Airway Stenting for Malignant Respiratory Complications in Esophageal Cancer

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Abstract. *Airway stenting is required for the palliative treatment of advanced esophageal cancer. This study retrospectively analyzes the outcomes of airway stenting for esophageal cancer at our institution. Data from nine patients who underwent airway stenting were reviewed. All patients had poor respiratory status due to esophagorespiratory fistula and/or respiratory stenosis. We retrospectively assessed the results of airway stenting as five grades of respiratory symptoms, regarding stent-related complications and clinical course and survival. Six silicone and six covered self-expandable metallic stents were deployed in five and six patients, respectively. Two types of airway stents were deployed in two patients, and double stents were positioned in the airway and in the esophagus of three other patients. The grade of respiratory symptoms improved in seven patients. The mean dyspnea grade was 3.0±0.9 and 1.3±1.3 before and after airway stenting, respectively. Stent-related complications comprised of chest pain, incomplete closure of the ERF, sputum retention and stent migration. The mean±SD survival of all patients was 103±108 (range, 0 to 325) days, and the survival of patients without relapsed cancer at the time of stenting, who underwent cancer-specific therapy after stenting, was prolonged. Although the airway should be stented according to the status and the prognosis of each patient individually stenting can relieve symptoms and improve the prognosis even when esophageal cancer is at very advanced stages. Airway stenting could play a role in the multidisciplinary management of advanced esophageal cancer.*

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Esophageal cancer is often already advanced, unresectable or metastatic at the time of presentation (1). The quality of life (QOL) of patients with esophageal cancer is extremely poor due to esophageal stricture or airway invasion. Esophageal cancer and airway invasion that progresses to esophagorespiratory fistula (ERF) or respiratory stenosis (RS) results in a rapid decline of the overall health status due to respiratory failure (2, 3) and thus, prompt treatment is required. However, the options for treating ERF and RS are frequently limited and challenging due to the poor general status of the patient. Although stent therapy is a useful modality for managing ERF and RS (4-8), it is often associated with complications (2).

Here we describe the outcomes of airway stenting in nine patients with esophageal cancer. We discuss matters of disease management, stent-related complications and options on how to cope with them.

Patients and Methods

Patients' characteristics. We retrospectively reviewed the medical records of nine patients with unresectable advanced or relapsed esophageal cancer after airway stenting between 1999 and 2010. Table I shows the characteristics of the six male and three female patients aged 61.1±10.9 (mean±SD; range, 41-79) years. Eight patients were diagnosed with esophageal squamous cell carcinoma and one (patient 4) had carcinosarcoma. All had respiratory symptoms, aspiration pneumonia and malnutrition at the time of stenting, and poor performance status (PS, ECOG 2-4). Patients 1, 2 and 8 were treated and ventilated in the emergency room for severe respiratory failure.

Airway disorders comprised of ERF (n=5), RS (n=2), and both ERF and RS (n=2). Patient 3 was treated for secondary ERF due to an esophageal stent. The sites of ERF or RS were the trachea in patients 5 and 9, the tracheal bifurcation in patients 1, 7 and 8, the main left bronchus in patients 2, 4 and 6 and the main right bronchus in patient 3.

Deployment of silicone stents and SEMS. ERF and RS in patients with esophageal cancer were managed using silicon stents (Dumon Tube BD; Novatech, Aubagne, France) and covered self-expandable metallic stents (SEMS, Covered Ultraflex Stent System; Boston

Table I. *Patients' characteristics*.

