Thoracic Cancer ISSN 1759-7706

INVITED REVIEW

Updates on endoscopic therapy of esophageal carcinoma

Hajime Isomoto

Department of Gastroenterology and Hepatology, Nagasaki University Hospital, Nagasaki, Japan

Keywords
Barrett's adenocarcinoma; early esophageal cancer; endoscopic mucosal resection; endoscopic submucosal dissection; squamous cell carcinoma.

Correspondence
Hajime Isomoto, Department of Gastroenterology and Hepatology, Nagasaki University Hospital, 1-7-1 Sakamoto, Nagasaki 852-8501, Japan.
Tel: +81 95 819 7567
Fax: +81 95 819 7568
Email: hajimei2002@yahoo.co.jp

Received: 22 December 2011; accepted 26 December 2011.

doi: 10.1111/j.1759-7714.2012.00109.x

Abstract

Endoscopic submucosal dissection (ESD) has the advantage over endoscopic mucosa resection (EMR), permitting removal of gastrointestinal neoplasms *en bloc*, but is associated with a relatively high risk of complications. Early esophageal cancer (EEC) is indicated when the tumors are confined to the two-third layer of the lamina propria. Esophageal stricture following semicircular or complete circular esophageal ESD is relatively frequent even if treated by multiple pre-emptive endoscopic balloon dilatation. Oral prednisolone may offer a novel, safe, and effective option for prevention of post-ESD stricture associated with ESD for extensive esophageal neoplasms. The procedures include marking, submucosal injection, circumferential mucosal incision and exfoliation of the lesion along the submucosal layer. Complete ESD can achieve a large one-piece resection, allowing precise histological assessment to prevent recurrence. Clinical outcomes of esophageal ESD have been promising, and the prognosis of EEC patients treated by ESD is likely to be excellent, though further long-term follow-up studies are warranted. Notification of a risk of perforation is essential for esophageal ESD. Bleeding during ESD can be managed with coagulation forceps, and postoperative bleeding may be reduced with routine use of the stronger acid suppressant, proton pump inhibitors.

Introduction

Endoscopic mucosal resection (EMR) has been used for the resection of early gastrointestinal (GI) neoplastic lesions.[1] EMR is widely accepted as a standard treatment for early GI cancer with nominal risk of lymph node metastasis, as it is minimally invasive, safe, and convenient.[2,3] Nevertheless, EMR of larger lesions with more than 2 cm in size requires piecemeal resection. The conventional EMR is associated with a high risk of local recurrence in such cases, especially when resections are accomplished in multiple segments or the margins are not clear.[4]

Endoscopic submucosal dissection (ESD) was initially developed in Japan for the resection of early gastric cancer (EGC).[5] ESD has the advantage over EMR in enabling the removal of GI tumors in an *en bloc* manner, irrespective of their size.[5,6] This allows precise histological assessment of specimens excised in one piece with tumor-free lateral/basal margins, preventing residual disease and local recurrence.[6,7] More recently, ESD has been successfully applied for early esophageal cancer (EEC) including squamous cell carcinoma and Barrett's adenocarcinoma.[8–14] In this review, we will discuss the applications and advances in ESD techniques with a focus on esophageal epithelial neoplasms including EEC.

Indications of ESD

EMR is widely accepted as a standard treatment for EGC with a nominal risk of lymph node metastasis, as it is minimally invasive, safe, and convenient.[2,3] The same is true for EEC and early colorectal cancer. However, the snaring procedure is not reliable for lesions larger than 20 mm in diameter or lesions with ulcer findings.[4,15] These lesions must be differentiated adenocarcinoma confined to the mucosa with no lymphatic or vascular involvement. However, it has been observed clinically that the accepted indications for EMR can be too strict, leading to unnecessary surgery.[4,16] In fact, attempts to expand the indications for ESD to treat EGC are currently underway in many Japanese institutes.[6,16,17]

