

New Design Esophageal Stents for the Palliation of Dysphagia From Esophageal or Gastric Cardia Cancer: A Randomized Trial

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BACKGROUND & AIM: Stents are often used for the palliation of inoperable esophageal or gastric cardia cancer. One of the drawbacks of the currently used stents is the high percentage of recurrent dysphagia due to stent migration and tissue growth. New stents have been designed to overcome this unwanted sequela of stent placement. In the present study, we investigated whether results of stent placement could be improved with newer stent designs.

METHODS: Between June 2004 and May 2006, 125 patients with dysphagia from inoperable carcinoma of the esophagus or gastric cardia were randomized to placement of an Ultraflex stent (N = 42), Polyflex stent (N = 41), or Niti-S stent (N = 42). Patients were followed by scheduled telephone calls at 14 days after treatment, and then monthly for 6 months or until death. Technical and functional outcome, complications, recurrent dysphagia, and survival were analyzed with, χ^2 tests, Kaplan-Meier curves, and log-rank tests.

RESULTS: Stent placement was technically successful in all patients with an Ultraflex stent, in 34/41 (83%) patients with a Polyflex stent, and in 40/42 (95%) patients treated with a Niti-S stent ($P = 0.008$). Dysphagia score improved from a median of 3 (liquids only) to 1 (ability to eat some solid food) in all patients. There were no differences in complications among the three stent types. Recurrent dysphagia, caused by tissue in- or overgrowth, migration, or food obstruction, was significantly different between patients with an Ultraflex stent and patients with a Polyflex stent or Niti-S stent (22 [52%] vs 15 [37%] vs 13 [31%], $P = 0.03$). Stent migration occurred more frequently with Polyflex stents, whereas tissue in- or overgrowth was more frequently seen with Ultraflex stents, and to a lesser degree, Niti-S stents. No differences were found in survival (median survival: Ultraflex stent 132 days vs Polyflex stent 102 days vs Niti-S stent 159 days) among the three stent types.

CONCLUSIONS: All three stents are safe and offer adequate palliation of dysphagia from esophageal or gastric cardia cancer. Nonetheless, Polyflex stents seem the least preferable in this patient group, as placement of this device is technically demanding and associated with a high rate of stent migrations.

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INTRODUCTION

Despite recent advances in the curative treatment of esophageal and gastric cardia cancer (1), more than 50% of patients have inoperable disease at presentation. For these patients, palliative treatment to relieve progressive dysphagia is usually the only treatment option. Self-expanding metal stents are often used for the palliation of obstruction from inoperable esophageal or gastric cardia cancer (2). One of the drawbacks of the presently used stents is the high percentage of recurrent dysphagia due to stent migration and tissue growth. New stents have been designed to overcome this unwanted sequela of stent placement.

Two newly designed stents, the fully covered Polyflex stent (Rüsch AG, Kernen, Germany) and the Niti-S stent (Taewoong Medical, Seoul, Korea), were recently introduced with the specific objective to overcome the problem of recurrent dysphagia. The completely covered Polyflex stent is a silicone device with an encapsulated monofilament braid made of polyester (3). This material has been proposed to be able to reduce nontumoral tissue in- and overgrowth (4). The Niti-S stent combines two specific characteristics to reduce stent migration. First, the Niti-S stent flares to 26 mm at both ends. Second, it has a double layer configuration, consisting of an inner polyurethane layer over its

entire length and an outer uncovered nitinol wire tube to allow the mesh of the stent to embed itself in the esophageal wall (5).

The aim of this study was to compare the worldwide most commonly used Ultraflex stent with the newly designed Polyflex stent and Niti-S stent in patients with dysphagia from carcinoma of the esophagus or gastric cardia.

METHODS

Study Population

Between June 2004 and May 2006, 125 patients with dysphagia due to esophageal or gastric cardia cancer were randomized to treatment with an Ultraflex stent, Polyflex stent, or Niti-S stent (Fig. 1). Inclusion criteria included an inoperable malignant obstruction of the esophagus or gastric cardia, or recurrent dysphagia after prior radiation with curative or palliative intent for esophageal cancer. A tumor was considered inoperable if the patient had distant metastases or local tumor infiltration in neighboring organs (as defined by the TNM classification), and/or poor health because of concomitant disease. All patients gave written informed consent. Exclusion criteria were a tumor length of more than 13 cm, tumor growth within 2 cm of the upper esophageal sphincter, a fistula between the esophagus and respiratory tree, and previous metal stent placement. Patients who were unfit to undergo conscious sedation were also excluded. Stent placement was performed in two hospitals, the Erasmus MC University Medical Center Rotterdam, The Netherlands (N = 120) and the Istituto Clinico Humanitas, Milan, Italy (N = 5). The study was approved by the Institutional Review Board of both hospitals.