Patient no.	Age, years Gender	Stage† and disease status	Previous therapy	ECOG PS	Respiratory symptoms before stenting	ERF	RS	Site
1	59/M	T4bN2M0 Stage IIIC	–	4	Mechanical ventilation	–	+	Bifurcation
2	79/M	Relapse after CRT (T3N1M0 Stage IIIA)	CRT, EB	3	Mechanical ventilation	+	+	Left bronchus
3	41/M	T4bN1M0 Stage IIIC	CRT	2	Dyspnea and cough	+	–	Right bronchus
4	58/M	Relapse and distant metastasis after CRT (T4bN0M0 Stage IIIC)	EB, CRT	2	Dyspnea and cough	+	–	Left bronchus
5	53/M	Relapse after CRT (T4bN1M0 Stage IIIC)	CRT	2	Dyspnea and cough	+	–	Trachea
6	58/F	T4bN1M0 Stage IIIC	CRT	2	Dyspnea and cough	+	–	Left bronchus
7	66/F	T4bN2M1 Stage IV	RT	3	Dyspnea and cough	+	+	Bifurcation
8	71/F	T4bN1M0 Stage IIIC	–	4	Mechanical ventilation	–	+	Bifurcation
9	65/M	Local recurrence after surgery (T3N1M0 Stage IIIA)	TTE, CRT	3	Dyspnea and cough	+	–	Trachea

M, Male; F, female; CRT, chemoradiotherapy; ERF, esophagorespiratory fistula; PS, performance status; RS, respiratory stenosis; RT, radiation therapy; TTE, transthoracic esophagectomy; EB, esophageal bypass. †TNM grades according to the criteria of the TNM Classification of Malignant Tumors, 7th edition (9).

Scientific, Natick, MA, USA) that were deployed using fluoroscopic guidance under general anesthesia in the operation room. Silicone stents were deployed mainly in the trachea and at the tracheal bifurcation using a rigid bronchoscope. Very severe RS caused by tumors protruding into the airway was ablated using a neodymium yttrium-aluminium garnet (Nd YAG) laser and was mechanically debulked using an external cylinder for the rigid bronchoscope, in order to restore the airway diameter. Compressed RS, due to esophageal cancer, was dilated using a balloon before inserting silicone stents.

The SEMS were inserted into the trachea and the bronchus using a flexible bronchoscope, mainly for ERF. Covered SEMS were deployed in order to tightly close the ERF and to prevent RS recurrence due to tumor growth between the wires of the SEMS.

Assessment of respiratory symptoms. We classified the respiratory symptoms as grades 0-5 based on the Common Terminology Criteria for Adverse Events Version 4.0 (10) in order to assess the results of the airway stenting as follows: no symptoms, shortness of breath with moderate exertion, shortness of breath with minimal exertion that limits instrumental activity of daily living, shortness of breath at rest that limits self-care activity of daily living, and life-threatening consequences indicating urgent intervention, respectively.

Results

Airway stenting and assessment of symptoms. Table II shows the results of deploying 12 stents into the airways of nine patients. Six silicone stents and six SEMS were placed in five and six patients, respectively. Both types of stents were used in patients 3 and 7.

Stents were deployed in the airway and the esophagus of patients 1, 3 and 6. Patient 1 received a silicone Y-stent in the tracheal bifurcation for severe RS, and then an esophageal stent for esophageal stenosis. This strategy improved the respiratory failure and the oral intake in this patient. Although patients 3 and 6 initially received esophageal stents for ERF which developed after chemoradiotherapy, their symptoms did not improve completely. Therefore, stents were deployed in their airways and their symptoms improved.

The grade of respiratory symptoms improved in seven patients after airway stenting (Table II). The mean dyspnea grade was 3.0±0.9 and 1.3±1.3 before and after airway stenting, respectively. Although patients 1 and 8 were under mechanical ventilation, the respiratory failure did dramatically improve due to resolution of the RS using the silicone Y-stent.

All patients were unable to consume any oral nutrition due to airway complications before stenting. However, oral intake remarkably improved in patients 1, 3 and 8 and improved slightly in patients 6, 7 and 9 by relieving respiratory distress or by closing an ERF after airway stenting and/or cancer-specific therapy. Four patients improved sufficiently to be discharged despite having cancer at an advanced stage.

Stent-related complications. Table III shows stent-related complications and the prognosis of the patients. The airways of all nine patients were successfully stented, but patient 4 died of massive hematemesis immediately after treatment. An autopsy of this patient showed that death was not associated with the airway stenting but was caused by rupture of the carotid artery due to relapsed cancer.

