Bronchoscopic Findings and Bleeding Control Predict Survival in Patients with Solid Malignancies Presenting with Mild Hemoptysis

Horiana B. Grosu[1], Roberto F. Casal[2], Rodolfo C. Morice[1], Graciela M. Nogueras-González[3], Georgie A. Eapen[1], David Ost[1], Mona G. Sarkiss[4], and Carlos A. Jimenez[1]

[1]Department of Pulmonary Medicine, The University of Texas MD Anderson Cancer Center, Houston; [2]Department of Pulmonary and Critical Care Medicine, Baylor College of Medicine, Houston; [3]Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston; and [4]Department of Anesthesiology and Perioperative Medicine, The University of Texas MD Anderson Cancer Center, Houston, Texas

Abstract

Background: Regardless of its volume, hemoptysis is a concerning symptom. Mild hemoptysis and its significance in patients with solid malignancies has not been studied.

Methods: We conducted a retrospective chart review of patients with solid malignancies who presented for evaluation of mild hemoptysis. In this population, we studied the impact of bronchoscopic findings and endobronchial therapies on overall survival and bleeding recurrence. Patients were categorized into four groups on the basis of the presence or absence of active bleeding and endobronchial disease at the time of initial bronchoscopy: active bleeding with endobronchial lesion (AB/EBL), active bleeding without endobronchial lesion (AB/no-EBL), absence of active bleeding but with endobronchial lesion (no-AB/EBL), and absence of active bleeding and endobronchial lesion (no-AB/no-EBL).

Measurements and Main Results: Ninety-five of the 112 patients with solid malignancies and mild hemoptysis underwent bronchoscopies. There was a significantly lower median survival time for patients with bronchoscopic findings of active bleeding and endobronchial lesion compared with patients with no active bleeding and/or no endobronchial lesion (3.48 mo; 95% confidence interval [CI], 2.14–6.05). On a multivariate analysis, factors independently associated with improved survival were higher hemoglobin values (hazard ratio [HR], 0.78; 95% CI, 0.67–0.91) and cessation of hemoptysis without recurrence at 48 hours (HR, 0.43; 95% CI, 0.22–0.84). Variables independently associated with worse survival were disease stage (HR, 10.8; 95% CI, 2.53–46.08) and AB/EBL (HR, 3.20; 95% CI, 1.74–5.89).

Conclusions: In patients with solid malignancies presenting with mild hemoptysis, bronchoscopic findings of AB/EBL are associated with decreased survival. Hemoptysis control without recurrence at 48 hours after endobronchial intervention may improve survival.

Keywords: hemoptysis; cancer; bronchoscopy

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Correspondence and requests for reprints should be addressed to Carlos A. Jimenez, Department of Pulmonary Medicine, Unit 1462, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030. E-mail: cajimenez@mdanderson.org

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Hemoptysis is a distressing symptom for patients with or without a known history of cancer. It disrupts patients' quality of life and provokes significant anxiety. For these reasons, evaluation and treatment of mild hemoptysis is important (1).

Morbidity and mortality in patients with hemoptysis depend not only on the volume of expectorated blood but also on the rate of bleeding, the ability of the patient to clear blood from the airways, and the extent and severity of underlying lung disease. A large body of literature on hemoptysis exists for the general population without known history of cancer (1–11). However, most studies have focused on massive hemoptysis because of its high mortality rate (2). Mild hemoptysis may be considered less meaningful because $< 20\%$ is due to an underlying malignancy and classically ascribed to inflammatory disease, such as acute or chronic bronchitis (1, 3, 4, 8, 12). Mild or minor hemoptysis is generally defined as blood-tinged, blood-streaked sputum; small blood clots within the sputum; or hemoptysis that is < 20 ml in 24 hours (3, 4).

