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The role of fiberoptic and rigid bronchoscopy in the diagnosis of malignant central airway pathologies

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Abstract:

BACKGROUND AND AIM: This study aims to identify the factors influencing the decision to proceed with fiberoptic bronchoscopy (FB) or rigid bronchoscopy (RB) when the initial FB does not provide a diagnosis, and it assesses the outcomes of these procedures.

METHODS: We performed a retrospective analysis of 158 patients who underwent diagnostic RB and 50 patients who underwent recurrent diagnostic FB among those diagnosed with malignant airway tumors.

RESULTS: There were no significant differences in age, comorbidities, or anticoagulant use between the groups. When initial FB procedures were analyzed, the rate of procedure failure was higher in the RB group due to central airway obstruction and intraprocedural complications, whereas the rate of inconclusive diagnoses was significantly higher in the recurrent FB group ($p<0.001$). Likewise, the proportion of patients in the RB group who underwent only airway assessment or bronchial lavage during the first FB was higher ($p<0.001$). The recurrent FB group experienced more complications during the second procedure ($p=0.005$). The incidence of neuroendocrine tumors or tracheal lesions was higher in the RB group ($p=0.005$). Patients in the RB group also had higher hospitalization rates (59.5%) and longer stays (6.38 days) ($p=0.001$). Moreover, patients in the RB group received significantly faster diagnoses ($p<0.001$).

CONCLUSIONS: Our findings suggest that for patients with central airway lesions, particularly those situated in the trachea, due to the risk of life-threatening complications such as hemorrhage during FB, and considering that recurrent FBs can prolong the time to diagnosis and increase the risk of complications, RB should be prioritized as the diagnostic approach.

Keywords:

Rigid bronchoscopy, fiberoptic bronchoscopy, malignancy

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Introduction

All bronchoscopic procedures are planned following the assessment of a patient's clinical and radiological features. Despite thorough clinical evaluations, there are instances where interventional procedures fail to yield a definitive diagnosis, necessitating repeat bronchoscopic examinations. In such cases, it is crucial to determine the primary diagnostic bronchoscopic method to employ.

Flexible bronchoscopy (FB) accounts for 90% of all bronchoscopic procedures. Its primary advantages include its ease of application with mild sedation and topical anesthesia, as well as its adaptability for use through a nasal, oral, tracheostomy, or endotracheal tube.[1] Rigid bronchoscopy (RB) has been a longstanding tool in diagnosing and treating various primary lung and respiratory tract diseases, the removal of tracheobronchial foreign bodies, and therapeutic interventions for central airway pathologies. Rigid bronchoscopy is typically administered by experienced teams in specialized centers.

Rigid bronchoscopy is superior to FB in terms of its wide-ranging capabilities, particularly in managing hemorrhages originating from the main bronchi and trachea, foreign body removal, the tamponade effect offered by the rigid bronchoscope body, and the large working channel for tools such as lasers, cautery devices, and cryotherapy.[2,3] While RB is currently employed for therapeutic purposes in addressing endobronchial tumors, lesions causing external pressure on the airways, and benign stenosis, it also offers advantages for diagnostic interventions by providing larger biopsy samples.[4] However, its use is restricted by the need for general anesthesia, specialized equipment, and skilled personnel, rendering it less common in most medical centers.

The diagnostic sensitivity of FB in central lesions causing airway obstruction typically ranges from 65% to 85%, particularly with the use of endobronchial or transbronchial biopsies.[5] However, in certain patient groups, FB may fail to yield a conclusive diagnosis, necessitating repeat bronchoscopic procedures. In such cases, when there is a definite need for a diagnostic bronchoscopic procedure, clinicians face a choice between conducting repeat FB or transitioning to RB, depending on the resources available at their institution. Currently, there is a lack of clear data to guide clinicians on which patient groups should proceed with repeated FB or opt for RB. In this study, we aimed to identify the factors influencing the decision to continue with FB or transition to RB in cases where FB initially failed to provide a diagnosis within the interventional bronchoscopy unit of a tertiary hospital. Furthermore, we evaluated the outcomes of these procedures.

