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Research Article

Hemoptysis in adult patients: Etiology, recurrence and risk of mortality

Erişkin hastalarda hemoptizi: Etyoloji, rekürrens ve mortalite riski

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Abstract

Aim: The etiology of hemoptysis varies according to population differences, time, geographical region, and diagnostic tests used. The aim of this study is to investigate the etiological causes, recurrence and mortality risk of hemoptysis in a university hospital.

Material and Methods: The data of 391 patients who applied to our hospital with hemoptysis between June 2011 and February 2022 were analyzed using the hospital electronic file system. Demographic characteristics, smoking information, radiological findings and related diagnoses of the patients were recorded. The obtained data were analyzed.

Results: A total of 391 patients, including 229 males and 162 females, were included in the study. The mean age of all patients was 54.5±20.0 years. Pneumonia (49.7%), lung cancer (21%), pulmonary embolism (17.8%) were the most common causes of hemoptysis. 48.5% of our cases had idiopathic hemoptysis. There was no difference between men and women in terms of diagnoses related to hemoptysis (p=0.937). The mean hemoptysis recurrence rate was 10.2% and the recurrence time was 375 days (min:6-max:2886) in all patients. The overall mortality rate was 6%. In the correlation analysis, only the length of stay in the first hemoptysis was found to be associated with mortality (p<0.05).

Conclusion: In our study; the overall mortality rate was 6%, and the risk of recurrence and mortality was high, and the risk of recurrence was higher in patients using anticoagulants or antiaggregants and in patients with lung cancer.

Keywords: Hemoptysis, etiology, recurrence, mortality

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Öz

Amaç: Hemoptizinin etiyolojisi, popülasyon farklılıklarına, zamana, coğrafi bölgeye, kullanılan tanısal testlere göre değişmektedir. Bu çalışmanın amacı bir üniversite hastanesinde hemoptizinin etyolojik nedenlerini, rekürrens ve mortalite riskini araştırmaktır.

Gereç ve Yöntemler: Hastanemize Haziran 2011-Şubat 2022 tarihleri arasında hemoptizi nedeniyle başvuran 391 hastanın verileri hastane elektronik dosya sisteminden faydalanılarak incelendi. Hastaların demografik özellikleri, sigara kullanım bilgileri, radyolojik bulguları, ilişkili tanıları kaydedildi. Elde edilen veriler analiz edildi.

Bulgular: Çalışmaya 229 erkek 162 kadın olmak üzere 391 hasta dahil edildi. Tüm hastaların yaş ortalaması 54.5±20.0 idi. Pnömoni (%49.7), akciğer kanseri (%21), pulmoner emboli (%17.8) en sık hemoptizi nedenleriydi. Olgularımızın %48.5'i idiopatik hemoptiziydi. Hemoptiziyle ilişkili tanılar açısından kadın-erkek arasında farklılık saptanmadı (p=0.937). Tüm hastalarda ortalama hemoptizi rekkürrens oranı %10.2, rekürrens süresi 375 gün (min:6-max:2886) bulundu. Genel mortalite oranı %6 olup, Korelasyon analizinde sadece ilk hemoptizde yatış süresinin mortalite ile ilişkisi bulundu (p<0.05).

Sonuç: Çalışmamızda; genel mortalite oranı %6 bulunmuş olup, rekürrens ve mortalite riskinin yüksek olduğu, antikoagülan ya da antiagregan kullanan hastalarda ve akciğer kanseri tanılı hastalarda rekürrens riskinin daha yüksek olduğu görüldü.

Anahtar Kelimeler: Hemoptizi, etyoloji, rekürrens, mortalite

Introduction

Hemoptysis is expectoration of bleeding from the tracheobronchial tree or lung parenchyma. The annual incidence of hemoptysis is 0.1% in outpatients and 0.2% in inpatients. It is a potentially life-threatening medical emergency and carries a high risk of death (1). The etiology of hemoptysis varies according to differences in patient population, time, geographical region, and diagnostic tests used. Lung cancer, pulmonary embolism and bronchiectasis are the leading causes of hemoptysis. The predominant cause of hemoptysis has changed from tuberculosis and bronchiectasis to lung cancer (2). Chest radiography is recommended as the initial diagnostic test in hemodynamically stable patients with hemoptysis. Bronchoscopy is recommended after computed tomography in patients with massive hemoptysis, abnormal radiographic findings, and risk factors for malignancy despite normal radiographic findings (3,4,5).

