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Gel immersion endoscopic mucosal resection for early gastric neoplasms: a multicenter case series study

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ABSTRACT

Several cases have been reported that suggest the efficacy of gel immersion endoscopic mucosal resection (GI-EMR) for gastric neoplasms. However, no study has evaluated treatment outcomes of GI-EMR for gastric neoplasms. This study aimed to investigate the efficacy and safety of GI-EMR for early gastric neoplasms. Nine patients (17 lesions) undergoing gastric GI-EMR were included, with a median lesion size of 10 mm (interquartile range [IQR] 5–13 mm). All lesions were protruding or flat elevated. The median procedure time was 3 minutes (IQR 2–5) and en bloc resection was achieved in all cases. Among 15 neoplastic lesions, the R0 resection rate was 86.7% (13/15 lesions). Adverse events included immediate bleeding requiring hemostasis in two cases, which was controlled endoscopically. No delayed bleeding or perforation occurred. In conclusion, GI-EMR may be a safe and effective treatment for early, small gastric neoplasms. However, due to the small sample in the present study, further investigation is required regarding the indication for this technique.

Introduction

Endoscopic submucosal dissection (ESD) is widely performed for early gastric neoplasms due to its superior en bloc and R0 resection and lower local recurrence rates compared with endoscopic mucosal resection (EMR). However, ESD demands high technical expertise and prolonged procedure time, which is associated with a risk of complications such as bleeding and perforation. ESD may not always be necessary for removing gastric lesions, especially for small (≤20 mm) gastric elevated tumors, because the European Society of Gastrointestinal Endoscopy (ESGE) guidelines indicate that EMR is acceptable for small Paris 0-IIa lesions with low likelihood of malignancy [1]. Nevertheless, conventional EMR often results in piecemeal resection, even for gastric tumors < 20 mm, leading to a higher local recurrence rate [2]. Therefore, there is a need for less invasive therapeutic options for gastric lesions.

Although underwater EMR (UEMR) is a potentially minimally invasive treatment with higher en bloc and R0 resection abilities and a lower local recurrence rate for colorectal neoplasms

than conventional EMR [3], UEMR for gastric neoplasms has several issues: 1) water mixing with gastric mucus over time, resulting in a poor visual field and difficulty in snaring under direct vision; 2) if immediate bleeding is observed after resection, it can lead to a compromised visual field and difficulty in stopping the bleeding; and 3) prolonged water immersion sometimes leading to backflow into the esophagus and pharynx, causing aspiration pneumonia.

To address these issues, a new endoscopic resection technique called gel immersion EMR (GI-EMR) has been developed, using ViscoClear (Otsuka Pharmaceutical Factory, Tokushima, Japan), an endoscopic field-of-view securing gel with a three-dimensional network structure consisting of xanthan gum, locust bean gum, concentrated glycerin, and purified water. The major advantage of this technique is that the gel does not mix with mucus, blood, or other residuals, maintaining a clear field of view over time and allowing for more accurate resection under direct vision than UEMR. A previous study reported that GI-EMR for duodenal tumors shortened the treatment time and improved the R0 resection rate compared with UEMR [4], suggesting that GI-EMR may enhance treatment outcomes while maintaining the same simplicity as UEMR. Despite several case reports of gastric GI-EMR [5], no studies have evaluated treatment outcomes with GI-EMR for gastric neoplasms. Thus, this study aimed to investigate the efficacy and safety of GI-EMR for early gastric neoplasms.

Patients and methods

Study design and patients

In this multicenter, retrospective case series, the records of patients who underwent GI-EMR for early gastric neoplasms between April 2021 and October 2023 at three institutions (Shiga University of Medical Science Hospital, Shizuoka Cancer Center, and Kobe City Medical Center General Hospital) were extracted. The principal indications for GI-EMR are as follows: 1) lesion size ≤20 mm; 2) protruding or flat elevated intramucosal lesion; and 3) location at the greater curvature or near the greater curvature side. Although these indications are similar to those for UEMR [6], UEMR is generally not performed at the three institutions because of concerns about poor visual field due to water mixing with gastric mucus over time. Conventional EMR was generally indicated only for pedunculated lesions. The final decision was reached through discussion at a gastroenterology conference. Written informed consent for endoscopic treatment was obtained from all patients preoperatively.

