

Oral prednisolone and triamcinolone injection for gastric stricture after endoscopic submucosal dissection

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Background: The expansion of the indications for endoscopic submucosal dissection (ESD) to include early gastric cancers has enabled extensive resection. However, post-ESD stenosis after large resections applied to the gastric cardia or pylorus is often difficult to manage. The aim of this study was to evaluate the benefit of oral prednisolone and triamcinolone injection for stenosis after gastric ESD.

Methods: Eight patients who underwent ESD for large neoplastic lesions that extended more than three-fourths of the luminal circumference were enrolled in this study. Four patients underwent ESD for gastric cardia cancer, and four patients were treated for pyloric lesions. To prevent post-ESD stricture, oral prednisolone was started at 30 mg daily on the second day after ESD and then tapered gradually in two cases, while topical injection of 80 mg triamcinolone was performed once immediately after ESD in six cases. Endoscopic balloon dilatation (EBD) was used for stricture-related symptoms or signs including nausea, vomiting, or food residuals observed on endoscopy. EBD was also applied if a 10-mm-diameter endoscope was not able to pass through the lumen. The incidence of stenosis, the frequency and period required for EBD, the duration required for ulcer healing after ESD, and the incidences of post-procedural bleeding and perforation were assessed.

Results: One of the eight patients had post-ESD stenosis requiring EBD. The median ulcer healing period after ESD was 87.5 (range, 56-133) days. No patients experienced post-procedural bleeding or perforation. There were no adverse events due to steroid therapy.

Conclusions: The results of the present study showed the safety and usefulness of steroid therapy for management of stenosis after large ESD in the gastric cardia or pylorus.

Keywords: Endoscopic submucosal dissection (ESD); cardia; pylorus; stricture; steroids



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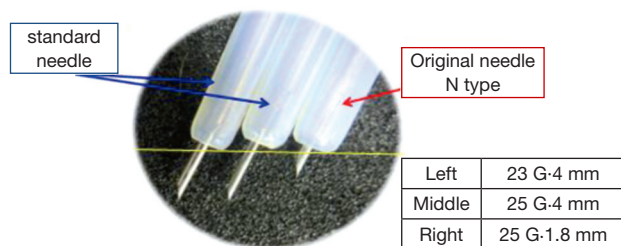
Introduction

The expansion of the indications for endoscopic submucosal dissection (ESD) to include early gastric cancers has enabled extensive resection (1,2). However, post-ESD stenosis after large resections applied to the gastric cardia or pylorus is often difficult to manage, requiring multiple endoscopic balloon dilatation (EBD) (3). Iizuka *et al.* reported the frequency of post-ESD stenosis as 1.9% of all gastric ESD; Tsunada *et al.* reported 0.9%; and Nonaka *et al.* reported 1.0% (4-6).

However, they reported that 17% of patients who underwent ESD for gastric cardia cancer had post-ESD stenosis, and 7% of patients who underwent ESD for pyloric cancer had post-ESD stenosis (6). Coda *et al.* reported the risk factors for post-ESD stenosis for the gastric cardia or pylorus; a resection of more than three-fourths of the circumference of the gastric cardia or pylorus is a significant factor related to stenosis (3). Again, all patients who had post-ESD stenosis were symptomatic (3). Dysphagia was the main symptom related

Table 1 Clinicopathological features of eight patients who underwent endoscopic submucosal dissection for large gastric cardia or pyloric lesions that extended more than three-fourths of the luminal circumference

Resection size (mm)	Tumor size (mm)	Depth of tumor invasion	Ulcer scar	Method of stricture prevention	Stricture	Endoscopic balloon dilatation	Follow-up period (days)	Period of ulcer healing (days)
100	85	m	-	Oral prednisolone	-	0	989	132
60	18	m	-	Triamcinolone injection	-	0	742	80
62	38	m	+	Oral prednisolone	-	0	721	133
55	30	m	-	Triamcinolone injection	-	0	357	88
58	40	m	-	Triamcinolone injection	+	3	288	123
42	10	-	-	Triamcinolone injection	-	0	364	84
40	16	m	-	Triamcinolone injection	-	0	185	87
63	25	sm1 (100 μ m)	-	Triamcinolone injection	-	0	87	56
Mean 59	Mean 27.5					Mean 0	Mean 360.5	Mean 87.5

**Figure 1** A short-type injection needle (N-type, Top Co, Tokyo, Japan) for safe injection onto the post-ESD ulcer. The length of the needle should be shorter than a conventional needle (1.8 vs. 4.0 mm for the novel and conventional needles, respectively).

to post-ESD stenosis in cases of gastric cardia cancer, whereas nausea or vomiting was most common for pyloric lesions (3). The median symptomatic period was 22 (range, 16-33) days and 27 (range, 15-46) days for gastric cardia and pyloric cancer, respectively (3). On the other hand, post-ESD stenosis occurs rarely following ESD for lesions of the body of the stomach (7). Thus, the risk of post-ESD stenosis varies depending on resection size and location.

