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# Self-Expanding Covered Metallic Stent as a Bridge to Surgery in Esophageal Cancer: Impact on Oncologic Outcomes



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- BACKGROUND:** Self-expanding metallic stents (SEMSs) have been used as a bridge to surgery, relieving dysphagia and maintaining nutrition, in patients with operable but obstructive esophageal cancer (EC). However, the impact of SEMSs on oncologic outcomes is unknown. The aim of this study was to evaluate the impact of SEMS insertion before EC surgery on oncologic outcomes.
- STUDY DESIGN:** From 2000 to 2010, two thousand nine hundred and forty-four patients who underwent an operation for EC with a curative intent were included in a multicenter European cohort. Through propensity score analysis, patients who underwent SEMS insertion (SEMS group,  $n = 38$ ) were matched 1:4 to control patients who did not undergo SEMS insertion (control group,  $n = 152$ ).
- RESULTS:** The SEMS and control groups were comparable according to age, sex, tumor location, clinical stage, American Society of Anesthesiologists score, dysphagia, malnutrition, neoadjuvant treatment administration, histology, and surgical procedure. Self-expanding metallic stent insertion was complicated by tumoral perforation in 2 patients. The in-hospital postoperative mortality and morbidity rates for the SEMS vs control groups were 13.2% vs 8.6% ( $p = 0.370$ ) and 63.2% vs 59.2% ( $p = 0.658$ ), respectively. The R0 resection rate (71.0% vs 85.5%;  $p = 0.041$ ), median time to recurrence (6.5 vs 9.0 months;  $p = 0.040$ ), and 3-year overall survival (25% vs 44%;  $p = 0.023$ ) were significantly reduced in the SEMS group, and the 3-year locoregional recurrence rate was increased (62% vs 34%;  $p = 0.049$ ). The results remained significant after excluding SEMS-related esophageal perforations. After adjusting for confounding factors, SEMS insertion was a predictor of poor prognosis (hazard ratio = 1.6;  $p = 0.038$ ).
- CONCLUSIONS:** Self-expanding metallic stent insertion, as a bridge to surgery, has a negative impact on oncologic outcomes in EC. [Clinicaltrials.gov](http://dx.doi.org/10.1016/j.jamcollsurg.2014.11.028) ID: NCT 01927016. (J Am Coll Surg 2015;220:287–296. © 2015 by the American College of Surgeons)
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**Disclosure Information:** Nothing to disclose.

Disclosures outside the scope of this work: Dr Mariette is a consultant and receives payment for lectures for Nestlé, has grants from Nestlé and Merck, is paid for manuscript preparation by Lifecell, and is paid for developing educational presentations by Sanofi, Takeda, Nestlé, and Lifecell. Dr Lefevre received payment for lectures for Vifa-Pharma and expenses for meetings by Sanofi and Eumedica.

The FREGAT (French Eso-Gastric Tumors) working group—FRENCH (Fédération de Recherche en Chirurgie)—AFC (Association Française de Chirurgie) collaborators are listed in [Appendix 1](#).

Presented at the European Surgical Association meeting in Athens, Greece, May 2014 and at the French Congress of Digestive Surgery SFCD-ACHBT, Paris, France, December 2013.

Received August 19, 2014; Accepted November 21, 2014.

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Esophageal cancer (EC) patients commonly present with substantial dysphagia and malnutrition because they often have advanced tumors at the time of diagnosis.<sup>1</sup> Malnutrition during multimodal therapy can lead to treatment delays, higher morbidity and mortality, poorer treatment response, and a compromised long-term prognosis.<sup>2</sup> There are several options for ensuring adequate caloric intake in malnourished EC patients, all of which have potential drawbacks. Gastrostomy placement can compromise the stomach before surgery and expose patients to infection.<sup>3</sup> Nasogastric or nasojejunal feeding is uncomfortable, can lead to aspiration pneumonia, and can decrease the patient's quality of life.<sup>4</sup> Operative or radiologic jejunostomy has a risk of infection, displacement, obstruction, or surgical complications.<sup>5</sup> Parenteral nutrition is inferior to enteral nutrition because of the risks for thrombophlebitis, sepsis, and gut bacterial translocation, as well as increased costs.<sup>2</sup> Endoscopic dilation offers only a transient benefit and can increase the rate of tumoral perforation.<sup>6</sup>