This study was approved by the Institutional Review Board of the Shiga University of Medical Science (Institutional No. R2023–080), Shizuoka Cancer Center (Institutional No. T2023–41–2023–1-3), and Kobe City Medical Center General Hospital (Institutional No. zn231205). Informed consent for participation was obtained using the opt-out method.

Endoscopic procedures and patient management

For all procedures, a therapeutic endoscope (GIF-H290T or GIF-Q260J; Olympus Medical Systems) with a distal attachment (D201–11804; Olympus Medical Systems or elastic touch [top]) was used. In some cases, other types of endoscopes (GIF-H290Z, GIF-H260Z, and GIF-2TQ260M; Olympus Medical Systems) were used. A standard electrosurgical generator (VIO300D or VIO3; ERBE) was used. Before resection, forceps or snares with predetermined diameters were used to measure lesion size. Marking around the lesion was performed using a snare tip or needle knife.

For GI-EMR, after a syringe was attached to the BioShield irrigator (U.S. Endoscopy), the gel was injected via the accessory channel into the stomach and the lesion was then carefully snared and resected with a blended cut current (Endocut Q; effect 3, time interval 2, time duration 2) using a 10-mm or 15-mm oval snare (SnareMaster Plus; Olympus Medical Systems) or a 15-mm or 20-mm rounded stiff snare (Captivator II; Boston Scientific) (▶ **Fig. 1**, ▶ **Video 1**). Prophylactic clipping after GI-EMR was performed according to endoscopist preference. The specimens were transported to the Pathology Division after being fixed in 10% formalin for histological assessment.

Patients who underwent GI-EMR were followed with a brief hospital admission. If R0 resection was achieved, endoscopic follow-up was performed 6 months to 1 year later. If the pathological margins were positive or indistinct, an endoscopy was performed within 6 months to biopsy the post-resection ulcer scar.