EEC involving the epithelium (m1: carcinoma in situ) or the lamina propria (m2) are candidates for endoscopic therapies including ESD and EMR, because no lymph node metastasis have been reported in EEC confined to these layers.[7] For EEC invading the muscularis mucosa (m3), the

lymph node metastasis rate is reported as 9%, and for cancer with minute submucosal invasion the rate is increased to 19%.[18] Therefore, for patients unwilling to undertake esophagectomy or patients with comorbid diseases, endoscopic treatment may be a relative indication for m3 or slightly submucosal invasive cancer. EEC spreading more than three-quarters of the circumference of the esophagus are not absolutely indicated even if the invasion depth is limited to m1 or m2.[7,18] Although such lesions can be removed *en bloc* with ESD, they are considered as the relative indication. Nevertheless, intensive balloon dilatations or tentative stent insertion may prevent stricture.[7,8,19] Previous studies have suggested a satisfactory prognosis after EMR, and EMR has been used for the treatment of EEC or high-grade dysplasia.[20] Despite its efficacy, this method is sometimes associated with local recurrences, especially when lesions larger than 20 mm are resected in a piecemeal manner. In turn, ESD allows *en bloc* resection for EEC, irrespective of size. In fact, successful resection of large esophageal cancers by ESD has been reported in a relatively small number of cases.[8,20] When the efficacy of ESD for smaller lesions ≤20 mm was compared with that of EMR, ESD was found to be the best endoscopic resection method, even for the smaller EEC.[20]

Endoscopic treatment is an alternative to esophagectomy in Barrett's esophagus patients with superficial adenocarcinoma, due to the nominal risk of lymph node involvement or distal metastases.[7] For Barrett's adenocarcinomas, EMR has limitations with respect to the resectable tumor size; in many cases, piecemeal resection is unavoidable and has been occasionally linked to local recurrence.[7] Recently, ESD has been used to remove esophagogastric junction tumors including Barrett's neoplasms with promising results.[9–11] However, there is no available data about nodal metastases from the large numbers of surgically resected cases of Barrett's adenocarcinoma at an early stage. Indeed, there is no or nominal risk of nodal metastasis for the intramucosal Barrett's adenocarcinoma, but the tumors with massive sm involvement are associated with considerable risk for metastatic disease.[7] There is no consensus whether the same criteria for gastric epithelial neoplasms or esophageal squamous cell neoplasms should also apply to Barrett's adenocarcinomas confined within the upper third of the submucosa.[7]

ESD techniques

ESD is performed using special endoscopic knives such as the insulated-tipped diathermic knife (IT knife), which was developed for *en bloc* resection of EGC.[5] For the ESD procedures, a single-channel upper GI endoscope with a water-jet system (GIF-Q260J, Olympus Optical Co., Tokyo, Japan) was used with a transparent cap attached to the endoscope tip. The ESD procedure, described previously in detail,[6] is usually performed using the following steps. EGC are first identified and demarcated using white-light endoscopy and chromoendoscopy with indigo-carmine solution, and then marking around the lesions is carried out with spotty cautery. A 10% glycerin plus 5% fructose in 0.9% saline solution (Glyceol; Chugai Pharmaceutical Co., Tokyo, Japan) or a ready-to-use hyaluronic acid solution (MucoUp, Seikagaku Co., Tokyo, Japan) is injected into the submucosal layer to lift the mucosa. A circumferential mucosal incision is made around the lesion using the IT knife (Olympus). In our hospital, a high-frequency generator (VIO300D; ERBE Elektromedizin GmbH, Tübingen, Germany) is employed for ESD.[13] The hyaluronic acid solution is injected into the submucosal layer to lift the surrounding mucosa. The ceramic ball at the tip of IT knife prevents perforation of the muscle layer. Then, submucosal dissection is performed for exfoliation of the lesion using the IT-knife and/or the Hook-knife (Olympus) in technically difficult situations. The solution can be injected into the submucosa at any time to raise and confirm the submucosal layer. Complete submucosal dissection can achieve a large one-piece resection.

The ESD procedures for EEC are performed in a similar process to those for EGC, but with several modifications for the esophagus.[13,21,22] A mucosal incision is made circumferentially around the lesion using the FlushKnife (Fujinon-Toshiba ES System Co., Omiya, Japan). The ready-to-use hyaluronic acid solution is exceptionally injected into the submucosal layer to lift the surrounding mucosa. The distal half of the mucosal incision is completed first. The proximal half is incised after the submucosal layer is dissected slightly, as described in the following steps. Before incising all the way around the markings, dissection of the submucosa is started beneath the area where the mucosal incision is made. This is done to avoid flattening the remaining area lifted by the cushioning solution as time passes. The submucosal dissection is done using the FlushKnife and/or the Hook knife, until the lesion is detached. Even if the invasion depth of EEC spreading more than three-quarters of the circumference of the esophagus is limited to m1 or m2, this is considered the relative indication due to the unavoidable stricture.

