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EC PULMONOLOGY AND RESPIRATORY MEDICINE

Research Article

Higher Diagnostic Yield by Adding Conventional Bronchoscopic Sampling to Radial Probe EBUS for Peripheral Pulmonary Lesions

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Received: September 10, 2018; **Published:** September 25, 2018

Abstract

Rationale: Radial probe Endobronchial Ultrasound (RP-EBUS) is used to guide sampling of peripheral lung lesions. There is minimal data regarding combined conventional bronchoscopic sampling and RP-EBUS guided sampling in the same patient.

Objective: We aimed to assess the utility of this combined approach and evaluate rates of complications in our cohort.

Methods: We performed a retrospective single center study which included patients who had RP-EBUS combined with conventional bronchoscopic sampling from August 2012 to October 2016 at the John Hunter Hospital, Newcastle, New South Wales, Australia.

Results: 71 patients were eligible with mean (SD) age 71 (7) years. 43 were male. Mean (SD) lesion size was 26 (3.5) mm. The localization rate with RP-EBUS was 82%. RP-EBUS sampling provided positive diagnoses in 41 patients (58%). Combining patients who were diagnosed based on conventional biopsy and RP-EBUS, diagnostic rate increased significantly to 68% (p-value = 0.016).

Seven patients who were diagnosed based on conventional sampling but were negative on RP-EBUS samplings. There was one small pneumothorax managed conservatively and one episode of moderate bleeding requiring local adrenaline therapy.

Conclusion: RP-EBUS sampling provides much higher success rate for diagnosis for peripheral lung lesions in comparison to traditional bronchoscopic sampling. When EBUS sampling is combined with conventional bronchoscopic sampling, it increases the diagnostic yield without significantly increasing complication rate.

Keywords: *Radial probe Endobronchial Ultrasound (RP-EBUS); Peripheral Lung Lesions; Conventional Bronchoscopic Sampling*

Introduction

Lung cancer is the second most common cancer in the world and the leading cause of cancer related mortality [1]. Early lung cancer is generally asymptomatic and may pose a significant diagnostic challenge depending upon the location of the lesion in the lung parenchyma. Central endobronchial lesions are easily accessible with fiber-optic bronchoscope and biopsies can be taken under direct vision. Pleural based lesions can be sampled with transthoracic needle biopsies with 90% success rate but associated with significant risk of pneumothorax [2].

Blind bronchoscopic brushing and transbronchial biopsies yield diagnosis in 20% patients and with fluoroscopic guidance, diagnostic yield can increase to 45% [3]. Radial Endobronchial ultrasound (RP-EBUS) is a frequently utilized tool for sampling of peripheral pulmonary lesions [4,5]. It involves localizing the tumor in peripheral lung using a radial ultrasound probe passed through a guide sheath (GS)

which is inserted through the working channel of a bronchoscope into the lung segment of interest. Real time fluoroscopy may also be utilized to localize the lesion. Once the lesion is localized, the ultrasound probe is removed, leaving the guide sheath in place. Through the guide sheath, brushings and transbronchial biopsies are performed.

The utility of RP-EBUS for peripheral pulmonary lesions is well recognized. Chan., *et al.* reported a single center retrospective study which included 467 patients and reported 69% diagnostic yield [6]. A meta-analysis was performed of studies using RP-EBUS for diagnosis of peripheral pulmonary lesion (PPL). 1420 patients were studied in 16 studies. It showed point specificity of 1.00 (95% CI 0.99 - 1.00) and point sensitivity of 0.73 (95% CI 0.70 - 0.76) overall [7]. Ali., *et al.* performed a recent meta-analysis of 57 studies having 7872 lesions biopsied using radial EBUS. They reported diagnostic yield 70.6% (95% CI: 68 - 73.1%). Overall complication rate was 2.8% [4].

Given the small size of the forceps used in RP-EBUS, biopsy samples are smaller in size as compared to conventional transbronchial biopsies using standard forceps [8]. There is limited published data about utility and benefit of combining traditional bronchoscopic samplings with RP-EBUS sampling in the same patient cohort.

Aim of the Study

We planned to study retrospectively the utility of performing conventional bronchoscopic sampling after RP-EBUS samplings for diagnosis of peripheral pulmonary lesions.