For randomization, patients were stratified for location of the tumor (esophagus or gastric cardia), radiation and/or chemotherapy prior to treatment, and center. Randomization was performed by the Trial Office of the Department of On-

cology, Erasmus MC Rotterdam, using a computer-generated allocation protocol.

Stents and Stent Placement Procedure

Patients were treated with an Ultraflex stent, Polyflex stent, or Niti-S stent (Fig. 1). The Ultraflex stent (Boston Scientific, Natick, MA) consists of a knitted nitinol wire tube and has a polyurethane layer, which covers the midsection of the stent extending to within 1.5 cm of either end of the stent. The stent has a proximal flare of 23 mm and a body diameter of 18 mm. It is available in three lengths: 10, 12, and 15 cm. The stent can be deployed gradually either from the proximal to distal end or *vice versa*. It is delivered in a compressed form inside an introducer sheath. The Polyflex stent (Rüsch AG, Kernen, Germany) is a silicone device with an encapsulated monofilament braid made of polyester. The meshes are completely covered by a silicone layer with a smooth inner surface and a more structured outer surface. The edges of the monofilaments are protected with silicone to avoid impaction and/or tissue damage at the proximal and distal ends. The stent has a proximal flare of 23 mm and a body diameter of 18 mm. It is available in three lengths: 9, 12, and 15 cm. The stent needs to be loaded in the introducer sheath prior to placement. This introduction device has a diameter of 13 mm. The Niti-S stent (Taewoong Medical, Seoul, Korea) has a double layer configuration over its entire length, consisting of an inner polyurethane layer over its complete length and an outer uncovered nitinol wire. The stent flares to 26 mm at its proximal and distal ends with a body diameter of 18 mm. It is available in three lengths: 9, 12, and 15 cm. The stent is delivered in a compressed form inside an introducer sheath.

During stent insertion, all patients were consciously sedated with midazolam (DormicumR, Roche Nederland BV, Mijdrecht, The Netherlands). If tumor obstruction did not allow passage of a standard endoscope, the tumor was either dilated to a maximum of 12 mm by a Savary-Miller Esophageal Dilator (Wilson-Cook Medical, Winston-Salem, NC) or, in most cases, the standard diameter (8.9 mm) endoscope (GIF-Q160; Olympus B.V., Zoeterwoude, The Netherlands) was changed for a small diameter (5.9 mm) endoscope (GIF-XP160; Olympus B.V.). The upper and lower tumor margins were marked with sclerotherapy needle-injected radiographic contrast material. The stents were advanced over a guide wire into the esophagus. During and following stent placement, deployment of the stent was endoscopically and radiographically assessed. A stent, which was 2–4 cm longer than the stricture, was chosen to allow for a 1–2 cm extension above and below the proximal and distal tumor shoulder. A proton pump inhibitor (PPI) was prescribed to all patients in whom the distal end of the stent was positioned across the gastroesophageal (GE) junction to prevent GE reflux after the procedure.

Study End Points

The primary outcome of the study was recurrent dysphagia. Secondary outcomes included technical and functional

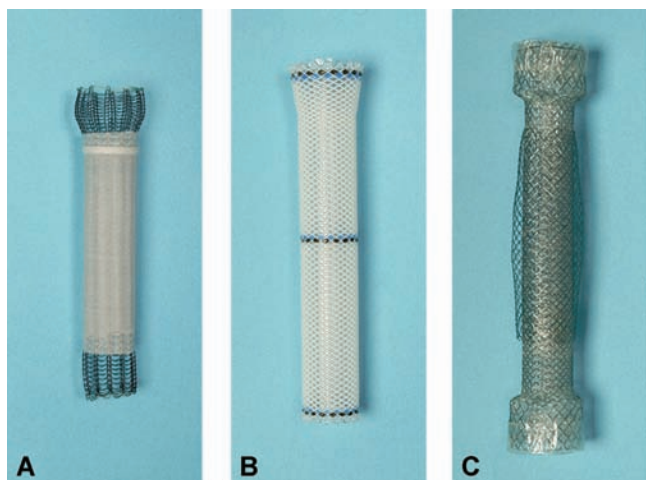


Figure 1. Stents that were used in this trial: Ultraflex stent (A), Polyflex stent (B), and Niti-S stent (C).

(dysphagia score, WHO performance score) outcome, complications, and survival.

Recurrent dysphagia was defined as occurrence of tissue in- or overgrowth, stent migration, and food obstruction. Technical outcome was defined as ease of placement of the stent at the desired location. Dysphagia was scored as: 0 = ability to eat a normal diet, 1 = ability to eat some solids, 2 = ability to eat some semisolids only, 3 = ability to swallow liquids only, 4 = complete dysphagia (6). Major complications were defined as life-threatening or severe complications, such as perforation, hemorrhage, fistula, aspiration-pneumonia, and severe pain, whereas minor complications were defined as not life-threatening or moderately severe complications, such as mild pain and GE reflux. Survival included 30-day mortality and long-term survival.

