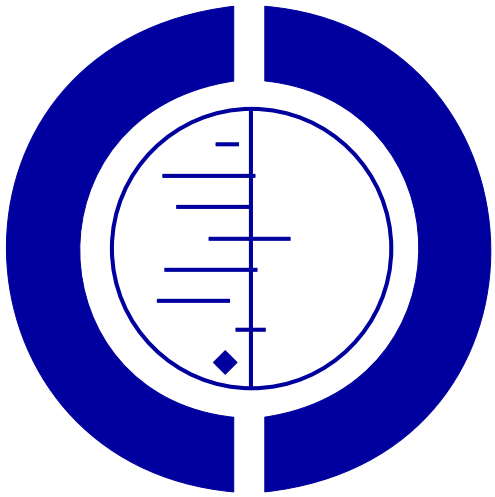
Endoscopic mucosal resection for early gastric cancer (Review)

YP Wang, C Bennett, T Pan



This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2007, Issue 1

http://www.thecochranelibrary.com

TABLE OF CONTENTS

Endoscopic mucosal resection for early gastric cancer (Review)

YP Wang, C Bennett, T Pan

This record should be cited as:
YP Wang, C Bennett, T Pan. Endoscopic mucosal resection for early gastric cancer. *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD004276. DOI: 10.1002/14651858.CD004276.pub2.

This version first published online: 25 January 2006 in Issue 1, 2006.
Date of most recent substantive amendment: 16 February 2006

ABSTRACT

Background
The treatment of early gastric cancer (EGC) using endoscopy, namely endoscopic mucosal resection (EMR), has been adopted for about 20 years, but the effectiveness and safety of the modality are still controversial. Furthermore, the quality of trials of this technique has not been assessed systematically.

Objectives
The purpose of this review was to compare the effectiveness and safety of endoscopic mucosal resection with gastrectomy for the treatment of early gastric cancer.

Search strategy
Searches were conducted on the Cochrane Central Register of Controlled Trials (CENTRAL) which includes the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group (UGPD) Trials Register (The Cochrane Library 2005, Issue 1), MEDLINE (1966 to March 2005), EMBASE (1980 to March 2005), CINAHL (1985 to March 2005) and CBM (Chinese BioMedical Database 1982 to 2002). The searches of CENTRAL, MEDLINE and EMBASE were updated in February 2006. Reference lists from trials selected by electronic searching were handsearched to identify further relevant trials. Published abstracts from conference proceedings from the United European Gastroenterology Week (published in Gut) and Digestive Disease Week (published in Gastroenterology) were handsearched. Members of the Cochrane UGPD Group, and experts in the field were contacted and asked to provide details of outstanding clinical trials and any relevant unpublished materials.

Selection criteria
All randomised controlled trials of early gastric cancer patients involving a treatment arm of EMR and a comparison arm of gastrectomy were to be included, but no RCTs were found.

Data collection and analysis
Three review authors (YP Wang, C Bennett and T Pan) independently assessed the eligibility of potential trials and extracted the data.

Main results
There were no randomised controlled trials identified for systematic review. Available evidence derived from non-randomised controlled trials is discussed in the main text of this review.

Authors' conclusions
There is a lack of randomised controlled trials in which endoscopic mucosal resection (EMR) is compared with gastrectomy for early gastric cancer. There is, therefore, a need for well-designed randomised controlled trials to determine the effects of EMR compared to gastrectomy.

PLAIN LANGUAGE SUMMARY

Endoscopic mucosal resection for early stomach cancer

There is a lack of randomised controlled trials (RCTs) in which endoscopic mucosal resection (EMR) is compared with surgery for early stomach cancer. There is a need for well-designed randomised controlled trials to determine the effects of EMR compared to gastrectomy.

BACKGROUND

Stomach cancer is the fourth most common cancer worldwide. In the UK, it is the fifth most common cancer for men and the ninth most common cancer for women (Cancer Research UK). It is the second most common cause of death from cancer worldwide. Geographically, there are some high risk areas, such as China and Japan, and lower rates of occurrence in North America, Australia and New Zealand (Parkin 2002).

Early gastric cancer (EGC) was defined in 1962 by the Japanese Research Society for Gastric Cancer as tumours with invasion limited to the mucosa or submucosa of the stomach irrespective of lymph node involvement (Kojima 1998). Surgical gastrectomy was the only method of treatment for EGC before endoscopic mucosal resection (EMR) or endoscopic mucosectomy was introduced in Japan (Hiki 1996). However, accumulated histopathological data on surgical gastric cancer specimens have revealed that many early gastric cancer patients did not have any metastatic lesions (Gotoda 2000; Tada 2000). That is, gastrectomy for resection of regional lymph nodes is not always required and the option of treating EGC using endoscopy, namely endoscopic mucosal resection (EMR), can be considered when the probability of lymph node metastasis is low.

The indications for EMR according to the Japanese Gastric Cancer Association Guidelines include:

(1) a tumour with a low risk of lymph node metastasis;

(2) differentiated adenocarcinoma, intramucosal cancer;

(3) a tumour of less than 20 mm in size, regardless of macroscopic type, and without ulcer findings (Japanese GCA 1998; Eguchi 2003).

