* resection was defined as one piece removal with tumor-free vertical and lateral margins.

Data collection and extraction

Articles were searched for in Medline, Pubmed, Ovid journals, Japanese language literature, Cumulative Index for Nursing & Allied Health Literature, ACP journal club, DARE, International Pharmaceutical Abstracts, old Medline, Medline non-indexed citations, OVID Healthstar, and the Cochrane Controlled Trials Registry. The search terms used were EMR, endoscopic mucosal resection, colon polyps, lateral spreading tumors, large polyps, nonpolypoid colon lesions, flat colon polyps, and flat adenomas. Two authors (SP and YK) independently searched and extracted the data for revising into an abstracted form. Any differences were resolved by mutual agreement.

Quality of studies

Clinical trials with a control arm can be assessed for the quality of the study. A number of criteria have been used to assess the quality of a study (e.g. randomization, selection bias of the arms in the study, concealment of allocation, and blinding of outcome)[15,16]. There is no consensus regarding how to assess studies without a control arm. Hence, these criteria do not apply to studies without a control arm[16]. Therefore, for this meta-analysis and systematic review, studies were selected based on completeness of data and inclusion criteria.

Statistical methods

This meta-analysis was performed by calculating pooled proportions, i.e. pooled proportion of *en-bloc* resections and complete cure *en-bloc* resections. Firstly, the individual study proportions of successful resections were transformed into a quantity using Freeman-Tukey variant of the arcsine square root transformed proportion. The pooled proportion was calculated as the back-transform of the weighted mean of the transformed proportions, using inverse arcsine variance weights for the fixed effects model and DerSimonian-Laird weights for the random effects model[17,18]. Forrest plots were drawn to show the point estimates in each study in relation to the summary pooled estimate. The width of the point estimates in the Forrest plots indicated the assigned weight to that study. The heterogeneity among studies was tested using Cochran's Q test based upon inverse variance weights[19]. If P value was > 0.10, the null hypothesis was rejected that the studies were heterogeneous. The effects of publication and selection bias on the summary estimates were tested by Begg-Mazumdar bias indicator[20]. Also, funnel plots were constructed to evaluate potential publication bias using the standard error and diagnostic odds ratio[21,22].

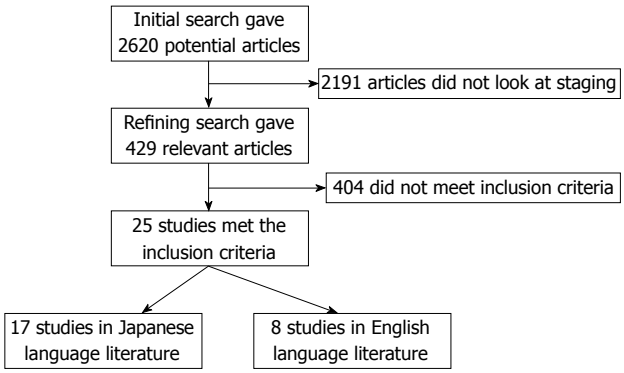

Figure 1 Search results.

RESULTS

An initial search identified 2620 reference articles from which 429 relevant articles were selected and reviewed. Data was extracted from 25 studies (n = 5221) which met the inclusion criteria[23-46]. The search results are shown in Figure 1. All the studies used snare to perform EMR. Two studies used a strip biopsy technique[42,43]. The mean size of the polyps was 22.48 ± 4.52 mm. There were 3755 successful *en-bloc* resections. The study characteristics are shown in Table 1.

The pooled proportion of *en-bloc* resections using a random effect model was 62.85% (95% CI: 51.50-73.52). Forest plot in Figure 2A depicts the individual study proportion of successful *en-bloc* resections in relation to the pooled estimate. The pooled proportion for complete cure *en-bloc* resections using a random effect model was 58.66% (95% CI: 47.14-69.71). Figure 2B shows Forrest plot depicting the individual study successful cure *en-bloc* resections in relation to the pooled estimate. The fixed effect model was not used because of the heterogeneity of studies.

Subgroup analysis was carried out by grouping studies according to the study population. This was done because the expertise needed to perform procedures might have affected the outcome. Studies were categorized into three groups: < 100 patients, 100-200 patients and > 200 patients. The proportions for successful *en-bloc* and successful cure *en-bloc* resections are shown in Table 2.

The publication bias calculated by Begg-Mazumdar bias indicator for successful cure *en-bloc* resections concluded that the Kendall's tau b value was -0.19 (P = 0.17). The funnel plot in Figure 3 shows that there was no publication bias for successful cure *en-bloc* resections.

