RESEARCH ARTICLE

Two-Endoscope Technique of Endoscopic Mucosal Resection for the Treatment of Gastric Intestinal Metaplasia

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ABSTRACT

Background and Aim: Gastric intestinal metaplasia (GIM) is precancerous with a worldwide prevalence of 25%. Eradicating Helicobacter pylori prevented about half of gastric cancers; failure to prevent the rest was attributed to GIM. GIM is irreversible and often extensive. There is no treatment. Existing endoscopic mucosal resection (EMR) is designed to treat early gastric cancer of usually <2 cm. A two-endoscope technique of EMR for extensive GIM had been designed and successfully applied. Our aim is to describe the technique in detail.

Two-endoscope technique of endoscopic mucosal resection: Patients with histologically confirmed moderate to severe GIM (operative link on GIM [OLGIM] classification) received the treatment in a daycare center. Chromoendoscopy with methylene blue was first performed to disclose and mark the GIM. Submucosal saline injections were used to lift the stained mucosa to form multiple safety cushions, which were then transformed into artificial polyps by suction and ligation, using a cap for ligation of esophageal varices. EMRs were then achieved by snare polypectomy. By rotating two gastroscopes, one designated to perform lift and snare and the other to perform suction and ligation, cycles of lift–ligate–snare were carried out until all stained mucosa was removed. Assessment chromoendoscopy with ≥seven biopsies was performed at 6 months.

Results: A total of 227 EMRs were performed in 40 patients, with a median of 3.5 per patient. Bleeding was uncommon and minimal. Gastric perforation ascribable to loss of a safety cushion occurred in one patient. Chromoendoscopy at 6 months in 36 willing patients showed no recurrence of GIM.

Conclusion: The two-endoscope technique of EMR for GIM was essentially safe and effective, with no recurrence at 6 months. It could be performed by endoscopists with standard skills.

Introduction

Gastric cancer is the 5th most common cancer in the world, and is the 4th leading cause of cancer deaths worldwide, following lung, colorectal and liver cancer in overall mortality; over a million new cases are diagnosed, worldwide, each year.[i] The age-standardized rate ($\times 1/10^5$) of gastric cancer is 32.8 in East Asia (China, Japan, S Korea), 16.8 in European Union, and 4.2 in USA.[ii] Gastric intestinal metaplasia (GIM) is a precursor to gastric cancer, with a pooled odds ratio (OR) of 3.6 in a meta-analysis of 21 studies comprising 402,636 participants,[iii] and an OR of 29.3 in rural China.[iv] It has a 1.6% 10-year baseline risk of progression to non-cardia intestinal-type gastric adenocarcinoma.[v] GIM has a worldwide prevalence of 25% in a meta-analysis of 107 studies involving 30,960 subjects,[vi] and prevalence varies between western and eastern countries, being 7–25% in USA and Europe,[vii,viii,ix,x] and 24–84% in east Asia.[xi,xii,xiii,xiv,xv]

GIM is described as mild, moderate, and severe using the OGIM system, which has an almost perfect interobserver agreement at 0.9 and has super-ceded the OLGA system (operative link on gastritis assessment), which is based on assessment of atrophic gastritis, for which the interobserver agreement was low.[xvi] Because of its simplicity and practicality, OLGIM has also super-ceded the complete and incomplete classification of GIM[xvii]; while no study is available to correlate the two systems, moderate to severe GIM most probably correlates with incomplete GIM, since both are associated with cancer development.[xvii,xviii] OLGIM is also preferred to classification by dysplasia,[xix] which is the ultimate stage before cancer but is known to associate with synchronous cancer,[xx] and interobserver variability on dysplasia is inevitable.[xxi,xxii] Moderate to severe OLGIM has been shown to associate with cancer development.[xxiii]

Helicobacter pylori is known to start a cascade of chronic gastritis, gastric atrophy, GIM, and gastric cancer.[xxiv] In a meta-analysis of 24 studies involving 48,064 individuals, eradication of H. pylori reduced the consequence of cancer by 54%[xxv]; the failure in the rest was attributed to pre-existing GIM[xxvi,xxvii] as affirmed by a meta-analysis of 16 studies involving 52,363 subjects.[xxviii] GIM is not reversible.[xxix,xxx,xxxi] Attempts to treat GIM with long-term anti-oxidative supplements[xxxii] or selective COX-2 inhibitor[xxxiii] had failed. There appears to be no treatment for GIM.

