Diagnostic Yield of Endobronchial Ultrasound Guided Transbronchial Needle Aspiration in Mediastinal Lesions - Mass / Lymphadenopathy

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Abstract

Introduction: Lymphoma, thymoma, germ cell tumors, neurogenic tumors, mediastinal goitres, and other conditions with mass manifestations tend to occur in the mediastinum. A precise diagnosis and staging of mediastinal Lymph nodes and disease are imperative to administer suitable treatment. Endobronchial ultrasound-guided transbronchial needle aspiration is a notably accurate and secure technique for procuring histological and cytological samples from enlarged mediastinal lymph nodes. Furthermore, EBUS is indispensable for the evaluation and clinical monitoring of mediastinal lymphadenopathy. Hence, the purpose of our study was to assess the diagnostic efficiency of TBNA with Endobronchial Ultrasound guidance in Mediastinal Lesions (mass/lymphadenopathy).

Materials and method: The present study was carried out as a hospital-based cross-sectional study on 60 patients with Mediastinal Mass/lymphadenopathy (above 18 years of age) of either sex, attending the Respiratory Medicine Department of a tertiary care teaching hospital in Puducherry. Approval for the study was obtained from the Institutional Ethical Committee and written informed consent from each patient was taken before the study.

Results: The majority of cases within our study were within the age group of 41 to 60 years. In our study, the incidence of mediastinal lesions in males is 63%, while in females it is 37%. In our study among benign cases, constituting 41.7% of patients, tuberculosis was the primary ailment (56%), followed by sarcoidosis (36%) and reactive lymphadenitis (8%). Malignant diagnoses were evident in half of the patients (50%), with primary lung cancer being the most common (53.3%), followed by secondary metastasis to the lung (23.3%). Hodgkin's lymphoma and non-Hodgkin's lymphoma were each identified in 6.7% of patients, while 8.3% of cases were deemed non-diagnostic. EBUS-TBNA exhibited a diagnostic yield of 100% for mediastinal masses, whereas for lymphadenopathy cases, the procedure achieved a diagnostic rate of 91%.

Conclusion: Our study has shown that the EBUS-TBNA had a diagnostic yield of 91.7% in mediastinal lesions with 91% in mediastinal lymphadenopathy and 100 % in mediastinal mass. Hence, we conclude that the EBUS-TBNA far surpasses alternate modalities, making it a superior diagnostic tool for evaluating mediastinal lesions.

***Keywords*:** Mediastinal Mass, Mediastinal Lymphadenopathy, Endobronchial ultrasound guided transbronchial needle aspiration.

INTRODUCTION

Lymphoma, thymoma, germ cell tumors, neurogenic tumors, mediastinal goitres, and other conditions with mass manifestations tend to occur in the mediastinum. [(1)] A proper diagnosis and staging of mediastinal lymph nodes and disease is necessary to provide appropriate treatment. Precise lesion location also provides useful information in formulating a differential diagnosis. [(2)]

Endobronchial ultrasound-guided transbronchial needle aspiration is a highly precise and secure method for taking samples of enlarged mediastinal lymph nodes. [(3)] Real-time endobronchial ultrasound-guided transbronchial needle aspiration combines high-frequency ultrasound imaging and endoscopic visualization to extract histological and cytological samples from lesions next to the tracheobronchial tree. This makes it

easier to identify the lymph nodes that need to be sampled. [4]

Tissue confirmation of nodal involvement is recommended in individuals with mediastinal lymph node enlargement and without distant metastases. [5] The gold standard for invasive mediastinal staging was mediastinoscopy, which offered a definitive tissue diagnosis with about 80% sensitivity and 100% specificity. [6] For many years, transbronchial needle aspiration (TBNA) biopsy has been used to obtain tissue for mediastinal staging; However, because of variations in operator skill, perceived risk, training, and diagnostic yield, this technique has not been utilized as often as it may be. However, its use is increasing due to recent advancements in bronchoscopic technology. Specifically, EBUS guided by transbronchial needle aspiration. [5]

