Bronchial brushing and biopsy: a comparison of diagnostic yield in lung cancer patients at King Hussein Medical Center

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ABSTRACT

Objective: This study assessed the diagnostic yield of bronchial biopsy and bronchial brush, obtained through fibreoptic bronchoscopy, in patients with a visible endobronchial tumor diagnosed at King Hussein Medical Center (KHMC).

Methods: This prospective study included 114 patients who were referred for fibreoptic bronchoscopy in the bronchoscopy unit at KHMC to evaluate suspicious lung masses between June 2016 and January 2019. Inclusion criteria were: age > 14 years and radiological evidence of a lung mass. Exclusion criteria were: patients who did not have a visible endobronchial tumor during fibreoptic bronchoscopy or who were found not to be fit for bronchoscopy due to medical reasons. Through fibreoptic bronchoscopy, bronchial forceps biopsies followed by bronchial brush were obtained and then sent for histological and cytological study. At least five bronchial biopsy samples from the tumor were taken. Biopsy or brush results that showed suspicious cells suggestive of malignancy were considered non-diagnostic and were regarded as negative for malignancy in our study. We reviewed the results obtained by bronchial forceps biopsy and by bronchial brushing and compared the diagnostic yield of each one of them separately. Subsequently, we examined the yield when both techniques were combined in diagnosing lung cancer.

Results: Out of the 114 patients enrolled in our study, 87 (76.3%) were male and 27 (23.7%) were female. The mean age ± standard deviation was 64 ± 9.2 years (males) and 60.1 ± 12.9 years (females). Bronchial biopsy was positive in 91 patients (79.8%), while bronchial brush was positive in 30 patients (26.3%). Bronchial biopsy and bronchial brush were both positive in 29 cases (25.4%). Bronchial brush was the only positive result in 1 case (0.9%), while bronchial biopsy was the only positive result in 62 cases (54.4%). Both techniques were negative in 22 cases (19.3%). The overall positive diagnosis using both techniques was 80.7% (92 cases). The most common tumor type diagnosed by bronchial biopsy was squamous cell carcinoma, followed by small cell carcinoma. On the other hand, adenocarcinoma was the most common cytological diagnosis obtained by bronchial brush, followed by squamous cell carcinoma.

Conclusion: In our study, diagnostic fibreoptic bronchoscopy was a sensitive method for diagnosing visible endobronchial lung tumors. Bronchial biopsy was more sensitive in diagnosing lung tumors compared to bronchial brushing. Combining both techniques did not significantly improve the diagnostic yield. Future studies regarding the causes of low sensitivity of bronchial brush in our hospital should be performed in order to improve the bronchial brush diagnostic yield.

Keywords: bronchial biopsy, bronchial brush, lung tumor

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Introduction

Bronchogenic carcinoma is considered to be one of the most frequent malignancies worldwide. Indeed, it is the leading cause of death due to malignancy worldwide. Despite the fact that the incidence of lung cancer is higher in males, the incidence is rising in females.[1]

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Bronchoscopy was performed for the first time in 1887 by Gustav Killian in Germany. [2] At that time, the main indications for the use of bronchoscopy were therapeutic, e.g., removing foreign bodies. Modern rigid Bronchoscopies were invented in the early 20th century by Chevalier Jackson, who significantly helped to advance bronchoscopy techniques. [3] However, the main use of rigid bronchoscopies remained therapeutic.

In 1967, fibreoptic bronchoscopy (FOB) was developed by S. Ikeda. [4] Since then, FOB has become the mainstay investigation in diagnosing patients with suspicion of lung cancer. During FOB, samples from the visible endobronchial tumor are usually taken by different methods, including bronchial biopsy, bronchial brushing and bronchial lavage. These samples are sent for histological and cytological analysis in order to identify the exact histological tumor type. This identification will play an integral role in determining the therapeutic options. Despite the fact that FOB is an important and essential tool to diagnose lung cancer, it can give variable diagnostic yields. [5-8] one possible reason for this variability is the fact that it is sometimes hard to obtain a representative sample from the neoplastic area because of limitations in the tissue sampling technique. The concurrent use of different sampling techniques, such as bronchial biopsy and brush, may have a positive impact on improving the diagnostic yield. [9]

In our study, we compared the diagnostic yield of forceps biopsy and bronchial brush obtained through FOB in patients with lung masses suspicious of malignancy in King Hussein Medical Center (KHMC). Our aim was to determine whether there was a difference in the diagnostic yield between the techniques, and whether combining the two techniques would improve the diagnostic accuracy.