The aim of this study is to investigate the demographic and etiological characteristics, recurrence risk, recurrence time and mortality rate of patients admitted to our hospital with hemoptysis.

Materal and Methods

The data of 391 patients admitted to our hospital between June 2011 and February 2022 due to hemoptysis, were analyzed using the hospital electronic file system. Patients over the age of 18 were included in the study. Patients with missing file data were excluded from the study. The patients' demographic characteristics, smoking status, radiological findings and related diagnoses were recorded. The collected data were analyzed. The amount of hemoptysis was determined as <30 ml/day mild, 30-100 ml/day moderate, 100-600 ml/day severe, and >600 ml/day massive. Except for the first episode of hemoptysis, recurrent episodes at least 30 days apart were considered as recurrent hemoptysis (6).

Statistical analysis

Nominal and ordinal data were defined by frequency analysis, measurement data were defined by mean and standard deviation values. Fischer's Exact and Chi-Square Similarity Ratio tests were used for difference analysis of nominal and ordinal data. Before the difference analysis of the measurement data, Kolmogorov Smirnov analysis was performed for normality test. Mann-Whitney U test was used for the difference in measurement data between groups, as all measurement data did not fit the normal distribution. In relational screening analysis, Spearman's rho correlation was used for univariate analysis and Binary Logistic Regression analysis was used for multivariate analysis. All analyzes were performed in SPSS 17.0 for Windows software, at 95% confidence interval and 0.05 significance level.

Results

A total of 391 patients, comprising 229 males and 162 females, were included in the study. The mean age of all patients was 54.5±20.0 years (Table 1). Atelectasis (22.8%), nodule (20.9%), and emphysematous changes (13.3%) were the most common tomography findings (Table 2). There was no difference between males and females in terms of tomography

findings (p=0.214). Pneumonia (49.7%), lung cancer (21%), pulmonary embolism (17.8%) were the most common causes of hemoptysis (Table 3). There was no difference between males and females in terms of diagnoses related to hemoptysis (p=0.937). The observed recurrence rate of hemoptysis in all patients was 10.2%. Mean hemoptysis recurrence time was 375 days (min:6-max:2886). In the patient population we examined, massive hemoptysis was observed in 35 (8.95%) patients. Among the patients with massive hemoptysis, 10 patients were diagnosed with lung cancer (2.55%), 11 with pneumonia (2.81%), 8 with bronchiectasis (1.53%), 3 with pulmonary embolism (0.76%), 1 with anticoagulant use (0.25%), 1 with endometriosis (0.25%), and 1 (0.25%) with active tuberculosis. Twenty-four (6.1%) of these patients were lost. In our study, the mortality rate in massive hemoptysis was found to be 68.57%. Therapeutic bronchoscopy was performed in 1 patient (0.25%), bronchial artery embolization in 3 patients (0.76%), and surgical treatment in 17 (4.3%) patients.

Table 1. Demographic data of patients

Age	n:391	54.5±20.0
Gender n(%)		
Male	229	(58.6)
Female	162	(41.4)
Smoking n(%)		
Quit smoking	80	(20.5)
Never smoked	160	(40.9)
Active smoker	140	(35.8)
Thorax computed tomography n(%)	263	(67.3)
Diagnostic Bronchoscopy n(%)	88	(22.5)
Hemoptysis Recurrence n(%)	40	(10.2)
Hospital Mortality n(%)	24	(6.1)

Table 2. Thorax computed tomography findings

Thorax computed-tomography findings	n	%
Atelectasis	60	22.8
Nodule	55	20.9
Emphysematous changes	35	13.3
Ground glass	28	10.6
Bronchiectasis	28	10.6
Consolidation	23	8.7
Solid mass	19	7.2
Peribronchial infiltration	15	5.7
Cavity	9	3.4
Pulmonary artery dilatation	6	2.2
Tuberculosis sequelae	5	1.9
Aneurysm	2	0.7
Fungus ball	1	0.3

Table 3: Hemoptysis-related diagnoses

Hemoptysis-related diagnoses	n	%
Pneumonia	78	49.7
Lung cancer	33	21
Pulmonary embolism	28	17.8
Use of anticoagulant or antiaggregant	14	8.9
Bronchiectasis	12	7.6
Bronchitis	10	6.4
Active lung tuberculosis	4	2.5
Vascular malformation	4	2.5
Pulmonary edema	4	2.5
Bronchial benign tumor	1	0.6
Endometriosis	1	0.6
Aspergillosis	1	0.6

In the group with hospital mortality, cavity, a thoracic computed tomography finding, was more common (12.5% vs. 1.6%) (p<0.05). Among the diagnoses associated with hemoptysis, lung cancer (33.3% vs. 7.1%) and pneumonia (45.8% vs. 18.3%) were more common in the group with hospital mortality, and the differences between the groups were statistically significant (p<0.05). The mean hospital stay at first hemoptysis was higher in the group with hospital mortality (p<0.05). Moreover, the distribution of all demographic, clinical, thoracic computed tomography and hemolysis-related diagnoses examined in the study in terms of mortality was not statistically significant (Table 4).

