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ORIGINAL ARTICLE

Predictive factors for improved diagnostic accuracy with the use of radial-probe EBUS

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Study carried out in the Serviço de Endoscopia Respiratória, Departamento de Pneumologia, Instituto do Coração, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo (SP) Brasil.

ABSTRACT

Objective: To assess predictive factors for improved diagnostic accuracy with the use of radial-probe EBUS (RP-EBUS). **Methods:** This was a retrospective review of consecutive patients undergoing RP-EBUS between February of 2012 and January of 2020. Parameters including the presence of a bronchus sign on CT scans, the position of the radial EBUS probe, lesion size, lesion location, and lesion type were analyzed in relation to two defined outcomes (final diagnosis or no diagnosis). Univariate analysis was used in order to explore the individual effects of each parameter on diagnostic accuracy. Multivariate logistic regression was performed to identify significant predictors of diagnostic accuracy. **Results:** RP-EBUS was used for diagnostic purposes in 101 patients. The lesion was < 3 cm in size in 59 patients (58.4%) and predominantly solid in 60.3%. There was a positive correlation between radial EBUS probe position and diagnostic accuracy (p = 0.036), with 80.9% of the patients showing a bronchus sign on CT scans. Furthermore, 89% of the patients showed a bronchus sign on CT scans and a correlation with diagnostic accuracy (p = 0.030), with 65.8% of the lesions being located in the left/right upper lobe (p = 0.046). When the radial EBUS probe was within the target lesion, the diagnostic yield was = 80.8%. When the probe was adjacent to the lesion, the diagnostic yield was = 19.2%. A bronchus sign on CT scans was the only parameter that independently influenced diagnostic accuracy (adjusted OR, 3.20; 95% CI, 1.081-9.770; p = 0.036). **Conclusions:** A bronchus sign on CT scans is a powerful predictor of successful diagnosis by RP-EBUS.

Keywords: Diagnostic techniques, respiratory system; Ultrasonography; Bronchoscopy.

INTRODUCTION

EBUS was initially described by Hürter & Hanrath in 1992.[1] Since then, it has become a valuable tool for bronchoscopists to visualize the airway wall, lung, and mediastinum.[1] With the advances in EBUS, a growing number of chest diseases can now be detected by bronchoscopy.

A flexible, rotating transducer is employed in the radial EBUS probe, which can be inserted with or without a guide sheath through the working channel of a bronchoscope. This device creates a 360° (radial) image of the surrounding structures outside the airway wall, enabling the detection of peripheral lung lesions. As a result, radial-probe EBUS (RP-EBUS) has the potential to improve the diagnostic yield of conventional bronchoscopy.

RP-EBUS has gained widespread recognition as an effective procedure for enhancing the sensitivity and accuracy of diagnosing peripheral lung lesions. In fact, RP-EBUS can precisely identify the location of pulmonary nodules or masses by leveraging the distinct echogenic properties of different lung tissues. This not only aids in pinpointing the location of the lesion but can also provide valuable insights into its underlying cause.

During transbronchial lung biopsy with a flexible bronchoscope, certain anatomical factors, such as the significant branching angles of subsegmental bronchi from their parent bronchi and variations in branching angles during breathing, can present challenges.[2] As a result, identifying the correct bronchus to approach with a flexible bronchoscope can prove difficult. However, using RP-EBUS as an adjunct can provide additional information on the path leading to the lesion, thus improving success rates in biopsy procedures.

Because of its favorable risk profile when compared with transthoracic needle aspiration (with pneumothorax rates of 0.8% and 25%, respectively),[3-5] RP-EBUS has become a critical tool for diagnosing peripheral lung lesions worldwide. In this study, we sought to assess predictive factors for improved diagnostic accuracy with the use of RP-EBUS.

METHODS

Patients

Medical records of patients undergoing bronchoscopy between February of 2012 and January of 2020 at the

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University of São Paulo School of Medicine *Hospital das Clínicas* Heart Institute, located in the city of São Paulo, Brazil, were retrospectively reviewed. The present study was approved by the Research Ethics Committee of the University of São Paulo School of Medicine *Hospital das Clínicas* (Protocol no. 4.535.270). All participating patients gave written informed consent before undergoing bronchoscopy.

