

Therapeutic bronchoscopic interventions for malignant airway obstruction

A retrospective study from experience on 547 patients

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Abstract

There is no definitive consensus about the factors affecting the choice of interventional bronchoscopy in the management of malignant airway obstruction. The present study defines the choice of the interventional bronchoscopic modality and analyzes the factors influencing survival in patients with malignant central airway obstruction. Totally, over 7 years, 802 interventional rigid bronchoscopic procedures were applied in 547 patients having malignant airway obstruction. There was a significant association between the type of stent and the site of the lesion in the present study. Patients with tracheal involvement and/or involvement of the main bronchi had the worst prognosis. The sites of the lesion and endobronchial treatment modality were independent predictors of survival in the present study. The selection of different types of airway stents can be considered on the base of site of the lesion. Survival can be estimated based on the site of the lesion and endobronchial bronchoscopic modality used.

Abbreviations: APC = Argon plasma coagulation, COPD = chronic obstructive pulmonary disease, ICU = intensive care unit.

Keywords: bronchoscopy, lung cancer, malignant airway stenosis, stent, survival

1. Introduction

Endobronchial treatment with or without stenting is commonly used as a tumor debulking method for malignant central airway obstruction.^[1,2]

A clinically significant airway obstruction may be caused by growth of an intraluminal tumor or by compression from an extrinsic tumor. Bronchogenic tumors, malignant lymphomas, esophageal tumors, tumors of larynx or thyroid, or metastases from an extrathoracic tumor may involve the central airways.^[3] The clinical symptoms and signs of these advanced malignancies include stridor, dyspnea, and obstructive pneumonia.

To the best of our knowledge, there is no absolute consensus about the factors influencing the choice of interventional bronchoscopic modality in the management of malignant airway stenoses with or without stenting. The purposes of the present study were to define the clinical factors which have potential to influence the choice of the interventional modality with or

without stenting for patients having malignant central airway obstruction. This study includes a large number of clinical experiences from the literature with a favorable follow-up period.

2. Methods

2.1. Study design and selection of patients

The present study was designed as a retrospective cohort study in which all the available data were retrospectively reviewed for patients referred to the Interventional Pulmonology Unit for central airway obstruction between August 2005 and January 2013 and for patients who were diagnosed as having malignant airway obstruction and who underwent endobronchial treatment. All the patients in the cohort were followed up till January 2014.

In studies with a retrospective analysis of standard diagnostic data, no ethical approval is needed in Turkey.

The Dumon (Novatech, France) stents were inserted using appropriate equipment as described in the literature.^[4]

A diode laser operating at a wavelength of 980 nm with 4 to 25 Watt, pulsed mode (Biolitec, Ceralas D 25; Jena, Germany) was applied for the endobronchial treatment. Argon plasma coagulation (40 Watt, blended mode-continuous flow) was applied using an instrument manufactured by ERBE Elektromedizin GBMH (Tübingen, Germany). Standardized protocols for appropriate power selections were used in accord with the manufacturer's recommendations.

Cryotherapy was performed using the ERBOKRYO system (Elektromedizin GBMH, Tübingen, Germany).

All the patients were intubated by a rigid bronchoscope (Efer Endoscopy, Paris, France) under general anesthesia using standardized techniques and mechanical debridement was applied when it was necessary. All the patients had symptomatic relief after endobronchial treatment and stenting.

2.2. Collection of data, statistical analysis, and measurements

Clinical and radiological data were obtained by using the hospital electronic database, chart reviews, and radiological systems. The

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Table 1**Demographical findings and number of patients according to clinical features and type of the tumor in the study population.**

	Small cell carcinoma	Nonsmall cell carcinoma	Lymphoma	Thyroid cancer	Malignant mesothelioma	Neuroendocrine tumor	Carcinoid	Malignant mesenchymal tumor	Other metastasis
Age (years \pm SD)	61.25 \pm 10.25	62.50 \pm 10.30	65.2 \pm 17.04	60.25 \pm 10.84	64 \pm 11.31	68.33 \pm 10.35	51.90 \pm 16.73	49.67 \pm 18.00	53.29 \pm 17.87
M:F ratio	42:11	351:60	6:3	1:3	2:0	5:4	12:17	5:4	4:10
Smoking history	44	352	5	3	2	8	19	5	8
COPD	12	55	3	—	—	1	4	2	2
ICU stay	16	71	1	—	—	3	5	2	2
Dyspnea	40	274	8	1	1	5	10	4	13
Cough	17	178	6	1	—	4	5	2	4
Hemoptysis	2	89	—	2	2	1	2	2	—
Sputum production	10	81	4	1	—	1	2	1	3