Materials and Methods

Study settings and ethics

Approximately 500 RB, 5,900 FB, and endobronchial ultrasonography procedures are performed annually in our tertiary hospital. Yedikule Chest Diseases and Chest Surgery Training and Research Hospital Clinical Research Ethics Committee approved the study protocol (Approval Number: 2020-38, Date: 15.10.2020). This study was performed in line with the principles of the Declaration of Helsinki. No artificial intelligence application was used in the production of the submitted work.

Study population

The study included 208 patients with suspected malignant airway pathology who underwent a diagnostic FB procedure. The final pathological diagnosis of all included patients was compatible with airway malignancy. In 158 patients, referred to as the RB group, the procedure was continued with RB due to the failure of the first FB procedure. In 50 patients, referred to as the FB group, despite the failure of the first FB procedure, FB was performed again for diagnostic purposes.

Patients in whom diagnostic methods other than FB were used as the initial procedure (RB, endobronchial ultrasound (EBUS), etc.), whose first FB procedure was diagnostic, or who were previously definitively diagnosed and underwent only therapeutic RB were excluded [Fig. 1].

Technique

Patients in the RB group were intubated with RB (Dumon Series II, Efer Endoscopy, La Ciotat, Paris, France), and their respiration was maintained with the conventional balloon method. Fiberoptic bronchoscopy was used through a rigid tube (Model 1T-180; Olympus America Inc., Melville, NY, USA) to clear secretions and blood from the airways, evaluate the openness of distal segments, and assess peripheral lesions. Endobronchial biopsy (EBB), bronchial lavage (BL), and transbronchial needle aspiration (TBNA) were applied via FB. Pathological materials were obtained by passing biopsy forceps of various sizes