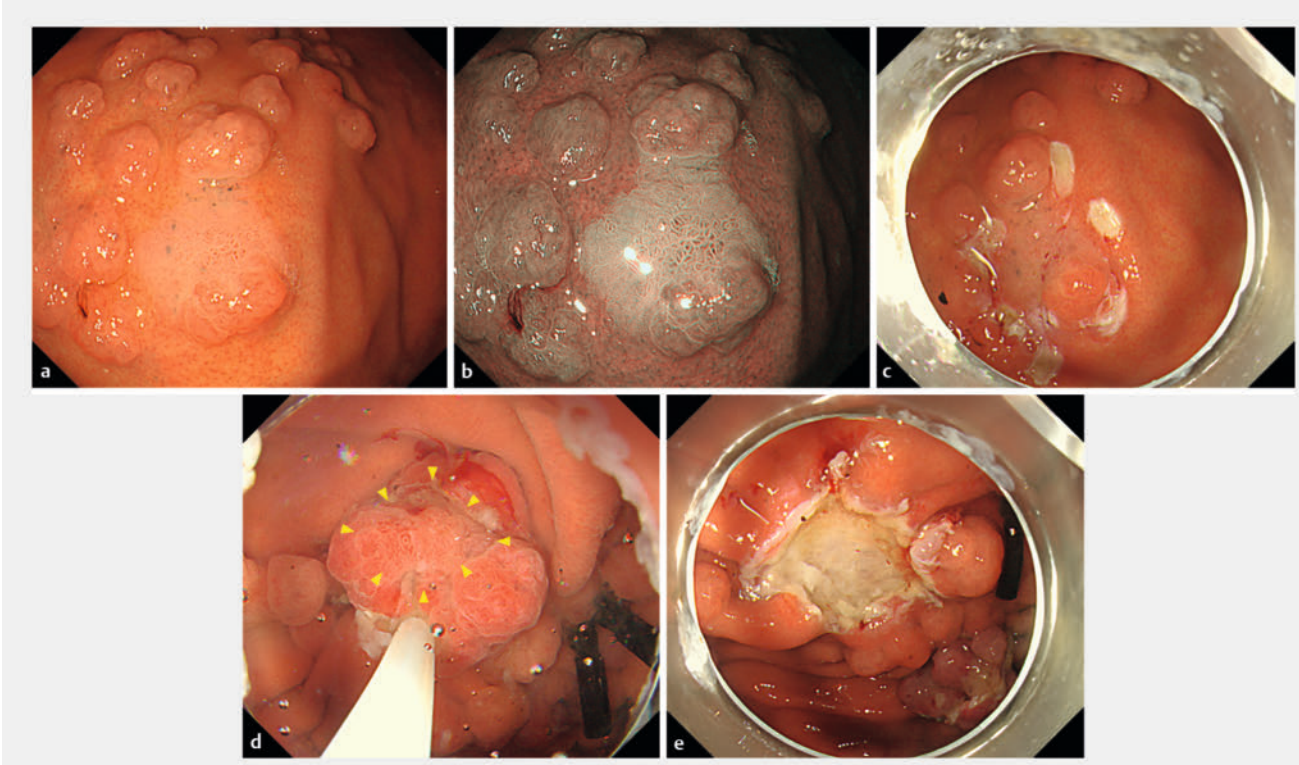
Data collection and definition

We retrospectively collected clinicopathological information from institutional electronic records. We analyzed the following treatment outcomes: en bloc resection rate, R0 resection rate, procedure time, and adverse events (AEs), such as immediate or delayed bleeding and perforation.

En bloc resection was defined as the endoscopic removal of the lesion in one piece. R0 resection was defined as an en bloc resection with free histological tumor margins. Procedure time was defined as the time from the start of the irrigating gel to the end of the resection. Immediate bleeding was defined as intraprocedure bleeding requiring endoscopic or surgical hemostasis such as continuous oozing or spurting. Delayed bleeding was defined as hematemesis or melena after EMR requiring blood transfusion or endoscopic or surgical intervention. A perforation was defined as a defect in the muscular layer of the ulcer after endoscopic resection.

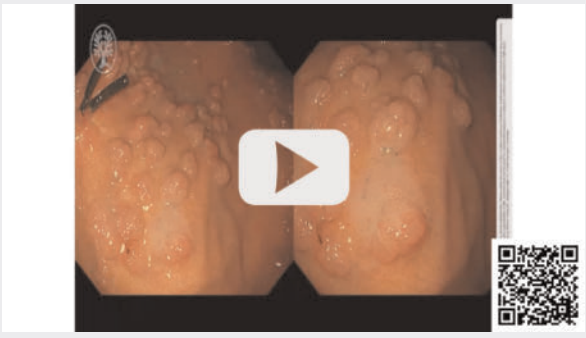
Results

Nine patients (17 lesions) who underwent gastric GI-EMR were included. Baseline characteristics of the patients are summarized in ▶ **Table 1**. The median patient age was 54 years (interquartile range [IQR], 47–59). The median lesion size was 10 mm (IQR, 5–13). Among the lesions, 82.4% (14 of 17) were located in the upper third of the stomach, and 70.6 % (12 of 17) at the greater curvature site. More than half of the lesions (10 of 17) were gastric neoplasms in patients with familial adenomatous polyposis (FAP), and three sporadic foveolar-type gastric neoplasms with a raspberry-like appearance [7] (pretreatment diagnosis) were included.



▶ **Fig. 1** GI-EMR procedure. **a** A whitish flat elevated lesion at the greater curvature of the upper gastric body with fundic gland polyposis in a FAP patient. **b** NBI view. **c** Marking was performed. **d** Snaring under gel immersion (the lesion was yellow arrowhead). **e** Mucosal defect without perforation. GI-EMR, gel immersion endoscopic mucosal resection; FAP, familial adenomatous polyposis; NBI, narrowband imaging

VIDEO



▶ **Video 1** Successful gel immersion endoscopic mucosal resection for the flat elevated lesion at the greater curvature of the upper gastric body with fundic gland polyposis.

Treatment outcomes for GI-EMR are shown in ▶ **Table 2**. Median procedure time was 3 minutes (IQR, 2–5). En bloc resection was achieved in all cases. In most cases (88%), the amount of gel used did not exceed 200 g (one pack of ViscoClear). Pathological examination revealed adenocarcinoma, adenoma, and non-neoplastic in five, 10, and two lesions, respectively. Among the 15 neoplastic lesions, the R0 resection rate was 86.7% (13 of 15). Of the cases in which R0 resection could not be achieved, all had unclear horizontal margins and did not show local recurrence at a follow-up period of 19 months. Clip closure after resection was performed in all the cases. AEs included immediate bleeding requiring hemostasis in two cases, which was controlled endoscopically. No delayed bleeding or perforation occurred.

Discussion

To the best of our knowledge, this is the first study to evaluate treatment outcomes of gastric GI-EMR. In this study, we demonstrated that GI-EMR resulted in favorable treatment outcomes, including en bloc and R0 resection rates. Immediate bleeding requiring hemostasis was endoscopically controllable, whereas neither delayed bleeding nor perforation occurred. These results suggest that GI-EMR might be a safe and effective treatment for small (≤20 mm) gastric neoplasms.