Wholly circumferential esophageal ESD is also performed using a similar process, with additional modifications.[13,21,22] The distal mucosal incision is completed first all the way around the markings with the FlushKnife. The proximal mucosa is then incised in the same circular fashion. The submucosa is incised using the FlushKnife, starting beneath the proximal mucosal incision in each quadrant. The submucosal dissection is advanced to reach the distal side of the mucosal incision, thus creating a submucosal tunnel. Then, the submucosa between the 3 to 4 longitudinal tunnels is dissected to connect together until the lesion is detached.

To control bleeding during ESD or to prevent possible bleeding from visible vessels in the artificial ulcer immedi-

ately after the resection, hemostatic forceps (Coagrasper, Olympus) are employed in the soft coagulation mode.

All patients are sedated by intravenous injection of 5–7.5 mg diazepam (Cercine; Takeda Pharmaceutical Co., Osaka, Japan) and 15 mg pentazocine (Pentazin, Daiichi-Sankyo Pharmaceutical Co., Tokyo, Japan), and 2.5 mg diazepam was additionally given for sedation as needed throughout the procedure.

The excised specimens are fixed in 10% buffered formalin, paraffin-embedded, sectioned perpendicularly at 2-mm intervals and stained with hematoxylin and eosin. Macroscopic appearance, histological type, the tumor size, the depth of invasion, the presence of ulcerative changes, lymphatic and vascular involvement, and tumor involvement to the lateral and vertical margins are assessed.[17] En bloc resection refers to a resection in one-piece. When the lesion has to be removed in multiple segments, the piecemeal-resected specimens are reconstructed as completely as possible. Resections are deemed curative when removal is achieved with tumor-free lateral and vertical margins.[17] By definition, there should be no lymphatic and vascular involvement. In addition, there should be no submucosal invasion deeper than 500 μm from the muscularis mucosae for EGC or be limited to the m1 or m2 in cases of EEC.[7,9,13]

Management of complications following ESD

The complications of endoscopic resection for EGC include pain, bleeding, and perforation.[16] Pain after resection is typically mild. Bleeding is the most common complication, occurring in up to 1.2–11.6% of patients undergoing standard EMR and in up to 7% of patients undergoing ESD.[16] During ESD, minor bleeding is commonly seen but can be successfully treated by grasping the bleeding vessels with Coagrasper as described above. Endoclips are sometimes needed for aggressive bleeding. Thereafter, a sodium alginate powder (Alto, Kaigen Co., Osaka, Japan) or sucrose-aluminum hydroxide gel (Chugai Pharmaceutical Co.) is sprayed onto the artificial ulcer base.[19] Delayed bleeding, manifested by hematemesis or melena at 0–30 days after the procedure, may require emergent endoscopy. The stronger acid suppressant, proton pump inhibitor (PPI) is used in order to prevent postoperative bleeding and promote ulcer healing; the standard dose of PPI is administered for patients with EGC or EEC treated by ESD.[22] Even large ulcers after ESD have recently been reported to heal within eight weeks after resection under the antacid treatment.[16] Nevertheless, most delayed bleeding (75%) occurs within 12 hours after ESD,[16] and patients must typically fast for one day, followed by a liquid diet on the second day, and a soft diet for three consecutive days thereafter. The patients remain hospitalized for at least eight days. In cases of semicircular or circumferential EECs, intraluminal stenosis of the esophagus often occurs postoperatively,[13,14,19] and such patients should undergo repeated (i.e., twice per week in our hospital) mechanical dilation with the specialized balloon catheter (Boston Scientific Japan Co., Tokyo, Japan), and would then be discharged several weeks after ESD.[19]

Perforation is rare with EMR but occurs more frequently with ESD. The risk of perforation during ESD for EGC is about 4% as per a large study from the Japanese Cancer institute.[16] Gastric perforation during endoscopic resection can be conservatively treated by complete endoscopic closure with endoclips (HX-600-090, Olympus), without peritoneal dissemination of the cancer cells. In addition, nasogastric suction is applied, and a broad-spectrum antibiotic is efficiently given for two to three days. If abdominal fullness due to air leakage from the perforated lesion is severe, decompression of the pneumoperitoneum by puncture needle must be performed. On the other hand, a delayed perforation due to the artificial ulcers following ESD is rare but may require surgical intervention.

