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 ≥20 years; (6) Eastern Cooperative Oncology Group performance status 0 to 2; (7) adequate organ function (white blood cell counts ≥3000/mm^3 and ≤12,000/mm^3, hemoglobin ≥9.0 g/dL, platelet count ≥100,000/mm^3, serum total bilirubin level ≤2.0 mg/dL, both alanine transferase and aspartate aminotransferase ≤100 IU/L, serum creatinine level ≤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.

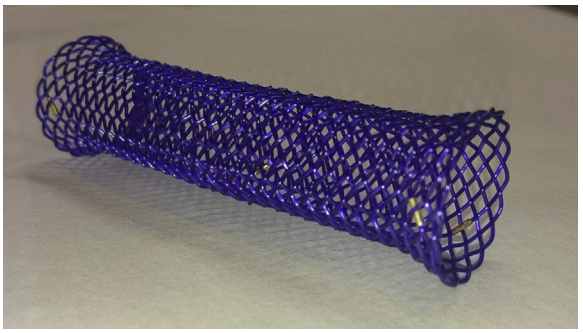


Figure 1. The biodegradable stent used in the study (SX-ELLA Stent Esophageal Degradable BD; ELLA-CS, Hradec Kralove, Czech Republic).

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

expansion was confirmed with both fluoroscopy and endoscopy.

Date and follow-up

Food and water intake was prohibited on the day of placement (day 1). Food and water intake then commenced the next day (day 2), if severe adverse events such as bleeding or perforation were not observed. Patients were discharged a week after stent placement (day 8) if there were no adverse events related to the placement. We allowed a lengthy hospital stay because esophageal stent is usually performed under hospitalization in Japan, and all participating investigators wanted 1 week to carefully observe patients before the study launch, because it was our first clinical experience with this biodegradable stent. Patients were assessed by physical examination, evaluation of DS with interview, and endoscopic observation at day 7. In addition, chest radiograph studies were performed at 2 and 4 weeks after stent placement and every month thereafter for 24 weeks or until confirmation of complete stent degradation or restricture with endoscopic observation.

We used a DS with 5 grades, and score was determined by 2 investigators at each institution independently. The 5 grades were as follows: 0, able to eat a normal diet/no dysphagia; 1, able to swallow some solid food; 2, able to swallow only semisolid foods; 3, able to swallow liquids only; 4, unable to swallow anything/total dysphagia. In addition, the DS was re-evaluated by the central evaluation committee consisting of a gastroenterologist and a nutritionist who were independent to the investigators in this study. The centrally assessed DS was used as a supplemental analysis to assess the reproducibility of DS, because the central evaluation was incorporated based on a recommendation from the committee of the Advanced Medical Care B program of the Ministry of Health, Labour and Welfare in Japan.

To be approved for this program endoscopists had to have several treatment experiences using this device. Thus, our study was done in a 2-step framework. We first enrolled 2 patients and evaluated the preliminary efficacy and safety data. Second, we then enrolled an additional 16 patients. The committee of Ministry of Health, Labour and Welfare was held after step 1, so the central evaluation was adopted for only 16 patients in step 2.

Endpoints

The primary endpoint was the proportion of patients whose DS was improved at 12 weeks after stent placement. The definition of DS improvement was when the DS was decreased to less than 2 or when the DS was 2 or worse but improved to 1 or 0 at least 1 week after supportive treatment involving removal of food impaction or argon plasma coagulation (APC) for reactive hyperplastic nodules because of stent. Patients were not classified as DS improved until assessment time when any reintervention for esophageal stricture was done. Patients who died or were lost to follow-up before assessment time were planned not to be classified as DS improvement cases.

Secondary endpoints were the proportion of DS improvement at 24 weeks, dysphagia-free survival (DFS), stricture improvement rate at 12 or 24 weeks, success rate of stent placement procedure, stent migration rate, and adverse events. Stricture improvement was defined as follows: (1) DS was decreased to lower than 2, (2) DS was 2 or worse but improved to 1 or 0 at least 1 week after supportive treatment involving removal of food impaction or APC for reactive hyperplastic nodules due to stent, or (3) a standard size endoscope could pass through the stricture. Patients were not classified as stricture improved until assessment time when any reintervention for esophageal stricture was done. The definition of stricture improvement consisted of the ability for endoscope passage, and it was the major difference from DS improvement.