Follow-Up

Patients were evaluated before stent placement, at 14 days and 1 month after placement, and then monthly until death. For patients still alive at the end of the study (October 31, 2006), follow-up was at least 6 months. Evaluations were performed by scheduled telephone calls to patients, and included the following items: (a) ability to eat and/or swallow (dysphagia score); (b) general health as assessed by the WHO performance score (graded as: 0 = normal activity, 1 = symptoms but ambulatory, 2 = in bed less than 50% of time, 3 = in bed more than 50% of time, 4 = 100% bedridden); and (c) specific symptoms such as pain, heartburn, regurgitation, and weight loss. If indicated, for example, in case of complications or recurrent dysphagia, patients were seen for evaluation and treatment. All evaluation items were recorded in a case record form.

Statistics

We calculated that for the primary end point of the study, *i.e.*, a difference in recurrent dysphagia in favor of at least one of the newer stent designs (Polyflex stent or Niti-S stent), three groups of 39 patients each would be sufficient to detect a reduction in recurrence of dysphagia by at least 40% of that found with Ultraflex stents as was found in previous studies (3, 7, 8) (Ultraflex stent 40% vs Polyflex stent 21% vs Niti-S stent 12%), with a 2-sided $\alpha = 5\%$ and power of 80%.

All analyses were performed on an intention-to-treat basis. Patients were compared for the following baseline characteristics: age, gender, dysphagia score before stent placement, WHO performance score before treatment, tumor length, tumor location, histology, dilation before stent placement, and prior radiation and/or chemotherapy. Outcome included dysphagia score after stent placement, WHO performance score after placement, complications, recurrent dysphagia, and survival (30-day and long-term).

Results were expressed as mean \pm standard deviation (SD) and as median with interquartile range (IQR), if appropriate; long-term survival was expressed as median survival. The χ^2 test was used for categorical variables. Complica-

tions and recurrent dysphagia among the three groups were compared with Kaplan-Meier and log-rank tests to adjust for time of occurrence of the event and survival differences. The risk of developing complications or recurrent dysphagia was calculated using Cox regression analysis with prior radiation and/or chemotherapy and chemotherapy after stent placement as covariates. Dysphagia scores at 4 wk after stent placement were analyzed using covariance analysis with dysphagia score at baseline taken as covariate. Survival of the three groups was calculated and compared using Kaplan-Meier curves and the log-rank test. A *P* value < 0.05 was considered statistically significant. All analyses were conducted using SPSS version 11.5 (SPSS Inc., Chicago, IL).

RESULTS

Patient Characteristics

The patient groups were similar with respect to clinical characteristics (Table 1). In approximately 20% of patients, the malignant stricture was located in the gastric cardia, whereas in the other patients the tumor was located in the esophagus. Approximately one-third of the patients had undergone radiation and/or chemotherapy prior to stent placement. There were no differences in total stent length among the three patient groups; however, corrected for the part of the stent that was covered, Ultraflex stents were shorter ($P < 0.001$). In addition, no differences in total stent length to tumor length ratios were found among the three stent types ($P = 0.37$), whereas length of the covered part of the stent to length of the tumor ratios were also lower for Ultraflex stents ($P < 0.001$).

Recurrent Dysphagia

Recurrent dysphagia occurred more frequently in patients with an Ultraflex stent ($P = 0.03$), which was caused by tissue in- or overgrowth, stent migration, and/or food obstruction (Table 2). Tissue in- or overgrowth occurred more frequently with Ultraflex stents compared to Polyflex stents or Niti-S stents ($N = 13$ [31%] vs $N = 4$ [10%] vs $N = 10$ [24%], respectively), and was observed after a median of 79 days after stent placement. Tissue in- or overgrowth was in the majority of patients (24/27 [89%]) treated by placement of a second stent.

Stent migration occurred more frequently in patients with a Polyflex stent ($N = 12$ [29%]) (Fig. 2A) compared to Ultraflex stents ($N = 7$ [17%]) and Niti-S stents ($N = 5$ [12%]). In 5/12 patients with a Polyflex stent, the stent migrated proximally, and in 7/12 patients stent migration was distally. None of the Ultraflex stents and Niti-S stents migrated proximally. Stent migration was mainly treated with a second stent (15/24, 63%) or repositioning of the stent (4/24, 17%) (Fig. 2B). One patient developed abdominal pain after placement of a Niti-S stent. Repeat endoscopy did not reveal a stent in the esophagus and an additional X-ray showed that the stent had migrated to the small bowel. As the stent caused obstruction and

Table 1. Clinical Characteristics of 125 Patients Treated With an Ultraflex Stent, Polyflex Stent, or Niti-S Stent for Palliation of Dysphagia Due to Inoperable Carcinoma of the Esophagus or Gastric Cardia

