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Endoscopic incision for the treatment of refractory esophageal anastomotic strictures: outcomes of 13 cases with a minimum follow-up of 12 months

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ABSTRACT

Background and aim: Endoscopic incision is an alternative method for refractory esophageal strictures; however, little is known about its long-term efficacy. The aim of the study is to assess the long-term outcomes of endoscopic incision for treating refractory esophageal anastomotic strictures.

Methods: Between September 2011 and September 2014, 13 patients with refractory esophageal anastomotic strictures were treated with endoscopic incision. Their clinical data were retrospectively collected to evaluate the efficacy and safety of the technique.

Results: All the 13 patients underwent the procedure successfully with median operation duration of 15 minutes. A total of 27 sessions were necessary to maintain lumen patency until September 2015, and 7 patients needed retreatment. The
symptoms relieved in all the cases, and the median dysphagia score decreased from 4 to 1 during a median follow-up of 25 months. The median diameter of stricture was enlarged from 4 mm to 12 mm. As a short-term effect, dysphagia symptoms improved in 100% (13/13), 84.6% (11/13) and 76.9% (10/13) of the patients one, three and six months after a single treatment. As long-term effect, the dysphagia improved in 61.5% (8/13), 63.6% (7/11) and 60% (6/10) of the patients 12, 18 and 24 months after a single treatment.

**Conclusions:** The efficacy of endoscopic incision is favorable in the short term. However, retreatment is needed to maintain the long-term lumen patency for parts of the patients.

**Key words:** Anastomotic stricture. Endoscopic gastrointestinal surgery. Esophageal cancer. Esophageal stricture. Therapeutic efficacy.

**INTRODUCTION**

Anastomotic stricture is one of the most frequent complications after surgical treatment of esophageal cancer, with an incidence of 5% to 46% (1,2). Most of the strictures can be successfully managed with endoscopic dilation. However, refractory strictures that do not respond to repeated dilations are difficult to be managed (3,4). Affected patients often suffer from recurrent dysphagia and vomiting, which severely impair their quality of life and adequate food intake (5). Surgical resection is recommended in cases of established refractory stricture; however, extensive injury and postoperative restenosis often ensue. The efficacy of intralesional steroid injection combined with dilation is controversial for refractory anastomotic strictures, and the frequency of injection, the dosage of drugs, remains to be established (6-8). Esophageal stent insertion is an alternative method, but the rate of migration is high and the long-term efficacy remains unsatisfactory (9).

Endoscopic incision (EI) is a novel technique for the treatment of refractory esophageal stricture and has shown exciting results in a few case series (10-13). However, little is known about the long-term efficacy of the technique. We herein report our results of
refractory esophageal anastomotic stricture treated with EI at our hospital, among whom a minimum follow-up of 12 months was completed.

METHODS

Patients information
The retrospective study was approved by the ethics committee of our hospital. The inclusion criteria of the study were as follows: a) anastomotic stricture after surgical treatment of esophageal cancer, diagnosed on the basis of clinical symptoms, esophagogastroduodenoscopy (EGD) and barium meal, and a malignant stricture was excluded based on the findings of a histological examination; b) refractory stricture was considered because the stricture could not be improved to a diameter of 10 mm or dysphagia symptom was not relieved after 3 or more sessions of endoscopic treatment (i.e., dilation or stenting) (3,10); c) the stricture was shorter than 5.0 cm; and d) patients consent to undergo an EI procedure at our hospital. Those with severe cardiopulmonary disease or blood coagulation disorders were excluded from the candidates for EI.

Thirteen consecutive patients were enrolled between September 2011 and September 2014. Informed consent was obtained from all patients before the procedure was performed. All the patients were informed of possible adverse events and other possible treatment options.

EI procedure
EI was performed under conscious sedation using a single-channel endoscopy (GIF-Q260J; Olympus, Japan) with a transparent cap (D-201-11802, Olympus, Japan) attached to the front. Carbon dioxide insufflator (UCR; Olympus, Japan) was used. Other equipment and accessories included a high-frequency generator (VIO 200; ERBE, Tübingen, Germany), an argon plasma coagulation unit (APC 300; ERBE), and an insulation-tip (IT) knife (KD611L, IT2, Olympus, Japan).

EI was performed as described previously (13). Radical incisions were made along a virtual line connecting the esophageal lumen on the oral side and the lumen on the
caudal side of the stricture, and the tissue located between two adjacent incisions was sliced off. After the procedure, the wound surface of incision was closely observed for any occurrence of perforation and hemorrhage. Figure 1 depicts an example of EI.

