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KLİNİK ÇALIŞMA
RESEARCH ARTICLE

Airway stents: a retrospective evaluation of indications, results and complications in our 10-year experience

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ABSTRACT

Airway stents: a retrospective evaluation of indications, results and complications in our 10-year experience

Introduction: *Tracheobronchial stents (TBS) are the principal modalities in the management of central airway obstruction with intrinsic tracheobronchial pathology and extrinsic airway compression. The aim of the study is to assess the indications, surveillance management, complications, and long-term outcomes of the TBS managed by rigid bronchoscopy (RB) in our 10-year experience.*

Materials and Methods: *The files of all patients who underwent stenting in two centers from November 2008 to September 2018 were reviewed for background data, type of disease, and indication for the placement of stents, symptoms, treatment, complications and outcome.*

Results: *305 patients were stented with 342 TBS. TBS were placed in both malignant (n= 223) and benign airway diseases (n= 82). The median length of stent stay was 88 (34-280) days in patients with malignancies and 775 (228-2085) days in benign diseases. There was no stent-related mortality. Mucostasis (19%) and granulation tissue formation (17%) were the most common stentrelated complications. Benign nature of the disease, tumors metastatic to tracheobronchial tree, lenght of stent stay, and shape of stent were associated with the development of complications.*

Conclusion: *TBS offer a safe and effective therapy for patients with both benign and malign tracheobronchial pathologies.*

Key words: *Tracheobronchial stents; stent complication; central airway obstruction*

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ÖZ

Hava yolu stentleri: endikasyonların, sonuçların ve komplikasyonların retrospektif olarak değerlendirilmesi; 10 yıllık tecrübemizle

Giriş: *Trakeobronşiyal stentler (TBS), santral hava yolu obstrüksiyonlarındaki iç trakeobronşiyal patolojiyi ve dış hava yolu kompresyonunu yönetmek için kullanılan başlıca yöntemdir. Bu çalışmanın amacı 10 yıllık tecrübemiz ile rijid bronkoskopi (RB) ile uygulanan TBS'nin endikasyonlarını, sürveyans yönetimini, komplikasyonlarını ve uzun vadeli sonuçlarını değerlendirmektir.*

Materyal ve Metod: *Kasım 2008-Eylül 2018 tarihleri arasında iki merkezde TBS yerleştirilmiş olan tüm hastaların dosyaları; arka plan verileri, hastalık tipi ve stentlerin yerleştirilmesi, semptomlar, tedavi, komplikasyonlar ve sonuç endikasyonları açısından incelendi.*

Bulgular: *Toplam 305 hastaya 342 TBS yerleştirildi. TBS'ler malign (n= 223) ve benign hava yolu hastalıkları (n= 82) olan hastalara yerleştirildi. Ortanca stent kalış süresi malign hastalığı olanlarda 88 (34-280) gün, benign hastalığı olanlarda 775 (228-2085) gündü. Stent ilişkili mortalite görülmedi. Mukostaz (%19) ve granülasyon dokusu oluşumu (%17) en sık görülen stent komplikasyonlarıydı. Hastalığın benign olması, trakeobronşiyal metastatik tümörler, stent kalış süresi ve kullanılan stentin şekli komplikasyonların gelişimi ile ilişkiliydi.*

Sonuç: *TBS'ler, benign ve malign trakeobronşiyal patolojisi olan hastalar için güvenli ve etkili bir tedavi sunar.*

Anahtar kelimeler: *Trakeobronşiyal stent; stent komplikasyonu; santral hava yolu obstrüksiyonu*

INTRODUCTION

Central airway obstruction (CAO) is defined as obstruction of major airways, namely, the trachea and the main bronchi. In adult patients, CAO can occur due to several benign and malignant etiological causes. Patients with significant CAO often experience dyspnea, respiratory distress, and obstructive pneumonia, and frequently die due to suffocation within hours or days. Although surgical resection with reconstruction is the first-line treatment, many patients with comorbidities are not suitable candidates for surgery (1). For these patients, therapeutic bronchoscopy (dilation, argon plasma coagulation (APC), laser vaporization, cryotherapy, and electrocautery) provides rapid palliation that can be lifesaving and improve quality of life (2). However, none of these therapeutic bronchoscopy techniques provide a remedy for intrinsic airway pathology or extrinsic compression. Airway stenting with tracheobronchial stents (TBS) via rigid bronchoscopy (RB) is a well-established procedure in the management of such conditions (3).

TBS, also known as tracheobronchial prostheses, are tubular devices that are used to treat various benign and malignant CAO's and tracheobronchoesophageal fistulas (TBEF) in order to maintain luminal patency and integrity (4). Several studies have proved the effectivity of stents in palliative and curative treatment of CAO and TEF; in fact, they lead to a significant improvement not only in symptoms and lung function but also in quality of life and survival, if stenting is done on time (5).

TBS are made of different types of materials and have advantages and disadvantages according to their structure. TBS have complications such as migration, granulation tissue formation, impaired mucociliary clearance, recurrent lumen obstruction of the stent, and increased bacterial colonization (6-8). Although stenting with TBS is becoming a very popular therapeutic option for patients with tracheobronchial disorders, most interventional pulmonologists do not have well-defined follow-up schedules or protocols (9). This study represents our institutional experience of various airway stenting and follow-up period for the management of obstructive benign and malignant tracheobronchial disorders.