Evaluating lymph nodes using EBUS biopsy has enabled excellent and more accurate assessment of the right and left paratracheal and subcarinal regions. Furthermore, two-way access to the Hilar and Interlobar areas is offered by EBUS. Radial mini-probes will also make it feasible to access intrapulmonary nodes. Additionally, EBUS is essential for evaluating and clinically monitoring mediastinal lymphadenopathy. By utilizing the EBUS technique, biopsy results have been significantly improved. [7] A novel and innovative approach called EBUS-guided mediastinal cryo-biopsy (EBUS-MCB) offers bigger nodal biopsy samples with higher diagnostic yield. [8]

Therefore, the purpose of our study was to evaluate the diagnostic yield of TBNA with Endobronchial Ultrasound guidance in mediastinal lesions (mass/ lymphadenopathy).

Objectives

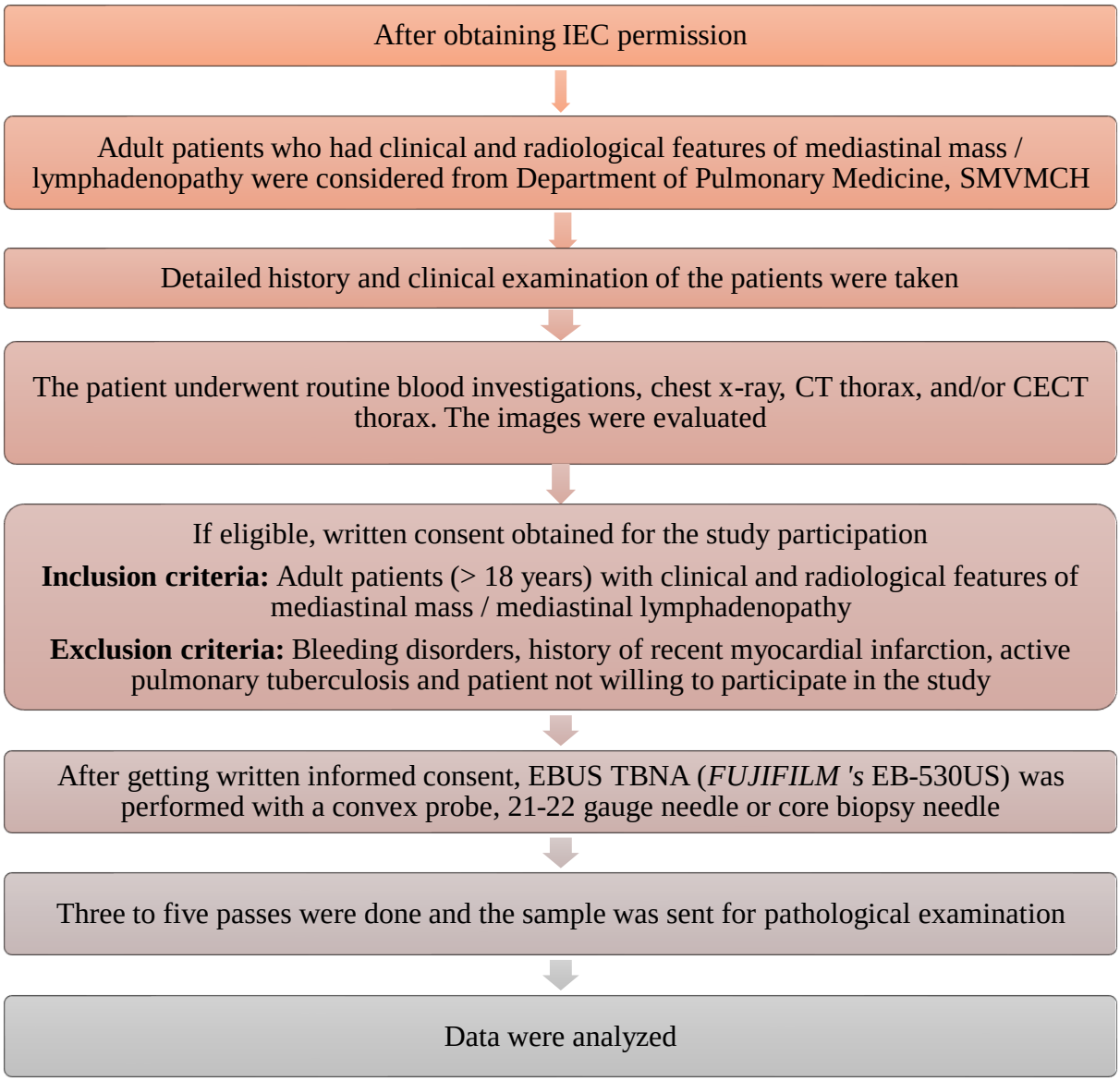
1. To assess the diagnostic yield of Endobronchial ultrasound guided transbronchial needle aspiration in mediastinal lesions.