DFS was measured from the date of stent placement to the first date of DS of at least or worse except for the dysphagia that improved with supportive treatment as noted earlier, initiation of another intervention for esophageal stricture, or any death. Adverse events were evaluated and graded according to Common Terminology Criteria for Adverse Events, version 4.0.[10] After confirmation that the DS was 2 or worse with stricture progression, any treatment for esophageal stricture except for biodegradable stent replacement was allowed.

Statistical analysis

The sample size was determined by assuming a binomial distribution. The expected proportion of DS improved was set to 40% and the threshold proportion set to 10% with a one-sided alpha of .05 and power of .90; therefore, the required number of patients was determined to be 18. The threshold value of 10% was determined based on a previous survey reporting that stricture improvement by an additional EBD was 10.4% (7/67) for the same target population as in the present study.[6] If more than 5 patients showed an improved DS at 12 weeks, the primary endpoint of this study was considered to have been met. DFS curve was estimated via the Kaplan-Meier method. All statistical analyses were performed using SAS software (release 9.4; SAS Institute, Cary, NC).

RESULTS

Between June 2012 and February 2015, 18 patients were enrolled and treated with biodegradable stents. The data were fixed at October 2015. Patient characteristics are presented in Table 1. Of those 18, 15 patients were men and 3 were women; median age was 72 years (range, 53-80). At enrollment, patients' DSs were 2 in 10 patients (55.6%), 3 in 7 patients (38.9%), and 4 in 1 patient (5.6%). The median length of stricture was 3.0 cm (range, 1.5-6.0). Treatments for esophageal cancer and causes of stricture

TABLE 1. Baseline patient characteristics

Patient number	Age (y)	Sex	DS	Stricture etiology	Length of stricture (cm)	Number of prior treatments for stricture		
						EBD	Bougie	Radial incision and cutting
1	72	M	4	Surgery	4.0	37	0	7
2	74	M	3	ER and CRT	3.0	36	0	32
3	74	M	3	Surgery	2.0	25	3	9
4	71	M	3	Surgery	2.0	182	0	0
5	63	F	2	Surgery and CRT	2.0	60	135	8
6	79	M	2	ER	5.0	24	22	0
7	72	M	3	Surgery	4.0	22	0	2
8	70	M	2	ER	1.5	13	0	0
9	76	M	2	ER	4.0	7	0	0
10	56	M	3	Surgery	4.0	22	18	0
11	72	M	2	Surgery	6.0	3	19	1
12	72	M	2	Surgery	3.0	17	1	0
13	73	M	2	Surgery	3.3	25	1	1
14	73	F	2	ER	3.0	24	0	0
15	80	F	2	ER and CRT	5.0	7	0	0
16	53	M	3	CRT	3.0	5	3	0
17	70	M	2	Surgery	2.0	6	1	1
18	74	M	3	Surgery	2.0	38	6	0

DS, Dysphagia score; *EBD*, endoscopic balloon dilation; *ER*, endoscopic resection; *CRT*, chemoradiotherapy.

were ESD in 6 patients (33.3%), esophagectomy in 11 patients (61.1%), and CRT in 4 patients (22.2%; 3 overlap cases). The median total number of prior treatments for esophageal stricture was 23 EBD (range, 3-182), 4.5 bougie (range, 1-135), and 4.5 radial incision and cutting (range, 1-32) procedures. A 60-mm-long stent was used in 14 patients, 80-mm long in 3 patients, and 100-mm long in 1 patient. The procedure of stent placement was successful in a single session in all patients.

Efficacy

Treatment results and efficacy are summarized in Table 2. Twelve patients were assessed as demonstrating DS improvement at 12 weeks after stent placement; therefore, the DS improvement rate at 12 weeks was 66.7% (12/18; 90% confidence interval [CI], 44.6%-84.4%). A representative case is shown in Figure 2. In addition, the subset analyses of DS improvement at 12 weeks after stent placement in each treatment were 8 of 11 patients (72.7%; 95% CI, 39.0%-94.0%) after esophagectomy, 3 of 4 patients (75%; 95% CI, 19.4%-99.4%) after CRT, and 4 of 6 patients (66.7%; 95% CI, 22.3%-95.7%) after ESD. Also, DS improvement without any supportive endoscopic treatments involving APC for reactive hyperplastic nodules at 12 weeks was 55.6% (10/18; 95% CI, 30.8%-78.5%). Among all 18 patients, only 3 patients improved their DS at 24 weeks (16.7%, 95% CI, 3.6%-41.4%). All 3 patients had been treated with esophagectomy for esophageal cancer.