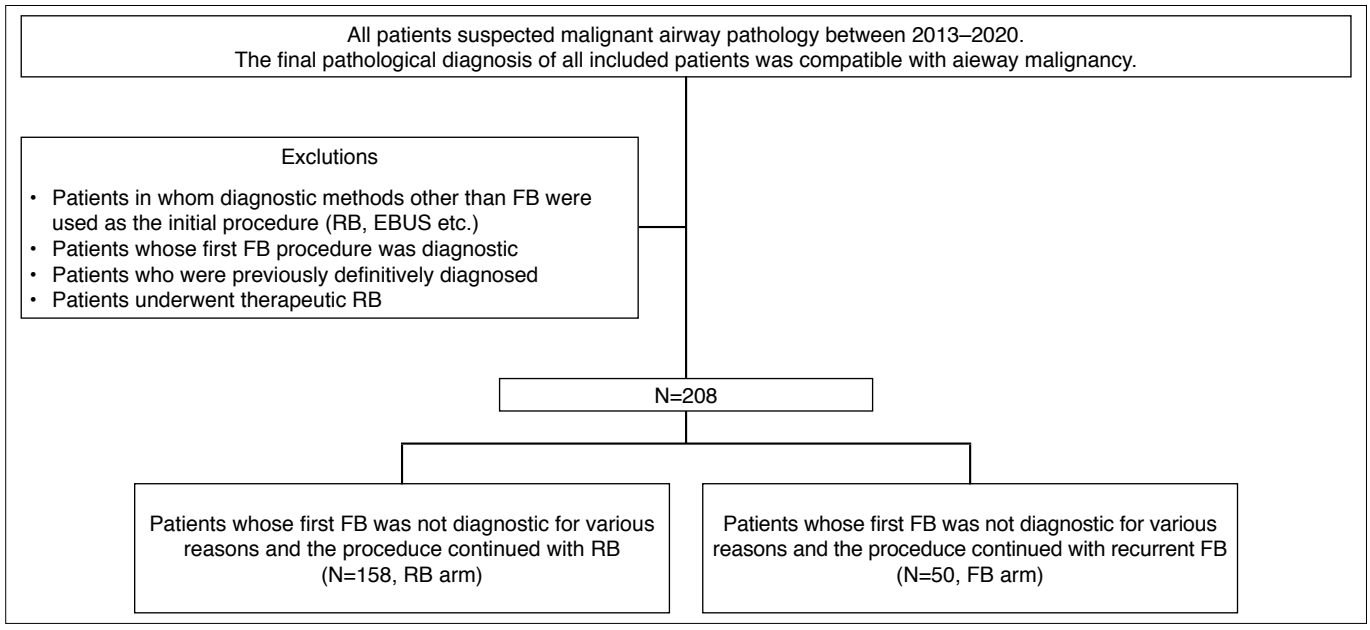

Figure 1: Flow chart

FB: Fiberoptic bronchoscopy, RB: Rigid bronchoscopy, EBUS: Endobronchial ultrasound

through RB. In both procedures, EBB was applied, and after removing any secretion and necrotic material, approximately 4–5 biopsies were taken to achieve an optimal diagnosis. After the FB procedure, patients were monitored based on the amount of sedative agent administered in the recovery room and the patient's clinical status. Post-RB patients were monitored in the post-anesthesia care unit next to the operating room for less than 2 hours and then transferred to an appropriate care area (intensive care unit or ward) depending on the need for ventilation. Patients without any complications were discharged.

Data collection

Procedure reports and pathology reports of all patients were examined. Data regarding age, gender, comorbidities, anticoagulant use, malignancies, laboratory parameters, and radiological findings were evaluated using the hospital information system.

Definitions

Intraprocedural complications were defined as situations where either no pathological sampling could be performed due to complications occurring during imaging with FB, or the procedure could not be completed due to complications developing after a biopsy was taken.

Central airway obstruction was defined as airway narrowing exceeding 50% during FB, preventing pathological sampling or allowing only BL to be performed.

Failure to reach a definitive diagnosis was defined as the inability to provide a pathological diagnosis despite completing the FB procedure by standard methods.

Uncontrolled arterial blood pressure elevation was considered when patients exhibited values over 20% of their initial blood pressure measurements.[6]

Hemorrhage severity was classified as follows: mild hemorrhage was self-limiting bleeding requiring aspiration; moderate hemorrhage was bleeding that stopped with bronchoscopy in the wedge position, administration of adrenaline, or cold normal saline; severe hemorrhage was bleeding necessitating the use of any endobronchial blocker (solid or liquid), catheter, cautery, resuscitation, blood transfusion, transfer to the intensive care unit, or resulting in death.[7]

Hypoxemia was defined as a drop in oxygen saturation below 90%, regardless of its duration, and in necessary situations, 2 liters per minute (L/min) of oxygen support was provided using a nasal cannula.[8]

For patients using anticoagulants for various reasons, consultation was requested from the physicians who initiated the treatment in the preoperative period. Vitamin K antagonists (VKA) were discontinued 5–7 days before the procedure, and low molecular weight heparin (LMWH) treatment was started. Low molecular

weight heparin treatment was also stopped 12 hours before the procedure and restarted based on postoperative hemorrhage. New generation oral anticoagulants (NOACs) were discontinued 24–48 hours before the procedure, following a similar protocol.

Data analyses and statistical methods

Statistical analysis was conducted using SPSS (SPSS Inc., Chicago, IL, USA) 21.0 software package.

The normality of the variables was examined using visual (histogram and Q-Q plot) and analytical methods (Kolmogorov-Smirnov test). Results were presented as mean ± standard deviation, or median and minimum-maximum for continuous variables. Categorical variables were reported as percentages and frequencies. The Mann-Whitney U test was used for comparisons between non-normally distributed continuous variables. Pearson's chi-square test and, if necessary, Fisher's exact test were used for comparisons between categorical variables. A p-value below 0.05 was considered statistically significant.

