

Treatment of complications caused by metallic stent placement in esophageal cancer

Özofagus kanserinde metal stent uygulamasının neden olduğu komplikasyonların tedavisi

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ABSTRACT

Background: This study aims to present the complications arising from self-expanding metallic stents placed in patients with esophageal cancer and the treatment methods for these complications.

Methods: The study included 268 patients with inoperable esophageal cancer (140 males, 128 females; mean age 64.4±16.3 years; range 28 to 91 years) who were placed 334 metallic stents in our clinic between January 2000 and December 2014. Patients who developed complications and treatment approaches adopted for these complications were evaluated retrospectively.

Results: Totally, we observed 365 complications. We detected major complications in 30 patients [13 hemorrhages (4.8%), 9 aspiration pneumonias (3.4%), 3 tracheal compressions (1.1%), 2 perforations (0.7%), and 3 esophagorespiratory fistulas (1.1%)] and minor complications in 334 patients [245 chest pains (91.4%), 36 tumor overgrowths (13.4%), 1 tumor ingrowth (0.4%), 10 partial stent migrations (3.7%), 8 falling of stents into the stomach (2.9%), 12 gastroesophageal refluxes (4.5%), 8 stent placement failures (2.9%), 5 hiccups (1.9%), 2 foreign body sensations (0.7%), 2 stent expansion failures (0.7%), 1 granulation tissue formation (0.4%), 3 food bolus obstructions (1.1%), 1 skin erosion (0.4%), and 1 stent fracture (0.4%)]. Before and after stent placement, mean dysphagia scores were 3.6 and 2.4, respectively. Mortality was observed in four patients (1.5%) after stent placement.

Conclusion: Although esophageal stent placement is a safe and effective method, it leads to many complications. Knowing how to treat these complications may increase patient's quality of life and decrease morbidity and mortality.

Keywords: Complication; esophageal cancer; stent; treatment.

ÖZ

Amaç: Bu çalışmada özofagus kanserli hastalarda uygulanan, kendi kendine genişleyen metal stentlere bağlı gelişen komplikasyonlar ve bu komplikasyonların tedavi yöntemleri sunuldu.

Çalışma planı: Çalışmaya kliniğimizde Ocak 2000 - Aralık 2014 tarihleri arasında 334 metal stent yerleştirilen 268 ameliyat edilemez özofagus kanserli hasta (140 erkek, 128 kadın; ort. yaş 64.4±16.3 yıl; dağılım 28-91 yıl) dahil edildi. Komplikasyon gelişen hastalar ve bu komplikasyonlar için benimsenen tedavi yaklaşımları retrospektif olarak değerlendirildi.

Bulgular: Toplam 365 komplikasyon görüldü. Otuz hastada majör komplikasyon [13 kanama (%4.8), 9 aspirasyon pnömonisi (%3.4), 3 trakeal kompresyon (%1.1), 2 perforasyon (%0.7) ve 3 özofagorespiratuvar fistül (%1.1)], 334 hastada minör komplikasyon [245 göğüs ağrısı (%91.4), 36 tümörün aşırı büyümesi (%13.4), bir tümörün içe doğru büyümesi (%0.4), 10 kısmi stent migrasyonu (%3.7), 8 stentin mideye düşmesi (%2.9), 12 gastroözofageal reflü (%4.5), 8 stentin yerleştirilememesi (%2.9), 5 hıçkırık (%1.9), 2 yabancı cisim hissi (%0.7), 2 stentin genişlememesi (%0.7), 1 granülasyon dokusu gelişimi (%0.4), 3 stentin gıda ile tıkanması (%1.1), 1 cilt erozyonu (%0.4) ve 1 stent kırılması (%0.4)] tespit edildi. Stent uygulaması öncesi ve sonrasında ortalama disfaji skoru sırasıyla 3.6 ve 2.4 idi. Stent uygulaması sonrası dört hastada (%1.5) mortalite gözlemlendi.

Sonuç: Özofageal stent uygulaması güvenli ve etkili bir yöntem olmasına rağmen birçok komplikasyona neden olmaktadır. Bu komplikasyonların nasıl tedavi edileceğini bilmek hastanın yaşam kalitesini artırıp morbidite ve mortaliteyi azaltabilir.

Anahtar sözcükler: Komplikasyon; özofagus kanseri; stent; tedavi.



