Turkish Journal of Thoracic and Cardiovascular Surgery 2021;29(3):360-369
http://dx.doi.org/doi: 10.5606/tgkdc.dergisi.2021.19927

Original Article / *Özgün Makale*

Secondary pulmonary malignancies requiring interventional bronchoscopic procedures

Girişimsel bronkoskopik işlem gerektiren sekonder pulmoner maligniteler

Efsun Gonca Uğur Chousein, Demet Turan, Mehmet Akif Özgül, Erdoğan Çetinkaya

Department of Chest Diseases, Health Sciences University, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey

ABSTRACT

Background: In this study, we aimed to share our single-center experience and to investigate the effect of interventional bronchoscopic procedures on secondary pulmonary malignancies in terms of complications, success, and survival rates.

Methods: A total of 83 patients (42 males, 41 females; mean age: 57.8±15.2 years; range, 18 to 94 years) with secondary pulmonary malignancies who underwent interventional bronchoscopic procedures between January 2009 and December 2019 were retrospectively reviewed. Data including demographic and clinical characteristics of the patients, complications, and success and survival rates were recorded.

Results: The most common secondary pulmonary malignancies were kidney and thyroid tumors with the complaints of cough, shortness of breath, and hemoptysis. The mean duration before the diagnosis was 34.7±52.8 (range, 0.1 to 219.3) months, and the mean survival after the diagnosis were 10±13.1 (range, 0.2 to 44.4) months. A total of 92% of the patients had an airway obstruction of >50% and the interventional bronchoscopic procedures such as argon plasma coagulation, laser, cryo, and mechanical resection were successful in achieving airway patency. Laser application was found to significantly improve survival (p=0.015). Acute complication rate was 8.4% and mortality rate was 0%.

Conclusion: In patients with tracheobronchial lesions due to secondary pulmonary malignancies, interventional bronchoscopic procedures, regardless of the stage of the disease, provide rapid palliation in life-threatening symptoms such as dyspnea and hemoptysis due to airway obstruction, prolonging patient's survival and gain time for additional treatments to take effect for primary disease.

Keywords: Interventional pulmonology, secondary pulmonary malignancy, tracheobronchial system.

ÖZ

Amaç: Bu çalışmada tek merkezli deneyimimiz sunuldu ve girişimsel bronkoskopik işlemlerin komplikasyonlar, başarı ve sağkalım oranları açısından sekonder pulmoner maligniteler üzerindeki etkisi araştırıldı.

Çalışma planı: Ocak 2009 - Aralık 2019 tarihleri arasında girişimsel bronkoskopik işlem yapılan sekonder pulmoner maligniteli toplam 83 hasta (42 erkek, 41 kadın; ort. yaş: 57.8±15.2 yıl; dağılım, 18-94 yıl) retrospektif olarak incelendi. Hastaların demografik ve klinik özellikleri, komplikasyonlar ve başarı ve sağkalım oranları dahil olmak üzere veriler kaydedildi.

Bulgular: En sık görülen sekonder pulmoner maligniteler öksürük, nefes darlığı ve hemoptizi şikayetleri ile böbrek ve tiroid tümörleri idi. Tanıya kadar geçen ortalama süre 34.7±52.8 (dağılım, 0.1-219.3) ay ve tanı sonrası ortalama sağkalım 10±13.1 (dağılım, 0.2-44.4) ay idi. Hastaların toplam %92'sinin hava yolu obstrüksiyonu %50'nin üzerindeydi ve argon plazma koagülasyon, lazer, kriyo ve mekanik rezeksiyon gibi girişimsel bronkoskopik işlemler hava yolu açıklığını sağlamada başarılı idi. Lazer uygulaması sağkalımı anlamlı düzeyde iyileştirdi (p=0.015). Akut komplikasyon oranı %8.4 ve mortalite oranı %0 idi.

Sonuç: Sekonder pulmoner malignitelere bağlı trakeobronşiyal lezyonu olan hastalarda, hastalığın evresinden bağımsız olarak, girişimsel bronkoskopik işlemler, hava yolu obstrüksiyonuna bağlı dispne ve hemoptizi gibi hayatı tehdit eden semptomlarda hızlı bir iyileşme sağlayarak, hastaların sağkalımını uzatır ve primer hastalıkları için alabilecekleri ek tedaviler için onlara zaman kazandırır.

Anahtar sözcükler: Girişimsel pulmonoloji, sekonder pulmoner malignite, trakeobronşiyal sistem.