Results

Among the comorbidities, hypertension (HT) was the most common in the RB group, while HT and cardiovascular diseases (CVD) were the most common in the FB group. When both groups were compared in terms of intraprocedural complications during the first FB, the rate of complications was statistically higher in the RB group. The rate of failure due to central airway obstruction was higher in the RB group, while the rate of patients failing to reach a definitive diagnosis was significantly higher in the FB group ($p<0.001$). In both groups, hemorrhage was the most common complication during the first FB, and there was no difference between the groups in terms of complication types (Table 1).

The rate of biopsy during the first FB in the RB group (35.4%) was lower than in the FB group (100%) ($p<0.001$). The number of patients who only had an airway evaluation or only underwent BL in the RB group was statistically higher ($p<0.001$). When both groups were compared in terms of the types of biopsies taken during the first FB, the rates of EBB + BL and EBB + TBNA + BL were statistically significantly higher in the FB group (Table 1).

When the distribution of intraprocedural complications of the first FB according to lesion location was examined in both groups, no statistically significant relationship was found between lesion location and complications (Table 1).

There were no significant differences between the two groups in terms of the types of biopsies that led to a diagnosis. The FB group had a higher rate of diagnoses obtained with EBB+BL (Table 2). After secondary procedures, a diagnosis could not be reached with any material in eight patients (5.1%) in the RB group and in five patients (10%) in the FB group. However, these patients were subsequently diagnosed using techniques such as endobronchial ultrasound or mediastinoscopy. In the FB group, the rate of complications during diagnostic FB was statistically higher compared to diagnostic RB ($p=0.005$). There was no statistically significant difference between the groups in terms of achieving a diagnosis as a result of all biopsy procedures.

The rate of complications during diagnostic FB was found to be statistically higher compared to the rate of complications during diagnostic RB ($p=0.005$). Hemorrhage was the most common complication in both groups (Table 2). Notably, there were no emergency bronchoscopic procedures in the FB group, while in the RB group, seven patients (4.4%) required such procedures. Respiratory failure requiring intensive care occurred in seven patients (4.4%) in the RB group, while there were no cases of respiratory failure in the FB group (Table 2).

The RB group had a statistically significantly higher number of patients diagnosed with neuroendocrine tumors ($p=0.005$). Tracheal lesions were more frequent in the RB group ($p=0.001$) (Table 2) [Fig. 2].

The proportion of hospitalized patients (59.5%) in the RB group was higher, and the duration of hospitalization (6.38 days) was found to be longer ($p=0.001$). Patients in the RB group received a significantly faster diagnosis compared to the FB group ($p<0.001$) (Table 3). In the RB group, seven (4.4%) patients underwent RB for the second time, while in the FB group, nine (18%) patients underwent FB for the third time, and one (2%) patient had FB for the fourth time. The number of procedures performed in the FB group was statistically higher than in the RB group ($p<0.001$).

In a comparison excluding patients with central tumoral infiltration or those in whom the procedure was terminated due to the development of intraprocedu-