MATERIALS and METHODS

The study enrolled from November 2008 to September 2018 in the interventional pulmonology department of Yedikule Chest Disease and Thoracic Surgery Research and Training Hospital. Databases of our center was searched for records of subjects who underwent stenting with TBS. Before TBS placement, informed consent was obtained from patients and/or parents outlining all potential risks (including airway perforation, infection, dislocation, obstruction, respiratory distress, and death). In studies with a retrospective analysis of standard diagnostic data, no ethical approval is needed in Turkey. Scientific Study Committee of our hospital reviewed and approved the database.

The following information was retrieved from the database: Demographic details, clinical diagnosis, bronchoscopic findings (site of lesion, type of obstruction, and stenosis percentage), treatment modalities (surgery, chemotherapy, radiotherapy), indication for stenting, features of stents, success of stenting, proce-

dure and stent-related complications, duration of follow-up, and survival time. Before the airway stenting, each patient underwent a standard pre-operative and clinical assessment, including physical examination, performance status [the American Society of Anesthesiologists (ASA)], routine laboratory tests, computed tomography (CT) of the chest and flexible bronchoscopy (FB) under local anaesthesia to evaluate airway anatomy and plan the optimal approach for treatment. Multiple therapeutic modalities were used including mechanical debulking and dilatation with the rigid broncoscopes (RB), balloon dilatation, Neodymium-Doped Yttrium Aluminium Garnet (Nd: YAG) laser photocoagulation, and argon plasma coagulation (APC). The equipment used included the Dumon Series II RB (Efer Endoscopy, La Ciotat, Paris, France) with an optical system, stent introducer, and forceps, and FB (model 1T-180; Olympus America Inc, Melville, N.Y, USA). APC (40 W, blended mode/ continuous flow) was applied using an instrument by ERBE Elektromedizin GmbH (Tubingen, Germany). A diode laser operating at a wavelength of 980 nm with 4 to 25 W in pulsed mode (Biolitec Cerals D25; Jena, Germany) was used for the endoluminal treatment. Cryotherapy was performed using the ERBOKRYO system (Elektromedizin GmbH, Tubingen, Germany). TBS used in the procedures could be classified in 3 groups according to material there are made of as follows; silicon stents (SS), metallic stents (MS), and hybrid stents (HS) and in 5 groups according to the shapes as; Y-shaped, straight, J-shaped, Oki, and stenotic stents.

The first phase of the procedure started with an evaluation of the airway and followed by treatment of endoluminal disease with any of the following techniques; mechanical debulking, laser ablation, APC, cryotherapy, and balloon dilatation. The stenotic segment of the airway was mechanically dilated directly with increasing sizes of the RB rotating it around itself. If the stenotic segment could not be treated with the RB then a rapid balloon bronchoplasty was performed. Endobronchial tumors were managed primarily by the Nd: YAG laser and/or APC than this procedure was followed by mechanical débridement and the retrieval of the debrided mass with the help of biopsy forceps and cryo-probe. The next step was the measurement of the diameter and length of the disease-affected trachea and main bronchi. The trachea was intubated with a larger lumen RB (internal diameter, 14 mm). The stent was loaded into a spesific designed introducer and deployed using the applicator through the RB utilizing either "pushing" or the "pulling" technique.

FB was performed 24 hours after stenting. Hypoxemia (desaturation below 90% for more than 1 min), and respiratory insufficiency requiring mechanical ventilation (MV), arrhythmia, hemorrhages, and death within 24 hours after the procedure, were considered to be acute complications. During every visit, FB under local anesthesia was also performed, to evaluate stent position and potential chronic complications such as migration, granulation tissue formation at the edges of the stent, stent fracture and secretion plugs. The primary outcomes of the present study were defined as the assessment of technical and clinical success of TBS, and the complications of the stenting. Technical success was defined as successful placement in the appropriate site in one bronchoscopic session. Clinical success was considered in terms of clinical improvement when the patient was weaned off mechanical ventilation or a dramatic improvement in respiratory symptoms in the subsequent period after the procedure.

Statistical Analysis

Statistical analyses of the data obtained in the study were made using R software. Variables were given as the mean or median with a standard deviation value. Student's t-test was used to compare means and Mann-Whitney U test was used to compare medians. Frequencies were compared with Chi-square and Fisher's Exact test. Spearman and Pearson correlation tests were used for correlation analysis. The date of stenting was considered as zero-day, last check date or date of death was considered as last day on survival analysis. Kaplan-Meier survival analysis was performed for univariate survival analysis. Log-rank or Cox tests were used for comparison of survival rates of groups. Cut-off values for continuous variables were identified using receiver operating characteristic (ROC) analysis (R Software). Variables that were associated with survival at $p< 0.10$ in univariate analysis were included in multivariate analysis. The Cox relative risks model was used for multivariate analysis of these factors that were likely to affect the survival. Forward stepwise analysis method was preferred to show that the variable independently affects the survival. A p-value of less than 0.05 was considered to be significant.