	Ultraflex Stent N = 42	Polyflex Stent N = 41	Niti-S Stent N = 42
Age, years, mean ± SD	69 ± 13	70 ± 10	65 ± 12
Gender, no. of patients (%)			
Male	28 (67)	28 (68)	30 (71)
Female	14 (33)	13 (32)	12 (29)
Median dysphagia score before treatment (IQR*)	3 (1)	3 (0)	3 (0)
Median WHO performance score before treatment (IQR)	1 (2)	1 (2)	1 (2)
Tumor length, cm, mean ± SD	8.1 ± 3	7.5 ± 2	7.5 ± 3
Stent length, cm, mean ± SD			
Total	12 ± 2	11 ± 2	12 ± 2
Covered part only [†]	9 ± 2	11 ± 2	12 ± 2
Ratio stent /tumor length, cm ± SD			
Total	1.6 ± 0.4	1.6 ± 0.3	1.7 ± 0.7
Covered part only [†]	1.2 ± 0.3	1.6 ± 0.3	1.7 ± 0.7
Location of tumor, no. of patients (%)			
Esophagus	35 (83)	33 (81)	35 (83)
Mid-esophagus	12	7	10
Distal esophagus	23	26	25
Gastric cardia	7 (17)	8 (19)	7 (17)
Tumor histology, no. of patients (%)			
Adenocarcinoma	30 (73)	27 (66)	28 (68)
Squamous cell carcinoma	11 (27)	14 (34)	12 (30)
Other	0 (0)	0 (0)	1 (2)
Prior radiation and/or chemotherapy, no. of patients (%)			
Total	14 (33)	12 (29)	11 (26)
Chemotherapy	8 (19)	7 (17)	7 (17)
Radiation	3 (7)	0 (0)	1 (2)
Radiation and chemotherapy	3 (7)	5 (12)	3 (7)

*IQR = interquartile range; [†]P < 0.001.

could not be retrieved endoscopically with double-balloon enteroscopy, the stent was surgically removed. The patient received another stent type because of increasing dysphagia. At the end of the study, this patient was still alive. Stent migration was observed in 8/24 (3 with an Ultraflex stent, 1 with a Polyflex stent, and 4 with a Niti-S stent; P = 0.41)

patients who additionally received chemotherapy following stent placement. More patients with an Ultraflex stent underwent upper endoscopy for cleansing of the stent because of food obstruction than patients with a Polyflex stent or Niti-S stent (N = 10 [24%] vs N = 2 [5%] vs N = 1 [2%], respectively; P = 0.002). Additional statistical analysis showed no

Table 2. Recurrent Dysphagia in 125 Patients Given an Ultraflex Stent, Polyflex Stent, or Niti-S Stent for Palliation of Dysphagia Due to Inoperable Carcinoma of the Esophagus or Esophagogastric Junction

	Ultraflex Stent N = 42	Polyflex Stent N = 41	Niti-S Stent N = 42	P Value*
Recurrent dysphagia, total no. of patients (%)	33 in 22 pts (52)	18 in 15 pts (37)	17 in 13 pts (31)	0.03
	33 in 22 pts (52)	18 in 15 pts (37)		0.42
	33 in 22 pts (52)	18 in 15 pts (37)	17 in 13 pts (31)	<0.01
Tissue growth, no. of patients (%)			17 in 13 pts (31)	0.06
	15 in 13 pts (31)	4 in 4 pts (10)		0.09
	15 in 13 pts (31)	4 in 4 pts (10)		0.04
	15 in 13 pts (31)	4 in 4 pts (10)	11 in 10 pts (24)	0.16
Stent migration, no. of patients (%)			11 in 10 pts (24)	0.49
	7 in 7 pts (17)	12 in 12 pts (29)		0.01
	7 in 7 pts (17)	12 in 12 pts (29)	5 in 5 pts (12)	0.07
	7 in 7 pts (17)	12 in 12 pts (29)	5 in 5 pts (12)	0.39
Food obstruction, no. of patients (%)			5 in 5 pts (12)	<0.01
	11 in 10 pts (24)	2 in 2 pts (5)		<0.01
	11 in 10 pts (24)	2 in 2 pts (5)	1 in 1 pt (2)	0.04
	11 in 10 pts (24)	2 in 2 pts (5)	1 in 1 pt (2)	<0.01
		1 in 1 pt (2)	0.40	

*Log-rank test for time to first event of recurrent dysphagia.

