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From radiological assumption to pathological conviction: experience with video mediastinoscopy at a tertiary cancer center

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SUMMARY

Purpose: To describe the role of mediastinoscopy in the setting of mediastinaladenopathy secondary to pulmonary and non-pulmonary cancers.

Methods: Retrospective analysis of patients undergoing video mediastinoscopy from November 2016 to December 2018 at tertiary cancer center for mediastinaladenopathy from lung cancer and non-pulmonary cancers with mediastinal nodes.

Results: Twelve patients were included out of which 11 patients underwent diagnostic mediastinoscopy. The median age was 58 years. Seven patients had lung cancer. The mean number of nodes sampled was 10.5 (range: 2-28 nodes). Five patients had mediastinaladenopathy from non-pulmonary cancer like endometrial, oropharyngeal and Hodgkin's lymphoma. Recurrent laryngeal nerve palsy was noted in one patient.

Conclusion: Mediastinoscopy serves as a valuable asset for staging of lung cancer and in the assessment of suspicious nodes in the setting of non-pulmonary cancers. However, training and expertise is in the need of the hour to prevent redundancy of this valuable procedure.

Key words: mediastinoscopy, mediastinaladenopathy, lung cancer, suspicious nodes

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INTRODUCTION

Cervical mediastinoscopy is a time tested tool for the invasive staging of mediastinal nodes. Standard cervical mediastinoscopy helpsin approaching lymph node stations viz. right upper paratracheal (station 2R), right lower paratracheal (4R), left upper paratracheal (2L), right lower paratracheal (4L) and sub-carinal (7). Hilar nodes (station 10) can also be accessed byexperienced surgeons, although it can be technically challenging. Overall, this procedure is accurate and carries minimal morbidity [1]. The role of mediastinoscopy in the evaluation algorithm is changing after the availability of endobronchial ultrasound guided trans-bronchial needle aspiration technique (EBUS-TBNA) [2]. Likewise, the opportunity for training the residents in mediastinoscopy is dwindling [2, 3]. However, mediastinoscopy still remains a tool in the evaluation of lung cancer and other malignancies [2]. At our institute, we perform cervical video mediastinoscopy in patients with lung cancer and non-pulmonary malignancies where invasive evaluation of mediastinal lymph nodes is indicated. We also perform mediastinoscopy for patients in whom the results of EBUS-TBNA remain inconclusive or negative, where further evaluation is clinico-radiologically indicated. In this article, we describe our experience with mediastinoscopy performed at a tertiary cancer center.

MATERIALS AND METHODS

This was a retrospective study conducted at a single centre. All patients undergoing standard cervical video mediastinoscopy for lymph node biopsy or lymphadenectomy from November 2016 to December 2018 were included. There was no specific exclusion criteria applicable to this study. All procedures were performed by a single surgical oncologist with special interest in thoracic oncology. The mediastinoscope used for the procedures was 10972 SP, Linder Hurtgen video mediastinoscope (Karl Storz SE and Co. KG, Tutlingen, Germany®). The study was approved by the institutional review board. Data was obtained from the medical records, surgical registers and investigation charts.

Under general anesthesia, neck extension was obtained by placing a pillow under the shoulder blades. A small transverse cervical incision was made in the lower neck just above the suprasternal notch. Strap muscles were dissected until the trachea was exposed. The mediastino scope was introduced

and gradually advanced, dissecting the pretracheal space. Right and left upper and lower paratracheal and sub-carinal stations were dissected. Nodal dissection was commenced only when the mediastinal anatomy is clear. This would require dissection to expose the carina and bronchi. The lymph nodes were dissected using the suction coagulation cannula before taking punch biopsies. The nodes from stations 2R, 4R, 2L, 4L and 7 were sampled separately and sent for pathological evaluation. Occasionally, the nodes of 2R and 4R stations when pushed up by the advancing blade of the mediastinoscope, would necessitates low withdrawal of the scope to allow the nodes to descend and come to the field of the camera before dissection. Careful finger examination after withdrawing the scope would help to identify the position of the nodes if they were masked by the anterior blade of the scope.

When evaluation of a particular nodal station or stations was required, usually when the primary cancer is non-pulmonary, a more selective approach was chosen. However, in lung cancer, dissection of all five stations approachable by the scope was performed. The contralateral mediastinal nodes (N3) were dissected first and sent for frozen section analysis in lung cancer.

If contralateral mediastinum was positive for metastasis, procedure is stopped and patient was referred for nonsurgical treatment like chemoradiation or radical radiotherapy. If ipsilateral nodes were positive, and nodes were limited to a single station and not bulky, neoadjuvant chemotherapy was preferred over chemoradiation.