Patients > 18 years of age who had a lung lesion that was visible on RP-EBUS and who had adequate clinical follow-up until confirmation of the diagnosis were included. Patients whose lesion was not visible on RP-EBUS, those who were lost to follow-up, and those diagnosed by endobronchial biopsies visible on conventional bronchoscopy were excluded.

CT analysis

All participating patients underwent CT scans of the chest. The scans were performed with patients lying in a supine position, in the craniocaudal direction, at the end of inhalation. The CT images were analyzed for various parameters, including the presence of a bronchus sign, lesion size, lesion type, and lesion location. The target bronchus for each case was identified through group discussion, and the results were confirmed accordingly. The CT scans were examined for the bronchus sign, which was defined as the presence of a bronchus leading directly to the target lesion.

RP-EBUS

After administration of topical anesthesia, all patients were lightly sedated with individually calculated doses of intravenous fentanyl, midazolam, and/or propofol.

A flexible bronchoscope with an outer diameter of 5.5 mm and a working channel of 2.2 mm and a 20-MHz flexible radial ultrasound probe (UM-S20-20R; Olympus Medical Systems Corp., Tokyo, Japan) were used. After placement of the bronchoscope near the affected bronchial segment (chosen after analysis of the chest CT images), the ultrasound probe was directed to the target area to locate the lesion. The probe was then removed from the working channel, allowing the introduction of the sampling instrument (biopsy forceps, a cytology brush, or an aspiration needle).

Study definitions

Lesions were stratified on the basis of size (≤ 3 cm or > 3 cm) and type (solid lesion, solid cavitated lesion, cavitary lesion, ground-glass opacity, or infiltrate). Lesion location was stratified into right upper lobe, right middle lobe, right lower lobe, left upper lobe, or left lower lobe. The CT bronchus sign was stratified into present or absent. The radial EBUS probe was classified as being within the lesion (when it was in the center of the lesion or surrounded by it) or adjacent to the lesion (when it was adjacent to the lesion and not completely in contact with it). The lesions were classified as being either malignant or benign on the basis of the findings of RP-EBUS biopsy.

Statistical analysis

The characteristics of the study population were described by means and interquartile ranges (for continuous variables) or absolute frequencies (for categorical variables). The Kolmogorov-Smirnov test was performed in order to test the normality of the distribution. Given that none of the variables showed a normal distribution ($p > 0.05$), nonparametric tests were performed. Spearman's correlation coefficient was used in the bivariate analysis. In the multivariate analysis, forward stepwise logistic regression was performed in order to investigate factors affecting diagnostic accuracy, which was evaluated as a dichotomous variable (accurate or inaccurate diagnosis), being considered the dependent variable. The independent variables were sex (male/female), age, lung disease, lesion size, lesion type, lesion location, CT bronchus sign, and position of the radial EBUS probe. The choice of the reference group for categorical variables (dichotomous or not) was based on the lowest absolute frequency of the category (for the variable sex) or on the first category of the variable under study (for the remaining variables). The Hosmer-Lemeshow test was used in order to fit the model with the independent variables. For model validation, its discriminatory ability, sensitivity, and specificity were analyzed by means of the AUC. All OR values were presented with their respective 95% CIs. The level of significance was set at $p = 0.05$. All statistical analyses were performed with the IBM SPSS Statistics software package for Windows, version 23.0 (IBM Corporation, Armonk, NY, USA).

RESULTS

Of the 101 patients who underwent biopsy by means of RP-EBUS, 56 (55.4%) were men and 45 (44.6%) were women. Most (56.4%) of the patients were < 65 years of age. The lesion was < 3 cm in 59 (58.4%) of the patients and predominantly solid in 60.3%. The most common lesion location was the right upper lobe (in 27.3%), followed by the left upper lobe (in 22.3%). Most of the patients (n = 85; 84.2%) had a bronchus sign on CT scans, and the probe was located within the lesion in 76 (75.2%). During the procedure, 89 patients (81.1%) had no complications. The baseline characteristics of the patients included in the study are summarized in Table 1.