TABLE 2. Percent of dysphagia score improvement after stent placement

	12 Weeks (95% confidence interval)	24 Weeks (95% confidence interval)
All patients	66.7% (12/18)	16.7% (3/18)
	(44.6%-84.4%*)	(3.6%-41.4%)
After esophagectomy	72.7% (8/11)	27.3% (3/11)
	(39.0%-94.0%)	(6.0%-61.0%)
After CRT	75.0% (3/4)	0% (0/4)
	(19.4%-99.4%)	(0%-60.2%)
After ESD	66.7% (4/6)	0% (0/6)
	(22.3%-95.7%)	(0%-45.9%)

CRT, Chemoradiotherapy; *ESD*, endoscopic submucosal dissection.
*This confidence interval is 90% because of primary endpoint.

In addition, the subset analyses of DS improvement at 24 weeks after stent placement showed 3 of 11 patients (27.3%; 95% CI, 6.0%-61.0%) after esophagectomy, 0 of 4 patients (0%; 95% CI, 0%-60.2%) after CRT, and 0 of 6 patients (0%; 95% CI, 0%-45.9%) after ESD. The DS improvement without any supportive endoscopic treatments involving APC for reactive hyperplastic nodules at 24 weeks was 16.7% (3/18; 95% CI, 3.6%-41.4%). From the re-evaluation by the central evaluation committee, DS improvement rates at 12 weeks and 24 weeks were 87.5% (14/16; 95% CI, 61.7%-98.5%) and 18.8% (3/16; 95% CI,