Indeed, EBD has been a treatment option for stenosis after large ESD, but EBD is sometimes complicated by perforation (8-10). In addition, repeat EBD substantially compromises patients' quality of life. Therefore, a new treatment strategy for post-procedural stenosis is necessary for large gastric ESD. In this regard, endoscopic triamcinolone injection and oral prednisolone have shown promising results for the prevention of luminal stricture following extensive esophageal ESD (11,12). The aim of the present study was to evaluate the benefit of oral prednisolone and triamcinolone injection for stenosis after extensive gastric ESD.

Methods

Patients

A total of eight patients (all men; mean age, 68.5 years; range 42-85 years, mean follow-up period, 360.5 days; range 87-989 days) who underwent large ESD was enrolled in this study. The clinicopathological features of each patient are summarized in *Table 1*. Written informed consent was obtained from each patient before ESD. The tumor was demarcated using indigocarmine or crystal violet staining to determine resection size.

Management of stricture after ESD

Large ESD was defined as ESD done for lesions that extended more than three-fourths of the luminal circumference of the gastric cardia or pylorus in accordance with previous studies (3,4,7). Four patients underwent ESD for gastric cardia cancer, and four patients were treated for pyloric lesions. Steroid (oral prednisolone or endoscopic triamcinolone injection) was administered to prevent stenosis after ESD in these cases. In two patients with gastric cardia cancer, oral prednisolone was started at 30 mg daily on the second day after complete circular ESD. Prednisolone was then tapered gradually (daily 30, 25, 20, 15, 10, and 5 mg for 14 days each) and discontinued at 12 weeks. In six patients (two gastric cardia lesions, four pyloric lesions), topical injection of 80 mg triamcinolone via endoscopy was performed once immediately after ESD using the short-type needle (N-type, Top Co, Tokyo, Japan; *Figure 1*) for safe injection onto the post-ESD ulcer. Triamcinolone injection has sometimes caused esophageal perforation with the conventional endoscopic needle, and, hence, the length of the

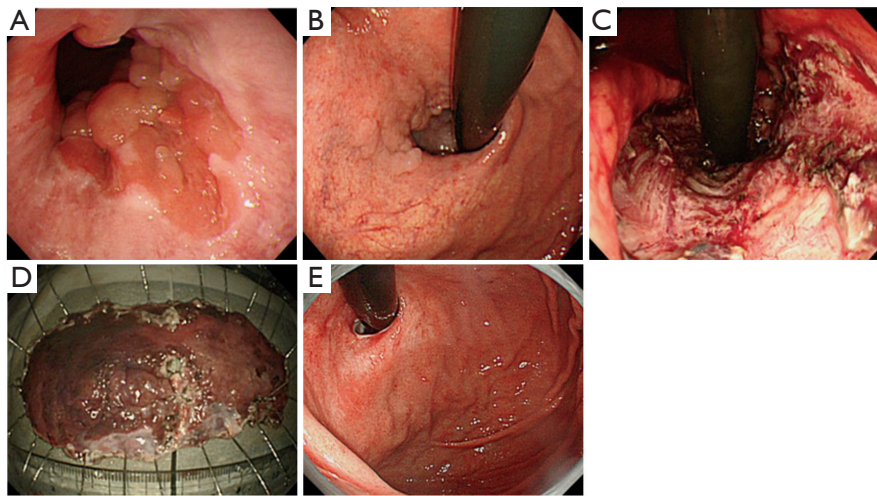


Figure 2 A 72-year-old man who had complete circular cardiac lumen resection for early gastric cancer and was given oral prednisolone for 12 weeks avoided post-ESD stenosis (case No. 1 in *Table 1*). (A) and (B) show before ESD from the oral and anal sides; (C) shows after ESD from the anal side; (D) shows the specimen; (E) shows 21 months after ESD, with no stricture.

needle should be shorter than the conventional needle (1.8 vs. 4.0 mm for the novel and conventional needles, respectively), to achieve safe application of gastric triamcinolone injections.

Follow-up endoscopy was performed one week, two weeks, and one month after ESD, and continued once a month until ulcer healing (epithelialization of the post-ESD ulcer). The patients were then followed at six months and one year after ESD, and annually thereafter.

EBD was used in cases with stricture-related symptoms or signs including nausea, vomiting, or food residuals observed on endoscopy. EBD was also used if a 10-mm-diameter endoscope could not be passed through the lumen. The incidence of stenosis, the frequency and period required for EBD, the duration required for ulcer healing after ESD, and the incidences of post-procedural bleeding and perforation were assessed. Post-procedural bleeding was defined as bleeding that required transfusion or bleeding that caused the hemoglobin level to fall 2 g/dL (2). Post-procedural perforation was diagnosed based on the presence of free air on abdominal computed tomography (13).