EMR has the advantage of not only allowing the lesion to be examined histologically to reveal its extent and infiltration depth but also the outcome of treatment can be evaluated on the basis of macroscopic and histological findings. Therefore, EMR provides significant benefits for an accurate final diagnosis and eradication of submucosal lesions. The procedure is less invasive than surgical gastrectomy without sacrificing the possibility of a cure (Hiki 1996; Ono 2001). Because of this, EMR appears to be a good therapeutic modality for EGC, especially in patients at high risk of having severe complications or refusing surgery (Hamada 1996). Endoscopic treatment has become increasingly popular in recent years as an alternative to surgical treatment and with the hope of offering superior quality of life for the patient. EMR is considerably cheaper compared with conventional surgery (O'Mahony 2001). A low incidence of post-operative complaints and no severe complications have been reported (Takeshita 1997a; Suzuki 1999). No deaths related to complications of EMR were registered in a review of 1832 patients treated with EMR in Japan over 10 years (Kojima 1998). Due to technological advances in detection methods, almost 10,000 cases of early gastric cancer are diagnosed every year in Japan, corresponding to 40% to 50% of all gastric cancers (Kojima 1998). The five-year survival rate of patients with EGC in that country is about 90% after gastrectomy and complete removal of primary and secondary lymph nodes (Ono 2001). Five and 10-year survival rates of EMR are similar to conventional surgery (Tada 2000). Thus, in differentiated gastric adenocarcinoma with minimal submucosal invasion and not accompanied by peptic ulcer or other risk factors, such as lymphatic invasion EMR alone may have a curative potential, without the necessity for further radical surgery (Kashimura 1999:Tada 2000). Because of the excellent results of EMR, experts believe that early detection of cancerous lesions and their treatment using EMR is the ideal goal of cancer treatment in people with cancers of the gastrointestinal tract (Ono 2001; Inoue 2002). EMR for mucosal gastric carcinoma without lymph node metastasis is the currently accepted curative procedure in Japan. Many other countries have adopted EMR treatment for EGC, such as China, the Americas and Western countries (Zhou 1995; Giovannini 1999; Llorens 2000; Wehrmann 2001; Ahmad 2002).

There are numerous techniques and many published studies evaluating EMR available (Zhou 1995; Kajiyama 1996; Takeshita 1997b; Giovannini 1999; Suzuki 1999; Kim 2000; Wehrmann 2001; Yoshikane 2001; Ahmad 2002). However, the quality of these trials has not been assessed systematically even though the technique of EMR has been in use for about 20 years.

OBJECTIVES

The purpose of this review was to compare the effectiveness and the safety of EMR with gastrectomy for the treatment of EGC.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

We searched for all randomised and quasi-randomised controlled trials of EGC patients involving a treatment arm of EMR and a comparison arm of gastrectomy. Abstracts or unpublished articles were included.

Types of participants

Participants included patients with EGC defined as tumours with invasion limited to the intermucosa and submucosa, using the Japan or Vienna Criteria (Schlemper 2000; Eguchi 2003), as these types of lesions have a low risk of metastasis (Yamao 1996).

Types of intervention

Endoscopic mucosal resection (EMR) was compared with gastrectomy (including partial, distal and total gastrectomy) in the treatment of EGC.

Types of outcome measures

Primary outcome
* Five-year survival rate.
Secondary outcomes
* Recurrence.
* Metastasis after therapy.
* Failure cases of EMR (patients whose EGC is not resected by EMR).
* Reports of complications, including bleeding, perforation and death associated with EMR.
* Quality of life measures.
Cost assessments were not performed.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Upper Gastrointestinal & Pancreatic Diseases Group methods used in reviews.

Searches were conducted to identify all published and unpublished randomised controlled trials. Articles published in any language were included.
Trials were identified by searching the following electronic databases: Cochrane Central Register of Controlled Trials (CENTRAL) which includes the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group Trials Register (The Cochrane Library 2005, Issue 1), MEDLINE (1966 to March 2005), EMBASE (1980 to March 2005), CINAHL (1985 to March 2005) and CBM (Chinese BioMedical Database 1982 to 2002). The searches of CENTRAL, MEDLINE and EMBASE were updated in February 2006. To identify randomised controlled trials (RCTs), the following search was combined with the Cochrane highly sensitive search strategy phases, one two and three as contained in the Reviewer's Handbook (Higgins 2005).
MEDLINE search strategy
exp gastrectomy/
gastrectom$.tw.
(total adj3 gastrectom$).tw.
(subtotal adj3 gastrectom$).tw.
(partial$ adj3 gastrectom$).tw.
(distal adj3 gastrectom$).tw.
(radical$ adj3 gastrectom$).tw.
(gastr$ adj10 resect$).tw
(stomach adj10 resect$).tw.
or/30-38
(endoscopic adj3 mucosal adj3 resection).tw.
(endoscop$ adj3 mucosectomy).tw.
or/40-41
39 and 42
Reference lists from trials identified by electronic searching were handsearched to identify further relevant trials. Published abstracts of conference proceedings from the United European Gastroenterology Week and British Society of Gastroenterology (published in Gut) and Digestive Disease Week (published in Gastroenterology) were handsearched. The authors also handsearched conference abstracts from the World Congress of Gastroenterology, Digestive Disease Week of China and the International Gastric Cancer Congress.
In addition, members of the Cochrane UGPD Group and experts in the field were contacted and asked to provide details of outstanding clinical trials and any relevant unpublished materials.

METHODS OF THE REVIEW

Study selection
All identified trials were reviewed to determine if they were RCTs or quasi-RCTs. The review of eligibility was carried out independently by three authors (YP Wang, C Bennett and T Pan). There was no difference in opinion. Trials published only in abstract form were included if full details of the protocol were given. Duplicate publications were excluded.
Eligibility
Studies were assessed for eligibility by T Pan, checked by YP Wang and independently assessed by C Bennett. No randomised trials were found.

