Malignant Tracheobronchial Strictures: Palliation with Covered Retrievable Expandable Nitinol Stent

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PURPOSE: To evaluate the safety and clinical effectiveness of a covered retrievable expandable nitinol stent for the treatment of malignant tracheobronchial stricture and/or esophagorespiratory fistula (ERF).

MATERIALS AND METHODS: With fluoroscopic guidance, stents were placed in 35 symptomatic patients with malignant tracheobronchial stricture and/or ERF in most cases caused by lung or esophageal cancer. The site of stricture was most commonly at the trachea or left main bronchus. If there were complications, the stent was removed with a retrieval set. Nine patients had combined symptomatic ERF.

RESULTS: A total of 47 tracheobronchial stents were placed and were technically successful and well-tolerated in all patients. Improvement of dyspnea was achieved in 92% of the patients (24 of 26 patients). Associated ERF in nine patients was effectively treated with tracheobronchial stent placement with or without esophageal stent placement. Stent migration, tumor overgrowth, symptomatic sputum retention, and hemoptysis occurred in 17% (6/35), 6% (2/35), 20% (7/35), and 17% (6/35) of patients, respectively. There were no documented cases of tumor ingrowth. Stent removal was performed easily in five patients when stent migration (n = 2), severe pain (n = 1), tumor overgrowth (n = 1), or persistent gastrobronchial fistula (n = 1) developed. All patients died 2 days to 26 weeks (mean, 9.62 weeks) after stent placement because of disease progression (n = 18), pneumonia (n = 9), hemoptysis (n = 5), or unknown cause (n = 3).

CONCLUSION: Use of a covered retrievable expandable nitinol stent is a safe and effective method for relieving dyspnea. This procedure contributed to improved quality of life for patients with malignant tracheobronchial stricture and/or ERF. Stent retrievability was useful in resolving stent-related complications.

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Abbreviation: ERF = esophagorespiratory fistula

IT is well known that fluoroscopic placement of an uncovered or covered expandable metallic stent is a safe, easy, and effective treatment for patients with inoperable malignant strictures of the tracheobronchial tree with resultant dyspnea. In addition, metallic stent placement is believed to considerably reduce the morbidity and complication rates associated with conventional nonexpandable plastic tubes (1–3). It is also well known that uncovered expandable metallic stents have a high recurrence rate of stricture because of progressive tumor ingrowth or granulation tissue and are not suitable for esophagorespiratory fistula (ERF) (4–10). There is also a slightly higher chance of stent fracture with possible wall perforation but less chance of stent migration (4–10). However, covered stents have less chance of tumor ingrowth, granulation tissue formation, or stent disruption and are suitable for ERF but there is a greater chance of stent migration (1,2,11–14).

To overcome the shortcomings of the uncovered stent and the difficult or impossible retrievability of uncovered and covered stents, Song et al designed a covered retrievable expandable nitinol stent and reported their initial experience in patients with benign and malignant tracheobronchial strictures (4). In their report, tumor ingrowth was effectively prevented and stent relocation or removal was possible when the stents were misplaced or had migrated. However, their study had only 13 patients, including eight patients with malignant tracheobronchial strictures, and a limited follow-up period.

The purpose of this study is to evaluate the safety and clinical effectiveness of a covered retrievable expand-
Hugh-Jones Classification for Assessment of Breathlessness on the Basis of Daily Activities (15,16)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>The patient’s breathing is as good as that of others of the same sex, age, and build while at work, on walking, or on climbing hills or stairs</td>
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<tr>
<td>II</td>
<td>The patient is able to walk with healthy persons of the same sex, age, and build on the level but is unable to keep up on hills or stairs</td>
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<tr>
<td>III</td>
<td>The patient is unable to keep up with healthy persons on the level but is able to walk a mile or more at a slow speed</td>
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<td>IV</td>
<td>The patient is unable to walk more than 100 yards on the level without a rest</td>
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<tr>
<td>V</td>
<td>The patient is breathless on talking or undressing or is unable to leave the house because of breathlessness</td>
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Figure 1. Left to right: Straight type tracheal stent for middle or upper tracheal strictures, the distal flared type tracheal stent for lower tracheal strictures, the hinged type stent for lower tracheal strictures extending to the main stem bronchus, and the bronchial stent which is flared proximally and distally.

