Original Article

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Palliative Esophageal Stenting for Esophagorespiratory Fistula in Patients with Esophageal Cancer

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Abstract:

Objective: This study aimed to evaluate the clinical outcomes following the placement of self-expandable metal stents (SEMS) in patients with esophagorespiratory fistula (ERF), due to esophageal squamous cell carcinoma (ESCC).

Material and Methods: Forty-three patients with ERF in ESCC underwent esophageal SEMS placement at Songklanagarind Hospital, Thailand, from January 2008 to June 2023. Data on initial clinical success and failure, complications, stent patency, and survival were collected.

Results: Technical success was achieved in all patients, with an initial clinical success rate of 28 of 43 (65.1%) and initial clinical failure occurring in 15 of 43 (34.9%). Among the 28 patients with initial clinical success, 13 developed recurrent symptoms: aspiration symptoms recurred in 61.5% (8 of 13) and dysphagia symptoms recurred in 38.5% (5 of 13). Persistent aspiration pneumonia, 53.3% (8 of 15), and persistent dysphagia symptoms, 46.7% (7 of 15), occurred in the 15 patients who had initial clinical failure. The overall major complication rate was 34.9% (15 of 43). The median stent patency duration was 38.5 days (interquartile range (IQR), 25.8–112.2) and the median survival duration was 40 days (IQR, 14–89.5). Survival was significantly lower in cases of initial clinical failure (14 days, IQR 6.5–32 days) compared to initial clinical success (72 days, IQR 27–197.2 days) (p-value<0.001).

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Conclusion: Palliative esophageal SEMS placement for ERF in patients with ESCC is technically easy, effective, safe, and provides short-term relief of aspiration, including dysphagia. Initial clinical success led to longer survival than initial clinical failure.

Keywords: complication, esophageal cancer, esophagorespiratory fistula, patency, stent, survival

Introduction

Esophageal cancer is a common gastrointestinal disease (global cancer statistics)[1]. Additionally, it is the 7th most common disease with 604,100 new cases and the 6th leading cause of death (544,100 people) in cancer patients[1]. Due to the loss of serosa of the esophagus, esophageal cancer can easily invade adjacent organs, such as the airway, lungs, and aorta, making for a poor prognosis. Esophagorespiratory fistula (ERF) develops in 5–15% of patients with advanced esophageal cancer[2,3]. ERF development is attributed to direct invasion, chemotherapy, or radiotherapy[4], presenting a severe and life-threatening complication. Patients with ERF struggle with swallowing, leading to chronic aspiration, respiratory infection, respiratory failure, sepsis, and eventual mortality.

The use of esophageal self-expandable metal stents (SEMS) has become a widely accepted and effective intervention for malignant ERF, emphasizing its superiority over supportive treatment in overall survival and quality of life[5–7]. This study focused on evaluating the clinical outcomes and survival following palliative SEMS placement in patients with malignant ERF from esophageal squamous cell carcinoma (ESCC).

Material and Methods

Study design

A single-center, retrospective cohort study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the Faculty of Medicine, Prince of Songkla University (REC. 64-164-10-4).

Study population

The study included all ESCC patients who underwent esophageal self-expandable metal stent (SEMS) placement for the treatment of ERF at Songklanagarind Hospital from January 2008 to June 2023. Patients with a history of non-esophageal cancer were excluded from the study.

Stent placement technique

ERF was confirmed by computed tomography (CT) and bronchoscopy. Flexible gastroscopy was performed to evaluate the anatomy, length, and location of the fistula. A guidewire was inserted across the esophagus, and the covered SEMS was positioned over the guidewire across the ERF and stenosis area, under fluoroscopic guidance[7].

Definition of outcomes

Initial clinical success was defined as: clinical improvement of dysphagia or aspiration symptoms within 7 days after stent placement.

Initial clinical failure was defined as: persistent dysphagia or aspiration symptoms within 7 days after stent placement.

Stent patency was calculated from the day of stent placement to the day of stent dysfunction causing symptom recurrence.

Survival period was calculated from the day of stent placement to the day of death.