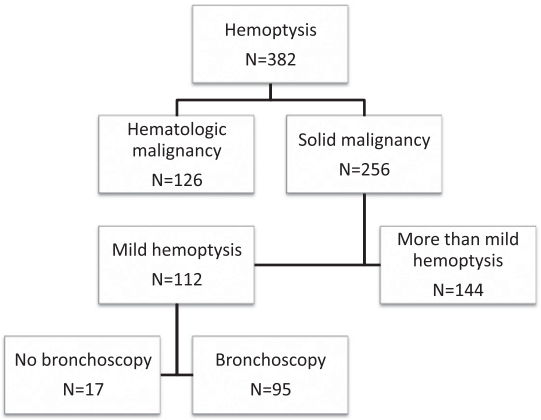

Figure 1. Number of patients evaluated and number of patients who underwent bronchoscopy.

We conducted this study to better understand the association of bronchoscopic findings and overall survival of patients with solid malignancies presenting with mild hemoptysis. We also wanted to evaluate the impact of invasive treatments on bleeding recurrence and outcomes in this population.

Methods

The University of Texas MD Anderson Cancer Center Institutional Review Board approved this study (protocol DR08–0273).

We conducted a retrospective chart review of inpatients and outpatients with solid malignancies referred to the departments of Pulmonary Medicine and Thoracic and Cardiovascular Surgery at The University of Texas MD Anderson Cancer Center for evaluation of and treatment for hemoptysis from November 2003 to July 2007.

Subjects and Data Collection

We defined mild hemoptysis as blood-tinged, blood-streaked sputum or small blood clots within the sputum. All patients with solid malignancies and mild hemoptysis were included. Patients with hematologic malignancies were excluded. Patients in whom hemoptysis exceeded the above definition were also excluded.

A diagnosis of acute bronchitis was made if patients presented with cough with or without phlegm production lasting for up to 3 weeks with no infiltrate on chest X-ray.

The diagnosis of pneumonia was made on patients who were given a new antibiotic prescription and had at least two of the following findings: new infiltrate on radiographic imaging; increase in cough; and increase in purulent sputum, fever, white blood cell count, or neutropenia.

For the patients who met the inclusion criteria, data on demographics, tumor histology, comorbid conditions, smoking history, Eastern Cooperative Oncology Group (ECOG) performance status, and treatment with antiplatelet or anticoagulant therapy were extracted from the patient records. Data on the stage of the disease were collected. We categorized the patients into early versus advanced disease based on their stage using the TNM system (early stage TNM stage I and II and advanced TNM stage III and IV). The results of laboratory studies, including renal function, hemoglobin values, platelet counts, and coagulation profile, were collected. Bronchoscopy date, time from onset of hemoptysis to bronchoscopy, and findings at bronchoscopy were also noted.

The treatment modalities for hemoptysis and results of the intervention were collected. We also recorded whether hemoptysis had stopped and not recurred 48 hours after bronchoscopy.

Overall survival (OS) was calculated as the time (in months) from the date of bronchoscopy to the date of death or censoring. Survival was censored at the date of last follow-up if death had not been reported.

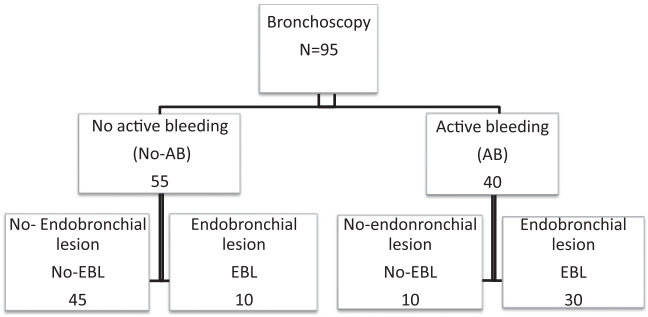

Figure 2. Number of patients with active bleeding (AB)/no active bleeding (no-AB) and endobronchial lesion (EBL)/no endobronchial lesion (no-EBL).

Statistical Analysis

Summary statistics were used to describe the clinical and demographic characteristics of the study population. Wilcoxon rank-sum tests or *t* tests were used to assess differences between patients with and without active bleeding for continuous variables.

We used Pearson's χ^2 test or Fisher's exact test to assess differences between patients with and without active bleeding for categorical variables.