Oral nutrition can be restored with the use of self-expanding covered metallic stents (SEMSs), and the use of SEMSs is established for the palliation of dysphagia in unresectable EC.<sup>6</sup> The indications for SEMS use have expanded to include relief from dysphagia in patients with resectable EC and for those who require neoadjuvant treatment before resection.<sup>7-16</sup> Self-expanding covered metallic stent insertion can immediately relieve dysphagia and allow for the maintenance of oral nutrition,<sup>17</sup> and a series of articles highlight that their use is associated with safe early results.<sup>7-16</sup> However, the impact of SEMS insertion on oncologic outcomes in the neoadjuvant setting is unknown. The objective of this multicenter study was to evaluate the impact of SEMS insertion before EC surgery on oncologic outcomes.

## METHODS

### Patients

Data from 2,944 consecutive adult patients undergoing surgical resection for EC (including Siewert type I and II junctional tumors) with curative intent, in 30 French-speaking European centers between 2000 and 2010, were retrospectively collected through a dedicated website (<http://www.chirurgie-viscerale.org>). The collected data included demographic parameters, details on the perioperative and surgical treatments, postoperative outcomes, histopathologic analysis, and long-term oncologic outcomes. Missing or inconsistent data were obtained from e-mail exchanges or phone calls with the referral center. Patients were not included if the surgical, tumoral and/or nutritional data required for the analysis

were missing. Additionally, only patients with squamous cell cancer or adenocarcinoma were included, resulting in 2,279 available patients. As part of an initial exploratory analysis, we established the relationship between SEMS and the patient's age, sex, American Society of Anesthesiologists score, dysphagia, malnutrition (weight loss >10% of physical weight during a 6-month period), pretherapeutic clinical tumor stage (cTNM) and location, histologic subtype, neoadjuvant treatment and radiotherapy administration, and the extent of surgery. All patients who underwent SEMS insertion (SEMS group, n = 38) were matched, through a propensity score analysis, 1:4 to a control group of patients who did not undergo SEMS insertion (control group, n = 152). Investigators were blinded to the postoperative and oncologic outcomes during the selection process. The study was accepted by the regional IRB on July 15, 2013, and the database was registered on the [Clinicaltrials.gov](http://Clinicaltrials.gov) website under the identifier NCT 01927016.

### Pretherapeutic workup

Pretherapeutic investigations were performed according to national guidelines ([www.tnccd.org](http://www.tnccd.org)) and were reported elsewhere.<sup>18</sup> The pretherapeutic cTNM classification, performed before any stenting, was based on endoscopic ultrasound and/or CT scan in cases where tumor stenosis precluded full endoscopic ultrasound examination.

### Therapeutic strategy

All patients were evaluated by a multidisciplinary team and treated with curative intent according to French national guidelines ([www.tnccd.org](http://www.tnccd.org)).

### Neoadjuvant treatment

Patients with cT3/T4 tumors and/or cN+ disease received neoadjuvant treatment. Neoadjuvant chemotherapy was based on 5-FU and platinum-based drug administration for 2 to 4 cycles, and neoadjuvant chemoradiation—usually combined with 5-FU and platinum-based drugs as well as concomitant 45 Gy radiotherapy—was used for locally advanced tumors for which preoperative staging suggested that R0 resection would be questionable as well as in squamous cell carcinomas.

### Surgical resection

Details of the resection technique have been described elsewhere.<sup>19</sup> Briefly, curative resection consisted of a transthoracic en bloc esophagectomy, including abdominal and mediastinal lymphadenectomy, as well as anastomosis placement above the level of the azygos vein. For supracarinal tumors, cervical lymphadenectomy was performed, and the anastomosis was placed in the neck. A transhiatal

esophagectomy was performed, with an abdominal and inferior mediastinal lymphadenectomy, for patients with respiratory insufficiency, limited lower third esophageal tumors, and no evidence of lymph node metastasis.