Constituting only one percent of all cancers, esophageal cancer ranks seventh among cancer-related deaths.^[1] While the prognosis for this disease is poor, about half of all cases are diagnosed during the inoperable stage. In general, five-year survival is less than 20%.^[2] Self-expanding metallic stents (SEMS) constitute one of the most important methods of palliation in inoperable cases.^[3] In this study, we aimed to present complications arising from self-expanding metallic stents placed in patients with esophageal cancer and the treatment methods for these complications.

PATIENTS AND METHODS

At the Atatürk University of Thoracic Surgery Department, totally 334 metallic stents were placed in 268 patients with inoperable esophageal cancer (140 males, 128 females; mean age 64.4±16.3 years; range 28 to 91 years) between January 2000 and December 2014. Our indications of stent placement were as follows: patients with inoperable tumors refusing chemoradiotherapy, patients with inoperable tumors with no improvement in dysphagia after chemoradiotherapy, patients with esophageal cancer not eligible for surgery and refusing other methods of treatment, patients with malignant trachea-esophageal fistula, and patients with recurrent malignant esophageal stenosis. We analyzed the complications which developed in patients and the adopted treatment approaches retrospectively. We recorded patients' age, gender, tumor location, tumor histopathology, radiochemotherapy history, length of stent, major and minor complications as well as treatment methods. The study protocol was approved by the Medical Faculty of Atatürk University Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographic characteristics of patients are given in Table 1. Before stent placement, localization and length of contrast-enhanced esophagogram and stricture, and presence of any trachea-esophageal fistula were shown. Esophageal stent was placed under fluoroscopy and guidance of endoscopy. In all patients, a self-expanding metallic Ultraflex type esophageal stent (Boston Scientific, Natick, MA, USA) was used. Before stenting, the length of tumoral lesion was evaluated with computed tomography, barium radiography and endoscopy, and the length of the stent to be placed was determined. Primarily, a guide wire was used to pass through the distal parts of the tumor. After fluoroscopic confirmation of intragastric placement of guide wire, the stent was placed to the lesion area through the guide wire. Special attention

was paid on whether the stent placed involved the tumor-free area of 3 cm from the proximal and distal part of the tumoral lesions. In patients whose distal part of tumor could not be reached with the guide wire, stent placement procedure was not carried out. In addition, in cervical spine tumors, no stent was placed in patients with a lesion close to esophageal orifice less than 2 cm. Lengths of the stents placed were 12 cm in 183 patients (54.8%), 10 cm in 76 patients (22.7%), 14 cm 35 patients (10.5%), 15 cm in 19 patients (5.7%), 8 cm in 14 patients (4.2%), and 16 cm in seven patients (2.1%). No stent was placed in eight patients whose distal part of tumor could not be reached with guide wire. Prior to stent placement, 48 patients (17.9%) received chemoradiotherapy. After stenting, eight patients (3.0%) were treated with chemotherapy.

RESULTS

While double stents were placed in 63 patients, four stents were placed in one patient. Major complications developed in 30 patients (11.2%), whereas 330 stent-related minor complications were observed (Table 2). Hemorrhage, although not massive, was observed in 13 patients (4.8%). Hemorrhages in all patients were managed with medical treatment. No bleeding-related mortality was observed.

Aspiration pneumonia was observed in nine (3.4%) patients. Broad-spectrum antibiotics and anti-reflux medical treatment were administered to all patients. Three patients who developed aspiration pneumonia died because of not responding to medical therapy.

After stent placement, tracheal compression was observed in three (1.1%) patients. Stents were removed

Table 1. Patient characteristics (n=268)

	n	%
Gender		
Male	140	52.2
Female	128	47.8
Histology		
Squamous cell carcinoma	161	60
Adenocarcinoma	92	34.4
Other	15	5.6
Tumor localization		
Upper esophagus	8	3
Middle esophagus	85	31.7
Distal esophagus and GEJ	175	65.3
Initial radiochemotherapy		
Yes	77	28.7
No	191	71.3

GEJ: Gastroesophageal junction.