Univariate Cox proportional hazards regression models were used to determine the association between each potential prognostic factor and OS. The Kaplan-Meier product limit method was used to estimate the median OS. Full and reduced multivariate Cox proportional hazards regression models were used to assess the prognostic factors and OS. Variables considered clinically relevant and those with *P* value of ≤ 0.10 in the univariate analysis were included in the multivariate model. A backward elimination strategy was used to choose the most parsimonious model. A *P* value of < 0.05 was considered statistically significant.

Statistical analysis was performed using STATA/SE version 12.1 statistical software (Stata Corp., College Station, TX).

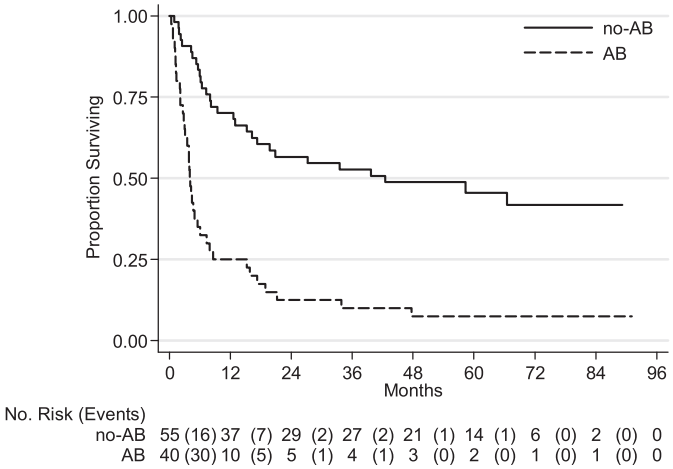

Figure 3. Kaplan-Meier survival estimation curves for patients in the active bleeding (AB) and no active bleeding (no-AB) groups ($P < 0.001$).

Results

Patient Characteristics

A total of 382 patients with hemoptysis were evaluated from November 2003 to July 2007; 126 had hematologic malignancy upon referral, and 256 had a solid malignancy. Of those with a solid malignancy, 112 (44%) had mild hemoptysis, and 95 (85%) underwent bronchoscopy (Figure 1).

The 95 patients who underwent bronchoscopy were categorized into two main groups based on the finding of active bleeding (AB) or absence of active bleeding (no-AB) at the time of initial bronchoscopic evaluation. These two groups were further divided into the following subgroups: active bleeding with endobronchial lesion (AB/EBL), active bleeding without endobronchial lesion (AB/no-EBL), absence of active bleeding but with endobronchial lesion (no-AB/EBL), and absence of active bleeding and endobronchial lesion (no-AB/no-EBL) (Figure 2).

Table 1 illustrates a comparison of the baseline characteristics of the patients with and without active bleeding. The most common malignancy was lung cancer, comprising 48% of patients. In the no-AB group, there were 26 patients with non–small lung cancer staged at the time of bronchoscopy as stage I (no. 4), stage III (no. 11), and stage IV (no. 11). In the AB group, there were 20 patients with non–small lung cancer staged at the time of bronchoscopy as stage I (no. 2), stage III (no. 7), and stage IV (no. 11). There was one patient with small cell lung cancer in the no-AB group, and there were five patients in the AB group.

In the no-AB group, there were 10 patients with localized non–lung cancer solid malignancies and 18 with advanced non–lung cancer solid malignancies. In the AB group, there was one patient with a localized non–lung cancer solid malignancy, and there were 14 with advanced non–lung cancer solid malignancies. Non–lung cancer solid malignancies included laryngeal carcinoma, thyroid carcinoma, breast carcinoma, renal carcinoma, melanoma, mesothelioma, prostate carcinoma, colorectal carcinoma, sarcoma, cervical carcinoma, parotid carcinoma, pancreas, adenocarcinoma of unknown origin, chordoma, malignant ciliary epithelioma, thymoma, carcinoma of the mouth, hepatocellular carcinoma, nasopharyngeal carcinoma, and bladder carcinoma.

No differences in age, sex, ethnicity, comorbid conditions, smoking history, or antiplatelet/anticoagulant therapy were found between the AB and the no-AB groups. Also, no differences were observed between the groups on values of renal function, platelet counts, and coagulation profiles. The ECOG performance status of most patients was between 1 and 2.

