Niti-S Esophageal Covered stent (double anti-reflux type). An observational patient registry/post-market clinical follow-up study

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Abstract

Background: Relieving dysphagia is the main goal of palliative care in advanced esophageal cancer. We aimed to evaluate the safety and clinical performance of the Niti-S esophageal double covered, anti-reflux stent (Taewoong Medical, Seoul, Korea) in inoperable carcinoma of the esophagus or gastric cardia.

Methods: This was a retrospective patient registry/post-market clinical follow-up study of all patients with esophageal malignant strictures undergoing self-expandable metal stent (SEMS) placement with the Niti-S Esophageal covered stent, double anti-reflux in a community hospital (AZ St Maarten Mechelen, Belgium) between March 2013 and July 2021.

Results: In twenty-nine patients, thirty self-expandable metal stents (SEMS) were placed. The median dysphagia score before stent placement was 3 and 0 after stent placement ($p < 0.001$). Stent migration did not occur. Two patients (7%) had new onset reflux symptoms. The most common adverse event was retrosternal pain (5 patients, 17%). One patient (3%) had recurrent dysphagia due to proximal tumoral overgrowth and two patients (7%) because of proximal benign tissue overgrowth. There were no perforations, fistula formations or episodes of food impaction.

Conclusion: The Niti-S esophageal double covered, anti-reflux stent (Taewoong Medical, Seoul, Korea) is an effective and safe treatment option for malignant esophageal stenosis. (Acta gastroenterol. belg., **2022,** 85, **1-5**).

Keywords: ???

Introduction

Esophageal cancer is the number eight of the most common type of cancer worldwide. Although esophageal squamous cell carcinoma continues to be the most prevalent type worldwide, esophageal adenocarcinoma (EAC) is quickly becoming the most prevalent type in developed countries. EAC is thought to be related to Barrett's esophagus and typically occurs in the distal third of the esophagus and at the gastroesophageal junction. Esophageal cancer is rarely found before being advanced or metastasized; 40% of cases have already distant metastasis (1).

In a palliative setting dysphagia is an important cause of impairment of the quality of life and relieving dysphagia is the main goal of palliative care.

The aim of this study is to retrospectively evaluate the safety and clinical performance of the Niti-S Esophageal Covered stent (double anti-reflux type) in inoperable carcinoma of the esophagus or gastric cardia.

Patients and methods

Methods

This observational patient registry/post-market clinical follow-up study is designed to collect data on the clinical performance and the safety of the Niti-S Esophageal covered stent, double anti-reflux type.

A retrospective audit was performed in a community hospital (AZ St Maarten Mechelen, Belgium) between March 2013 and July 2021. All patients with esophageal malignant strictures undergoing SEMS placement with the Niti-S Esophageal covered stent, double anti-reflux type were reviewed. All these patients were inoperable because of metastatic spread, locally advanced disease, or the presence of severe medical comorbidities. We used a score for grading dysphagia modified from the score of Mellow and Pinkas (1): 0 = normal diet, 1 = able to eat some solid food, 2 = able to eat semi-solids only, 3 = able to swallow liquids only, 4 = complete dysphagia (2).

Data collection and statistical analysis

Clinical data were collected by reviewing the electronic patient files. Collected data included patient demographics, symptomatology, adverse events, pathological data and SEMS insertion details. Procedural success was defined as stent implantation on the desired site and full expansion within 3 days. Data were collected until death or 6 months post-procedure. The change of dysphagia score was analysed with the Wilcoxon signed-rank test using SPSS software.

The Niti-S Esophageal Covered stent (double anti-reflux type)

The Niti-S stent (Taewoong Medical, Seoul, Korea) is delivered in a compressed form inside an introducer sheath with a diameter of 18 or 20 F. The stent has a

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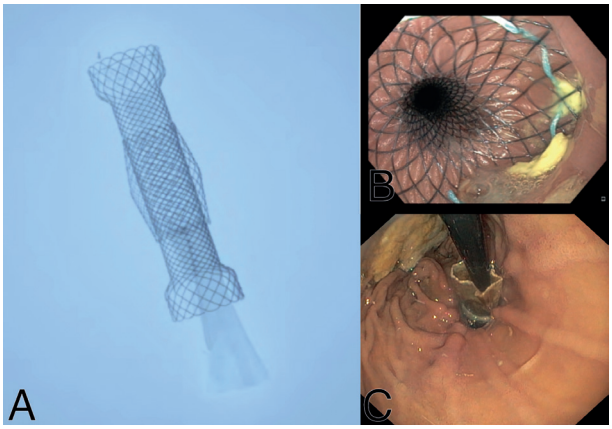

Figure 1. — A: The Niti-S stent, B: proximal end, C: distal end.

double layered design with a full silicone covering preventing tumour ingrowth and an additional uncovered outer nitinol mesh to resist migration. A polytetrafluoroethylene skirt blocks gastric reflux with the stent placed at the esophageal gastric junction. It has 4 radiopaque markers at both ends and 2 in the middle. A retrieval string at the proximal end helps to reposition if necessary (Fig. 1 A: the Niti-S stent, B: proximal end, C: distal end). The stents used in this registry had a body diameter of 18 or 20 mm and a length of 8, 10, 12 or 15 cm. The stent flares are 26 mm at its proximal and distal ends.