Stent Construction and Stent Introducer and Retrieval Set

The stent was woven from a single thread of 0.2-mm-diameter nitinol wire in a tubular configuration and covered by being dipped in a 12% polyurethane solution (Chronoflex; Cardiotech International, Woburn, MA) to prevent tumor growth or granulation tissue through the stent wires. Four types of retrievable nitinol stents were used (Fig 1). The tracheal stent was 16 or 20 mm in diameter when fully expanded and 40–50 mm long, and the bronchial stent was 10 or 12 mm in diameter and 30–40 mm long. The hinged stent was placed in the bifurcation area, a tracheal stent was placed in the lower trachea, and a bronchial stent was placed in the left main bronchus. To make a hinged stent, the ends of a tracheal stent and a bronchial stent were connected at one point without overlap with use of nylon monofilament. To make the stent removable, a 2-mm-diameter nylon loop was hooked inside of each bend in the upper end of the stent and another nylon thread was passed through each of the nylon loops to form a larger loop (drawstring) that filled the circumference of the inside of the proximal stent. The stent was constructed according to these specifications by a local manufacturer (Tae-woong, Seoul, Korea).

A tracheal stent introducer set includes a 21-F sheath, a 12-F breathing tube, a pusher catheter, and a balloon-guided catheter 8 mm in diameter and 3 cm long (Meditech/Boston Scientific, Watertown, MA) (Fig 2). After passing the tracheal stent introducer set over a guidewire, the balloon-
guided catheter is deflated and removed from the breathing tube so that the patient can breathe during the procedure. A bronchial stent introducer set includes a 14-F sheath, a dilator, and a pusher catheter (Fig 2). A stent retrieval set consists of a 13-F sheath, a 10-F dilator, a hook wire, and a 0.035-inch guidewire (Terumo, Tokyo, Japan) (Fig 3). The hook wire was constructed in the research laboratory with a nitinol wire. The end of the hook wire was constructed in a question mark configuration to hook the drawstring of the stent.

Stent Placement and Removal

Stent placement and removal were performed by one of four interventional radiologists (J.H.S., G.S.J., G.Y.K., H.Y.S.). The site, severity, and length of the stricture were evaluated before tracheal or bronchial stent placement by means of conventional radiography/fluoroscopy, computed tomography (CT), and bronchoscopy. The detailed technique of tracheal or bronchial stent placement as well as stent removal is the same as described in the authors’ previous report (4). A stent at least 10 mm longer than the stricture, was selected so that the proximal and distal parts would rest on the upper and lower margins of the stricture, respectively.

The stent was removed if complications such as severe pain or migration occurred. After the nylon drawstring was grasped with the hook wire, the hook wire was withdrawn into the sheath to collapse the proximal stent and the entire assembly was removed together (Fig 3).

Follow-up

All patients underwent conventional radiography 1–3 days after stent placement to verify the state of expansion and the stent position. If follow-up conventional radiography showed full expansion of the stent, bronchoscopy was routinely performed to verify stent patency and position.

Interviews with the patients as well as fluoroscopic examinations were performed 1 week after stent placement and then every month to obtain detailed clinical information and to detect stent migration, ERF, or formation of tumor ingrowth or granulation tissue. Follow-up bronchoscopy was performed only in patients with recurrent aggravated dyspnea or unusual symptoms. When interview and fluoroscopic examination were not practical because a patient was severely ill, the patient or their family was contacted by telephone every month for as long as the patient remained alive. During the follow-up period, the following information was specifically requested and documented: degree of
dyspnea; chest pain; symptoms of aspiration or sputum retention; hemoptysis; and whether these symptoms were severe enough to require treatment.