DESCRIPTION OF STUDIES

None of the forty-five potential RCTs was suitable for inclusion. None of these excluded studies was an RCT, these trials being largely retrospective reviews of therapy for EGC, either single arm or controlled against other modalities of EMR or against surgery. There were only four trials which directly compared EMR

with surgery (Mizumoto 1992; Nishida 1993; Fukase 1994; Kim 2000). One further trial reviewed EMR and surgery cases retrospectively but this was not a direct comparison as it reported lymph node metastasis and mode of invasion in the EMR cases and background factors and treatment results in the surgery cases (Misumi 1991). All four of these were non-randomised trials and were excluded.

METHODOLOGICAL QUALITY

There were no included studies.

RESULTS

There were no included studies.

DISCUSSION

Many studies of EMR have been published, particularly in the Japanese literature. There are currently no randomised controlled trials (RCTs) which evaluate the efficacy and safety of endoscopic mucosal resection (EMR) for early gastric cancer (EGC), or which compare EMR to gastrectomy for EGC. This discussion is, therefore, based on available evidence derived from reports of non-randomised studies. It is difficult to draw conclusions from the data obtained from non RCTs as selection bias in the series quoted will be present.

Updated searches will be carried out on a regular basis. If RCTs or potential RCTs become available they will be assessed and, where appropriate, incorporated into an updated review. If further details are required to assess the trials, for example method of randomisation, the study investigators will be contacted to obtain further details. A routine update of the review is due within two years of publication.

Indications for endoscopic mucosal resection

Based on the Japanese classification of gastric carcinoma (Japanese GCA 1998), the indications for endoscopic therapy are (Tada 2000) as follows.

1) Well-differentiated adenocarcinoma.
2) A tumour of size 20 mm or less in elevated types.
3) A tumour of size10 mm or less in depressed types.
4) Not associated with peptic ulcer.
5) Invasion limited to the mucosa.

The incidence of lymph node metastasis from intramucosal EGCs fulfilling these criteria is small, reported as only 0.36% (Yamao 1996).

EMR can be used to completely resect small EGCs restricted to the mucosa or can be considered when the degree of invasion into the submucosa is minute (Noda 1997). In this review the participants' characteristics were predetermined by the characteristics of patients who were enrolled by the individual studies. Perhaps as a result of this, most of the trials we assessed only included people who had tumours with apparently limited local invasion and low risk of metastasis. The true depth of invasion is not normally known at the time of EMR and one of the advantages of EMR is that it provides detailed information on depth of invasion and risk of lymph node metastasis. If cases in which lesions were found to invade deeper than expected are excluded from studies, the potential advantage of EMR in such cases cannot be assessed. Some studies do report the application of EMR to patients with such expanded criteria (Kojima 1998). Kajiyama et al 1996 evaluated the diagnostic accuracy and therapeutic value of EMR for the treatment of sub-mucosal lesions in the gastrointestinal tract. In a series of 77 patients, they concluded that EMR can be used to eradicate some types of sub-mucosal lesions (Kajiyama 1996). In an assessment of local curability of early gastric cancer, that is, no recurrence of tumour in the stomach two years after treatment, patients who did not satisfy then current therapeutic indications were treated by EMR. These patients should have been treated by surgery but had severe concomitant disease. Local cure rate in these cases was only 67% compared with a 98% local cure rate for tumours that met the standard criteria (Amano 1998). Noda 1997 cautions that as surgical gastrectomy has a five-year survival rate of 98%, any expansion of endoscopic therapy in EGC should at present only be in cases where there are clinical contraindications for surgical treatment. However, results from studies which support the use of EMR in patients having larger, well-differentiated mucosal carcinomas and developments in EMR techniques may influence widening the present indications for EMR.

Resection rates

Reported resection rates varied. In a review of 1832 cases in the Japanese literature, Kojima1998 reported that compete resection was achieved in 73.9% of cases (Kojima 1998). Higher rates have been reported: 90.4% (Giovannini 1999), 97.7% (Tani 1997) and O-izumi et al report only 9.7% residual lesions in patients with standard indications for EMR (O-izumi 1991). Lower rates of complete resection have been noted in series which expanded the indications for EMR (Hiki 1995). A large study, which prospectively recruited patients with early gastric cancer for treatment with EMR, gave an overall complete excision rate of 71.9% for patients who completed the study and had small, moderately to well-differentiated intramucosal carcinomas but only 46.3 % for cases with larger differentiated carcinomas of size 2.1 to 4 cm. Completeness of resection was assessed histopathologically and suitable incompletely resected cases underwent additional endoscopic treatment. Subsequent endoscopic findings, including biopsies, showed no residual tumour, indicating that in some cases of incomplete EMR repeat treatment can be successful in eliminating tumours (Ida 2004).

Factors which influence incomplete resection by EMR are probably related to the resection technique used, the definition of clear margins and the inclusion of patients with expanded criteria, for

example patients who have tumours with some degree of submucosal invasion (Kojima 1998).

Techniques

Numerous types of and modifications to the technique of EMR have been described (Takeshita 1997b; Chonan 1998) and discussed in Tanabe et al (Tanabe 1999). Additionally, there is debate over single fragment or piecemeal resection with it being suggested that EMR for EGC be performed en bloc rather than by dividing the lesion (Miyata 2000; Ono 2001; Eguchi 2003). Resection rates are reduced in lesions that are difficult to remove as a result of their size or location on the anterior or posterior wall rather than the lesser curvature of the stomach (Takekoshi 1994). To ensure adequate resection, it is suggested that a 'security margin' of 2 mm between the edge of the resected specimen and the margin of cancer should be preserved (Mizumoto 1992; Hamada 1996).