2. To compare the diagnostic yield between mediastinal mass and lymphadenopathy.

Materials and methods:

The study was done in the Department of Respiratory Medicine, Sri Manakula Vinayagar Medical College & Hospital,(SMVMCH) Madagadipet, Puducherry.The study was cleared by the Research Committee of SMVMCH and the Institutional Ethics Committee (Human studies) (IEC No – EC/74/2022) of SMVMCH, Pondicherry. The design employed in our study was a hospital-based cross-sectional study. Adult patients who had clinical and radiological features of mediastinal mass / lymphadenopathy availing the outpatient and inpatient services of the Department of Pulmonary Medicine, SMVMCH, Pondicherry were included in the study after getting informed consent from the patients. Patients eligible for recruitment to the study met all the following criteria: Adult patients (> 18 years) with clinical and radiological features of mediastinal mass / mediastinal lymphadenopathy. Patients were excluded for any of the following: Bleeding disorders, history of recent myocardial infarction, active pulmonary tuberculosis and patient not willing to participate in the study. Considering the diagnostic accuracy of 97.02% seen for EBUS-TBNA in diagnosing mediastinal and hilar lymphadenopathy, in a study by Ye T et al.,[4] the sample size for the present study was calculated to be 56 at 95% confidence interval and 4.5% absolute precision using OpenEpi, Version 3, open-source calculator--SSPropor. Considering the 10% non-response rate, the sample size is rounded off to 60 as the final sample size. All adult patients with clinical and radiological features of mediastinal mass / lymphadenopathy availing outpatient and inpatient services of the Department of Pulmonary Medicine in SMVMCH, fulfilling the inclusion and exclusion criteria were considered for the study using simple random sampling. Thus, the total sample size of 60 was achieved over 18 months. The duration of the study was 18 months from the date of approval by IEC committee (September 2022 -March 2024).

Flowchart 1: Flow of study procedure



The collected data was initially entered into Microsoft Excel and subsequently imported into Jamovi 2.3.38 for detailed analysis. Descriptive statistics, represented as frequencies, were calculated to summarize the key characteristics of the dataset.

RESULTS

Table 1:

Variable	Count %
Age	
11 – 20	1.7 %
21 – 40	16.7%
41 – 60	51.7%
61 – 80	28.3%
Above 80	1.7%
Gender	
Female	37%
Male	63%
Chief complaints	
Dyspnoea	40 (66.7)
Cough	49 (81.6)
Loss of appetite	35 (58)
Loss of weight	39 (65)
Fever	15 (25)