**Statistical Analysis**

To evaluate the improvement of dyspnea based on Hugh-Jones classification, a Wilcoxon signed rank test was used. When a patient died, their cause of death was determined after review of the medical records or a telephone interview. The Kaplan-Meier method was used to determine the cumulative survival period from the time of stent placement and the log rank test was used to evaluate the survival period according to the cause of death. To evaluate if there was a significant difference in the survival period according to the cause of death, the patients were divided into two groups according to disease progression and other causes. It was surmised that disease progression could reflect the natural course of the patient and the other causes could include the stent-related complications. The SPSS version 10.0 statistical package (SPSS, Chicago, IL) was used to perform the analyses. A P value of < .05 was considered statistically significant.

**RESULTS**

**Stent Placement**

A total of 47 tracheobronchial stents (21 tracheal stents, 22 bronchial stents, and four hinged stents) were placed to treat tracheobronchial stricture or combined ERF or to treat complications (Fig 4, 5). In seven patients the stent was misplaced but was immediately relocated successfully. Thus, stents were placed successfully in all 35 patients. Twenty-four patients with tracheobronchial stent placement experienced dull chest pain for 1–3 days after stent placement, and one patient complained of severe pain and required stent removal. No serious procedural complications occurred. In addition to the tracheobronchial stents, 11 esophageal stents were placed to treat ERF or associated complications. An improvement of more than one grade of the Hugh-Jones classification was seen in 92% of patients (24 of 26 patients); grade V in two patients, grade IV in two patients, grade III in seven patients, and grade II in 15 patients. Bronchoscopy performed after full stent expansion showed that the lumen remained patent within the stent.

In nine patients with ERF, the tracheobronchial stent (n = 6) or both tracheobronchial and esophageal stents (n = 3) were placed to seal off the fistula. Tracheobronchial stents were placed because of previous Ivor-Lewis surgery (transthoracic esophagectomy with bowel interposition) (n = 3), extrinsic tracheal compression by previous esophageal stent (n = 2), presence of an esophageal stent (n = 1), combined tracheal and esophageal strictures (n = 1), moderate tracheal stricture without esophageal stricture (n = 1), or mild state of esophageal stricture after esophageal stent removal (n = 1). Both tracheal and esophageal stents were placed in three patients; simultaneously in one patient who showed combined tracheal and esophageal stricture, and 4 days or 2 weeks after initial esophageal stent placement in two patients with extrinsic tracheal compression by the esophageal stent. After stent placement, the fistula was controlled completely in eight patients, but controlled incompletely in one patient; however, there was much improvement in the aspiration symptoms in this patient.

**Stent Removal or Expectoration**

Removal of the stent was performed and well tolerated in five patients, but complete migration (spontaneous expectoration) of the bronchial stent occurred in two patients. The cause of stent removal was partial stent migration in two patients, severe pain or aggravation of dyspnea caused by tumor overgrowth in two patients, and persistent gastrobronchial fistula in the remaining patient. Re-insertion of the stent followed in four patients: two patients with complete stent migration, one patient with partial stent migration who underwent bronchial stent placement immediately after detection of stent migration, and one patient who underwent a slightly wider second bronchial stent (14 mm diameter) placement just after removal of the original bronchial stent (12 mm diameter) because there was persistent gastrobronchial fistula (Fig 5).

**Complications and Reintervention**

Stent migration occurred in six patients (six of 35 patients, 17%) 1 day to 2 weeks (average, 5 days) after stent placement. It was complete (expectoration) in two patients and partial in four patients. As a treatment, additional bronchial stent placement was performed in four patients and intubation in one patient. The one remaining patient with partial stent migration did not undergo further treatment because of deteriorating clinical status and the patient died 1 day after the stent migration. The four patients who underwent second stent placement showed marked symptom improvement until death.

Besides ERF detected before stent placement in nine patients, esophageal bronchial and esophagotracheal fistulas occurred with aspiration symptoms 16 weeks after bronchial stent placement in one patient with recurrent esophageal cancer. During follow-up, this patient underwent placement of four esophageal stents and one tracheal stent with a decreased amount of contrast material passed through the fistula. In this patient, esophagobronchial fistula was presumed to be a possible complication after bronchial stent placement because the fistula site corresponded to the proximal margin of the inserted bronchial stent; however, there was no evidence of bronchial stent breakage.