**Postoperative management**

Patients were kept *nil-by-mouth* for 2 days, with a liquid diet for 5 days, and returned gradually to a soft diet within a month. Intravenous proton pump inhibitor (PPI) was used for 3 days for all the patients and prophylactic antibiotics were used for 3 days for those who were at high risk of infection. Oral PPI administration was recommended for at least 4 weeks after the procedure. Patients were scheduled for a follow-up visit at 1, 3, 6 and 12 months after EI and then annually for EGD to observe the healing of the wound and check for any sign of recurrence. Patients were contacted via telephone to obtain a current dysphagia score.

**Evaluation of dysphagia before and after EI**

We evaluated the grade of dysphagia symptoms using dysphagia score (14): 0, able to eat a normal diet; 1, unable to swallow certain solids; 2, able to swallow semisolid foods; 3, able to swallow liquids only; and 4, unable to swallow liquids.

**Definition of failure and indication of retreatment**

Treatment failure was defined as the inability to pass an endoscope with a diameter of 10 mm through the stricture site after EI and as a dysphagia score higher than 2 (10). The diameter of the stricture was measured based on the contrast to the tip of an IT knife (2 mm). We performed additional EI treatment when the patient had treatment failure.

**Statistical analysis**

Statistical analysis was performed using SPSS 17.0. Continuous variables were
expressed as medians and ranges and analyzed by the Wilcoxon test. P < 0.05 was considered to be significant.

RESULTS

Patients characteristics

Of the 13 patients, 9 were male and 4 female, aging from 48 to 72 years old. As for the surgery of esophageal cancer, 12 of them received esophagogastrostomy and 1 received end-to-end esophageal anastomosis. Five cases received postoperative chemotherapy and one received radiotherapy. They had received a median of 4 sessions (range 3-8) of endoscopic treatments before EI, and the median duration of repeated dilation was 2 months (range 0.5-15 months). The dysphagia score was 3 or 4 before the procedure. Detailed clinical data are shown in table I.

Efficacy of EI

All the patients were given fluid food 48 hours postoperatively. The median follow-up was 24 months, ranging from 12 to 42 months. As a short-term effect, the dysphagia symptom improved in 100% (13/13), 84.6% (11/13) and 76.9% (10/13) of the patients 1, 3 and 6 months after a single treatment. As a long-term effect, the dysphagia improved in 61.5% (8/13), 63.6% (7/11) and 60% (6/10) of the patients 12, 18 and 24 months after a single treatment. The median diameter of the strictures increased from 4 mm (range 1-6 mm) to 12 mm (range 8-16 mm) (p < 0.05) (Fig. 2). The dysphagia score decreased to 0 or 1 in 92.3% (12/13) of the cases. In case 9, 7 sessions of EI were performed. The estimated diameter was 8 mm and dysphagia score was 2 until September 2015, but he refused an additional therapy.

Safety of EI
EI was successfully performed in all the 13 cases with a median operation time of 15 minutes (range 9-25 min). Re-EI was needed to maintain patency for 7 cases (1 re-EI in 4 patients; 2 re-EI in 2 patient, and 6 re-EI in 1 patient), and the median period of time elapsed since treatment ended to the recurrence of symptoms of EI was 9 months (range 2-18 months), which was longer than that of balloon dilation (BD) (9 vs 2 months, p < 0.05). The median hospital stay was 4 days (range 3-6 days). Case 5 suffered from chest pain which was relieved within 2 days by oral administration of a painkiller. No major complication such as bleeding and perforation occurred.

DISCUSSION

Current strategies to manage refractory stricture mainly include surgical resection and endoscopic therapy (15). Surgical resection is associated with extensive injury and postoperative restenosis. Endoscopic methods include local steroid injection, stent insertion and endoscopic incision. Intralesional steroid may reduce the risk of recurrent stricture formation because it can locally inhibit the inflammatory response and reduce collagen formation. A few retrospective studies have shown that a combination of steroid injection and balloon dilation (BD) could reduce the total number of dilations required for esophageal anastomotic stricture (6,7). However, these studies were small and uncontrolled. Hirdes et al. (8) conducted a multicenter, randomized study of 60 patients with benign esophagogastric anastomotic strictures and they found that endoscopic corticosteroid injections do not provide a statistically significant decrease in frequency of repeat dilations or prolongation of the dysphagia-free period. So the efficacy of steroid injection is still controversial and needs further confirmation. Stent insertion is an alternative method, and available stents include self-expandable metal/plastic stents, biodegradable stents, etc. (16). A few studies have demonstrated the feasibility of stenting for refractory esophageal anastomotic stricture, but long-term efficacy is not that satisfactory, and their complications, such as tissue overgrowth, migration and pain, are not negligible (9,17).