Table 2. Complications

Complication	n	%	1/3 Upper		1/3 Middle		1/3 Lower	
			n	%	n	%	n	%
Hemorrhage	13	4.8	2	11.1	3	2.6	8	3.6
Aspiration pneumonia	9	3.4	2	11.1	5	4.3	2	0.9
Tracheal compression	3	1.1	2	11.1	1	0.8		
Perforation	2	0.7			1	0.8	1	0.4
Esophagorespiratory fistula	3	1.1	2	11.1	1	0.8		
Chest pain	245	91.4	8	44.4	79	68.0	158	68.7
Tumor overgrowth	36	13.4			13	11.0	23	10.0
Tumor ingrowth	1	0.4					1	0.4
Incomplete migration	10	3.7			3	2.6	7	3.0
Complete fall into stomach	8	2.9			1	0.8	7	3.0
Gastroesophageal reflux	12	4.5			2	1.7	10	4.4
Failed stent placement	8	2.9			2	1.7	6	2.6
Hiccup	5	1.9			1	0.8	4	1.8
Sensation of foreign body	2	0.7	1	5.6	1	0.8		
Incomplete stent expansion	2	0.7			1	0.8	1	0.4
Formation of granulation tissue	1	0.4			1	0.8		
Food bolus obstruction	3	1.1			2	1.7	1	0.4
Skin erosion	1	0.4	1	5.6				
Stent fracture	1	0.4					1	0.4
<i>Total</i>	365		18	100	117	100	230	100

in two patients with stenotic lesion in proximal esophagus. Dyspnea disappeared following the removal of stent. In the third patient, the lesion was obliterating the left main bronchus and was also removed. However, patient died during follow-up.

Perforation occurred in two patients (0.7%) while placing the esophageal stent. Perforation diameter was less than 1 cm in both patients (Figure 1). Perforation

areas in both patients were effectively covered using a second stent.

Esophagorespiratory fistula was observed in three patients after one, two, and four months following stent placement, respectively. In one patient, the fistula was close to the cricopharyngeal sphincter. No new stent was placed in this patient, while a feeding jejunostomy was placed. In the other two patients, the fistula was

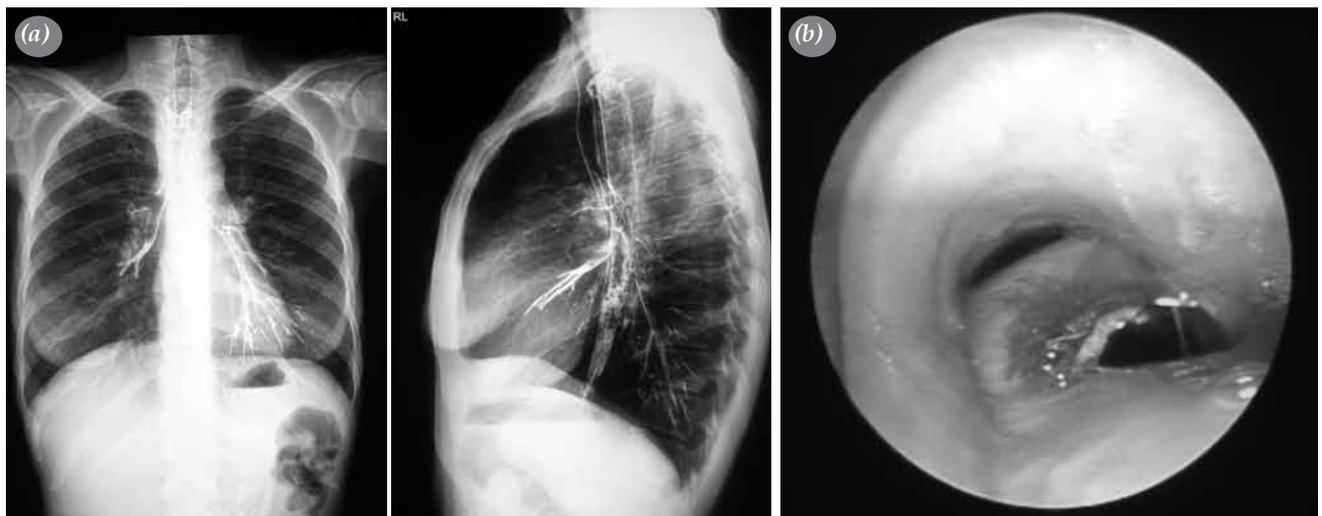


Figure 1. (a) Stent-related tracheal rupture, (b) bronchoscopic image of same patient.



Figure 2. A case of three stenting.

closed using a second esophageal stent. One of these patients died after 15 days due to empyema.