Tumor overgrowth occurred at the margin of the tracheal stent in two patients (two of 35 patients; 6%), one with thyroid cancer and one with lung cancer. Tumor overgrowth manifested as aggravation of dyspnea in each patient 5 and 10 weeks, respectively, after tracheal stent placement. The patient with thyroid cancer underwent removal of protruded tumor including the tracheal stent 1 week after detection of the tumor overgrowth but died from airway obstruction by uncontrollable tumor regrowth 3 weeks after stent removal. The other patient with lung cancer underwent left bronchial stent placement after detection of tumor overgrowth at the lower margin of the tracheal stent because the right main bronchus was nearly obstructed by the tumor mass and the right lung
Figure 4. A 63-year-old man with luminal narrowing of the trachea by invasion of metastatic paratracheal lymphadenopathy from rectal adenocarcinoma. (a) A three-dimensional CT image shows irregular narrowing of the tracheal lumen (arrows). (b) An axial CT image through the trachea shows an irregular soft tissue mass (arrows) protruding into the tracheal lumen. (c) A fluoroscopic image obtained during stent placement shows a tracheal stent introducer set (arrows) passing over the narrow segment of the trachea. (d) A fluoroscopic image obtained immediately after stent placement shows the stent fully expanded.
was nearly destroyed and had collapsed; this patient died from airway obstruction by tumor overgrowth at the distal portion of the left bronchial stent 10 weeks after bronchial stent insertion.

Sputum retention was symptomatic and aggravated during the 1-month follow-up after stent placement in seven patients (seven of 35 patients; 20%). In these seven patients, the sputum was yellowish and purulent.

Figure 5. Images from a 54-year-old man with gastrobronchial fistula after Ivor-Lewis surgery for esophageal cancer. (a) An axial CT image at the level of the carina shows a large gastrobronchial fistula (arrow). (b) Esophagography shows definite contrast in the right side bronchus (arrows). (c) Esophagography obtained immediately after stent placement (12 mm in diameter) shows the stent fully dilated; however, the gastrobronchial fistula is still persistent. (d) Stent removal was performed 5 days after stent placement because of persistent fistula. (e) Esophagography obtained immediately after insertion of the second, slightly larger diameter (14 mm) bronchial stent shows that the fistula has disappeared. (continues)
Among them, two patients died from increased sputum and subsequent pneumonia.

Hemoptysis occurred in six patients (six of 35 patients; 17%) 1–7 weeks (average, 3.8 weeks) after stent placement. It was sudden and massive and was the cause of death in five patients, while in one patient with tracheal cancer, the oozing-like bleeding was detected at the upper portion of the stent on bronchoscopy 3 weeks after tracheal stent placement. It was surmised that it originated from the friable tracheal tumor mass but it disappeared spontaneously within 2 days.

Statistical Analysis

The grade of dyspnea significantly decreased after stent placement in 26 patients without associated ERF (Wilcoxon signed rank test, \( P < .05 \)).
During the follow-up period, all 35 patients died 2 days to 26 weeks after stent placement because of disease progression \((n = 18)\), pneumonia \((n = 9)\), hemoptysis \((n = 5)\) or an unknown cause \((n = 3)\). The mean survival period \(\pm SD\) was 9.62 \(\pm\) 8.35 weeks. A test was performed to determine whether there was a significant difference in the survival period according to the cause of death between disease progression \((n = 18)\) and other causes \((n = 17)\). The mean survival period \(\pm SD\) was 13.94 \(\pm\) 2.37 weeks in patients who died from disease progression and 4.47 \(\pm\) 1.07 weeks in patients who died from other causes. There was a statistically significant difference in the survival period of the two groups (log rank test; \(P < .01\)) (Fig 6).