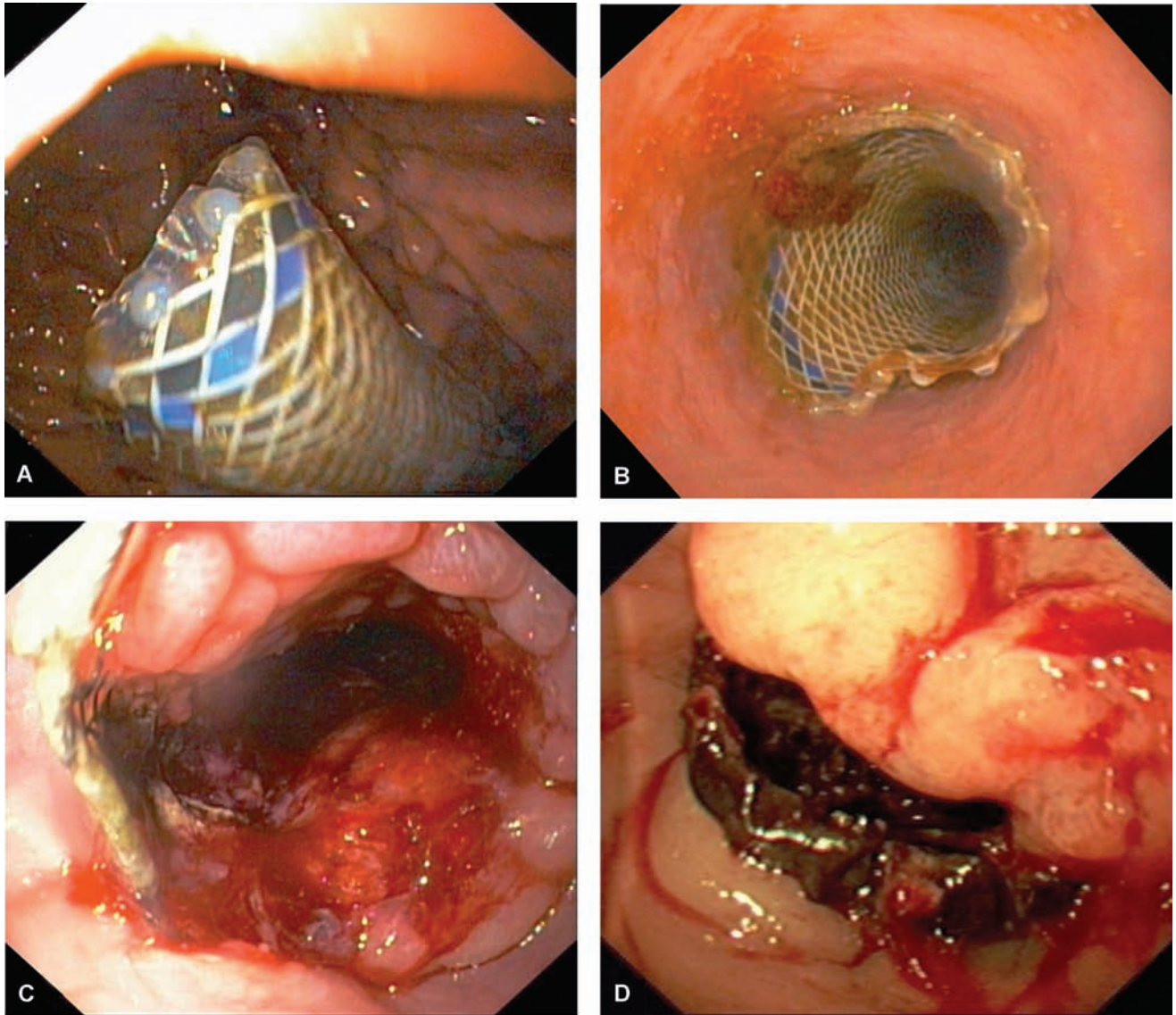


Figure 2. Stent migration with a Polyflex stent (A), which was endoscopically repositioned (B). Nontumoral tissue in- and overgrowth with an Ultraflex stent (C) and tumoral tissue overgrowth with a Niti-S stent (D).

association between food obstruction and tumor/tissue in- or overgrowth for each of the stent types.

Two months after stent placement, all patients were invited to undergo upper endoscopy to investigate whether evidence of tumoral or nontumoral tissue in- or overgrowth could be detected. In total, 33/125 patients (9 with an Ultraflex stent, 11 with a Polyflex stent, and 13 with a Niti-S stent) agreed. Twenty-seven patients refused to undergo upper endoscopy, whereas 26 patients were deemed unfit and 25 were already deceased at that time. In 15/33 (45%) patients (all three stents $N = 5$), evidence of tissue in- or overgrowth at the proximal end of the stents was observed. Three (20%) of these patients also had symptoms of dysphagia and a second but different type of stent was placed. Following additional stent placement, the dysphagia score improved. In all patients, biopsies were taken at the upper and lower end of the stent in case

tissue growth was observed. Nontumoral tissue in- or overgrowth was found in 3/6 (50%) patients with an Ultraflex stent (Fig. 2C), in 4/5 (80%) patients with a Polyflex stent, and in 3/4 (75%) patients with a Niti-S stent, whereas the remaining patients had tumoral tissue in- or overgrowth (Fig. 2D). None of the patients with nontumoral tissue in- or overgrowth was symptomatic.