Others	26 (43.3)
Past history	
Diabetes Mellitus	13 (22)
Hypertension	11 (18.3)
Tuberculosis	8 (13)
Others	42 (41)
CT Thorax findings	
Right paratracheal LN	24 (40)
Subcarinal LN	19 (31.6)
Left paratracheal LN	13 (21.7)
Pre-tracheal LN	12 (20)
Right hilar LN	9 (15)
Lung Mass	5 (8.3)
CECT Thorax findings	
Right paratracheal LN	26 (43.3)
Subcarinal LN	21 (35)
Left hilar LN	14 (23.3)
Right hilar LN	13 (21.7)
Lung Mass	11 (18.3)
Necrotic LN	5 (8.3)
Mediastinal mass	5 (8.3)
Cytological features	
Well-defined granuloma with Necrosis	14 (32.3)
Ill-defined granuloma without Necrosis	9 (15)
Atypical Cells Arranged in a Glandular Pattern	8 (13.3)
Atypical Squamous Cells in Sheets & Clusters	5 (8.3)
Small Round Blue Cell with Crush Artifact	10 (16.7)
Atypical Clusters	3 (5)
Sub-Optimal for Evaluation	5 (8.3)
Reactive Lymphadenitis	2 (3.3)
Reed Sternberg Cells	2 (3.3)
Diffuse Infiltrate of Large Atypical B Lymphoid Cells	
Lymph nodes sampled	
Station 7	40 (66.7)
Station 4R	38 (63.3)
Station 4L	6 (10)
Station 10R	6 (10)
Station 10L	3 (21.7)
Station 2R	1 (18.3)
Diagnosis	
Benign	25 (41.7)
Tuberculosis	14 (56)
Sarcoidosis	9 (36)
Reactive lymphadenitis	2 (8)
Malignant	30 (50)
Primary lung cancer	16 (53.3)
Secondary metastasis to thorax	7 (23.3)
Suspicious of malignancy	3 (10)
Hodgkin's lymphoma	2 (6.7)
Non-Hodgkin's lymphoma	2 (6.7)
Non diagnostic	5 (8.3)
Stations sampled	
Tuberculosis (N=14)	
7	10 (71.4)
4R	9 (64.3)
2R	1 (7)
10R	1 (7)
Sarcoidosis (N=14)	
7	9 (100)
4R	7 (78)
4L	1 (11)
10R	4 (44.4)
Adenocarcinoma (N=8) **4R**	7 (87.5)
7	4 (50)
4L	2 (25)
Squamous Cell Carcinoma (N=5)	3 (60)
4R	2 (40)
4L	1 (20)
7	1 (20)
10L	
Small Cell Carcinoma (N=10)	9 (90)
4R	4 (40)
7	

Table 2:

Mediastinal Lesion	Diagnosed	Inconclusive/not diagnosed	Yield (%)
Mass (N=5)	5	0	100
Lymphadenopathy (N=55)	50	5	91

Table 1 :The age distribution of adult patients with clinical and radiological features of mediastinal lesions indicates that most cases occur in the 41 to 60 age range, accounting for 51.7% of the total. This suggests that middle-aged adults are the most affected group. Following this, the 61 to 80 years age group represents 28.3% of the patients. Patients in the 21 to 40 years age group comprise 16.7% of the total. Younger individuals aged 11 to 20 years and the oldest group, those above 80 years, each constitute a small proportion of the population, at 1.7%. Overall, these figures highlight that mediastinal lesions are most commonly observed in middle-aged and older adults, particularly those between 41 and 60 years old. The gender distribution of the 60 patients with clinical and radiological features of mediastinal lesions, males make up 63% of the patient population, while females account for 37%. The most common chief complaint is cough, reported by 81.6% of the patients. This is followed by dyspnea, affecting 66.7% of the patients, and loss of weight, which is noted by 65% of the patients. Additionally, 58% of patients reported a loss of appetite, and 25% experienced fever. The data highlights that cough, dyspnea, and loss of weight are the predominant symptoms among these patients.The most common past medical condition reported was diabetes mellitus, affecting 22% of the patients, followed by hypertension, which was present in 18.3% of the cases. Tuberculosis was noted in 13% of the patients. Among those who underwent CT Thorax, enlarged right paratracheal lymph nodes were the most commonly observed finding, present in 40% of the patients. Enlarged subcarinal lymph nodes were noted in 31.6% of cases, followed by enlarged left paratracheal lymph nodes in 21.7%. Enlarged pre-tracheal lymph nodes were identified in 20% of the patients, and enlarged right hilar lymph nodes were found in 15%. Among those who underwent CECT Thorax, the most frequent finding was enlarged right paratracheal lymph nodes, observed in 43.3% of the patients. Subcarinal lymph nodes were seen in 35% of cases, while enlarged left hilar lymph nodes were present in 23.3%. Enlarged right hilar lymph nodes were identified in 21.7% of patients, and lung masses were found in 18.3%. Enlarged para-aortic lymph nodes were noted in 16.7% of cases, and enlarged sub-aortic lymph nodes in 15%. Additionally, enlarged left paratracheal lymph nodes were found in 13.3% of patients, and enlarged supra clavicular lymph nodes in 3.3%. Necrotic findings and mediastinal masses were each observed in 8.3% of cases. The most frequent cytopathological finding was well-defined granuloma with necrosis, seen in 23.3% of the patients. Ill-defined granuloma without necrosis was detected in 15% of the patients. Small round blue cells with crush artifacts were observed in 16.7% of cases. Atypical cells in a glandular pattern were detected in 13.3% of patients, while atypical squamous cells in sheets and clusters were identified in 8.3% of cases. Similarly, 8.3% of the samples were considered sub-optimal for evaluation. Less frequently observed findings included atypical clusters in 5% of patients, as well as reactive lymphadenitis, Reed Sternberg cells, and diffuse infiltrate of large atypical B lymphoid cells, each found in 3.3% of cases. In 66.7% of patients, Station 7 was sampled. Station 4R was sampled in 63.3% of patients. Stations 4L and 10R were each sampled in 10% of patients. Station 10L was sampled in 21.7% of patients, and Station 2R was sampled in 18.3% of patients. These percentages indicate a higher concentration of sampling in Stations 7 and 4R compared to the others. Among the benign diagnoses, which accounted for 41.7% of the patients, tuberculosis was the most common (56%), followed by sarcoidosis (36%) and reactive lymphadenitis (8%). Malignant diagnoses were found in half of the patients (50%), with primary lung cancer being the most prevalent (53.3%), followed by secondary metastasis to the lung (23.3%). Cases under suspicious of malignancy, specifically those with atypical clusters in cytopathology, constituted 10% of the malignancies. Both Hodgkin's lymphoma and non-Hodgkin's lymphoma were diagnosed in 6.7% of the patients. Lastly, 8.3% of the cases were deemed non-diagnostic. This distribution highlights the significant presence of both malignant and benign