**DISCUSSION**

Tracheobronchial stenosis or obstruction caused by end-stage malignancies produces severe dyspnea and is associated with high morbidity and possibility of early death \((3,4)\). It is well known that different kinds of uncovered or covered expandable metallic stents have been used safely and effectively to treat patients in whom surgery is contraindicated. The advantages of the use of a conventional uncovered expandable metallic stent are the superior mucociliary clearance and low incidence of stent migration as well as the benefit of extrinsic tumor compression. The superior mucociliary clearance with resultant decreased sputum and the low incidence of stent migration occur because only a small area of mucosa is covered by the stent and the metal lattice becomes overgrown with ciliated respiratory epithelium \((2-5,17,18)\).

However, the use of uncovered expandable metallic stents in the treatment of malignant tracheobronchial stenosis has some limitations. Progressive tumor ingrowth/overgrowth or granulation tissue through the openings between the wire filaments tends to cause progressive dyspnea and there is a slightly higher chance of stent fracture and possible laceration or perforation of the bronchial mucosa. Furthermore, they are not suitable for use in treatment of ERF \((4-10,17,19)\). To overcome the shortcomings of uncovered expandable metallic stents, covered expandable metallic stents have been developed \((1-4,10-13,19)\). Although they may improve the long-term patency of the stent lumen, they may also increase the risk of stent migration and occlusion of upper or middle bronchi or smaller bronchi \((2,3,12,20)\). Some investigators have tried to develop a partially covered stent to overcome the shortcomings of uncovered and covered stents \((12,13)\). Miyayama et al \((12)\) placed Gianturco stents partially covered with polyurethane in two patients with malignant bronchial stricture and asserted that stent migration and occlusion of small bronchi by the covered portion may decrease if the covered portion is kept to a minimum. Kishi et al \((13)\) placed two Z-stents partially covered with dacron in both main bronchi in one patient with lung cancer and reported that the stent was effective in preventing tumor ingrowth into the stent. Recently, Madden et al \((11)\) reported that the Ultraflex expandable metallic stents partially covered with polyvinyl chloride were effective in 25 patients with malignant and benign tracheobronchial strictures, and that there was no stent migration. However, the length of this kind of partially covered stent must be longer than the expected length to cover the stricture because the uncovered part must be present to prevent stent migration; they are also difficult and dangerous to remove, especially if the metallic mesh of the bare portion is overgrown by granulation tissue.

Therefore, it is believed that covered stents are superior to uncovered stents if they can be removed if there are complications, such as stent migration, or when they are no longer necessary as in patients with malignant lymphoma, who may have stents removed after chemotherapy or radiation therapy \((21)\). In this study, stent retrievability was technically easy and very useful when stent migration occurred or the patient’s clinical status worsened after stent placement. In the report by Filler et al \((22)\), stent removal was performed through a bronchoscope with use of general anesthesia and grasping forceps in children with previous Palmaz stent insertion. The investigators held and twisted the stent several times to decrease its diameter and then withdrew the smaller twisted stent into the bronchoscope; there was a potential risk of mucosal bleeding and airway occlusion during the procedure in cases of tight welding of the stent into the tracheal wall. However, the removal technique used in this study is very safe because the stent can easily be collapsed with the hook-like device, pulled upward into the sheath, and the entire assembly withdrawn without difficulty because the stent is completely covered and optimally designed for removal.

In this study, tracheal or bronchial stent placement with or without esophageal stent placement was performed as a first treatment or during the follow-up period in nine study patients with associated ERF not only because there was a higher chance of esophageal stent migration owing to previous Ivor-Lewis surgery but also because some patients had associated dyspnea secondary to tracheobronchial stricture or tracheal compression. All study patients experienced either disappearance or great improvement of their symptoms of aspiration and dyspnea after the tracheobronchial stent placement. After Ivor-Lewis surgery, the replaced stomach or colon shows a large lumen compared with the lumen of the original esophagus. Therefore, a stent with a large diameter is necessary to cover the large surface of the lumen when a stent is inserted into the replaced stomach or colon. Otherwise, tracheal or bronchial stent placement may be a good alternative, especially in cases of associated tracheobronchial stricture. Morgan et al \((23)\) placed two covered stents in the trachea when ERF of the upper esophagus was difficult to treat with esophageal stents; they obtained encouraging results. Nomori et al \((24)\) reported placement of double stents in both the esophagus and trachea for the treatment of esophageal or bronchogenic carcinoma with both esophageal and tracheobronchial stricture. However, they documented that there is a high risk of fistula developing or growing because of necrosis of both the esophageal and tracheobronchial walls from the pressure of the stents. In this study, there were no patients who showed development or enlargement of fistula after both esophageal and tracheal stent placement.

