Diagnostic utility of flexible bronchoscopy in mediastinal and hilar lymphadenopathies

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Background Mediastinal and/or hilar lymphadenopathy with or without parenchymal lesions are difficult in the diagnosis via noninvasive techniques.

Objective To assess the role of flexible fiberoptic bronchoscopy (FOB), in particular, blind transbronchial needle aspiration (TBNA) in the diagnosis of mediastinal and/or hilar lymphadenopathies.

Patients and methods A cross-sectional study was carried out on 42 out of 83 patients presented by chest radiography of hilar and/or mediastinal lymphadenopathies with or without parenchymal lesions. Contrast-enhanced computed tomography chest and FOB, TBNA, and bronchoalveolar lavage were done for all patients. Forceps biopsy and bronchial brushing were done for some patients with bronchoscopic airway abnormalities.

Results A total of 52 patients underwent FOB procedures; among them 10 (19.2%) patients were excluded due to nonconclusive diagnosis for further evaluations; final histopathological and/or microbiological diagnosis was confirmed in 42 (80.8%) patients, and they were included in data analysis. Among them, 25 (59.5%) patients had malignant lymphadenopathies (five patients had small cell lung cancer, 18 patients had nonsmall cell lung cancer, and two patients had lymphoma) and 17 (40.5%) had benign lymphadenopathies (eight patients had sarcoidosis, three patients had tuberculosis, six patients had reactive lymphadenitis). The overall sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of TBNA in the diagnosis of intrathoracic lymphadenopathies were 75.00, 54.50, 60.00, 70.60, and 64.29%, respectively.

Conclusion Bronchoscopy with TBNA has good sensitivity and negative predictive value with fair specificity and positive predictive value in the diagnosis of intrathoracic lymphadenopathies. TBNA is a safe, effective procedure and can be performed easily during routine diagnostic bronchoscopy, and minimize the requirement for mediastinoscopy and thoracotomy.

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Keywords: bronchoscopy, hilar and mediastinal lymphadenopathy, intrathoracic lymphadenopathy, transbronchial needle aspiration

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Introduction

Tuberculosis (TB) and/or fungal infection, neoplasm, and reactive hyperplasia are the most common causes of mediastinal and hilar lymphadenopathies [1]. Immunologic, endocrine, and lipid storage diseases such as sarcoidosis, histiocytosis X, and Castleman's disease are other causal factors for lymphadenopathies [2].

Intrathoracic lymphadenopathies are mainly due to sarcoidosis. Malignant causes of lymphadenopathies include lymphoma, leukemia, and metastatic carcinoma involving the lung, esophagus, and breast cancers [3]. Lymph node diameter exceeding 1–2 cm indicates anomalies. Bilateral symmetrical hilar lymphadenopathy is characteristic of sarcoidosis, but in older people is most likely due to small cell lung cancer, while bilateral asymmetry was described in lymphoma. Unilateral hilar lymphadenopathy in young people can be caused by TB and metastases from bronchogenic carcinoma in older people [4]. Lymphoid proliferations present as reflections of either benign lesions (reactive hyperplasia and lymphadenitis) or malignant lymphomas. An atypical lymphoid proliferation is an expression utilized when it is not adequate for the pathologist to discriminate between benign and malignant features of lymphoid infiltration [5].

The computed tomography (CT) scan allows better delineation of lymphadenopathy and/or parenchymal changes. However, in many cases, biopsy is essential to verify the final diagnosis [6]. For mediastinal adenopathy/mass, the gold standard for histologic diagnosis is mediastinoscopy, mediastinotomy, or an open lung biopsy; still these techniques are invasive with hazardous complications [7]. Fiberoptic bronchoscopy (FOB) using transbronchial needle aspiration (TBNA) and transbronchial lung biopsy should be considered before mediastinoscopy and diagnostic thoracotomy [4]. TBNA is currently a

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well-recognized bronchoscopic procedure for sampling mediastinal/hilar adenopathy and masses. TBNA is indicated for any enlarged lymph node lining the trachea or the main bronchi or a parenchymal lesion adjacent to the main or segmental bronchi demonstrated by a CT scan [8]. Endobronchial ultrasound (EBUS)-TBNA has shown that it is advanced to TBNA regarding safety and the diagnostic yield due to direct visualization of the needle while pursuing the tracheobronchial wall and sampling the lesions [9–11]. However, the requirements of expensive equipment as well as the access or expertise for performing EBUS-TBNA may not be available at all centers restrict the extensive use of EBUS-TBNA in less developed regions. On the other hand, blind TBNA with the use of ordinary equipment, lower cost, easy application, and practice is related to widespread performance [12,13]. Unfortunately, EBUS is not available in most Egyptian hospitals. Therefore, the aim of this study was to assess the role of flexible FOB, in particular, blind TBNA in the diagnosis of mediastinal and/or hilar lymphadenopathies.

Patients and methods

A cross-sectional, prospective study was carried out at the Chest Diseases Department, Al-Zahraa University Hospital, Cairo, Egypt, in the period from January 2014 to August 2017.

Inclusion criteria

Patients having hilar and or mediastinal lymphadenopathy detected on plain chest radiography and /or enhanced thoracic CT with or without parenchymal abnormalities.

Exclusion criteria

Patients with severe bleeding tendencies and those in whom FOB is contraindicated and/or prematurely terminated were excluded from the study.

Ethical considerations

The ethics committee of the Faculty of Medicine for Girls, Al-Azhar University approved the study. Every participant gave his/her informed written consent before enrollment into the study. Each participant had the right to refuse participation or withdraw from the study at any point without affecting their rights to medical care. All the data were coded to ensure confidentiality.