Table 1: Patient and clinical characteristics of the first fiberoptic procedures

	RB group (n=158)		FB group (n=50)		p
	n	%	n	%	
Gender					
Male	122	77.2	47	94	**0.008***
Age (mean±standard deviation) (median, min-max)	61.15±12.63 63 (21–89)		64.9±9.8 65 (43–89)		0.077***
Anticoagulant use	23	14.55	10	20	0.359*
Presence of comorbidities	94	59.5	30	60	0.949*
DM	26	16.5	12	24	0.229*
HT	42	26.6	14	28	0.844*
COPD-asthma	28	17.7	12	24	0.326*
CVD	32	20.3	14	28	0.250*
NMD	2	1.3	3	6	0.091*
CKD	3	1.9	2	4	0.596**
Past malignancy	13	8.2	7	14	0.228*
PD	3	1.9	0	0	1**
OSAS	1	0.6	0	0	1**
First FB failure evaluation					
Intraprocedural complication	65	41.1	12	24	**<0.001****
Central airway obstruction	33	20.9	0	0	**<0.001****
Failure to reach a definitive diagnosis	60	38	38	76	**<0.001****
Evaluation of intraprocedural complications of the first FB					
Uncontrolled arterial blood pressure elevation	11	7	4	8	0.760**
Hypoxemia	10	6.3	0	0	0.120**
Hemorrhage	61	38.6	14	28	0.170*
Patient non-compliance	11	7	3	6	1**
Procedures performed during the first FB					
Airway evaluation only	57	36.1	0	0	**<0.001***
Biopsy	56	35.4	50	100	
BL	45	28.5	0	0	
Pathological sample collection methods					
EBB	4	2.5	2	4	**<0.001****
EBB+BL	24	15.2	25	50	
TBNA+BL	10	6.3	1	2	
EBB+TBNA + BL	10	6.3	22	44	
TBNA	5	3.2	0	0	
EBB+TBNA	3	1.9	0	0	
BL	45	28.5	0	0	
Airway evaluation only	57	36.1	0	0	
Lesion locations in patients with intraprocedural complications					
Trachea	11	13.1	0	0	0.204*
Right main bronchus	21	25	6	37.5	0.302**
Left main bronchus	17	20.2	3	18.8	0.892**
Lobar bronchus	62	73.8	10	62.5	0.356**

*: Pearson Chi-square test, **: Fisher's exact test, ***: Mann-Whitney U test. RB: Rigid bronchoscopy, FB: Fiberoptic bronchoscopy, DM: Diabetes mellitus, HT: Hypertension, COPD: Chronic obstructive pulmonary disease, CVD: Cardiovascular disease, NMD: Neuromuscular disease, CKD: Chronic Kidney disease, PD: Psychiatric disease, OSAS: Obstructive sleep apnea syndrome, BL: Bronchial lavage, EBB: Endobronchial biopsy, TBNA: Transbronchial needle aspiration

ral complications in both groups, no differences were found between the groups regarding age, comorbidity, or anticoagulant use. There was no statistical difference between the groups in terms of the type of biopsy performed during the first FB or the type of biopsy during the second diagnostic interventional procedure. There was also no statistical difference between the groups concerning tumor localization. In the RB group, seven patients (11.7%) had neuroendocrine tumors, while there were none in the FB group. The rate of intraprocedural complications was statistically higher in the FB group. The number of hospitalized patients was higher in the

Table 2: Characteristics of second interventional procedures (rigid bronchoscopy [RB] for RB group, second flexible bronchoscopy [FB] for FB group)

	RB group		FB group		p
	n	%	n	%	
Diagnostic evaluation	150	94.9	45	90	0.311*
Methods of obtaining pathological samples					
EBB	114	76	25	50	0.053*
BL	1	0.7	0	0	
TBNA	7	4.7	2	4	
EBB+BL	15	10	10	20	
BL+TBNA	1	0.7	1	2	
EBB+TBNA	10	6.6	7	14	
EBB+TBNA+BL	2	1.3	0	0	
Rate of intraprocedural complications in diagnostic procedure	14/158	8.86	12/50	24	**0.005****
Uncontrolled arterial blood pressure elevation	0	0	2	4	0.057*
Desaturation	4	2.5	1	2	1*
Hemorrhage	9	5.7	6	12	0.133**
Patient non-compliance	0	0	3	6	**0.013***
Exitus	1	0.63	0	0	1*
Respiratory failure requiring intensive care	7	4.4	0	0	0.2*
Tumor type distribution					
NSCLC	111	70.3	39	78	**0.005***
SCLC	12	7.6	6	12	
Sarcomatoid carcinoma	5	3.2	1	2	
Metastatic carcinoma	12	7.6	1	2	
Neuroendocrine carcinoma	16	10.1	0	0	
Carcinoma in situ	2	1.3	3	6	
Tumor location					
Trachea	29	18.4	0	0	**0.001****
Right main bronchus	54	34.2	12	24	
Left main bronchus	37	23.4	13	26	
Lobar bronchus	101	63.9	37	74	

