Low morbidity after palliation of obstructing gastro-oesophageal adenocarcinoma to restore swallowing function

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ABSTRACT

INTRODUCTION: This study describes the procedure-related complications and survival after deployment of self-expanding metal stents (SEMS) or use of argon plasma coagulation (APC) in patients with obstructing gastro-oesophageal junction (GEJ) adenocarcinoma.

MATERIAL AND METHODS: During an 8-year period, 312 patients with non-resectable, obstructing adenocarcinoma at the GEJ were treated with SEMS and/or APC and thereafter followed with endoscopies.

RESULTS: A total of 707 procedures (246 SEMS procedures and 461 ablations) were performed. No patients died in relation to the procedures. Minor bleeding during APC was seen in 20 patients. Early complications to SEMS were migration and misplacement. A single perforation with the guide-wire was seen. Late complications were tumour overgrowth and food impaction. A single treatment with SEMS or APC was performed in 115 (37%) and 49(16%) patients, respectively. SEMS replacement was necessary in 17 (5%) patients. Repeated APC treatments were necessary in 57 (18%) patients. The median time of survival in patients treated with SEMS, APC or both procedures was 134 days, 114 days and 215 days (p = 0.004), respectively. The survival in patients palliated with SEMS and/or APC alone was significantly lower compared to those who were palliated with SEMS and/or APC in combination with chemoradiotherapy. The median time of survival was 120 days in SEMS and 203 days in APC patients (p = 0.05).

CONCLUSION: SEMS and APC are safe treatment options for restoration of the swallowing function in patients with obstructing GEJ adenocarcinoma. SEMS or APC are equivalent treatment modalities in terms of survival.

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Surgical resection is the primary treatment for malignant tumours in oesophagus and at the gastro-oesophageal junction (GEJ). However, more than 50% of the patients have reached a non-resectable stage at the time of presentation [1]. The vast majority of these patients will require palliative intervention to diminish dysphagia and restore the ability to swallow, either at the time of presentation or later as the tumour expands and obstructs the oesophageal lumen.

In patients with malignant tumour stenosis, the use of self-expanding metal stents (SEMS), argon plasma coagulation (APC) or brachytherapy has become the treatment of choice, often in combination with palliative chemoradiation [2]. In APC, a jet of ionised argon is conducted as high-frequency electrical energy of uniform intensity to the target area. Tumour tissue is thereby resected or vaporized and superficial oozing stopped [3]. The APC destroys tissue to a depth of approximately 1-2 mm.

The purpose of this retrospectively designed study was to present the procedure-related complications of deployment of SEMS or the use of APC in patients with obstructing GEJ adenocarcinoma. Furthermore, the aim was to investigate whether there was any difference in survival between patients palliated with SEMS or APC alone or in combination with chemotherapy or chemoradiation.

MATERIAL AND METHODS

From 1 January 2003 to 31 December 2010, all patients referred to our institution with biopsy-verified adenocarcinoma in the oesophagus or at the GEJ with symptoms of obstruction requiring palliative treatment with SEMS and/or APC were prospectively registered in a separate database and data were retrospectively analysed. Symptoms of obstruction were defined as either complete inability to sink or ability to sink fluid only. All patients were at a non-resectable stage either because of metastatic disease or because of T4 tumour as evaluated by computed tomography, gastroscopy and/or endoscopic ultrasound. A small number of the patients were at a resectable stage, but did not undergo surgery due to their advanced age, severe co-morbidity or on the patient's own request.

The following data were retrieved at first visit: Age, gender, tumour-node-metastasis (TNM)-stage, date of stent deployment and/or date of APC, type of SEMS, early complications (within 48 hours) and late complications (> 48 hours). Finally, information regarding treatment with palliative chemotherapy or chemoradiation was collected.

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TABLE 1

Patient characteristics, tumour-node-metastasis-stage and palliative oncological therapy.

	SEMS (n = 134)	APC (n = 106)	SEMS + APC (n = 72)	p-value	Oncological therapy and SEMS or APC (n = 144)	SEMS/APC alone (n = 168)	p-value
Males/females, n	99/35	86/20	58/14	0.33	117/27	126/42	0.19
Age, years, mean ± SD	68 ± 12	71 ± 12	70 ± 13	0.15	66 ± 11	73 ± 12	< 0.0001
T-stage, n				0.09			< 0.0001
T2	10	5	5		13	7	
T3	76	48	44		91	77	
T4	27	26	7		32	28	
Unknown	21	27	16		8	56	
N-stage, n				0.35			< 0.0001
N0	16	15	11		16	26	
N1	91	59	45		115	80	
Unknown	27	32	16		13	62	
M-stage, n				0.23			< 0.0001
M0	59	38	34		71	60	
M1	45	33	17		53	42	
Unknown	30	35	21		20	66	
Oncological therapy, n				0.54			
Chemotherapy	31	13	14		–	–	
Chemoradiation	39	26	21		–	–	

APC = argon plasma coagulation; M = metastasis; N = node; SD = standard deviation; SEMS = self-expanding metal stents; T = tumour.