Study design

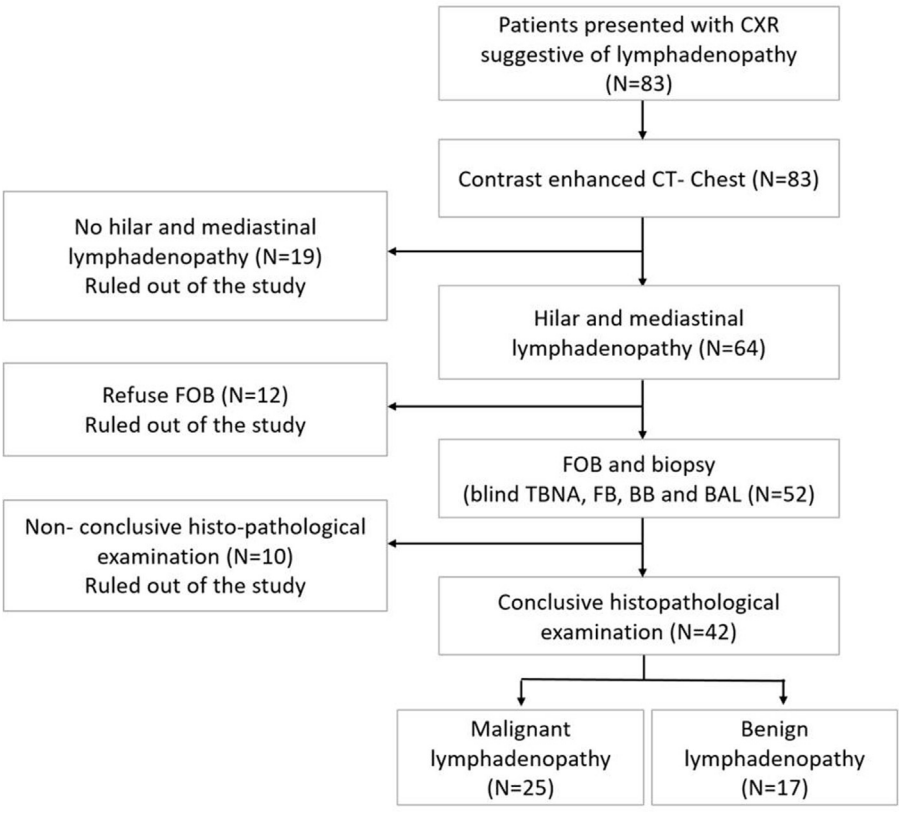
A cross-sectional study was carried out on 83 patients presented by chest radiography of hilar and/or mediastinal lymphadenopathies with or without parenchymal lesions. All of them were subjected to contrast-enhanced CT chest which showed no lymphadenopathy in 19 patients, while there was evidence of lymphadenopathy (hilar, mediastinal, or both) in 64 patients; 12 of them refused FOB procedure and ruled out of the study. For the remaining 52 patients, FOB and biopsy [TBNA, forceps biopsy (FB), bronchial brushing (BB), or bronchoalveolar lavage (BAL) either as single modalities or combined] were done. For 10 patients, histopathological examination showed atypical lymphoid hyperplasia for immunophenotyping and further evaluations; therefore, they were ruled out of the study. Final histopathological diagnosis was confirmed in the remaining 42 patients (25 malignant lymphadenopathies and 17 benign lymphadenopathies) and they were enrolled into this study and were included in final data analysis (Fig. 1).

(1) Demographic data including age, sex, smoking habits, radiographic findings (pulmonary lesions, enlarged lymph node location, site, and size), bronchoscopic findings (types of airway abnormalities, wide carina location), simultaneous use of biopsy forceps, or BB for biopsy of associated airway abnormalities, diagnostic bronchoscopic methods (TBNA, biopsy forceps, BB, BAL), and pathological diagnosis were recorded. All selected patients had no accessible peripheral lymph node, not previously diagnosed as malignancy or other inflammatory diseases like TB or sarcoidosis.
(2) Contrast-enhanced chest CT scan was done using multidetector scanner (160 detectors; Toshiba, Prime Aquilion, Tokyo, Japan). The scans were obtained in the supine position and during full inspiration. Chest CT scan was performed from the lower part of the neck to the adrenal gland. Scanning parameters of CT examinations were as follows: slice thickness 5 mm, slice interval 0.5 mm, collimation 2.5 mm, scan time 3.9 s, feed/rotation 15 mm. A scout was taken with 120 kV and 100 mA, and then helical scanning in the caudo-cranial direction to minimize the respiratory artifacts was done. Scans were performed after intravenous administration of the contrast agent. In our hospital, all chest CT scans were reported/interpreted routinely by an experienced radiologist. Additionally, for this study, the pulmonologist author interpreted the CT scan separately and when there is conflict, a consensus was held with the radiologist.
(3) Flexible fiberoptic bronchoscopy: flexible FOB (FB 1T 160; Olympus, Tokyo, Japan), along

with BB (BC-5C), FB (FB-15C) and TBNA (NA-411D-152; Olympus) supplied with them were used. Supplemental oxygen, pulse oximetry, sphygmomanometer, and equipment for resuscitation were available at the time of the procedure. Platelet count and prothrombin time were extracted before the procedure and are within normal values. The patients were maintained without oral intake for at least 6 h prior to the procedure. Premedication included 0.5 mg atropine injected intramuscularly to decrease secretions 30 min before the procedure. The patients were sedated with intravenous midazolam (2.5–5 mg) in incremental doses to achieve conscious sedation, before and after the insertion of the bronchoscope if not contraindicated. The procedure was performed transnasally on the patient in supine position. Just before insertion of the bronchoscope, 2–3 ml of 2% viscous lidocaine was applied to the nose and lidocaine spray into the oral cavity. Additional small quantities of 1% xylocaine were instilled through FOB for topical bronchial anesthesia, as needed. Oxygen was administered by a nasal cannula and flows were adjusted upward from 2 l/min to keep the oxygen saturation at more than 90%. BAL, TBNA of adjacent tracheobronchial lymph nodes, BB, and FB from associated airway abnormalities were performed as decided by the bronchoscopist. TBNA was performed blindly and as per the international recommendations [14].