Patients 3, 6, 7 and 8 developed the following complications after airway stenting: incomplete closure of the secondary ERF after esophageal SEMS, chest pain after SEMS deployment in the esophagus and the airway, incomplete closure of an ERF after deploying a silicone stent and a SEMS into the airway, and sputum retention as well as stent migration after deploying a silicone Y-stent in the tracheal bifurcation, respectively. Chest pain after stenting the esophagus and the main left bronchus for ERF was resolved by administration of morphine hydrochloride suppositories.

Table II. *Treatment for esophagorespiratory fistula and respiratory stenosis and outcomes of airway stenting.*

Patient no.	Airway stent		Esophageal stent	Dyspnea grade		Oral intake		Hospital discharge after stenting
	Type	Duration (days)†		Before	After	Before	After	
1	Silicone Y	13	+	4	0	No	Possible	+
2	Silicone I	255	–	4	4	No	No	–
3	Silicone Y, I, SEMS	575	+	2	1	No	Possible	+
4	SEMS	224	–	3	NE	No	NE	–
5	SEMS	353	–	2	1	No	Only tubal feeding	–
6	SEMS	140	+	2	1	No	Small meals	–
7	Silicone Y, SEMS	54	–	3	2	No	Small meals	+
8	Silicone Y	4	–	4	0	No	Possible	+
9	SEMS	52	–	3	1	No	Small meals	–

NE, Not evaluable; silicone stent (Dumon type); SEMS, self-expandable metallic stent (Ultraflex type). †Period between diagnosis of esophageal cancer and stent deployment.

Table III. *Complications of airway stenting and prognosis.*

Patient no.	Airway stent-related complications	Post-treatment	Cause of death	Prognosis after stenting (days)†
1	None	CRT	Cancer	197
2	None	–	Cancer	10
3	Incomplete ERF closure	CT	Hematemesis	168
4	None	–	Hematemesis‡	0
5	None	–	Cancer	19
6	Chest pain	–	Cancer	62
7	Incomplete ERF closure	–	Cancer	101
8	Sputum retention and stent migration	CRT	Cancer	325
9	None	–	Cancer	48

ERF, Esophagorespiratory fistula; CRT, chemoradiotherapy. †Period between airway stent placement and death. ‡Carotid artery ruptured by cancer invasion.

A secondary ERF that developed due to an esophageal SEMS in patient 3 could not be completely closed by two silicone stents deployed in the airway. We therefore deployed an additional covered SEMS in the trachea to bridge the gap between the two silicone stents, and this strategy covered several large ERFs (11) (Figure 1).

Esophageal cancer in patient 7 had extensively invaded the tracheal bifurcation and the bronchus, and several ERFs and RS had developed (Figure 2A). Bronchoscopy revealed large ERFs in the tracheal bifurcation and the main left bronchus, and a silicone Y-stent and a SEMS were inserted in the bifurcation and left bronchus, respectively (Figure 2B). Although this strategy did not completely cover the large ERFs, the respiratory symptoms slightly improved and the patient was able to consume small semisolid meals.

Patient 8, who developed sputum retention and stent migration, had esophageal cancer that had extensively invaded the tracheal bifurcation and respiratory failure due to RS, as well as extreme subcutaneous and mediastinal emphysema that probably arose due to communication between the mediastinum and the airway through the tumor (Figure 3A). This patient was referred to our hospital on an urgent basis from another institution where she had already been intratracheally intubated and mechanically ventilated. We deployed a silicone Y-stent at the tracheal bifurcation after YAG-laser ablation and coring of the intratracheal tumor in order to restore the airway caliber (Figure 3B) and concurrently created a tracheotomy and a gastrostomy. The retained sputum required essentially weekly removal through the tracheotomy using a suction device and a flexible bronchoscope. Radiation therapy had considerably reduced the size of the primary tumor and the airway caliber was restored. Thereafter, the stent migrated within the trachea and we removed it through the tracheotomy using forceps. The tracheotomy was useful for addressing the complications of sputum retention and stent migration in this patient. The patient received nutrition through the gastrostomy until radiation therapy improved her ability to consume food orally.