Spearman's rho correlation analysis results demonstrated that, there was a significant and positive correlation between the first hemoptysis and hospital mortality and length of stay (r=0.394; p<0.01), cavity (r=0.174; p<0.01), tuberculosis sequelae (r=0.103; p<0.05), bronchial artery embolization (r=0.100; p<0.05), surgical treatment for hemoptysis (r=0.102; p<0.05), lung cancer (r=0.224; p<0.01), pneumonia (r=0.166; p<0.01), and endometriosis (r=0.198; p<0.01) (Table 5).

Among the variables that were significantly correlated in the correlation analysis, there was a statistically significant difference between the groups with and without mortality only in terms of length of stay at first hemoptysis (B=0.097; p<0.05). The contributions of cavity, bronchial artery embolization, surgery, lung cancer, pneumonia and endometriosis parameters in multivariate analysis were not statistically significant (p>0.05) (Table 6).

According to the ROC analysis results regarding the diagnostic value of the length of stay in the first hemoptysis on hospital mortality, the diagnostic value of the length of stay in the first hemoptysis was found to be 85.3% (Area Under Curve (AUC)= 0.853; p<0.01). When the cut-off value of 14.5 days of hospitalization in the first hemoptysis was taken, the sensitivity and specificity of hospital mortality were found to be 85.7% and 86.8%, respectively (Figure 1).

Table 4. Distribution of some clinical, radiological and hemoptysis-related findings according to mortality groups and results of difference analysis

	Hospital Mortality		p
	None (n=367)	Yes (n=24)	
Gender n (%)			
Male	218 (59.4)	11 (45.8)	0.137[a]
Female	149 (40.6)	13 (54.2)	
Average age ± SS	54.25±20.11	58.08±17.57	0.412[b]
Hospital unit n (%)			
Policlinic	273 (74.4)	14 (58.3)	0.231[c]
Inpatient service	93 (25.3)	10 (41.7)	
Intensive care unit	1 (0.3)	-	
Thorax computed tomography n (%)	248 (67.6)	15 (62.5)	0.379[a]
Thorax computed tomography findings n (%)			
Bronchiectasis	25 (6.8)	1 (4.2)	0.514[a]
Cavity	6 (1.6)	3 (12.5)	0.013[a]
Solid mass	16 (4.4)	3 (12.5)	0.103[a]
Consolidation	21 (5.7)	2 (8.3)	0.420[a]
Ground-glass	28 (7.6)	-	0.159[a]
Nodule	52 (14.2)	3 (12.5)	0.556[a]
Fungus	1 (0.3)	-	0.939[a]
Aneurysm	2 (0.5)	-	0.881[a]
Tuberculosis sequelae	7 (1.9)	2 (8.3)	0.100[a]
Emphysematous changes	31 (8.4)	4 (16.7)	0.157[a]
Pulmonary artery dilatation	6 (1.6)	-	0.682[a]
Atelectasis	56 (15.3)	4 (16.7)	0.518[a]
Peribronchial infiltration	15 (4.1)	-	0.380[a]
Diagnostic bronchoscopy n (%)	82 (22.3)	6 (25.0)	0.464[a]
Therapeutic bronchoscopy n(%)	1 (0.3)	-	0.939[a]
Bronchial artery embolization n (%)	2 (0.5)	1 (4.2)	0.173[a]
Surgery n (%)	14 (3.8)	3 (12.5)	0.078[a]
Hemoptysis-related diagnoses n (%)			
Lung cancer	26 (7.1)	8 (33.3)	0.000[a]
Bronchitis	11 (3.0)	-	0.494[a]
Pneumonia	67 (18.3)	11 (45.8)	0.003[a]
Aspergillosis	1 (0.3)	-	0.939[a]
Active pulmonary tuberculosis	3 (0.8)	1 (4.2)	0.225[a]
Bronchiectasis/Cystic fibrosis	11 (3.0)	1 (4.2)	0.538[a]
Vascular malformation	4 (1.1)	-	0.775[a]
Anticoagulant-antiaggregant use	13 (3.5)	1 (4.2)	0.594[a]
Pulmonary edema	4 (1.1)	-	0.775[a]
Pulmonary embolism	25 (6.8)	3 (12.5)	0.242[a]
Systemic disease	21 (5.7)	-	0.255[a]
Bronchial benign tumor	1 (0.3)	-	0.939[a]
Endometriosis	-	1 (4.2)	0.061[a]
Recurrence n (%)	38 (10.4)	2 (8.3)	0.546[a]
Smoking n (%)			
None	156 (42.5)	15 (62.5)	
Quit Smoking	76 (20.7)	4 (16.7)	0.143[c]
Active smoker	135 (36.8)	5 (20.8)	
Length of stay at first hemoptysis (mean) ± SS	8.25±10.13	23.57±12.25	0.001[b]
Time to recurrence (mean)± SS	375.90±576.57	366.50±94.04	0.412[b]