Extensive moderate to severe GIM, however, had been successfully treated endoscopically, using a novel two-endoscope technique of endoscopic resection, with no endoscopic recurrence after 6 months.[xxxiv] This report describes in detail this endoscopic technique, with an attached video presentation, with the purpose that the technique would gain wide adoption.

Two-endoscope technique of endoscopic mucosal resection

Patients

In our first report,[xxxiv] 40 consecutive patients were studied (including 20 males, mean age 62.3 ± SE 2.9 years and 20 females, mean age 58.6 ± SE 2.4 years). A prior gastroscopy with five biopsies, as recommended by the updated Sydney classification of gastritis,[xxxv] plus two prepyloric biopsies confirmed the presence of moderate to severe GIM using the OLGIM system.

Instruments and materials

two standard gastroscopes (Olympus GIFHQ290), one fitted with a cap for band ligation of esophageal varices (caps with up to 10 bands are available from Boston Scientific or Wilson Cook) and the other uncapped (Figure 1A), endoscopic cannula, injection needle, and snare, normal saline, and chromoendoscopy solutions[xxxvi] including n-acetyl choline, and methylene blue at 1:1 dilution mixed with adrenaline at 1:10,000. Methylene blue has been known for its safety.[xxxvii]

Chromoendoscopy

After an overnight fast, patients undergo the procedure in a daycare center under monitored anesthetic care with propofol for sedation. Chromoendoscopy is first performed with the uncapped endoscope using a cannula to spray the entire stomach with n-acetyl choline to remove any mucus, followed by methylene blue to stain and demonstrate the GIM (Figure 1B). Three minutes are allowed for the stain to take hold, followed by vigorous flushing with water to remove the stain and frequent suctions of the solutions to prevent esophageal reflux and bronchial aspiration. Persistently stained mucosa indicates GIM.[xxxvii] Chromoendoscopy showed that GIM was patchy and affected the distal half of the antrum[xxxiv] in all 40 patients, extending proximally to involve the whole antrum in 10 patients and further to the distal gastric body in another 10 (Table 1).

Table 1. Distribution of GIM, and Endoscopic mucosal resections (EMRs) performed, by gender and site, and cycles of endoscope exchanges per patient. Results of the first study[xxxiv] showed that GIM under chromoendoscopy was patchy and affected the distal half of the antrum in all 40 patients, extending proximally to involve the whole antrum in 10 patients and further to the distal gastric body in another 10 (Table 1).
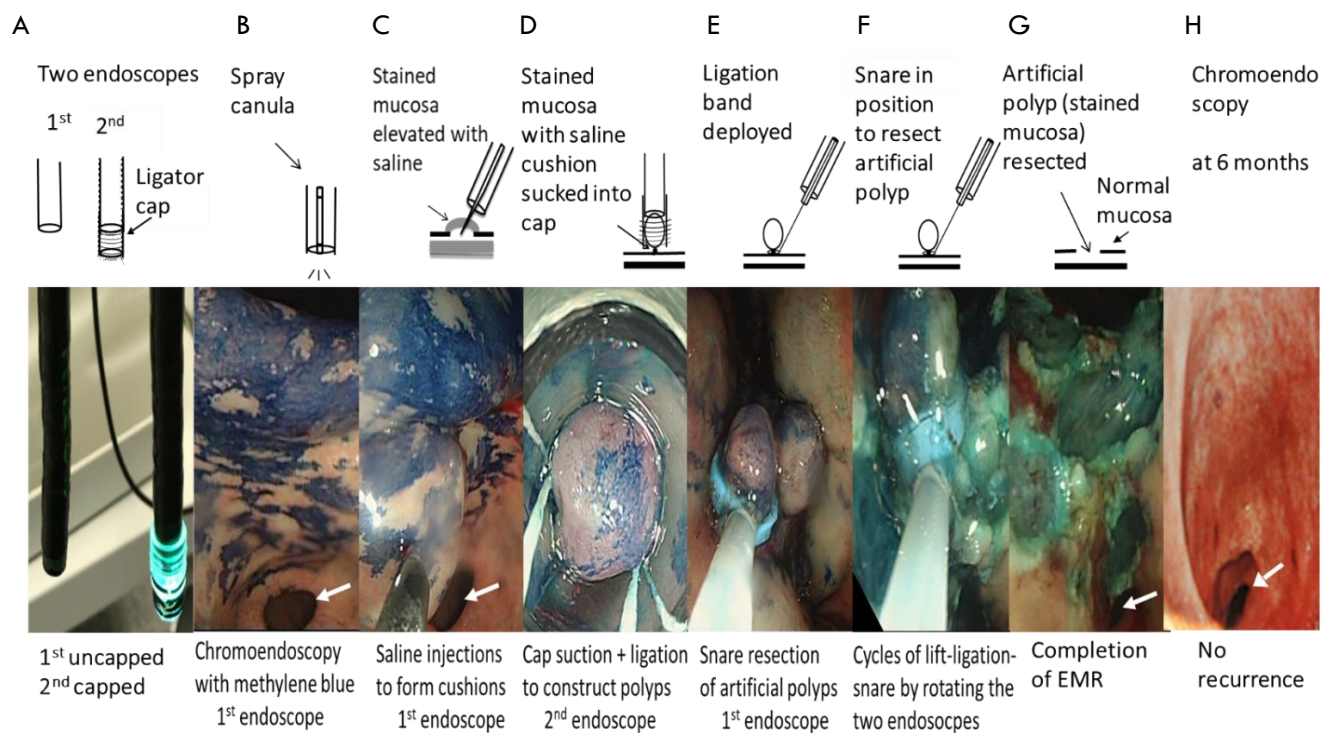
Table 1:

Patients	EMRs performed		
	Male	Female	Total
n	20	20	40
Distal half of antrum	20	25	23	48
Entire antrum	10	43	18	61
Entire antrum + distal body	10	71	47	118
Total	40	139	88	227

Two-endoscope technique of endoscopic mucosal resection

Using the same endoscope, an injection needle is inserted through the stained mucosa into the submucosa. A total of 10–50 ml of normal saline is injected to elevate the stained mucosa to form a cushion; multiple injections can be carried out to form multiple cushions (Figure 1C,1D). The endoscope is withdrawn and replaced with the capped endoscope immediately to minimize the diffusion of saline to the neighbor tissue, thereby losing the safety cushions. The capped endoscope is positioned over the elevated cushion of stained mucosa; suction is applied to draw the mucosa into the cap; and a band is deployed to ligate the mucosa, transforming it to an artificial polyp containing saline (Figure 1E). In one sitting, multiple artificial polyps can be constructed.

Figure 1: Two-endoscope technique of endoscopic mucosal resection
(white arrow indicates pylorus)

A	B	C	D	E	F	G	H
Two endoscopes 1st 2nd Ligator cap	Spray canula	Stained mucosa elevated with saline	Stained mucosa with saline cushion sucked into cap	Ligation band deployed	Snare in position to resect artificial polyp	Artificial polyp (stained mucosa) resected Normal mucosa	Chromoendoscopy at 6 months
1st uncapped 2nd capped	Chromoendoscopy with methylene blue 1st endoscope	Saline injections to form cushions 1st endoscope	Cap suction + ligation to construct polyps 2nd endoscope	Snare resection of artificial polyps 1st endoscope	Cycles of lift-ligation-snare by rotating the two endosocpes	Completion of EMR	No recurrence

Video 1 : Video (9:29:04 minutes) showing chromoendoscopy and the two-endoscope technique of EMR in a patient with severe antral intestinal metaplasia.

EMR Severe GIM of antrum.wfp

This capped endoscope is then withdrawn, and the uncapped endoscope is reinserted to perform snare polypectomy of the artificial polyps (Figure 1F). All resected specimens are to be retrieved, usually with a basket, for pathological examination to confirm GIM and to detect the presence of any dysplasia and/or malignancy.

Cycles of endoscope exchanges are carried out until all stained mucosa has been resected (Figure

1G). The EMR wounds can be clipped, but this is generally not necessary as practically all wounds are superficial. Small residual spots of stained mucosa, usually 2–5 mm, can be destroyed by electrocoagulation and retrieved using hot biopsy forceps. Patients can be discharged after the procedure with a proton-pump inhibitor and sucralfate.

