

Our Clinical Experience of Self-Expanding Metal Stent for Malignant Central Airway Obstruction

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Abstract

Background: We studied the safety, effectiveness, and limitations of airway stenting using self-expanding metal stent (SEMS) in patients with malignant central airway obstruction (CAO).

Methods: A retrospective review of records of patients undergoing SEMS placement for malignant CAO during year 2013 - 2014 was done.

Results: Sixteen patients (11 males and five females) underwent SEMS placement for malignant CAO. Median (range) age was 66 (54 - 78) years. No perioperative or immediate postoperative complications were seen except acute myocardial infarction (AMI) in one patient. Three patients were transferred to intensive care unit (ICU) for closer monitoring after the procedure and were discharged the next day. All four patients with lung atelectasis on presentation experienced complete re-expansion of the lung post-stenting. The dyspnea was substantially relieved in 14 (87.5%) patients. Two of the three patients who had been intubated were weaned off from the ventilator following stent insertion. Stent patency was maintained until death in all patients except one. Median survival from the date of diagnosis and the date of stent placement in lung cancer, esophageal cancer, and thyroid cancer were 140 (21 - 564) and 85 (15 - 361), 288 (80 - 419) and 61 (60 - 171), and 129 (71 - 187) and 67 (16 - 118) days, respectively. This survival was similar to reported expected survival associated with the underlying malignancy. During follow-up, granulation tissue (n = 1), mucostasis (n = 1), and tumor ingrowth (n = 2) were the most frequently encountered complications.

Conclusion: SEMSs are safe and effective in reversing respiratory failure caused by malignant CAO, averting premature death, allowing application of cancer targeted therapy, and restoring impending shortened survival to expected life expectancy associated with the underlying malignancy.

Keywords: Lung cancer; Bronchoscopy; Central airway obstruction; Stent

Introduction

Central airway obstruction (CAO) is an uncommon but potentially life-threatening condition that can be due to a number of malignant diseases. For example, airway obstruction complicates approximately 20-30% of patients with lung cancer [1]. This can result from either the direct endobronchial extension of a tumor or extrinsic compression from parenchymal lung mass, lymph-node, and esophageal or thyroid cancer [2]. Clinically, malignant CAO presents with dyspnea, stridor, or cough. Radiologically, it can present with lobar or complete lung atelectasis. Physiologically, it can manifest as air flow obstruction on spirometry with characteristic changes in flow volume loop (FVL) such as blunting of the expiratory and inspiratory limb of the FVL in case of fixed airway obstruction, or biphasic FVL in case of unilateral mainstem bronchus obstruction [2, 3]. Interventional bronchoscopy with airway stenting by virtue of re-establishment of the patency of the airway provides immediate relief of dyspnea, resolution of radiological and physiological changes, improves functional status, and confers stabilization of clinical condition to allow administration of definitive therapies targeted at cancer [2]. Other interventional bronchoscopic techniques used for the recanalization of the malignant CAO are the laser resection, coring of the tumor with the rigid tube, and brachytherapy [2]. In addition to palliation, survival benefit has also been described if performed early [4]. In CAO from extrinsic compression, two types of stents are used for recanalization. Silicone stents are preferred for benign diseases, whereas metal stents can be used for malignant CAO [5]. We describe our clinical experience in using self-expanding metal stent (SEMS) for malignant CAO.

Materials and Methods

We performed a retrospective analysis of 16 patients treated with SEMS for malignant CAO from January 1, 2014 to November 30, 2015. We collected data on oxygenation, radio-