p<0.05 was considered statistically relevant. In the bold areas, although there was no statistically significant difference, a noteworthy percentage difference was observed. *: Fisher's exact test, **: Pearson Chi-square. EBB: Endobronchial biopsy, BL: Bronchial lavage, TBNA: Transbronchial needle aspiration, NSCLC: Non-small cell lung cancer, SCLC: Small cell lung cancer

RB group, and the duration of hospital stays was longer. The time from the first bronchoscopic procedure to the diagnosis was longer in the FB group.

Discussion

The findings of our study provide important perspectives on the use of RB as a diagnostic intervention in patients with central airway pathologies. It was observed that RB provides a shorter time to diagnosis and is a more reliable option for controlling life-threatening complications. Hemorrhage was the most common complication in all patients. Our study found that factors such as anticoagulant use, the presence of comorbidities, and age did not significantly influence the choice of RB as a diagnostic intervention. In patients referred for RB, the frequency of tumor localization in the trachea was notably high. Despite the longer hospitalization and increased number of hospitalization days for patients undergoing RB, a diagnosis was achieved more promptly.

It has been reported that the overall risk of adverse events related to FB increases with patient age. However, since no widespread or severe adverse events have been observed, increasing age should not deter bronchoscopy.[9] A multi-center retrospective study (n=20,986) reported a 0.02% mortality rate for bronchoscopic procedures (therapeutic-diagnostic FB, RB, FB + RB combination) and a 1.1% rate of serious complications. Hemorrhage was the most common complication at 41%, followed by desaturation at 11%, pneumothorax at 9.77%, and pulmonary edema at 6.22%.[10] Malignancy has been associated with an increased