Methods

We performed a single center retrospective analysis of patients who have RP-EBUS sampling and conventional bronchoscopic sampling for diagnosis of peripheral pulmonary lesions from August 2012 to October 2016 at a tertiary care hospital, New South Wales, Australia. The ethics approval was not sought due to retrospective nature of study and institutional policy. The RP-EBUS sampling included transbronchial biopsies, brushings and guide sheath aspirate by using Olympus® GuideSheath Kit K-201. Conventional transbronchial biopsies were performed with 2 mm Boston Scientific Radial Jaw™ biopsy forceps. Conventional brushings were obtained with TeleMed® bronchial cytology brush 3.0mm. Standard washings were also obtained from the segment of interest.

All bronchoscopy procedures were performed in the bronchoscopy suite and attended by at least two respiratory physicians. Patients had conscious sedation for the procedure with intravenous midazolam and fentanyl along with 1% topical lignocaine therapy. Sedation was performed by a separate respiratory physician who has been accredited to perform sedation for bronchoscopic procedures. CT scans were reviewed prior to the procedure to determine the segmental/subsegmental location of lesion which guided the radial EBUS to the segment of interest. Fluoroscopy image guidance was used for sampling. Once lesions were identified, the ultrasound probe was withdrawn leaving the guide sheath in place. Brushing and biopsy samples were taken via the guide sheath in all patients. It was followed by conventional transbronchial biopsies and brushings. The number of biopsies performed were decided by the proceduralist depending upon visual size and adequacy of sample and generally ranged from 3 - 5. Samples were labelled separately and reported by pathologist separately. Results were considered positive if any sampling method resulted a positive diagnosis. All patients were monitored in a recovery area and investigated with chest X-ray only if they developed chest pain, dyspnea or physician was concerned about pneumothorax. Patients were discharged home on the same day if they remained clinically stable.

Result

There were 73 patients who had RP-EBUS guided biopsy of a peripheral lung lesion. Two patients who were excluded from analysis. One patient had obvious endobronchial tumour on bronchoscopy and did not need RP-EBUS. Positive diagnosis was obtained on conventional sampling alone. Another patient was excluded due to RP-EBUS machine malfunction. Only conventional sampling was performed which was diagnostic of malignancy.

71 patients were included in the analysis. Mean (SD) age of patients was 71 (11) years. 41 were male. Mean (SD) lesion size was 26 (3.5) mm.

RP-EBUS detected lesions in 58 patients with localization success rate of 82%. The lesions were concentric on ultrasonography in 44 patients and eccentric in 12 and data was missing for 2 lesions. In the remaining 13 patients, only standard bronchoscopic sampling was performed which was diagnostic in 5 patients (38% success rate) (Figure 1).