### Self-expanding covered metallic stent insertion

Self-expanding covered metallic stent insertion is not commonly used for resectable EC in the tertiary referral centers that participated in the current study, reflecting the overall reluctance to consider stents for operable disease because of the perforation risk and unknown oncologic outcomes. The indications for SEMS placement were dysphagia, for the majority of patients, and/or locally advanced tumor and/or the requirement for neoadjuvant treatment. Self-expanding covered metallic stent insertion was usually performed in peripheral centers before discussion at a tertiary center multidisciplinary team. Only patients for whom SEMS placement was performed as a bridge to curative surgery and before beginning oncologic treatment were included. Covered SEMSs were deployed in the standard manner over guidewires, with the aid of radiologic imaging. Self-expanding covered metallic stents were sized based on the tumor location and length and severity of the stricture. Radiologic and endoscopic confirmation of the stent position was obtained. As a consequence of both the time period and multicenter nature of the study, a variety of SEMS brands were used. Because the aim of the study was to examine the impact of SEMS on oncologic outcomes, only patients who underwent successful stent placement were considered, and no data on the feasibility of SEMS are available.

### Histopathologic analysis

Histologic staging of tumors was based on the seventh edition of the International Union Against Cancer TNM classification.<sup>20</sup> Resections were designated R0 when removal was both macroscopically and microscopically complete, R1 for a microscopically positive resection margin and R2 for a macroscopically positive resection margin. All patients with pTNM stage IV were considered to have an R2 resection. Tumors with a complete pathologic response were graded pT0.

### Follow-up

All patients surviving the operation were followed until death or June 2013, according to a previously reported protocol,<sup>18</sup> resulting in a follow-up of at least 30 months for the surviving patients. In R0 patients, the first site of recurrence was used to document the time to disease recurrence and was classified as locoregional (in the upper abdomen or mediastinum), distant (including cervical recurrences for infracardinal tumors), or mixed (both).

### Study end points

The primary objective was to evaluate the impact of SEMS insertion before EC surgery on the 3-year overall survival (OS). The secondary objectives were to analyze the impact of stent insertion on the R0 resection rate, time to recurrence, and 3-year locoregional recurrence rate.

### Statistical analysis

The survival status of the patients was determined in June 2013, and median follow-up was 43.6 months (range 4.8 to 143.3 months), which was comparable between the SEMS and control groups ( $p = 0.761$ ). Seven patients (3.7%) were lost to follow-up. Quantitative variables are expressed as the mean  $\pm$  SD or the median (range), and qualitative variables are expressed as a percentage. Student's *t*-test or Mann-Whitney test was used for intergroup comparisons of quantitative variables, and a chi-square test or Fisher exact test was used to compare categorical data. We conducted propensity score matching analysis to compensate for the differences in some baseline characteristics between the two treatment groups. First, we compared all available patient, tumor, and treatment variables using a chi-square test. Next, a propensity score was calculated using logistic regression with the imbalanced variables mentioned. Finally, all patients in the SEMS group were matched 1:4 according to the propensity scores for control patients, leading to an even distribution of potential confounding factors to the treatment groups. Survival distributions were estimated using the adjusted Kaplan-Meier method and compared using a log-rank test. A binary logistic regression was used to identify predictors of R0 resection. Univariate and multivariate Cox proportional hazards models were used to assess pretherapeutic prognostic factors for the OS and to compute hazard ratios and their 95% CIs. All tests were 2-sided and the threshold for statistical significance was set at  $p < 0.05$ . Analyses were performed with SPSS software, version 19.0 (SPSS, Inc).