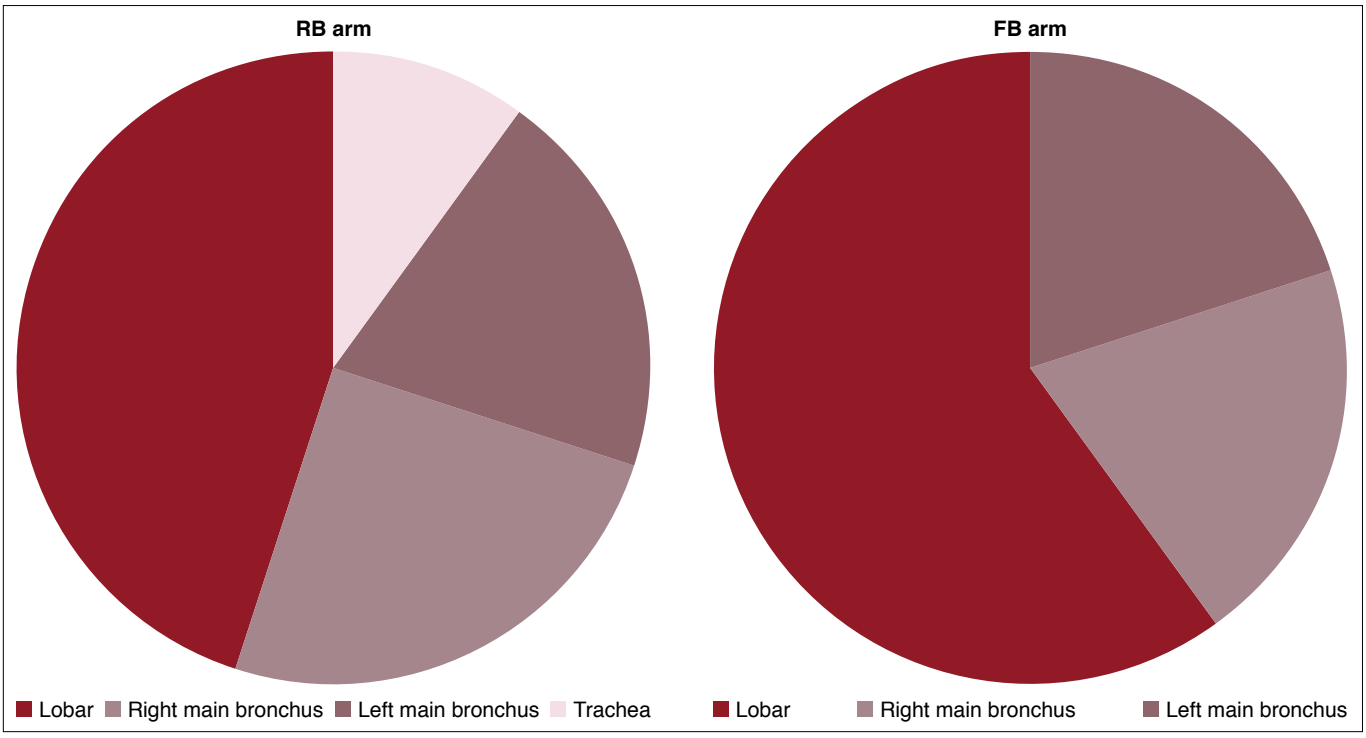

Figure 2: Lesion locations

RB: Rigid bronchoscopy, FB: Fiberoptic bronchoscopy

risk of post-bronchoscopic hemorrhage.[11] In our study, a higher rate of hemorrhage during FB was observed, which may be attributed to the fact that the entire patient population had malignancy. The literature suggests that the risk of hemorrhage during FB is influenced by the type of endoscopic biopsy, the patient's coagulation status, anticoagulant use, and comorbidities. In experienced centers, FB-related hemorrhage is typically managed with RB, allowing for the rapid removal of blood from the bronchial tree and the use of advanced bronchoscopic methods such as Argon Plasma Coagulation (APC) and laser coagulation.[12] We believe that RB is an effective and reliable method in cases where airway safety needs to be ensured, such as hemorrhage, and in repeated diagnostic procedures.

The diagnostic success rate of EBB varies widely, ranging from 30% to 70%, depending on the size and

Table 3: Number of patients hospitalized during the diagnostic procedure, length of hospitalization, and time between the first interventional procedure and pathological diagnosis in both groups

	RB group		FB group		p
	n	%	n	%	
Number of hospitalized patients	94	59.5	15	30	**<0.001***
Hospitalization duration (mean±standard deviation, median (min-max))	6.38±7.3 3.5 (0-40)		3.8±8.9 0 (0-54)		**0.001****
Time elapsed from the first interventional procedure to the provision of a pathological diagnosis					
<30 days	128	81	18	36	**0.001*****
1–3 months	25	15.8	27	54	
3–6 months	4	2.5	4	8	
Longer than 6 months	1	0.6	1	2	
Number of days, mean±standard deviation, median (min-max)	22.92±21.3 16 (4–126)		43.82±38.3 35.5 (10–213)		**0.001****

p<0.05 was considered statistically significant and significance was detected in the data shown in bold. *: Pearson Chi-square test, **: Mann-Whitney U test, ***: Fisher's exact test. RB: Rigid bronchoscopy, FB: Fiberoptic bronchoscopy

location of the lesion.[13,14] Although there was no significant difference between the groups regarding the type of biopsy providing a diagnosis, a higher percentage of diagnoses in the RB group was associated with larger biopsy samples.

While a study comparing FB under local anesthesia with RB under general anesthesia reported a higher rate of major complications in the RB group, our study found a higher complication rate during recurrent diagnostic FBs compared to diagnostic RBs.[15] Another study examining complications of FB under local anesthesia noted that the complication rate increased with the number of procedures performed.[16] Insisting on the use of FB for diagnosis after the first FB evaluation increases the risk of complications.