Following stent placement, 245 patients (91.4%) complained of chest pain in various degrees. In patients with mild to moderate pain, pain was managed with simple analgesics. Opioid agents were used in 35 patients with severe pain. A permanent epidural catheter was fitted to a patient with no improvement in pain despite medical therapy.

While tumor overgrowth was observed in 36 patients (13.4%), tumor ingrowth was observed in one patient (0.4%). A new stent was placed in the esophagus in all of these patients (Figure 2).

Stent migration was observed in 18 patients (6.7%). While there was incomplete migration in 10 patients (3.4%), stents had completely dislodged into the stomach in eight patients (2.9%). In patients with incomplete migration, stents were taken to their normal location by rigid esophagoscopy using forceps. By this method, success was achieved in all patients. No procedure-related complications or mortality was observed. Stent was removed by performing gastrotomy after a mini-laparotomy in five of the eight patients in which migration to stomach was observed. In three patients, however, the stents which had fallen into the stomach were removed by flexible endoscopy. A new esophageal stent was simultaneously placed in all patients with total migration.

Gastroesophageal reflux complaint emerged in 12 patients (4.5%). In our study, histamine H₂-receptor antagonists and/or proton pump inhibitors were given routinely to all patients after esophageal stent placement. In addition, patients were recommended to lie down with a 45 degree-pillow, to sleep from four hours after dinner, and to avoid eating reflux-inducing foods. No additional procedures were implemented in patients with gastroesophageal reflux.

Esophageal stent was not correctly placed in eight patients (2.9%) because of the failure to pass through the distal part of the tumor with guide wire. Feeding gastrostomy/jejunostomy was applied to these patients.

Hiccup was observed in five patients (1.9%) following stent placement. Four patients were treated successfully through oral metoclopramide (40 mg per day for three days) and chlorpromazine (50 mg per day for two days). However, one patient did not respond to metoclopramide and chlorpromazine. In this patient, hiccup was treated with baclofen.^[4]

Foreign body sensation was observed in two patients (0.7%). No additional procedures were implemented to these patients and they adapted to esophageal stent in time.

Incomplete stent expansion was detected in two patients (0.7%). In both patients, stents were expanded by balloon dilatation. Subsequently, no migration was observed in any of the patients.

In one patient (0.4%), granulation tissue formation was observed and a new esophageal stent was placed in this patient.

Food bolus obstruction was observed in three patients (1.1%). In these patients, food residues were removed by rigid esophagoscopy and the lumen was reopened.

In one patient (0.4%), fracture was observed in the stent eight months after stent placement. Stent pieces were removed by endoscope and a new stent was placed into the esophagus.^[5]

A patient (0.4%) applied to our clinic with complaint of skin erosion. In this patient, the stent had been placed into proximal esophagus from the external center and esophagoscope could not be inserted into the esophagus due to excessive granulation tissue. The stent could not be removed in this patient who received gastrostomy feeding.^[6]

Using the modified Takita's dysphagia grading system, dysphagia was evaluated in all patients one day before and 48 hours after the procedure. Mean

dysphagia grades before and after the procedure were 3.6 and 2.4, respectively. In our patients, mean survival was 177.7 ± 59.3 days (range 2 to 993 days). The quality of life scores, which were evaluated in 137 (95.1%) patients one day before and one month after the procedure, were 73 ± 10.3 (range 57 to 85) and 112 ± 12.6 (range 90 to 125), respectively.

After stent placement, hospital mortality was observed in four (1.5%) patients (aspiration pneumonia in two patients, fistula-related empyema in one patient, and tracheal compression in the other patient).

DISCUSSION

Esophageal SEMSs are used as a simple, safe, and effective method of palliation in the treatment of obstruction, fistulas or anastomotic leakage due to esophageal cancer.^[7,8] However, complications are still observed in the early (within the first week after stenting) and late periods (after one week) due to the use of metallic stents. Most common major complications in the early period are migration, hemorrhage and perforation, and are reported at an average rate of 6 to 7%.^[9] Frequency of migration, hemorrhage, tumor overgrowth, fistula formation, and food bolus obstruction increase particularly in patients with long lifetimes. In our study, although the ratio of these three complications in early period was 12.3%, no mortality was observed in any of the patients due to perforation, hemorrhage or migration. Among minor complications, chest pain was observed in 91.4% of the patients. Except for the pain, the rate of minor complications comprising migration, gastroesophageal reflux, stent placement failure, hiccup, foreign body sensation, incomplete stent expansion, granulation tissue formation, food bolus obstruction, stent fracture, and skin erosion was 33.6%.