Received: April 26, 2020 *Accepted:* July 23, 2020 *Published online:* July 26, 2021

Correspondence: Efsun Gonca Uğur Chousein, MD. SBÜ Yedikule Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları Kliniği, 34020 Zeytinburnu, İstanbul, Türkiye. Tel: +90 505 - 649 37 01 e-mail: efsungoncachousein@yahoo.com

Cite this article as:

Uğur Chousein EG, Turan D, Özgül MA, Çetinkaya E. Secondary pulmonary malignancies requiring interventional bronchoscopic procedures. Turk Gogus Kalp Dama 2021;29(3):360-369

Malignancies occupy the first rank within major areas of interest of interventional pulmonology. Airway obstructions, life-threatening hemorrhage, post-obstructive pneumonia, and atelectasis secondary to malignancies are pulmonary disorders within the field of interventional pulmonology.[1-4]

The lungs are the organs most susceptible to metastatic spread of all malignant tumors. Lung parenchyma and lymphatics are the usual sites affected by secondary pulmonary malignancies; however, the possibility of metastases within the tracheobronchial tree is rare and underestimated.[5-8] Such tumors can be difficult to differentiate from primary pulmonary malignancies, due to very similar appearance and histology.[9] They may present as endoluminal masses with irregular margins, masses causing external compression, or mucosal/submucosal infiltrations.[10]

Tracheobronchial involvement due to secondary pulmonary malignancies is usually a late-stage finding of primary disease, but can occur at any stage.[6] The medical literature contains scant information about secondary pulmonary malignancies requiring interventional bronchoscopic procedures. As they are rarely encountered, the current literature consists either of case reports or series of patients pooled from different centers, rather than large-scale studies.

Irrespective of disease stage, interventional bronchoscopic procedures can provide acute palliation of -life-threatening conditions, such as dyspnea due to airway obstruction, hemoptysis and fistulas, and also improve quality of life, prolong survival, and gain time for treatment addressing the primary disease.[11,12] Therefore, this group of patients should not be overlooked at any stage of their diseases and should be always followed closely according to pulmonary symptoms, clinical course, and radiological findings.[13] In the present study, we aimed to share our single-center experience and to investigate the effect of interventional bronchoscopic procedures on secondary pulmonary malignancies in terms of complications, success, and survival rates.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Health Sciences University, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital, Department of Chest Diseases between January 2009 and December 2019. A total of 83 patients (42 males, 41 females; mean age: 57.8±15.2 years; range, 18 to 94 years) with secondary pulmonary malignancies who underwent interventional bronchoscopic procedures were included. Cases that were not reported as definitely diagnosed metastases of tumors of extrapulmonary origin according to histopathologic examination were excluded. The patients were evaluated based on their medical records for demographic data, histopathological features of primary extrapulmonary malignancies, tracheobronchial distributions, the timing of occurrence following the primary diagnosis, bronchoscopic findings, complications related to the procedure, and survival. Patients were included in the study if their bronchoscopic examination revealed external compression, mucosal/submucosal infiltration, an endoluminal mass or fistula in the tracheobronchial system, and had a histopathologically confirmed diagnosis of secondary pulmonary malignancy according to biopsy results. A written informed consent was obtained from each patient. The study protocol was approved by the Scientific Board of Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital (22.01.2020/237-2) and Ethics Committee of University of Health Sciences (46418926-050.03.04: 20/128). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients presenting with preliminary diagnoses such as malignant airway obstruction and hemoptysis were initially evaluated with thoracic computed tomography (CT), and if possible, by fiberoptic bronchoscopy (FOB).

Malignant airway obstruction was defined as more than 50% obliteration in the tracheobronchial system lumen within the reach of a rigid bronchoscope. The degree of obstruction was determined based on the Cotton-Myer grading for tracheal stenosis. Success of treatment was defined as more than 50% relief of the obstruction and reconnection with the distal airway, accompanied by clinical improvement. Bronchoscopic findings in the tracheobronchial system were classified as external compression, mucosal/submucosal infiltration, endoluminal mass, and fistula.

From the perspective of interventional pulmonology, cases with secondary pulmonary malignancies were first compiled and, then, classified into two categories, according to whether the primary malignancy had an intra- or extrathoracic location. Esophageal, thyroid, parathyroid tumors, and lymphomas were accepted as intrathoracic malignancies. All other secondary pulmonary malignancies, including kidney, colon and breast tumors were considered as extrathoracic malignancies.

Rigid bronchoscopic procedures were performed under general anesthesia. All patients were monitored

with electrocardiography and oxygen saturation (SpO_2) during the procedure, with arterial blood pressure measured every 5 min. General anesthesia induction was achieved with midazolam 0.05 to 0.10 mg/kg, propofol (maximum dose 1,000 mg), remifentanil (maximum dose 2 mg), and rocuronium bromide (maximum dose 50 mg) according to the patient's condition. The equipment used in the procedures included the DuMoN™ Series II Rigid Bronchoscope (Efer Endoscopy, La Ciotat, France) with optical system. The argon plasma coagulation (APC) applicator (40 W, blended mode/ continuous flow) was used via an instrument by Erbe Elektromedizin (Erbe Elektromedizin GmbH, Tubigen, Germany). Endoluminal treatment was accomplished with a diode laser operating at a wavelength of 980 nm with 4 to 25 W in pulsed mode (Biolitec® Ceralas D25; Germany). Cryotherapy was performed with the ERBOKRYO® system (Erbokryo®; Erbe Elektromedizin GmbH, Tubingen, Germany).

Statistical analysis

Statistical analysis was performed using the R software version 3.6.3. Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency, where applicable. For continuous variables, the Student t-test and Mann-Whitney U test were used, while chi-square and Fisher's exact tests were used for categorical variables that met the normality assumption. In survival analysis, the first interventional bronchoscopic procedure date was accepted as zero-day, while the last check date or date of death was accepted as the last day. The Kaplan-Meier survival analysis was used for univariate survival analysis. Log-rank test was applied for comparison of survival rates of groups. A p value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics of the patients are shown in Table 1. The most common complaints were cough, shortness of breath, and hemoptysis.