RESULTS

Clinical Features of the Study Population

From November 2008 to September 2018, 305 patients underwent stenting with 342 TBS (a median of one stent per patient; range 1-4) in two hospitals. All patients were symptomatic; principal symptoms were dyspnea in 88%, stridor in 33%, hemoptysis in 22%, and respiratory failure in 14%. The mean ASA patient score prior to intervention was 2.94 ± 0.64 (range 1-4). The majority of patients (73%) had an obstruction ratio of airways greater than 75%. Malignancy (223, 73%) was the most common cause of stenting. The most frequent malignancy responsible for stenting was non-small cell lung cancer (NSCLC) (Table 1). Of the 223 patients with malignant disease (MD), 205 (92%) had undergone previous radiation, chemotherapy, or both. Twenty-nine patients (23%) had a history of previous surgery. Leading benign indication for airway stenting (82 patients) was the post-intubation tracheal stenosis (PITS) (40, 48%) (Table 1).

Table 1. Demographic and clinical details of the study population (n= 305)

Variables	Value
Age, years[a]	57.7 ± 11.5
Gender (male), n (%)	218 (71)
Etiology	
Benign, n (%)	82 (26)
Anastomotic (PA/PT)	8 (10)
PITS	40 (48)
PTTS	15 (18)
TBM	9 (10)
TBEF	7 (8)
Vascular compression	3 (4)
Idiopathic	3 (4)
Malignant, n (%)	223 (74)
Primary tracheobronchial or lung tumors	186 (83)
Non-small cell lung cancer	94 (42)
Small cell lung cancer	70 (31)
Bronchial carcinoid	8 (4)
Malign mesenchymal tumor	6 (3)
Adenoid cystic carcinoma	3 (1)
Others +	5 (2)
Tumors metastatic to tracheobronchial	37 (17)
Eosephagus	12 (5)
Thyroid	6 (3)
Lymphoma	5 (2)
Colorectal	4 (2)
Renal cell	3 (1)
Ovarian	3 (1)
Others ++	4 (2)
Site of lesion	
Trachea	122 (40)
Left main bronchus	23 (8)
Right main bronchus	32 (11)
Trachea and each or both bronchi	128 (41)
Type of stenosis	
Intrinsic obstruction	116 (38)
Extrinsic obstruction	76 (25)
Complex	113 (37)

[a] Results given as mean ± SD; n: Number of cases, PITS: Post-intubation tracheal stenosis, PTTS: Post-tracheostomy tracheal stenosis, TBM: Tracheobronchomalacia, TBEF: Tracheobronchoesophageal fistula, PA: Post-anastomotic, PT: Post-transplantation, Others+; carcinoma in situ (2), low grade neuroendocrine tumor (2), malign epithelial tumors (1); Others++; malignant melanoma (1), endometrium (1), parotis (1), breast (1), larynx (1) cancer.

Procedure of Stenting

A total of 342 TBS were placed, and the stent was successfully deployed in all cases. The indications for TBS placement were CAO (82%) and TBEF (5%), TBM (13%). The majority of patients (90%) required only one stent procedure, but a significant number of patients required two stent procedures (7%), 3 stent procedures (2%), and 4 stent procedures (1%) to maintain stent patency and airway palliation. The placement of TBS resulted in immediate relief of symptoms in 95.2% (289/305) subjects at once. Seventy-seven percent of the patients had additional procedures (Table 2).

Analysis of Stent Complications

Acute complications (< 24 h) were recorded in 30 patients (10%). No severe hemorrhage was observed (Table 3). Chronic complications (> 24 h) of the stents occurred in 98 of 342 procedures (32%). The most common chronic complication was mucostasis of the stent (Table 3). Complications in patients with malignant conditions presented earlier than those in patients with benign conditions (p= 0.04). The complication rates following stenting were as follows, stent migration (15% vs. 6%; p= 0.01), granulation tissue formation (23% vs. 14%; p< 0.05), and mucostasis (26% vs. 11%; p= 0.02) and were significantly different in patients with benign conditions and those with malignant conditions (Table 3).

Complications were directly correlated with tumors metastatic to tracheobronchial (r= 0.16, p= 0.004), follow-up days after airway stenting (r= 0.4, p< 0.001), stent shape (r= 0.21, p< 0.01), and inversely