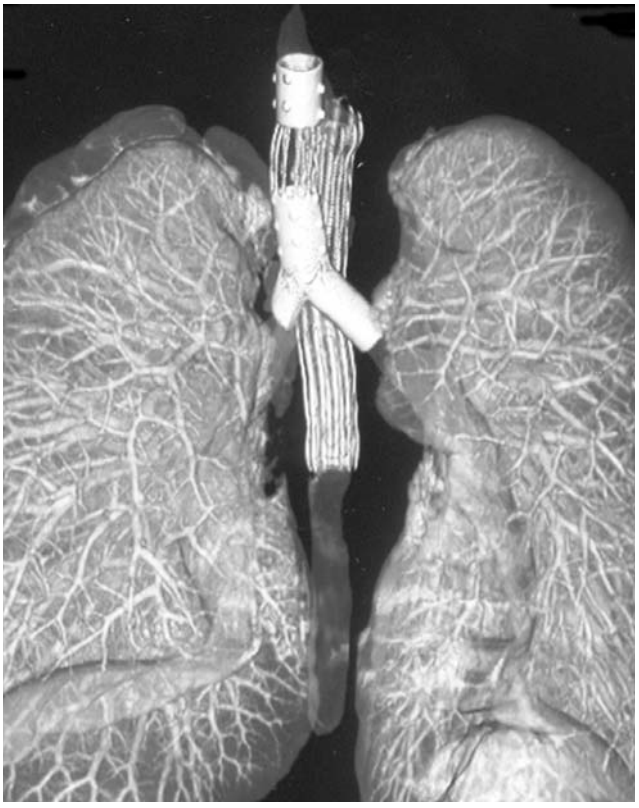

Figure 1. *Three-dimensional computed tomographic (CT) image. Esophageal self-expandable metallic stent and three airway stents consisting of two types.*

Clinical course and survival after airway stenting. Table III shows the clinical course and survival of patients after airway stenting. The mean±SD survival of the nine patients after airway stenting was 103±108 (range, 0 to 325) days. Seven patients died of cancer progression. Patient 3 died of massive bleeding due to hematemesis 168 days after deployement of two stents. Although whether the bleeding was due to cancer progression or the stent was unclear, given the delay between the double stenting and the hematemesis, death might have been caused by cancer progression. Patients 2 and 5 died within 30 days of airway stenting due to multiple organ failure and disseminated intravascular coagulation syndrome caused by cancer progression, respectively.

Chemotherapy and/or radiation therapy were administered after airway stenting in patients 1, 3 and 8 and their mean±SD survival was 230±84 (range, 168 to 325) days compared to 40±38 (range, 0 to 101) days for the six patients who did not undergo these additional therapies after stenting. The mean±SD survival periods after stenting four patients with, and five without cancer relapse or recurrence at the time of stenting were 19±21 (range, 0 to 48) and 171±101 (range, 62 to 325) days, respectively. The prognosis was obviously better for the patients without cancer relapse or recurrence at the time of stenting who could undergo subsequent cancer-specific therapy.

Discussion

Airway complications are thought to affect between 4.7% and 9.4% of patients with esophageal cancer (12-14). Airway complications frequently become life-threatening for patients with an already extremely poor QOL and general condition. Although airway stenting can remarkably improve the QOL of patients with advanced esophageal cancer (8), it can also be associated with morbidity and even mortality (2, 15). We have described the cases of nine patients who underwent airway stenting for esophageal cancer accompanied by ERF and/or RS, and analyzed the value of this procedure as well as the associated complications.

We deployed two types of stents with different advantages and disadvantages. The advantages of silicone stents are the relatively low rates of trauma and perforation, since they are not expandable, they can be easily and safely removed and the stent wall is impervious to intraluminal tumor progression. The disadvantages include a relatively higher rate of migration, granulation tissue formation at the ends of these stents and intraluminal plugging with sputum. Often regarded as a disadvantage of silicone stents, rigid bronchoscopy conversely allows, superior airway control while offering the capacity to maintain ventilation, which might actually render the procedure safer for patients with airway complications (2, 6). On the other hand, SEMS can be easily deployed in the airway and they exert expansion force on the airway walls, resulting in relatively lower migration rates. However, the rates of vascular and airway trauma are potentially higher, and adjustment of the position of such stents or their removal is impossible (2, 6, 16, 17).