Methods

In this prospective study, 114 patients—who were referred for FOB in the bronchoscopy unit in KHMC to evaluate suspicious lung masses between June 2016 and January 2019—were enrolled in this study. The ethics committee approved this study. Inclusion criteria were: age > 14 years and radiological evidence of a lung mass. Exclusion criteria were: patients who did not have a visible endobronchial tumor during FOB or who were found not to be fit for bronchoscopy due to medical reasons.

All patients provided written informed consent prior to the procedure. The patients underwent proper evaluation before the procedure, including medical history and physical examination. Platelet count and bleeding profile were sent for all patients. All FOBs were performed by senior pulmonologists in the bronchoscopy unit of KHMC. Patients were fasted for at least 6 h prior to the bronchoscopy. All patients received midazolam (Dormicum) intravenously prior to the procedure, with an initial dose of 2 mg, after which increments of 1 mg were added to reach the desired sedation. Xylocaine (4%) was used for topical anesthesia. Oxygen saturation and pulse rate were monitored throughout the procedure using a pulse oximeter. After visualizing the endobronchial tumor, bronchial forceps biopsies were collected, followed by bronchial brush. At least five bronchial biopsy samples from the tumor were taken using a fenestrated or toothed forceps. The samples were fixed in 10% formalin and sent for histopathological analysis. Subsequently, bronchial brush was performed using a sheath protected brush from the same site. The brushes were smeared on four clean slides using a circular motion to avoid air drying, [10] and then fixed in 95% ethanol immediately for cytological examination. Bronchial brush slides were stained using the Papanicolaou technique, whereas specimens that were taken for histological examination via forceps biopsy were stained with haematoxylin and eosin after being processed. A senior histopathologist examined all the slides. Biopsy or brush results that showed suspicious cells suggestive of malignancy were considered non-diagnostic and were regarded as negative for malignancy in our study.

At the end of the study, we reviewed the results obtained by bronchial forceps biopsy and bronchial brushing, compared the diagnostic yield of each one of them separately and then examined the yield when both techniques were combined in diagnosing lung cancer.

Continuous variables are expressed as mean ± standard deviation; categorical variables are expressed as percentages.

Results

The patients' characteristics are shown in (Table I). Of the 114 patients who underwent FOB, 92 patients (80.7%) had positive results for malignancy. Bronchial biopsy was superior to bronchial brushing in diagnosing lung cancer in our study, as shown in (Table II). Only 1 case had a positive bronchial brush and a negative bronchial biopsy result. Cytology showed evidence of adenocarcinoma for this case.

The most common histopathological type of lung cancer diagnosed by bronchial biopsy in our study was squamous cell carcinoma, followed by small cell carcinoma. However, the most common cytological type diagnosed by bronchial brush in our study was adenocarcinoma, followed by squamous cell carcinoma (Table III). In all of the 29 cases that were diagnosed by both techniques, there was an agreement on the cell type via histological and cytological techniques.

Table I: Age and sex distribution of the patients included in this study.

	Male	**Female**
Number (%)	87 (76.3)	27 (23.7)
Age range (years)	43-80	34-80
Mean age ± standard deviation (years)	64.2 ± 9.2	60.1 ± 12.9

Table II: Accuracy of bronchial brushing and bronchial biopsy in the 114 cases examined in this study.

Group	**Number (%) of cases**
Brush positive, Biopsy positive	29 (25.4%)
Brush positive, Biopsy negative	1 (0.9%)
Brush negative, Biopsy positive	62 (54.4%)
Brush negative, Biopsy negative	22 (19.3%)
Bronchial brushing positive	30 (26.3%)
Bronchial forceps biopsy positive	91 (79.8%)
Total positive	92 (80.7%)

Table III: Comparison of cell types obtained by bronchial biopsy and bronchial brush.