Table 2. General characteristics of cases with airway stenting

	All patients (n= 305)	Patients with BD (n= 82)	Patients with MD (n= 223)	p
Ages, years[a]	57.7 ± 11	56.3 ± 14	57.9 ± 10	NS
Gender (male), n (%)	218 (71)	45 (54)	173 (77)	< 0.001
Comorbidities, n (%)	76 (25)	32 (39)	44 (19)	< 0.001
Diabetes mellitus	28 (9)	14 (17)	14 (6)	
Cardiovascular disease	36 (11)	26 (31)	10 (9)	
Cerebrovascular disease	19 (6)	10 (12)	9 (4)	
Pulmonary disease	21 (7)	9 (10)	12 (5)	
Others[b]	11 (4)	3 (4)	8 (3)	
Stent Indication, n (%)				NS
CAO	251 (82)	64 (78)	187 (83)	
TEF	17 (5)	6 (7)	11 (6)	
TBM	37 (13)	12 (15)	25 (11)	
Stent location; n (%)				
Trachea	103 (33)	45 (54)	58 (26)	< 0.01
Left main bronchus	11 (4)	2 (3)	9 (4)	NS
Right main bronchus	29 (10)	7 (9)	22 (9)	NS
Trachea and bronchi	162 (53)	15 (18)	147 (65)	< 0.001
Stent shape, n (%)	342	98	244	
Y-shaped stent	189 (55)	22 (22)	167 (68)	< 0.001
Straight stent	73 (21)	7 (7)	66 (27)	< 0.001
Stenotic stent	64 (18)	64 (65)	-	NA
Oki stent	9 (3)	8 (10)	1(1)	< 0.001
J stent	7 (2)	-	7 (2.3)	NA
Stent type, n (%)	342	98	244	
Silicon stent	292 (85)	93 (94)	219 (9)	< 0.001
Metallic stent	46 (13)	6 (6)	21 (8)	NS
Hybrid stents	4 (1)	-	4 (2)	NA
AD, n (%)	237 (77)	64 (78)	173 (77)	NS
APC	118	8	110	
Laser	37	2	35	
Cryo	123	11	112	
MD	95	61	34	
Ballon	39	34	4	

[a] Results given as mean ± SD; [b] Other chronic diseases such as renal failure, thyroid diseases, n: Number of cases, AD: Additional procedures, APC: Argon plasma coagulation, MD: Mechanical dilatation, CAO: Central airway obstruction, TBM: Tracheobronchomalacia, TBEF: Tracheobronchoesophageal fistula, BD: Benign diseases, MD: Malign diseases, NS: Statistically nonsignificant, NA: Not available.

correlated with malign diseases (r= -0.15, p= 0.007) (Table 4). While granulation tissue development was more frequent in tumors metastatic to tracheobronchial (p< 0.001), MS (p< 0.05), prior treatment (non-KT and non-RT) (p< 0.01), and additional processing (p< 0.01), migration was observed more frequently in benign diseases (p< 0.05) and with straight stents (p< 0.001) (Table 4). Univariate analysis showed stent complications were most closely associated with ASA score (p< 0.01), presence of benign disease (p= 0.008), presence of extrathoracic origin (p= 0.006), stent shape (p< 0.01), additional processing (p= 0.004), and length of follow-up period (p< 0.001). In the multivariate analysis, patients with the presence of stent complications were only significantly more likely to the length of the follow-up period (p= 0.003) (Table 5).

Outcomes and Follow-Up

After airway interventions 298 of 305 patients (95%) noted a significant improvement in their symptoms. There was no procedure-related mortality. The mean

Table 3. Complications and follow-up results of cases with airway stenting

	All patients (n= 305)	Patients with BD (n= 82)	Patients with MD (n= 223)	p
Acute complications, n (%)	30 (10)	6 (7)	24 (10)	NS
Respiratory distress needing MV	13 (4)	2 (2)	11 (5)	NS
Minimal-moderate bleeding	10 (3)	-	10 (4)	NA
Atrial fibrillation	3 (1)	2 (2)	1 (1)	NS
Trauma to teeth	4 (1)	2 (2)	2 (1)	NS
Excessive bleeding	-	-	-	NA
Procedure-related death	-	-	-	NA
Chronic complications, n (%)	98 (32)	36 (43)	62 (27)	**< 0.05**
Mucostasis	58 (19)	22 (26)	26 (11)	**0.02**
Granulation	52 (17)	19 (23)	33 (14)	**< 0.05**
Tumor regrowth	21 (7)	-	21 (10)	NA
Stent migration	27 (9)	13 (15)	14 (6)	**0.01**
Breakage	2 (0.5)	-	2 (1)	NA
Treatment of stent complications				
Aspiration of secretion	52 (15)	15 (18)	37 (16)	NS
AD (Cryo, APC, MD)	62 (18)	17 (20)	45 (20)	NS
Stent removel	34 (10)	21 (25)	13 (6)	**< 0.01**
Stent replacement	37 (11)	27 (32)	10 (4)	**< 0.001**
Time of complication (day)[a]	22 (7-80)	8 (1-15)	45 (12-145)	**0.04**
Follow-up after TMS (mounth)[a]	4.8 (1-21)	25 (7-69)	2.9 (1-9.3)	**< 0.001**
Mortality ratios, n (%)	229 (75)	32 (39)	197 (88)	**< 0.001**

[a] Results given as median (quarter intervals); n: Number of cases, APC: Argon plasma coagulation, MV: Mechanical ventilation, AD: Additional procedures, BN: Benign diseases, MD: Malign diseases, APC: Argon plasma coagulation, MD: Mechanical dilatation, NS: Statistically nonsignificant, NA: Not available.

follow-up duration was 5 (2-20) months. The overall 5-year survival rate of the patients was calculated as 21%. The 5-year survival rate was 58% for patients with benign diseases and 7% for patients with malign diseases (p< 0.001) (Figure 1).