There have been few reports on the complications of ESD in the esophagus. Fujishiro *et al*. reported that perforation occurred in 6.9% (4/58) patients with esophageal squamous cell neoplasms during ESD, whereas there was no evidence of significant bleeding.[8] The patients with the complication were managed by conservative medical treatments after endoscopic closure of the perforation. Here, notification of risk of perforation in esophageal ESD is essential, since it may cause severe or even life-threatening conditions including mediastinal emphysema and mediastinitis.[8]

Outcomes of ESD

Despite the increasing use of ESD for EGC, the long-term clinical outcomes have not been fully evaluated. The 3-year overall survival after ESD seems excellent, with the rate being nearly 99%.[17] In a multicenter study of endoscopic resection for EGC, Oda *et al*. reported a comparable 3-year overall survival between the EMR and ESD groups (99.7% and 98.5%, respectively).[23] The 5-year survival rate after ESD reached 97.1%, which was equivalent to the rate after EMR documented in previous reports.[24,25] Of note, both the 3-year and 5-year disease-specific survival rates after ESD were 100%,[17] similar to those after EMR in 12 major Japanese institutions.[24] In general, EGC has had excellent clinical outcomes, with 10- and 20-year survival rates after gastrectomy with removal of lymph nodes as high as 95%.[24] Confirmation of whether ESD can equal surgery will require further long-term prospective studies.

Outcomes of esophageal ESD are summarized in Table 1. A total of 248 cases of esophageal neoplasms consisting of 160 superficial squamous cell carcinomas, 81 severe dysplasia and seven intramucosal Barrett's adenocaricnomas underwent

Table 1 Representative outcomes of endoscopic submucosal dissection for esophageal epithelial neoplasms

Authors	Case No.	*En bloc* resection	Curative resection	Complications		Postprocedural stricture	Subjects
				Perforation	Bleeding		
Fujishiro *et al*	58	100%	78%	6.9%	0%	16%	Esophageal squamous cell neoplasms
Kakushima *et al*	30	97%		3.3%	0%	–	Esophagogastric junction tumors
Yoshinaga *et al*	25	100%	72%	0%	0%	8%	Esophagogastric junction adenocaricinoma
Hirasawa *et al*	58	100%	79%	0%	5.2%	1.7%	Esophagogastric junction adenocaricinoma
Takahashi *et al*	116	100%	99.1%	2.6%	–	17.2%	Early esophageal squamous cell carcinoma
Ours	248	99.6%	91.9%	0%	0.4%	6%	Early esophageal squamous cell carcinoma Barrett's adenocarcinoma high-grade intraepithelial neoplasia

ESD in our hospital between April 2006 and October 2011 (Table 1). On the whole, *en bloc* resection was achieved in almost all patients (247/248), and the rate of *en bloc* with tumor-free lateral/vertical margins was 91.9% (228/248). There was no perforation and bleeding, but intramural stricture occurred in 15 of the 248 cases. All of the 15 lesions extended more than three-quarters of the circumference of the esophagus. Fujishiro *et al*. reported that the rate of *en bloc* resection was 100% (58/58) for esophageal squamous cell neoplasms, and *en bloc* resection with tumor-free lateral/basal margins was achieved in 78% (45/58).[8] Of 40 lesions occurring in 31 patients fulfilling the criteria of node-negative tumors (mean follow-up, 17 months), one lesion resected by *en bloc* resection with nonevaluable tumor-free lateral margins recurred locally six months after ESD, which was treated successfully by a second ESD procedure.

For 30 lesions of esophagogastric tumors including Barrett's adenocarcinoma treated by ESD, the *en bloc* resection with the tumor-free lateral/vertical margins was achieved in 97% (29/30).[9] Histological evaluation of the resected specimens revealed five cases of angiolymphatic invasion and five cases of submucosal invasion deeper than 500 μm. Local recurrence was not observed in any patient during follow-up (mean 14.6 months, range six–31 months) in their study. In another study, the *en bloc* resection rate was 100% in 25 superficial adenocarcinoma located at the esophagogastric junction. Seventeen lesions (72%) were judged as curative resection with the tumor-free lateral/vertical margins and showed no local or distant recurrence during a median follow-up period of 30.1 months.[10] More recent study on long-term outcomes of ESD for the superficial adenocarcinoma of the esophagogastric junction supported the favorability.[11] Thus, ESD can be safely and effectively performed for the esophagogastric junction tumors, albeit the study numbers of these preliminary studies were limited.