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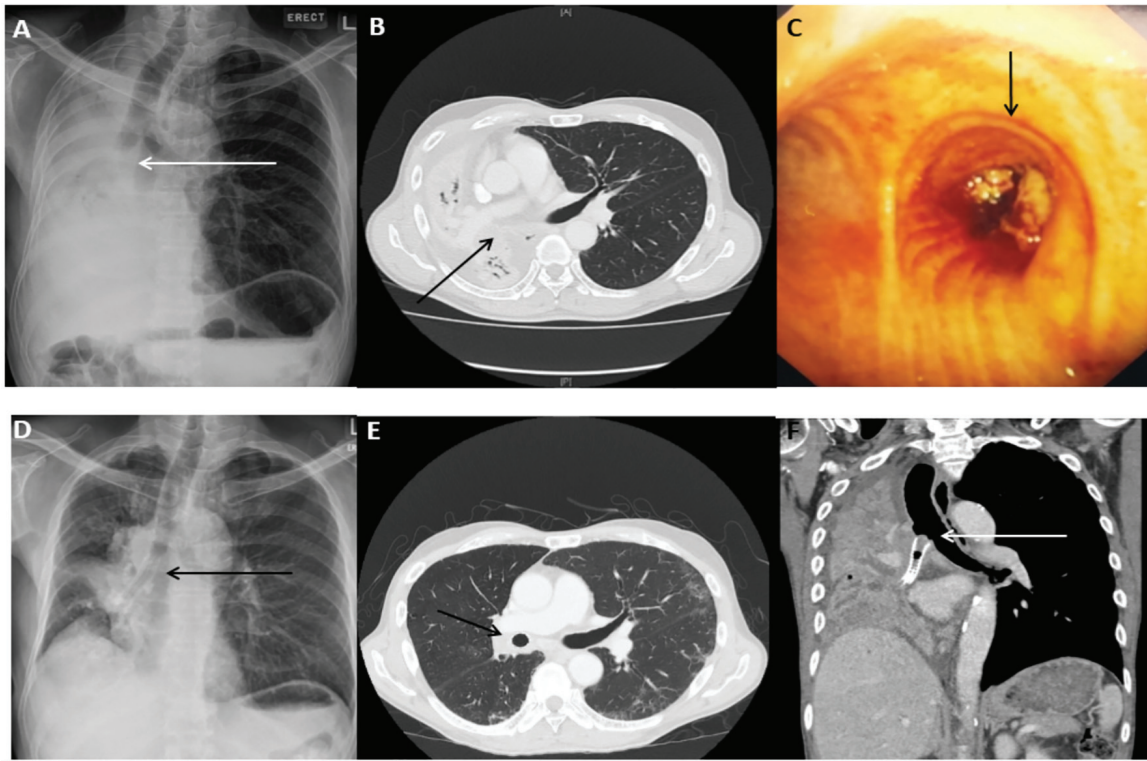


Figure 1. Representative case of malignant central airway obstruction in a 60-year-old male with squamous cell carcinoma. (A) Complete right lung collapse on the radiograph at the time of initial presentation with the cut off of the right main bronchus (arrow). (B) CT scan of the chest (axial view) showing collapsed right lung. (C) Visible endobronchial tumor obstructing the right main bronchus on bronchoscopy. (D) Re-expansion of the right lung following the SEMS placement in the right main bronchus and bronchus intermedius (arrow). (E) Post-stent placement CT scan of the chest (axial view) showing re-expansion of the right lung and stent in-situ (arrow). (F) CT scan of the chest 1 year later showing tumor ingrowth and recurrence of lung collapse.

graphic changes, bronchoscopic appearance, type of intervention, complications of intervention, safety, and effectiveness of SEMS. Approval from our institutional review board was obtained.

Flexible and rigid bronchoscopies were performed using standard techniques [1]. Nd-YAG laser resection (Laser sonic Model 8000; Heraeus Surgical, Milpitas, CA) was performed using 15- to 30-W pulses and pulse duration of 0.5 - 1.0 s. Coring of the tumor was carried out using the rigid tube where necessary. Flexible bronchoscopy through the rigid tube was employed as necessary to help clear the airways of secretions and blood. In cases with extrinsic compression from malignant obstruction, Boston Scientific Ultraflex SEMSs were deployed using the Ultraflex™ Tracheobronchial Stent System via standard technique. Only covered Ultraflex self-expanding stents were used. Covered SEMSs are coated with a silicone sheath except 0.5 cm of their proximal and distal end.

Definitions

CAO was defined as the obstruction of the trachea and main-stem bronchi. Respiratory failure was defined as stridor, need for supplemental oxygen, or need for mechanical ventilation. Survival was calculated from date of diagnosis-to-date of

death or November 30, 2015.

Data analysis

We used software (SPSS, version 17; SPSS, Chicago, IL) for all statistical analyses. The results were compared using a Wilcoxon two-sample test or Fisher's exact test. P values were two-sided and considered indicative of a significant difference if less than 0.05.