In the guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer [8], differentiated mucosal gastric cancer ≤ 20 mm without ulceration is designated as an absolute indication for EMR or ESD. However, ESD is mainly performed over conventional EMR for such lesions due to higher piecemeal resection and local recurrence rates for EMR than for ESD [2]. Recently, gastric UEMR has become a simple and useful alternative to conventional EMR with relatively good treatment outcomes [6]. However, the evidence is insufficient due to the small sample size, and there are several

▶ **Table 1** Baseline characteristics.

Patients	**N = 9**
Age, years, median (IQR)	54 (47–59)
Male sex (%)	4 (44)
Hereditary disease (%)	
▪ FAP	3 (33)
▪ Lynch syndrome	1 (11)
▪ None	5 (56)
Lesions	**N = 17**
Lesion size, mm, median (IQR)	10 (5–13)
Location 1 (%)	
▪ Upper third	14 (82)
▪ Middle third	1 (5.9)
▪ Lower third	0 (0)
▪ Remnant stomach	2 (12)
Location 2 (%)	
▪ Greater curvature	12 (71)
▪ Lesser curvature	0 (0)
▪ Anterior wall	3 (18)
▪ Posterior wall	2 (12)
Morphology (%)	
▪ Protruding	8 (47)
▪ Flat elevated	9 (53)
Antithrombotic agents (%)	1 (5.9)
Pathology of biopsy specimen before treatment (%)	
▪ Adenocarcinoma	5 (29)
▪ Adenoma	9 (53)
▪ Difficult to determine neoplastic or non-neoplastic	1 (5.9)
▪ Non-neoplastic	1 (5.9)
▪ Biopsies were not performed	1 (5.9)
Pretreatment diagnosis (%)	
▪ Gastric neoplasms in patients with FAP	10 (59)
▪ Foveolar-type gastric neoplasms with a raspberry-like appearance	3 (18)
▪ Gastric neoplasms in patients with Lynch syndrome	2 (12)
▪ Gastric hyperplastic polyp with adenocarcinoma	1 (5.9)
▪ Fundic gland polyp with dysplasia	1 (5.9)

IQR, interquartile range; FAP, familial adenomatous polyposis.

▶ **Table 2** Treatment outcomes of gel immersion endoscopic mucosal resection for gastric neoplasms.

Lesions	**N = 17**
En bloc resection (%)	17 (100)
R0 resection (%)*	13 (87)
Procedure time, minutes, median (IQR)	3 (2–5)
Pathology (%)	
▪ Adenocarcinoma	5 (29)
▪ Adenoma	10 (59)
▪ Non-neoplastic lesion	2 (12)
Clip closure after resection (%)	17 (100)
Immediate bleeding (%)	2 (12)
Delayed bleeding (%)	0 (0)
Perforation (%)	0 (0)

IQR, interquartile range.
*The R0 resection rate was calculated among 15 neoplastic lesions.

issues: poor visual field due to water mixing with gastric mucus or bleeding over time and the risk of aspiration pneumonia due to prolonged water immersion. Thus, we focused on GI-EMR [5], which may contribute to better treatment outcomes while maintaining the same simplicity as UEMR [4]. In fact, en bloc resection was achieved in all cases in this study and the R0 resection rates for gastric adenocarcinomas and adenomas were similar to those of UEMR previously reported [6] (86.7% [13 of 15] vs. 86.4% [19 of 22]).

Furthermore, median procedure time tended to be shorter than that previously reported for UEMR [6] (3 vs. 4 minutes). Therefore, GI-EMR may yield similar resection ability and shorter procedure time than UEMR. As for aspiration pneumonia after endoscopic resection, one case of aspiration pneumonia after UEMR was observed previously [6], while no aspiration pneumonia after GI-EMR occurred in this study. Although there are currently no reports about the amount of water used in gastric UEMR, procedure time can be sometimes prolonged depending on mucus or residue in the stomach and post-resection bleeding, which may increase the amount of water and risk of aspiration pneumonia. However, although aspiration pneumonia due to food residue and gel reflux is still a possibility with GI-EMR, the gel is more viscous than water and resection can be performed with a good field of view without the gel mixing with residue, which contributes to shorter procedure time. Therefore, risk of aspiration pneumonia may be lower with GI-EMR than with UEMR. The only identified disadvantage of GI-EMR compared with UEMR is the cost of the gel. Considering the advantages of GI-EMR compared with UEMR mentioned above, GI-EMR may be a more desirable method for small elevated lesions.

