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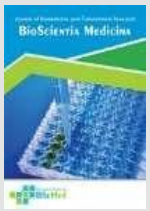

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Airway Stent in Lung Cancer: A Narrative Literature Review

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A B S T R A C T

Lung cancer complications are the leading cause of death in lung cancer patients. This study aimed to describe the prevalence of stent placement, indications for stent placement, success and complication rates, and prognosis of airway stent placement in patients with lung cancer. Malignant central airway obstruction (MCAO) is one of the significant complications. Insertion of airway stent can restore airway patency in more than 90% of patients with MCAO. Airway stent placement is indicated in patients with extrinsic lesions, obstruction of ≥ 50%, have patent airway below the obstruction, and are not in the terminal state. The technical success was reported to be very high and consistent with the range of 95-100%. Early complications were relatively rare; however, up to 87% of long-term complications were reported. Stent placement is a risk factor for lower respiratory tract infection, an adverse prognostic factor in lung cancer survival. Airway stents should be indicated and used with caution and discretion. With the advancement and development of technology, various materials and types of airway stents are being developed to minimize adverse outcomes.

1. Introduction

Lung cancer is the most deadly malignancy among other diseases. Most deaths from lung cancer are related to complications from the course of the disease. Main airway obstruction is one of the complications leading to hemoptysis, atelectasis, and obstructive pneumonia. These complications cause disability in the patient's daily life activity and increase the risk of repeated hospitalization due to respiratory failure.[1,2]

Malignant central airway obstruction (MCAO) is defined as occlusion of 50% main airway cross-sectional area and occurs in 20-30% of primary lung malignancy cases. The trachea and the main bronchus branches are both included in the definition of "main airway." In contrast to the lobar and segmental bronchus, known as the lower airway, the main airway only contain a small amount of collateral ventilation.[3,4] The majority of patients with MCAO have endoluminal metastases or extrinsic compression of massive lymphadenopathy as the underlying etiology. In patients with MCAO, surgical intervention is not effective in relieving the acute symptoms of airway obstruction. Chemotherapy or radiotherapy takes a long time to relieve symptoms of MCAO. Interventions through bronchoscopy, such as mechanical debulking, cauterization, and stent placement, can

immediately reduce MCAO symptoms and improve quality of life.[5,6] Several studies have demonstrated the effectiveness of these procedures in reducing the frequency and severity of dyspnea and improving clinically relevant endpoints. The reported success rate is over 90%, with a low complication rate.[7,8]

Compared to other interventional bronchoscopy procedures, airway/bronchial stent placement is one of the most frequently performed interventions, especially in extrinsic lesions that cause airway obstruction. The success rate of stent placement is high and consistent (95-100%).[8–10] Complications are common despite symptom relief, especially in long-term follow-ups due to the complex anatomy of the central airways and physiology. This procedure was introduced by Dumon in 1989. The placement of an airway stent has become a hot subject in interventional pulmonology. Various types of stents and stent materials are available, although the ideal stent under various conditions has not been found.[11] This study aimed to describe the prevalence of stent placement, indications for stent placement, success and complication rates, and prognosis of airway stent placement in patients with lung cancer.

Prevalence of airway stent placement in lung cancer

An airway stent is a prosthesis made of various materials used to support and maintain a patent airway. In the management of MCAO, there are two types of stents, namely silicone and metal/hybrid.[12] Meanwhile, in terms of design, the latest development reports on the types of stent designs are grouped into four areas, which are three-dimensional (3D) printed stents, drug-eluting stents, biodegradable stents, and mini stents.[10] Airway stents are more suitable for use in extrinsic malignant compression cases. Although less frequently, stents are utilized to maintain airway patency of post-ablation intrinsic or mixed endobronchial tumors, as well as persistent airway narrowing cases.[8,12] Stents provide a rapid and durable palliative treatment, with 84-100% of patients experiencing dyspnea symptom alleviation.[12] Patients with advanced malignant obstruction and tracheobronchial stents have been found to have a good correlation with improved survival and quality of life.[7]

It is expected that thirty percent of individuals with lung cancer may develop central airway obstruction at some point throughout their treatment (MCAO).[1,7] Saji et al. conducted a cohort study of lung cancer patients from 1994 to 2008 in the United States and reported that 69% of lung cancer patients with MCAO require insertion of a tracheobronchial stent during interventional bronchoscopy therapy (IBT).[1] Another study by Chung et al. analyzed the outcome of self-expandable metallic stent (SEMS) application and reported MCAO-associated SEMS placement counted for 81%.[13] The cohort study conducted by Kim et al.,[7] and Mohan et al.[14] suggested a lower prevalence of tracheobronchial stent placement, which are 50.4% and 56.6% in each study. This is related to the use of other procedures in interventional bronchoscopy (mechanical debulking, cryodebulking, etc.), which also have increased success and good prognosis compared to those reported in previous studies.[7,14]