The mean time from the diagnosis of the primary tumor until the detection of tracheobronchial involvement was 34.7±52.8 (range, 0.1 to 219.3) months. The longest time interval until tracheobronchial involvement was seen in colon tumors with 83.8±80.1 (range, 24.7 to 219.3) months and lymphomas with 50±57.9 (range, 0.1 to 185) months, while the shortest time interval was in tumors of the esophagus with 8.9±10.8 (range, 0.1 to 37.7) months (Table 2).

The mean survival time after the diagnosis of endobronchial metastasis was 10±13.1 (range, 0.2 to 44.4) months. The shortest survival time was seen in cervix and prostate tumors (Table 2). Considering the four largest groups of malignancies including the majority of secondary pulmonary malignancies, the mean survival times of thyroid was 9.3±10.1 (range, 0.3 to 26.1) months, kidneys were 17.6±15.6 (range 0.4 to 40.5) months, esophagus was 6.2±12.8 (range, 0.2 to 44.4) months, and lymphoma was 6.4±9.6 (range, 1.5 to 28.1) months.

There was a wide variety of subgroups, but the most prominent malignancies in order of frequency were thyroid and kidney tumors (Table 2). According to their

Table 1. Baseline features of study population (n=83)

Variables	n	%	Mean±SD	Min-Max
Age (year)			57.8±15.2	18-94
Sex				
Female	41			
Male	42			
Complaints				
Cough	43		32.8	
Shortness of breath (dyspnea)	25		19	
Hemoptysis	18		13.8	
Sputum	12		9.2	
Chest pain	9		6.9	
No complaints	17		13	
Other	7		5.3	

SD: Standard deviation.

Table 2. Pathological characteristics of patients with secondary pulmonary malignancies

	Primary tumor type	n	%	*Time (months) Mean±SD	*Time (months) Min-Max	†Survival (months) Mean±SD	†Survival (months) Min-Max	Alive/Dead
Intrathoracic origin	Thyroid	14	16.9	19.8±32.3	0.1-87.4	9.3±10.1	0.3-26.1	4/10
	Esophagus	13	15.6	8.9±10.8	0.1-37.7	6.2±12.8	0.2-44.4	2/11
	Lymphoma	13	15.6	50±57.9	0.1-185	6.4±9.6	1.5-28.1	5/8
	Parotid gland	1	1.2	- ¶		- ¶		0/1
Extrathoracic origin	Kidneys	14	16.9	43.8±37.7	0.1-100.5	17.6±15.6	0.4-40.5	0/14
	Colon	5	6	83.8±80.1	24.7-219.3	11.9±15.9	0.9-38.1	0/5
	Ovarian	5	6	10.6±13.1	0.1-26.9	10.6±19.4	0.3-39.7	0/5
	Breast	4	4.9	20.7±22.9	0.1-45.4	0		2/2
	Larynx	3	3.7	51.3±88.8	0.1-153.9	20.8±27.7	1.2-40.5	1/2
	Skin	2	2.4	0		5.8±5	2.2-9.4	0/2
	Endometrium	2	2.4	-		8.8±11.9	0.4-17.2	0/2
	Rectum	2	2.4	64.2±51.9	27.5-100.9	alive		2/0
	Others‡	5	6	80±119.4	3-217.6	4.9±3.9	2.2-10.5	1/4
	Total	83	100	34.7±52.8	0.1-219.3	10±13.1	0.2-44.4	17/66

SD: Standard deviation; * Interval between diagnosis of primary tumor and endobronchial metastasis; † Survival time from diagnosis of endobronchial metastasis. ¶ This type (parotid gland) of tumor was detected in only 1 case so that a mean, a SD, min and max values could not be given. The interval between diagnosis and detection of endobronchial metastasis was 154 months and and survival time from diagnosis of endobronchial metastasis was 2.2 months. ‡ Other types of tumors: Cervix tumor in 1 case, with 19.7 months of interval between diagnosis and detection of endobronchial metastasis and 2.2 months of survival time from diagnosis of endobronchial metastasis, Testis tumor in 1 case, with 217.6 months of interval between diagnosis and detection of endobronchial metastasis who is still alive, Bladder tumor in 1 case with a 4.5 months of survival after detection of endobronchial metastasis. Prostate tumor in 1 case who was diagnosed and treated in the same session with a 2.2 months of survival time from diagnosis of endobronchial metastasis, Synovial sarcoma in 1 case, with 3 months of interval between diagnosis and detection of endobronchial metastasis and 10.5 months of survival time from diagnosis of endobronchial metastasis.