conditions among patients with mediastinal lesions, with primary lung cancer and tuberculosis being the most common diagnoses in their respective categories. For tuberculosis (N=14), the stations most frequently sampled were 7 (71.4%) and 4R (64.3%). For adenocarcinoma (N=8), the most commonly sampled station was 4R (87.5%), followed by station 7 (50%) and 4L (25%). In squamous cell carcinoma (N=5), station 4R was sampled in 60% of cases. For small cell carcinoma (N=10), station 4R was sampled in 90% of case.

Table 2 : EBUS-TBNA for mediastinal mass had a diagnostic yield of 100%, successfully diagnosing all 5 cases. For lymphadenopathy, the technique had a yield of 91%, diagnosing 50 out of 55 cases, with 5 cases remaining non-diagnostic.

DISCUSSION

Mediastinal mass / lymphadenopathy poses the greatest challenge to pulmonologists in their day-to-day clinical practice. The etiologies of mediastinal lesions are diverse, encompassing various infectious, neoplastic, and inflammatory conditions. [9] Endobronchial ultrasound-guided trans-bronchial needle aspiration represents an innovative bronchoscopic approach facilitating real-time sampling of mediastinal lesions. The evidence supporting the efficacy of EBUS-TBNA in diagnosing mediastinal lymph nodes is progressively mounting. [10]