Factors significantly affecting survival in malign diseases using the univariate analysis were type of malignancy (p< 0.012), degree of airway obstruction (p< 0.1), stent shape (p= 0.051), and treatment modality (p= 0.04). Multivariate analysis showed that the type of malignancy were independent predictors of survival (Table 6, Figure 2). In benign diseases, factors that were found to affect the survival rate on the univariate analysis (p< 0.1) (age, the type of underlying benign disease, degree of airway obstruction, and presence of comorbidities) were also used in multivariate analysis of the factors that may affect the survival rate. The analysis showed that age was independently prognostic factors (Table 7, Figure 3).

DISCUSSION

Airway stenting is an appealing mini-invasive palliative treatment option for patients with tracheobronchial disorders, who are not surgical candidates. Recent technological advances have increased the popularity of TBS with interventional pulmonologists and chest physicians, particularly because stenting is effective for both extraluminal and intraluminal lesions and promptly relieves acute airway obstruction-related disorders. We evaluated the indications-complications and follow-up period of the stents we applied in past 10-years in this retrospective study and discussed them in the context of the recent literature. Technical success was achieved in 100% of patients and clinical success in 76%. There was no stent-related mortality. The results of our study suggest that placement of TBS is a safe and effective treatment option in the management of benign and malignant disorders.

TBS are made of silicone, metallic or a combination of both (hybrid stents). Most stents are available in

Table 4. Correlation coefficients between demographic variables and stent complications

Variable	TBS complication	
	r coefficient	**p**
Malign diseases	**-0.15**	**0.007**
Type of stenosis	-0.01	NS
Tumors metastatic to tracheobronchial	**0.16**	**0.004**
Follow-up days after stenting	**0.4**	**< 0.001**
Treatment modality	0.1	NS
Age, years	0.01	NS
Presence of comorbidities	0.02	NS
Stent shape (SS)	**0.14**	**0.01**
Type of stent	0.04	NS
AD	0.02	NS
	Migration	
	r coefficient	**p**
Malign diseases	**-0.14**	**0.009**
Type of stenosis	-0.05	NS
Tumors metastatic to tracheobronchial	0.07	NS
Follow-up days after stenting	**0.2**	**< 0.001**
Treatment modality	0.1	NS
Stent shape (Y-S)	**-0.25**	**0.001**
Type of stent	0.06	NS
	Granulations	
	r coefficient	**p**
Malign diseases	-0.09	NS
Type of stenosis	-0.01	NS
Tumors metastatic to tracheobronchial	**0.16**	**0.04**
Follow-up days after stenting	**0.3**	**< 0.001**
Treatment modality (KT and RT)	**-0.13**	0.01
Stent shape	0.03	NS
Type of stent (MS)	**0.12**	**< 0.05**
	Mucostasis	
	r coefficient	**p**
Malign diseases	**-0.18**	**0.001**
Type of stenosis	-0.06	NS
Tumors metastatic to tracheobronchial	0.03	NS
Follow-up days after stenting	**0.2**	**< 0.01**
Treatment modality	0.04	NS
Stent shape (SS)	**0.18**	**0.02**
Type of stent	0.08	NS

TBS: Tracheobronchial stents, AD: Additional processing (laser, argon plasma coagulation, cryotherapy, mechanical dilatation), CT: Chemotherapy, RT: Radiotherapy, SS: Straight stent, Y-S: Y stent, MS: Metallic stent, NS: Statistically nonsignificant.

various shapes (straight, stenotic, Oki, Y-shaped, J-shaped), diameters, and lengths (10). The main indication for airway stenting is to reduce the symptoms associated with airway obstruction caused by benign or malignant diseases in which medical, surgical, or endoscopic treatments are not sufficient. In both intrinsic and extrinsic airway obstructions, TBS can be used to provide airway patency. In addition, patients with degenerative expiratory central airway collapse (tracheobronchomalacia or selected dynamic airway collapse disease), postsurgery/transplantation anastomotic strictures or patients with TBEF should benefit from stenting (4,11). In our retrospective study, there were numerous diversity of indica-

Table 5. Univariate and multivariate analysis for the presence of any stent-related complications among patients

Variable	Univariate analysis p-value OR (95% CI)	Multivariate analysis p-value OR (95% CI)
Age, years	0.7 (0.5-0.11)	
Male, gender	0.2 (0.09-0.4)	
ASA score	**0.01 (0.001-0.12)**	0.09 (-0.22-0.1)
Presence of comorbidities	0.66 (0.61-0.68)	
Presence of benign disease	**0.008 (0.006-0.011)**	0.63 (-0.4-0.25)
Tumors metastatic to tracheobronchial tree	**0.006 (0.004-0.02)**	0.07 (-0.11-0.45)
Type of stenosis	0.47 (0.45-0.48)	
Stent shape	**0.005 (0.003-0.07)**	0.7 (-0.11-0.08)
Type of stent	0.7 (0.6-0.8)	
Treatment modality	0.2 (0.1-0.3)	
Additional procedure	**0.05 (0.03-0.07)**	0.08 (-0.22-0.37)
Percentage of lumen obstruction	0.6 (0.6-0.8)	
Follow-up period	**0.001 (0.001-0.01)**	**0.003 (0.005-0.02)**

ASA: American Society of Anesthesiologists.