Results

Sixteen patients (11 males and five females) underwent stenting in 1 year. Median (range) age was 66 (54 - 78) years. Eighteen stents were placed in 16 patients, with one patient needing two stents in both bronchi and one needing two adjacent stents in right main bronchus and bronchus intermedius (Fig. 1). Nine (56.2%) patients had primary lung cancer, five (31.2%) had esophageal cancer, and two (12.5%) had thyroid cancer. Three patients received mechanical ventilation before the procedure (Table 1). Two patients underwent concurrent laser prior to stent placement. Four patients had lobar or complete lung atelectasis on presentation. Procedures were done

Table 1. General Characteristics of Patients (n = 16)

SN/age/gender	Type of cancer	Airway lesions	Radiology findings	Site of stent	Stent dimensions	Other therapy
Lung cancer (n = 9)						
1/78/F	Non-small cell carcinoma	Mid-trachea stenosis	4.4 × 3.5 cm mass in superior mediastinum compressing the trachea	Mid-trachea	16 × 40 mm	Nil
2/63/M	Sarcomatoid cancer	RMB obstruction	RUL mass	RMB	12 × 40 mm	RT
3/61/M	Squamous cell carcinoma lung	RMB and BI obstruction	4.5 × 4.7 × 4.6 cm Rt. hilar mass with complete collapse if Rt. lung	RMB and BI	14 × 40 and 14 × 40 mm	RT and chemotherapy
4/58/M	Adenocarcinoma lung	RMB obstruction	12.8 × 7.7 × 7.5 cm RUL mass with SVC obstruction	RMB	16 × 40 mm	Nil
5/74/F	Adenocarcinoma lung	RMB obstruction	RUL mass with collapse of RUL	RMB	12 × 40 mm	RT (9#)
6/70/M	Squamous cell carcinoma	Mid-tracheal and RMB obstruction	-	Trachea	16 × 40 mm	Chemotherapy and RT
7/70/M	Squamous cell carcinoma	Distal trachea, proximal Rt. Main and proximal Lt. main obstruction	Infiltrate	Right and LMB	12 × 40 and 12 × 40 mm	RT (35#)
8/77/M	Squamous cell carcinoma	-	-	RMB	10 × 40 mm	RT
9/67/F	Squamous cell carcinoma	Distal trachea narrowing to 0.4 cm and Rt. Main obstruction	6.1 × 5.5 × 6.5 cm RUL mass with tracheal compression	Distal trachea	16 × 40 mm	RT (12#)
Esophageal cancer (n = 5)						
10/58/M	Squamous cell carcinoma	LMB obstruction	5.2 × 3.8 × 2.4 cm mass in posterior mediastinum	LMB	14 × 40 mm	Ivor-lewis surgery with chemotherapy and RT prior to stenting
11/66/M	Squamous cell carcinoma	LMB obstruction	-	LMB	14 × 40 mm	Chemotherapy and RT
12/68/M	Squamous cell carcinoma	LMB obstruction	-	LMB	14 × 40 mm	Chemotherapy and RT
13/55/M	Squamous cell carcinoma	LMB obstruction	-	LMB	18 × 40 mm	Chemotherapy
14/63/M	Adenocarcinoma	LMB esophageal fistula	Bilateral infiltrates from aspiration pneumonia	LMB	18 × 40 mm	Ivor-lewis surgery prior to stenting
Thyroid cancer (n = 2)						
15/54/F	Anaplastic thyroid carcinoma	Upper tracheal narrowing to 0.5 cm	5.2 × 6.2 × 6.4 cm mass in the thyroid gland	Upper trachea		Nil
16/76/F	Anaplastic thyroid carcinoma	Sub-glottis and upper tracheal stenosis	6.6 × 3.3 × 5.6 cm mass in the thyroid gland	Upper trachea	18 × 60 mm	Nil

RUL: right upper lobe; Rt.: right; LMB: left main bronchus; RMB: right main bronchus; BI: bronchus intermedius; RT: radiotherapy; #: number of fractions of radiotherapy.

Table 2. Survival of Patients Having Malignant COA and Treated With SEMS in Comparison to the Expected Survival Associated With the Underlying Malignancy (n = 16)