COPD, Chronic obstructive pulmonary disease; ICU, Intensive care unit.

primary outcomes of the present study were defined as the response to stenting and endobronchial treatment of the patients, the rate of complications of the stenting and endobronchial treatment. Multiple and recurrent applications of stenting and total procedures for endobronchial treatment were also recorded. The chi-square test was used to assess the significance of factors influencing the choice of interventional bronchoscopic treatment modality. A Kaplan–Meier log-rank analysis was used to determine the factors for survival. Factors which were significant on the basis of a univariate analysis were then analyzed using the Cox regression model. A *P* value of <0.05 was accepted as statistically significant.

3. Results

3.1. Clinical features of the study population

Totally, 802 interventional rigid bronchoscopic procedures were applied in 547 patients having a malign airway obstruction. The male to female ratio was 432 to 115 and median age was 63 years. The median follow-up period was 5.3 months (range, 0–100 months). Demographical findings and clinical features of the study population were summarized in Table 1.

3.2. Interventional bronchoscopic features of study population

The total laser application was performed in 250 procedures for 178 patients, argon plasma coagulation was used in 373 procedures for 257 patients, cryotherapy was performed in 93 procedures for 54 patients, and stents were applied during 171 procedures in 147 patients. Overall, 94 Y-stents and 52 tube stents (Novatech, La Ciotat, France) were placed into the central airways of patients having malign airway obstruction. Total flexible bronchoscopy (Olympus Evis Exera, Tokyo, Japan) was used in 391 patients for follow up of endobronchial treatment and/or stenting. For follow up, a flexible bronchoscopy was used in 100 patients after they had stenting. A laser was most commonly used in lung malignancies and was combined with stenting in 36 patients in the present study. Argon plasma coagulation (APC) was most commonly used for lung malignancies and was combined with stenting in 65 patients in the present study. Cryotherapy was most commonly used in lung malignancies and was combined with stenting in 5 patients in the present study.

The diagnoses and types of the malignancies are summarized in Table 2. Bronchoscopic view of the lesions and stents were shown in Figs. 1 and 2. Bronchogenic lung cancers were the most common

type of malignancy causing central airway obstruction followed by lymphoma and metastases from extra extrathoracic sites. The placement of an endobronchial stent was most commonly used for primary lung cancers in the present study. The primary lesions were confined only to the trachea in 65 (11.9 %) patients; confined to the trachea plus right main bronchus in 87 (15.9 %) patients; confined to the trachea plus left main bronchus in 20 (15.9 %) patients; confined to the trachea plus both main bronchi in 121 (22.1 %) patients, and the right bronchial system and as well as left bronchial system were involved in 9 (1.6%) patients.

There was a significant association between the type of stent used and the site of the lesion ($P=0.013$). Insertion of Y stent alone was most frequently used for the lesions confined to both the left and the right bronchial system combined with a coexisting tracheal involvement. Tube stents were more frequently placed for lesions located in only the trachea or in left main bronchus. All patients reported substantial improvement in their dyspnea after stenting. There was no significant association between the use of the laser alone and the site of the lesion ($P>0.05$). There was a significant association between the use of Argon plasma coagulation and the site of the lesion ($P=0.029$). The Argon plasma coagulation was more frequently used for the lesions involving both trachea plus a main bronchus.

4. Complications

The complications were seen in total in 10.8% (59 out of 547) patients. Complications following endobronchial treatment were observed in 59 patients. Arrhythmias during endobronchial treatment were seen in 4 patients, a hypertensive attack was seen

Table 2**Causes of airway obstruction and distribution of patients.**

Underlying malignancy causing of airway obstruction	Number of patients n = 547
Squamous cell cancer	199
Small cell cancer	53
Adenocarcinoma	31
Nonsmall cell lung cancer undefined	181
Carcinoid tumor	29
Lymphoma	9
Thyroid cancer	4
Renal cell cancer	4
Malign mesothelioma	2
Neuroendocrine tumor	9
Malign mesenchymal tumor	9
Other metastasis	17

