Prospective trial of biodegradable stents for refractory benign esophageal strictures after curative treatment of esophageal cancer

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Background and Aims: Biodegradable stents are reportedly effective for refractory benign esophageal strictures; however, little is known about their use in patients with refractory stricture after endoscopic submucosal dissection (ESD) or chemoradiotherapy (CRT) for esophageal cancer. This study aimed to evaluate the effectiveness of biodegradable stents for these patients.

Methods: Patients with refractory benign esophageal stricture with a dysphagia score (DS) of 2 or worse and for whom the passage of a standard size endoscope was not possible were eligible. The primary endpoint was the proportion of those who improved their DSs (% DS improved) at 12 weeks after stent placement, and the secondary endpoints were the proportion of those who improved their DSs at 24 weeks, dysphagia-free survival (DFS), and adverse events.

Results: Eighteen patients (men:women, 15:3; median age, 72 years; range, 53-80) were enrolled. Twelve patients improved their DS at 12 weeks (% DS improved, 66.7%; 90% CI, 44.6%-84.4%). Also, 8 of 11 patients (72.7%) after esophagectomy, 4 of 6 patients (66.7%) after ESD, and 3 of 4 patients (75%) after CRT improved at 12 weeks. Three patients who were treated with esophagectomy maintained their DS improvement at 24 weeks (% DS improved, 16.7%; 95% CI, 3.6%-41.4%). The median DFS was 14.1 weeks (95% CI, 13.0-19.0). One patient who had ESD and CRT developed an esophagobronchial fistula 3 months after stent placement.

Conclusions: Biodegradable stents are effective and tolerable for refractory benign esophageal strictures after treatment for esophageal cancer; however, long-term efficacy was limited, especially after ESD or CRT. (Clinical trial registration number: UMIN000008054.) (Gastrointest Endosc 2017;86:492-9.)

The incidence rate of benign esophageal stricture is reported to be approximately 30% after esophagectomy[1] and up to 40% after radiotherapy for patients with advanced esophageal cancer.[2] Endoscopic resection (ER) is a key treatment for superficial esophageal cancer without metastasis. The post-ER stricture rate is reported at approximately 15%, and a mucosal defect after ER of three-fourths luminal circumference or larger is a

Abbreviations: APC, argon plasma coagulation; CRT, chemoradiotherapy; DFS, dysphagia-free survival; DS, dysphagia score; EBD, endoscopic balloon dilation; ER, endoscopic resection; ESD, endoscopic submucosal dissection.

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significant risk for benign esophageal strictures.[3] Endoscopic submucosal dissection (ESD) has made en-bloc resection of large lesions possible and has become popular, causing concern that the incidence of benign esophageal strictures will increase.[4] Dysphagia because of benign esophageal strictures is a major problem for patients even if their cancers are cured, and it can sometimes cause weight loss, nutritional disorders, and aspiration pneumonia.[5] Although patients with benign esophageal stricture are usually treated with endoscopic balloon dilation (EBD) or bougie in clinical practice, some cases may require many repeat treatments, causing long delays before dysphagia relief.[6]

The biodegradable stent (SX-ELLA Stent Esophageal Degradable BD; ELLA-CS, Hradec Kralove, Czech Republic; Fig. 1) is made of polydioxanone and is degraded by hydrolysis 8 to 12 weeks after placement; therefore, there is no need to remove the device. It is reported as an effective option for refractory benign esophageal stricture,[7] but little is known about the efficacy and safety for patients with cancer, especially after ESD or chemoradiotherapy (CRT). Therefore, the aim of this study was to evaluate the efficacy and safety of biodegradable stents for refractory benign esophageal stricture after curative treatment including esophagectomy, ESD, or CRT for esophageal cancer.

METHODS

Study design

This multi-institutional, nonrandomized, single-arm phase II study complied with the Declaration of Helsinki requirements. The study protocol was approved by the institutional review boards of all participating hospitals, and all patients provided written informed consent. The study was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN000008054) and was conducted within a framework of the Advanced Medical Care B program of the Ministry of Health, Labour and Welfare Japan.

Eligibility

Eligibility criteria were as follows: (1) esophageal cancer considered as cured with radical esophagectomy, ER, radiotherapy, or CRT; (2) a dysphagia score (DS) of 2 or worse, inability to pass a standard size endoscope (major axis, 9-11 mm), and absence of cancer recurrence with endoscopic finding; (3) refractory benign esophageal stricture as referred to by Kochman's criteria[8] and defined as persistent after 5 or more treatments of EBD or bougies and/or at least once by the radial incision and cutting method[9]; (4) possibility of safe stent insertion that meets the criteria of absence of esophageal fistula, distance from esophageal orifice 3 cm or longer, and length of stricture 8 cm or shorter; (5) age $\geq$20 years; (6) Eastern Cooperative Oncology Group performance status 0 to 2; (7) adequate organ function (white blood cell counts $\geq$3000/mm^3 and $\leq$12,000/mm^3, hemoglobin $\geq$9.0 g/dL, platelet count $\geq$100,000/mm^3, serum total bilirubin level $\leq$2.0 mg/dL, both alanine transferase and aspartate aminotransferase $\leq$100 IU/L, serum creatinine level $\leq$2.0 mg/dL); and (8) written informed consent provided by the patient. Exclusion criteria were as follows: (1) delivery system (28F) could not pass the stricture even if endoscopic dilation was conducted before biodegradable stent insertion; (2) active infection that required systemic treatment; (3) synchronous active cancer in other organs except for carcinoma in situ, intramucosal cancer, or watchful waiting for prostate cancer; (4) radiation treatment was performed for the esophagus within 6 months before enrollment; (5) presence of Lugol's voiding lesion near the stricture or multiple Lugol's voiding lesions throughout the whole esophagus; (6) opioid analgesic therapy; (7) inability to discontinue antithrombotic drugs; (8) abolition or severe disorder of swallowing function; (9) pregnancy or nursing; (10) chronic steroid treatment; (11) patient judged to be inappropriate for enrollment in the study for any reason by the investigator; and (12) prior treatment using biodegradable stent placement.

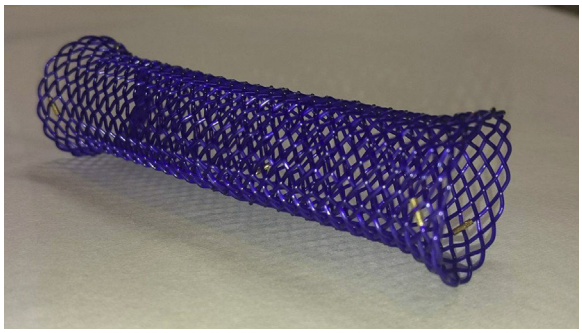

Figure 1. The biodegradable stent used in the study (SX-ELLA Stent Esophageal Degradable BD; ELLA-CS, Hradec Kralove, Czech Republic).

Procedure

To participate in the study, endoscopists needed to have performed 5 or more cases of esophageal stent placement. Details of the biodegradable stent placement procedure are as follows. First, length and major axis of the stricture were confirmed, and markers were placed at the body surface of the proximal and distal end of the stricture. Second, previous treatment with EBD, bougie, or radial incision and cutting was allowed, if the delivery device insertion was expected to be difficult to pass through the stricture. Third, the major axis of the stent was set at 18 mm, and the length of stent was selected based on the patient's stricture at 60, 80, or 100 mm. The biodegradable stent was extended and mounted into the delivery device and inserted through the guidewire under fluoroscopic guidance. Fourth, the stent was released at the appropriate position between markers, and, finally, stent