Hemorrhage is the most frequently observed late-term complication, which has been reported between 1 to 12% in different series.^[9,10] Nonetheless, hemorrhage rate in patients with esophageal cancer untreated due to the natural course of the underlying malignancy is 5 to 8%.^[11] The exact cause of hemorrhage has not been clearly understood. However, it is thought that both prosthesis placement and disease progression contribute equally to hemorrhage.^[1] The relationship between patients who received chemoradiotherapy previously and hemorrhage has been found to be significant.^[12] In patients with stents, evaluating the focus of hemorrhage is not possible. In this case, pharmacological treatment should be considered. In post-mortem examinations, it has been shown that, after stent placement, the edge of stent causes necrosis

of the aorta and esophageal wall, and leads to fatal hemorrhage. In addition, stent placement in patients with aortal wall-invasive esophageal tumors may lead to rupture and hemorrhage.^[13] Hemorrhage is usually mild or of a self-limiting type. Mortality may be observed in patients developing severe hematemesis. In case of a severe hemorrhage, angiography should be performed after resuscitation. In rare patients with severe hemorrhage, the bleeding vessel can be managed using angiography and gel foam or coils.^[14] In our study, all patients with hemorrhage were treated pharmaceutically and no hemorrhage-related mortality was observed.

Tracheal compression is a rare but serious complication, secondary to esophageal stent placement. Esophageal stent placement is not recommended in patients with tracheal compression detected by computed tomography or respiratory distress caused by bronchoscopy or balloon dilatation.^[15] Acute tracheal compression can be treated with prompt removal of an esophageal or tracheal stent placement. In our study, stents were removed in patients with stent-related perforation. However, mortality was observed in one patient.

Perforation in SEMSs is one of the challenging complications with high mortality. It has been reported as less than 5% in SEMSs.^[9,16] Perforation is reported to be more frequent in patients who previously received radiotherapy, chemotherapy or laser treatment.^[15] Iatrogenic perforation is usually detected during procedure, however, pneumomediastinum, pneumothorax and leakage in the contrast esophagogram can be detected in radiography. Esophageal perforation detected during the procedure requires emergency intervention. In order to close the perforation, coated stent placement and broad-spectrum antibiotic therapy should be implemented promptly as the least invasive and safest method of treatment in inoperable esophageal cancer. In our study, two patients with stent-related perforation were successfully treated with a second stent.

Malignant esophagorespiratory fistula (ERF) develops most commonly due to esophageal cancer. Risk of ERF in patients with esophageal tumors is 5 to 15%.^[17] The gold standard today in the treatment of these patients is stent placement into the esophagus. However, due to esophageal cancer, ERF may develop in patients with stent due to erosion caused by the stent. During follow-up, ERF has developed in three of our patients due to the stent placed into the esophagus. In these patients, we think that the best approach would be a second coated stent

placement into the esophagus provided that the fistula localization is suitable for this.

Pain after SEMS placement is usually mild and observed in the majority of patients. In these patients, pain continues for a shorter time (two to three days) contrary to rigid prosthesis.^[18] The most probable cause of pain is dilation and distention of the esophageal lumen invaded by tumoral tissue and the expansion of the stent. In addition, esophageal

spasm secondary to acid reflux may also affect pain. While chest pain is observed in almost all of the patients in the early period, prolonged chest pain is observed in less than 13% of patients.^[19] If there are no perforation findings after stent placement, retrosternal pain disappears usually within a few days with analgesic treatment.^[15] However, pain might be severe in some patients who may not respond to anesthetics. Nonsteroidal antiinflammatory analgesic