(4) Bronchoscopic biopsy techniques: 20-G and 19-G TBNA needles (NA-411D-152; Olympus) were used, with a needle length of 12 mm. Once the bronchoscope reached the target area, the TBNA needle was advanced to penetrate through the intercartilaginous space, inserted into the target lymph node pursuing the tracheobronchial wall perpendicularly. The exact sites of aspiration for TBNA were determined by endobronchial abnormality (endobronchial lesions, bulge due to extrinsic compression, and widening of carina). In cases where there was no endobronchial abnormality, the site of aspiration was determined by CT scan findings. With the needle inserted suction was applied at the proximal port using a 20 ml syringe with the needle moved in and out by 3–4 mm. The needle was then withdrawn from the target site after releasing suction. The contents of the needle were expelled by using air from the 20 ml syringe

Figure 1



Flowchart for patient selection. BAL, bronchoalveolar lavage; BB, bronchial brushing; CT, computed tomography; CXR, chest radiography; FB, forceps biopsy; FOB, fiberoptic bronchoscopy; TBNA, transbronchial needle aspiration.

Table 1 Comparison of the studied variables between malignant and benign lymphadenopathies

	Total (*N*=42)	Malignant LN (*N*=25)	Benign LN (*N*=17)	Test value[a]	*P* value
Age (mean±SD) (years)	48.8±12.1	54.2±9.3	40.8±11.6	4.2[b]	0.001
Sex [*n* (%)]					
Male	20 (47.6)	17 (68.0)	3 (17.6.2)	8.0[a]	0.050
Female	22 (52.4)	8 (32.0)	14 (82.4)		
Smoking status [*n* (%)]					
Nonsmokers	14 (33.3)	6 (24.0)	8 (47.1)	2.4[a]	0.043
Smokers	28 (66.7)	19 (76.0)	9 (52.9)		
CT findings [*n* (%)]					
Parenchymal lesions	23 (54.8)	17 (68.0)	6 (35.3)	5.9[a]	0.042
Lymphadenopathies location					
Hilar	12 (28.6)	5 (20.0)	7 (41.2)	10.3[a]	0.013
Mediastinal	15 (35.7)	10 (40.0)	5 (29.4)		
Hilar and mediastinal	15 (35.7)	10 (40.0)	5 (29.4)		
Unilateral	16 (38.1)	13 (52.0)	3 (17.6)	5.2[a]	0.047
Bilateral	26 (61.9)	12 (48.0)	14 (82.4)		
Lymphadenopathies size					
Less than 2 cm	15 (35.7)	6 (24.0)	9 (52.9)	6.3[a]	0.027
Equal or more than 2 cm	27 (64.3)	19 (76.0)	8 (47.1)		
Bronchoscopic findings [*n* (%)]					
Wide carina					
No wide carina	12 (28.6)	6 (24.0)	6 (35.3)	7.6	0.023
Wide main carina	20 (47.6)	16 (64.0)	4 (23.5)		
Wide C1 or C2 carina	10 (23.8)	3 (12.0)	7 (41.2)		
Airway abnormalities					
No airway abnormalities	18 (42.8)	6 (24.0)	12 (70.6)	3.4	0.018
Endobronchial nodule	11(26.2)	10 (40.0)	1 (5.9)		
Airway compression	13(31.0)	9 (36.0)	4 (23.5)		
Bronchoscopic procedures					
TBNA	17 (40.5)	14 (56.0)	3 (17.6)	7.8	0.019
FB	12 (28.6)	7 (28.0)	5 (29.4)		
TBNA+FB	29 (69.0)	21 (84.0)	8 (47.1)		
BAL	6 (14.3)	1 (4.0)	5 (29.4)		
BB	3 (7.1)	0 (0.0)	3 (17.6)		

BAL, bronchoalveolar lavage; BB, bronchial brushing; CT, computed tomography; FB, forceps biopsy; LN, lymph node; TBNA, transbronchial needle aspiration. This is the statistical method of calculation.

and smears were made. TBNA has to be performed, before bronchial mucosal biopsy to avoid contamination. Direct smear technique was used for the preparation of TBNA specimens. The specimen was smeared on a glass slide applying pressure from the same syringe and was immediately covered with a second slide and while exerting gentle continuous pressure the slides were drawn apart. The TBNA and brushing specimens were immediately smeared on clean glass slides and immediately fixed with 95% ethanol for cytological examination. Bronchial biopsy was performed by using FB if there are associated airway abnormalities, whenever possible three to five biopsies were obtained from the center of the most abnormal area; care was taken to avoid biopsied obvious necrotic area that could affect the diagnostic yield. The specimens were immediately fixed in 10% buffered formalin. BAL was taken by instilling 50 ml of normal saline into the affected area in all cases. Lavage samples were submitted for cytology, acid fast bacilli smears and culture examination. An examination was considered complete if at least three adequate TBNA or FB specimens and four brushing specimens were taken. FOB was prematurely terminated if the patient appeared unstable (e.g. severe tachycardia or desaturation), has severe bleeding, or the procedure was prolonged for more than 45 min postbronchoscopy chest radiograph and arterial blood gases (ABG) were performed routinely 4 h after TBNA.

(5) Definite malignancy was considered when the malignant cells were detected by histopathological examination. Cells suspicious of malignancy were not included in the definition of positive diagnostic yield; further investigations were done for these patients and not included in the study. All patients in whom diagnosis was confirmed by any FOB sampling techniques were included into the study.

Table 2 Comparison of transbronchial needle aspiration positive yield and transbronchial needle aspiration negative yield in malignant lymphadenopathies