## RESULTS

### Demographic and pretherapeutic tumor characteristics

The characteristics of the study population ( $n = 190$ ) are summarized in Table 1. The patients' median age was 64.5 years (range 34 to 81 years) with a male to female ratio of 7.3:1. Malnutrition affected 55.3% of the patients. In 52.6% of the patients, the American Society of Anesthesiologists score was I or II. The majority of the cases were adenocarcinomas (57.9%), which were mostly located in the lower two thirds of the esophagus (93.7%). In total, 58.4% of the patients had a clinical stage III tumor, with

**Table 1.** Demographic and Therapeutic Characteristics of the Study Population

Demographic and therapeutic characteristics	Study population (n = 190)		SEMS group (n = 38)		C group (n = 152)		p Value
	n	%	n	%	n	%	
Age							0.537
Younger than 60 y	62	32.6	14	36.8	48	31.6	
60 y and older	128	67.4	24	63.2	104	68.4	
Sex							0.824
Male	167	87.9	33	86.8	134	88.2	
Female	23	12.1	5	13.2	18	11.8	
ASA score							1.000
I	35	18.4	7	18.4	28	18.4	
II	65	34.2	13	34.2	52	34.2	
III	85	44.8	17	44.8	68	44.8	
IV	5	2.6	1	2.6	4	2.6	
Tumor location							0.895
Upper	12	6.3	3	7.9	9	5.9	
Mid	49	25.8	10	26.3	39	25.7	
Lower	129	67.9	25	65.8	104	68.4	
Dysphagia							1.000
No	10	5.3	2	5.3	8	5.3	
Yes	180	94.7	36	94.7	144	94.7	
Pretherapeutic cTNM stage							0.757
I	36	19.0	7	18.4	29	19.1	
II	43	22.6	7	18.4	36	23.7	
III	111	58.4	24	63.6	87	57.2	
Neoadjuvant treatment							0.852
No	78	41.0	15	39.5	63	41.5	
Yes	112	59.0	23	60.5	89	58.5	
Neoadjuvant radiotherapy							0.648
No	124	65.3	26	68.4	98	64.5	
Yes	66	34.7	12	31.6	54	35.5	
Histologic type							1.000
SCC	80	42.1	16	42.1	64	42.1	
ADC	110	57.9	22	57.9	88	57.9	
Malnutrition							1.000
No	85	44.7	17	44.7	68	44.7	
Yes	105	55.3	21	55.3	84	55.3	
Surgical resection							0.945
TT 2 fields	147	77.4	30	79.0	117	77.0	
TT 3 fields	23	12.1	4	10.5	19	12.5	
Transhiatal	20	10.5	4	10.5	16	10.5	
Postoperative treatment							0.394
No	145	76.3	27	71.0	118	77.6	
Yes	45	23.7	11	29.0	34	22.4	

ADC, adenocarcinoma; ASA, American Society of Anesthesiologists; SEMS, self-expanding metallic stents; SSC, squamous cell carcinoma; TT, transthoracic.

neoadjuvant treatment administered in 59.0% of the patients. The cT and cN classifications were similar between groups (not shown). A transthoracic approach was performed in 89.5% of the patients. Due to propensity score matching, the SEMS and control groups were comparable for the age, sex, tumor location and stage, American Society of Anesthesiologists score, dysphagia, malnutrition, neoadjuvant treatment and radiotherapy administration, histology, and surgical procedure. The two groups were comparable in dysphagia severity, which was assessed at the initial presentation (no dysphagia/able to swallow solid food/semi-liquids only/liquid only/unable to swallow;  $p = 0.246$ ). Self-expanding covered metallic stent insertion was complicated by tumor perforation in 2 patients and was treated by immediate curative surgery.

### Postoperative course

The in-hospital mortality and morbidity rates in the SEMS and control groups were 13.2% vs 8.6% ( $p = 0.370$ ) and 63.2% vs 59.2% ( $p = 0.658$ ), respectively (Table 2). Although there was no difference for each complication when considered individually, the Dindo-Clavien grade 3/4 postoperative complication rates were significantly higher in the SEMS group compared with the control group (44.7% vs 27.0%;  $p = 0.033$ ).