Outcome and Survival

Stent placement was technically successful in all patients with an Ultraflex stent, in 34/41 (83%) patients with a Polyflex stent, and in 40/42 (95%) patients treated with a Niti-S stent ($P = 0.008$) (Table 3). Reasons for technical difficulties were too proximal (Polyflex stent $N = 4$) or too distal (Polyflex stent $N = 3$, Niti-S stent $N = 2$) stent placement as noticed immediately after the procedure. In six patients, the stent

Table 3. Outcome and Survival in 125 Patients Treated With an Ultraflex Stent, Polyflex Stent, or Niti-S Stent for Palliation of Dysphagia Due to Inoperable Carcinoma of the Esophagus or Gastric Cardia

	Ultraflex Stent N = 42	Polyflex Stent N = 41	Niti-S Stent N = 42	P Value
Technical success, no. of patients (%)	42 (100)	34 (83)	40 (95)	0.008
Dilation before treatment, no. of patients (%)	4 (10)	5 (12)	6 (14)	0.80
Median dysphagia score 4 wk after treatment (IQR*)	0 (1)	1 (2)	0 (1)	0.07
Median WHO performance score 4 wk after treatment (IQR)	1 (2)	1 (2)	1 (1)	0.31
Chemotherapy after treatment, no. of patients (%)	7 (17)	2 (5)	15 (36)	0.002
30-Day mortality, no. of patients (%)	2 (5)	7 (17)	2 (5)	0.07
Median survival in days	132	102	159	0.13
Still alive, no. of patients (%)	5 (12)	6 (15)	11 (26)	0.19
Cause of death, no. of patients (%)				0.49
Stent-related	1 (2)	2 (5)	–	
Tumor progression	35 (84)	33 (80)	30 (72)	
Not related to tumor	1 (2)	–	1 (2)	

*IQR = interquartile range.

was successfully repositioned with a grasping forceps. In two patients, the Polyflex stent was again loaded in the introducer sheath and placed, while in another patient randomized to a Polyflex stent, a second, but other, stent type was placed.

At 4 wk after stent placement, the dysphagia score had improved from a median of 3 (liquids only) to 1 (ability to eat some solid food) (Table 3). We found no significant differences in the degree of improvement among the three patient groups over 4 wk time ($P = 0.22$). At 4 wk, no differences in WHO performance score were observed ($P = 0.31$). Following stent placement, 24/125 (19%) patients, mainly with Niti-S stents ($N = 15$) or Ultraflex stents ($N = 7$), received additional palliative chemotherapy and were treated with cisplatin and paclitaxel (Table 3). After six courses of chemotherapy, the tumor was considered to be resectable in 5 patients and surgery with curative intent was performed.

Median survival was 132 days in patients with an Ultraflex stent, 102 days in those with a Polyflex stent, and 159 days

in those with a Niti-S stent ($P = 0.13$). Twenty-two of 125 (18%) patients were still alive at the end of follow-up of at least 6 months. The majority of deceased patients (98/103, 95%) died from tumor progression, whereas three patients, two with a Polyflex stent and one with an Ultraflex stent, died from stent-related complications (Table 3).

Complications

Complications occurred in 9 (21%) patients with an Ultraflex stent, in 10 (24%) with a Polyflex stent, and in 9 (21%) with a Niti-S stent (Table 4). Of the early (≤ 7 days) major complications, perforations were seen in two patients treated with a Polyflex stent. One of these patients died from septic complications. In the other patient, a palliative resection was performed because of ongoing leakage in spite of seemingly adequate stent placement. Late (> 7 days) major complications consisted predominantly of hemorrhage ($N = 11$). Hemorrhage occurred more frequently with Ultraflex stents ($N = 5$) and Polyflex stents ($N = 5$). Five patients with

Table 4. Complications in 125 Patients Treated With an Ultraflex Stent, Polyflex Stent, or Niti-S Stent for Palliation of Dysphagia Due to Inoperable Carcinoma of the Esophagus or Gastric Cardia

	No. of Patients (%)			P Value*
	Ultraflex Stent N = 42	Polyflex Stent N = 41	Niti-S Stent N = 42	
Total complications	12 in 9 pts (21)	11 in 10 pts (24)	10 in 9 pts (21)	0.89
Major complications	9 in 9 pts (21)	8 in 8 pts (20)	5 in 5 pts (12)	0.48
≤7 days				
Perforation	–	2	–	
Severe pain	1	–	2	
Fever	1	–	–	
Aspiration pneumonia	–	1	–	
Hemorrhage	–	–	1	
>7 days				
Hemorrhage	5	5	1	
Fistula	2	–	1	
Minor complications	3 in 3 pts (7)	3 in 3 pts (7)	5 in 4 pts (10)	0.94
Mild retrosternal pain	2	1	2	
Gastroesophageal reflux	1	2	3	

*Log-rank test for time to first complication.

hemorrhage were successfully treated with external beam radiation therapy (EBRT), and three patients required at least one blood transfusion. Three patients were treated with a combination of EBRT and blood transfusion, whereas one of these patients was additionally treated with endoscopic argon plasma coagulation. No patient died as a consequence of hemorrhage. Three patients, two with an Ultraflex stent and one with a Niti-S stent, developed an esophagorespiratory fistula, which was successfully sealed with a second stent in all patients. However, one of these patients died from progressive respiratory failure. Another patient, treated with a Polyflex stent, died from progressive respiratory failure following aspiration pneumonia.