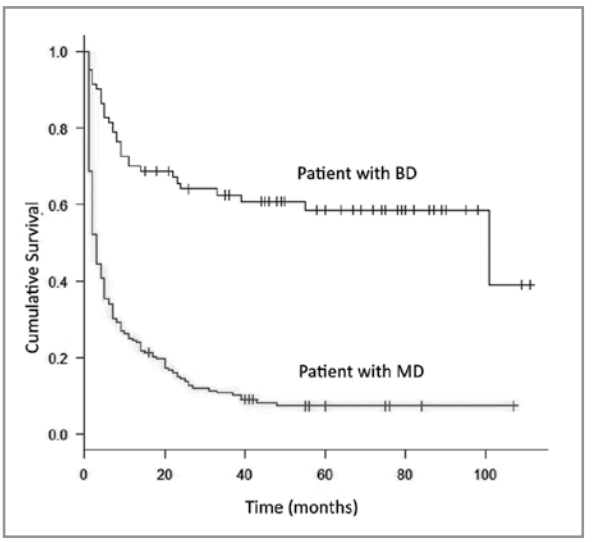

Figure 1. Overall survival of patients after interventional bronchoscopy (MD: Malign diseases, BD: Benign diseases, p< 0.001 by log-rank test).

tions for stenting and central airway obstructions (CAO) that were the highest, consistent with the literature. In addition, our study showed that all the patients had symptomatic relief after stenting.

The majority of TBS indications are CAO due to malignant airway tumors. These patients branded with a poor prognosis and should not benefit from surgery with curative intent; however, they will require procedures for palliation with the hope of being provided with an improved quality of life (2). TBS does not treat the tumor; so, the objective of an airway stent is either entirely palliation or treatment and prevention of symptoms of CAO to give an opportunity to those patients to receive systemic therapy (12). In patients with malignancies, the most common indication for TBS placement is bronchogenic carcinoma, which can present as extraluminal compression with or without an intraluminal lesion. Approximately 30% of patients with bronchogenic carcinoma develop CAO and may require airway stents as part of their management (13). Metastases from both intrathoracic organs such as malignant lymphomas, esophageal tumors, tumors of larynx or thyroid, and extrathoracic organs can also invade the central airways in addition to primary lung malignancies (11). Primary lung cancers were the most common indication for stenting in this study. And metastasis from extrathoracic organs including lymphoma, tumors of the larynx was also seen.

Indications for stenting in benign tracheal stenosis (BTS), include long tracheal strictures, stenosis due to inflammatory diseases, post lung transplantation strictures, tracheobronchomalacia, postintubation tracheal stenosis (PITS) and post tracheostomy tracheal stenosis (PTTS). The treatment algorithm of BTS is well defined and surgery is considered as the first treatment of choice. When surgery is not possible,

Table 6. Characteristics of the study population affecting survival after interventional bronchoscopic procedures for malignant diseases

	Survival				p	
Characteristics	**Mean months (%95 CI)**	**3 months (%)**	**6 months (%)**	**12 months (%)**	**Univariate**	**Multivariate**
Type of underlying malignancy					**0.012**	**0.04 (0.01-1.2)**
Non-small cell lung cancer	3 (1-9)	36	24	19		
Small cell lung cancer	1 (1-5)	23	7	-		
Tumors metastatic to TBT	2 (1-16)	49	37	27		
Site of the lesion					0.32	
Trachea	2.5 (1-9.5)	36	27	19		
Right main bronchus	2 (1-16)	34	19	17		
Left main bronchus	3 (1-9)	40	31	22		
Trachea + right + left main bronchus	3 (1-9)	53	32	20		
Degree of airway obstruction (%)[a]					**0.1**	**0.9 (0.8-1.1)**
Grade 1 (< 50%)	3 (1-8.5)	69	53	32		
Grade 2 (50%-74%)	3 (1-11.7)	65	39	21		
Grade 3 (75%-89%)	2.4 (1-17)	40	33	22		
Grade 4 (90%-100%)	2 (1-7)	40	25	15		
Type of lesion					0.4	
Intrinsic obstruction	3 (1-11)	47	32	23		
Extrinsic obstruction	2 (1-13)	40	32	26		
Complex	3 (1-8)	43	31	16		
Treatment modality					**0.04**	**0.63 (0.6-2.3)**
Surgery	6.5 (1.25-26)	68	50	42		
CT	2 (1-10)	44	34	24		
RT	9.5 (2-14)	58	45	23		
CT and RT	12 (2-33)	67	43	27		
Sytent type					0.69	
SS	3 (1-9.25)	46	34	23		
MS	2 (1-6.6)	35	29	15		
HS	1.5 (1-11)	50	25	-		
Stent shape					**0.051**	**0.3 (0.2-11.6)**
Y-shaped stent	3 (1-8)	42	29	20		
Straight stent	3 (1-16)	51	22	49		
Oki stent	8 (1.7-51)	55	45	-		
J stent	9 (2-43)	66	33	-		

CT: Chemotherapy, RT: Radiotherapy, SS: Silicon stent, MS: Metallic stent, HS: Hybrid stents, [a] Myer-Cotton stenosis grading system, TBT: Tracheobronchial tree.

mechanical dilatation is usually proposed and stents are placed only when dilatation fails to offer an acceptable result (14). PITS and PTTS compose the majority causes of BTS (15). In these cases, stents are often considered as better options, essentially because of their retrievable character. Several representative studies of clinical experience with TBS in BTS have been reported (16-18). All patients had immediate symptomatic relief after stent placement with no procedure-related mortality. The majority of our patients with BTS who had airway stenting were PITS and PTTS (64%). We found symptomatic relief and 100% technical success in all cases. We preferred stenotic stents (SS) and we noticed that S-S were stable and efficacious if the narrowed part of SS was placed in the stenotic segment correctly.