TABLE 2

Numbers of early and late complications to argon plasma coagulation or self-expanding metal stents deployment and the type of stent used.

	SEMS (n = 246)	APC (n = 461)
Early complications ≤ 48 hours		
Bleeding	2	20
Perforation	1	0
Misplacement	1	–
Migration	1	–
Late complications > 48 hours		
Overgrowth	25	–
Food impaction	11	–
Migration	8	–
Material failure	5	–
Ingrowth	3	–
Stent type		
Ultra flex	134	–
Choo	43	–
Hanaro	19	–
Niti	2	–
Data not available	8	–

APC = argon plasma coagulation; SEMS = self-expanding metal stents.

All patients were referred to the hospital's oncological centre. Patients with good performance (performance status 0-2) and normal kidney and liver function were offered chemotherapy or chemoradiation.

Argon plasma coagulation and stenting procedures

During gastroscopy it was evaluated whether the tumour was passable. APC was performed if the scope could pass through the tumour since the deployment of SEMS in these cases may cause the stent to migrate into the stomach.

APC was performed with a flexible argon gas coagulation probe (Erbe, Elektromedizin GmbH) through the gastroscope and at a power setting at 60 watt, all visible tumour tissue was ablated. A subsequent chest X-ray was performed to exclude perforation of the oesophagus during the APC procedure. If the tumour was non-passable, a SEMS was deployed.

Before metal stent deployment, the extent of the tumour stenosis was evaluated. Fluoroscopy was used and the proximal and distal margins of the tumour were marked with a radiopaque contrast and a tissue clip, respectively. A guide-wire was introduced through the gastroscope and through the stenosis. Hereafter the scope was removed. Under fluoroscopic control, the stent catheter was advanced over the wire through the tumour stenosis. Chest X-ray to verify stent expansion was performed on the following day. Patients were discharged if they were able to swallow solid food and chest X-ray showed no signs of perforation and if no bleeding was observed.

Both procedures were performed with the patient in left lateral position under conscious sedation with midazolam and morphine.

Follow-up

A follow-up gastroscopy was scheduled four weeks later or earlier if severe dysphagia emerged.

The dates of new stent deployment and/or dates of renewed APC and data on the number of treatments, early complications (within 48 hours) and late complications (> 48 hours) were retrieved from the follow-up visits. All patients were followed until death. Finally, the date of death was collected from the CPR registry.

Statistical analyses

The survival was estimated using the Kaplan-Meier method, and log rank test was used to evaluate the statistical significance of the differences. The censoring date for survival was 1 December 2011.

A two-sided p-value < 0.05 was accepted as statistically significant. The SPSS statistical package (version 18.0; SPSS inc., Chicago, IL) was used for all analyses.

The Danish Data Protection Agency approved the processing of data (2001-41-1452).

Trial registration: not relevant.

RESULTS

During the eight-year period, 707 procedures (246 SEMS deployments and 461 ablations) were performed in 312 patients with obstructing oesophageal or GEJ adenocarcinoma who underwent gastroscopic therapy with APC (244 ablations), SEMS deployment (153 procedures) or both procedures (93 SEMS procedures and 217 APC therapies). The patient characteristics, TNM-stage and palliative chemotherapy or chemoradiation are shown in **Table 1**.

The complications to APC or stent deployment are shown in **Table 2**. In the majority of the patients, the procedures were uneventful and well tolerated. No patients died in relation to the procedures.

One perforation of the oesophagus occurred during introduction of the guide-wire through the tumour, but the SEMS was deployed after replacement of the wire. The patient had an uneventful post-operative period and lived for 351 days.

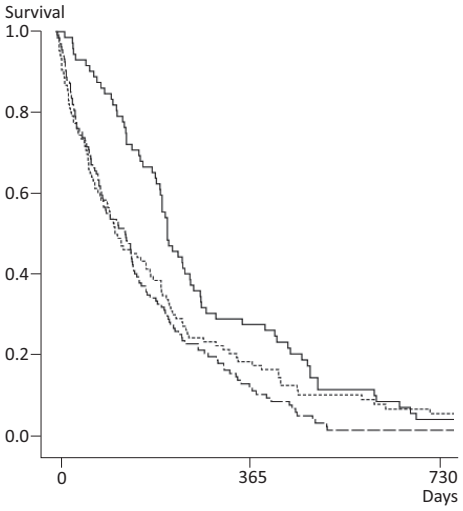
A single treatment with SEMS was performed in 115 (37%) of the patients, and a single aragon plasma ablation was sufficient in 49 (16%) patients.