DISCUSSION

Some colorectal cancers develop from adenomas. The risk of high grade dysplasia and cancer increases with the size of the lesion. Endoscopic removal of large (> 2 cm) sessile and flat polyps represents a difficult challenge for conventional snare resection and they are frequently managed by piecemeal resection or surgically[6,47]. EMR was the definitive procedure in all the collated studies. The data for complications was not available for the majority of the studies, so this data was not collected. EMR is a technique that can be applied to sessile and flat

Table 1 Study characteristics

	Author, yr	Instrument used	*n*	Type of polyp	Technique
1	Matsushita *et al*[23], 2003	Snare	935	No information	EMR
2	Imai *et al*[24], 1999	Snare	30	No information	EMR
3	Igarashi *et al*[25], 1999	Snare	884	No information	EMR
4	Oka *et al*[26], 2005	Snare	410	Lateral spreading tumor	EMR
5	Sano *et al*[27], 2004	Snare	392	Lateral spreading tumor	EMR
6	Hotta *et al*[28], 2003	Snare	284	Protrusion 68, flat 213, depressed 3	EMR
7	Matsuda *et al*[29], 2006	Snare	154	Is,Isp 33, LST-G 96, NG 25	EMR
8	Yasumoto *et al*[30], 2005	Snare	240	LST-G 180, NG 60	EMR
9	Terai *et al*[31], 2003	Snare	223	Lateral Spreading tumor	EMR
10	Nozaki *et al*[32], 2006	Snare	198	Ip 3, Isp 34, Is 7, LST-G 85, NG 28	EMR
11	Watari *et al*[33], 1998	Snare	186	Lateral spreading tumor	EMR
12	Sugisaka *et al*[34], 2003	Snare	162	No information	EMR
13	Matsunaga *et al*[35], 1999	Snare	134	No information	EMR
14	Nomura *et al*[36], 2001	Snare	54	No information	EMR
15	Kobayashi *et al*[37], 1999	Snare	131	No information	EMR
16	Nakajima *et al*[38], 2006	Snare	52	No information	EMR
17	Cho *et al*[39], 1999	Snare	34	No information	EMR
18	Saito *et al*[40], 2001	Snare	170	Lateral spreading tumor	EMR
19	Tanaka *et al*[13], 2001	Snare with needle spike	81	Lateral spreading tumor	EMR
20	Ahmad *et al*[41], 2002	Snare with suction	41	Colon and rectum	EMR
21	Hurlstone *et al*[42], 2004	Strip technique of Karita	80	Rectal villous adenoma	EMR
22	Hurlstone *et al*[43], 2005	Strip technique of Karita	62	Rectal villous adenoma	EMR
23	Su *et al*[44], 2005	Snare with needle spike	152	Colonic nonpolypoid lesions	EMR
24	Uraoka *et al*[45], 2005	Snare	113	Lateral spreading tumor	EMR
25	Kawamura *et al*[46], 1999	Snare	19	Submucosal invasive colorectal cancers	EMR