Residual and recurrent cancers

Incomplete resection may result in persistence or reappearance of a tumour. Clinicians then need to explore the options of further endoscopic therapy, observation or surgery depending on the status and fitness of the patient for major surgery and the degree of invasiveness of the tumour (Kojima 1998). Tada 2000 discussed this and reported the development of a protocol to follow up incomplete resection.

Endoscopic re-treatment of recurrences after EMR can result in local cure. In one study the patients were followed up by endoscopic examination up to five years after the completion of initial treatment (and extended for a further three years after endoscopic re-treatment for recurrence). With respect to small, moderately to well-differentiated intramucosal carcinomas, in patients that completed the study "the long term results, including cases of additional treatment for residual cancer following the original EMR, showed that recurrence occurred in 8 out of 199 cases (4.0%) in five of whom local cure was achieved with endoscopic treatment, giving a local final cure of 98.5%". The remaining three recurrent tumour patients, who underwent surgery, had no lymph node metastases (Ida 2004).

Local recurrence may occur in completely resected cases and may be explained by the inappropriate assessment of multi-fragment specimens (Ono 2001). In a large prospective study by Ida et al, published in 2004, there were no cases of recurrence following complete excisions in a single procedure. The authors do, however, conclude that in the cases of incomplete resection there were still recurrences after additional treatments and that in order to achieve radical cure by EMR the lesion must be initially detected and treated at the stage of local intramucosal disease (Ida 2004). Endoscopic surveillance of patients treated by EMR is recommended with suggested schedules of every six months for five years (Miyata 2000) or every three to six months for the first year and yearly thereafter (Kondo 2001). Endoscopic monitoring may reveal the development of metachronous cancers.

Complications and mortality due to endoscopic mucosal resection

Mortality due to EMR is low. No cases were reported by Kojima et al 1998.

Complications associated with EMR include bleeding and perforation (Nelson 2000). Bleeding and haemorrhage are managed by local coagulation therapy. Bleeding is more frequent when large lesions are removed or piecemeal resection techniques are employed (Noda 1997; Tanabe 1999).

Rates of bleeding vary from 1.2% (O-izumi 1991) to 20.5% (Tanabe 1999) and are also described as 'frequent' (Ono 2001).

Perforation rates vary from 0.4% (O-izumi 1991) to 5.2 % (Kondo 2001), this being managed by clipping or surgery.

A multi-centre collaborative prospective study of endoscopic treatment of early gastric cancer reported haemorrhage rates of 1.7% (7/409) and only one case of perforation (0.2%) (Ida 2004). Only one trial reported a comparison of complications of surgery compared with EMR. In a report comparing EMR with 256 radical surgery cases, postoperative complications occurred in 7.8% with an operative mortality of 0.78% in the radical surgery group. In the 56 EMR cases, nine experienced slight bleeding which was treated by ethanol injection using endoscopy (Mizumoto 1992).

Survival

Only one death after EMR was due to gastric cancer in the series reported by Kojima et al (Kojima 1998); with survival rates nearing 100% for small tumours with minimal submucosal invasion (Ponchon 2001).

In a retrospective evaluation of endoscopic treatment (116 cases) for gastric cancer compared with surgical treatment (59 cases), survival rates with Kaplan-Meier curves were calculated. In patients who were younger than 65 years, five-year survival was 92.8% for EMR cases and 100% for surgery cases. The 10-year survival rates for patients less than 65 years of age were 92.8% for EMR treated cases and 91.7% for surgery cases. In patients older than 65 years of age, five-year survival was 80.8% for EMR treated cases and 100% for surgery cases. The 10-year survival rates for patients older than 65 years of age were 80.8% for EMR and 75.0% for surgery cases. There were no significant differences between the results for patients older or younger than 65 or between the survival of EMR treated cases and surgically treated cases (Fukase 1994). Similar rates were noted by (Kim 2000), that is two and five-year survival rates for EMR versus surgery were 95% and 100% for EMR and 100% and 100% for surgically treated patients. Nishida et al (Nishida 1993) showed that in elderly patients (older than 75 years of age) endoscopic therapy showed better results than conventional surgery in the first two years and almost the same results after three years. Tada et al (Tada 2000) looked at survival in 410 patients treated over a 15-year period by strip EMR. Survival rates over five and ten years for EMR compared with surgery were 84.9% and 83.5% and 90.9% and 87.4% respectively, with no significant differences between the two groups.

Quality of life (QoL)

Only one study discussed QoL. Takeshita 1997a referred to a report which indicated poor quality of life after gastrectomy. They suggested that QoL after EMR was favourable in terms of healing, diet, ability to work, drug therapy and performance status.

Cost

A cost assessment was not included in the protocol for this review as it was considered to be outside the scope of a Cochrane review. In the trials assessed, no data regarding cost were reported. The EMR procedure requires a shorter hospital stay than surgical gastrectomy but the cost saving may be offset by the need for long-term endoscopic surveillance post EMR.

Long-term outcomes

These were not described in any study.