Bronchoscopic evidence of endobronchial lesion was found more often in the AB group than in the no-AB group (75 vs. 25%; $P < 0.001$). Additionally, patients in the AB group were more likely to have advanced stage disease.

Bronchitis and pneumonia as a cause of mild hemoptysis was found in 8 out of 95 patients.

In patients who had evidence of metastatic disease to the chest on radiographic imaging, we presumed the bleeding was from distal metastatic lung parenchymal lesions once all other causes of bleeding were ruled out.

Treatment Modalities

In the AB/EBL group (n = 30), bleeding was managed bronchoscopically in 26 (87%) patients. Argon plasma coagulation (APC) was used in 25 patients, and neodymium-doped yttrium aluminum perovskite lasers were used in the remaining patient. Endoscopic treatment resulted in immediate cessation of hemoptysis without recurrence during the following 48 hours in

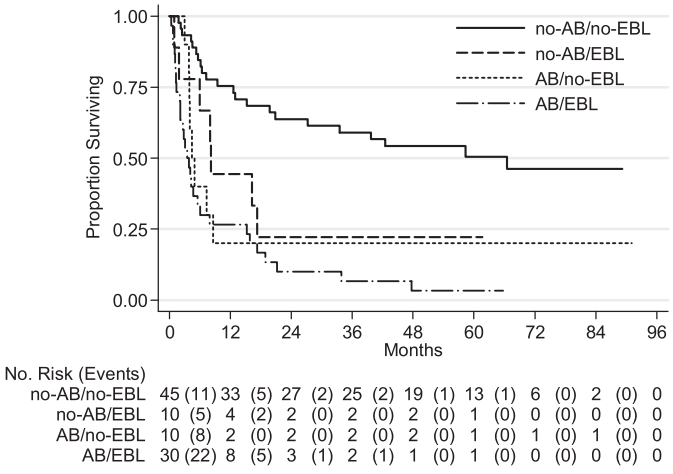

Figure 4. Kaplan-Meier survival estimation curves for patients in the groups with active bleeding with endobronchial lesion (AB/EBL), active bleeding with no endobronchial lesion (AB/no-EBL), no active bleeding with endobronchial lesion (no-AB/EBL), and no active bleeding and no endobronchial lesion (no-AB/no-EBL) ($P < 0.001$).

Table 1. Summary statistics of clinical and demographic characteristics

	Active Bleeding		*P* Value
	Yes	No	
Age, yr	40	55	
Median (range)	61.6 (23.9–82.1)	61.1 (20.3–86.9)	
Gender, n (%)			
Male	24 (60.0)	23 (41.8)	
Female	16 (40.0)	32 (58.2)	
Ethnicity, n (%)			
White	29 (72.5)	42 (76.4)	
Black	6 (15.0)	7 (12.7)	
Hispanic	3 (7.5)	5 (9.1)	
Asian	2 (5.0)	1 (1.8)	
Basal malignancy, n (%)			
Lung	20 (50.0)	26 (47.3)	
Metastatic cancer	20 (50.0)	29 (52.7)	
Smoking, n (%)			
Positive	7 (17.5)	15 (27.3)	
Negative	33 (82.5)	40 (72.7)	
Heart disease, n (%)			
No	25 (62.5)	27 (49.1)	
Yes	15 (37.5)	28 (50.9)	
Lung disease, n (%)			
No	19 (47.5)	23 (41.8)	
Yes	21 (52.5)	32 (58.2)	
Kidney disease, n (%)			
No	38 (95.0)	52 (94.5)	
Yes	2 (5.0)	3 (5.5)	
Liver disease, n (%)			
No	39 (97.5)	54 (98.2)	
Yes	1 (2.5)	1 (1.8)	
Radiation therapy to chest, n (%)			
No	27 (67.5)	37 (67.3)	
Yes	13 (32.5)	18 (32.7)	
Antiplatelet therapy, n (%)			
No	32 (80.0)	45 (81.8)	
Yes	8 (20.0)	8 (14.5)	
Anticoagulant therapy, n (%)			
No	38 (95.0)	52 (94.5)	
Yes	2 (5.0)	2 (3.6)	
Hemoglobin, g/dl			0.124*
n	38	48	
Mean (SD)	11.5 (1.8)	12.1 (2.1)	
PTT			0.466*
n	37	49	
Mean (SD)	28.4 (3.4)	29.0 (4.0)	
INR			0.103†
n	37	50	
Median (range)	1.1 (0.8–1.5)	1.1 (0.8–3.3)	0.103†
Platelets			
n	38	50	
Mean (SD)	320.1 (136.9)	277.2 (107.3)	
Median	288.5	273.5	
Creatinine, mg/dl			0.060†
n	38	52	
Median (range)	0.9 (0.5–1.8)	1.0 (0.5–2.3)	
Time from hemoptysis onset to consultation, d			0.265†
n	40	54	
Median (range)	14.0 (1.0–180.0)	14.0 (1.0–150.0)	
Time from consultation to bronchoscopy, d			0.073†
n	40	55	
Median (range)	1.0 (0.5–7.0)	1.0 (0.5–14.0)	