Insertion technique

Stents were initially inserted at the radiological unit or at the operating room using a mobile fluoroscopic system and subsequently, since October 2018, at the endoscopy unit equipped with Siemens Artis Zee multipurpose fixed angiography system and anaesthesiologic equipment.

Table 1. — **Clinical characteristics of 29 patients**

		numbers	**%**
Patients		29	
Niti-S stents		30	
Median age (range) - Y		75 (34-90)	
Gender	male	25	86
	female	4	14
Tumour histology	adenocarcinoma	21	70
	Squamous cell carcinoma	6	20
	extrinsic	3	10
Prior radiation and/or chemotherapy	chemotherapy	14	48
	Palliative radiation therapy	1	3
	Chemoradiation therapy	1	3

Patients were positioned in the left decubitus. If there was a clinical suspicion of aspiration risk (for instance stasis of food or liquids on previous endoscopy), patients were installed in the supine position and endotracheally intubated using crush induction to secure the airway.

Direct visualisation of the tumour was performed using Olympus adult gastroscopes. A metal guidewire (0.057'') with a floppy tip was placed along the entire tumour length reaching the stomach. Proximal and distal extents of the esophageal stricture were marked externally using skin surface markers. In case of an endoscopically inaccessable tumorous stricture, the residual lumen and the extents were visualised using contrast agent applied through a diagnostic ERCP catheter and using fluoroscopy.

Under fluoroscopic control, the SEMS were then inserted over the guidewire ensuring overlap of the radio-opaque markers within the stent delivery system and the skin markers. Subsequentially the SEMS was deployed under fluoroscopic and/or endoscopic control.

Results

Patients and stents

In twenty-nine patients, thirty self-expandable metal stents (SEMS) were placed using the Niti-S Esophageal covered stent, double anti-reflux type. The indication of stent placement was dysphagia. Clinical characteristics of the patients treated with the Niti-S stent are shown in Table 1.

All stents were positioned with the anti-reflux valve in the cardia. The diameter of the stents used were 18 or 20 mm and the length 120, 150 or 180 mm, depending on the size of the tumour.

SEMS insertion

Successful deployment and technical success were obtained in 29/30 stent placements (97%). In one patient (with extrinsic malignant compression) full expansion of the stent was not reached within 3 days. Seven (23%) SEMS were inserted in day care patients, 20 (66%) were inpatients (information not available in 3 patients).

Patient outcomes

The dysphagia score was available in 29 patients. The median dysphagia score before stent placement was 3 and 0 after stent placement ($p < 0.001$)(data collected until death or maximal 6 months post-procedure).

After stent placement 17 (59%) had a 0 score, 3 (10%) had a 1 score, 5 (17%) had a 2 score, 4 (14%) a 3 score and none had a 4 score. Mortality after stent placement is displayed in table 2. The cause of death was disease progression, no one died because of the stent placement. Five patients were alive during follow-up in December 2021 with last follow-up after stent placement at 9, 12,

Table 2. — **Mortality**

	numbers	%
0 - <1W	0	0
1 - <4 W	3	10
4 - <12 W	17	57
12 - <24 w	3	10
> 24 W	2	7
alive	5	17

Table 3. — **Adverse events**

	number	%
New reflux symptoms	2	7
Stent migration	0	0
Retrosternal pain > 48 h	5	17
Tumoral ingrowth	1	3
Proximal overgrowth	2	7
perforation	0	0
pneumonia	1	3
bleeding	4	13
fistula	0	0
Food impaction	0	0

15, 19 and 84 weeks. Adverse events are shown in table 3.

Two patients had new onset reflux symptoms. One patient developed pyrosis 4 weeks after stent placement and was treated with pantoprazole 40 mg twice a day with good result. The other patient developed 16 weeks after stent placement an oesophagitis grade D despite a good position and normal appearance of the anti-reflux valve (Fig. 2). Pantoprazole 2 × 40 mg a day was started but a peptic stenosis was formed at the proximal end under PPI treatment and a second covered stent was placed 24 weeks after the first stent placement. Nevertheless, a new peptic stenosis proximal of the second stent developed at 64 weeks after the first stent placement. The anti-reflux valve was noticed to have eroded. A new anti-reflux stent was placed (20 × 150 mm) with good result so far (patient is still alive, 84 W follow-up).