In this study, GI-EMR was mainly performed for protruding or flat elevated lesions. Most morphologies of sporadic *Helicobacter pylori*-associated gastric neoplasms are of the depressed

type, which can cause them to slip during snaring and convert to ESD. Furthermore, a previous report about duodenal EMR and UEMR showed that depression was an independent risk factor for conversion to ESD [9]. Therefore, it is difficult to apply GI-EMR to these lesions. On the other hand, the major morphologies of gastric neoplasms located in the upper or middle third of the stomach in FAP patients [10] and sporadic foveolar-type gastric neoplasms with a raspberry-like appearance in *H pylori*-naïve patients [7] are the protruding or flat elevated type, which accounted for most of the patients included in this study and they could be easily removed with snaring EMR. Furthermore, gastric neoplasms with FAP are often accompanied by fundic gland polyposis around the tumor, which makes mucosal dissection difficult during ESD; however, during GI-EMR, fundic gland polyps around the lesion are caught in the snare, making it easier to remove. Thus, GI-EMR may be a good indication for gastric neoplasms, which usually have a protruding or flat elevated morphology.

This study has several limitations. First, it was retrospective with a small sample size, resulting in potential selection bias. Further multicenter prospective studies are required to validate these results. Second, GI-EMR was mainly performed by experienced endoscopists, which limits the generalizability of the results. Third, the procedure time for GI-EMR may have been underestimated because some patients had two lesions resected on the same day and the gel used for the first lesion may have remained during resection of the second lesion, which may have affected the treatment time.

Conclusions

In conclusion, GI-EMR may be a safe and effective treatment for small early gastric neoplasms. However, given the small sample in this study, further investigation is required regarding indications for this technique and its appropriate use compared with other resection techniques.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

[1] Pimentel Nunes P, Libânio D, Bastiaansen BAJ et al. Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2022. Endoscopy 2022; 54: 591–622

[2] Oda I, Saito D, Tada M et al. A multicenter retrospective study of endoscopic resection for early gastric cancer. Gastric Cancer 2006; 9: 262–270 doi:10.1007/s10120-006-0389-0

[3] Nagl S, Ebigbo A, Goelder S et al. Underwater vs conventional endoscopic mucosal resection of large sessile or flat colorectal polyps: a prospective randomized controlled trial. Gastroenterology 2021; 161: 1460–1474.e1 doi:10.1053/j.gastro.2021.07.044

[4] Miyakawa A, Kuwai T, Sakuma Y et al. A feasibility study comparing gel immersion endoscopic resection and underwater endoscopic mucosal resection for superficial nonampullary duodenal epithelial tumors. Endoscopy 2023; 55: 261–266 doi:10.1055/a-1924-4711

[5] Kimura H, Oi M, Morita Y et al. Gel immersion endoscopic mucosal resection for a gastric neoplasm with a background of fundic gland polyposis. Endoscopy 2022; 54: E1011–E1012

[6] Yamamoto S, Takeuchi Y, Uedo N et al. Underwater endoscopic mucosal resection for gastric neoplasms. Endosc Int Open 2022; 10: E1155–E1158 doi:10.1055/a-1854-3373

[7] Shibagaki K, Fukuyama C, Mikami H et al. Gastric foveolar-type adenomas endoscopically showing a raspberry-like appearance in the Helicobacter pylori-uninfected stomach. Endosc Int Open 2019; 7: E784–E791 doi:10.1055/a-0854-3818

[8] Ono H, Yao K, Fujishiro M et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer (second edition). Dig Endosc 2021; 33: 4–20 doi:10.1111/den.13883

[9] Kiguchi Y, Kato M, Nakayama A et al. Feasibility study comparing underwater endoscopic mucosal resection and conventional endoscopic mucosal resection for superficial non-ampullary duodenal epithelial tumor <20 mm. Dig Endosc 2020; 32: 753–760 doi:10.1111/den.13524

[10] Shimamoto Y, Ishiguro S, Takeuchi Y et al. Gastric neoplasms in patients with familial adenomatous polyposis: endoscopic and clinicopathologic features. Gastrointest Endosc 2021; 94: 1030–1042.e2