We mainly used silicone stents for patients with RS in the tracheal bifurcation and for patients with improved respiratory status due to stenting, who could undergo cancer-specific therapy. These stents are suitable for deployment in the bifurcation and the absence of an expansion force is unlikely to result in airway trauma after radiation therapy. We deployed covered SEMS to tightly close ERFs. We initially deployed a covered SEMS in the esophagus for the inflammation subsides, approximately one month after radiation therapy. If this did not control the symptoms, we deployed a second covered SEMS in the airway. The features of these two types of stent should be fully utilized according to the status and type of treatment administered to individual patients.

Chemotherapy and radiation therapy can also relieve dysphagia and respiratory symptoms of esophageal cancer. We generally perform chemoradiotherapy as a first-line therapy, with high-calorie infusion for patients with less severe respiratory symptoms who cannot consume oral nutrition, even if esophageal cancer has invaded the airway. Therefore, all nine

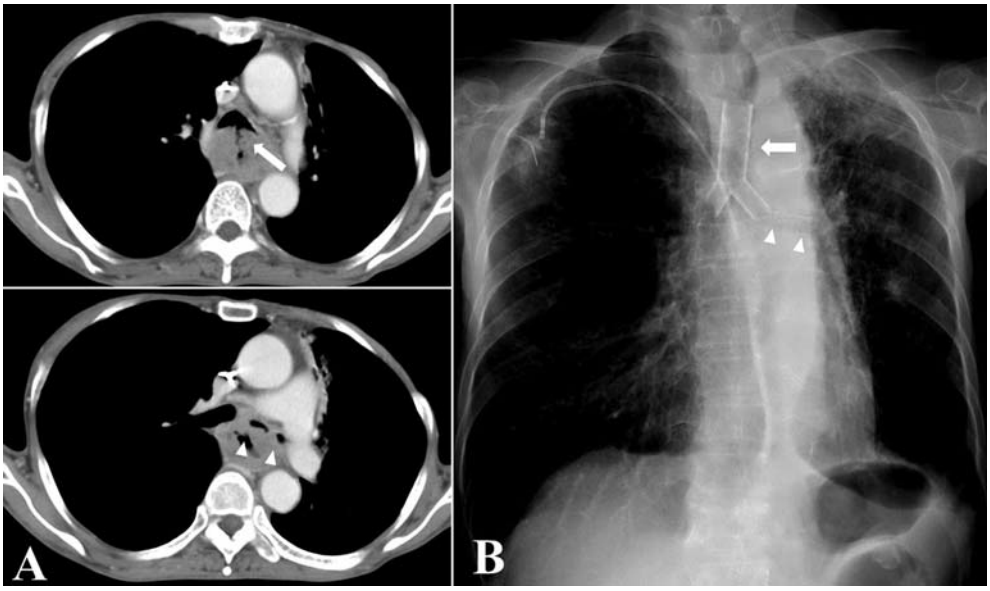

Figure 2. *Chest and radiographic images. A: Chest CT shows the esophagorespiratory fistula at tracheal bifurcation (arrow) and a stenosis of the left main bronchus (arrowheads). B: Chest radiography shows the silicone Y-stent (arrow) and the self-expandable metallic stent (arrowhead) deployed in the bifurcation and the left main bronchus, respectively.*