Figure 1 shows the correlation between the final diagnosis obtained by RP-EBUS biopsy and the clinical characteristics of the patients. There was a positive correlation between the position of the radial EBUS probe and diagnostic accuracy ($p = 0.036$), with

Table 1. Baseline characteristics of the study population.

Characteristic	(N = 101)
Age, years	
Mean [IQR]	62 [55-71]
Minimum-maximum	19-88
Sex, n (%)	
Male	56 (55.4)
Female	45 (44.6)
Lung disease, n (%)	
Malignant	60 (59.4)
Benign	41 (40.6)
Lesion size, n (%)	
≤ 3 cm	59 (58.4)
> 3 cm	42 (41.6)
Lesion location, n (%)	
Right upper lobe	33 (32.7)
Left upper lobe	27 (26.7)
Left lower lobe	19 (18.8)
Right lower lobe	16 (15.9)
Right middle lobe	6 (5.9)
Lesion type, n (%)	
Solid lesion	73 (72.3)
Ground-glass opacity	11 (10.9)
Solid cavitated lesion	8 (7.9)
Cavitary lesion	6 (6.0)
Infiltrate	3 (2.9)
Bronchus sign on CT scan, n (%)	
Yes	85 (84.2)
No	16 (15.8)
EBUS probe position, n (%)	
Within the lesion	76 (75.2)
Adjacent to the lesion	25 (24.8)

80.9% of the patients showing the CT bronchus sign. In addition, 89% showed the CT bronchus sign and a correlation with diagnostic accuracy ($p = 0.030$), with 65.8% of the lesions being located in the left/right upper lobe ($p = 0.046$).

Table 2 shows the results of the logistic regression analysis with diagnostic accuracy as the dependent variable. The model showed a value of $p < 0.001$. The Hosmer-Lemeshow test revealed a value of $p = 0.834$, and the AUC was = 0.918, indicating that the model had excellent sensitivity and specificity (Figure 2).

DISCUSSION

The main objective of our study was to explore factors associated with improved diagnostic accuracy with the use of RP-EBUS. Thus, univariate analysis was used in order to consider the individual effects of each parameter on diagnostic accuracy. We found that the position of the probe (within the lesion), the presence of a bronchus sign on CT scans, and the location of the lesion (in the left/right upper lobe) were positively correlated with diagnostic accuracy.

The second major objective of the present study was to identify significant predictors of diagnostic accuracy. After adjusting the variables for the demographic characteristics of the study population, multivariate logistic regression clearly demonstrated that the bronchus sign is a stronger predictor than are the other parameters evaluated and is the only parameter that independently influences diagnostic accuracy.

The findings of this study differ from those of previous studies on the relationship between RP-EBUS and the bronchus sign. For instance, Yamada et al. conducted a retrospective analysis of 158 lesions and found that only RP-EBUS–based lesion identification was a significant predictor of biopsy success based on multivariate analysis.[6] However, only 58 patients were eligible for CT evaluation of the bronchus sign, and several adjuvants were used in the study, which might have reduced the significance of the bronchus sign.

Multiple studies have shown that the size of the lesion has a considerable impact on the diagnostic accuracy of RP-EBUS.[7-11] In our study, the diagnostic yield of lesions > 3 cm was higher than that of lesions < 3 cm (54.8% vs. 45.2%), but the difference was not statistically significant ($p = 0.233$).

Several factors have been consistently linked to increased diagnostic accuracy of RP-EBUS. First, using RP-EBUS to identify the target lesion has been shown to improve accuracy.[12] Second, placing the radial probe in the center of the lesion (rather than adjacent to it) has also been found to improve accuracy.[13,14] However, these factors are only identifiable during the procedure and cannot be used in order to select patients beforehand. Therefore, careful examination of the CT scan before the procedure, particularly in order to assess the presence of the bronchus sign, is crucial to enhance the diagnostic outcome.