Management of esophageal stricture after ESD for large EEC

Although the exact incidence of luminal stricture after esophageal ESD is unknown, it is related to the extent of the circumference being resected.[5] In particular, esophageal stricture occurs commonly following ESD involving the entire circumference of the esophageal lumen.[5,13,21] The resultant dysphagia substantially decreases patients' quality of life (QOL), requiring multiple sessions of endoscopic balloon dilatation (EBD).[6,13,21,22] Although EBD has been a treatment of choice in the setting of benign esophageal strictures,[15] intralesional steroid injection into corrosive or anastomotic strictures can achieve remission of dysphagia or reduce the need for repeated EBD.[26,27] However, certain patients with recalcitrant esophageal stricture do not respond to local steroid therapy, although systemic steroid administration often resolves the problem in such cases.[28,29] Therefore, we have been treated with the post-ESD stricture via systemic prednisolone; oral prednisolone was started at 30 mg/day on the third day post-ESD, tapered gradually, and then discontinued eight–12 weeks later. An additional EBD was performed on demand whenever dysphagia appeared. Our recent studies documented that stricture at three months after ESD was found in seven of 22 patients in the preemptive EBD group but only one of 19 in the oral prednisolone group. The average number of EBD sessions required was 15.6 in the preemptive EBD group and 1.7 in the oral prednisolone group. After complete circular ESD, 32.7 EBD sessions were needed on average in the preemptive EBD group, whereas fewer were needed in the oral prednisolone group.[13] Thus, post-ESD esophageal strictures were persistent even if treated preemptively with multiple EBD sessions, but oral prednisolone may offer a useful preventive option. Further prospective studies on the preventive effects of oral prednisolone in comparison with local infection of triamcinolone,[14] a long-acting steroid derivative, are warranted and should be attempted in the setting of post-procedural stenosis following ESD. We are currently investigating this possibility.

Conclusion

Endoscopic resection of EGC and EEC is well established as a standard therapy in Japan and is increasingly becoming accepted and regularly used in the other countries. ESD, an innovative application modality of EMR, has been developed

to allow the resection of larger lesions in an *en bloc* manner; the earlier results so far have been promising in EGC, EEC and esophagogastric junction tumors including Barrett's adenocarcinoma. It is feasible to assess the histopathological curability of the resected specimens precisely, reducing recurrence. ESD still has relatively high complication rates; notification of perforation risk is essential in particular when performing esophageal ESD. Bleeding during ESD can be managed by endoscopic closure with endoclips, and delayed bleeding is rare with the use of oral and/or intravenous PPIs. The relatively long-term outcomes may be excellent in EGC after ESD. Nevertheless, continued surveillance is necessary for recurrent tumors in cases of non-curative resection and for metachronous cancers even after curative ESD.

Disclosure

The author has no conflict of interest.