Malignant cases	Positive yield (*N*=15)	Negative yield (*N*=10)	Test value	*P* value
CT findings [*n* (%)]				
Parenchymal lesions	13 (83.7)	4 (40.0)	8.5	0.048
Location of lymphadenopathies				
Hilar	4 (26.7)	1 (10.0)	6.9	0.050
Mediastinal	4 (26.7)	6 (60.0)		
Hilar and mediastinal	7 (46.7)	3 (30.0)		
Unilateral	4 (26.7)	9 (90.0)	4.12	0.041
Bilateral	11 (73.3)	1 (10.0)		
Lymphadenopathies size				
Less than 2 cm	2 (13.3)	4 (40.0)	9.4	0.023
Equal or more than	13 (86.7)	6 (60.0)		
Bronchoscopic findings [*n* (%)]				
Wide carina				
No wide carina	12 (28.6)	6 (24.0)	7.6	0.023
Wide main carina	20 (47.6)	16 (64.0)		
Wide C1 or C2 carina	10 (23.8)	3 (12.0)		
Airway abnormalities				
No airway abnormalities	0 (00.0)	6 (50.0)	4.4	0.010
Endobronchial nodule	3 (60.0)	1 (8.3)		
Airway compression	2 (40.0)	5 (41.7)		
Bronchoscopic procedures				
TBNA	13 (86.7)	1 (10.0)	21.2	0.001
FB	0 (0.0)	7 (70.0)		
TBNA+FB	2 (13.3)	0 (0.0)		
BAL	0 (0.0)	2 (20.0)		
BB	0(0.0)	0 (0.0)		
Simultaneous use of BB	13 (86.7)	6 (60.0)	6.8	0.018
Simultaneous use of FB	12 (80.0)	5 (50.0)	6.3	0.019
Final diagnosis				
SCLC	4 (26.7)	1 (10.0)	1.8	0.18
NSCLC	9 (60.0)	9 (90.0)		
Lymphoma	2 (13.3)	0 (0/0)		

BAL, bronchoalveolar lavage; BB, bronchial brushing; CT, computed tomography; FB, forceps biopsy; NSCLA, nonsmall cell lung cancer; SCLA, small cell lung cancer; TBNA, transbronchial needle aspiration.

Statistical data analysis

Using the statistical package for social sciences program, version 17.0 (SPSS Inc., Chicago, Illinois, USA). Descriptive analysis was done and the results were expressed as mean±SD for quantitative continuous variables, and as percentages for qualitative (categorical and nominal) variables. The effect of each variable was evaluated in the univariate analysis using the χ^2 test for categorical variables and Student's *t* test for continuous variables. Multivariate logistic regression analysis was performed to identify the factors predicting the diagnostic yield of the TBNA sampling technique. The strength of relevance between the studied factors and the positive yield was determined according to the value of the beta regression coefficient (*B*) for each variable. *P* value less than or equal to 0.05 (with a confidence limit at 95%) were considered significant. Sensitivity, specificity, and negative predictive values (NPVs) were calculated; with 95% confidence intervals calculated using the modified Wald method. The diagnostic yield of each sampling technique was defined as the total number of patients in whom a diagnosis was obtained by this method over the total number of patients examined.

Results

Flexible FOB procedures were performed for 52 patients; 10 (19.2%) patients were excluded due to nonconclusive diagnosis (atypical lymphoid hyperplasia for further evaluations), while in the remaining 42 (80.8%) patients, the diagnosis was confirmed microbiologically and/or histopathologically (25 malignant lymphadenopathies and 17 benign lymphadenopathies) (Table 1).

Table 1 showed male predominance (*P*=0.05) with significantly higher age (*P*=0.001) and smoking in

Table 3 Multivariate logistic regression analysis for transbronchial needle aspiration yield cases with malignant and benign lymphadenopathies

Variables	*B*	SE	Wald	Significance	95% CI for Exp (*B*)	
					Lower	Upper
Malignant lymphadenopathy						
Bilateral lymphadenopathies	1.8	0.93	3.5	0.002*	0.028	0.97
Parenchymal lesions	2.1	1.5	3.4	0.050*	0.93	2.3
Mediastinal lymphadenopathies	2.3	1.4	4.1	0.033*	1.32	2.3
Lymphadenopathies of size ≥2 cm	2.8	1.7	4.0	0.002*	0.16	144.81
Wide main carina	2.2	2.4	7.4	0.050*	0.29	1.01
Endobronchial nodule	1.41	0.63	4.95	0.026*	0.08	0.85
Simultaneous use of FB	1.6	1.3	3.69	0.060	1.42	8.87
Simultaneous use of BB	1.1	1.1	1.4	0.056	0.31	1.03
Benign lymphadenopathy						
Bilateral lymphadenopathies	2.7	0.90	4.4	0.030*	0.029	0.90
Lymphadenopathy of size ≥2 cm	2.9	0.92	3.8	0.001*	0.027	0.96
Wide main carina	1.8	1.47	3.64	0.056	0.95	294.3
Simultaneous use of FB	2.3	1.1	4.9	0.028*	1.30	144.70

BB, bronchial brushing; FB, forceps biopsy. *Significant.

Table 4 Comparison of transbronchial needle aspiration positive yield and transbronchial needle aspiration negative yield in benign lymphadenopathies

Benign cases	Positive yield (*N*=5)	Negative yield (*N*=12)	Test value	*P* value
CT findings [*n* (%)]				
Parenchymal lesions	2 (40.0)	4 (33.3)	0.004	0.94
Location of lymphadenopathies				
Hilar	2 (40.0)	5 (41.7)	0.49	0.78
Mediastinal	1 (20.0)	4 (33.3)		
Hilar and mediastinal	2 (40.0)	3 (25.0)		
Unilateral	0 (0.0)	3 (25.0)	5.6	0.044
Bilateral	5 (100.0)	9 (75.0)		
Size of lymphadenopathies				
Less than 2 cm	1 (20.0)	8 (66.7)	9.1	0.014
Equal or more than	4 (80.0)	4 (33)		
Bronchoscopic findings [*n* (%)]				
Wide carina				
No wide carina	0 (00.0)	6 (50.0)	12.0	0.036
Wide main carina	3 (60.0)	1 (8.3)		
Wide C1 or C2 carina	2 (40.0)	5 (41.7)		
Airway abnormalities				
No airway abnormalities	3 (60.0)	9 (75.0)	3.2	0.19
Endobronchial nodule	1 (20.0)	0 (00.0)		
Airway compression	1 (20.0)	3 (25.0)		
Bronchoscopic procedures				
TBNA	3 (60.0)	0 (0.0)	17.0	0.002
FB	1 (20.0)	4 (33.3)		
TBNA+FB	1 (20.0)	0 (0.0)		
BAL	0 (0.0)	5 (41.7)		
BB	0 (0.0)	3 (25.0)		
Simultaneous use of BB	1 (20.0)	3 (25.0)	1.3	0.25
Simultaneous use of FB	4 (80.0)	3 (25.0)	9.0	0.011
Final diagnosis [*n* (%)]				
Sarcoidosis	4 (80.0)	4 (33.3)	2.4	0.11
TB	1 (20.0)	2 (16.7)		
Reactive lymphadenitis	0 (0.0)	6 (50)		