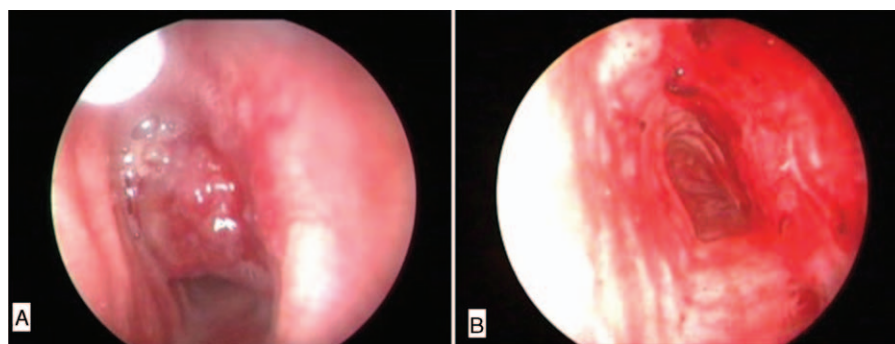


Figure 1. (A) A 57-year-old patient with squamous cell carcinoma type and lobulated mass lesion located in midportion of the trachea causing 65% of the lumen obstruction before the endobronchial treatment. (B) Tumor was coagulated with diode laser and obstruction was relieved totally by rigid bronchoscopic intervention. Scabbard trachea was also seen and noticed easily after the endobronchial treatment.

in 9 patients, and oxygen desaturation was seen 24 patients. Restenosis due to the tumor progression during an acute follow-up period was seen in 20 patients.

The patency of the airway lumen, the control of bleeding, and reduction of tumor size were achieved in all of the cases.

4.1. Prognosis and survival analysis

A total of 151 patients were still alive at the end of follow-up period. The median follow-up time was 5.3 months (range 0–100 months). Factors significantly affecting survival using the Kaplan–Meier log-rank analysis were type of malignancy causing central airway obstruction ($P < 0.01$) (Fig. 3), site of lesion ($P < 0.01$) (Fig. 4), and the type of endobronchial treatment modality ($P = 0.01$) (Fig. 5). Multivariate analysis using a Cox regression model showed that site of lesion and endobronchial treatment

modality were independent predictors of survival (Fig. 6) (Table 3).

5. Discussion

The primary indication for endobronchial treatment is palliation of central airway obstruction.^[2,5] The common indications for airway stenting are presence of intrinsic lesions, extrinsic compression, complex strictures, or a central airway fistula.^[3] There are no definitive data about factors such as type of disease or site of the lesion which may affect the use of a single or combined modality or stenting in the treatment of endoluminal lesions. The location, shape, and length of stenosis is an important consideration to determine the choice of stent.^[1] A significant association between the type of stent and the site of the lesion was seen in the present study. A bifurcated Y stent alone