Table 3. Distribution of secondary pulmonary malignancies in the tracheobronchial system

	Number of patients	Trachea		Right bronchial system		Left bronchial system	
	n	n	%	n	%	n	%
Thyroid	14	14		-		-	
Esophagus	13	11		4		5	
Lymphoma	13	11		8		10	
Kidneys	14	3		4		7	
Colon	5	3		2		5	
Ovarian	5	3		4		1	
Breast	4	2		1		1	
Larynx	3	3		-		1	
Skin	2	1		1		-	
Endometrium	2	2		1		-	
Rectum	2	1		-		1	
Cervix	1	1		-		-	
Parotid gland	1	-		1		1	
Testis	1	-		1		-	
Bladder	1	1		1		1	
Prostate	1	-		-		1	
Synovial sarcoma	1	-		1		-	
Total	83	56	67.4	29	34.9	34	40.9

origins, the distribution of intra- and extrathoracic origins were detected in close ratios; 49.4% and 50.6%, respectively.

The trachea was the site where secondary pulmonary malignancies were most often detected within the tracheobronchial tree and mostly affected by malignancies of intrathoracic origin (i.e., thyroid and esophageal tumors). Regarding the right and left bronchial systems, malignant lymphomas were the most common in both right and left bronchial systems (Table 3).

According to the degree of obstruction caused by the secondary pulmonary malignancies in the tracheobronchial system, it was over 50% in 77 (92%) of cases and below 50% in seven (8%) cases. These seven cases were treated in our interventional pulmonology unit, as they either could not tolerate FOB under sedation or had hemorrhage.

Based on the bronchoscopic findings, 50.6% of these malignancies most commonly took the mixed form pattern, while the remaining ones were in close ratios of an isolated endoluminal mass, external compression or mucosal/submucosal infiltration. Also, fistulas accompanied other malignant forms in small numbers. Types of bronchoscopic findings from our case series, such as a mixed type of tumoral lesion composed of external compression, endoluminal mass, and mucosal tumoral infiltration due to malignant melanoma (Figure 1a), a mucosal tumoral infiltration due to breast cancer (Figure 1b), an external compression due to lymphoma (Figure 1c), and an endoluminal mass due to thyroid tumor (Figure 1d) are shown in Figure 1.

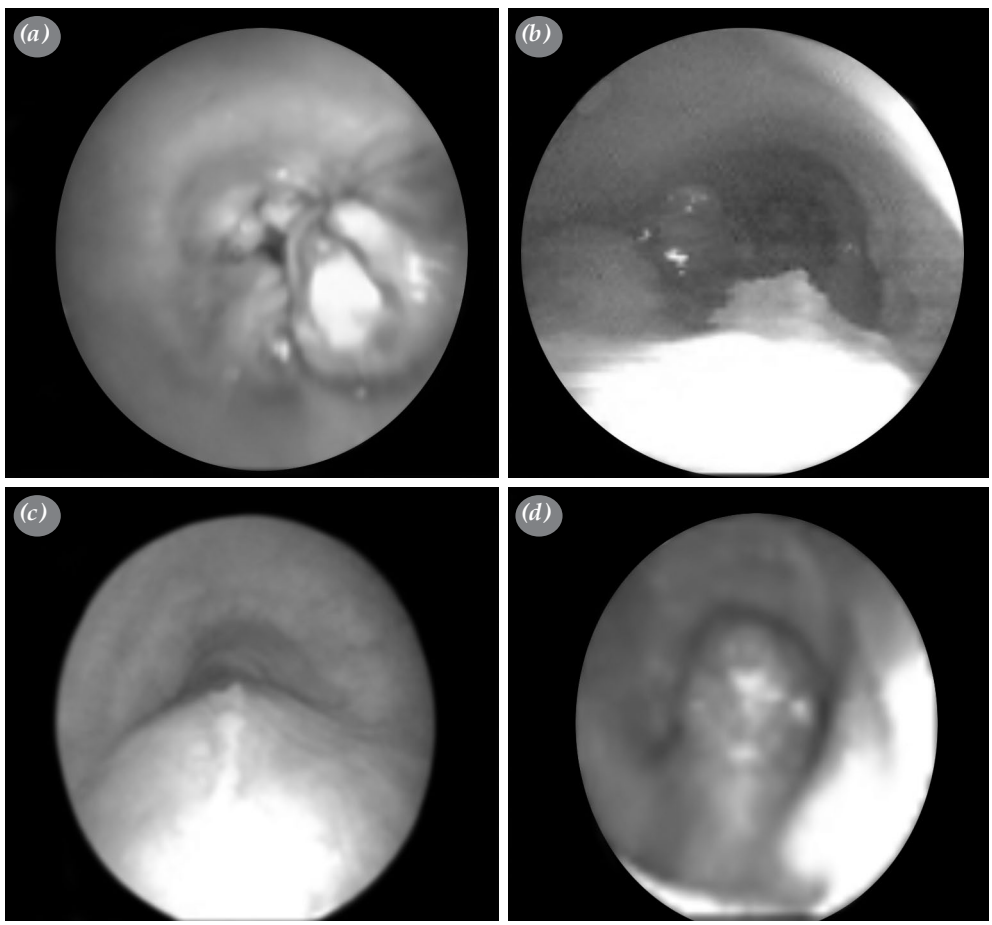

Figure 1. Bronchoscopic findings of secondary pulmonary malignancies. **(a)** A mixed type of tumoral lesion which is composed of external compression, endoluminal mass, and mucosal tumoral infiltration due to malignant melanoma. **(b)** A mucosal tumoral infiltration due to breast cancer. **(c)** An external compression due to lymphoma. **(d)** An endoluminal mass due to a thyroid tumor.

