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Management of Malignant Stricture of the Esophagogastric Junction with a Newly Designed Self-Expanding Metal Stent with an Antireflux Mechanism

Background and Study Aims: When stents are placed across the esophagogastric junction for palliative treatment of malignant strictures, they may lead to esophagogastric reflux. The aim of this study was to compare the effectiveness of a newly designed antireflux stent with that of a standard open stent and a currently available antireflux stent (Dostent) in preventing gastroesophageal reflux symptoms in patients with inoperable cancer at the esophagogastric junction.

Patients and Methods: Thirty-six consecutive patients with cancer at the esophagogastric junction were randomly assigned to undergo placement of a newly designed antireflux stent (n = 12), a Dostent (n = 12), or a standard open stent (n = 12). Technical and clinical success, dysphagia score, reflux symptoms, complications and ambulatory 24-h esophageal pH monitoring were assessed.

Results: The technical success rates were 100 %. After 1 week, dysphagia had improved in all patient groups ($P < 0.05$), but the degree of improvement did not differ between the three groups. The DeMeester score was significantly lower in the group with the newly designed antireflux stent than in the other groups. The fraction of the total recording time during which esophageal pH was below 4 was 3.14 ± 5.78 % using the newly designed antireflux stent, in comparison with 29.25 ± 15.41 % in the Dostent group and 15.01 ± 11.72 % in the standard open stent group ($P < 0.001$). Fewer reflux episodes occurred with the newly designed antireflux stent than with the Dostent or standard open stent. There were no complications with any of the three stents.

Conclusions: The newly designed antireflux stent is effective in relieving dysphagia caused by malignant cancer at the esophagogastric junction. The newly designed antireflux stent is significantly more effective in preventing gastroesophageal reflux than currently available antireflux stents.

Introduction

Esophageal cancer is frequently unresectable at the time of diagnosis, due to local invasion or metastasis to other organs. Therapy is therefore usually palliative in nature, with the major aims being relief of dysphagia, maintenance of nutrition, and closure of tracheoesophageal fistulas. Placement of self-expanding metal stents (SEMS) has become the treatment of choice for palliative therapy in patients with unresectable malignant esophageal strictures, as it is safe and minimally invasive [1,2]. However, the optimal palliative therapy for patients with strictures of the esophagogastric junction is still a matter of debate, as severe gastroesophageal reflux and aspiration pneumonia, which can in turn adversely affect the patient's quality of life, often develop [3]. Weston and Sharma [4] reported a high incidence of gastroesophageal reflux disease, including cases of aspiration and death, in patients who had SEMS placed across the esophagogastric junction. Valbuena [5] also reported cases of heartburn and coughing spells in 27 % of patients in whom a standard open stent was used for palliative treatment of esophagogastric junction cancer.

Several previous attempts have been made to solve this problem by developing esophageal stents with an antireflux mechanism

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[5–9]. However, few studies have investigated the efficacy of SEMS with an antireflux mechanism using objective methods such as ambulatory 24 h esophageal pH monitoring. The aim of the present study was to compare the effectiveness of a newly designed antireflux stent with that of a standard open stent and a currently available antireflux stent (Dostent) in patients with inoperable esophagogastric junction cancer, using ambulatory 24 h esophageal pH monitoring.

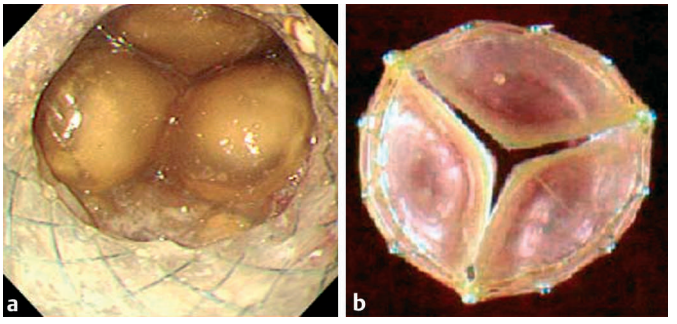

Figure **1** The Dostent. The stent has a disconnected body, and the material used for both the valve and the covering is polyurethane. The valve is placed on the inner aspect of the stent's distal end and has the shape of a tricuspid valve. **a** As seen from the upper end of the stent. **b** As seen from the lower end.