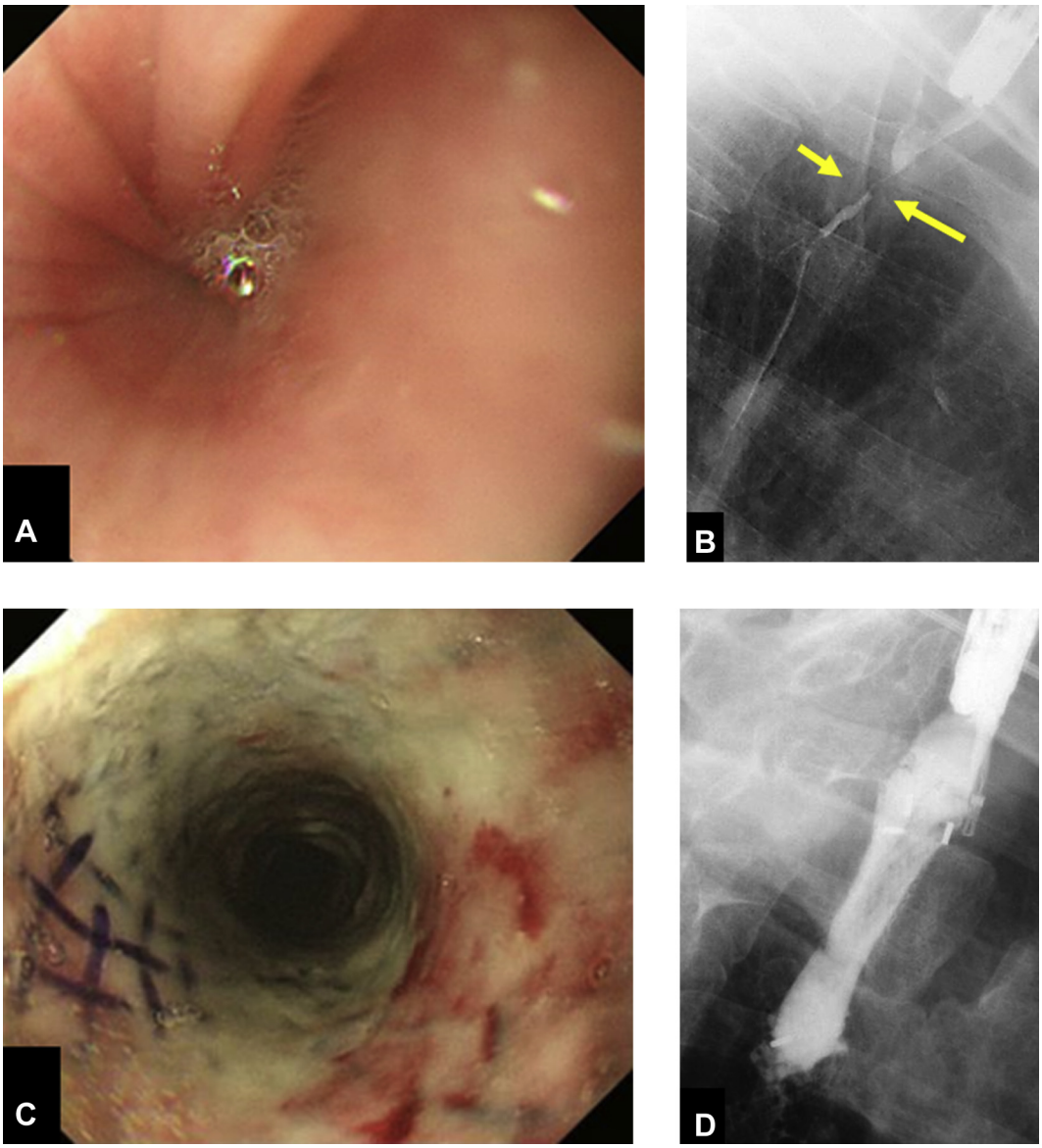


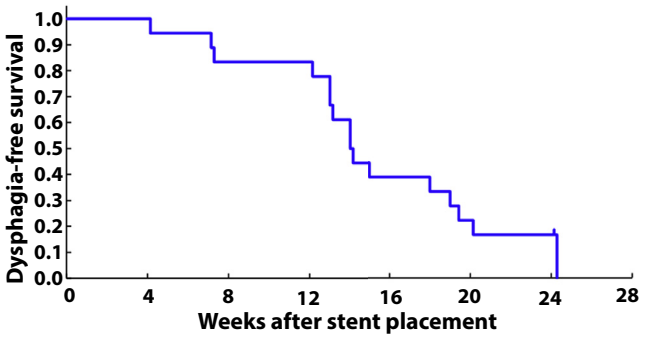
Figure 2. A patient with refractory esophageal stricture after endoscopic resection followed by chemoradiotherapy for esophageal cancer (case number 2 in Table 1). **A,** Endoscopic imaging of stricture before stent placement. The patient's dysphagia score was 3 before stent placement. **B,** Fluoroscopic imaging of stricture before stent placement. The narrowest point was at the *yellow arrow*. **C,** Endoscopic image of stricture at 4 weeks after stent placement. Patient's dysphagia score improved to 0 after placement. **D,** Fluoroscopic imaging of stricture after stent placement.

4.1%-45.7%), respectively. Furthermore, the median DFS was 14.1 weeks (95% CI, 13.0 months to 19.0 weeks), and DFS at 12 weeks and 24 weeks were 83.3% (95% CI, 56.8%-94.3%) and 16.7% (95% CI, 4.1%-36.5%), respectively (Fig. 3). The stricture improvement rate at 12 and 24 weeks were 61.1% (11/18, 95% CI, 35.7%-82.7%) and 11.1% (2/18, 95% CI, 1.4%-34.7%), respectively. The median period between placement and complete degradation of stents was 127 days (range, 98-219).

Safety

The only intraoperative adverse event was a case of grade 2 nausea and grade 1 vomiting just after stent placement. Stent migration was not experienced in any patients during their follow-up. Reactive hyperplastic nodules because of the stent were endoscopically observed in 13 patients (72.2%), 10 of whom received APC for the nodules.