Table 4. Interventional bronchoscopic procedure options and frequency of applications

			Interventional bronchoscopic procedure options and frequency of applications											
			APC		Cryotherapy		Cryoextraction		Laser		MR		Stenting	
Primary tumor	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Thyroid	14	16.9	7	50	7	50	3	21.4	0	0	9	62.3	6	42.8
Esophagus	13	15.6	7	53.8	5	38.5	3	23.1	0	0	4	30.7	12	92.3
Lymphoma	13	15.6	7	53.8	3	23.1	2	15.4	0	0	6	46.1	9	6.9
Kidneys	14	16.9	13	92.8	6	42.8	7	50	5	35.7	7	50	2	14.3
Colon	5	6	4	80	4	80	2	40	2	40	4	80	1	20
Ovarian	5	6	3	75	3	75	2	50	0	0	1	25	3	75
Breast	4	4.8	3	75	1	25	1	25	0	0	2	50	2	50
Larynx	3	3.6	1	33.3	1	33.3	0	0	0	0	2	66.7	1	33.3
Skin	2	2.4	2	100	1	50	0	0	0	0	1	50	1	50
Endometrium	2	2.4	1	50	1	50	1	50	1	50	1	50	0	0
Rectum	2	2.4	1	50	0	0	0	0	0	0	0	0	1	50
Cervix	1	1.2	1	100	0	0	0	0	0	0	0	0	1	100
Parotid gland	1	1.2	1	100	1	100	1	100	1	100	1	100	0	0
Testis	1	1.2	1	100	1	100	1	100	0	0	1	100	0	0
Bladder	1	1.2	1	100	0	0	0	0	0	0	0	0	0	0
Prostate	1	1.2	1	100	1	100	1	100	0	0	0	0	0	0
Synovial sarcoma	1	1.2	1	100	1	100	0	0	0	0	1	100	0	0
Total	83		55	62.3	36	43.4	24	28.9	9	10.8	40	48.2	39	47

APC: Argon plasma coagulation; MR: Mechanical resection.

Mortality was 81% in patients with mixed type lesions and 78% in those with single type lesions. The mean survival time defined as the time from diagnosis until death was 8.7±11.6 (range, 0.3 to 40.4) months for mixed type lesions and 10.2±14.2 (range, 0.2 to 44.4) months for single type lesions.

Interventional bronchoscopic procedures performed through a rigid bronchoscope such as APC, cryo-extraction, cryotherapy, laser, mechanical resection, and stenting were carried out as part of a multimodal therapy. Nineteen (22%) of patients underwent ≥2 interventional procedures. Regarding thermal treatments, APC was performed in 55 (62.3%), cryotherapy in 36 (43.4%), laser in nine (10.8%), and cryo-extraction in 24 (28.9%) cases. Mechanical resection was performed in 40 (48.2%) and stenting was performed in 39 (47%) cases (Table 4).

Evaluation of the stents according to their shapes revealed that 22 Y-shaped, 20 straight-shaped, and two tracheal stenotic stents were used. Of these, 33 were silicone, eight were polyflex, and three were semi-covered metallic stents. In four patients, more than one stents were applied (Table 4).

Table 5. Relationship between interventional bronchoscopic procedure and survival

	Survival time		
	Mean±SD	Min-Max	*p*
APC			
Yes	3.5±1.1	0.3-40.5	0.220
No	1.2±0.6	0.23-44.4	
Cryotherapy			
Yes	5.4±2.6	0.3-40.5	0.883
No	2.5±0.9	0.23-44.4	
Cryoextraction			
Yes	3.4±5.4	0.3-40.5	0.526
No	3.3±0.9	0.23-44.4	
Laser			
Yes	17.2±1.7	3.26-40.5	0.015
No	2.2±0.9	0.23-44.4	
MR			
Yes	5.4±2.1	0.43-40.5	0.525
No	2.2±0.7	0.23-44.4	
Stenting			
Yes	2.7±2.2	0.23-44.4	0.911
No	3.4±0.2	0.26-40.5	

APC: Argon plasma Coagulation; MR: Mechanical resection.

For the preferred interventional bronchoscopic procedures, the patients to whom laser was applied (17.2±1.7 days) had longer mean survival time than those who did not (2.2±0.9 days), indicating statistical significance (p=0.015) (Table 5).

Airway patency was achieved through interventional bronchoscopic procedures applied to the lesions (Figure 2a and Figure 2a) and ensured with the support of stents, if needed (Figure 2b and Figure 2b), as seen in bronchoscopic views from our series (Figure 2).

All 80 patients whose clinical progression and outcomes were available for follow-up had symptomatic palliation with a procedure related-mortality rate of 0%. Three patients who required intensive care were not eligible for progression and outcome evaluation. The procedure-related acute complication rate was 8.4%. Acute complications that we encountered were in order of frequency arrhythmia (3.6%), intensive care unit admission for extubation failure due to post-procedural hypoxia and/or hypercarbia (3.6%), and hemorrhage (1.2%).

All patients underwent regular bronchoscopic follow-up after interventional bronchoscopic procedures according to our follow-up and treatment protocol. While there were no complications related to the procedure during stenting, 23 (60%) patients developed stent-related complications during follow-up which were mostly migration, granulation formation, and mucostasis.