(Continued)

23 (88%) of these 26 patients. All three patients who had recurrence of bleeding at 48 hours were successfully treated a second time (two patients with APC and one with arterial embolization).

In the AB/no-EBL group (n = 10), one patient was effectively treated with bronchial artery embolization, and this patient had no evidence of recurrence at 48 hours after treatment. Nine patients did not undergo intervention for mild hemoptysis. In five (55%) of these patients, hemoptysis resolved with medical treatment at 48 hours after presentation.

In the no-AB/EBL group (n = 10), one patient underwent APC treatment to the endobronchial lesion that had stigmata of prior bleed and had no recurrence of bleeding at 48 hours after therapy. Of nine patients who did not undergo therapeutic intervention, three (33%) had a recurrence of bleeding by 48 hours after presentation.

In the no-AB/no-EBL group (n = 45), none of the patients underwent endobronchial intervention, and five (11%) patients had recurrence of bleeding at 48 hours after presentation.

The presumed bleeding source in most patients without EBL was distal airway metastatic disease; only eight patients were treated as bronchitis or pneumonia as a cause of mild hemoptysis.

Overall Survival

The median survival times for patients in the subgroups were as follows: AB/EBL, 3.48 months (95% CI, 2.14–6.05); AB/no-EBL, 4.40 months (95% CI, 2.99–8.54); no-AB/EBL, 8.15 months (95% CI, 0.95–NE); and no-AB/no-EBL, 66.50 months (95% CI, 20.80–NE) (Table 2).

Hazard ratios in the multivariate Cox survival analysis were significantly higher for the AB/EBL group compared with the no-AB/no-EBL group; the HRs of the no-AB/EBL and AB/no-EBL groups were not statistically different when compared with the no-AB/no-EBL group. As expected in the multivariate analysis, advanced stage disease was associated with worse survival (HR, 10.80; 95% CI, 2.53–46.08). Factors independently associated with improved survival in the multivariate analysis were higher hemoglobin levels (HR, 0.78; 95% CI. 0.67–0.91) and cessation of hemoptysis without recurrence at 48 hours after bronchoscopy (HR, 0.43; 95% CI, 0.22–0.84) (Table 3). Kaplan-Meier survival estimation curves for patients in the AB and no-AB

Table 1. (CONTINUED)

	Active Bleeding		*P* Value
	Yes	No	
ECOG PS, n (%)			0.197‡
PS 0	3 (7.5)	7 (12.7)	
PS 1	17 (42.5)	32 (58.2)	
PS 2	13 (32.5)	12 (21.8)	
PS 3	7 (17.5)	4 (7.3)	
Resolved in 48 h, n (%)			0.068‡
No	12 (30.0)	8 (14.5)	
Yes	28 (70.0)	47 (85.5)	
Blood transfusion, n (%)			0.229
No	35 (89.7)	53 (96.4)	
Yes	4 (10.3)	2 (3.6)	
Endobronchial lesion, n (%)			<0.001§
No	10 (25.0)	45 (81.8)	
Yes	30 (75.0)	10 (18.2)	
Stage, n (%)			0.010‡
Early	3 (7.5)	16 (29.1)	
Advanced	37 (92.5)	39 (70.9)	

Definition of abbreviations: ECOG = Eastern Cooperative Oncology Group; INR = international normalized ratio; PS = performance status; PTT = partial thromboplastin time.
**t* Test.
†Wilcoxon rank-sum test.
‡Fisher's exact test.
§Pearson chi-square test.

groups are shown in Figure 3; curves for AB/EBL, AB/no-EBL, no-AB/EBL, and no-AB/no-EBL are shown in Figure 4.