	Respiratory failure	Diagnosis-to-stenting time (days)	Diagnosis-to-death time or last follow-up time (actual life expectancy in days)	Stenting-to-death or last follow-up (days)	Expected life expectancy
Non-small cell lung cancer	Yes	14	74	60	
Sarcomatoid cancer	Yes	40	220	180	
Squamous cell carcinoma lung	Yes	1	362	361	
Adenocarcinoma lung	Yes	39	54	15	
Adenocarcinoma lung	No*	11	347	336	
Squamous cell carcinoma	No	516	564	48 (alive)	
Squamous cell carcinoma	Yes	-12	140	152 (alive)	
Squamous cell carcinoma	No	4	89	85 (alive)	
Squamous cell carcinoma	Yes	6	21	15 (alive)	
Lung cancer (n = 9), median (range)		11 (-12 - 516)	140 (21 - 564)	85 (15 - 361)	10 (8 - 12) months [13]
Squamous cell carcinoma	Yes	323	419	96	
Squamous cell carcinoma	No	299	360	61	
Squamous cell carcinoma	Yes	117	288	171	
Squamous cell carcinoma	No	20	8	60	
Adenocarcinoma	Yes	56	117	61	
Esophageal cancer (n = 5), median (range)		117 (20 - 323)	288 (80 - 419)	61 (60 - 171)	9 (8 - 10) months [15-17]
Anaplastic thyroid carcinoma	Yes	55	71	16	
Anaplastic thyroid carcinoma	Yes	69	187	118	
Anaplastic thyroid cancer (n = 2), median (range)		62 (55 - 69)	129 (71 - 187)	67 (16 - 118)	3.8 (3 - 4.6) months [14]
All (n = 16)		39.5 (-12-516)	163.5 (21 - 564)	73 (15 - 361)	

*Patients without respiratory failure in the lung carcinoma group underwent stent placement to prevent worsening of the airway obstruction secondary to radiation therapy. Patients without respiratory failure in the esophageal carcinoma group underwent stent placement prior to esophageal stenting to prevent airway compromise from esophageal stenting.

under general anesthesia in operation room via the rigid bronchoscopy. No perioperative or immediate postoperative complications were seen except acute myocardial infarction (AMI) on day after the procedure in one patient. Three patients were transferred to intensive care unit (ICU) for closer monitoring after the procedure and were discharged the next day. All four patients with lung atelectasis on presentation experienced complete re-expansion of the lung post-stenting. The dyspnea was substantially relieved in 14 patients (87.5%). All three patients who were intubated prior to intervention were weaned off from the ventilator following stent insertion.

During follow-up, granulation tissue (n = 1), mucostasis (n = 1), and tumor ingrowth (n = 2) were the most frequently encountered complications. Median survival from the date of diagnosis and the date of stent placement in from lung cancer, esophageal cancer, and thyroid cancer were 140 (21 - 564) and 85 (15 - 361), 288 (80 - 419) and 61 (60 - 171), and 129 (71 - 187) and 67 (16 - 118) days, respectively. This survival was similar to expected survival based on the life expectancy of the

underlying malignancy (Table 2) [6-10].

Discussion

This study illustrates that SEMS are safe and effective for managing malignant CAO. They provide prompt reversal of respiratory failure and re-expansion of the collapsed lung. By reversing respiratory failure, they avert premature death and allow cancer targeted therapy to be undertaken. This restores the length of survival to the expected life expectancy associated with the primary cancer.

CAO develops secondary to endoluminal disease, external compression by a mediastinal or hilar tumor, bulky lymphadenopathy, or a combination of endoluminal and extrinsic disease [11]. There are a variety of treatment options that can restore airway patency in this group of patients [12-15]. Stents are employed when extrinsic compression is the dominating cause of the CAO. However, generally, airway stenting is

Table 3. Complications of Stent Placement in Malignant Central Airway Obstruction

	McGrath et al [19] (n = 68)	Saad et al [20] (n = 82)	Cavaliere et al [2] (n = 306)	Breitenbacher et al [21] (n = 60)	Current study (n = 16)
Type of stent	Ultraflex SEMS	Ultraflex SEMS	Silicone stents	Ultraflex SEMS	Covered Ultraflex SEMS
Covered/uncovered	Uncovered (94%)	Uncovered (66%)	Not applicable	Uncovered (18.3%)	Uncovered (0)
Migration	4(5.8%)	4.7%	18 (6%)	5%	0
Granulation tissue	3 (4.4%)	14.6%	3 (0.9%)	5%	1 (6.2%)
Mucostasis	Not reported	Not reported	3 (0.9%)	8%	1 (6.2%)
Tumor ingrowth	1 (1.4%)	Not reported	Not reported	5%	2 (12.5%)
Pneumonia	2 (2.9%)	15.9%	5 (1.6%)	10%	0

combined with some form of endoscopic tumor resection to achieve patency of the airway.