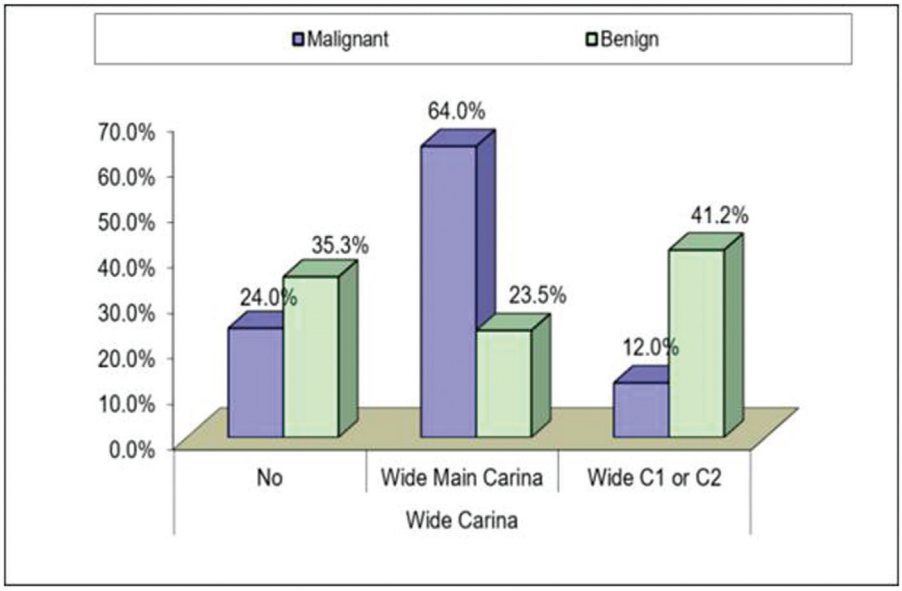
BAL, bronchoalveolar lavage; BB, bronchial brushing; CT, computed tomography; FB, forceps biopsy; TB, tuberculosis; TBNA, transbronchial needle aspiration.

Table 5 Overall sensitivities, specificities, positive predictive value, negative predictive value, and accuracy of transbronchial needle aspiration among the studied cases

Diagnosis	Positive yield [*n* (%)]	Negative yield [*n* (%)]		Test value	*P* value
Malignant	15 (75.0)	10 (45.5)		3.796	0.050
Benign	5 (25.0)	12 (54.5)			
TBNA yield	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
	75.00	54.50	60.00	70.60	64.29

NPV, negative predictive value; PPV, positive predictive value; TBNA, transbronchial needle aspiration.

Figure 2



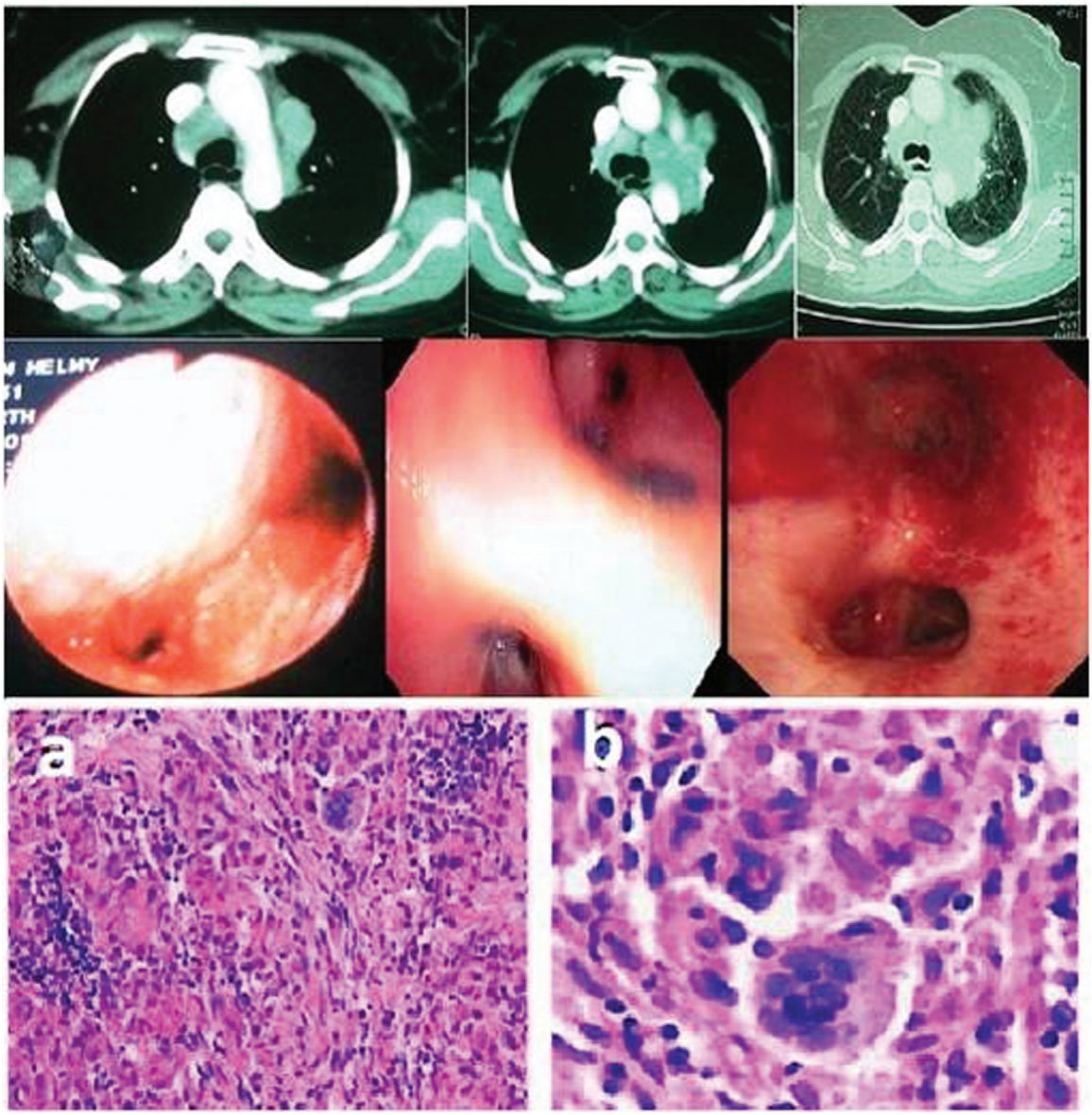
Distribution of wide carina locations between patients with malignant and benign lymphadenopathies.