Discussion

This study suggests that the presence of active bleeding and endobronchial lesion during the initial bronchoscopic evaluation of patients with mild hemoptysis and advanced stage diseases is independently associated with decreased survival. Higher hemoglobin levels at the time of bronchoscopy and bleeding control at 48 hours were significantly associated with improved survival. No other statistically significant associations between outcome and other prognostic factors were found.

Our study shows that patients with lung cancer and non–lung cancer solid malignancies presenting with mild hemoptysis are very likely to have active bleeding and endobronchial disease that is identifiable at bronchoscopy and amenable to bronchoscopic therapies. Etiologies of hemoptysis reported in various series depend on the year of the publication and the health care environment and geographic location of patients. Ours is the first study addressing the significance of mild hemoptysis in patients with a known history of a solid malignancy.

Hirshberg and colleagues reviewed 208 patients without history of malignancy who presented with hemoptysis at a university hospital in Jerusalem, Israel, between 1980 and 1995 (3). Of these, 80 patients presented with mild hemoptysis, defined similarly as in our study. The most common cause of mild hemoptysis reported in this publication was bronchitis, followed in decreasing frequency by pneumonia, lung cancer, and bronchiectasis. These authors reported "positive results" after bronchoscopy in 54% of patients with mild hemoptysis. However, neither the definition of "positive results" nor the bronchoscopic findings was described. Also, although 18% of these patients with mild hemoptysis were diagnosed with lung cancer, the presence or absence of endobronchial disease was not reported.

Johnston and colleagues retrospectively reviewed 148 patients with hemoptysis who underwent diagnostic bronchoscopy (1). Seventy-two patients had mild hemoptysis, defined as < 20 ml per 24 hours. Similar to the study by Hirshberg and colleagues (3), the most common cause of mild hemoptysis in this publication was bronchitis (47%).

In our study, 46% of the patients had endobronchial disease visible by bronchoscopy, and 42% had active bleeding at the time of bronchoscopy. Only 8 of these 95 patients in our cohort had bronchitis or pneumonia as a cause of mild hemoptysis, which is a much lower frequency than described for the general population. In patients who had evidence of metastatic disease to the chest without other clear cause for bleeding, we presumed that the bleeding was from distal metastatic lesions. Our findings are different from those reported in the literature because our studied population included only patients with a known history of a solid malignancy.

Knowing the site of bleeding is critical for managing hemoptysis, and bronchoscopy is essential to accomplishing this goal. Not only the bronchoscopic intervention itself can be therapeutic, but we believe the bronchoscopic findings can help plan additional measures in case the bleeding increases or assist in guiding bronchial artery embolization procedures if necessary. In the current study, bronchoscopic treatments for bleeding control were implemented when active bleeding and endobronchial lesions were identified. Of these, APC was most commonly used. Similar to a previous report from our group, APC was successful for achieving hemostasis in most cases (13).

Hemoptysis is a common symptom in patients with intrathoracic tumors and one that is responsible for significant alteration in quality of life (17). Given the overall poor outcome of bronchopulmonary malignancies, symptom palliation is of utmost importance.

The observed decreased survival in the AB/EBL group could be a reflection of advanced disease rather than the presence of active bleeding and endobronchial lesion during bronchoscopy. However, after adjusting for different factors, including disease stage, AB/EBL remained as an independent risk factor for worse survival. We hypothesize that central airway involvement by metastatic disease has a worse prognosis than parenchymal lung metastasis. Smaller, centrally located tumors can result in major complications, such as respiratory insufficiency from airway obstruction, postobstructive pneumonia, and asphyxiation from bleeding. In contrast, distal parenchymal metastatic disease often remains without symptoms or complications until tumor burden is large. Bleeding control without recurrence at 48 hours after bronchoscopy had a favorable effect on survival in our study, and endobronchial treatment was also effective to alleviate hemoptysis. One of the strengths of our study is that it consists of data averaged over a long period (mature cohort) instead of single-year data. This is useful for reducing