Patients and Methods

Patients

From July 2001 to March 2004, 36 consecutive patients with dysphagia caused by inoperable carcinoma of the esophagogastric junction were randomly assigned to undergo insertion of either a newly designed antireflux stent, a Dostent, or a standard open stent. Patients with incurable malignant esophageal strictures involving the esophagogastric junction or within 2 cm of the esophagogastric junction were included. Patients with benign strictures, previous esophagogastric surgery, high portal blood pressure, coagulation disorders, pregnant or breastfeeding women, and terminally ill patients with an estimated life expectancy of less than 6 weeks were excluded. There were 32 men and four women, aged 49–83 years (mean 65.7 years). Twenty-eight patients had squamous-cell carcinoma of the distal esophagus, seven patients had advanced gastric cancer with distal esophageal invasion, and one patient had gastric lymphoma. The diagnosis was established by means of endoscopic biopsy and computed tomography. In these 36 patients, 12 received standard open stents, 12 received Dostents, and 12 received the newly designed antireflux stent.

Stent Design

The standard open stent is a covered self-expandable metal stent (M.I. Tech. Co., Inc., Pyongtack, Korea). The stent is made from a strand of nitinol wire. The individual stent bodies have an internal diameter of 18 mm and a length of 20 mm. Multiple stent bodies can be interconnected with a polyurethane membrane to produce stents of 4–18 cm in length. The stent is flare-shaped, with flanges at the proximal and distal ends measuring 24 mm in diameter. The stent is completely covered with a polyurethane membrane. The Dostent (M.I. Tech. Co., Inc., Pyongtack, Korea) is an early-model antireflux stent dating from 1996 in which the valve was manufactured into the shape of a tricuspid valve. The stent has a disconnected body and the material used for both the valve and the covering is polyurethane. The valve is placed on the inner aspect of the stent's distal end. The leaflet contacting the three wings of the valve is 1 mm in length and 30 mm in diameter (Figure **1**). This product had problems in functioning properly when the reflux pressure was high, with the valve easily flipping over or small gaps occurring at the contact points of the tricuspid valve. A new model was therefore designed.

The modified antireflux stent (M.I. Tech. Co., Inc., Pyongtack, Korea) is an esophageal stent that is fully covered except for the proximal flange, to impede tumor ingrowth through the wire mesh, which has an S-type antireflux valve with a long leaflet inside the stent body. The antireflux valve is attached to the stent wall in order to minimize acid reflux and prevent inversion of the valve (Figure **2**). The length of the valve's leaflet is 70 mm and its diameter at 18 mm is smaller than that of the earlier models because of its position within the body of the stent. However, it has