Tumor type	Number (%) by bronchial biopsy	Number (%) by bronchial brush
Squamous	32 (28.1%)	12 (10.5%)
Adenocarcinoma	24 (21.5%)	7 (14%)
Small cell carcinoma	28 (24.6%)	10 (8.8%)
Adenosquamous	1 (0.9%)	0 (0%)
Large cell	1 (0.9%)	1 (0.9%)
Carcinoid	2 (1.8%)	0 (0%)
Metastasis	2 (1.8%)	0 (0%)
Lymphoma	1 (0.9%)	0 (0%)
Negative for malignant cells	23 (20.2%)	84 (73.7%)

Discussion

In this study, the overall positive diagnostic yield of bronchial biopsy and brushing combined together was 80.7% (92 of 114 patients). Previous studies reported variable results regarding the overall positive diagnostic yield of FOB: Buirski *et al.* showed 80%,[11] Quorian *et al.* reported 58%[12] Ono *et al.* stated 97.8%,[13] Matsuda *et al.* indicated 93.7%[14] and Chajjed *et al.* showed the lowest level at 50%.[15] The reason behind this variation could be related to the technical experience of the pulmonologist performing the procedure, specimen handling prior to submitting them to the laboratory and the different ways to interpret the cytological changes depending on the histopathologist.

In our study, bronchial biopsy showed positive results for malignancy in 91 cases (79.8%). Previous studies found a variable positive yield of bronchial biopsy: 71% for Kvale *et al.*,[16] 89% for Knight and Clarke [17] and 91% for Macdonald[18] and Webb and Clarke.[19] However, Knight and Clarke interpreted biopsy samples reported as "suggestive of carcinoma" as being positive for malignancy, a decision that may explain the high sensitivity of the bronchial biopsy in their study. Another possible explanation for the varying positive yield based on bronchial biopsy could be attributed to the different number of biopsy specimens taken during FOB. A study by Gellert *et al.* showed that the positive diagnostic yield of bronchial biopsy increases from 75% when taking three biopsies to 90% when taking five biopsies.[20] Popovich *et al.* found that the maximum yield was reached after the fourth specimen.[21] In our study, we took at least five bronchial biopsies from all visible endobronchial tumours to ensure optimal diagnostic yield.

Bronchial brush was positive in only 30 cases (26.3%) in our study. This diagnostic yield is low when compared to many studies. Alam[22] and Fuladi *et al.*[10] specified a positive bronchial brush diagnostic yield of 84% and 80.76%, respectively. Gaur *et al.* reported a positive yield as high as 93.90%.[23] In fact, many studies found that bronchial brushing was more sensitive in the diagnosis of lung cancer compared to bronchial biopsy.[16, 24-28] The cause of false negative bronchial brush results has been addressed in many studies. Giti *et al.*[1] determined that out of the 31 patients found to have negative bronchial brush results in his study, which constituted 31% of the

patients; 12 cases (38.7%) were missed because of sampling and fixation errors. Another 8 cases were missed (25%) due to screening error by the pathologist. Another study by Nodit *et al*.[29] found that 75% of the false negative bronchial brush results were caused by sampling issues (i.e., crush artifacts and inadequate cells). In our study, we did not investigate the cause of the low sensitivity of the bronchial brushing. We can pursue this endeavour in future studies.

Combining both sampling techniques did not significantly impact the sensitivity in detecting lung malignancies in our study when compared to positive bronchial biopsy results alone (80.7% and 79.8%, respectively).

In 29 cases (25.4%), both bronchial biopsy and bronchial brush were positive. In all of these cases, there was an agreement on the cell type via histological and cytological analysis. Bronchial brush was the only positive result in just 1 case (0.9%).

The most common tumour diagnosed by bronchial biopsy was squamous cell carcinoma (28.1%), followed by small cell carcinoma (24.6%). These results are consistent with previous studies. Choudhury *et al.* reported that squamous cell carcinoma was the most common malignancy, followed by small cell carcinoma (as confirmed by histological examination).[30] Similar findings were reported by Rawat *et al*.[31] However, the most common tumour diagnosed by bronchial brush was adenocarcinoma, followed by squamous cell carcinoma. In 2 cases, lung metastases were diagnosed only by bronchial biopsy, and the bronchial brush result was negative in both cases. The primary origin of the metastases was identified by histological study of the bronchial biopsy samples (one of ovarian origin and the other from breast origin). One lymphoma case was also diagnosed only by bronchial biopsy, as well as 2 cases of atypical carcinoid in which the bronchial brush was also negative.

Conclusion

In our study, diagnostic FOB was a sensitive method for diagnosing visible endobronchial lung tumours. However, bronchial biopsy was more sensitive in diagnosing lung tumours compared to bronchial brushing. Combining both techniques did not significantly improve the diagnostic yield. Future studies regarding the causes of low bronchial brush sensitivity in our hospital should be done in order to improve the bronchial brush diagnostic yield.

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