Our study revealed that most of our cases were within the age group of 41 to 60 years, constituting 51.7% of the total cases. The gender distribution in our research exhibited a higher representation of males, constituting 63% of the patient cohort, with females making up 37%. This suggested a greater incidence of mediastinal lesions among males in this particular demographic area. Predominant symptoms among patients in our study encompassed cough (81.6%), dyspnea (66.7%), and weight loss (65%). By combining the findings of Computed tomography (CT) thorax and Contrast Enhanced Computed Tomography (CECT) thorax in our study, enlarged right paratracheal lymph nodes were the most prevalent followed by subcarinal lymph node enlargement and enlarged left paratracheal lymph nodes. Lung masses were observed in 8.3% of cases in CT and 18.3% of cases in CECT. Necrotic lymph nodes and mediastinal masses were each documented in 8.3% of cases in CECT. In our study, Station 7 was sampled in 66.7% of the patients, while Station 4R was sampled in 63.3% of the patients. In the research conducted by Chung et al, Station 7 was sampled in 35% of the patients, while Station 4R was sampled in 29% of the patients. These findings reveal a notable disparity in sampling preference between Stations 7 and 4R compared to the other stations. [11] The most prevalent benign cytopathological manifestations was well defined granuloma with necrosis followed by ill defined granuloma without necrosis. In the study by Tanushree Gahlot et al involving 100 patients displaying mediastinal lymph node enlargement, 71 were identified as granulomatous lymphadenitis – tuberculosis (44.5%) and sarcoid-like granuloma in 30 (32.2%) patients. [12] In our study, cytological features of small round blue cells with crush artifacts were noted in 16.7% of cases. Atypical cells in a glandular arrangement were detected in 13.3% of individuals, whereas atypical squamous cells in clusters and sheets were recognized in 8.3% of scenarios similar to a study done by Tanushree Gahlot et al. [12] 8.3% of the specimens were considered sub-optimal for diagnosis. In our research, the final diagnoses among the 60 patients involving mediastinal lesions were classified as benign, malignant, or non-diagnostic. Among them, benign lesions constituted 41.7 % of the study followed by malignant lesions in 50 % of the participants and non-diagnostic in 8.3% of the study participants. Among the benign lesions in our study, tuberculosis was identified as the most prevalent followed by sarcoidosis and reactive lymphadenitis. In contrast, Adil Can Gungen et al's investigation revealed that most patients were diagnosed with sarcoidosis followed by tuberculosis, and other benign lesions. [13] Within our study group of 23 patients diagnosed with bronchogenic carcinoma, the most prevalent lesion was small cell carcinoma followed by adenocarcinoma and squamous cell carcinoma. Additionally, small cell carcinoma was detected in 10 patients. Ting Ye et al discovered that within their study, the most common malignant tumors were adenocarcinoma followed by small cell carcinoma and squamous carcinoma.[4]Amidst malignant lesions identified in our research, primary lung cancer accounted for 53.3% of cases, followed by secondary metastasis to the thorax at 23.3%. Cases under suspicion for malignancy, particularly those exhibiting atypical clusters in cytopathology,

represented 10% of the malignant cases. Chung et al. in their study diagnosed 5 % of cases of lung cancer and 7% of cases of metastatic lymphadenopathy from extra thoracic malignancy. [11] Our study signifies prevalence of both malignant and benign conditions among individuals with mediastinal lesions, with primary lung cancer and tuberculosis emerging as the most common diagnoses in their respective categories. By comparing the diagnostic yield of EBUS-TBNA between mediastinal lymphadenopathy and mass, it was found that EBUS-TBNA was diagnostic in all 5 cases (100%). In our research for mediastinal lymphadenopathy, the technique yielded 91%, diagnosing 50 out of 55 cases, with 5 remaining non-diagnostic. In a study by Zemaitis et al., 215 patients underwent EBUS-TBNA, and only 176 (81.9%) cases were diagnosed cytologically.[6] The majority of research studies suggest a higher prevalence of malignant conditions in comparison to benign conditions. On the contrary, our research demonstrated a higher occurrence of benign conditions as opposed to malignant ones, with tuberculosis cases being more common, a rarity when compared to results from other studies. In various studies conducted by Shahab et al. and Tanushree Gahlot et al., EBUS-TBNA demonstrated a diagnostic yield of 85% and 92% respectively for mediastinal lymphadenopathy. [12,14]In our research with 60 participants of mediastinal lesions, using EBUS-guided TBNA, we identified 55 satisfactory samples that were diagnostic. Thus, indicating a robust diagnostic yield rate of 91.7%

CONCLUSION

Our study has shown that the EBUS-TBNA had a diagnostic yield of 91.7% in mediastinal lesions with 91% in mediastinal lymphadenopathy and 100 % in mediastinal mass. Hence, we conclude that the EBUS-TBNA far surpasses alternate modalities, making it a superior diagnostic tool for evaluating mediastinal lesions.

LIMITATIONS

✓ The main limitation of our research is the small sample size.

✓ There were fewer mediastinal mass cases to compare with the diagnostic yield of EBUS TBNA in mediastinal lymphadenopathy.

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