References

1 Sano T, Kobori O, Muto T. Lymph node metastasis from early gastric cancer: endoscopic resection of tumour. *Br J Surg* 1992; **79**: 241–4.
2 Rembacken BJ, Gotoda T, Fujii T, Axon AT. Endoscopic mucosal resection. *Endoscopy* 2001; **33**: 709–18.
3 Soetikno R, Kaltenbach T, Yeh R, Gotoda T. Endoscopic mucosal resection for early cancers of the upper gastrointestinal tract. *J Clin Oncol* 2005; **23**: 4490–8.
4 Gotoda T. Endoscopic resection of early gastric cancer. *Gastric Cancer* 2007; **10**: 1–11.
5 Gotoda T, Kondo H, Ono H *et al*. A new endoscopic mucosal resection procedure using an insulation-tipped electrosurgical knife for rectal flat lesions: report of two cases. *Gastrointest Endosc* 1999; **50**: 560–3.
6 Isomoto H, Shikuwa S, Yamaguchi N *et al*. Endoscopic submucosal dissection for early gastric cancer: a large-scale feasibility study. *Gut* 2009; **58**: 331–6.
7 Fujishiro M. Perspective on the practical indications of endoscopic submucosal dissection of gastrointestinal neoplasms. *World J Gastroenterol* 2008; **14**: 4289–95.
8 Fujishiro M, Yahagi N, Kakushima N *et al*. Endoscopic submucosal dissection of esophageal squamous cell neoplasms. *Clin Gastroenterol Hepatol* 2006; **4**: 688–94.
9 Kakushima N, Yahagi N, Fujishiro M, Kodashima S, Nakamura M, Omata M. Efficacy and safety of endoscopic submucosal dissection for tumors of the esophagogastric junction. *Endoscopy* 2006; **38**: 170–4.
10 Yoshinaga S, Gotoda T, Kusano C, Oda I, Nakamura K, Takayanagi R. Clinical impact of endoscopic submucosal dissection for superficial adenocarcinoma located at the esophagogastric junction. *Gastrointest Endosc* 2008; **67**: 202–9.
11 Hirasawa K, Kokawa A, Oka H *et al*. Superficial adenocarcinoma of the esophagogastric junction: long-term results of endoscopic submucosal dissection. *Gastrointest Endosc* 2010; **72**: 960–6.
12 Takahashi H, Arimura Y, Masao H *et al*. Endoscopic submucosal dissection is superior to conventional endoscopic resection as a curative treatment for early squamous cell carcinoma of the esophagus (with video). *Gastrointest Endosc* 2010; **72**: 255–64.
13 Yamaguchi N, Isomoto H, Nakayama T *et al*. Usefulness of oral prednisolone in the treatment of esophageal stricture after endoscopic submucosal dissection for superficial esophageal squamous cell carcinoma. *Gastrointest Endosc* 2011; **73**: 1115–21.
14 Hashimoto S, Kobayashi M, Takeuchi M, Sato Y, Narisawa R, Aoyagi Y. The efficacy of endoscopic triamcinolone injection for the prevention of esophageal stricture after endoscopic submucosal dissection. *Gastrointest Endosc* 2011; **74**: 1389–93.
15 Oka S, Tanaka S, Kaneko I *et al*. Endoscopic submucosal dissection for residual/local recurrence of early gastric cancer after endoscopic mucosal resection. *Endoscopy* 2006; **38**: 996–1000.
16 Gotoda T, Yamamoto H, Soetikno RM. Endoscopic submucosal dissection of early gastric cancer. *J Gastroenterol* 2006; **41**: 929–42.
17 Isomoto H. Global dissemination of endoscopic submucosal dissection for early gastric cancer. *Intern Med* 2010; **49**: 251–2.
18 Oyama T, Miyata Y, Shimaya S. Lymph nodal metastasis of m3, sm1 esophageal cancer [in Japanese]. *Stomach Intestine* 2002; **37**: 71–4.
19 Fujishiro M, Yahagi N, Kakushima N, Kodashima S, Ichinose M, Omata M. En bloc resection of a large semicircular esophageal cancer by endoscopic submucosal dissection. *Surg Laparosc Endosc Percutan Tech* 2006; **16**: 237–41.
20 Kakushima N, Fujishiro M. Endoscopic submucosal dissection for gastrointestinal neoplasms. *World J Gastroenterol* 2008; **14**: 2962–7.
21 Isomoto H, Yamaguchi N, Nakayama T *et al*. Management of esophageal stricture after complete circular endoscopic submucosal dissection for superficial esophageal squamous cell carcinoma. *BMC Gastroenterol* 2011; **11**: 46.
22 Isomoto H, Yamaguchi N. Endoscopic submucosal dissection in the era of proton pump inhibitors. *J Clin Biochem Nutr* 2009; **44**: 205–11.
23 Oda I, Saito D, Tada M *et al*. A multicenter retrospective study of endoscopic resection for early gastric cancer. *Gastric Cancer* 2006; **9**: 262–70.
24 Kojima T, Parra-Blanco A, Takahashi H, Fujita R. Outcome of endoscopic mucosal resection for early gastric cancer: review of the Japanese literature. *Gastrointest Endosc* 1998; **48**: 550–4.
25 Uedo N, Iishi H, Tatsuta M *et al*. Longterm outcomes after endoscopic mucosal resection for early gastric cancer. *Gastric Cancer* 2006; **9**: 88–92.
26 Lee M, Kubik CM, Polhamus CD, Brady CE III, Kadakia SC. Preliminary experience with endoscopic intralesional steroid injection therapy for refractory upper gastrointestinal strictures. *Gastrointest Endosc* 1995; **41**: 598–601.

27 Kochhar R, Makharia GK. Usefulness of intralesional triamcinolone in treatment of benign esophageal strictures. *Gastrointest Endosc* 2002; **56**: 829–34.
28 Morikawa N, Honna T, Kuroda T *et al*. High dose intravenous methylprednisolone resolves esophageal stricture resistant to balloon dilatation with intralesional injection of dexamethasone. *Pediatr Surg Int* 2008; **24**: 1161–4.
29 Hishiki T, Kouchi K, Saito T *et al*. Successful treatment of severe refractory anastomotic stricture in an infant after esophageal atresia repair by endoscopic balloon dilation combined with systemic administration of dexamethasone. *Pediatr Surg Int* 2009; **25**: 531–3.