### Secondary end points

The R0 resection rate was significantly lower in the SEMS group (71.0% vs 85.5%;  $p = 0.041$ ). After adjusting for confounding factors, SEMS insertion was a significant predictor of R1/R2 resection (odds ratio = 2.4; 95% CI, 1.02–5.5;  $p = 0.046$ ), and patients in the SEMS group had more advanced pTNM stage tumors, even though both groups had comparable tumors at the initial presentation. Median time to recurrence was significantly lower in the SEMS group (6.5 months [range 0 to 18 months] vs 9.0 months [range 0 to 42 months];  $p = 0.040$ ), with an increased 3-year locoregional recurrence rate (62% vs 34%;  $p = 0.049$ ). All of these results remain significant after exclusion of the two SEMS-related esophageal perforations. With respect to the outcomes of the two perforated cases, one pathologically staged III patient experienced pneumonia in the postoperative setting and a cancer-related death at 3 months, and the other patient, pathologically staged II, had an uneventful postoperative course with a cancer-related death after 28.4 months of follow-up (Table 3).

### Overall survival

Median OS was 25.8 months (range 18.7 to 32.9 months), which was significantly lower in the SEMS group than in the control group (17.4 months [range

**Table 2.** Postoperative Complications in the Study Population and in SEMS and C Groups

Postoperative complications	Study population (n = 190)		SEMS group (n = 38)		C group (n = 152)		p Value
	n	%	n	%	n	%	
In-hospital postoperative complication							0.657
No	76	40.0	14	36.8	62	40.8	
Yes	114	60.0	24	63.2	90	59.2	
In-hospital postoperative mortality							0.277
No	172	90.5	33	86.8	139	91.5	
Yes	18	9.5	5	13.2	13	8.5	
Anastomotic leakage							0.645
No	169	88.9	33	86.8	136	89.5	
Yes	21	11.1	5	13.2	16	10.5	
Surgical site infection							0.184
No	163	85.8	30	78.9	133	87.5	
Yes	27	14.2	8	21.1	19	12.5	
Pulmonary complication							0.344
No	108	56.8	89	58.6	19	50	
Yes	82	43.2	63	41.4	19	50	
Cardiovascular complication							0.453
No	173	91.1	34	89.5	139	91.5	
Yes	17	8.9	4	10.5	13	8.5	
Thromboembolic event							NA
No	186	97.9	37	97.4	149	98.0	
Yes	4	2.1	1	2.6	3	2.0	
Sepsis							NA
No	180	94.7	37	97.4	143	94.1	
Yes	10	5.3	1	2.6	9	5.9	
Dindo-Clavien classification (n = 114)							0.027
I	13	6.8	1	2.6	12	7.9	
II	43	22.6	6	15.8	37	24.3	
IIIa	4	2.1	0	0	4	2.6	
IIIb	14	7.4	2	5.3	12	7.9	
IVa	17	9.0	9	23.7	8	5.3	
IVb	5	2.6	1	2.6	4	2.6	
V	18	9.5	5	13.2	13	8.6	
Reoperation							0.381
No	159	83.7	30	78.9	129	84.9	
Yes	31	16.3	8	21.1	23	15.1	

NA, not applicable due to very low number of events; SEMS, self-expanding metallic stents.

11.7 to 23.1 months] vs 27.5 months [range 29.0 to 35.1 months];  $p = 0.023$ ). Three-year OS was 40%, which was significantly reduced in the SEMS group (25% vs 44%) (Fig. 1). After excluding the SEMS-related esophageal perforations, the 3-year OS remained significantly reduced in the SEMS group (28% vs 44%;  $p = 0.043$ ). In the R0 population, median OS was again decreased in the SEMS group (19.0 vs 32.2 months), but this was not significant, most likely due a type II error ( $p = 0.232$ ). After adjusting for pretherapeutic confounding

factors, SEMS insertion was an independent predictor of poor prognosis (hazard ratio = 1.6; 95% CI, 1.02–2.5;  $p = 0.038$ ).