AUTHORS' CONCLUSIONS

Implications for practice

No evidence has been found from RCTs to evaluate the safety and efficacy of endoscopic mucosal resection (EMR compared with gastrectomy for early gastric cancer (EGC). It is difficult to draw too many conclusions from the data obtained from non-RCTs as selection bias in the series quoted will be present.
As patients with EGC can expect a five-year survival of greater than 90% with surgical gastrectomy, and there are no prospective randomised controlled studies that evaluate the effectiveness of EMR compared with gastrectomy in EGC, it is difficult to assess if EMR should be adopted as the primary method of treatment for small EGCs. In terms of quality of life after treatment and its utility in patients who are unfit for surgery EMR does seem to be an attractive alternative (O'Mahony 2001). However, complications are not infrequent and there is a risk of incomplete resection or the development of recurrent or new cancers at a later date. Long-term regular endoscopic surveillance may be unacceptable to patients and would incur costs to the provider. Wide uptake of this technique in the West may require the provision of specialist centres with appropriately trained personnel.

Implications for research

There is a wide variation in the range of results reported in published non-randomised studies, the reasons for this being unclear. A review of the different recurrence rates, metastasis rates and complication rates with the reasons for this variation is outside the scope of this review but if undertaken elsewhere could provide useful background information for practitioners and patients and may inform the design of properly controlled trials. It is recommended that future trials should analyse survival, employing Kaplan Meier curves and hazard ratios, this being a more powerful tool than assessment of survival at five and ten years only. Quality of life and cost effectiveness should also be investigated. The condition of patients and different modalities of EMR should be considered, if possible. Ideally, guidelines for the management of EGCs, including protocols for treatment of patients who are unsuitable for EMR or whose tumours are not completely resected, should be guided by results from properly designed controlled trials conducted by individuals who have had proper training in EMR.

POTENTIAL CONFLICT OF INTEREST

None known.

ACKNOWLEDGEMENTS

We acknowledge the support and the invaluable help of the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group in this review.

SOURCES OF SUPPORT

External sources of support

- China Medical Board of New York (Grant number 98-680) CHINA

Internal sources of support

- Chinese Cochrane Center, Chinese Center of Evidence-based Medicine, West China Hospital of Sichuan University CHINA

REFERENCES

References to studies excluded from this review

Abe 1995

Abe T, Itho M. Endoscopic mucosal resection for the early gastric cancer. *Progress of Digestive Endoscopy* 1995;**17**:146–7.

Akiyama 1997

Akiyama M, Ota M, Nakajima H, Yamagate K, Munakata A. Endoscopic mucosal resection of gastric neoplasms using a ligating device. *Gastrointestinal Endoscopy* 1997;**45**:182–6.

Amano 1998

Amano Y, Ishihare K, Amano K, Hirakiwa K, Adachi R, Fukuda M, et al. An assessment of local curability of endoscopic surgery in early gastric cancer without satisfaction of current therapeutic indications. *Endoscopy* 1998;**30**:548–52.

Atsumi 1993

Atsumi M, Kodama T, Uehira H, Kashima K. Surveillance after endoscopic resection and early diagnosis of local recurrence. *Stomach Intestine* 1993;**28**:1433–9.

Barreda 1998

Barreda B, Sanchez L. Endoscopic treatment of early gastric cancer [Tratamiento endoscopio del cancer gastrico temprano y lesiones premalignas gastricas mediante mucosectomia]. *Revista de Gastroenterologia Peru* 1998;**18**(3):214–26.

Chonan 1998

Chonan A, Mochizuki F, Ando M, Atsumi M, Mishima T, et al. Endoscopic mucosal resection of early gastric cancer - usefulness of aspiration EMR using a cap fitted scope. *Digestive Endoscopy* 1998; **10**(1):31–6.

Fujisaki 1997

Fujisaki J, Ikegama M, Oota Y, Arai Y, Okuwaki S, Oomasa R, et al. Endoscopic mucosal resection for early gastric cancers; its follow up and management for problematic cases. *Progress of Digestive Endocopy* 1997;**50**:70–3.

Fukase 1994

Fukase K, Matsuda T, Suzuki M, Toda M, Okuyama Y, Sakai J-I, et al. Evaluation of the efficacy of endoscopic treatment for gastric cancer considered in terms of long-term prognosis. A comparison with surgical treatment. *Digestive Endoscopy* 1994;**6**(3):241–7.

Giovannini 1999

Giovannini M, Berrardini D, Moutardier V, Moges G, Houvenaeghel G, Seitz JF, et al. Endoscopic mucosal resection (EMR): results and prognostic factors in 21 patients. *Endoscopy* 1999;**31**(9):698–701.

Hamada 2001

Hamada T, Kondo K, Saito S, Kitamura S. Endoscopic mucosal resection for early gastric cancer. *Nippon Geka Gakkai Zasshi (Journal - Japan Surgical Society)* 2001;**102**(10):745–8.

Hiki 1995

Hiki Y, Shimao H, Mieno H, Sakakibara Y, Kobayashi N, Saigenji K. Modified treatment of early gastric cancer: evaluation of endoscopic treatment of early gastric cancer with respect to treatment indication groups. *World Journal of Surgery* 1995;**19**:517–22.

Ida 2002

Ida K, Katoh T, Nakajima T, et al. Outcome after using EMR according to standard guideline for endoscopic treatment of early gastric cancer. *Stomach Intestine* 2002;**37**:1137–43.

Ida 2004

Ida K, Nakazawa S, Yoshino J, Hiki Y, Akamatsu T, Asaki S, et al. Multicentre collaborative prospective study of endoscopic treatment for early gastric cancer. *Digestive Endoscopy* 2004;**16**:295–302.

Ikeda 1984

Ikeda Y, Hirao M, Hase Y, Sugihara T, Takahashi Y, Okuyama T, et al. Endoscopic resection of early gastric carcinomas and other gastric lesions with malignant potential. *Gastroenterological Endoscopy* 1984; **26**:1655–61.