EI was first reported for the treatment of Schatzki rings (18,19). Subsequently, EI was
added to BD, and was shown to be effective in small series of patients with refractory esophageal anastomotic stricture (20,21). As a primary treatment, Lee et al. (22) reported their experience of EI for benign esophageal anastomotic strictures; 24 patients were included. After two years of follow-up, 87.5% of the patients were dysphagia-free after a single session. However, a randomized prospective study of 62 cases with primary esophageal anastomotic stricture failed to demonstrate the superiority of EI over BD regarding the required dilations sessions and success rate (23). So the efficacy of EI for primary treatment of anastomotic stricture is still controversial. As an alternative treatment for refractory anastomotic stricture, EI has shown exciting short-term results in several cases series (11-13), and a retrospective cohort study revealed that the short-term efficacy of EI and BD was comparable, but the 6-month and 12-month patency rate of EI was superior to that of BD (10). However, little is known about the long-term efficacy of EI. In the present study, all the 13 patients had several previous attempts of dilation/stenting, but failed to obtain a sustained symptomatic improvement. They were all treated with EI. The results showed that the short-term efficacy of EI is favorable as more than 75% of the cases were dysphagia-free after a single session, which is consistent with the published studies. Though the long-term efficacy is not that satisfactory and 53.8% (7/13) of the cases needed retreatment, the duration of required retreatment is longer than that of BD. This indicates that EI could serve as an alternative treatment for refractory esophageal anastomotic stricture. Stricture recurrence is the major concern for patients receiving EI and it was demonstrated that the efficacy of EI was associated with the stricture length. Hordijk et al. (11) found that all the 12 patients with a short stricture (< 1.0 cm) were dysphagia-free during a 12-month follow-up after a single treatment, while a mean of 3 sessions were needed to maintain patency for the 8 cases with a long stricture (1.5-5.0 cm).

In the present study, recurrence was observed in 7 cases and they all received re-EI. Several methods have been developed to reduce recurrence. In Muto’s study, a weekly preventive endoscopic balloon dilatation was performed to maintain patency, and a median of four BD sessions were needed (10). Tan et al. (24) reported that fully-covered stent is useful to prevent restenosis after EI. Stenting has potential advantages
over BD in its ability to provide continuous, radially oriented dilation pressures over a longer period of time, and a stent could protect the incision area from gastric acid erosion. Thus, stenting may be better than BD in preventing restenosis after EI, especially for those with a long stricture (25). A randomized study is ongoing in Japan concerning the efficacy of EI combined with steroid injection (26). What is more, EI leads to a wound surface like circumferential endoscopic submucosal dissection, which facilitates formation of postoperative stricture (27). Tan et al. (28) modified the method as endoscopic incision and selective cutting for refractory colorectal stricture, but its safety and efficacy for esophageal stricture remain unknown. Thus the efficacy of the above methods to prevent restenosis after EI should be evaluated by a large scale, prospective study. Gastroesophageal reflux is one of the common causes of benign esophageal stricture (15), and it may be a risk factor of recurrence after EI treatment. We noticed that 6 of the 7 patients who needed retreatment had received esophagogastrostomy, thus reflux after treatment may encounter. What is more, no recurrence was observed in the first 4 weeks administrating an oral PPI. Another patient who needed 6 sessions of retreatment received radiotherapy before EI treatment. As radiation therapy itself is a cause of benign esophageal stricture (15), a radiotherapy history may also affect the efficacy of EI. However, whether the two factors are risk factor of recurrence or not should be evaluated by further studies. Limitation of the study includes its small sample size and retrospective design.

In conclusion, the efficacy of EI for the treatment of refractory esophageal anastomotic stricture is favorable in the short term. However, retreatment is sometimes needed to maintain the long-term lumen patency for parts of the patients. Large comparative studies are warranted to further confirm our findings.

REFERENCES


### Table I. Clinical characteristics of the 13 patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Age (years), median (range)</td>
<td>62 (48~72)</td>
</tr>
<tr>
<td>Sex. M/F</td>
<td>9/4</td>
</tr>
<tr>
<td>Distance from the incisors, cm, median (range)</td>
<td>20 (15~24)</td>
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</table>

#### Surgery procedures of esophageal cancer

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagogastrostomy</td>
<td>12/13</td>
</tr>
<tr>
<td>End-to-end esophageal anastomosis</td>
<td>1/13</td>
</tr>
</tbody>
</table>

| Diameter of the stricture, cm, median (range)        | 0.4 (0.1~0.6) |
| Length of the stricture, cm, median (range)          | 1.5 (0.8~1.8) |
| Total sessions of previous treatment before EI, median (range) | 4 (3~8)       |
| Period of time elapsed since treatment ended to the recurrence of symptoms of balloon dilation before EI, months (range) | 2 (0.5~15)    |
Fig. 1. A. Procedure of endoscopic incision. B. Preoperative stricture. C. Radial endoscopic incision with an IT knife. D. Dilated esophageal lumen after incision.

Fig. 2. The diameter enlarged obviously 12 months after EI.