Stent migration did not occur.

The most common adverse event was retrosternal pain (5 patients, 17%), including one of the two patients with previous radiotherapy. One patient had esophageal spasm with a good response on nifedipine. The other patients were treated with analgesics.

One patient (3%) with a marked longitudinally extending tumour even before stenting, had recurrent dysphagia due to proximal tumoral overgrowth (Fig. 3), which could be solved by placing a second stent.

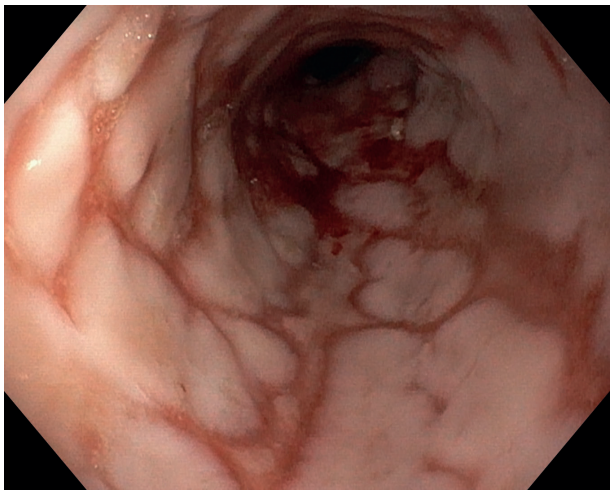

Figure 2. — Oesophagitis after stent placement.

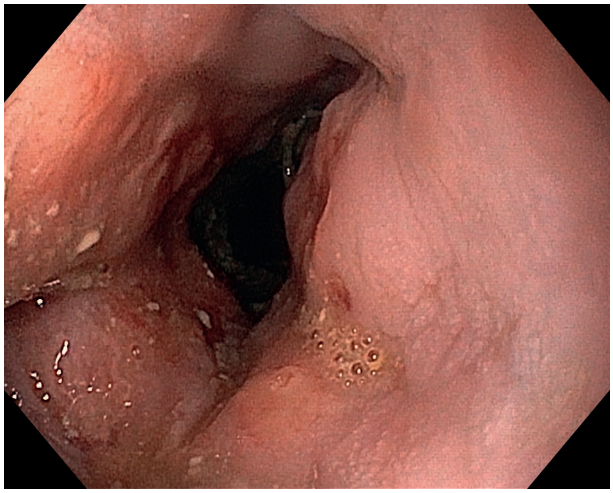

Figure 3. — Proximal tumoral overgrowth.

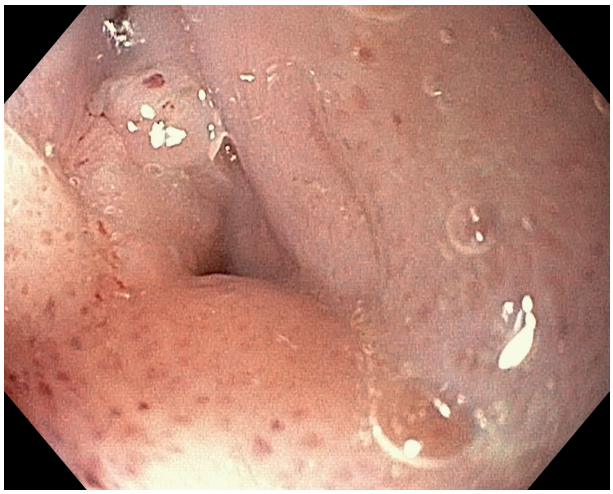

Figure 4. — Proximal benign tissue overgrowth.

Two patients (7%) had recurrent dysphagia at 12 weeks and 16 weeks post stenting because of proximal benign tissue overgrowth (Fig. 4) for which an additional fully covered stent was placed, bridging the stenosis.

The fully covered stent stayed in place during the further follow-up in one patient. In the second patient the fully covered stent dislocated and disappeared two months after placement with recurrent dysphagia; a new double layer (non- anti-reflux) stent was placed to bridge the proximal stenosis.

One patient developed pneumonia the day after the procedure, which was treated with amoxycillin-clavulanic acid with good result. Four patients went through a bleeding episode (13%): 1 patient at 1 week, 2 patients at 4 weeks and 1 patient at 24 weeks after placement. These bleedings were considered tumour related.

There were no perforations, fistula formations or episodes of food impaction.

Discussion

According to the current guidelines there are two therapeutic options to relieve dysphagia in inoperable esophageal carcinoma: the placement of a SEMS or brachytherapy (3).