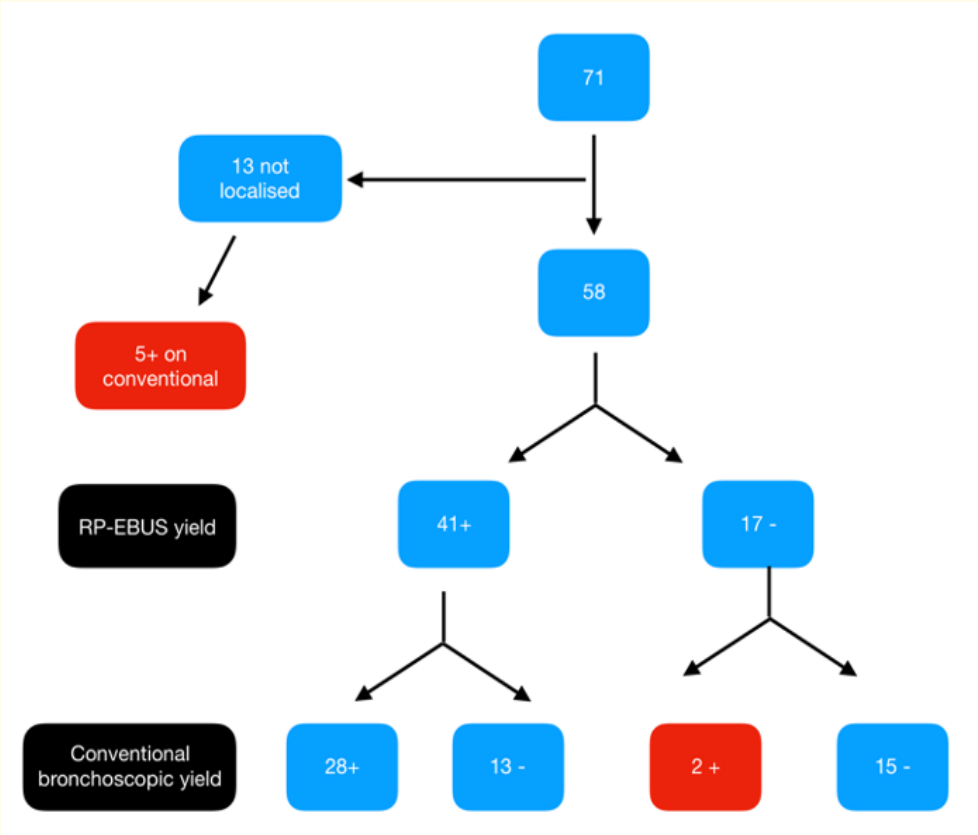

Figure 1: *Flow diagram showing number of patients diagnosed with conventional and RP-EBUS sampling.*

In patients with RP-EBUS localizable lesions (58), 41 patients were diagnosed based on RP-EBUS sampling with diagnostic yield of 71%. Out of 41 patients diagnosed based on RP-EBUS, conventional sampling missed the diagnoses in 12 patients.

Of 17 patients not diagnosed with RP-EBUS despite localizable lesion, 2 were diagnosed based on conventional sampling (12%). Overall RP-EBUS gave positive diagnoses in 41 patients (58%) out of 71 included patients. The diagnostic yield increased significantly from 58% to 68% after combining all patients diagnosed with RP-EBUS and conventional bronchoscopy together, p-value = 0.016 (McNemar test).

We studied the factors which could be predictors of positive result using RP-EBUS sampling in our cohort. These factors included age, location of lesions, size of the lesion, and sonographic location of lesion (concentric vs eccentric). Lobar location was divided into two groups, upper lobes in one group and middle/lingula and lower lobes in other group. None of the mentioned factors showed positive correlation (Table 1).

Parameters	Odd ratio	95% Confidence interval	p-value
Age	0.988	0.937 - 1.041	0.65
Upper lobe vs middle/lower lobes	0.323	0.090 - 1.159	0.083
Size of lesion < 30 mm vs lesion size > 30 mm	0.529	0.127 - 2.204	0.382
Location Adjacent vs concentric	2.429	0.632 - 9.339	0.197

Table 1: *Predictors of positive diagnosis for RP-EBUS. None of the predictors showed positive correlation with final diagnosis in our cohort.*

Discussion

Our results showed 10% increased diagnostic yield when RP-EBUS sampling is coupled with conventional bronchoscopic sampling and found to be statistically significant (p value = 0.016). In other words, the diagnosis would have been missed had conventional sampling not been performed in all patients.

There is no consensus or recommendations regarding conventional sampling along with RP-EBUS sampling. Different centers have different approaches. This has not been systematically studied previously. There is only one published study to our knowledge which assessed the utility of adding bronchoscopic sampling to EBUS-GS sampling [8]. It included 88 patients, 57 of whom were diagnosed based on EBUS TBLBx (64%). Out of 31 not diagnosed by EBUS samplings, 15 were diagnosed with conventional TBLBx. It increased the diagnostic yield from 64% to 81%. Their population (88%) was selected from 266 patients who went for diagnostic procedures for peripheral pulmonary lesions and only those patients who had localizable lesions were included in the analysis. Our results reinforce that combining conventional bronchoscopic procedures increases the diagnostic yield substantially.

Adding conventional sampling takes a little more time during the same sedation or anesthesia and avoids repeat procedure. Conventional biopsy forceps are larger and the biopsy material obtained with conventional TBBx is generally three times bigger than RP-EBUS TBBX tissue [8]. In addition to increasing diagnostic yield, it could also provide extra tissue for immunohistochemistry and genetic testing to assess need for targeted therapy. It is not uncommon that repeat procedures are performed to get more tissue for advanced genetic/molecular tests.

There was one small pneumothorax (1.4% incidence) in our cohort which was managed conservatively and an episode of moderate bleeding post biopsy that was managed with topical cold saline and adrenaline. The complication rate is low in our cohort and comparable to other published studies [4,6]. It also reinforced that combing conventional bronchoscopic sampling to RP-EBUS does not increase the complication rate significantly.

Conclusion

Adding conventional bronchoscopic sampling to RP-EBUS sampling for peripheral pulmonary lesions increases the diagnostic rate significantly without any apparent increase in complication rate.

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Volume 7 Issue 10 Octobert 2018