In this study, tumor overgrowth along the margin of the stent was detected in two patients with dyspnea
aggravation, but there was no documented case of tumor ingrowth. These results show that a covered stent is very effective in preventing tumor ingrowth compared with previous studies with uncovered stents that included more than five and fewer than 36 patients and reported tumor ingrowth of up to 24% (5,7,8,18). Prevention of tumor ingrowth is considered to be the strongest indication for use of covered stents in malignant tracheobronchial strictures.

Symptomatic sputum retention was 20% in this study, but it was reported to be as much as 38% after covered stent placement and less than 20% after uncovered stent placement (1,6,11). Covered stents have the potential disadvantages of impeding mucociliary clearance, thereby fostering sputum retention (11). However, the description of sputum retention has been poor in previous reports probably because it is difficult to discern whether the symptomatic sputum retention occurred as a consequence of the placed stent or because of combined lung parenchymal abnormality especially when it was present before stent placement. In instances where a covered stent is used, the occurrence of sputum retention could be reduced if the internal surface of the covering material was smoother or hydrophobic (1).

Hemoptysis has been reported to be 6%–18% in previous studies with uncovered stents (5,6,8,25) that included more than seven and fewer than 36 patients. If it is presumed that massive hemoptysis originates from eroded vessels because of broken stents (6), it can be expected that the incidence of fatal hemoptysis might be reduced in patients with covered stent placement. However, the fatal hemoptysis rate was still high, at about 17% (6 of 35 patients), in this study with covered stents. It is difficult to determine whether hemorrhage was related to the inserted stent or the patient’s underlying disease or natural disease course.

That the survival period of the patients who died from disease progression was significantly longer than those who died from the other causes such as pneumonia, hemoptysis, or an unknown cause (13.94 ± 2.57 weeks versus 4.47 ± 1.07 weeks), and pneumonia or hemoptysis could be regarded as stent-related complications, indicates that their survival could be improved by preventing potential complications. The short mean survival period of 9.62 weeks along with the wide range of the standard deviation, suggests that the most of the patients in this study had advanced stages of malignancy although they varied in the severity of their general condition.

Bronchoscopic examination was useful for evaluating lesion characteristics as well as the degree of luminal narrowing before stent placement and its location and patency to the distal airway after placement. Bronchoscopic examination was also useful for locating the orifice of the stricture and for advancing a guidewire through it. However, it was not so difficult to insert a stent introducer and deploy the self-expandable metallic stents to appropriate locations under fluoroscopic guidance only. The fluoroscopic guidance has several advantages over endoscopic guidance for the placement of self-expandable metallic stents. First, the stricture length can be measured correctly with a sizing catheter and the proximal and distal locations of the stricture can be marked on the patient’s skin with radiopaque markers. Second, the stent can be deployed more accurately because the total length of the stricture and the deploying stent as a whole can be seen. Third, topical anesthesia of the larynx and pharynx is adequate for placing self-expandable metallic stents with fluoroscopic guidance because a smaller diameter introducer set can be used. However, general anesthesia is mandatory when a rigid bronchoscope is used.

In conclusion, the long-term follow-up results show that use of covered retrievable expandable nitinol stents offers a safe and effective method for relieving dyspnea and improves quality of life for patients with malignant tracheobronchial stricture and/or ERF. Furthermore, stent retrievability was useful when there were stent-related complications.

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References