## DISCUSSION

Dysphagia, the cardinal symptom of EC, is distressing to the patient, and it is frequently associated with malnutrition. Restoring the esophageal patency with a stent can relieve dysphagia and improve oral intake. For operable

**Table 3.** Pathologic Analysis in the Study Population and in SEMS and C Groups

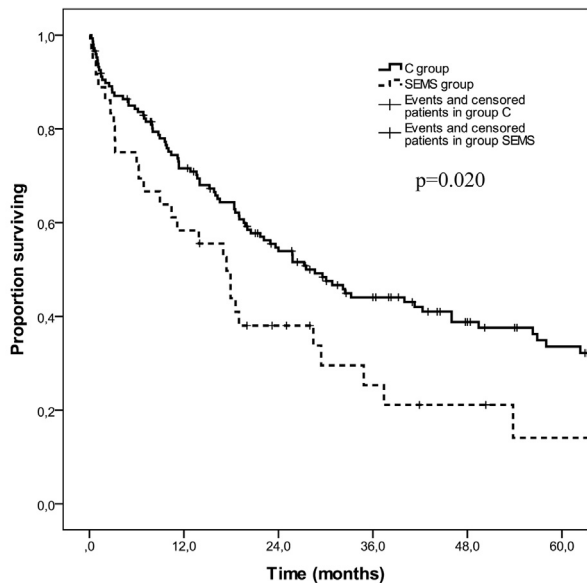
Variables	Study population (n = 190)	SEMS group (n = 38)	Control group (n = 152)	p Value
Resection radicality, n (%)				0.041
R0	157 (82.7)	27 (71.1)	130 (85.5)	
R1	24 (12.6)	5 (13.2)	19 (12.5)	
R2	9 (4.7)	6 (15.7)	3 (2.0)	
Circumferential margin, n (%)				0.011
Negative	164 (86.3)	28 (73.7)	136 (89.5)	
Positive	26 (13.7)	10 (26.3)	16 (10.5)	
pT, n (%)				0.507
pT0	14 (7.4)	3 (7.9)	11 (7.2)	
pT1a	11 (5.8)	2 (5.3)	9 (5.9)	
pT1b	10 (5.2)	1 (2.6)	9 (5.9)	
pT2	35 (18.4)	8 (21.1)	27 (17.8)	
pT3	101 (53.2)	17 (44.7)	84 (55.3)	
pT4a	15 (7.9)	6 (15.8)	9 (5.9)	
pT4b	4 (2.1)	1 (2.6)	3 (2.0)	
pN, n (%)				0.114
pN0	73 (38.4)	9 (23.7)	64 (42.1)	
pN1	57 (30.0)	12 (31.6)	45 (29.6)	
pN2	31 (16.3)	10 (26.3)	21 (13.8)	
pN3	29 (15.3)	7 (18.4)	22 (14.5)	
No. of LNs examined, median (range)	16 (1–56)	16 (3–41)	16 (1–56)	0.805
No. of positive LNs, median (range)	1 (0–21)	2 (0–19)	1 (0–21)	0.109
pTNM stage, n (%)				0.040
0	11 (5.8)	2 (5.3)	9 (5.9)	
Ia	15 (7.9)	2 (5.3)	13 (8.6)	
Ib	12 (6.3)	1 (2.6)	11 (7.2)	
IIa	31 (16.3)	4 (10.5)	27 (17.8)	
IIb	18 (9.5)	5 (13.2)	13 (8.6)	
IIIa	47 (24.7)	6 (15.8)	41 (27.0)	
IIIb	12 (6.3)	3 (7.9)	9 (5.9)	
IIIc	40 (21.1)	11 (28.9)	29 (19.1)	
IV*	4 (2.1)	4 (10.5)	0 (0)	
Tumor differentiation, n (%)				0.683
Well	53 (27.9)	8 (21.1)	45 (29.6)	
Moderate	7 (37.4)	17 (44.7)	54 (35.5)	
Poor	35 (18.4)	7 (18.4)	28 (18.4)	
NR	3 (16.3)	6 (15.8)	25 (16.5)	

\*Stage IV tumors were discovered at time of surgery and/or pathologic analysis.

LN, lymph node; NR, not reported; SEMS, self-expanding metallic stents.

disease, many surgeons are reluctant to consider stents, expressing concerns about perforation, difficulties in surgical dissection, and future tumoral resectability. Despite this, some studies have examined the role of stents as a bridge to surgery and reported that their insertion can be performed with safe early results, but none of these studies reported data on oncologic outcomes (Table 4).<sup>7-16</sup> The current study is the first to show that SEMS placement negatively impacts oncologic outcomes, with

significantly lower R0 resection rates, time to recurrence, and OS, and significantly higher rates of locoregional recurrence. The results remained significant after excluding SEMS-related esophageal perforations, highlighting that the complications of stent placement are not solely responsible for these poor outcomes. Additionally, SEMS insertion was an independent predictor of incomplete resection and poor prognosis after adjusting for pretherapeutic confounding factors.