Repeated stent placement was necessary in 17 (5%) patients (14 patients required two stents, two patients required three stents and a one patient required four stents). In nine (3%) patients re-stent deployment was necessary due to migration, and in five (2%) cases re-stenting was performed due to material failure (broken stent).

Repeated APC treatments were necessary in 57 (18%) patients (2-10 ablations).

The median time to re-stenting or repeated APC therapy was 179 days (range: 1-651 days) and 41 days (1-345 days), respectively.

FIGURE 1



Survival of patients treated with self-expanding metal stents (n = 134), argon plasma coagulation (n = 106) or both procedures (n = 72) (p = 0.004).

Numbers at risk

Days after treatment	0	180	365	540	730
APC + SEMS	72	47	20	8	3
APC	106	42	19	9	5
SEMS	134	46	14	2	2

APC = argon plasma coagulation; SEMS = self-expanding metal stents.

SEMS + APC APC SEMS

During APC, 20 patients experienced minor bleeding from the tumour in relation to the procedure. None of these patients required repeated endoscopy. The most common late complications to the SEMS were tumour overgrowth and food impaction.

Figure 1 shows the survival of patients treated with SEMS alone, APC alone or both procedures. At the censoring date, all patients were dead. The median time of survival was 134 days (confidence interval (CI): 95-173 days) for SEMS, 114 days (69-159 days) for APC and 215 days (183-247days) (p = 0.004) for both procedures. No significant differences in age, sex, TNM-stage, use of palliative chemotherapy or chemoradiation were seen between the groups (Table 1).

Palliative chemotherapy or chemoradiation were given to 132 (42%) patients. The treatment consisted of a combination of xeloda, carboplatin and taxotere as mono-therapy or in combination with radiation.

The survival in patients palliated with SEMS and/or APC alone was significantly lower than that of those who were palliated with SEMS and/or APC in combination with palliative chemotherapy or chemoradiation (**Figure 2**). The median time of survival was 120 days (CI: 97-143 days) and 203 days (CI: 174-232 days) (p = 0.05), respectively. Patients who were considered candidates for oncological therapy were generally younger, but had reached a more advanced T-stage and N-stage than the patients who received SEMS or APC alone (Table 1).

DISCUSSION

The incidence of adenocarcinoma at the GEJ is increasing. At the time of presentation, more than half of the patients have advance-staged disease and the demand for palliation procedures will therefore increase in the future [1]. Restoring the ability to swallow not only impacts the patient's general performance status through weight gain which might enable palliative chemoradiotherapy, but also increases the patient's remaining life-quality [4].

In general, studies dealing with APC as palliative therapy in patients with obstructive gastro-oesophageal cancer are scarce. Studies of ablation therapy mainly concern the yttrium-aluminum-garnet (YAG)-laser technique and were published in the early 1990s.

Our results demonstrate that palliation of obstructing GEJ adenocarcinoma with either APC and/or SEMS is a safe procedure for recovery of the ability to swallow.

Self-limiting bleeding (oozing from the tumour) was the only complication to APC.

The overall early complication rate to SEMS deployment is acceptable with only a single perforation as a major event. Tumour overgrowth and food impaction were the most common late complications also seen in similar reports on stenting procedures. Overgrowth, reported in 2-30% of the patients receiving a SEMS, may also be the result of epithelial hyperplasia and not tumour expansion alone [5-8].

Since we only deploy a SEMS if the tumour is not passable, only 8% experienced stent migration although nearly all stents were of the covered type. The frequency of stent migration is reported to range from 0% to 32% and the highest rates are observed in stents placed across the GEJ [9, 10].

In half of the patients, palliation with a single procedure with either SEMS or APC was necessary to restore the swallowing function. However, as the tumour gradually expands, tumour overgrowth in relation to the SEMS will eventually require APC. Similarly, patients treated with repeated argon plasma ablations may eventually end up requiring a SEMS when APC gets increasingly difficult. Thus, the longer survival observed in patients treated with either procedure reflects the repeated demand for tumour obstruction control due to longer survival in general, rather than a survival benefit triggered by APC in particular.

Only a few studies have investigated the effect of argon plasma ablation therapy versus stenting.