a. Fischer's Exact Test, b. Mann Whitney U Test, c. Likelihood Ratio, SS: Standard Deviation.

Table 5. Spearman's rho correlation analysis results for the relationship between hospital mortality and some clinical, radiological and hemoptysis-related findings

Hospital Mortality	r	p
Gender	0.066	0.192
Age	0.041	0.413
Hospital unit	0.087	0.087
Length of stay in first hemoptysis	0.394**	0.002
Thorax computed tomography	-0.026	0.609
Bronchiectasis	-0.025	0.615
Cavity	0.174**	0.001
Solid mass	0.091	0.073
Consolidation	0.027	0.599
Ground-glass	-0.071	0.161
Nodule	-0.012	0.820
Fungus ball	-0.013	0.799
Aneurysm	-0.018	0.718
Tuberculosis sequelae	0.103*	0.042
Emphysematous changes	0.069	0.173
Pulmonary artery dilatation	-0.032	0.529
Atelectasis	0.009	0.853
Peribronchial infiltration	-0.051	0.314
Diagnostic bronchoscopy	0.015	0.763
Therapeutic bronchoscopy	-0.013	0.799
Bronchial artery embolization	0.100*	0.049
Surgical	0.102*	0.043
Lung cancer	0.224**	0.000
Bronchitis	-0.044	0.391
Pneumonia	0.166**	0.001
Aspergillosis	-0.013	0.799
Active pulmonary tuberculosis	0.080	0.115
Bronchiectasis Cystic fibrosis	0.016	0.748
Vascular malformation	-0.026	0.608
Anticoagulant- antiaggregant use	0.008	0.874
Pulmonary edema	-0.026	0.608
Pulmonary embolism	0.053	0.296
Systemic disease	-0.061	0.229
Bronchial benign tumor	-0.013	0.799
Endometriosis	0.198**	0.000
Recurrence	-0.016	0.752
Time to recurrence	0.144	0.371

*p<0.05 **p<0.01

Discussion

Of all hemoptysis cases, 50% remain cryptogenic, with the most common causes that can be detected listed as airway infections (bronchitis, pneumonia, lung abscess) (22%), bronchial carcinoma or metastases (17.4%), bronchiectasis/ cystic fibrosis (6.8%), pulmonary cardiovascular causes such as edema, mitral stenosis (4.2%), pulmonary artery embolism (2.6%), tuberculosis (2.7%), anticoagulant or antiaggregant use (3.5%). In Western countries, the average age is 62, and