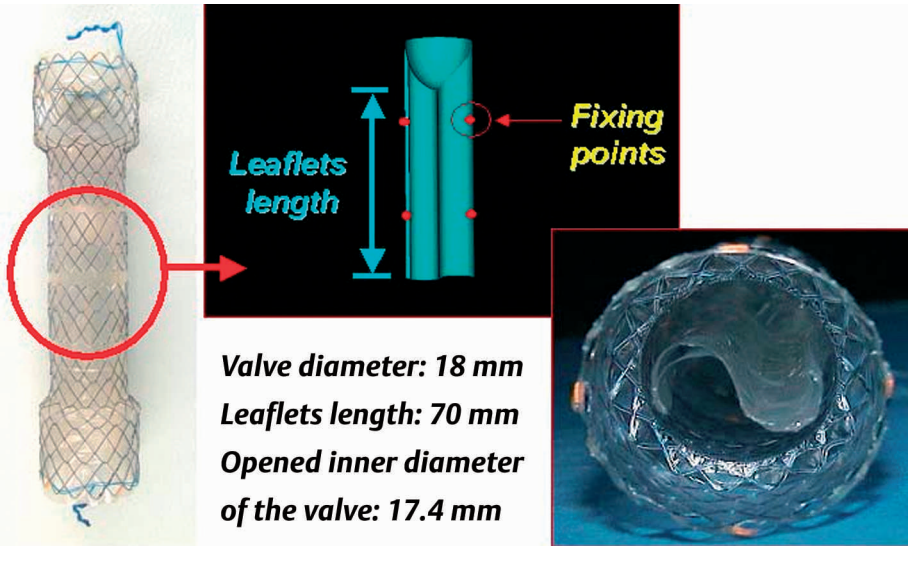

Figure **2** The newly designed antireflux stent (with an S-type valve and long leaflets). This modified antireflux stent is an esophageal stent that is fully covered, except for the proximal flange, to impede tumor ingrowth through the wire mesh, which has an S-type valve with long leaflets inside the stent's body. The antireflux valve is attached to the stent wall in order to minimize acid reflux and prevent inversion of the valve.

a strong antireflux effect, as it uses an S-type valve with a long leaflet and the open inner diameter of the valve is small at 17.4 mm.

Stent Insertion Procedures

This prospective study was approved by the ethics committee of Soon Chun Hyang University. In all cases, informed consent was obtained from the patients before the procedure. All of the patients had dysphagia at the initial evaluation. Dysphagia was graded on a scale of 0 to 4 (0, no dysphagia; 1, dysphagia to regular solids; 2, dysphagia to soft solids; 3, dysphagia to solids and liquids; 4, complete dysphagia including saliva). A reflux symptom score was also evaluated using a questionnaire (Table **1**). Each stenting procedure was carried out with the patient under intravenous conscious sedation using 2 – 5 mg midazolam hydrochloride and nalbuphine 10 mg for optimal effect. The pharynx was anesthetized with 2 % viscous lidocaine (Taejoon Pharmaceutical Co., Seoul, Korea). Oxygen was administered via a nasal cannula, and the patient's vital signs were continuously monitored during the procedure. The procedures were all conducted with endoscopic and fluoroscopic visualization. In patients with tight strictures, preinsertion dilation was carried out using a Savary–Gilliard bougie dilator under fluoroscopic guidance. To prevent stent migration, the stents were inserted in all cases using the technique described by Shim et al. [10], in which the silk thread attached to the proximal flange of the stent is drawn out and attached to the patient's earlobe. After placement of a 0.038-inch stiff guide wire in the stomach, the stent introducer was advanced over the guide wire into the esophagus under fluoroscopic guidance, and the stent was deployed by pulling back the introducer sheath.

Follow-Up

Proton-pump inhibitors and other antacid medications were not prescribed. The patients ingested a liquid diet on the first day after the procedure, were restricted to a soft diet for 2 days, and then progressed to a soft diet. Clinical and radiographic check-up examinations were subsequently scheduled on days 1 and 7 and every 4 weeks thereafter. To evaluate the status of the valve and correct positioning of the stent, endoscopic examinations were carried out on the fifth to seventh days after insertion of the stent. After confirmation of complete fixation of the stent to the esophageal mucosa, the silk thread connected to the patient's earlobe was removed. Gastroesophageal reflux into the esophagus was assessed using ambulatory 24 h esophageal pH monitoring, with pH electrodes positioned just above the upper flange of the stent. This examination was carried out on the seventh day after stent placement. The dysphagia score and reflux symptom score were reevaluated on day 7. Endoscopic and radiographic examinations were repeated if there was recurrent dysphagia or reflux symptoms.

Statistical analysis. The data are presented as means plus or minus standard deviation (SD). All statistical analyses were carried out using the SPSS software package (SPSS Inc., Chicago, Illinois, USA). The statistical significance of differences for non-normally distributed data was tested with the Mann–Whitney U test. The data were compared using the Kruskal–Wallis test for independent samples between groups. A P value of less than 0.05 was regarded as significant.