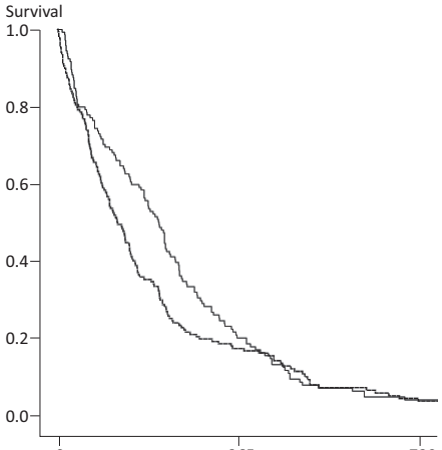
A large, randomised trial comparing three different SEMS types and non-stent treatment (ablasive therapies, intraluminal brachytherapy, etc.) found a significant survival advantage over patients who received a stent [11]. These findings were supported by Dallal et al who randomised 65 patients with oesophageal carcinoma to either thermal ablation or SEMS. Improved survival was seen in patients palliated by thermal ablative therapies when compared with SEMS [12]. In our material, the survival of patients who underwent APC did not differ significantly from that of those who were palliated with a SEMS.

The main disadvantage of APC, however, is the need to repeat the treatment which may be strenuous and tiring for weak, elderly patients. In our study, the median time to re-APC was 41 days. Unlike ablation therapy, SEMS leads to effective and lasting dysphagia relief, often in a single treatment session. However, patients undergoing SEMS deployment may experience post-treatment pain which is reported to be expected in 10-60% of the patients and possibly linked to the SEMS diameter [13-15]. Hence, SEMS may be a good choice in patients with a relatively short life expectancy. On the other hand, the treatment cost of a covered SEMS is 1,470 US$ whereas that of an argon coagulation probe is 260 US$.

In the present study, patients who received palliative chemotherapy or chemoradiation in addition to SEMS or APC had a longer median survival than those who were palliated with SEMS or APC alone. But this effect was temporary and after approximately one year, a "catch up" effect was seen and the survival curves merged. However, patients were selected for oncological therapy based on their physical performance and age. Thus, the observed survival benefit might depend

FIGURE 2

Survival of patients treated with self-expanding metal stents or argon plasma coagulation alone (n = 168) and patients treated with self-expanding metal stents or argon plasma coagulation in combination with palliative chemotherapy or chemoradiation (n = 144) (p = 0.05).



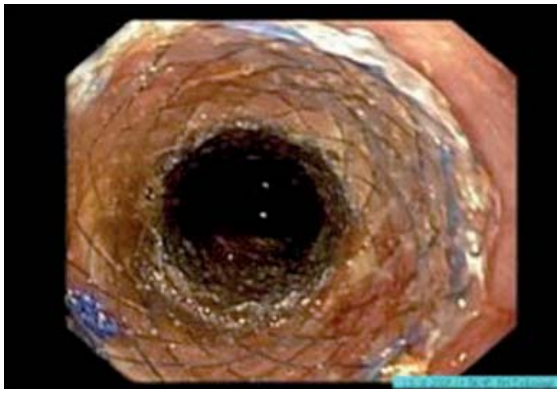
Numbers at risk

Days after treatment	0	180	365	540	730
APC + SEMS	168	59	28	10	5
APC + SEMS and palliative chemotherapy or chemoradiation	144	80	26	9	5

APC = argon plasma coagulation; SEMS = self-expanding metal stents.

SEMS or APC alone

SEMS or APC and palliative chemotherapy or chemoradiation



Self-expanding metal stent placed through tumour stenosis in the oesophagus.

on selection bias rather than being an effect of the oncological treatment. Interestingly, despite the better performance of these patients, their long-term survival (beyond one year) was almost the same.

Burstow et al reported a median survival of 153 days versus 72 days after SEMS and adjuvant therapy compared with SEMS alone in a study with 126 patients [16]. We have not found any published data on survival after APC.A drawback in the present study is the lack of dysphagia scores pre- and post procedure. Such scores would standardize the improvement in ability to swallow and facilitate comparison of the effect of SEMS and APC. Previous studies have shown an improvement in dysphagia score in 88% of patients with malignant dysphagia undergoing APC, of whom 66% had a normal diet following ablation though APC was used in combination with dilatation in some patients [17-19].

We conclude that SEMS and APC are safe treatment options for restoration of the swallowing function in patients with obstructing gastro-oesophageal adenocarcinoma. If the tumour is passable with the gastroscope, we recommend ablation by APC; otherwise, a SEMS is the treatment of choice. Stent obstruction by overgrowth may be treated with repeated APC ablations.

Regarding survival, SEMS or APC are equivalent treatment modalities. Temporary addition of palliative chemotherapy or chemoradiation increases survival.

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CONFLICTS OF INTEREST: none

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