In order to improve the pretest probability of a successful RP-EBUS procedure, several steps can be taken. First, it is important to have a solid understanding of bronchial segmentation. Second, a CT scan should be performed no later than 3-4 months before the RP-EBUS procedure. Third, the path from the major bronchus to the lesion subsegment should be traced. Fourth, the location of the lesion in the subsegmental bronchus should be identified by means of the radial EBUS probe. Finally, RP-EBUS screening should not be delayed, because of the possibility of atelectasis resulting from anesthesia or sedation.

It is important to acknowledge the limitations of our study. First, the fact that this was a single-center retrospective nonrandomized study might have introduced a selection bias. Second, the bronchoscopy procedures were not performed by the same bronchoscopist, and we did not measure the impact of differences in skill levels on diagnostic accuracy. Third,

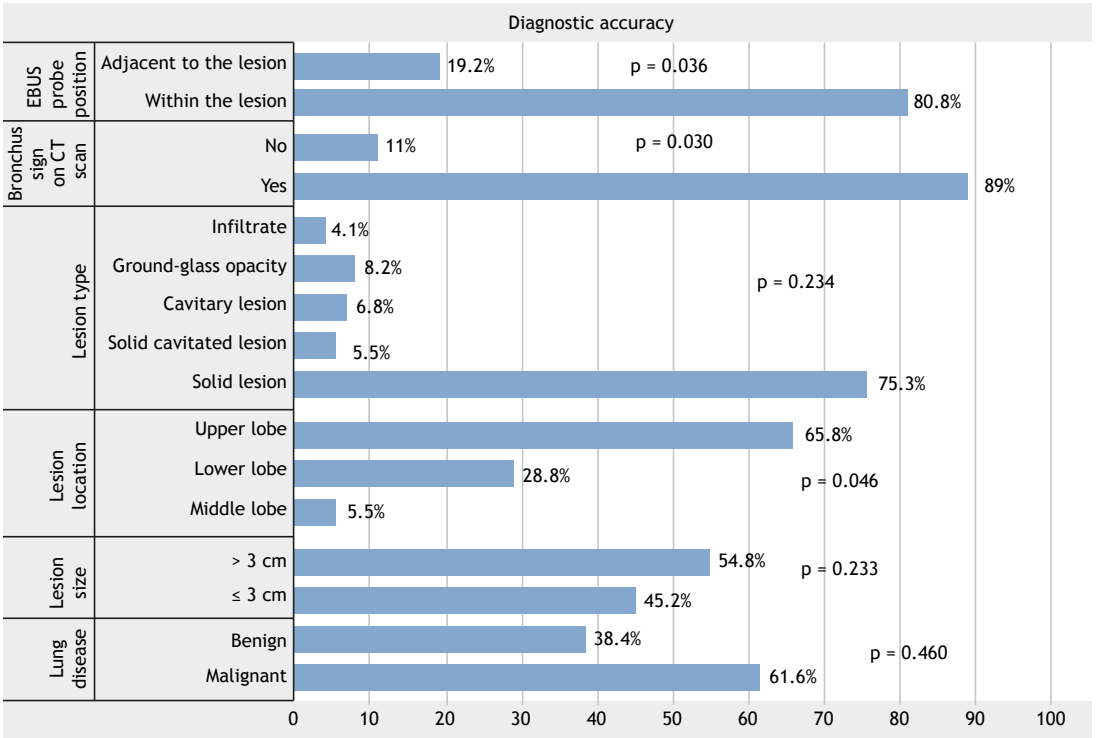

Figure 1. Diagnostic accuracy of radial-probe EBUS, on the basis of clinical characteristics. In the multivariate analysis, the presence of a bronchus sign on CT scans remained as the only independent predictor of diagnostic accuracy (adjusted OR, 3.20; 95% CI, 1.081-9.770; p = 0.036).