Kajiyama 1996

Kajiyama T, Hajiro K, Saki M, Inoue K, Konishi Y, Takakuwa H, et al. Endoscopic resection of gastrointestinal submucosal lesions: a comparison between strip biopsy and aspiration lumpectomy. *Gastrointestinal Endoscopy* 1996;**44**(4):404–10.

Katsube 2002

Katsube T, Ogawa K, Hamaguchi K, Shimao K, Yamaguchi K, Konno S, et al. Modification of endoscopic aspiration mucosectomy (EAM) for early gastric cancer: EAM with pre-cutting. *Hepato-Gastroenterology* 2002;**49**(48):1510–3.

Kim 2000

Kim H, Lee D, Baik S, Kim J, Kwon S, Kim D, et al. Endoscopic mucosal resection with a ligation device for early gastric cancer and precancerous lesions: comparison of its therapeutic efficacy with surgical resection. *Yonsei Medical Journal* 2000;**41**(5):577–83.

Kondo 2001

Kondo H, Gotoda T, Ono H, Oda I, Yamaguchi H, Saito D, et al. Early gastric cancer: endoscopic mucosal resection. *Annali Italian di Chirugia* 2001;**72**(1):27–31.

Llorens 2000

Llorens P, Pisano R, Pisano OR. Endoscopic mucosectomy in incipient gastric malignant lesions [Mucosectomia endoscopia en lesiones gastricas malignas incipientes]. *Revista Medica de Chile* 2000 Sep;**128** (9):969–76.

Matsushita 1997

Matsushita M, Hajiro K, Okazawi K, Takakuwa H. Endoscopic mucosal resection of gastric tumours located in the lesser curvature of the upper third of the stomach. *Gastrointestinal Endoscopy* 1997;**45** (6):512–5.

Matsuzaki 2003

Matsuzaki K, Nagao S, Atsushi K, Miyazaki J, Yoshida Y, Kitagawa Y, et al. Newly designed soft prelooped cap for endoscopic mucosal resection of gastric lesions. *Gastrointestinal Endoscopy* 2003;**57**:242–6.

Misaka 1997

Misaka R, Kawaguchi M, Saitoh T. A study of the efficiency of endoscopic mucosal resection and the additional treatment as the total planning treatment for early gastric cancer. *Progress in Digestive Endoscopy* 1997;**50**:79–83.

Misumi 1991

Misumi A, Mizumoto S, Misumi K, Harada K, Kako H, Honmyo U, et al. Indication and limitation of endoscopic surgery of early gastric cancer: an analysis of 290 early cancers operated on and 65 early cancers treated endoscopically. *Japanese Journal of Gastroenterological Surgery* 1991;**24**(10):2610–4.

Miyamoto 2002

Miyamoto S, Muto M, Hamamoto Y, Boku N, Ohtsu A, Baba S, et al. A new technique for endoscopic mucosal resection with an insulated-tip electrosurgical knife improves the completeness of resection of intramucosal gastric cancers. *Gastrointestinal Endoscopy* 2002;**55**: 576–81.

Miyata 2000

Miyata M, Yokoyama Y, Okoyama N, Joh K, Sasaki M, Ohara H, et al. What are the appropriate indications for endoscopic mucosal resection of early gastric cancer? Analysis of 256 endoscopically resected lesions. *Endoscopy* 2000;**32**(10):773–8.

Mizumoto 1992

Mizumoto S, Misumi A, Harada K, Arima K, Hirata T, Yoshinaka I, et al. Evaluation of endoscopic mucosal resection (EMR) as a curative therapy against early gastric cancer. *Nippon Geka Gakkai Zasshi* 1992; **93**(9):1071–4.

Nishida 1993

Nishida T, Naruma K, Tanaka S, Inoue K, Teshima H, Yoshihara M, et al. Comparison of endoscopic therapy and conventional surgery for treatment of early gastric cancer in elderly patients. *Nippon Romen lgakka Zasshi (Japanese Journal of Geriatrics)* 1993;**30**(5):376–81.

Noda 1997

Noda M, Kodana T, Atsumi M, Nakajima M, Sawai N, Kashima K, et al. Possibilities and limitations of endoscopic resection for early gastric cancer. *Endoscopy* 1997;**29**(5):361–5.

O-izumi 1991

O-izumi H, Matsuda T, Fukase K, Furasawa A, Mito S, et al. Endoscopic resection for early gastric cancer. The actual procedure and clinical evaluation. *Stomach & Intestine* 1991;**26**:289–300.

Ono 2001

Ono, H. Kondo, H. Gotoda, T. Shirao, K. Yamaguchi, H. Saito, D, et al. Endoscopic mucosal resection for treatment of early gastric cancer. *Gut* 2001;**48**(2):225–9.

Suzuki 1999

Suzuki Y, Hiraishi H, Kanke K, Watanabe H, Ueno N, Ishida M, et al. Treatment of gastric tumors by endoscopic mucosal resction with ligating device. *Gastrointestinal Endoscopy* 1999;**49**(2):192–8.

Takahashi 1997

Takahashi H, Kojima T, Parra A, Sakuri K, Handa K, Kirihara Y, et al. Clinical evaluation of endoscopic therapy for early gastric cancer (abstract). *Endoscopy* 1997;**29**:E21.

Takechi 1992

Takechi K, Mihara M, Saito Y, Endo J, Maekawa, H, Usui T, et al. A modified technique for endoscopic mucosal resection of small early gastric carcinomas. *Endoscopy* 1992;**24**:215–7.