Table 2. Univariate COX proportional survival analysis

	No. of Points	No. of Events	Median Survival	95% CI for Median	HR	95% CI for HR	*P* Value
Age, yr							
Unit change	95	66	12.62	6.05–19.75	1.00	0.99–1.02	0.618
Hemoglobin, g/dl							
Unit change	95	66	12.62	6.05–19.75	0.78	0.68–0.88	<0.001
PTT							
Unit change	95	66	12.62	6.05–19.75	0.96	0.89–1.03	0.244
INR							
Unit change	95	66	12.62	6.05–19.75	1.15	0.64–2.06	0.646
Platelets							
<50,000	2	2	2.99	2.99–NE	1.00	0.08–1.34	0.118
⩾50,000	86	59	12.62	6.05–18.86	0.32		
Creatinine, mg/dl							
Unit change	95	66	12.62	6.05–19.75	0.70	0.32–1.54	0.373
Time for hemoptysis onset to consultation, d							
Unit change	95	66	12.62	6.05–19.75	0.99	0.99–1.00	0.189
Time to bronchoscopy, d							
Unit change	95	66	12.62	6.05–19.75	0.91	0.82–1.00	0.057
Gender							
Male	47	36	6.14	3.78–16.23	1.00		
Female	48	30	17.28	7.20–66.50	0.61	0.37–0.99	0.044
Ethnicity							
White	71	47	15.84	5.59–33.87	1.00		
Black	13	10	6.34	3.48–9.40	1.42	0.71–2.81	0.321
Hispanic	8	7	6.14	0.69–20.80	1.58	0.71–3.51	0.265
Asian	3	2	17.28	17.28–NE	1.08	0.26–4.46	0.913
Basal malignancy							
Lung cancers	46	33	7.33	4.93–16.23	1.00		
Other cancers	49	33	17.25	5.29–47.70	0.80	0.49–1.30	0.362
Smoking							
Positive	22	15	17.28	4.24–NE	1.00		
Negative	73	51	7.89	5.55–18.86	1.27	0.71–2.25	0.423
Heart							
No	52	38	12.88	5.98–20.80	1.00		
Yes	43	28	8.54	5.29–42.48	0.89	0.55–1.45	0.641
Lung							
No	42	33	7.20	4.24–17.25	1.00		
Yes	53	33	20.80	6.34–58.38	0.63	0.39–1.03	0.064
Kidney							
No	90	62	12.62	6.05–18.86	1.00		
Yes	5	4	19.75	2.99–NE	1.07	0.39–2.93	0.901
Liver							
No	93	64	12.62	6.05–19.75	1.00		
Yes	2	2	6.14	6.14–NE	1.36	0.33–5.59	0.668
Antiplatelet therapy							
No	77	56	8.54	5.59–17.25	1.00		
Yes	16	10	18.86	3.48–NE	0.73	0.37–1.44	0.368
Anticoagulant therapy							
No	90	62	12.88	6.14–19.75	1.00		
Yes	4	4	1.87	1.02–NE	2.62	0.95–7.24	0.063
ECOG PS							
PS 0	10	4	NR	7.98–NE	1.00		
PS 1	49	32	20.80	6.34–58.38	2.29	0.81–6.47	0.119
PS 2	25	21	5.98	3.81–9.40	4.35	1.48–12.76	0.007
PS 3	11	9	2.99	1.12–12.62	6.51	1.98–21.41	0.002
Active bleeding							
No-AB	55	29	42.48	16.23-NE	1.00		
AB	40	37	4.01	2.99-5.55	3.65	2.22–6.02	<0.001
Blood transfusion							
No	88	60	15.24	7.20-21.19	1.00		
Yes	6	5	2.99	0.66-NE	2.27	0.91–5.69	0.080

(Continued)

Table 2. (CONTINUED)