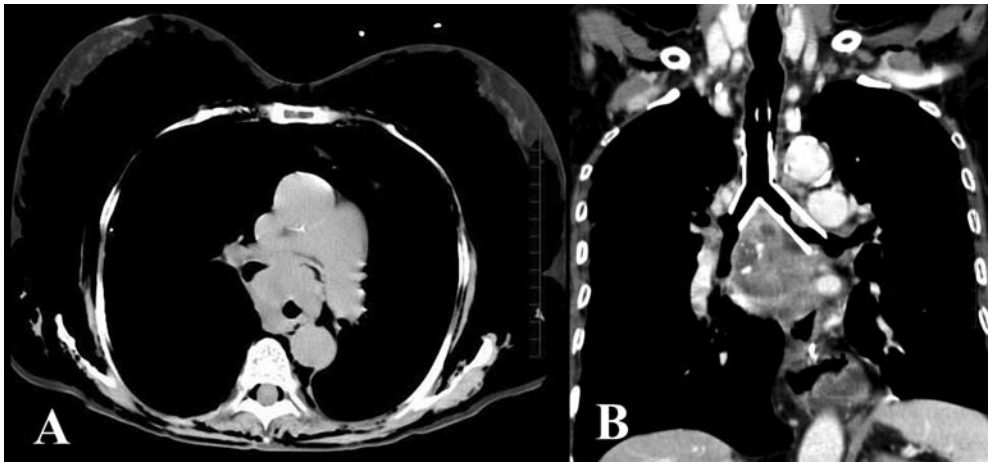

Figure 3. *Chest scans. A: Esophageal cancer has extensively invaded the tracheal bifurcation which is severely stenosed, and subcutaneous and mediastinal emphysema is evident. B: Chest CT scan shows silicone Y-stent at the tracheal bifurcation.*

patients in the present study had advanced-stage esophageal cancer with severe respiratory symptoms due to ERF and/or RS that required rapid treatment. Despite these extreme conditions, dyspnea grades improved in seven of them after airway stenting. Silicone Y-stents deployed in patients 1 and 8 with fatal disease and severe RS in the tracheal bifurcation resulted in improvement of their respiratory status to the extent that chemoradiotherapy could be administered.

Patients with airway complication, especially ERF, cannot take any oral nutrition. Airway stenting followed by cancer-specific therapy remarkably and slightly improved oral intake in three patients each. The combination of airway stenting and subsequent cancer-specific therapy improved the QOL for the patients, and reduced the tumors, which prolonged survival.

Various complications associated with airway stenting, such as migration, mucous plugging, tumor and granuloma overgrowth and airway trauma have been reported (2). The reported frequency of minor and major complications ranges from 15% to 60% (4, 5, 16, 18). Closure after airway stenting was incomplete in two of our patients (patients 3 and 7).

Several secondary ERFs due to esophageal stenting developed in patient 3 and three airway stents were subsequently needed to close and control them. This patient was managed by the use of two types of stents, which preserved his oral intake and QOL as an outpatient until the end of life (11).

Patient 8 developed sputum retention, which is a recognized complication following the use of silicone stents. We concurrently created a tracheotomy and a gastrostomy with airway stent deployment in this patient. One week later, the tracheotomy tube was changed to a vocable tube, through which the sputum was easily eradicated using a suction device or a flexible bronchoscope. Enteral nutrition was also administered until this patient was able to consume satisfactory amounts of oral nutrition due to improvements conferred by subsequent chemoradiotherapy. Tracheotomy and gastrostomy are also useful supportive procedures for patients with advanced esophageal cancer. Because the disease status of very advanced esophageal cancer considerably varies among patients, combining stents with supportive care is also needed in order to improve their QOL.

The survival of most patients with advanced esophageal cancer who undergo stent therapy typically ranges from 8 to 40 weeks (5, 12, 18, 19). The mean±SD survival of our patients after airway stenting was 103±108 (range, 0 to 325) days and the prognosis was similar to the results published by others. Furthermore, the present study uncovered a considerable difference in survival between patients with and without relapsed or recurrent cancer after cancer-specific therapy, and those with and without cancer-specific treatment after airway stenting. Not only the symptoms, but also the prognosis of patients without cancer relapse or recurrence can be improved by stenting followed by cancer-specific therapy.

In conclusion, stents should be deployed in the airway after consideration of the status and the prognosis of patients with esophageal cancer and malignant airway complications. They are also useful in regard to symptoms relief and improvement of prognosis of even patients with extremely advanced esophageal cancer. Stent-related complications can be addressed by appropriate supportive care. Despite the small patient cohort analyzed herein, we consider that airway stenting can play a drastic role in the multidisciplinary management of advanced esophageal cancer.

Conflict of Interest

There is no conflict of interest regarding the manuscript.

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