Table **1** Questionnaire for the reflux symptom score

Symptoms	*Intensity*	*Frequency*	*Score*
Heart burn	0 1 2 3 4	0 1 2 3 4	
Acid reflux	0 1 2 3 4	0 1 2 3 4	
Chest pain	0 1 2 3 4	0 1 2 3 4	
Foreign-body sensation	0 1 2 3 4	0 1 2 3 4	
Hoarseness	0 1 2 3 4	0 1 2 3 4	
Total			

Score	*Intensity*	*Frequency*
0	No symptoms	No symptoms
1	A minor problem likely to be forgotten unless careful attention is paid	At least once a month
2	May need some treatment but would not affect everyday life	At least once a week
3	A severe symptom affecting everyday life	About twice a week
4	A severe symptom requiring hospitalization	Three times a week

Table **2** Patient demographics relative to each type of stent

	A (n = 12)	*B (n = 12)*	*C (n = 12)*
Mean age (years, range)	62.7 (50 – 74)	69.2 (49 – 83)	65.3 (51 – 83)
Sex (M/F)	11/1	9/3	12/0
Histology			
Squamous-cell carcinoma	10	9	9
Adenocarcinoma	2	2	3
Other	0	1	0

A: standard open stent; B: Dostent (antireflux stent); C: the newly designed stent with an S-type valve with long leaflets.

Results

The patients' demographic data are summarized in Table **2**. No statistical differences were observed with regard to age, sex, histology, or mean stricture length. Stent insertion was technically successful in all of the patients, and no procedure-related complications occurred in any of the three groups. The stent usually showed some waisting at the site of the stricture immediately after insertion, but expanded fully after a few days. All of the patients had some dull chest pain following insertion for a few days. After stent placement, all of the patients had immediate improvement of their dysphagia ($P < 0.05$). The effectiveness of the palliative treatment for dysphagia was similar in all of the stent groups, with no statistically significant differences. In group A (standard open stent), the mean reflux symptom score increased from 4.42 ± 3.40 to 6.25 ± 2.70 ($P = 0.049$) after stent placement. Five patients in group A reported severe nocturnal reflux symptoms. In group B (Dostent), the mean reflux symptom score increased from 5.58 ± 3.40 to 5.75 ± 6.15 ($P = 0.798$). Four patients in group B reported severe nocturnal reflux symptoms, and one patient developed aspiration pneumonia. By contrast, in group C (the newly designed antireflux stent), the mean reflux

symptom score decreased from 5.42 ± 3.40 to 2.50 ± 1.78 ($P = 0.005$) after stent placement, and none of the patients reported nocturnal reflux symptoms or developed aspiration pneumonia (Table **3**). The results of ambulatory 24 h esophageal pH monitoring are shown in Table **4**. The DeMeester score was significantly lower in group C than in the other groups (group A, 60.44 ± 48.66; group B, 105.29 ± 51.96; group C, 12.00 ± 21.51; $P < 0.001$). The fraction of the total recording time during which esophageal pH was below 4 was only 3.14 ± 5.78 % using the newly designed antireflux stent, compared with 15.01 ± 11.72 % with the standard open stent and 29.25±15.41 % with the Dostent ($P < 0.001$). Fewer reflux episodes occurred with the newly designed antireflux stent than with the Dostent and standard open stent (group A, 87.50 ± 58.99; group B, 68.75 ± 61.52; group C, 24.00 ± 55.39; $P = 0.002$). No differences were detectable with regard to complications, need for repeat interventions, or survival periods. The 30-day mortality rate was 8 % in group A, 9 % in group B, and 12 % in group C; the median survival periods were 114 days, 107 days, and 109 days, respectively.

Table **3** Dysphagia and reflux symptom scores with the three types of stent (Mann–Whitney U test)

	A (n = 12)	*B (n = 12)*	*C (n = 12)*
Dysphagia score (mean)			
Pre	3.25 ± 0.45	3.08 ± 0.69	2.83 ± 0.58
Post	1.00 ± 0.60	1.08 ± 0.69	0.91 ± 0.51
P	0.002	0.001	0.001
Reflux symptom score (mean)			
Pre	4.42 ± 3.40	5.58 ± 3.40	5.42 ± 3.40
Post	6.25 ± 2.70	5.75 ± 6.15	2.50 ± 1.78
P	0.049	0.798	0.005

A: standard open stent; B: Dostent (antireflux stent); C: the newly designed stent with an S-type valve with long leaflets.