Table 3. Treatment of complications

Complications	Treatment
Hemorrhage	If bleeding is not severe, transfusion of fresh frozen plasma and erythroid suspension, Angiographic gelfoam or coil application in severe hemorrhage
Aspiration pneumonia	Prevent reflux and suppress acid secretion, Broad-spectrum antibiotics
Tracheal compression	Stents should not be placed closer than 2 cm from esophageal orifice, Removal of a placed esophageal stent or additional tracheal stent placements
Perforation	Covered stent placement, Broad-spectrum antibiotics
Esophagorespiratory fistula	Covered stent placement, Broad-spectrum antibiotics
Chest pain	Nonsteroid analgesics, Opioid analgesics, Epidural catheter
Tumor overgrowth/ingrowth	Argon-plasma coagulation, Endoscopic laser treatment, Electrocautery treatment, Second stent
Incomplete migration	Flexible endoscopy
Completely into the stomach	Removing via endoscopy or gastrostomy
Gastroesophageal reflux	H ₂ -receptor antagonists, Proton pump inhibitors, A 45 degree elevation of the head end of the bed during sleep, A time between meals and sleeping of at least four hours
Hiccup	Gastric decompression together with oral metoclopramide, chlorpromazine, baclofen
Sensation of foreign body	Stents should not be placed closer than 2 cm from esophageal orifice
Incomplete stent expansion	Balloon dilatation
Formation of granulation tissue	Endoscopic laser treatment, Electrocautery treatment, Second stent
Food bolus obstruction	Rigid esophagoscopy
Skin erosion	Stents should not be placed closer than 2 cm from esophageal orifice, If possible, be removed by surgery, Feeding gastrostomy/jejunostomy
Stent fracture	Endoscopic removal, Second stent
Failure stent placement	Feeding gastrostomy/jejunostomy

and opioid combination may be administered to these patients.

The most common late-term complication after stent placement is tumor infiltration affecting both ends of the stent. This complication has been reported in 10 to 20% of patients after an average of three months.^[1,3,20] Coated stent placement may inhibit tumor ingrowth. However, it cannot prevent tumor overgrowth and benign hyperplastic tissue development on the edge of the stent. These problems can be solved with a new stent placement.^[21] In these cases; argon plasma coagulation, endoscopic laser therapy or electrocautery may be employed. Again, in these cases, a second stent placement is also an appropriate method. Considering the tumor growth, we routinely pay attention to the presence of an intact tissue of 2 to 2.5 cm from the proximal and distal part of the tumor when placing the stent. Nevertheless, the rate of tumor overgrowth/ingrowth was 13.8% in our study and a second esophageal stent was placed in all patients.

Stent migration is another common complication. Due to tumor/tissue ingrowth, coated stents are preferred. However, the risk of migration in coated stents is higher.^[22] Particularly, when coated stents are placed in cardia, the migration rate is reported to be 25 to 32%.^[19,23] The reasons for migration may be insufficient expansion of the stent, tumor shrinkage due to chemotherapy or radiotherapy, malposition of the stent, over-dilation of stenosis before stenting or esophageal peristalsis.^[24] Although larger diameter stents seem to be more appropriate to prevent migration, they have been shown to lead to complications more frequently.^[25] If the stent did not migrate too far, it may be pulled back endoscopically to its location. However, removal of the migrated stent may not be achieved in all patients and sometimes may even be dangerous. Alternatively, a second stent may be placed inside the migrated stent. Asymptomatic stents in the stomach may be left there. However, if symptomatic, the stent should be removed by endoscopy or surgical incision.^[3] In our study, while an incomplete migration was observed in 3.7% of the patients, the stent displaced into the stomach in 2.9% of cases. While the stent was pulled back to its normal location by endoscope in all patients with incomplete migration, the stent was removed by employing gastrotomy after a mini-laparotomy in five of the eight patients with total migration to stomach. However, in three patients, the stents which had fallen into the stomach were removed by flexible endoscopy. A new esophageal stent was placed simultaneously to all patients with total migration.

Comprehensively, the rate of re-intervention after esophageal stent placement and the rate of mortality as a direct result of metallic stent placement have been reported to be approximately 25% and 0.5 to 2%, respectively.^[1,3,8,18] In our study, a re-intervention (new stent placement, removal of the stent, stent dilation, or removal of food residues) became necessary in 72 (26.9%) patients. Considering that the mortality rate was low (1.5%) and the mean survival rate was approximately six months in our study, we may conclude that esophageal stent provides significant palliation. Furthermore, we think that, in view of both the literature and our clinical experiences, the treatments presented in Table 3 might be useful in the management of esophageal stent complications.

Our study has several limitations which are usual for retrospective studies, such as selection bias. In addition, longer follow-up is required to fully evaluate the durability of the relief of symptoms and improvement in the quality of life.

In conclusion, self-expanding metallic stents are safe and effective for palliation in patients with inoperable esophageal cancer and permit oral intake by allowing passage in a short duration. However, many complications may arise due to use of these stents requiring re-intervention. Being aware of the methods for avoiding and treating these complications may reduce mortality and improve quality of life.

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