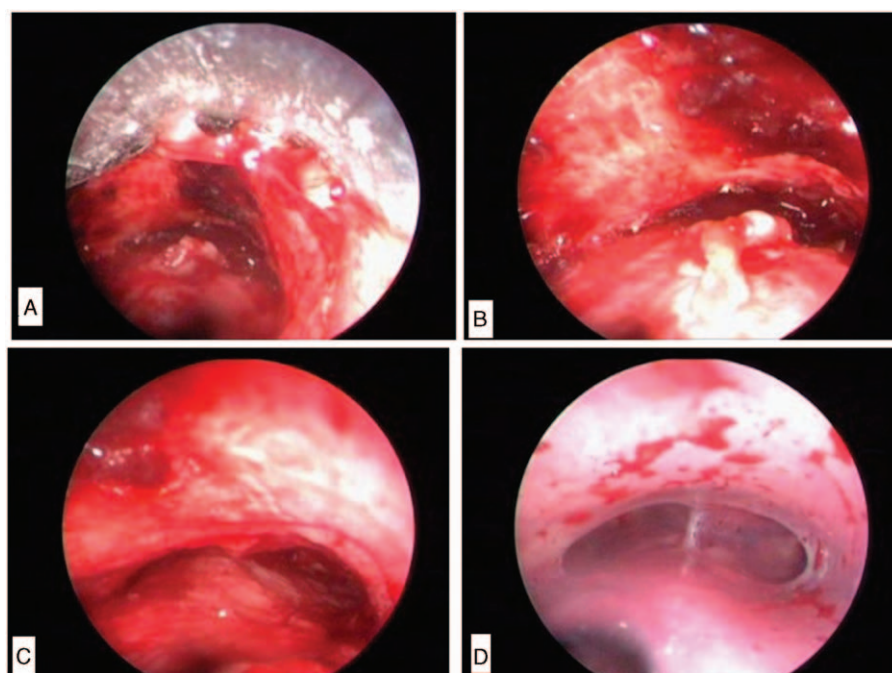


Figure 2. (A) A 54-year-old patient with internal and external tracheal tumoral compression who presented with respiratory insufficiency and tracheal lumen was obstructed >90%. (B) Early findings seen after dilatation of the distal trachea by rigid bronchoscopy. (C) Late findings seen after dilatation of the distal trachea by rigid bronchoscopy showing decreased tracheal obstruction. (D) Placement of Dumon Y stent that was located on carina.

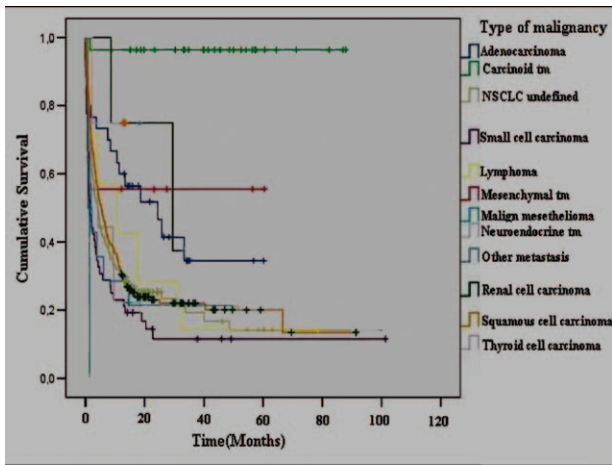


Figure 3. Type of malignancy causing central airway obstruction as a factor affecting survival of the study population represented as the Kaplan–Meier curve ($P < 0.01$).

was most frequently used for lesions confined to both the left and the right bronchial system, having a coexisting tracheal involvement in the present study and tube stents were more commonly used [employed] for the lesions located in only the trachea or in the left main bronchus in the present study. The Dumon Y-stent has been proved to be useful and has been proposed to be well-tolerated in the management of malignant disease involving the main carina.^[6] All the stents were well tolerated in the present study. Y stents are usually used when dealing with long stenoses and strictures involving the trachea and the main bronchi. The inner surface of Y stents is smoother and no tumor tissue can grow between the single stents. Prevention of migration is another advantage of Y stents as they are located on the carina. Tube stents or so called straight stents have been used for placement in the trachea or larger bronchi.^[3]

Follow-up flexible bronchoscopy was used in 100 patients after that had stenting in the present study. A study of this issue proposed the conclusion that routine follow-up bronchoscopies are not justified.^[7] However follow-up bronchoscopy may reveal a complication or a side-effect of stenting. If granulation tissue is present during follow-up bronchoscopy it is not obligatory that it

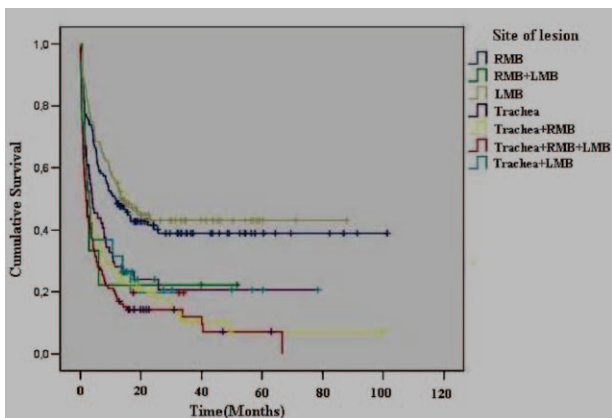


Figure 4. Site of the lesion as a factor affecting survival of the study population represented as the Kaplan–Meier curve ($P < 0.01$).