Takekoshi 1988

Takekoshi T, Fujii A, Katoh Y, Yanagisawa, Tainaka K. Radical endoscopic treatment of gastric cancer - indication for and evaluation of endoscopic resection. *Gan To Kagaku Ryoho (Japanese Journal of Cancer Chemotherapy)* 1988;**15**(4 pt 2-3):1449–59.

Takekoshi 1994

Takekoshi T, Baba Y, Ota H, Kato Y, Yanigawa A, Tagaki K, et al. Endoscopic resection of early gastric carcinoma, a retrospective analysis of 308 cases. *Endoscopy* 1994;**26**(4):352–8.

Takeshita 1997a

Takeshita K, Tani M, Inoue H, Saeki I, Hayashi S, Honda T, et al. Endoscopic treatment for early oesophageal or gastric cancer. *Gut* 1997;**40**(1):123–7.

Takeshita 1997b

Takeshita K, Tani M, Inoue H, Saeki I, Honda T, Kando F, et al. Endoscopic treatment for early oesophageal or gastric cancer. *Hepatogastroenterology* 1997;**44**(18):1602–11.

Tanabe 1999

Tanabe S, Koizumi W, Kokutou M, Imaizumi H, Ishii K, Kida M, et al. Usefulness of endscopic aspiration as compared with strip biopsy for the treatment of gastric mucosal cancer. *Gastrointestinal Endoscopy* 1999;**50**(6):819–2.

Tanabe 2002

Tanabe S, Koizumi W, Mitomi H, Nakai H, Murakami S, Nagaba S, et al. Clinical outcome of endoscopic aspiration mucosectomy for early stage gastric cancer. *Gastrointestinal Endoscopy* 2002;**56**(5):708–13.

Tani 1997

Tani M, Takeshita K, Saeki I, Hayashi S, Honda T, Inoue H, et al. Protection of residue or recurrence following endoscopic mucosal resection for gastric tumorous lesions (in Japanese with English abstracts). *Progress of Digestive Endoscopy* 1997;**50**:74–8.

Torii 1995

Torii A, Sakai M, Kajiyama T, Kishimoto H, Kin G, Inoue K, et al. Endoscopic aspiration mucosectomy as curative endoscopic surgery: analysis of 24 cases of early gastric cancer. *Gastrointestive Endoscopy* 1995;**42**:475–9.

Wehrmann 2001

Wehrmann T, Lange P, Nakamura M, Riphaus A, Stergious N. Endoscopic mucosal resection of premalignant lesions of the upper gastrointestinal tract. *Zeitschrift fur Gastroenterologie* 2002;**39**(11):919–28.

Yamamoto 2002

Yamamoto H, Kawata H, Sunada K, Kaneko Y, Ido K, et al. Success rate of curative endoscopic mucosal resection with circumferential mucosal incision assisted by mucosal injection of sodium hyaluronate. *Gastrointestinal Endoscopy* 2002;**56**:507–12.

Yoshikane 2001

Yoshikane H, Sakakibara A, Hidano H, Niwa Y, Goto H, Yokoi Y. Piecemeal endoscopic aspiration mucosectomy for large superficial intramucosal tumors of the stomach. *Endoscopy* 2001;**33**(9):795–9.

Zhou 1995

Zhou L, Lin S, Ye S. Endoscopic mucosectomy for resection of early gastric cancer and precancerous lesions. *Zhonhhua Nei Ke Za Zhi (Chinese Journal of Internal Medicine)* 1995;**34**(7):443–5.

Additional references

Ahmad 2002

Ahmad N, Kochman M, Long W, Furth E, Ginsberg G. Efficacy, safety and clinical outcomes of endoscopic mucosal resection: a study of 101 cases. *Gastrointestinal Endoscopy* 2002;**55**(3):390–6.

Cancer Research UK

Cancer Research UK. Stomach cancer incidence statistics for the UK (2001). http://info.cancerresearchuk.org/cancerstats/types/stomach/incidence/ (accessed 16 February 2006).

Eguchi 2003

Eguchi T, Gotoda T, Oda I, Hamanaka H, Hasuike N, Saito D. Is endoscopic one-piece mucosal resection essential for early gastric cancer?. *Digestive Endoscopy* 2003;**15**:113–6.

Gotoda 2000

Gotoda T, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, et al. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at 2 centers. *Gastric Cancer* 2000;**3**(4): 219–25.

Hamada 1996

Hamada T, Kondo K, Itagaki Y, Nishida J. Endoscopic mucosal resection for early gastric cancer. *Nippon Rinsho (Japanese Journal of Clinical Medicine)* 1996;**54**(5):1292–7.

Higgins 2005

Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5 [updated May 2005]. In: *The Cochrane Library*, Issue 3, 2005. Chichester, UK: John Wiley & Sons.

Hiki 1996

Hiki Y. Endoscopic mucosal resection (EMR) for early gastric cancer. *Nippon Geka Gakkai Zasshi (Journal - Japan Surgical Society)* 1996; **97**(4):273–8.

Inoue 2002

Inoue H, Fukami N, T. Yoshida, Kuda S-E. Clinical and public health challenge of cancer endoscopic mucosal resection for esophageal and gastric cancer. *Journal of Gastroenterology and Hepatology* 2002;**17**(4): 382–8.

Japanese GCA 1998

Japanese Gastric Cancer Association. Japanese Classification of Gastric Carcinoma - 2nd English edition. *Gastric Cancer* 1998;**1**(1):10–24.