Among the stent-related complications such as granulation tissue and mucostasis, 52.1% were seen with Y-shaped stents. As for stents placed for tracheal lesions, complications were seen more often in straight silicone stents than in polyflex stents. The risk of migration of polyflex stents was found to be less than that of straight silicone stents (12.5% vs. 44.4%, respectively). Stent complications were most frequently seen in the patients with an underlying diagnosis of lymphoma.

DISCUSSION

The number of malignant tumors diagnosed every year has been increasing worldwide. This can be attributed to the multifactorial nature of malignancies, aging population, and developments in the field of medicine enabling earlier diagnosis and expanded treatments options requiring high costs.[14]

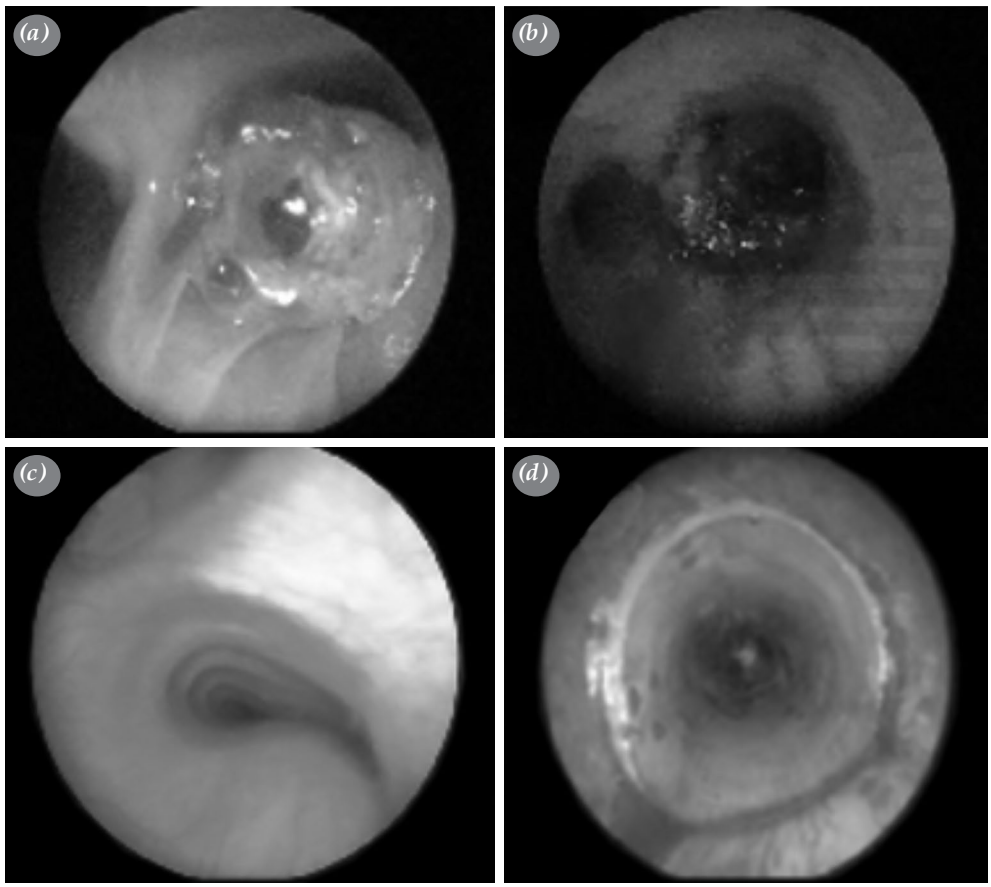

Figure 2. Bronchoscopic views before and after the procedure. **(a)** Endobronchial lesion of breast cancer in the right main bronchus before the procedure. **(b)** Bronchoscopic view of right main bronchus after the procedure. **(c)** Extrinsic compression of lymphoma in the trachea before the procedure. **(d)** Bronchoscopic view of the silicone Y-shaped stent after the procedure.

The likelihood of metastasis to the lung during the course of all malignancies is quite high, with reported rates between 25 and 30%.[15] Around 20 to 50% of all malignancies metastasize to the lungs, 2% of these located within the tracheobronchial tree.[7] Similar to primary lung malignancies, secondary pulmonary malignancies are known to cause life-threatening conditions such as malignant airway obstruction, respiratory distress, hemorrhage, fistula, atelectasis, and post-obstructive pneumonia, leading to loss of life and increased mortality.[6,16,17] However, review of the literature reveals that while there is a plethora of studies in patients with primary lung malignancies treated by interventional pulmonology, the current literature on this subset of patients consists of only case reports or pooled patients from several centers due to the rarity of secondary pulmonary malignancies involving the tracheobronchial tree.[16,17]

In our study, the most common presenting symptoms were cough (32.8%), shortness of breath (19%), and hemoptysis (13.8%) with a significant portion of patients not demonstrating any pulmonary symptoms (13%). The mean time from the diagnosis of the primary tumor until the detection of tracheobronchial involvement was 34.7±52.8 (range, 0.1 to 219.3) months with a similar period of Lee et al.'s[18] study. Different from their study, the longest mean interval until tracheobronchial involvement was seen in colon tumors with 83.8±80.1 (range, 24.7 to 219.3) months, while the shortest interval was in tumors of the esophagus with 8.9±10.8 (range, 0.1 to 37.7) months. The mean survival time after the diagnosis of endobronchial metastasis was 10±13.1 (range, 0.2 to 44.4) months. The mean survival duration from diagnosis to detection of endobronchial metastasis was 16.1 months in the

Lee et al.'s[18] study, which may be due to exclusion of lymphomas which have shorter survival times than the other malignancies.