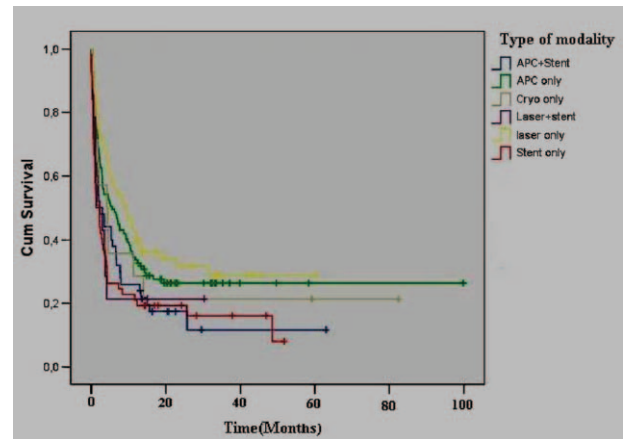


Figure 5. Type of endobronchial treatment modality as a factor affecting survival of the study population represented as the Kaplan–Meier curve ($P = 0.01$).

be removed. If the patient is not symptomatic, no action may be required. However, in the case of growth of further granulation tissue, the patient can be symptomatic and postobstructive pneumonia may be revealed. Therefore, early follow-up bronchoscopy may prevent this complication.^[3]

Endobronchial stents are most frequently used for re-establishing the patency of narrowed central airways in lung malignancies. Malignant lymphomas, esophageal tumors, tumors of larynx or thyroid, or metastases from extrathoracic organs can also involve the major airway in addition to primary lung malignancies.^[3] Primary lung cancers were the most common indication for endobronchial treatment and stenting in the present study. Other malignancies included lymphoma, tumors of the larynx, and metastases from extrathoracic organs in the present study.

The present study showed that all the patients had symptomatic relief after endobronchial treatment and stenting. Airway stenting is a useful treatment modality besides the other interventional bronchoscopic procedures. It not only provides rapid relief of symptoms and an improved quality of life but also gives additional time for adjuvant chemoradiotherapy that might provide prolonged survival.^[2,8,9]

Complications related to the placement of the stents include reobstruction of the lumen by tumor, granuloma formation at the

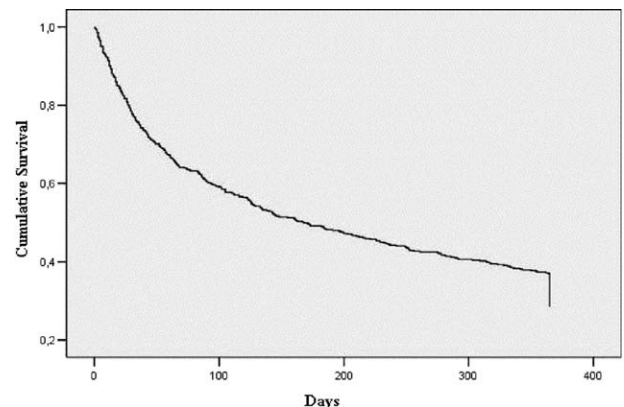


Figure 6. Cumulative survival of study cohort during 365 days (1 year) period.

Table 3**Characteristics of the study population affecting survival after interventional bronchoscopic procedures for malignant central airway obstruction.**

Characteristics	Survival			P	
	Mean months (%95 CI)	3 months %	6 months %	Univariate	Multivariate
Type of underlying malignancy				0.006	0.7
Squamous cell lung cancer	21.5 (16–27)	62	47		
Small cell lung cancer	15.3 (6.3–24.4)	38	28		
Adenocarcinoma	28.5 (18.9–38.1)	73	70		
Non-small cell lung cancer undefined	21 (14.4–27.6)	90	82		
Carcinoid tumor	84.8 (78.9–90.7)	96	96		
Lymphoma	20.8 (1.8–39.8)	71	57		
Thyroid cancer	10.7 (5.9–15.5)	75	75		
Renal cell cancer	25.6 (15.8–35.5)	100	100		
Malign mesothelioma	1 (0.3–1.6)	—	—		
Neuroendocrine tumor	7.1 (2.3–11.9)	55	44		
Malign mesenchymal tumor	33.8 (14.3–53.3)	55	55		
Other metastasis	13.4 (2.7–24)	42	28		
Site of the lesion				<0.001	<0.001
Trachea	20.1 (12.1–28)	56	43		
Right main bronchus	43.2 (34.6–51.8)	73	60		
Left main bronchus	41.6 (33.8–49.4)	77	68		
Trachea+right main bronchus	14.4 (8–20.8)	46	38		
Trachea+left main bronchus	10.1 (4.2–16)	47	36		
Trachea+right+left main bronchus	10 (6.4–13.6)	41	28		
Right main+Left main bronchus	13.3 (0.1–26.8)	33	13		
Endobronchial treatment				0.013	0.02
Laser only	22.4 (16–27.8)	71	57		
Argon plasma coagulation only	29.7 (21.7–37.9)	58	49		
Cryotherapy only	20.9 (3.9–37.8)	57	35		
Stent only	10.7 (5.9–15.4)	38	26		
Laser+stent	7.9 (1.8–14.1)	42	11		
Argon plasma coagulation +stent	11.9 (5.7–18.1)	48	38		