patients with malignant lymphadenopathies. Regarding CT abnormalities, parenchymal lesions (*P*=0.042), mediastinal or combined hilar and mediastinal lymphadenopathies and lymph node size more than or equal to 2 cm (*P*=0.027) are significantly higher in the malignant group, while hilar (*P*=0.013) and bilateral lymphadenopathies were significantly higher in patients with benign lymphadenopathies. Regarding bronchoscopic findings, wide main carina was significantly higher in the malignant group, while wide C1 or C2 was common in the benign group (*P*=0.023). Most cases with malignant lymphadenopathies were associated with bronchoscopic airway abnormalities, while 70.6% of cases with benign lymphadenopathies have no bronchoscopic airway abnormalities (*P*=0.018) (Fig. 2-6). Most cases of malignant lymphadenopathies were diagnosed via either TBNA plus FB (84.0%) or TBNA alone (56.0%) or FB (28.0%), while in benign lymphadenopathies most cases were diagnosed through FB or BAL (29.4% each) and only 17.6% were diagnosed via TBNA (*P*=0.019).

Table 2 demonstrated that among cases with malignant lymphadenopathies, the positive TBNA yield was related to the presence of parenchymal lesions (83.7%) (*P*=0.048), combined hilar and mediastinal lymphadenopathies (46.7%, 0.050), bilateral lymphadenopathies (73.3%, 0.041), lymphadenopathies size more than or equal to 2 cm (86.7%) (*P*=0.023), wide main carina (86.7%) (*P*=0.041), presence of endobronchial nodule (53.3%) (*P*=0.010), and simultaneous use of either BB or FB (86.7 and 80.0%) (*P*=0.018 and 0.019). Moreover, by multivariate logistic regression analysis, the most significant factors related to TBNA positive yield in malignant lymphadenopathies were lymphadenopathies size more than or equal to 2 cm (*B* coefficient=2.8), mediastinal lymphadenopathies (*B* coefficient=2.3), wide main carina (*B* coefficient=2.2), parenchymal lesions (*B* coefficient=2.1), and bilateral lymphadenopathies (*B* coefficient=1.8) in descending orders (Table 3).

Table 4 shows that in patients with benign lymphadenopathies the positive TBNA yield was related to the presence of bilateral lymphadenopathies (100.0%, *P*=0.044), lymphadenopathies size more than or equal to 2 cm (80.0%, *P*=0.014), wide main carina (60.0%, *P*=0.036), and simultaneous use of FB (80.0%,

Fig. 3



CT chest with intravenous contrast shows hugely enlarged retrocaval, RT and LT hilar, aorto-pulmonary, perivascular, subcarinal, and postmediastinal LN. FOB showed widening of the main carina and a wide RC1. Histopathological examination of TBNA showed a picture of sarcoidosis: (a) small noncaseating granuloma formed mainly from the epithelioid cells surrounded by a narrow rim of lymphocytes with scattered foreign body giant cells and (b) high power of the same picture (hematoxylin and eosin, original magnification a, ×200; b, ×500). CT, computed tomography; FOB, fiberoptic bronchoscopy; LN, lymph node; TBNA, transbronchial needle aspiration.

P=0.011). Additionally, by multivariate logistic regression analysis, the most significant factors relevant to TBNA positive yield in benign lymphadenopathies were lymphadenopathies of size more than or equal to 2 cm (*B* coefficient=2.9), bilateral lymphadenopathies (*B* coefficient=2.8) (*B* coefficient=2.7), and simultaneous use of FB (*B* coefficient=2.3) in descending order.