The most common secondary pulmonary malignancies showing tracheobronchial involvement in our study were tumors of the esophagus, thyroid, kidneys, and lymphomas which is similar to the rates reported by Niu et al.[19] and Madagaira and Gaissert[20] The most common site of involvement was the trachea (67.4%) consistent with the literature.[21] Thyroid and esophageal tumors and lymphomas, due to their adjacency to the trachea and bronchial system, frequently led to findings of external compression detected by bronchoscopy. Similar to the study by Shin et al.,[21] cases with mixed type lesions were found to compose nearly half of the lesions and had a shorter survival time (8.7±11.6; range, 0.3 to 40.4 months) than those with uniform type lesions (10.2±14.2; range, 0.2 to 44.4 months).

Interventional bronchoscopic procedures such as mechanical resection, thermal methods (cryo, argon, laser), and stenting implemented in interventional bronchology specialty centers positively contributes to patients' quality of life and survival, and gains them time to receive their systemic treatment.[5,22] Examination of interventional procedure records of our cases revealed that, in order of frequency, APC, mechanical resection, and stenting were the most commonly performed treatments as the part of a multimodality treatment. While 19 (22%) patients underwent interventional procedures in ≥2 sessions, this rate was 35% in the series of Shin et al.[21]

Modalities such as APC that can also assist in bleeding control, were selected less often, as intrathoracic tumors such as thyroid and esophagus tumors and lymphomas produce mostly external compression. The APC was applied more frequently to the remaining tumors with mucosal/submucosal involvement and also to renal tumors, which are known for their propensity for bleeding. Also, the frequent use of the laser device in the first years of our study has been superseded in recent years by the APC, owing to its lower cost and similar effectiveness profile in bleeding control.[23]

Considering the effects of applied interventional bronchoscopic procedures on survival, a statistically significant relationship was found between laser application and survival, compared to APC, cryo, and mechanical resection.[24] In our study, the success rate of the procedures performed for secondary pulmonary malignancies requiring an interventional bronchoscopic procedure was 97%. This rate is similar to the literature rates reported as 93%, which is the average success rate of all previous studies concerning central airway obstructions,[25] and to the rates reported by Shin et al.[21] as 90.8% in one of the few studies performed in cases with malignant airway obstruction due to secondary pulmonary metastases.

Clinical and symptomatic palliation was observed (97%) in nearly all of our cases, except for cases requiring admission to intensive care following the procedure (3%). All of the patients were referred to the oncology clinic for their oncological treatments. The survival of patients with extrapulmonary malignancies who develop pulmonary metastasis is reported as being less than six months in the literature.[13] In our study, the mean survival was 10 months, and it appears that interventional bronchoscopic procedures improve the survival of patients.

In the present study, the complication rate of 8.4% falls within the range of complications reported (0.9 to 11.7%) in previous studies of cases with malignant central airway obstruction.[22] The procedure-related mortality rate was 0%, indicating a low rate than those reported in previous studies. The complication and mortality rates reported by Shin et al.[21] in cases with central airway obstruction due to secondary pulmonary malignancies were 20.4% and 3.1%, respectively. They attributed their high rates to the fact that most of their patients were terminal cancer patients without other treatment options.[21]

In addition, 58.9% of the patients with stenting who develop stent-related complications were most frequent with Y-shaped stents and, in lymphomas, thyroid and esophageal tumors and these complications were detected during bronchoscopy either for routine follow-up or due to the changes in patients' clinical state. The reason for high complication rates due to Y-shaped stents can be explained by being the most frequently preferred stents in recent years, since they are known for a lower migration risk. The rate of stent-related complications in our series such as granulation formation, mucostasis, migration, and fistula formation were similar to those reported in other studies.[16,19,21,26]

One of the main limitations to this study is that, since our center is a referral hospital, our patients were evaluated in different institutions before their admissions and referred to us to receive further oncological treatment. In addition, if the quality of life questionnaires could have been administered before and after the procedure, a much more objective

comparison of the palliative effect of the procedure could have been made.