SEMS insertion provides rapid palliation of dysphagia when compared to brachytherapy. This difference in efficacy diminishes gradually over time, and brachytherapy seems to provide better relief of dysphagia after 3 months of follow-up. Therefore, ESGE guidelines states that brachytherapy is a valid alternative for patients with a longer life expectancy (4,5). In the study of Homs, one should consider that 45 of the 101 patients allocated to brachytherapy also received a SEMS during follow-up for recurrent or persistent dysphagia. Moreover, brachytherapy has limited availability. In addition, it is difficult for an individual, non-operable patient to prospectively estimate the life expectancy in terms of months. Therefore, in our centre SEMS placement is mostly used with these indications.

In this retrospective review of 29 patients (30 stents), the Niti-S stent was effective to alleviate dysphagia; the median dysphagia score before stent placement was 3 and 0 after stent placement ($p < 0.001$). In total 25/29 (86%) patients could at least eat semi-solid food after stent placement. Recurrent dysphagia remains a concern after SEMS placement and can occur in a setting of stent migration, tumour overgrowth/ingrowth or tissue overgrowth. Stent migration is an important issue, which is more frequently observed when a stent is placed across the gastroesophageal junction. This is probably the case because the distal stent end projects freely in the gastric lumen. Therefore, it is not fixed to the gastric wall as it is the case in these series. Migration rates of fully covered stents are very high (to 36%), higher than those of partially covered stents (to 23%). Embedding of the uncovered stent ends leads to better fixation (6).

In this series no stent migrations were experienced (0%). The design of the Niti-S seems very effective to prevent migration. The stent flares to 26 mm at its ends but (probably more important) it has a double-layer configuration with a full silicone covering, preventing tumour ingrowth and an additional uncovered outer nitinol mesh to embed itself in the esophageal wall (Fig. 1). Very low stent migration rate with the Niti-S stent was also noticed by Verschuur et. al. (7).

Stent occlusion because of tissue ingrowth through the mesh or overgrowth at the stent ends is another cause of recurrent dysphagia.

Tumoral ingrowth through the mesh didn't occur in the series because of the full silicone covering of the inner layer. As a standard stenting technique, a wide segment of proximal normal mucosa was always covered using stents that were substantially longer than the malignant stricture. Using this method, only one patient (3%) with a marked longitudinally extending tumour even before stenting, had recurrent dysphagia due to proximal tumoral overgrowth (Fig. 3), which problem could be solved by placing a second stent.

Two patients (7%) had recurrent dysphagia because of proximal benign, reactive tissue overgrowth at week 12 and week 16 post stenting (Fig. 4). In these two patients an additional fully covered stent was placed, bridging the stenosis up to the present double layer stent. Non-malignant tissue overgrowth is mostly due to granulation tissue, comprising a richly vascularized connective tissue with new capillary formation, numerous fibroblasts and a myriad of other inflammatory cells. The risk increases with longer dwell times. Radial force, diameter of the stent and the material of the stent seem to be other factors causing reactive tissue overgrowth (8).

Depending on the stent type, reported numbers for recurrent dysphagia due to tissue overgrowth are 3% to 30% (6). A low rate (7%) of tissue overgrowth has been noted in this series, as it was also noted in the Niti-S study of Verschuur et. al.: 2 of 42 patients (5%) (7).

Stent placement across the gastroesophageal junction may lead to reflux of gastric contents. Anti-reflux SEMS can prevent this complication, but results are widely variable for different stent types (9). PPI therapy was not started as routine practice after stenting. With the anti-reflux valve only 2/29 patients (7%) developed new reflux symptoms, which is a satisfactory result. The first patient could be managed by PPI therapy. The second patient developed an oesophagitis grade D (Fig. 2) and thereafter a peptic stenosis, additional stenting was necessary as described above.

The most common adverse events in this series were retrosternal pain in 5 patients (17%), including one of the two patients with previous radiotherapy. The rate of retrosternal pain after stent placement seems to vary depending on the type of stent, varying from 3% to 31%. Increased expansion force and decreased flexibility of some stent types may play a part in this. As previous radiation and/or chemotherapy is associated with a higher risk of pain, reported pain rates can be subject of bias (6). One patient had esophageal spasm with a good response on nifedipine. The other patients were treated with analgesics including opiates.

A low threshold was maintained to perform stent placement under general anaesthesia with orotracheal intubation and crush induction. The procedure was scheduled after a few days nil per os if necessary (for example in case of known stasis of fluid or food on previous gastroscopy); in that way stent placement related aspiration pneumonia could be prevented in all but one patient.

Conclusion

The Niti-S esophageal double covered, anti-reflux stent (Taewoong Medical, Seoul, Korea) is an effective treatment option for malignant esophageal stenosis as 86% patients could at least eat semi-solid food after stent placement. Only 7% had new reflux symptoms and no patient had stent migration. The most common adverse events were retrosternal pain (17%). Three patients had recurrent dysphagia: one patient had proximal tumoral overgrowth (3%) and two patients proximal tissue overgrowth (7%). These three patients could successfully be managed with additional stenting.

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