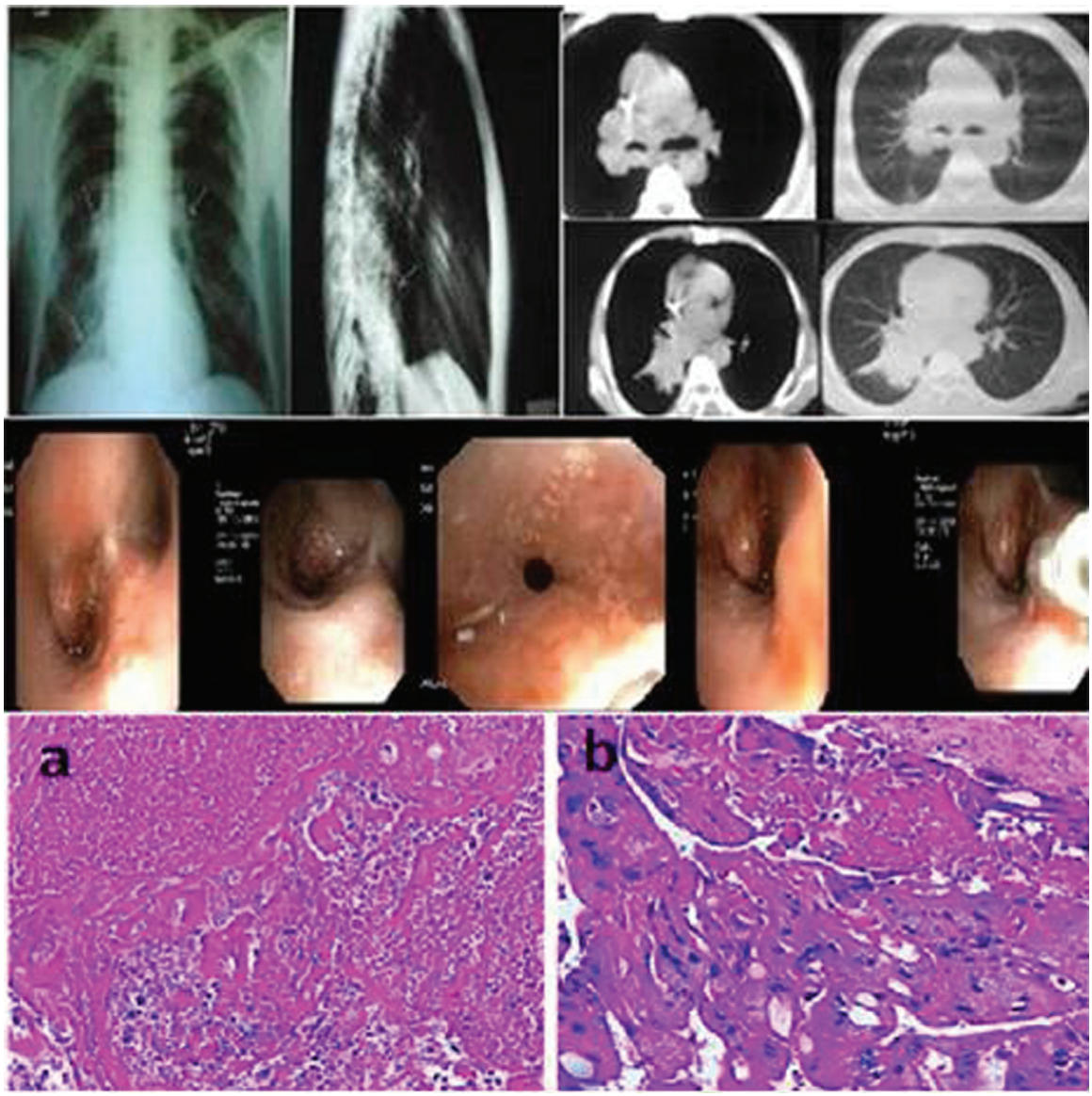
Table 5 demonstrated that the overall sensitivity, specificity, positive predictive value (PPV), NPV, and diagnostic accuracy of TBNA in the diagnosis of intrathoracic lymphadenopathies were 75.00, 54.50, 60.00, 70.60, and 64.29, respectively.

Discussion

A flexible bronchoscopic needle plays an important role in the diagnoses and staging of lung cancer or other metastatic cancers as well as other inflammatory diseases, that is sarcoidosis and TB [7].

The overall sensitivities of the current study showed that 42 (80.8%) out of 52 (100%) patients who underwent FOB were diagnosed with TBNA and other FOB procedures; 25 (48.1%) of them had malignant lymphadenopathies (five patients had small cell lung cancer, 18 patients had nonsmall cell lung cancer, and two patients had lymphoma) and 17 (32.7%) patients had benign lymphadenopathies (eight

Fig. 4

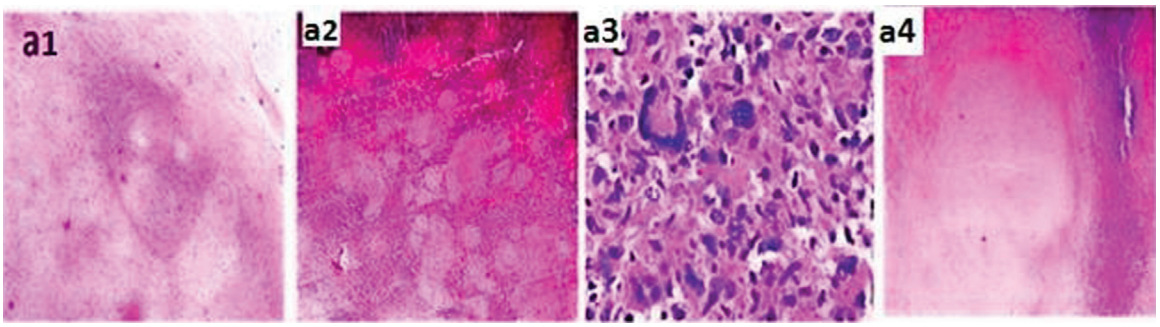


CXR: bilateral hilar shadow, opacity in the RT lower lung zone; CT chest: irregular soft tissue mass in post and medial segment of the RT lower lobe, encasing the lower lobe bronchus. FOB, BF, TBNA: widening of the main carina, large submucosal mass bulging at the RT main bronchus two cartilage below the carina at its post. Wall extending into bronchus intermedius with incomplete obstruction. Histopathology of TBNA-BF: (a) LN with metastatic squamous cell carcinoma and (b) high power picture showed atypical squamous cells, large pleomorphic hyperchromatic nuclei (hematoxylin and eosin, original magnification a, ×200; b, ×500). BF, biopsy forceps; CT, computed tomography; CXR, chest radiography; FOB, fiberoptic bronchoscopy; LN, lymph node; TBNA, transbronchial needle aspiration.

sarcoid patients, three tuberculous patients, and six patients with nonspecific lymphadenitis) (Tables 1, 3). Accordingly, TBNA had good sensitivity (75.0%) and NPV (70.6%), with fair specificity (54.5%), PPV (60.0%), and diagnostic accuracy (64.3%) for the diagnosis of intrathoracic lymphadenopathies (Table 5). In our research TBNA and other FOB procedures confirmed the diagnosis in 80.8% patients; similarly the results of other research [14,15] confirm that the sensitivity of TBNA for detecting and staging lung cancer is reported to be between 60 and 90%. On the other hand, the sensitivity of TBNA is lower than reported by other workers (45–60%) [1,16]; the accuracy of diagnosis of tuberculous lymphadenitis is 50–85% [16] and 20–60% in sarcoidosis [17,18].