In conclusion, as the number of patients diagnosed with cancer has been increasing globally, the use of interventional pulmonology procedures in the treatment of secondary pulmonary malignancies, although rare until now, is expected to increase. Patients with extrapulmonary malignancies should be closely monitored, irrespective of pulmonary symptoms. Particularly in the presence of life-threatening lesions in the tracheobronchial system, as in tracheobronchial involvement of primary pulmonary malignancies, interventional pulmonology can palliate the symptoms of these patients and positively contribute to their survival with low mortality and acceptable complication rates.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Chen CH, Wu BR, Cheng WC, Chen CY, Chen WC, Hsia TC, et al. Interventional pulmonology for patients with central airway obstruction: An 8-year institutional experience. Medicine (Baltimore) 2017;96:e5612.
2. Sakr L, Dutau H. Massive hemoptysis: An update on the role of bronchoscopy in diagnosis and management. Respiration 2010;80:38-58.
3. Mehta RM, Cutaia M. The role of interventional pulmonary procedures in the management of post-obstructive pneumonia. Curr Infect Dis Rep 2006;8:207-14.
4. Raoof S. Is bronchoscopy indicated in the management of atelectasis? Journal of Bronchology 2002;9:52-8.
5. Mudambi L, Miller R, Eapen GA. Malignant central airway obstruction. J Thorac Dis 2017;9(Suppl 10):S1087-S1110.
6. Marchioni A, Lasagni A, Busca A, Cavazza A, Agostini L, Migaldi M, et al. Endobronchial metastasis: An epidemiologic and clinicopathologic study of 174 consecutive cases. Lung Cancer 2014;84:222-8.
7. Stella GM, Kolling S, Benvenuti S, Bortolotto C. Lung-seeking metastases. Cancers (Basel) 2019;11:1010.
8. Çakmak H, Tokat AO, Karasu S. Is open surgery necessary for metastatic pulmonary tumors evaluated with thorax tomography? Turk Gogus Kalp Damar Cerrahisi Derg 2018;26:254-9.
9. Breta M, Arava S, Madan K, Singh A, Jain D, Guleria R. Endobronchial metastasis from extrathoracic malignancies: A clinicopathological study of 11 cases. Lung India 2019;36:212-5.
10. Scarlata S, Fuso L, Lucantoni G, Varone F, Magnini D, Antonelli Incalzi R, et al. The technique of endoscopic airway tumor treatment. J Thorac Dis 2017;9:2619-39.
11. Oberg C, Folch E, Santacruz JF. Management of malignant airway obstruction. AME Med J 2018;3:115.
12. Oviatt PL, Stather DR, Michaud G, Maceachern P, Tremblay A. Exercise capacity, lung function, and quality of life after interventional bronchoscopy. J Thorac Oncol 2011;6:38-42.
13. Deeb A, Haque SU, Olowokure O. Pulmonary metastases in pancreatic cancer, is there a survival influence? J Gastrointest Oncol 2015;6:E48-51.
14. Miller KD, Nogueira L, Mariotto AB, Rowland JH, Yabroff KR, Alfano CM, et al. Cancer treatment and survivorship statistics, 2019. CA Cancer J Clin 2019;69:363-85.
15. Davidson RS, Nwogu CE, Brentjens MJ, Anderson TM. The surgical management of pulmonary metastasis: Current concepts. Surg Oncol 2001;10:35-42.
16. Miwa K, Matsuo T, Takamori S, Sueyoshi S, Mitsuoka M, Fujita H, et al. Temporary stenting for malignant tracheal stenosis due to esophageal cancer: A case report. Jpn J Clin Oncol 2002;32:27-9.
17. Nakamura T, Tajima T, Ogimi T, Miyakita H, Nitta M, Myojin K, et al. Expandable metallic stent for endobronchial metastasis from colorectal cancer: Reports of 2 cases. Tokai J Exp Clin Med 2017;42:79-84.
18. Lee SH, Jung JY, Kim DH, Lee SK, Kim SY, Kim EY, et al. Endobronchial metastases from extrathoracic malignancy. Yonsei Med J 2013;54:403-9.
19. Niu JM, Zhang J, Qiu XJ, Wang J, Pei YH, Wang YL, et al. Comparison of clinical features and stent placement outcomes between airway stenosis caused by primary pulmonary malignancies and that caused by primary non-pulmonary malignancies. Chin Med J (Engl) 2019;132:431-6.
20. Madariaga ML, Gaissert HA. Secondary tracheal tumors: A systematic review. Ann Cardiothorac Surg 2018;7:183-96.
21. Shin B, Chang B, Kim H, Jeong BH. Interventional bronchoscopy in malignant central airway obstruction by extra-pulmonary malignancy. BMC Pulm Med 2018;18:46.
22. Ost DE, Ernst A, Grosu HB, Lei X, Diaz-Mendoza J, Slade M, et al. Therapeutic bronchoscopy for malignant central airway obstruction: Success rates and impact on dyspnea and quality of life. Chest 2015;147:1282-98.
23. Suyama H, Igishi T, Makino H, Kaminou T, Hashimoto M, Sumikawa T, et al. Bronchial artery embolization before interventional bronchoscopy to avoid uncontrollable bleeding: A case report of endobronchial metastasis of renal cell carcinoma. Intern Med 2011;50:135-9.
24. Khemasuwan D, Mehta AC, Wang KP. Past, present, and future of endobronchial laser photoresection. J Thorac Dis 2015;7(Suppl 4):S380-8.
25. Lin CY, Chung FT. Central airway tumors: Interventional bronchoscopy in diagnosis and management. J Thorac Dis 2016;8:E1168-E1176.
26. Ayub A, Al-Ayoubi AM, Bhora FY. Stents for airway strictures: Selection and results. J Thorac Dis 2017;9(Suppl 2):S116-S121.