Statistical analysis

Considered variables consisted of: age, gender,

body mass index (BMI), Eastern Cooperative Oncology Group (ECOG) score, clinical staging, location and length of tumor, fistula size, location of the fistula opening, prior cancer treatment, pre- and post-stent dysphagia score, weight change after stenting, prior pulmonary infection, and post-stent complications. Continuous data are reported as median±interquartile range (IQR). Comparisons between groups were performed via the chi-square test or Fisher's exact test for dichotomous variables. Median and IQR of the interval and cumulative rates for stent patency and survival were calculated using the Kaplan-Meier method. The data were analyzed using RStudio version 4.2.1.

Results

Clinical outcomes

The demographic and clinical characteristics of the 43 patients revealed a predominantly male population. The most common location was the middle thoracic area (76.7%), and the most common fistula opening was the left main bronchus (39.5%). In total, 46.5% underwent chemoradiotherapy before stent insertion. The median duration from chemoradiotherapy to stent placement was 87.5 days (IQR, 56-141.5); 93% had symptoms of dysphagia and 55.8% had pulmonary infection (Table 1).

SEMS placement in the esophagus was technically successful in all 43 patients, with no immediate procedure-related complications: initial clinical success was achieved in 65.1% (28 of 43). Among the 28 patients with initial clinical success, 46.4% (13 of 28) later developed recurrent symptoms: recurrent aspiration symptoms in 61.5% (8 of 13) and recurrent dysphagia symptoms in 38.5% (5 of 13). In patients with initial clinical failure, 34.9% (15 of 43), symptoms consisted of persistent aspiration at 53.3% (8 of 15) and persistent dysphagia at 46.7% (7 of 15) (Figure 1).

Table 1 Patients' baseline characteristics

Characteristic	Number of patients (%)
Gender (male:female)	41 (95.3):2 (4.7)
Age mean (S.D.)	58.1 (8.9)
BMI (<18.5:≥18.5)	35 (81.4):8 (18.6)
Pre-stent ECOG score (1:2:3:4)	6 (14):28 (65.1):9 (20.9):0
Pre-stent dysphagia score (0:1:2:3:4)	0:0:3 (7):18 (41.8):19 (44.2)
Clinical staging (I:II:III:IV)	0:0:16 (37.2):27 (62.8)
Tumor location	
Upper thoracic	5 (11.6)
Middle thoracic	33 (76.7)
Lower thoracic	5 (11.6)
Tumor length (cm)	7 (5, 10)
Fistula diameter (mm)	3 (2, 4.5)
Location of fistula opening	
Trachea	7 (16.3)
Right bronchus	8 (18.6)
Left bronchus	17 (39.5)
Lung parenchyma	6 (14)
Pleural cavity	5 (11.6)

S.D.=standard deviation, ECOG=Eastern Cooperative Oncology Group, cm=centimeters, mm=millimeters

Complications

Of the patients with initial clinical failure, 33.3% (5 of 15) had early complications. These consisted of severe neck or chest pain, which was improved with pain control in 3 patients. In another patient, we had to remove the stent due to persistent severe pain following pain control. One patient had stent migration, which was treated with stent repositioning and fixation to the mucosa with clips. The overall complication rate was 34.9% (15 of 43). The overall late complication rate was 23.2% (10 of 43). Details of the management of adverse events are summarized in Table 2.

Survival and stent patency

Median duration of stent patency was 38.5 days (IQR, 25.8–112.2). Cumulative stent patency rates at 3, 6, 9, and 12 months were 63.3%, 31.7%, 23.7%, and 11.9%. Median duration of survival was 40 days (IQR, 14–89.5). Cumulative survival rates at 3, 6, 9, and 12 months were 48.6%, 44.2%, 30.9%, and 30.9% (Figure 2). Survival of initial clinical failure (14 days, IQR 6.5–32 days) was significantly lower than initial clinical success (72 days, IQR 27–197.2 days) (p-value<0.001) (Figure 3).