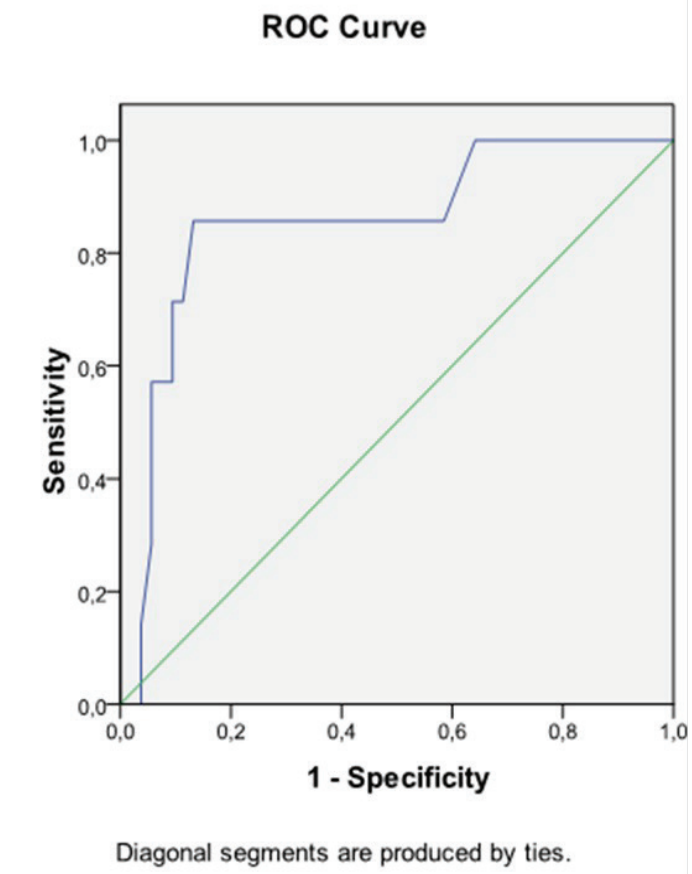

Figure 1. ROC analysis results on the diagnostic value of length of stay at first hemoptysis on hospital mortality.

In our study, male cases presenting with hemoptysis were more common, and pneumonia (49.7%), lung cancer (21%), pulmonary embolism (17.8%), use of anticoagulants (8.9%), and bronchiectasis (7.6%) were the most common causes. The reason why pneumonia is more common in etiology and has a higher mortality is that our hospital is a solid organ and hematological transplant center, and a reference hospital for solid and hematological malignancies. Community and hospital-acquired resistant viral, bacterial and fungal pneumonias are common in our hospital. In a study by Fidan et al. in 2002, lung cancer was the leading cause of hemoptysis (34.3%), followed by bronchiectasis (25.0%), tuberculosis (17.6%), pneumonia (10.2%), and pulmonary embolism (4.6%). Most of the lung cancer patients were male (p=0.002) (6). In our study, no gender difference was observed in terms of lung cancer, which may be due to the increased incidence of lung cancer in the female population over the years. Lung cancer mortality is higher in men than in women, but the size of this difference continues to decrease due to the higher incidence of lung cancer in women and increases in mortality (7,8,9).

Table 6. Binary logistic regression analysis results among parameters with significant correlation with hospital mortality

	B	S.E.	Wald	df	p	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Length of stay in first hemoptysis	0.097	0.046	4.476	1	0.034	1.102	1.007	1.205
Cavity(1)	-42.312	31663.892	0.000	1	0.999	0.000	0.000	.
Bronchial artery embolization(1)	-3.043	44471.720	0.000	1	1.000		0.000	.
Surgery(1)	19.231	19033.107	0.000	1	0.999	2.248E8	.000	.
Lung cancer(1)	-3.386	2.080	2.651	1	0.103	0.034	0.001	1.994
Pneumonia(1)	-2.174	1.765	1.517	1	0.218	0.114	0.004	3.617
Endometriosis(1)	-25.055	40192.957	0.000	1	1.000	0.000	0.000	.
Constant	51.239	65065.736	0.000	1	0.999	1.790E22		

-2 Log likelihood: 21.499; Cox & Snell R^2: 0.304; Nagelkerke R^2: 0.592.

In the study of Özgül et al., the most common etiology in hemoptysis patients was tuberculosis (43.8%), followed by lung cancer (21.7%) and chronic bronchitis (5.5%) (10). In the study of Ünsal et al., the most common causes of hemoptysis were bronchiectasis (22.4%), lung cancer (18.9%), active tuberculosis (11.2%) and inactive tuberculosis (10.5%) (11).

In Uzun et al's prospective cohort, lung cancer (53.3%), pulmonary embolism (23.1%) and bronchiectasis (23.1%) were the main causes of hemoptysis, consistent with our study. This study is the first to show that pulmonary embolism is the leading cause of hemoptysis. In our study, pulmonary embolism was found to be the cause of hemoptysis with a high rate and supports this study (2).

In our study, tuberculosis as the cause of hemoptysis was seen at a lower rate (2.5%) compared to other studies. After the effective tuberculosis control programs implemented in our country, the registered tuberculosis incidence has decreased by an average of 5% annually for the last 10 years. In 2005, a total of 20,535 tuberculosis patients were registered and the incidence was 29.4 per hundred thousand, while it was 14.6 per hundred thousand in 2017 (12). We thought that this change in the incidence of tuberculosis was the reason why the tuberculosis rates observed in our study were lower than in other studies conducted in our country. Widespread use of antibiotics and advances in radiological methods used in the diagnosis of lung malignancies have led to changes in the etiology of hemoptysis. In the study published by Lee et al. in 2000, bronchiectasis was found to be the most common cause of hemoptysis (13). In previous studies in our country, hemoptysis due to bronchiectasis was observed at higher rates compared to our study (2,6,10,11).