It is known that survival of patients with untreated malignant CAO is very poor and ranges from 1 to 2 months [16, 17]. Life expectancy in untreated advanced lung cancer is 4 - 5 months [6]. Platinum-based chemotherapy improves survival in this group to 8 - 12 months [6]. Similarly life expectancies in advanced esophageal carcinoma and anaplastic thyroid carcinoma are 9 (8 - 10) and 3.8 (3 - 4.6) months, respectively [7-10]. In this context, despite having CAO, patients in our cohort lived to the level of the expected life expectancy associated with the underlying malignancy. The described and perceived benefits of the stenting are mainly relief of dyspnea, improved functional status, and better quality of life [18]. However, it is noteworthy that even though stenting does not increase survival *per se*, it supports survival by preventing premature death from respiratory failure, post-obstructive pneumonitis, and sepsis. It is also shown that patients having advanced lung cancer with locally treated malignant CAO in combination with chemotherapy live as long as their counterparts without CAO [18].

The American College of Chest Physicians (ACCP) has published an advisory against using metal stents in benign airway obstruction. Silicone stents are preferable in such diseases due to their ease of removal and re-introduction [5]. Some centers prefer silicone stents even for malignant CAO. However, limited life expectancy of patients with malignant CAO obviates the need for removal of the stent upon resolution of the stenosis. We found SEMS effective in restoring and maintaining the airway patency and at the same time easy to introduce and safe with no peri-procedural complications or mortality. Relative ease of their insertion carries the potential to broaden the proportion of patients they can be offered to.

We found that lung cancer patient with CAO presents at the time of initial diagnosis, whereas patients with thyroid carcinoma and esophageal carcinoma develop CAO significantly later in the course of their disease. In our cohort, CAO developed at the median interval of 3.9 months after the diagnosis of esophageal cancer, and 2 months after the diagnosis of thyroid cancer. Since early intervention is preferable, this information can allow physicians to determine the timing of follow-up in outpatient clinic and time for repeating the imaging study to look for the development of CAO with the intent to identify and intervene early before the development of significant air-

way compromise.

Regarding complications of the SEMS, mucostasis, granulation tissue formation, and tumor ingrowth at the edges of the stent were seen, out of which tumor ingrowth was the most frequent and detrimental complication as it compromised the patency of the airway irreversibly. No patient experienced stent migration (the most significant and frequent complication of the silicone stents) in our cohort even after the resolution of CAO from radiotherapy and chemotherapy. Complications associated with SEMSs are well documented. In a retrospective analysis of 68 patients undergoing Ultraflex SEMSs insertion for malignant tracheobronchial stenosis, most of which were uncovered, complications included hemorrhage originating in the area of the stent placement during the insertion itself (one patient), mild hemoptysis (five patients), stent migration (four patients), severe granulation tissue (three patients), pneumonia (two patients), odynophagia, respiratory failure, stent occlusion, and deployment failure (one patient in each case). There were no episodes of fistula formation, lobe collapse, pneumothorax or sudden death [19]. In another study of 82 patients, Saad et al reported the occurrence of infection in 15.9%, obstructive granulomas in 14.6%, and migration in 4.7% [20]. Most of the patients received an uncovered stent in this cohort too. In a study by Breitenbacher et al in patients with malignant diseases, they observed a complication of mucus plugging in 8% of the cases, as well as stent migration, the formation of granulation tissue and the re-stenosis of the tumor in 5% of cases, each [21]. The lower incidence of stent migration in our cohort is consistent with the existing literature (Table 3) [2, 19-21]. In comparison with silicone stents, Ultraflex stents have a lower rate of migration due to their epithelialization, but with a higher rate of granulation tissue formation [21]. Stents were patent in most patients until the time of death as evidenced by computed tomography (CT) or bronchoscopy done close to the time of death indicating that prognosis of underlying cancer was the determinant of length of survival rather than stent failure.

In conclusion, SEMSs not only offer minimally invasive palliative therapy for patients suffocating from un-resectable malignant CAO with low complication risk, but also preserve survival by averting premature death from respiratory failure, and conferring clinical stability to allow cancer targeted therapy to take place. Tumor ingrowth at the uncovered edges of the stent is the most significant and irreversible complication.

Completely covered SEMSs may help to overcome this complication.

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Conflicts of Interest

AV, CKP, QMW, WYS, AWCR, SKG, BH, ACK, ASYW, AL, DYHT, and JA have no competing financial interests to disclose.

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