Major adverse events occurring during the follow-up are presented in Table 3. The most frequent adverse events after stent placement were esophageal pain in 9 patients (50%), GERD in 5 patients (27.8 %), and vomiting in 3 patients (16.8%); however, all these adverse events were grade 1 or 2. Three patients had severe adverse events (grade 3) that required hospitalization. A patient with benign esophageal stricture after esophagectomy and chemotherapy who had previously been treated 37 times with EBD and 7 times with radial incision and cutting and



Number of patients	Number of events	median DFS (weeks) (95% CI)	12-weekDFS (95% CI)	24-weekDFS (95% CI)
18	16	14.1 (13.0 - 19.0)	83.3% (56.8% - 94.3%)	16.7% (4.1% - 36.5%)

Figure 3. Kaplan-Meier curve of dysphagia-free survival (DFS) in patients given biodegradable stents for refractory benign esophageal strictures after curative treatment of esophageal cancer.

had a DS of 4 at enrollment experienced grade 3 esophageal stricture and was admitted to the hospital at 59 days after stent placement. The cause of stricture was hyperplastic reactive nodules due to the stent, and this was smoothly resolved with endoscopic intervention of APC and steroid administration. Another patient after esophagectomy who had previously been treated 182 times with EBD and had a DS of 3 at enrollment experienced grade 3 soft tissue infection approximately a week after placement; subsequently, his left clavicle bone became infected. His infection resolved with surgical drainage approximately 13 months after placement. Another patient with esophageal stricture after ESD followed by CRT previously treated 7 times with EBD and had DS of 2 at enrollment developed an esophagobronchial fistula approximately 3 months after stent placement. Her general status stabilized with continuous suction drainage from percutaneous transesophagostomy and feeding from percutaneous gastrojejunostomy. She was discharged approximately 10 months after admission. There was no treatment-related deaths in this study.

DISCUSSION

This is the first multi-institutional prospective trial of biodegradable stents for patients with refractory benign esophageal stricture after treatment for esophageal cancer including stricture after ESD. In the present study the DS improvement at 12 weeks after stents placement was 66.7% (12/18; 90% CI, 44.6%-84.4%); therefore, the primary endpoint was met. Furthermore, the efficacy of the biodegradable stent did not differ by the method of treatment for esophageal cancer at 12 weeks after placement.

We previously reported the efficacy of EBD for refractory benign esophageal strictures after curative treatment for esophageal cancer.[6] In that report we comparatively analyzed the efficacy of EBD for benign stricture between cohorts after esophagectomy and nonsurgical treatment including ESD or radiotherapy. We concluded that EBD for strictures after nonsurgical treatment requires a significantly large number of procedures to achieve a cure and contains a larger number of patients with refractory stricture. Therefore, we predicted that the efficacy of biodegradable stents would also differ between the causes of stenosis, and 4 patients were mandatory to enroll in each triggered treatment for esophageal cancer to comparatively assess differences between each treatment in this study. The strong point of this study was the comparative evaluation of efficacy of the biodegradable stent among individual treatments that were the causes of the esophageal strictures. The efficacy of the biodegradable stent at 24 weeks after placement was poorer than the efficacy that we had expected and was unsatisfactory, especially in patients with refractory stricture after nonsurgical treatment including ESD or CRT.

In the BEST (Biodegradable Esophageal Stent) study, Repici et al[7] reported the efficacy of biodegradable stents for refractory stricture mainly caused by peptic injury or surgery in a multi-institutional prospective study. In that study the DS improvement rate was 45% (9/20) at the median follow-up period of 53 weeks; therefore, it was a more favorable outcome compared with our present study. Although it is difficult to identify with certainty the reason for the difference between the studies, we could suggest that a difference in patient backgrounds or stent size might have influenced the outcome. In the BEST study the mean times of prior treatment for esophageal stricture was 2.2 ± .5 per month (range, 1-3), whereas the median times of prior treatment was 3 for EBD (range, 1-30) or 2.5 for bougie (range, 1-13) in our study. It also may be that the present study consisted of more difficult cases to relieve dysphagia. Moreover, we chose an 18-mm-diameter stent because of concern for possible damage to the refractory stricture mainly after radiation; however, a 25-mm major axis stent was chosen in the BEST study. It is difficult to estimate the adequate stent size for Japanese patients who are smaller, thinner, and prefer soft food as compared with a Western patient populations.