stent side, mucous plugging and migration of the stent, or with the use of a laser, both perforation of airway wall and fire.^[2,10] The stent-related complications were observed in 20 patients in the present study.

Total laser applications were performed in 250 procedures for 178 patients and there was no significant association between the use of the laser alone and the site of the lesion in the present study. One of the main indications for the use of laser bronchoscopy includes obstructive lesions of the trachea, the left and right main bronchi, the bronchus intermedius, and the lobar orifices that compromise ventilation and the severely symptomatic patients having dyspnoea, stridor, an intractable cough, or hemoptysis. The most common indication is inoperable lung malignancies having endobronchial features. In most cases, laser bronchoscopy is used together with other treatment modalities such as stenting, external beam irradiation, and brachytherapy.^[2] Lasers were most commonly used in lung malignancies and combined with stenting in the present study.

External compression of the airways is the only absolute contraindication for the use of a laser. Hypoxemia, bronchoesophageal fistula, and coagulopathy are other relative contraindications for laser use. Hypoxemia, bleeding, perforation, fistula formation, and fire are laser-related complications. Inspired oxygen concentration should be kept <40% to prevent the risk of fire.^[2] Hypoxemia was observed in 7 patients who had received laser application in the present study.

Argon plasma coagulation was used in 373 procedures for 257 patients as an interventional bronchoscopic modality. Argon plasma coagulation was more frequently used for lesions

involving both trachea plus a main bronchus. Argon plasma coagulation is used with an ionized argon gas jet flow to conduct electrons providing a noncontact mode of treatment.^[11] Indications for argon plasma coagulation include coagulation of hemorrhage from the tracheobronchial system, and treatment of granulomatous lesions in relation with airway stents. Immediate symptomatic relief is provided by using argon plasma coagulation for tumor coagulation followed by mechanical debulking; this has been the accepted consensus strategy.^[12]

Cryotherapy was used in 93 procedures for 54 patients. Cryotherapy is the endobronchial treatment modality of extreme cold for local destruction of viable tissue. Cryotherapy has a delayed action compared to laser or electrosurgery. The action of cryotherapy occurs from a few hours to a few days after application. Cryotherapy has been used for palliation of endobronchial exophytic obstructive lesions.^[12] Cryotherapy was most commonly used in lung malignancies and combined with stenting in 5 patients in the present study.

There is no consensus about the factors influencing the choice of interventional bronchoscopic modality in the management of malignant airway stenoses with or without stenting. This issue has been raised by Chhajed et al and reported that there was no significant year effect for the treatment modality (laser, stent, or both) and the underlying disease as well as the nature of the lesion. On the other hand, the use of laser alone was reported as significantly influenced by the presence of lesions below the main bronchi.^[13] In the present study, argon plasma coagulation was more frequently used for lesions involving both trachea plus a main bronchus.

The patients who had involvement of the trachea or both main bronchi had a worse prognosis than having a malignancy restricted to 1 lung. The patients in whom only laser therapy or only argon plasma coagulation was performed as an endobronchial treatment had a better survival compared to other modalities of endobronchial treatment.

There are some limitations of this study. All cases are initially Stage IIIB and stage IV patients, but unfortunately we do not have the data of final stages in this retrospective cohort. Survival analysis should be based on the final stages to reflect the association with endobronchial therapy.

In conclusion, there is no consensus about the factors influencing the choice of interventional bronchoscopic modality in the management of malignant airway stenoses with or without stenting. There was a significant association between the type of stent and the site of the lesion in the present study. Patients with tracheal involvement or with involvement of the main bronchi had the worst prognosis. The site of the lesion and the endobronchial treatment modality were independent predictors of survival in the present study. Further prospective randomized trials are needed to define the factors influencing the choice of interventional bronchoscopic modality in the management of malignant airway stenoses.

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