A total of 227 EMRs were performed with a median of 3.5 per patient. All patients had the procedure performed in one session, except two, both with GIM involving the entire antrum and distal body, with one requiring two and the other three sessions, approximately 8 weeks apart. Bleeding was uncommon and minimal and could be readily controlled by electrocoagulation. No patient had major gastrointestinal bleeding in the form of hematemesis or melena. In the patient who required three sessions, one EMR at the second session resulted in perforation, which was discovered during the procedure; laparoscopic repair of the perforation was performed. The patient returned on a later date to have the EMRs (total 31) completed. No patient had aspiration pneumonia. There was no mortality. All specimens were retrieved for pathological examination; no malignancy or dysplasia was present.

Follow up
Median follow up was 52 weeks. At 1 week, 62.5% of patients reported no complains; the others reported minor epigastric or chest discomfort in the first 2 days. No patient phoned up for an immediate appointment because of postoperative discomfort. In the 36 patients who agreed to have repeat chromoendoscopy and multiple biopsies at 6 months (Figure 1H), chromoendoscopy was negative in all except six patients, in whom fewer than ten 2–5 mm spots of persistent staining were present; these were most likely remnants of previous EMR and were removed by hot biopsy, which demonstrated mild GIM. All other biopsies indicated no GIM.

Discussion

A mafor advantage of the two-endoscope technique of EMR is its ability to resect gastric lesions larger than 2 cm, a limit beyond which has not been endoscopically achieved in the past,[xxxviii] and GIM is often larger than 2 cm [xxxix] and has hitherto been untreatable; it is now amenable to treatment. The technique is simple — chromoendoscopy, needle injection of saline to elevate mucosa, ligation, and snare resection are all familiar to endoscopists with standard skills. The instruments are readily available: methylene blue, two standard endoscopes, ligation cap for esophageal varices, and standard endoscopy instruments. The technique is safe — the saline mucosal cushions constructed before band ligation and snare resection help avoid perforation and bleeding. The cost of the procedure is low and involves the setting of a routine endoscopy center. A final advantage is that the procedure is performed in a daycare setting, with home discharge afterwards.

The disadvantages include (i) the need for multiple endoscope insertions and withdrawals with possible minor injury to throat, although this can generally be avoided with well-lubricated endoscopes or the use of a throat guard (which we found unnecessary), and (ii) perforation, as occurred in one of our 40 patients. In retrospect, this was related to the loss of the saline cushion, which could occur when a significant portion of the saline diffused to the neighbor tissue so that subsequent suction and ligation trapped all layers of the stomach, leading to perforation when snare resection was applied. This complication is preventable by ensuring that all safety cushions are adequately and generously filled with saline before applying suction and ligation. New devices and techniques have become available for endoscopic closure of gastrointestinal perforations.[xl]

Specially designed caps for EMR are available; these, however, are designed for EMR one site (< 2 cm) at a time. This approach is not applicable when large areas like those of IM are present.
Endoscopic submucosal dissection (ESD), while designed for small lesions such as early gastric cancer, can in theory be extended to treat extensive IM; it is typically performed by endoscopists with experience in the technique itself. ESD carries a significantly higher risk of perforation (3.2%) than EMR (1.2%), as shown in a meta-analysis study.[xli]

In this study, 36 patients agreed to a repeat chromoendoscopy and biopsies at 6 months; this confirmed the loss of IM, indicating that the treatment was effective and that there was no recurrence.

As indicated earlier, eradication of *H. pylori* reduced gastric cancer risk by only about half,[xxvi] and the failure in the other half could be attributed to the development of GIM,[xlii,xliii,xliv] a complication of *H. pylori* and has been regarded as a point of no return.[xlv,xlvi] This technique will help pave the way for the ultimate prevention of gastric cancer.

Conclusion

The two-endoscope technique of EMR can be applied to treat GIM, which is precancerous, often extensive, and for which there is no established treatment. It is essentially free from complications and can be readily performed by endoscopists with standard skills.

Ethics

This study was approved by Hong Kong Clinical Research Ethics Committee (No. 012019001).

Conflicts of interests

The authors have no conflict of interest or financial relationship relevant to this article. The technique reported in this study was accepted by the Australia Patent Office, patent number 2017272212 Title: Two-Endoscope Technique of Endoscopic Mucosal Resection and Kit with a Set of Endoscopes for the Method, and by the USA Patent Office, No. US 10,293,061, with the same Title.

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