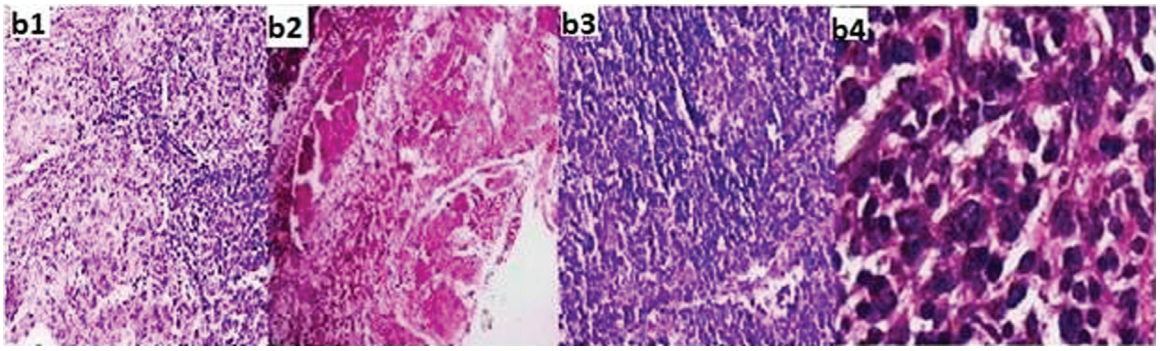
However, TBNA was diagnostic in 72% patients in the study carried out by Trisolini *et al.* [19]. Our results were slightly differed from that reported by Samaha *et al.* [7], as the yield of TBNA was positive in 61% patients, 25% of them were positive for malignancy, and 36% were diagnosed as inflammatory disease, that is TB or sarcoidosis. Rai *et al.* [4] reported that TBNA confirmed the diagnosis in 31.3%. It showed caseating granuloma in 16.7% and noncaseating granuloma in

Fig. 5



(a) Examples of benign lesions of LN: (a1) reactive lymphoid hyperplasia showed prominent lymphoid follicles with a germinal center; (a2) case of TB showed multiple caseating tubercles with a wide rim of lymphocytes; (a3) high power of a previous picture showed a tubercle formed mainly from epithelioid cells with scattered Langerhans giant cells; (a4) a case of TB with marked caseation (hematoxylin and eosin, original magnification a1, a2, a4, ×200; a3, ×500). LN, lymph node; TB, tuberculosis.

Fig. 6



(b) Examples of malignant lymphadenopathies: (b1) lymph node with metastatic ductal carcinoma in a patient with a history of breast carcinoma; (b2) lymph node with metastatic carcinoma of unknown origin; (b3) a case of lymphoma showed wide architectural effacement of the lymph node; (b4) high power of previous picture showed diffuse infiltration by mixed and large-sized lymphocytes with large irregular hyperchromatic nuclei (hematoxylin and eosin, original magnification b1, b2, b3, ×200; b4, ×500).

14.6% patients, suggesting the diagnosis of TB and sarcoidosis. Acid fast bacilli were grown in one (2.08%) patient on BAL. None of the patients showed malignancy/lymphoma. The difference is possibly because of the patient selection criteria as some of these studies are conducted only in benign lymphadenopathies, also due to the improvement of both CT and bronchoscopic techniques in the last few years.

Regarding malignant versus benign nature of the studied cases: Our study showed that patients with malignant lymphadenopathies were mainly men and smokers, while patients with benign lymphadenopathies were mainly women. Regarding CT abnormalities; our patients with malignant lymphadenopathies had higher parenchymal lesions, mediastinal, or combined hilar and mediastinal lymphadenopathies and lymphadenopathies of size more than or equal to 2 cm, while patients with benign lymphadenopathies have significantly higher hilar and bilateral lymphadenopathies.

Regarding bronchoscopic findings, our study has shown that widening of the main carina was significantly higher in the malignant group, while widening of the secondary carina (C1 or C2) was common in the benign group. Most cases with malignant lymphadenopathies were associated with bronchoscopic airway abnormalities, while 70.6% of cases with benign lymphadenopathies have no bronchoscopic airway abnormalities. Rai *et al.* [4] reported that FOB showed abnormality in 39.6% patients, for example widening of carina in 12.5, widening of secondary carina in 8.3%, bulge into airways because of extrinsic compression in 14.6%, and endobronchial nodule in 4.2% of patients. Additionally, out of the two patients with endobronchial nodules, TBNA and biopsy confirmed caseating granuloma in one and noncaseating granuloma in the other patient.

Our study demonstrated that most cases of malignant lymphadenopathies were diagnosed via either TBNA plus FB (84.0%) or TBNA alone (56.0%) or FB (28.0%) alone, while in benign lymphadenopathies most cases

were diagnosed through FB or BAL (29.4% each) and only 17.6% were diagnosed via TBNA (P=0.019). Aiming to identify the factors that may predict the successful diagnostic yield of TBNA in malignant and benign studied cases, the current study demonstrated that the positive TBNA yield in malignant lymphadenopathies was related to the presence of parenchymal lesions, combined hilar and mediastinal lymphadenopathies, bilateral lymphadenopathies, lymphadenopathies of size more than or equal to 2 cm, wide main carina, presence of endobronchial nodule, and simultaneous use of either BB or FB, while in patients with benign lymphadenopathies the positive TBNA yield was related to bilateral lymphadenopathies, lymphadenopathies of size more than or equal to 2 cm, wide main carina, and simultaneous use of FB. Sehgal *et al*. [20] did not identify any factor that predicted a successful diagnostic yield in sarcoidosis with conventional TBNA. However another study [21] reported that TBNA provides diagnosis in 95.6% of patients with endobronchial lesions, surpassing the combined yield of washing, brushing, and biopsy. Subsequently various workers [22] have reported the usefulness of TBNA, even in the absence of an endobronchial disease. TBNA has also been found useful in the diagnosis of mediastinal lymphadenopathy [23–27].

The main strength of this study is that it reflects the diagnostic value of FOB in a regular clinical practice in our country that has limited resources.

Conclusion

We concluded that bronchoscopy with TBNA has good sensitivity and NPV with fair specificity, PPV, and diagnostic accuracy in the diagnosis of intrathoracic lymphadenopathies. The procedure is inexpensive and can be performed easily during a routine diagnostic bronchoscopy. It cannot completely replace mediastinoscopy; it may certainly reduce the number of mediastinoscopy procedures.

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Conflicts of interest

There are no conflicts of interest.

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