Table 2. Multivariate logistic regression for factors affecting the accuracy of diagnosis.[a]

Multivariate analysis		
Independent variable	Adjusted OR (95% CI)	p
Bronchus sign on CT scan		
No (reference group)	1	
Yes	3.250 (1.081-9.770)	0.036

[a]Variables included in the model: sex, age, lung disease, lesion size, lesion location, lesion type, bronchus sign on CT scan, EBUS probe position, and complications.

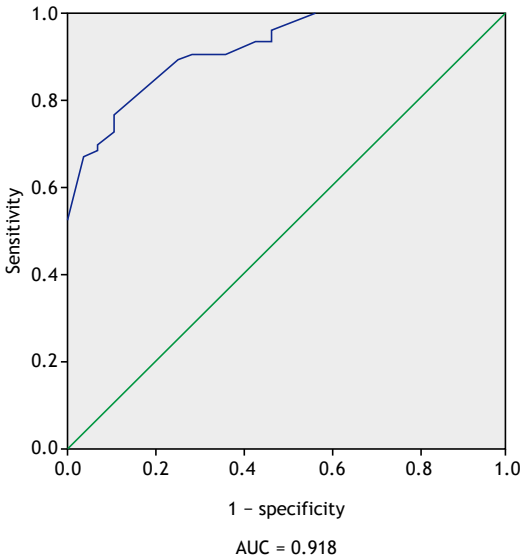

Figure 2. ROC curve for factors affecting the accuracy of diagnosis.

the choice of bronchoscope and sampling devices varied independently for each case. Fourth, we did not have access to rapid on-site evaluation during the procedure. Prospective randomized studies are needed for further evaluation of the diagnostic accuracy of RP-EBUS and to identify potential areas for improvement.

In conclusion, this study found that the presence of a bronchus sign on CT scans was a significant predictor of improved diagnostic accuracy with the use of RP-EBUS, regardless of lesion size, location, or type. This suggests that patients with a bronchus sign on CT scans may be good candidates for RP-EBUS because they have a higher probability of diagnostic success with this procedure.

AUTHOR CONTRIBUTIONS

AB: study conception and design; interpretation of the data; and drafting of the manuscript. MCC: analysis and interpretation of the data. FL, AP, SED,

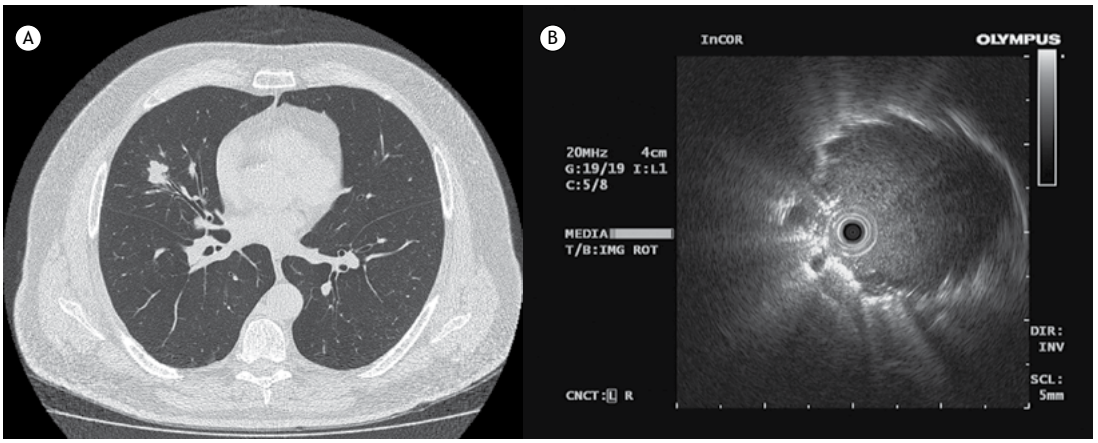

Figure 3. Comparison between CT (n A) and radial-probe EBUS with the probe positioned within the lesion (in B).

VRF, and MJ: critical revision of the manuscript for important intellectual content and final approval of the version to be published.

CONFLICTS OF INTEREST

None declared.

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