The advantages of SS are that they are easily repositioned or removed, minimal granulation formation, and cost-effectivity. Disadvantages of SS if compared to other stent types are; stent high rates of migration, mucostasis, adherence of secretions due to the impairment of mucociliary clearance, and necessity

Table 7. Characteristics of the study population affecting survival after interventional bronchoscopic procedures for benign diseases

	Survival				p	
Characteristics	**Mean months (95% CI)**	**3 months (%)**	**6 months (%)**	**12 months (%)**	**Univariate**	**Multivariate**
Age, years					**0.001**	**0.02 (0.08-0.5)**
< 58	55 (15-78)	90	87	82		
≥ 58	14 (5-37)	87	77	65		
Type of underlying benign diseases					**0.06**	0.37 (0.1-1.1)
PITS	21 (6-65)	85	75	69		
PTTS	69 (11-90)	86	80	73		
Anastomotic (PO/PT)	40 (14-74)	88	80	80		
TBM	11 (4-55)	83	58	44		
Degree of airway obstruction (%)[a]					**0.017**	0.1 (0.1-3.4)
Grade 1 (< 50%)	46 (12-68)	90	80	60		
Grade 2 (50%-74%)	24 (8-87)	88	81	72		
Grade 3 (75%-89%)	15 (8-36)	84	75	72		
Grade 4 (90%-100%)	7 (1-45)	72	54	45		
Type of lesion					0.46	
Intrinsic obstruction	36 (7-79)	89	83	70		
Extrinsic obstruction	14 (5-56)	87	69	52		
Complex	23 (8-69)	93	87	76		
Comorbidities	14 (4-80)	92	84	68	**0.001**	0.16 (0.06-9.1)
Diabetes mellitus	14 (5-73)	92	88	78		
Cardiovascular disease	14 (4-83)	94	89	77		
Cerebrovascular disease	32 (5-87)	94	88	80		
Chronic pulmonary disease	14 (4-55)	92	85	75		
Sytent type					0.8	
Silicon stent	26 (7-72)	94	89	82		
Metallic stent	23 (15-39)	50	50	50		
Stent shape					0.42	
Stenotic stent	33 (8-78)	89	84	77		
Y-shaped stent	44(19-68)	75	75	75		
Straight stent	14 (5-55)	86	79	71		
Oki stent	11 (5-38)	100	100	100		

PITS: Post-intubation tracheal stenosis, PTTS: Post-tracheostomy tracheal stenosis, TBM: Tracheobronchomalacia, [a] Myer-Cotton stenosis grading system, PO: Post-anastomotic, PT: Post-transplantation.

of performing under general anesthesia with RB (19). Metallic stents (MS) advantages are easily delivery with FB, well compatibility to the anatomic structure of the airway, low rates of migration and better mucociliary clearance. The disadvantages are it is permanent in the airways and can cause prominent granulation tissue within the stent (19). In our study, we used SS in the majority of our cases (88%) because of these advantages. However, the usage of MS was very low, we think that depends on the characteristics of our patient population.

Despite many benefits, TBS are foreign bodies prone to complications. Complications may occur during follow-up; but life-threatening serious complications are rare (20). Hemorrhage, migration, airway perforation and pneumothorax are acute but rare complications. We observed minimal or moderate hemorrhage in ten patients; all hemorrhages were easily controlled. We encountered no complication-related deaths, but thirteen patients required non-invasive mechanical ventilation after the procedure. In addition that, acute complications rates were similar with the recent studies (10%) than the previous studies with a ratio of 3-10% (21,22).

The reported rate of stent-related complications vary in the literature (mostly 40-60%, and as high as

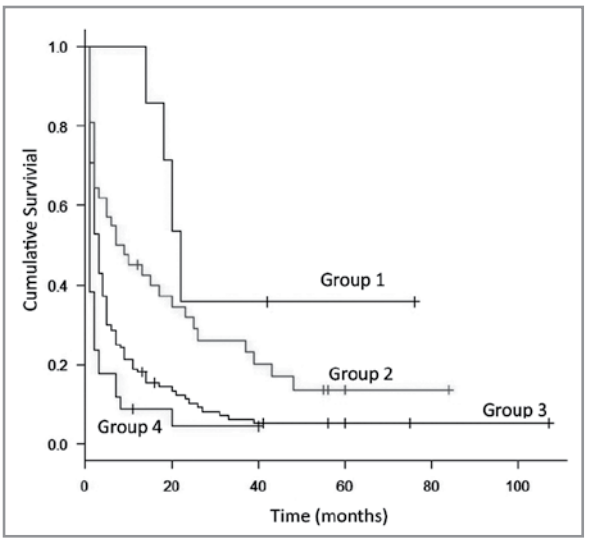

Figure 2. Factors significantly affecting survival in malign diseases using the Kaplan–Meier log-rank analysis (Group 1; patient with bronchial carcinoid, Group 2; patient with tumors metastatic to tracheobronchial tree, Group 3; patient with non–small cell lung cancer, Group 4; patient with small cell lung cancer, p< 0.001 by log-rank test).