Indications for placement of bronchial stents in lung cancer

The main anatomical indications for airway stent placement are (1) recurrence of endoluminal, infiltrative obstructive lesions following first endobronchial therapy, (2) constriction of the airway lumen by extrinsic airway lesions, and (3) mixed-type extrinsic or endoluminal malignant lesions. Less frequent indications include the treatment of malignant strictures that are refractory to dilatation and the management of tracheoesophageal fistula. The findings of current research indicate that this pattern has not altered, and the obstructive lesions are more often seen in the main bronchus and the trachea.

A recent study by Sabath and Ost described several indications that emphasize caution in certain cases. Their study described two categories of general indications for airway stent placement.[10] The blockage of the lumen of the major airway is the first sign to appear and is also the one that occurs most often. Both extrinsic compressions from the mass that is

located surrounding the airway and intrinsic blockage from the mass that is located inside the airway are frequent causes of airway obstruction. Mixed patterns are also common in some cases. In addition, tracheobronchomalacia is an example of a condition in which the airway wall loses its strength, which may lead to airway collapse and luminal blockage. Pure extrinsic compression and weakness of the airway wall are indications for stent placement in severe cases. Pure intrinsic obstruction can generally be treated with endoluminal ablatives and debulking alone. The case of mixed patterns often requires several intervention modalities.[6,10]

A defect in the airway wall is the second indication that may be present. Following lung transplantation, broncho-oesophageal fistula or anastomotic dehiscence can result in substantial airway wall defects. This problem can then develop into more airway complications and can be treated by airway stent placement. There is a wide selection of different types of airway stents that may be purchased commercially. As was indicated before, stents may be generally classified according to the material from which they are made, either metal or silicon. There are minor but clinically significant differences between the various types of stents, notwithstanding the fact that no single stent type is optimal for all situations.[6,10,15]

Several factors must be considered in determining whether or not an airway stent is required, one of which is whether the observed airway obstruction is significant. In general, airway occlusion, which is an indication for stent placement, is 50%.[5,12] Decreased tracheal lumen diameter of 8 mm often causes dyspnea on exertion. A lumen size of 5 mm usually causes dyspnea at rest. Intervention should be considered when the lesion is physiologically severe and causing worsening dyspnea.[16]

The absence of patency in the distal airway where the stent is attached is one of the contraindications to stent placement. As a result, the insertion will not be beneficial. In certain situations, this can be determined by preprocedural imaging; however, in most cases, this cannot be determined with certainty until a bronchoscopy is performed. Consideration is also given to the patient's general clinical status, especially in patients with advanced lung cancer. Although acute problems during therapeutic bronchoscopy are uncommon, long-term consequences, including infection, granulation tissue development, and stent migration, are rather common and may need repeat bronchoscopy in an already compromised patient. Similar considerations should also be given to the fact that stent placement often requires general anesthesia, so a relative contraindication is considered in patients who cannot tolerate general anesthesia or moderate sedation.

The success rate of airway stent installation in lung cancer

Most studies report a technical success rate of 95 to 100 percent for bronchial stent implantation in patients with lung cancer when performed by a professional and experienced practitioner.[10,16,18] The clinical success rates are quite variable (Table 1). In most cases, the decrease in dyspnea symptoms that occurs immediately after stent placement is used as a proxy for the clinical success of the procedure. There may be heterogeneity in the study population with various comorbidities, severity, and clinical circumstances contributing to the variable results among studies.

Table 1. The technical and clinical success rate of airway stent placement in lung malignancies.