RESULTS

During the study period, twelve patients underwent mediastinoscopy, eleven for diagnosis or staging and one was done for complete lymphadenectomy. The demographic and disease profile of patients are depicted in the Table 1.

In six cases of lung cancer, mediastinoscopy was done as part of staging. In one case, invasive mediastinal evaluation of unidentified mediastinal mass by mediastinoscopy led to diagnosis of lung cancer. The average duration of the procedure was 86 minutes. The number of mediastinal nodal station dissected in each patient is depicted in Table 2.

Tab. 1. Demographic and disease profile of the patients under the study

Variable		Results
Age (years)	Mean	58.41
	Median	58
Gender	Male	07
	Female	05
Indication	Staging	10
	Diagnostic	01
	Therapeutic	01
Site of primary cancer	Pulmonary	07 (6+1)
	Non-pulmonary	05
Site of primary in non-pulmonary cancers	Tongue	1
	Recurrent Oropharyngeal	1
	Endometrial	1
	Breast and thyroid (synchronous)	1
	Recurrent Hodgkin's lymphoma	1

Tab. 2. Number of nodal stations sampled and average number of nodes sampled

Number of nodal stations	Number of patients
5	5
4	2
3	3
2	1
1	1
Mean	10.5
Range	2-28

Three or more nodal stations were dissected in 10 patients. The average number of nodes identified in patients who underwent sampling of more than four nodal stations was 15.28. Intraoperative frozen section (FS) analysis was used in 10 patients in the study. Four patients were detected with positive nodes on FS. The final histopathology results were in concordance with the FS in all patients. The number of positive nodes ranged from one to two in each patient. Eight patients in the study had reactive changes in the mediastinal nodes of which two had granulomatous inflammation. The total number of nodes retrieved from each station in all patients put together is depicted in Figure 1.

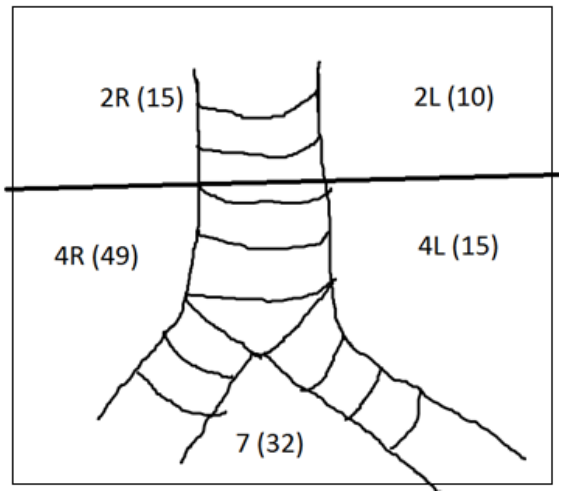

Fig. 1. Total number of lymph nodes retrieved at each mediastinal station (in brackets) for all patients combined

PET scan was performed in 10 patients in the study. Six of them had metabolically active enlarged lymph nodes with standard uptake value (SUV) of four or more (SUV>4) of which three had nodes positive for malignancy. It was found that PET positivity correlates with positive histopathology in 50% of cases and one out of four PET negative patients had a positive lymph node in the mediastinum.

One patient with Hodgkin Lymphoma (HL) developed second relapse after autologous stem cell transplantation in the right cervical lymph node. PET scan done for staging work up showed uptake in the left lower paratracheal station in addition to the cervical node. Mediastinoscopic biopsy of the metabolically active paratrachealnodes confirmed disease in the mediastinum. The patientunderwent Involved Field Radiotherapy (IFRT) to the neck and mediastinum after multispecialty board discussion. He remains disease free during the last follow up at one year.

Another patient with medullary cancer of the thyroidtreated with total thyroidectomy and neck dissection was found to have

Tab. 3. Morbidity associated with mediastinoscopy

Morbidity	Number of patients
Recurrent laryngeal nerve palsy	1
Bleeding	0
Tracheobronchial injury	0
Pneumothorax	0
Mediastinitis	0

residual nodes in the mediastinum. A mediastinal lymph node dissection was performed using Video Assisted Mediastinal Lymphadenectomy (VAMLA) technique. The calcitonin level normalized after the surgery and the patient is currently disease free 18 months following the treatment.

The morbidity of patients undergoing mediastinoscopy has been depicted in Table 3. The patient with recurrent Hodgkin's lymphoma developed left recurrent laryngeal palsy after the procedure.