Minor complications, mainly retrosternal pain and gastroesophageal reflux, were seen in 3 (7%) patients with an Ultraflex stent, in 3 (7%) with a Polyflex stent, and in 4 (10%) with a Niti-S stent (Table 4). The pain was stent-related in all patients and required treatment with analgesics, which was in most cases for a short (≤ 1 wk) period.

We performed a univariate analysis of patients previously treated with radiation and/or chemotherapy or subsequently treated with chemotherapy. This analysis showed that the occurrence of complications (hazard ratio [HR] 1.50, 95% CI 0.69–3.24) and recurrence of dysphagia (HR 1.57, 95% CI 0.86–2.86) were not associated with prior radiation and/or chemotherapy. In addition, complications (HR 0.53, 95% CI 0.18–1.55) and recurrent dysphagia (0.74, 95% CI 0.38–1.42) were also not associated with chemotherapy following stent placement.

DISCUSSION

In this randomized trial, we found that Ultraflex stents, Polyflex stents, and Niti-S stents were equally effective and safe for the palliation of dysphagia from inoperable or recurrent carcinoma of the esophagus or gastric cardia. Technical problems during stent placement were more frequently observed with Polyflex stents than with Ultraflex stents and Niti-S stents ($P = 0.008$). Recurrent dysphagia, however, occurred more frequently with Ultraflex stents than with the newer stent types ($P = 0.03$) (Table 2).

Stent placement was technically successful in the majority (116/125 [93%]) of patients (Table 3). Stents were, however, positioned too proximally or too distally in seven patients with a Polyflex stent and in two patients with a Niti-S stent, as became evident immediately after stent insertion. In the case of Polyflex stents, this was caused by uncontrollable stent deployment at its final stage, when the last 20–40% of the stent is released from the introduction catheter. At that stage, the stent tends to jump in an unpredictable way from the sheath (3, 9). We were successful in repositioning the stent in 8/9 patients, whereas in one patient an alternative stent type was placed.

Recurrent dysphagia was caused by tissue in- or overgrowth, stent migration, and food obstruction (Table 2). Tis-

sue in- or overgrowth at the stent end can be due to nonmalignant hyperplastic tissue growth (Fig. 2C) or progressive tumor growth (Fig. 2D). It has been demonstrated that tissue overgrowth from nonmalignant obstructive tissue is more likely to occur in patients with a prolonged survival. Mayoral *et al.* (4) showed the presence of nontumoral tissue at the ends of different types of partially and fully covered stents in 32% of patients after a mean interval of 22 wk. In our study, tissue in- or overgrowth was observed in 16/33 (48%) patients who had undergone a scheduled upper endoscopy for this indication 2 months after stent placement. Only three of these patients had symptoms of recurrent dysphagia. Biopsies confirmed in 10/16 (62%) patients the presence of nontumoral tissue in- or overgrowth. Symptomatic tissue in- or overgrowth occurred more frequently with Ultraflex stents (31%) and Niti-S stents (24%) compared to Polyflex stents (10%) (Table 2). This is not clearly different from the rather large range of reported tissue in- or overgrowth rates observed in other studies, varying from 3–31% (4, 7, 10, 11). Although not shown by the 2-month biopsy results in our study, which showed an equal distribution of tumoral and nontumoral tissue in- or overgrowth among the different stents types, it might well be that the material of the Polyflex stent, made of polyester and silicone, is able to prevent hyperplastic tissue formation in the long-term, in contrast to the nitinol braiding of both the Ultraflex stent and Niti-S stent. Another explanation for the observed differences could be that both stent ends of the Ultraflex stent are uncovered over a distance of 1.5 cm, allowing tissue to project into the esophageal lumen. Moreover, the ratio between the covered part of the stent and the total tumor length was shorter for Ultraflex stents than for Polyflex stents and Niti-S stents in this study (Table 1). This latter factor may additionally have contributed to the occurrence of tumoral tissue in- or overgrowth with Ultraflex stents. We therefore suggest that, if partially covered stents are used, the choice for stent length should also be determined by the length of the covered part of the stent.