Authors	Year	Type of Study	Study Population	Installation success rate	Clinical success rate
Han XW, Wu G, Li YD et al.[20]	2008	Retrospective	35 Tracheo-bronchial stenosis patients	100%	89%
Chung FT, Chen, HC, Chou, CL, et al.[13]	2010	Retrospective	77 MCAO patients	SEMS =100%	51,6% (In this study, patients were suspected of having pulmonary parenchymal involvement, lymphangitic spread, tumor embolism, and wasting syndrome, thereby decreasing the significance of improvement after stent placement.)
Saji H, Furukawa K, Tsutsui H, et al.[1]	2010	Retrospective	65 MCAO patients	100%	98%
Furukawa K, Ishida J, Yamaguchi G, et al.[21]	2010	Retrospective	58 MCAO patients	100%	100%
Li ZM, Wu G, Han XW, Ren KW, et al.[22]	2014	Retrospective	28 Tracheo-bronchial stenosis patients	SEMS =100%	100%
Mahmood K, Wahidi MM, Thomas S.[23]	2015	Retrospective	24 MCAO patients	100%	100%
Marchese R, Poidomani G, Paglino G, et al.[24]	2015	Retrospective	52 Tumor-induced tracheobronchial stenosis patients	100%	100%
Qiao Y, Fu YF, Cheng L. et al.[25]	2016	Retrospective	12 patients of carina stenosis caused by a tumor	Y shaped stent = 100%	100%
Fu YF, Lv LL, Xu H, Wei N.[26]	2016	Retrospective	11 patients of airway stenosis caused by malignancy	100%	100%
Huang S, Xu J, An Z, Yuan P, et al.[8]	2018	Retrospective	12 MCAO patients	Y-shaped stent =100%	66% It is believed that 28% of patients have cancer, whereas 6% of patients are reliant on ventilators and so cannot be assessed.
Bi Y, Ren J, Chen H, et al.[9]	2019	Retrospective	39 MCAO patients	97,4%	100%

Insertion of bronchial and airway stents requires good clinical judgment, adequate skill level, careful consideration, and anticipation of complications that may occur during or after insertion. A stent is a foreign body that can exacerbate certain symptoms, such as coughing, and put the patient at risk for further complications. The operator and clinician must be relatively sure that the symptoms are mainly due to airway obstruction. The likelihood of tumor development or recurrence, as well as the selection of systemic treatment, are other considerations.

Prognosis of airway stent placement in lung cancer

Multiple research has examined the safety and effectiveness of silicone stents and SEMS.10,12,16 Nonetheless, when used for long periods of time, stents can develop significant complications. Among the reported problems are migration, infection, granulation tissue formation, halitosis, stent fracture, metal fatigue, vascular and airway wall perforation, and mucosal tears.[9,10,12,14,16,19] It is recommended by professionals that a "stent alert" card be issued to each patient. This card should include the kind and size of the stent, as well as the position of the endotracheal tube, as well as its suitable size to be utilized in the event that emergency intubation is necessary.[12] The reported rates of stent-related complications vary in the literature based on the study population and the type/material of airway stents inserted (most reported in the 40-60% range and reached 87% at 20 months post-placement).

The silicone stent is folded and inserted into the airway through a special metal device that is inserted into the rigid bronchoscope, distal to the stenosis, and then pulled back into the desired position. These stents require bronchoscopy expertise to insert but are easily removed, well tolerated, and cause less granulation tissue reaction than other types. Another major advantage is the ease of adjustment at the placement site based on bronchoscopy and CT scan measurements.[27]

The Dumon stent is the most widely used silicone stent, at least in Europe and Japan (Figure 1). Straight or forked silicone stents for right and left carina stenosis (Y and Oki stents). The patient's symptoms and quality of life were reported to improve immediately in the majority of cases, both in malignant and non-malignant central airway obstruction. Granulation tissue reactions are less symptomatic, and the risk of migration is less in malignant cases. One of the disadvantages of silicone stents compared to SEMS is that they have a narrower internal diameter which can lead to mucus plugging (14% of cases), which can lead to bacterial colonization (Figures 2 and 3).[27,28]

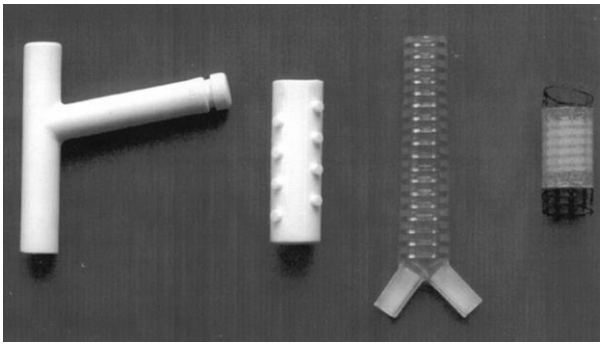

Figure 1. Various types of silicone-based stents.
From left to right: Montgomery, Dumon, Dynamic Stent (Rusch), and Closed Wallstent (Microvasive).[29]

SEMS is more suitable for use in tight, distorted stenosis, tracheoesophageal fistula (TEF), and more commonly for necrotic stenosis, as it is less rigid and reduces the risk of perforation. Lower migration risk, greater clearance, and larger internal diameter.[27] These stents are easy to insert and offer immediate success, particularly in cases of MCAO, as they rapidly reduce dyspnea and improve quality of life and respiratory function. SEMS have a higher risk of granulation tissue reactions (particularly partially closed SEMS); neo-epithelialization with mucosal integration, making it harder to remove the stent after

3–6 weeks; a lesser vault effect; and a higher chance of leakage.[10,11,27] The rate of major complications was 16% in the first month and 13% in subsequent months. Among the earliest consequences include pneumothorax, pneumonia, and migration. 10% of patients have both hemoptysis and infection. In benign airway stenosis, symptomatic granuloma development is reported in 15-27% of patients in later stages and rises with prolonged use.