We have set the primary endpoint of this study as DS improvement at 12 weeks, and the validity of this endpoint should be discussed. For timing of the primary endpoint, we determined under reference that biodegradable stents gradually degrade within 8 to 12 weeks after placement. In fact, the median period of complete degradation was approximately 18 weeks after placement; however, biodegradable stents gradually decrease in efficacy from the initiation of degradation. Hirdes et al[11] conducted a prospective follow-up study to evaluate the efficacy of single and sequential biodegradable stent placement. In that report the median dysphagia-free period after initial

TABLE 3. Adverse events related to stent placement

Event	Grade*				Total	
	1	2	3	4	Number	Percent
Esophageal pain	7	2	0	—	9	50
Fever	1	1	0	0	2	11.1
Esophageal bleeding	0	0	0	0	0	0
Nausea	0	0	0	—	0	0
Vomiting	3	0	0	0	3	16.7
Cough	1	0	0	—	1	5.6
Dysphagia	1	0	0	0	1	5.6
Malaise	0	1	—	—	1	5.6
Neck pain	1	0	0	—	1	5.6
Pain	0	1	0	—	1	5.6
Sore throat	1	0	0	—	1	5.6
GERD	3	2	0	—	5	27.8
Esophageal stricture	0	0	1	0	1	5.6
Esophagobronchial fistula	0	0	1	0	1	5.6
Bone infection†	—	—	1	0	1	5.6
Soft tissue infection†	—	0	1	0	1	5.6

*Grade 1: Mild, asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2: Moderate; minimal, local or noninvasive intervention indicated. Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated. Grade 4: Life-threatening consequences; urgent intervention indicated.
†Overlap case.

placement was 90 days (range, 14-618), similar to the results of the present study. Therefore, 3 months after placement might be an adequate timing as the primary endpoint for evaluation of the biodegradable stent.

Three of our patients experienced severe adverse events. A patient with esophageal stricture because of hyperplastic reactive nodules after placement required hospitalization. We performed APC for the hyperplastic nodules as referred to in the case report,[12] and the patient's restricture smoothly resolved. Unfortunately, an esophagobronchial fistula occurred in a patient with stricture after ESD and CRT. Before initiation of this study, the safety of stent placement for strictures after CRT was the largest concern, because 2 of 3 patients who had severe pain after placement in the BEST study had postradiation stricture.[7] Furthermore, prior radiotherapy was reported as a risk factor of severe adverse events, including esophageal perforation,[13] and there are several reports of severe adverse events after placement of several types of stents for patients with prior radiation.[14-16] Although it is hard to conclude with a small patient cohort, the balance of risks and benefits appears not to support the use of biodegradable stents after CRT because it is too invasive. We as investigators should pay special attention when performing procedures for patients who have had radiotherapy.

Although this is a multi-institutional prospective study, the total number of cases was relatively small. Although the total number of cases enrolled in this study was adequate to evaluate the efficacy, the cohort in each cause of stricture group was too small to draw conclusions, especially after CRT or ESD. In addition, this was not a randomized control trial that compared other modalities or types of stent. Some reports comparatively evaluate the temporary placement of plastic stents and fully covered metallic stents and the biodegradable stent. Although the efficacies of dysphagia improvement and migration rate were similar between the fully covered metallic stent and the biodegradable stent, poor long-term improvement and a high migration rate were confirmed in patients treated with plastic stents.[17] Self-expandable metallic stents are the preferred device for permanent placement in patients with malignant stricture but are sometimes used as a temporary method for benign esophageal strictures. Stent removal is mandatory in cases with benign stricture, and most of these stents are removed safely. In some cases, however, especially after a long period of placement, patients have had severe adverse events during removal, including perforation.[18] Indeed, biodegradable stents and plastic stents are not commercially available, and self-expandable metallic stents for benign strictures are positioned as a contraindication in Japan. Therefore, it is very difficult to conduct a randomized controlled trial.

In conclusion, the biodegradable stent is an effective and tolerable treatment for refractory benign esophageal stricture after curative treatment, including ESD or CRT.

Although the efficacy at 3 months did not differ by the type of treatment for esophageal cancer, the long-term efficacy of biodegradable stents is limited, especially in patients with refractory benign esophageal strictures after ESD or CRT.

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