However, despite advanced diagnostic methods, the cause of hemoptysis cannot be determined in most patients (50%) with hemoptysis (4). In our case, 48.5% of our cases were idiopathic hemoptysis.

Bleeding localization and hemoptysis can be detected in 33-82% and 35-50% of the cases, respectively, by chest X-ray, in 70-100% and 60-77%, respectively, by computed tomography, in 73-93% and 2.5-8%, respectively, by bronchoscopy (1). Computed tomography (CT) was used in 67.3% of our cases. It has been reported that up to 10% of pulmonary malignancies in patients with hemoptysis can remain hidden on chest X-ray and 96% of them can be detected by CT (13). In our cases, diagnostic bronchoscopy was performed in 22.5% of the patients. There are publications reporting that CT is superior to bronchoscopy in showing the centre of bleeding (14). Bronchial artery embolization (BAE), performed in 3 of our patients, is a minimally invasive procedure that has become the preferred treatment for recurrent and massive hemoptysis. When performed by an experienced operator with sufficient technical equipment, clinical success, defined as cessation of bleeding within 24 hours after BAE or in same-admission, can reach 75-98%, but the recurrence rate of bleeding varies between 1 and 27% (15). Surgery was performed in 17 of the patients enrolled in our study due to massive hemoptysis. Although lung resection is associated with high morbidity and mortality rates in the treatment of massive hemoptysis, it is the only permanent curative method when necessary (16). Recurrence was observed in 10.2% of our cases. Recurrence of hemoptysis is common (47%) even following embolization in hemoptysis and is associated with high mortality (17). In our study, recurrence was not found to be associated with mortality.

In a study from our country, lung cancer was shown to be the most common cause of recurrent hemoptysis (18). Fidan et al. revealed that the most common etiology in recurrent hemoptysis is bronchiectasis (6). In our study, the most common recurrence risk was seen in patients with lung cancer diagnosis and use of anticoagulant/antiaggregant. In a study evaluating long-term prognostic outcomes in patients with hemoptysis, bronchiectasis was found to be associated with an increased risk of recurrence (19). Fidan et al and Ryuge et al also found bronchiectasis to be the most common diagnosis in recurrent hemoptysis (6,20). Tobacco smoke and its bronchopulmonary inflammatory consequences constitute an etiology for bronchial bleeding, regardless of the severity of the underlying disease (21). Although it was not associated with hemoptysis mortality in our study, 56% of the patients presenting with hemoptysis had a history of smoking.

In our study, the overall mortality rate was 6%, and it was shown that there was a statistically significant and positive relationship between hospital mortality and length of stay at first hemoptysis, cavity, tuberculosis sequelae, bronchial artery embolization, surgery status, lung cancer, pneumonia and endometriosis. However, in the correlation analysis, only the length of stay in the first hemoptysis was found to be associated with mortality. Mondoni et al. reported that the overall mortality rate was 13.7%, increased from 18.1% to 31% after a one-year follow-up, and lung malignancy was the main determinant of mortality (19). Mortality rates are 50-100% in patients with massive hemoptysis treated conservatively (1). Massive hemoptysis is the expectoration of 600 mL of blood over 24 hours, usually in an adult. Massive hemoptysis was observed in 8.9% of the patient population we examined. Most of the patients with massive hemoptysis consisted of patients diagnosed with lung cancer, pneumonia and bronchiectasis. The etiologies of massive hemoptysis vary greatly according to demographic characteristics. Malignancy, bronchiectasis and chronic infection are the most common causes in adults (22). In our study, the mortality rate due to massive hemoptysis was 68.57%, which is consistent with the literature (1,22).

Conclusion

In our study, it was observed that the risk of recurrence and mortality in hemoptysis is high, it can recur even after a long time, and the risk of recurrence is higher in patients using anticoagulants or antiaggregants and in patients with lung cancer diagnosis. Patients and physicians should be careful and cautious in terms of hemoptysis-associated mortality, morbidity and recurrence risk.

Conflict of Interest and Source of Funding

The authors declare that there is no conflict of interest.

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Ethics Committee Approval

Ethics committee approval was obtained from Baskent University Medicine and Health Sciences Research Committee. (Ethics committee No:KA22/14 – Date:11.01.2022).

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