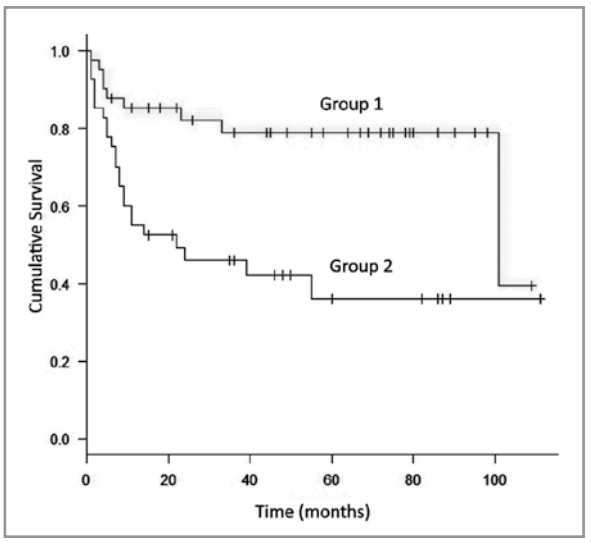

Figure 3. Factors significantly affecting survival in benign diseases using the Kaplan-Meier log-rank analysis (Group 1; patient age < 58 years, Group 2; patient age ≥ 58 years, p< 0.001 by log-rank test).

87%), based on the study population and the types/material of airway stents deployed (23-26). Among long-term complications, granulation tissue formation with subsequent restenosis, stent occlusion or tumor growth obstruction, mucostasis, stent-migration, stent-fracture are described. Moreover, these complications are more commonly seen with benign lesions than with malignant lesions (27,28). The rates of long-term complications like granuloma formation and stent fractures are low due to the short life expectancy of patients with malignancy. The long-term complication rate in our study (32%) is within this range. We observed a higher stenting complication rates in patients with BD (43%) than patients with MD (27%). In univariate analysis, benign airway stenosis, duration of follow-up and straight stent use were significant in the univariate analysis, whereas in the multivariate analysis only the follow-up period was significant.

Mucostasis is the most common stent complication (29). It is well known that stents impair mucus clearance, thus accumulation of secretions can be considered a slightly annoying problem or a severe complication. It consists of a coating of wires and polymers used for stents with biofilm. Secretions accumulate and block the stent lumen, causing severe shortness of breath in the patient. Halitosis develop due to bacterial and fungal colonization in the stent. The most common complication of our cases was mucostasis (19%). Also, there was a relationship between mucostasis and the stent shape and benignity of disease.

Granuloma formation (GF) rates vary depending on the underlying disorder and the type of stent used. GF may be more common in patients with benign airway obstructions than in those from the malignant disease group (30,31). This was probably due to the longer length of stent stay in the airways. In addition to that, the literature reports that GF is more common in MS than in SS (32). GF is the second most common complication in our cases (52 of 305 patients, 17%) and similar in the previously reported range in the literature (2.9-15.2%) and also in benign patients (26%) GF is more common than malignant patients (11%) (32-34). In addition, similar to the literature (2.9-15%), higher levels of GF were observed in MS (35%) than SS (15%) in our study. Likewise, we found an inverse correlation between the GF and the history of treatment (chemo and/or radiotherapy). This finding may suggest that chemo/radiotherapy contributes to the prevention of granulation development. The immunosuppressive effect of these therapies could have reduced the inflammatory response and as a consequence, the tissue granulation formation also.

Migration is another common complication associated with stents. SS have higher migration rates than

MS. It is seen in 10% of malignant patients and twice as often in benign patients (35). In our study, there was a higher rate of migration in benign patients (15%) than in malign patients (6%). In addition, we found very low rates of migration in our cases with Y-stents (2%), whereas the frequency of migration between type of stent was not significant. This can be attributed to the low (18%) usage of MS.

In patients with both benign and malignant airway obstruction, airway stenting may provide immediate and durable palliation that can rescue the patient from imminent death and assure an improved quality of life (36,37). In this study, we also investigated prognostic factors associated with overall survival after the airway stenting. In multivariate analysis, survival depends on the underlying malignancy type of patient with MD, and the age of the patients with BD (greater than 58 years). On the other hand, the site of the lesion, degree of airway obstruction, type of lesion, treatment modality, presence of comorbidities, type and shape of stents were not significantly associated with increased mortality in our study.

In conclusion; our study showed that all the patients had symptomatic relief after airway stenting. No stent-related-deaths were recorded in our population due to stent placement and permanence in the airways. The results of this study and the systematic review suggest that airway stenting is a safe and effective treatment option in the management of benign and malignant airway disorders.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: MAÖ, ECS

Analysis/Interpretation: ECS, EÇ

Data Acquisition: DT, EGUC

Written by: ECS, GÖ

Critical Revision: DD, EGUC, MAÖ

Final Approval: All of authors.

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