Group C	152	101	70	48	34	25
Group SEMS	38	21	11	6	4	2

**Figure 1.** Overall survival curves in the self-expanding metallic stent group (SEMS group,  $n = 38$ ) and in the control group (C group,  $n = 152$ ). The number of subjects at risk in each interval is shown in the table at the bottom of the figure.

Similar results have been reported in colon cancer,<sup>21</sup> where SEMSs have been used as a bridge to surgery for acute, left-sided colonic obstruction and for which the short-term feasibility of this approach has been demonstrated.<sup>22</sup> The following mechanisms have been suggested to explain the negative oncologic impact observed after stent placement: SEMSs generate peri-stent fibrosis secondary to expansive radial forces, compromising the normal planes of dissection and, therefore, the resectability<sup>23</sup>; SEMS fixating spurs might be responsible for microperforations, favoring tumor cell dissemination; SEMS insertion increases the levels of circulating neoplastic cells<sup>24</sup>; chemo(radio)therapy can accentuate the complications related to SEMS insertion, such as esophageal fistula<sup>11,25</sup>; and inability to accurately restage tumors after SEMS insertion makes it difficult to identify the tumors that progress and become unresectable. These factors might also explain the higher rate of severe postoperative complications in the SEMS group in the current study, compared with previous reports.<sup>26</sup> For patients who are eligible for surgery, recent innovations, such as self-expanding plastic stents,<sup>10,13,14,16</sup> which are easily removed and allow for accurate restaging, or biodegradable stents, which dissolve in a few months,<sup>7</sup> might be alternatives to SEMS. However, even with these innovations, the expansive radial forces, thought to be

the main mechanism responsible for the adverse oncologic outcomes, persist.

A literature review examining the results of the preoperative use of self-expanding stents for EC (Table 4) revealed that, after stenting, the rate of patients who did not complete their expected therapeutic sequence is high, ranging from 31% to 85%. This is largely related to the interval disease progression.<sup>9,10,12,14</sup> These data support our results, which question the oncologic safety of the use of SEMS in EC patients before surgery.

Substantial weight loss before surgery is associated with higher rates of postoperative morbidity and mortality and lower rates of resectability, response to chemotherapy, and survival.<sup>2</sup> Therefore, early enteral nutrition is important for improving tolerance and efficacy of neoadjuvant treatments. Because SEMS seem to compromise oncologic outcomes, several other options should be considered.<sup>2</sup> Nasogastric or nasojejunal feeding tubes can be used, but they are only practical for short time periods due to patient discomfort, and jejunostomy tubes have been the mainstay for providing enteral feeding, despite some well-known complications.<sup>5</sup> Recently, percutaneous gastrostomy has been shown to be a safe alternative in experienced hands.<sup>27</sup>

This study has some limitations. As with all retrospective surveys, this study has potential selection bias. This prompted us to use propensity score matching, a statistical technique that provides an odds ratio of the treatment effect that is very similar to that obtained in randomized trials.<sup>28</sup> The best way to assess the long-term impact of SEMS use is a multicenter, randomized controlled trial, however, such a trial has never been feasible in France because of surgeons' reluctance to use metallic stents in the preoperative setting. Only patients who underwent an operation were included in the database, therefore, we could not evaluate the feasibility of SEMS, which has already been reported in other small studies (Table 4). Additionally, because we only collected data on patients who underwent resection, we could not examine patients who underwent SEMS insertion with curative intent but would not benefit from surgery due to tumor progression or SEMS-related fistula.<sup>29</sup> Such data would have reinforced our findings. As only 38 patients underwent SEMS insertion, there is potential for selection bias. The small population reflects that few patient series have been reported and stent placement is not recommended in French guidelines ([www.tncd.org](http://www.tncd.org)). The practices reported here are those of nonspecialized physicians, and SEMSs were placed before multidisciplinary team consultation. Additionally, dedicated methodology has been used to avoid including more patients with advanced tumors in the SEMS group. This has been