In our study, the rates of hemorrhage and hypoxemia associated with RB were relatively high. In a population consisting of patients with malignant central airway obstruction undergoing therapeutic RB, RB-associated hemorrhage occurred in 2.3% of cases and hypoxemia in 1.5%.[17] Repeated bronchoscopic procedures, emergency procedures, and malignant lesions, especially those causing hemorrhage, have been associated with increased complications.[17,18] We believe that the elevated complication rates observed during RB in our study can be attributed to the fact that all patients included in the study had malignancies. Additionally, the fact that 4.4% of patients required emergency RB due to complications arising during FB procedures could be one of the reasons for the higher complication rates observed during the study.

While the literature lacks information on the development of hypoxemia during diagnostic RB procedures, a relevant study focused on therapeutic RB procedures. This study, involving RB for tumor excision and stenting in patients with tracheal and main bronchial lesions, reported a hypoxemia rate of 25%.[19] It is worth noting that the therapeutic procedures in this study differed from diagnostic RB, which was the focus of our investigation. Despite these differences, our study found a lower rate of intraoperative hypoxemia at 2.5%, suggesting a favorable outcome compared to the literature.

Neuroendocrine carcinomas are typically solitary tumors (70%) found in central airways, with rare metastasis to extrathoracic organs.[20,21] The higher rate of neuroendocrine tumors among patients referred for RB in our study is likely due to the central location of these tumors.

Patients who underwent RB reached a diagnosis much faster than those who underwent recurrent FB. It is known that early diagnosis of lung cancer increases the chance of treatment and reduces mortality.[22] Delayed acquisition of pathological results with repeated diagnostic procedures prolongs the process of diagnosing the disease. This finding suggests that the use of RB during the diagnostic stage in selected patients after the first FB accelerates the diagnostic process.

In the available literature, the time from the initial evaluation of a patient by a pulmonologist to the formal diagnosis is commonly referred to as the "diagnostic period," which typically averages around 15 days.[23] However, a multicenter study indicated that the mean time from evaluation by a pulmonologist to diagnosis can extend to 20.4±44.5 days.[24] In our study, the timeframe from the first FB to diagnosis was consistent with the literature's reported numbers in patients who underwent RB. In contrast, patients in the FB group were diagnosed significantly later than what is observed in the literature.

It is well-established that an early diagnosis of lung cancer significantly improves treatment prospects and reduces mortality rates.[23] Delays in obtaining pathological results due to repetitive diagnostic procedures can prolong the diagnostic process for patients. This underscores the potential benefit of implementing RB in the diagnostic phase for selected patients after the initial FB, as it can expedite the diagnostic process and contribute to better patient outcomes.

Conclusion

Our study emphasizes that considering the option of using RB following initial FB evaluations, particularly for tumors located in the central airways, including the trachea, can expedite the diagnostic process. Moreover, when intraprocedural complications such as moderate to severe hemorrhage or hypoxemia arise, prompt referral of the patient to a center capable of performing RB to ensure airway patency offers significant advantages in terms of complication management. This approach may contribute to improved procedural success and more effective management of malignant airway pathologies.

Ethics Committee Approval

The study was approved by the Yedikule Chest Diseases and Chest Surgery Training and Research Hospital Clinical Research Ethics Committee (No: 2020-38, Date: 15/10/2020).

Authorship Contributions

Concept – C.Ö.; Design – S.N.S.; Supervision – M.S.A.; Funding – M.S.A.; Materials – F.A.; Data collection &/or processing – C.Ö.; Analysis and/or interpretation – S.N.S.; Literature search – S.T.O.; Writing – M.S.A.; Critical review – C.S.

Conflicts of Interest

There are no conflicts of interest.

Use of AI for Writing Assistance

No AI technologies utilized.

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Nil.

Peer-review

Externally peer-reviewed.

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