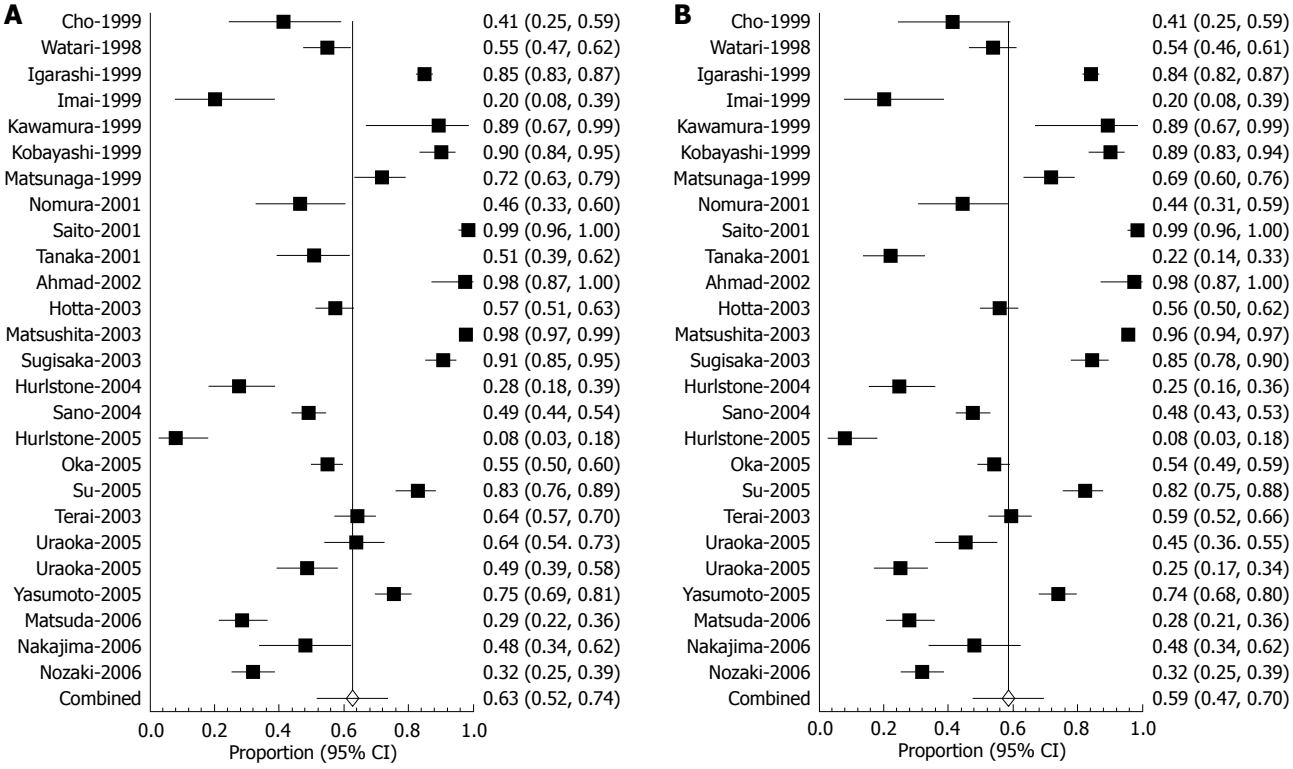

Figure 2 Forrest plot showing successful *en-bloc* (A) and cure *en-bloc* (B) resection.

lesions. Though initially used for the treatment of early gastric cancer in Japan, the technique has been expanded to the therapy of large colorectal neoplasms[7].

This meta-analysis revealed that *en-bloc* resection was achieved in 62.85% of lesions and tumor-free vertical and lateral margins were achieved in 58.6%. These results compare well to *en-bloc* resection rates achieved by conventional polypectomy snare, which have been reported to be between 7% and 34% for large sessile polyps[6,48].

Furthermore, our meta-analysis revealed that experience performing EMR plays an important role in achieving a better *en-bloc* resection and cure *en-bloc* tumor-free rate. Studies reporting more than 200 lesions removed reported a 71.39% *en-bloc* resection of lesions and tumor-free vertical and lateral margins in 69.17% of cases, while studies reporting less than a 100 lesions reported a

Table 2 Results based on study size

Study size	No. of studies	Successful *en-bloc* resection (95% CI)	Successful cure *en-bloc* resection (95% CI)
< 100 patients	9	48.07% (28.36-68.09)	44.19% (24.31-65.09)
100-200 patients	9	68.93% (50.39-84.76)	63.32% (43.50-81.04)
> 200 patients	7	71.39% (52.24-87.20)	69.17% (51.11-84.61)

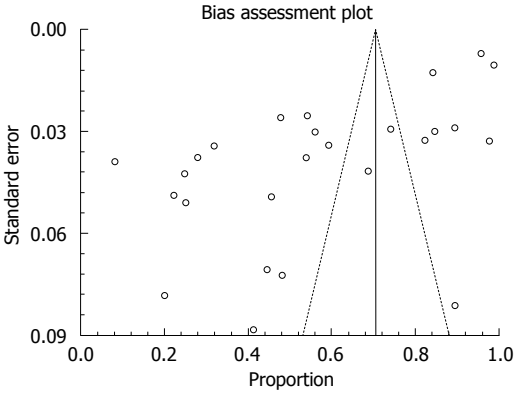

Figure 3 Funnel plot showing publication bias for successful cure *en-bloc* resection.

48.07% *en-bloc* removal and tumor-free vertical and lateral margins in 44.19% of cases. This indicates that experience in the technique of EMR increase the cure *en-bloc* rate.

In the present meta-analysis we searched the world literature which included articles published in Japanese language literature. We believe that our results are a reasonable reflection of the status of EMR in the therapy of large colorectal polyps.

EMR is an effective technique for resection of large colorectal polyps. The technique offers an alternative to surgery. This meta-analysis shows that the success rate for *en-bloc* margin-free resection is not high but improves with experience. Improvements in techniques and equipment are needed to increase complete cure *en-bloc* resection rates.

COMMENTS

Background

Endoscopic mucosal resection (EMR) has emerged as an alternative to surgery for the resection of large colorectal polyps. Complete cure with tumor-free lateral and vertical margins would prevent further therapy. Published data regarding successful *en-bloc* resection with tumor-free margins by EMR has been varied.

Innovations and breakthroughs

EMR has been shown to be useful in the removal of large colorectal sessile and flat lesions. However, there are limits to the size of lesions which can be removed *en-bloc* with the various EMR techniques, with 1.5-2 cm generally being the upper limit. *En-bloc* removal of large polyps is desirable as it facilitates thorough histological evaluation related to the completeness of resection, and is associated with a lower recurrence rate as compared to piecemeal removal.

Applications

EMR is an effective technique for resection of large colorectal polyps and offers an alternative to surgery. This meta-analysis shows that the success rate for *en-bloc* margin-free resection is not high but improves with experience. Improvements in techniques and equipment are needed to increase complete cure *en-bloc* resection.

Peer review

The authors evaluated the proportion of successful complete cure *en-bloc* resections of large colorectal polyps achieved by EMR. They found that EMR is an effective technique for resection of large colorectal polyps.This article is well written and easy to read.

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