**Table 4.** Results of the Use of Self-Expanding Stent (Plastic or Metallic) as a Bridge to Surgery in Esophageal Cancer in the English Literature

First author, year	Tumor n	Tumor stage	Tumor location, n	Type of stent	Additional enteral nutrition, n (%)	Perforation, n	Chest pain, n (%)	Fistula, n	Bleeding, n	Stent migration, n (%)	Completion of neoadjuvant therapy, n (%)	Surgical resection, n (%)	Complete resection	Long-term follow-up
Krokidis, <sup>7</sup> 2013	11	NR	Upper, 3 Mid, 1 Distal, 7	B-SEPS	NR	NR	NR	2	1	2/11 (18)	3/11 (27)	1/11 (9)	NR	NR
Pellen, <sup>8</sup> 2012	16	II–III	Upper, 1 Mid, 3 Distal, 12	SEMS	NR	0	NR	0	0	8/16 (50)	NR	10/16 (63)	8/10 (80)	NR
Siddiqui, <sup>9</sup> 2012	55	>IIa	Mid, 10 Distal, 45	SEMS	NR	1	13/55 (24)	1	0	17/55 (31)	55/55 (100)	8/55 (15)	NR	85% palliative care
Brown, <sup>10</sup> 2011	32	II–III	Mid, 5 Distal, 27	SEPS	1/32 (3)	0	2/32 (6)	1	NR	8/32 (25)	NR	20/32 (63)	20/20 (100)	NR
Lopes, <sup>11</sup> 2010	11	IIa–IIIc	Upper, 1 Mid, 4 Distal, 6	SEMS	NR	0	3/11 (27)	1	NR	2/11 (18)	10/11 (91)	2/11 (18)	NR	NR
Langer, <sup>12</sup> 2010	38	NR	Mid, 18 Distal, 20	25 SEMS 13 SEPS	NR	2	NR	3	1	12/38 (32)	32/38 (84)	20/38 (53)	NR	NR
Adler, <sup>13</sup> 2009	13	>IIa	Mid, 4 Distal, 9	SEPS	1/13	0	12/13 (92)	0	0	6/13 (46)	12/13 (92)	3/13 (23)	NR	NR
Bower, <sup>14</sup> 2009	25	IIa–IIIc	Mid, 5 Distal, 20	SEPS	2/25 (8)	0	1/25	0	0	6/25 (25)	23/25 (92)	14/25 (56)	NR	NR
Martin, <sup>15</sup> 2009	5	NR	Mid, 2 Distal, 3	SEPS	1/5 (20)	NR	NR	NR	NR	1/5 (20)	5/5 (100)	NR	NR	NR
Siddiqui, <sup>16</sup> 2009	12	NR	Upper, 1 Mid, 1 Distal, 10	SEPS	NR	0	8/15	0	0	4/11 (36)	NR	NR	NR	NR

SEPS, self-expanding plastic stent; SEMS, self-expanding metallic stent; B-SEPS, biodegradable SEPS; Mid, middle third of the esophagus; NR, not reported.



ensured in the following ways: including only patients who were eligible for curative surgery; identifying all factors that were predictive of stent placement for constructing the propensity score, which was used for matching; matching all SEMS patients to the maximum number of control patients, leading to a 1:4 ratio; and verifying the prognostic impact of SEMS placement after adjusting for other pretherapeutic variables.

## CONCLUSIONS

This multicenter case-control study allows us to conclude that the use of SEMS to relieve dysphagia as a bridge to surgery has a negative impact on oncologic outcomes in EC patients.

### Appendix 1: list of collaborators in the French Eso-Gastric Tumors Working Group

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**Acknowledgment:** The authors thank Prof Stéphane Benoist, Prof Xavier Dray, Dr Stéphane Lecleire, Dr Laetitia Dahan, and Dr Julien Branche for their valuable comment; Hélène Beal for her statistical assistance; and Dr William B Robb for critically revising the article.

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