Table **4** Ambulatory 24 hour esophageal pH monitoring (Kruskal-Wallis test)

	A (n = 12)	*B (n = 12)*	*C (n = 12)*	P
Total number of reflux episodes	87.50 ± 58.99	68.75 ± 61.52	24.00 ± 55.39	0.002
Longest duration (min)	35.89 ± 32.43	150.43 ± 110.61	11.86 ± 21.74	< 0.001
% total time with pH < 4	15.01 ± 11.72	29.25 ± 15.41	3.14 ± 5.78	< 0.001
DeMeester score	60.44 ± 48.66	105.29 ± 51.96	12.00 ± 21.51	< 0.001

A: standard open stent; B: Dostent (antireflux stent); C: the newly designed stent with an S-type valve with long leaflets.

Discussion

With the rising incidence of carcinoma involving the distal esophagus and gastric cardia, self-expanding metal stents are increasingly being deployed across the esophagogastric junction. This can lead to significant gastroesophageal reflux and aspiration pneumonia, which can in turn adversely affect the patients' quality of life. With a stent deployed across the esophagogastric junction, the stomach and the esophagus in effect become a common cavity. In addition to reflux resulting from an increase in intra-abdominal pressure, patients with SEMS also may experience "passive reflux" when gravity is eliminated [8]. To resolve this problem, several attempts have been made in recent years to develop esophageal stents with an antireflux mechanism. Nunes et al. [6] and Valbuena [5] attached latex sleeves to rigid plastic esophageal stents. Mizumoto et al. [7] used a cylindrical Gore-Tex modification to prevent reflux. Dua et al. [8] designed a modified self-expanding metal esophageal Z-stent to prevent reflux. The stent was modified by extending the polyurethane coating beyond the lower metal cage so as to form a "windsock" type of valve. The authors reported that this antireflux stent was effective in preventing reflux without interfering with physiological flow.

Several trials have been conducted in Korea in the effort to develop an ideal antireflux stent. In 1993, a modified self-expanding metal esophageal stent was developed to prevent reflux. The morphology of this stent was similar to that of the stent designed by Dua et al. [8], but it had certain limitations: insertion is more difficult with this type of stent than with conventional stents, and the antireflux valve can easily become inverted when high-pressure gradients occur – e.g., during belching, vomiting, and coughing. Once it has become inverted, it is difficult to revert the valve by drinking water, and an endoscopic procedure is sometimes needed to revert the valve.

In 1996, another modified antireflux esophageal stent (Dostent, M.I. Tech. Co., Inc., Pyongtack, Korea) was produced. This is a fully covered esophageal stent that has an antireflux valve with a larger distal band in order to prevent reflux. The antireflux valve consists of three leaflets, like the tricuspid valve in the heart. The valves are made of polyurethane and attached to the inner portion of distal end of the stent. Most patients who received this stent experienced relief of reflux symptoms, but some were found to have acid reflux on 24 h pH monitoring, with endoscopic examination showing that the valve had become reversed or distorted. A new model was therefore designed. This modified antireflux stent is a fully covered esophageal stent that has an S-type valve with long leaflets inside the body of the stent. The antireflux valve is attached to the stent wall in order to minimize acid reflux and prevent inversion of the valve.

Objective assessment of gastroesophageal reflux requires radiographic, scintigraphic, manometric, or pH monitoring techniques. Although barium and scintigraphic studies were not carried out in the present study, 24 h pH monitoring is the most reliable method of diagnosing gastroesophageal reflux disease. In this study, the modified antireflux stent was compared with conventional self-expandable metal stents and Dostents with regard to reflux symptoms, dysphagia score, and the ambulatory 24 h pH monitoring results. The dysphagia score improved significantly with all of the stents. Of the three stents, the newly designed S-type antireflux valve was found to the best for preventing acid reflux on ambulatory 24 h pH monitoring. The modification does not appear to interfere with the primary function of the stent-relieving dysphagia. On the basis of this experience with the new antireflux valve stent, we believe that the S-type valve

with long leaflets is more effective than conventional stents and the previous Dostent in preventing acid reflux and valve inversion.

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