Results

As shown in *Table 1*, there were six IIa and two IIc macroscopic types according to the Paris endoscopic classification (14). The mean resection size was 59 (range, 40-100) mm, and the mean tumor size was 27.5 (range, 10-85) mm. As for tumor invasion depth, there were six intramucosal carcinomas, one slightly invasive carcinoma

into the submucosa, and one adenoma. The mean period of ulcer healing was 87.5 (range, 56-133) days. One of the eight patients had post-ESD stenosis that required EBD, the median frequency and period required for EBD was 0 times and 0 days (range, 0-3 times, 0-74 days), respectively. The median ulcer healing period after ESD was 87.5 (range, 56-133) days, and no patient experienced post-procedural bleeding or perforation. There were no adverse events in association with steroid therapy.

The patient who had complete circular gastric cardia lumen resection for early gastric cancer and was given oral prednisolone for 12 weeks did not develop post-ESD stenosis (case No. 1, *Figure 2*). However, the patient who had complete circular ESD for early gastric cancer in the pylorus and was given topical triamcinolone injection developed post-ESD stenosis (case No. 5). EBD and additional triamcinolone injection were added, but the next week, a 10-mm-diameter scope could not pass again, and only EBD was added, because triamcinolone generally remains 3-4 weeks in the local area. Twelve weeks after ESD, a 10-mm-diameter endoscope could not pass again, and EBD and a triamcinolone injection were added in combination with oral prednisolone starting at 30 mg/day. Prednisolone was then tapered gradually (daily 30, 25, 20, 15, 10, and 5 mg for 14 days each) and discontinued at 12 weeks. After the combination therapy, the patient remained free from stricture for about one year (*Figure 3*).

On the other hand, the remaining six patients who underwent semicircular large ESD did not develop

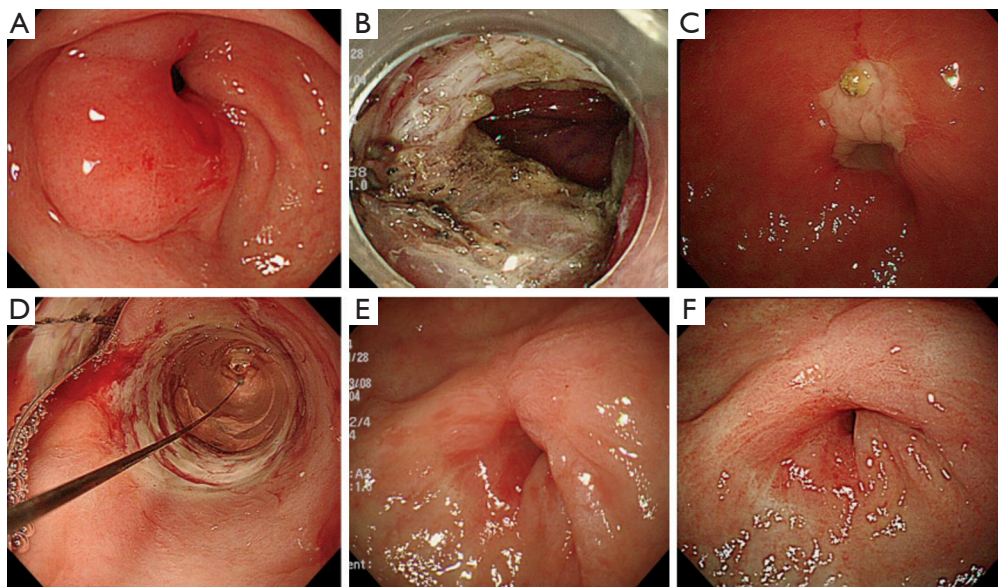


Figure 3 An 83-year-old man who had complete circular ESD for early gastric cancer in the pylorus (A,B) and was given topical triamcinolone injection developed post-ESD stenosis [case No. 5, (C); one month after ESD, (E); three months after ESD]. With combination treatment including multiple ESD (D), triamcinolone injection, and oral prednisolone, the patient who had post-ESD stricture has remained free from the stricture for about one year (F).