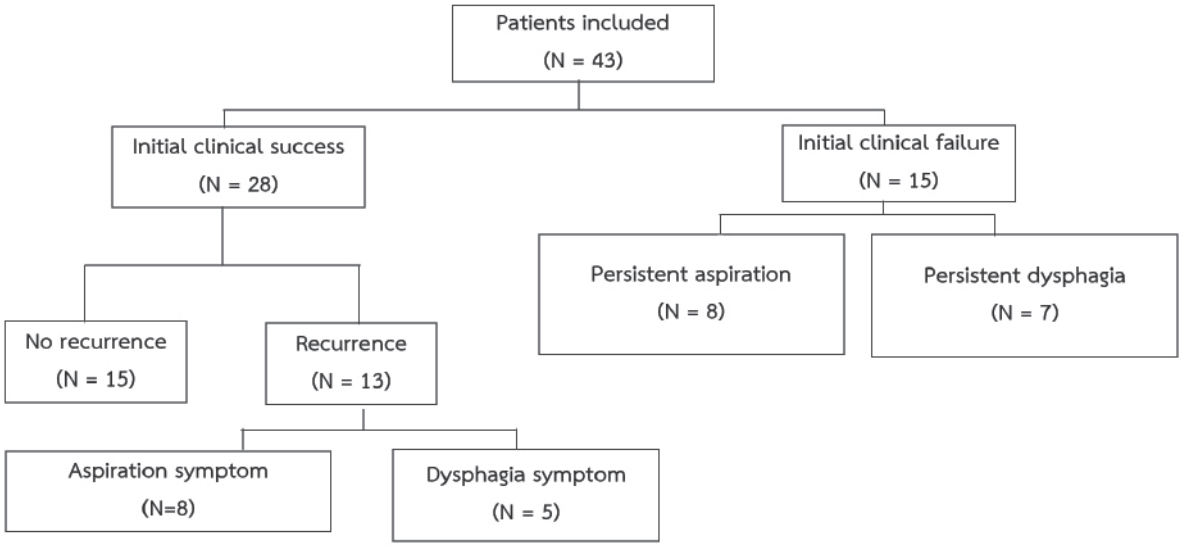

Figure 1 Flow chart summarizing the clinical outcomes of patients

Table 2 Overall late complications and management

Major complication (No.)	Management (No.)
Tumor overgrowth into stent (4)	Argon beam plasma coagulation (2) Re-stent placement (1)
Re-open of fistula (2)	Re-stent placement (1)
Tumor overgrowth into trachea (1)	Tracheal stent placement (1)
Stent eroded into trachea (2)	Tracheal stent placement (1)
Massive hematemesis (1)	Aggressive resuscitation and death (1)