Kashimura 1999

Kashimura H, Ajioka Y, Watanabe H, Nishikura K, Iiri T, Asakura H. Factors for nodal micrometastasis of submucosal gastric carcinoma: Assessment of indications for endoscopic treatment. *Gastric Cancer* 1999;**2**(1):33–9.

Kojima 1998

Kojima T, Parra-Blanco A, Takahaski H, Fujita R. Outcome of endoscopic resection for early gastric cancer: review of the Japanese literature. *Gastrointestinal Endoscopy* 1998;**48**(5):550–5.

Nelson 2000

Nelson D, Block K, Bosco J, Burdick J, Curtis W, Faigel D, et al. Technology status evaluation report. Endoscopic mucosal resection. *Gastrointestinal Endoscopy* 2000;**52**(6):860–3.

O'Mahony 2001

O'Mahony, S. Endoscopic mucosal resection for early gastric cancer. *Gut* 2001;**48**(2):151–2.

Parkin 2002

Parkin DM, Bray F, Ferlay J, Pisani P. Global Cancer Statistics, 2002. *CA A Cancer Journal for Clinicians* 2005;**55**:74–108.

Ponchon 2001

Ponchon T. Endoscopic mucosal resection. *Journal of Clinical Gastroenterology* 2001;**32**:6–10.

Schlemper 2000

Schlemper R, Riddell R, Kato Y, Borchard F, Cooper H, Dawsey S, et al. The Vienna classification of gastrointestinal epithelial neoplasia. *Gut* 2000;**47**(2):251–5.

Tada 2000

Tada M, Tanaka Y, Matsuo N, Shimamura T, Yanaguchi K. Mucosectomy for gastric cancer. Current status in Japan. *Journal of Gastroenterology and Hepatology* 2000;**15**(1):D98–D102.

Yamao 1996

Yamao T, Shirao K, Ono H, Kondo H, Saito D, Yamaguchi Y, et al. Risk factors for lymph node metastasis from intramucosal gastric carcinoma. *Cancer* 1996;**77**(4):597–8.

TABLES

Characteristics of excluded studies

Study	Reason for exclusion
Abe 1995	Non-controlled
Akiyama 1997	Non-controlled
Amano 1998	Non-controlled
Atsumi 1993	Non-controlled
Barreda 1998	Non-controlled

Chonan 1998	Non-controlled
Fujisaki 1997	Non-controlled
Fukase 1994	Non-randomised controlled trial
Giovannini 1999	Non-controlled
Hamada 2001	Non-controlled
Hiki 1995	Non-controlled
Ida 2002	Non-controlled
Ida 2004	Non-controlled
Ikeda 1984	Non-controlled
Kajiyama 1996	Non-controlled
Katsube 2002	Non-controlled
Kim 2000	Non-randomised controlled trial
Kondo 2001	Non-controlled
Llorens 2000	Non-controlled
Matsushita 1997	RCT but does not compare EMR with surgery (2 types of EMR compared)
Matsuzaki 2003	Non-controlled
Misaka 1997	Non-controlled
Misumi 1991	Non-randomised controlled trial
Miyamoto 2002	Non-controlled
Miyata 2000	Non-controlled
Mizumoto 1992	Non-randomised controlled trial
Nishida 1993	Non-randomised controlled trial
Noda 1997	Non-controlled
O-izumi 1991	Non-controlled
Ono 2001	Non-controlled
Suzuki 1999	Non-controlled
Takahashi 1997	Non-controlled
Takechi 1992	Non-controlled
Takekoshi 1988	Non-controlled
Takekoshi 1994	Non-controlled
Takeshita 1997a	Non-controlled
Takeshita 1997b	Non-controlled
Tanabe 1999	Non-controlled
Tanabe 2002	Non-controlled
Tani 1997	Non-controlled
Torii 1995	Non-controlled
Wehrmann 2001	Non-controlled
Yamamoto 2002	Non-controlled
Yoshikane 2001	Non-controlled
Zhou 1995	Non-controlled

GRAPHS AND OTHER TABLES

This review has no analyses.

INDEX TERMS

Medical Subject Headings (MeSH)

Gastrectomy; Gastric Mucosa [*surgery]; Gastroscopy [*methods]; Stomach Neoplasms [pathology; *surgery]

MeSH check words

Humans

COVER SHEET

Title	Endoscopic mucosal resection for early gastric cancer
Authors	YP Wang, C Bennett, T Pan
Contribution of author(s)	YP Wang conceived the topic and designed the review. C Bennett, YP Wang and T Pan, screened the papers against inclusion criteria, appraised the quality of the papers and extracted data from the papers. C Bennett and YP Wang wrote the review. C Bennett updated the review (February 2006)
Issue protocol first published	2003/3
Review first published	2006/1
Date of most recent amendment	22 May 2006
Date of most recent SUBSTANTIVE amendment	16 February 2006
What's New	This is an updated version of the review first published in January 2006. Searches of the bibliographies of trials excluded in the original version were conducted and any potential randomised controlled trials of endoscopic mucosal resection (EMR) compared with surgery were obtained and assessed for eligibility. No eligible trials were found.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	01 February 2006
Date authors' conclusions section amended	10 February 2006
Contact address	Dr Yiping Wang Gastrointestinal Department of West China Hospital Sichuan University Guoxuexiang 37 Chengdu 610041 CHINA E-mail: wyplm@mail.sc.cninfo.net Tel: 0086 0 288 55 44 437
DOI	10.1002/14651858.CD004276.pub2
Cochrane Library number	CD004276

Editorial group	Cochrane Upper Gastrointestinal and Pancreatic Diseases Group
Editorial group code	HM-UPPERGI