Stent migration is still a frequently occurring problem, particularly for distally located tumors (12). This cause of recurrent dysphagia was most frequently seen with Polyflex stents (29%) (Fig. 2A and B) compared to Ultraflex stents (17%) and Niti-S stents (12%) (Table 2). The design of the stent is probably important in reducing stent migration. The Ultraflex stent has uncovered proximal and distal segments, which, as has been stated previously, allows the normal mucosa above and below the tumor to project into the stent lumen. In the Dutch SIREC study, a similar stent migration rate was found with Ultraflex stents, *i.e.*, 17% (18/108 patients) (7). The Niti-S stent was specifically designed to reduce, if not eliminate, stent migration with the combination of a flare to 26 mm at both ends and an outer uncovered nitinol wire over a polyurethane layer for embedment in the esophageal wall. In a previous case series, stent migration was observed in 3/42 (7%) patients treated with a Niti-S stent (8). The relatively high migration rate of the Polyflex stent was not surprising, because the Polyflex stent is completely covered by a

relatively smooth silicone membrane. Nonetheless, reported results for migration with Polyflex stents are conflicting. In a study by Dormann *et al.* (3), migration was observed in only 6% (2/33) of patients with malignant dysphagia. In contrast, in a study from Rome, a comparable migration rate of 25% (4/16) was found (13).

For food obstruction of the stent, endoscopic cleansing was an effective treatment. Although both food obstruction and tissue in- or overgrowth occurred more frequently with Ultraflex stents (24%) than with Polyflex stents (5%) and Niti-S stents (2%), no association was found between these two causes of recurrent dysphagia. Prevention is important and consists of providing clear eating instructions to patients, specifically with regard to thorough chewing of food and drinking effervescent drinks between bites and after meals to flush the stent. Although all patients received a brochure with instructions on eating, food obstruction still occurred in 13/125 (10%) patients.

Complications were observed in 28/125 (22%) patients with no differences among patients treated with an Ultraflex stent, Polyflex stent, or Niti-S stent (Table 4). Perforation occurred in two patients during introduction of a Polyflex stent, resulting in the death of one patient, and surgery in the other patient. These perforations may have been caused by the size of the introduction system. The applicator, in which the stent is loaded prior to stent placement, has a diameter of 13 mm and is rather rigid. In addition, the stent seems to be less suitable for angulated strictures because the distal dilator is rather short. The inappropriate forced transmission of such an introduction sheath may complicate its passage across such strictures. A common late complication was the occurrence of late hemorrhage. This was also previously seen in the SIREC study (7). Hemorrhage in that study was observed in 14/108 (13%) patients treated with a stent, but only in 5/101 (5%) patients treated with brachytherapy ($P = 0.05$). Whether the radiation effect of brachytherapy had a protective effect on bleeding from the tumor through tumor reduction or a hemostatic effect on the tumor vasculature or the expanding force of a stent increased bleeding risk remained unclear. Although some studies have suggested that an increased risk of complications is associated with previous radiation and/or chemotherapy (14), this could not be confirmed in the current study, nor in other series (15–17).

The present study demonstrates that all three stents are safe and offer the same degree of palliation at the same level of safety in patients with inoperable or recurrent carcinoma of the esophagus or gastric cardia. We previously found that brachytherapy was favorable over (Ultraflex) stent placement with regard to long-term relief of dysphagia and the occurrence of fewer complications (7). The presently available new-generation stents probably offer no improvement for these two effects. Based on our findings, we conclude that Polyflex stents seem the least preferable in this patient group, as placement of this device is technically demanding and associated with a high rate of stent migration. We recommend the use of Niti-S stents or Ultraflex stents that are long enough

to cover the full tumor length in patients with dysphagia from esophageal or gastric cardia cancer, particularly in patients with a calculated life expectancy of less than 3 months (18).

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STUDY HIGHLIGHTS

What Is Current Knowledge

- Stents are often used for the palliation of dysphagia from inoperable esophageal or gastric cardia cancer.
- One of the drawbacks of the currently used stents is the high percentage of recurrent dysphagia due to stent migration and tissue growth.
- There is a need to improve results of stent placement by introducing new stent designs that should overcome the problems encountered with the older generation metal stents.

What Is New Here

- Two newly designed stents, the fully covered Polyflex stent and the Niti-S stent, were recently introduced with the specific objective to overcome the problem of recurrent dysphagia.
- Results from a randomized trial of 125 patients who received an Ultraflex stent ($N = 42$), a Polyflex stent ($N = 41$), or a Niti-S stent ($N = 42$) for malignant dysphagia demonstrate that all three stents are safe and offer the same degree of palliation at the same level of safety in patients with inoperable carcinoma of the esophagus or gastric cardia.
- Recurrent dysphagia, particularly related to stent migration (Niti-S stent) and tissue in- or overgrowth (Polyflex stent), was less frequently observed during follow-up with these new devices.

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CONFLICT OF INTEREST

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