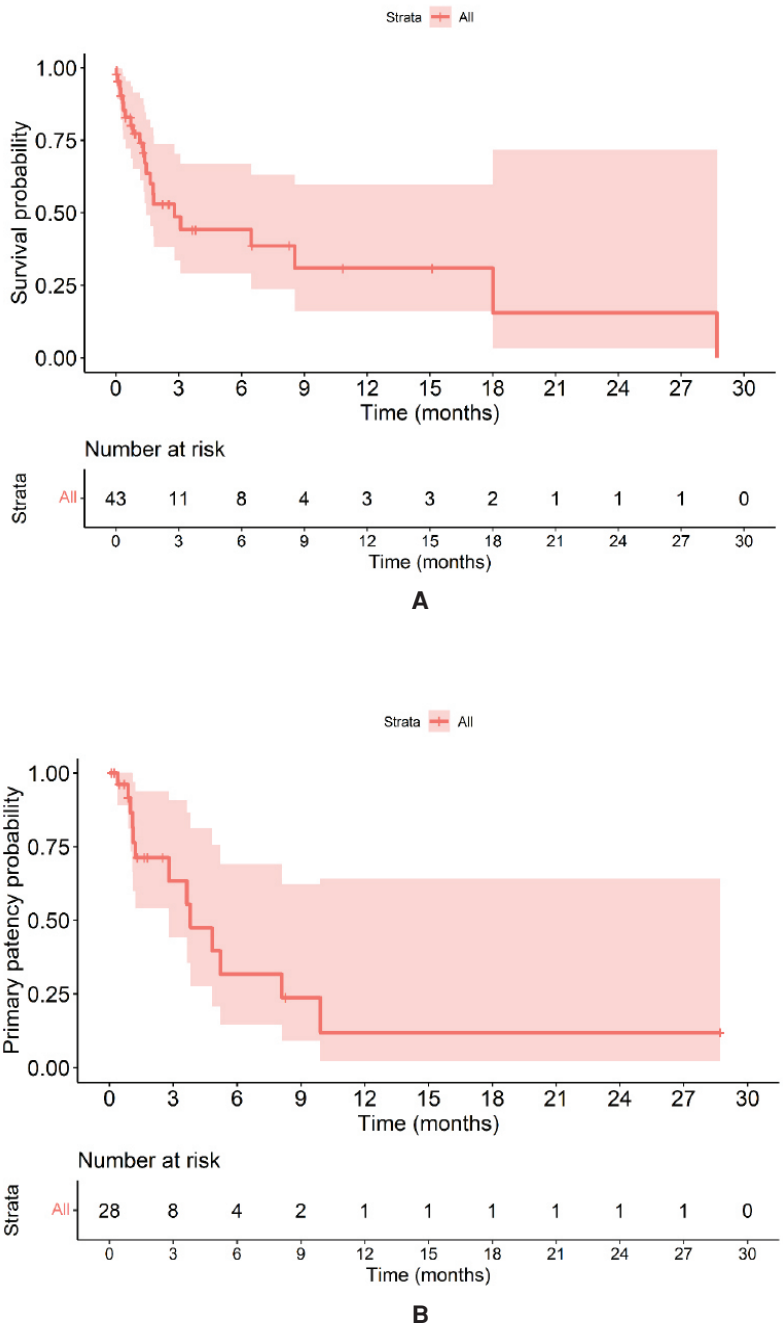

Figure 2 (A) Overall survival rate and (B) stent patency rates

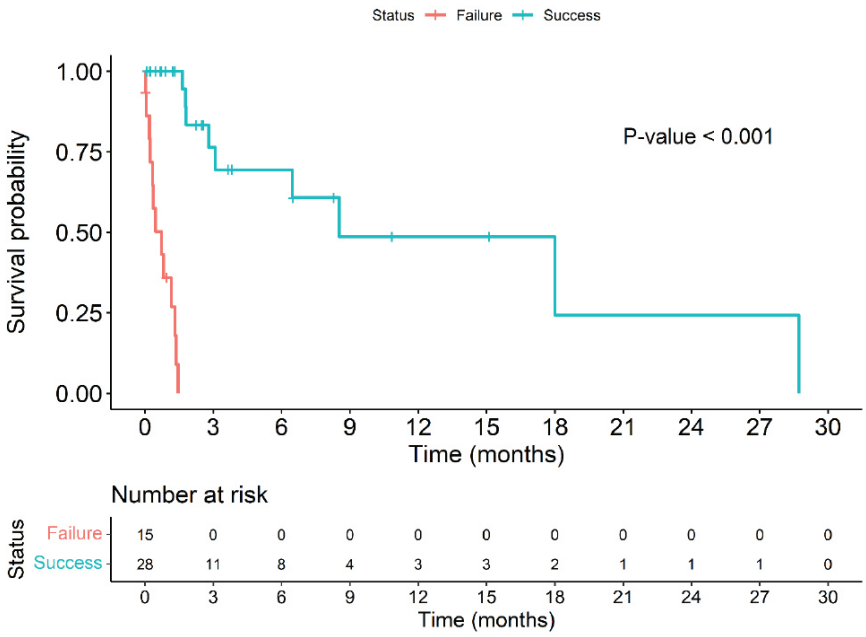

Figure 3 Overall survival rate compared between initial clinical success and initial clinical failure

Table 3 Predictors of initial clinical failure

Variable	Univariate analysis		p-value	Odds ratio
	Yes (n=15)	No (n=28)		
Age (mean)	57.8 (10.6)	58.3 (8.1)	0.875	
BMI	17.5 (1.3)	16.9 (2.2)	0.315	
Tumor location			0.544	
Upper thoracic	3 (20)	2 (7.1)		Ref:
Middle thoracic	11 (73.3)	22 (78.6)		0.33; 95% CI 0.05–2.3; p-value=0.265
Lower thoracic	1 (6.7)	4 (14.3)		0.17; 95% CI 0.01–2.82; p-value=0.214
Length of tumor (mean)	8.2 (3)	7.5 (2.7)	0.438	
Opening location			0.484	
Trachea	4 (26.7)	3 (10.7)		Ref:
Right bronchus	3 (20)	5 (17.9)		0.45; 95% CI 0.06–3.57; p-value=0.45
Left bronchus	4 (26.7)	13 (46.4)		0.23; 95% CI 0.04–1.5; p-value=0.124
Lung parenchyma	3 (20)	3 (10.7)		0.75; 95% CI 0.08–6.71; p-value=0.797
Pleural cavity	1 (6.7)	4 (14.3)		0.19; 95% CI 0.01–2.66; p-value=0.216