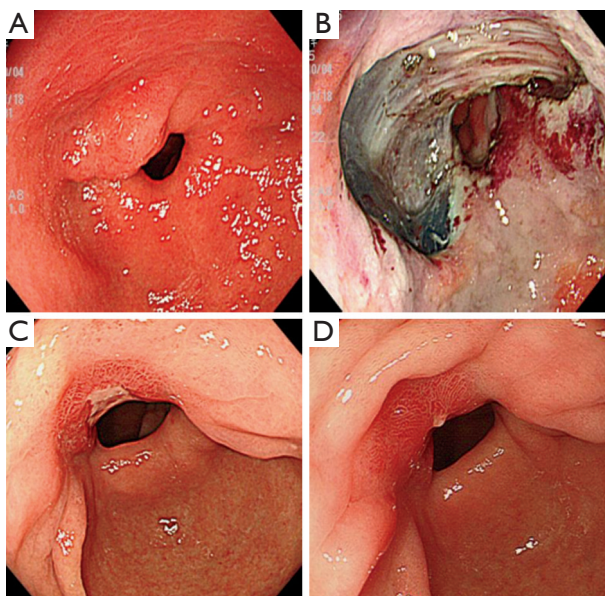


Figure 4 A patient who underwent three-fourths large gastric ESD for early gastric cancer avoided post-ESD stenosis with triamcinolone injection (case No. 7). (A) shows before ESD; (B) shows after ESD; (C) shows two months and (D) shows four months after ESD.

post-ESD stenosis with either triamcinolone injection (representative case No. 7, *Figure 4*) or oral prednisolone.

Discussion

ESD enables curative *en bloc* removal of gastrointestinal neoplasms irrespective of size in early non-invasive stage of the diseases (1,2). However, post-ESD stricture has become a major concern, particularly with superficial esophageal epithelial neoplasms (15). Esophageal stricture causes dysphagia and aspiration pneumonia and decreases patients' quality of life (11,15,16). Similarly, post-ESD stenosis causes symptoms such as dysphagia in cases of large ESD for gastric cardia cancer, and nausea or vomiting for pyloric cancer (6). Indeed, EBD has been a treatment option for stenosis after large ESD, but EBD is sometimes complicated by perforation (8-10). In addition, repeat EBD substantially compromises patients' quality of life, even in large gastric ESD. In fact, Nonaka *et al.* reported the median frequency and period required for EBD without prevention was 5 (range, 1-14) times and 42 (range, 1-120) days, respectively, for large gastric cardia lesions and 9 (range, 7-40) times and 50 (range, 28-198) days, respectively, for pyloric lesions (6).

Thus, a new treatment strategy for post-procedural stenosis is necessary for large gastric ESD. In this regard, endoscopic triamcinolone injection and oral prednisolone have shown promising results for the prevention of luminal stricture following extensive esophageal ESD (11). Isomoto *et al.* reported the usefulness of oral prednisolone

administration for the management of post-procedural stricture even in cases of complete circular ESD for extensive esophageal epithelial neoplasms (12). There were some case reports on the successful management of post-ESD stricture with steroid injection onto a post-large gastric ESD ulcer for pyloric lesions (17,18). Few reports for gastric cardia lesions were seen. Coda *et al.* reported the risk factors for post-ESD stricture for gastric cardia or pyloric lesions, as described previously (3). According to their studies, the length of tumor resection was important; resection over 50 mm in size was a significant risk factor (cardia, $P < 0.05$ and pylorus, $P < 0.01$) (3). In the present study, six patients had resections over 50 mm. Only one patient who underwent a 58-mm-long ESD developed post-ESD stenosis, but the other patients did not post-ESD stenosis with prophylactic steroid therapy.

It took no less than almost three months until ulcer healing following large gastric ESD in our study. Steroid use might exacerbate peptic ulcers and has not been established as safe for post-ESD ulcers of the stomach. There were no adverse events with steroid therapy in the present small series. Further observation and larger studies are warranted to draw conclusions about the relationship between steroid use and ulcer healing and safety.

One patient had post-ESD stenosis following complete circular resection for a large pyloric early gastric cancer, which was not prevented by triamcinolone injection. The intractable stricture was ultimately resolved with oral prednisolone treatment. Another patient who underwent complete circular ESD for gastric cardia cancer did not develop stenosis with oral prednisolone. Although the location of ESD was different (between the cardia and pylorus), the present study suggests that oral prednisolone could be more useful than triamcinolone injection for complete circular resection, as shown in prior studies in esophageal ESD (11).

There have been new technologies for the management of esophageal stricture, such as autologous oral mucosal sheets, temporary stent insertion, and so on (19,20). However, few modalities have been used for gastric stricture so far, and the present therapeutic experience with oral prednisolone administration or triamcinolone injection for large gastric ESD suggests that they can be useful options to prevent gastric stricture or to reduce the number and adverse events of EBD sessions.

Conclusions

Oral prednisolone and triamcinolone injection were effective

for the management of post-ESD stricture following large gastric ESD for gastric cardia and pyloric lesions without serious complications, indicating the safety and usefulness of the steroid treatment. Further evaluation in a large series is needed before steroid therapy is recognized as an option for the management of post-ESD stricture.

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