	No. of Points	No. of Events	Median Survival	95% CI for Median	HR	95% CI for HR	*P* Value
Resolved in 48 h							
No	20	17	4.40	2.99-7.89	1.00		
Yes	75	49	16.23	7.98-39.75	0.50	0.28–0.87	0.014
Active bleeding and endobronchial lesion							
No-AB/no-EBL	45	22	66.50	20.80-NE	1.00		
No-AB/EBL	10	7	8.15	0.95-NE	2.40	1.02–5.66	0.045
AB/no-EBL	10	8	4.40	2.99-8.54	2.96	1.31–6.71	0.009
AB/EBL	30	29	3.48	2.14-6.05	4.93	2.78–8.74	<0.001
Endobronchial lesion							
No-EBL	55	30	39.75	12.62-NE	1.00		
EBL	40	36	4.21	2.14-7.98	3.30	2.01–5.44	<0.001
Stage							
Early	19	4	NR	66.50-NE	1.00		
Advanced	76	62	6.14	4.40-12.62	8.81	3.17–24.46	<0.001

Definition of abbreviations: AB = active bleeding; CI = confidence interval; EBL = endobronchial lesion; ECOG = Eastern Cooperative Oncology Group; INR = international normalized ratio; NE = not estimable; NR = not reached; PS = performance status; PTT = partial thromboplastin time.

Table 3. Multivariate COX proportional survival analysis

	Full Model*		Reduced Model†	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Age				
Unit change	1.01 (0.99–1.03)	0.379		
Hemoglobin, g/dl				
Unit change	0.83 (0.71–0.98)	0.025	0.78 (0.67–0.91)	0.001
Time from consultation to bronchoscopy, d				
Unit change	1.00 (0.99–1.01)	0.689		
Gender				
Male				
Female	0.66 (0.37–1.17)	0.152		
Heart				
No				
Yes	0.89 (0.47–1.70)	0.724		
Anticoagulant therapy				
No				
Yes	3.07 (0.97–9.69)	0.056		
ECOG PS				
PS 0				
PS 1	2.00 (0.54–7.36)	0.298		
PS 2	3.61 (0.88–14.86)	0.075		
PS 3	6.28 (1.28–30.78)	0.023		
Stage				
Early				
Advanced	9.53 (2.09–43.41)	0.004	10.80 (2.53 –46.08)	0.001
Active bleeding and endobrochial lesion				
no-AB/no-EBL				
no-AB/EBL	1.58 (0.57–4.40)	0.383	1.29 (0.53 –3.16)	0.572
AB/no- EBL	3.24 (1.16–9.04)	0.025	2.40 (0.98 –5.85)	0.055
AB/EBL	2.80 (1.37–5.72)	0.005	3.20 (1.74 –5.89)	<0.001
Resolved in 48 h				
No				
Yes	0.66 (0.29–1.46)	0.302	0.43 (0.22–0.84)	0.014
Blood transfusion	0.84 (0.28–2.54)	0.759		
No				
Yes				

*$P < 0.10$ in the univariate analysis.
†$P < 0.05$ in the univariate analysis.

measurement error and capturing a long-term effect. Also, our database accurately recorded all the predictive variables considered important for this multivariate analysis. Although the 48-hour cut off for bleeding cessation is not meant to predict recurrence of hemoptysis, it is clinically useful to define prognosis shortly after bronchoscopy.

Our study is subject to the potential limitations of the use of observational data to evaluate the effects of outcomes and therapy: it is possible that the observed results are due to unmeasured confounders. Future studies will have to test the potential associations we found on our report. In spite of its retrospective nature, our study is the first to offer information on the survival of patients with solid malignancy presenting with mild hemoptysis. Finally, our study is based on a selected patient population attending a dedicated cancer center, which probably represents a self-selection and different threshold to request and accept advanced interventions when compared with the general population.

In summary, patients with an underlying solid malignancy of any origin who present with mild hemoptysis and have active bleeding and endobronchial lesions during bronchoscopy have decreased survival. Furthermore, these patients are likely to benefit from palliative interventions and should be approached differently than patients with mild hemoptysis without a history of malignancy. Bronchoscopy should be always considered in these patients as part of the diagnostic and prognostic investigations and for possible palliative treatments. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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