Previous studies have indicated that stent placement requires a level of expertise with experience, so it is generally only available in centers of excellence which reinforces the need to use extreme care while placing airway stents. A multi-center study based on the American College of Chest Physicians Quality Improvement Registry, Evaluation, and Education (AQuiRE) registry, examined the incidence of complications from 1,115 procedures performed on 947 patients at 15 centers. Of the 947 patients, 36% required airway stent placement. Overall, the mean short-term complication rate was 3.9% (0.9-11.7%). Six patients (0.5%) died from complications of the procedure. From this study, the risk factors for complications that were found to be significant were emergency procedures, American Society of Anesthesiology (ASA) scores above 3, repeat therapeutic bronchoscopy, and moderate sedation. There were no occurrences of problems linked to stent installation; nevertheless, 4.4% of patients experienced an unanticipated increase in hospitalization, 1.3% had respiratory failure, and 0.5% had bleeding needing intervention. Death within 30 days of the procedure was associated with an Eastern Oncology Group (ECOG) score greater than 1, an ASA greater than 3, and an intrinsic or mixed obstruction.

Figure 2. SEMS, Ultraflex® closed (covered) and opened (uncovered) (Boston Scientific, United States).

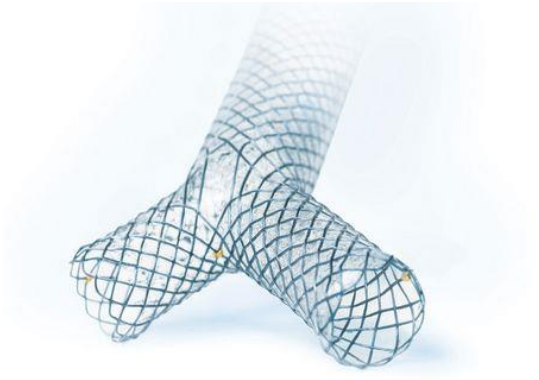

Figure 3. SEMS, nitinol monofilament self-expandable metal stent (InnovaMedica, Spain).

Figure 4. SEMS, Stent AERO®(Merit Medical System, Alveolus, North Carolina, USA).

In inpatients who had stents, the risk of lower respiratory tract infection (LRTI) was shown to climb by 13% each month. This was observed in comparison to the risk in patients who did not have stents. One out of every eight individuals using stents is estimated to acquire an infection. Grosu et al. found that the male gender was related to an increased incidence of LRTI in patients receiving airway stents.[32] An additional study that was noteworthy was a retrospective trial of complications in patients who were treated for MCAO with airway stents at a big referral cancer center over a period of 5.5 years. Overall, infection, migration, granulation tissue formation, and mucus clogging are the most prevalent consequences. The median incubation period was one month. The AERO type stent provides an increased risk of infection compared to other stents (Figure 4). The AERO stent is a fully covered third-generation SEMS stent to reduce the risk of granulation tissue formation. Migration complications have a mean time of occurrence of 1.4 months. When compared to metal stents, silicone tube stents are associated with a higher risk of migration [Hazard Ratio (HR) 3.52; P=0.007]. Granulation tissue formation also had a mean time of 1.4 months. In a multivariate study, silicone stents and LRTI were both shown to be related to an increased incidence of granulation. Mucous blockage generally occurs at 1.3 months. Silicone stents and placement on the left side are associated with an increased risk of mucus plugging.[33] This may be attributed to the smaller and longer diameter of the left bronchus than the right bronchus. The mean time to complications was mostly 1.4 months, and this time helps guide monitoring and follow-up techniques in patients after stent placement. The last few years have seen useful progress regarding complications of airway stents and therapeutic bronchoscopy for MCAO. The data may be put to use to help guide clinical decision-making and provide assistance in assessing some of the risks associated with airway stents.

2. Conclusion

Stents in lung cancer are indicated for obstructive lesions located in the main bronchus and trachea. The success rate of the procedure and clinical trials is quite high, although significant complications are still being reported. Various clinical trial studies need to be developed to be able to achieve a better prognosis without significant complications of bronchial stent placement in lung cancer.

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