BMI=body mass index

Predictors of initial clinical failure

The results of the logistic regression analysis for initial clinical failure are summarized in Table 3. Logistic regression analysis showed that age, BMI, tumor location, length of tumor, and fistula location cannot predict initial clinical failure after esophageal SEMS placement.

Discussion

ERF is an uncommon but critical event in patients with esophageal cancer. It arises from direct tumor invasion, or as an adverse event of therapies such as chemotherapy or radiotherapy. Prompt treatment is essential to prevent aspiration and respiratory infection. Furthermore, surgical correction is not popular in some cases due to the advanced stage of the disease, presence of pulmonary infection, or the patient simply being unfit for surgery. Esophageal SEMS placement has proven highly effective, with reported success rates ranging from 41% to 80%[3,5–9]. The initial clinical success rate in this study was 65.1%, which immediately improved quality of life by stopping aspiration and also providing relief of dysphagia symptoms. However, initial clinical failure occurred in 34.9%, consisting of persistent aspiration or dysphagia. This study could not determine the reasons or factors that predicted the outcomes of initial clinical success or failure, which might be due to the limited number of patients. Kim et al. reported stricture of the upper esophagus is an independent predictor of initial clinical failure and shorter stent patency[5].

We found that the initial clinical failure group had early complications, such as severe neck or chest pain and stent migration, which required repositioning of the stent. In contrast, the initial clinical success group had no early complications. The overall late complication rate was 23.2% compared to the previously reported rate of 28%[3]. In this study, the most common early complication was severe pain. Stent placement at the ERF close to the upper esophageal sphincter has been traditionally considered to be difficult because of pain at the neck. The most common late complication was stent stenosis, which usually occurs from tumor overgrowth, obstruction at the proximal or distal end of the stent, particularly in delays of over 30 days after stent placement. Patients required other modalities such as tumor ablation, re-stent placement, or esophageal dilation with a percutaneous endoscopic gastrostomy tube for nutritional support.

In this cohort, 2 cases had late complications, which required tracheal stent: tumor overgrowth into the trachea (1) and stent erosion into the trachea (1). Many studies have reported on dual stent placement at the same time as being safe and effective[10–12]. However, dual stenting should be performed carefully because of pressure necrosis between the esophageal and airway wall, due to competing radial forces. The European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommend esophageal SEMS placement for malignant ERF. Additionally, airway stenting may be considered in addition to esophageal SEMS placement in order to improve the success rate and prevent airway obstruction[13].

Median duration of stent patency was 38.5 days. Median duration of survival was 40 days. The duration of survival and stent patency varied in previous studies because of differences in patient conditions, such as stage of disease, pulmonary infection, and outcome after SEMS placement[3,5,6,8]. This study demonstrated that the survival of initial clinical failure (14 days, IQR 6.5–32 days) was significantly lower than initial clinical success (72 days, IQR 27–197.2 days) (p-value<0.001). The main cause of death in ERF patients from esophageal cancer is pneumonia. In the majority of patients, pulmonary infection may persist or recur, even after SEMS placement. Pulmonary infection should be intensively treated before and after the procedure. In our opinion, the benefit from esophageal SEMS placement is not only stopping aspiration, but also dysphagia relief, which increases the quality of life in the final stage. To increase patient survival, esophageal SEMS placement must be established in early ERF, ideally before the onset of aspiration or pneumonia.

This study is limited due to its retrospective nature, which could have led to some selection bias. We found that it is difficult to find the factors predicting clinical outcome after esophageal SEMS placement. Further studies with a larger sample size may be necessary in order to find these predictors.

Conclusion

Palliative esophageal SEMS placement for ERF in patients with ESCC is technically easy, effective, safe, and provides short-term relief of aspiration symptoms and dysphagia. Initial clinical success led to longer survival than initial clinical failure.

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Conflict of interest

This study has no conflicts of interest.

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