DISCUSSION

Involvement of mediastinal lymph nodes is an important therapeutic and prognostic factor in lung cancer. In non-pulmonary cancers, mediastinal lymph nodes can be involved by the disease. Metabolically active mediastinal node soften pose challenges during staging and management [4-8]. PET scan has high false positivity rate with several infections and other inflammatory conditions mimicking cancer with a high metabolic uptake [4, 9, 10]. Pathological confirmation of an involved node is recommended before deciding on the mode of treatment of lung cancer [8, 10].

Cervical mediastinoscopy is the gold standard in evaluating mediastinal nodes in pulmonary and non-pulmonary cancers. It was routinely performed before surgical treatment of lung cancer [11]. In the last decade, EBUS- TBNA and endo-ultrasound (EUS) guided transesophageal FNAC have been added to the armamentarium of the clinician [12]. Yasufuku and colleagues reported a prospective randomized trial comparing cervical mediastinoscopy with EBUS-TBNA in patients with lung cancer for evaluation of the mediastinal nodes. They found that EBUS-TBNA has equal accuracy in evaluating mediastinal nodes compared to mediastinoscopy when onsite evaluation of needle aspirates by a cytopathologist or cytotechnician was available [13]. Another study from the Europe found that combined endoscopic and surgical evaluation of the mediastinum is more sensitive than surgical evaluation alone [14].

EBUS-TBNA may not be sufficient when larger sample is required for diagnosis like lymphoma and inflammatory conditions. The accuracy of EBUS-TBNA is less in the community as compared to the trial setting [15, 16]. In EBUS negative patients with lung cancer, with high probability of positive mediastinal node, confirmation with mediastinoscopy is indicated if there is discrete me diastinal nodes (N2), a centrally placed lung lesion or a positive N1 node, all of which increase the possibility of finding positive N2 nodes [2].

In two large meta-analyses evaluatingneo-adjuvant chemotherapy (NACT)in lung cancer, NACT followed by surgery provided significantly improved five year survival compared to surgery alone [17, 18]. Similarly, the International Adjuvant Lung Cancer Trial showed that non-small cell lung cancer patients, staged I to III, benefitted with improved five year survival with adjuvant chemotherapy as compared to surgery alone [19]. This has led to the argument that, when chemotherapy benefits in both neoadjuvant and adjuvant settings, timing of chemotherapy may not be very relevant. In cases where adjuvant chemotherapy is anyway indicated by virtue of T stage (>T2a), and preoperative PET CT scan shows discrete N2 nodes, proceeding with NACT without obtaining pathological confirmation of N2 may be considered in institutions where NACT followed by surgery is routinely practiced in patients with limited N2 disease [20]. Exceptions are, patients with T1 or T2a primary who may not require adjuvant chemotherapy if mediastinal nodes are found to be negative for metastasis and those with suspected N3 disease (contralateral mediastinal nodes) where surgical treatment is not recommended. This again reduces the role of invasive mediastinal evaluation in a large subset of patients with lung cancer.

Due to multiple reasons, the number of mediastinoscopies performed has reduced worldwide [2, 3]. This has decreased the opportunity of the residents and trainees in thoracic oncology to get confidence in this procedure. This points to the importance of centralized training programs and frequent workshops to keep this skill alive.

Generally, mediastinoscopy carries low morbidity and mortality. In the study published by Yasufuku et al. [13], out of the 153 patients who underwent mediastinoscopy, only four experienced minor complications. In another large retrospective study published from the University of Alabama at Birmingham, out of the 1970 patients who underwent mediastinoscopy, morbidity occurred in 1.3% with major bleeding requiring sternotomybeing encountered in 2 (0.1%) patients [21].

Figure 2 summarizes the role of mediastinoscopy in the present era in the evaluation of lung cancer. In non-pulmonary cancers, the investigation of choice for a suspected mediastinal lymph node is EBUS-TBNA [22].

*Upfront mediastinoscopy is indicated if facility or expertise for EBUS is not available

Mediastinoscopy and biopsy is an option if facility and/or expertise for EBUS-TBNA is not available or the result of EBUS-TBNA is inconclusive. Figure 3 depicts the evaluation of mediastinal nodes in non-pulmonary cancer.

*Upfront mediastinoscopy is done if facility/expertise for EBUS is not available

In the developing world with more prevalence of tuberculosis, PET scan has a low specificity in mediastinal evaluation even though the sensitivity is unaffected [10]. Patients with non-pulmonary cancer occasionally present with incidentally detected enlarged mediastinal nodes which require invasive evaluation with EBUS or mediastinoscopy before treatment for the primary cancer and the intent of treatment can be decided.

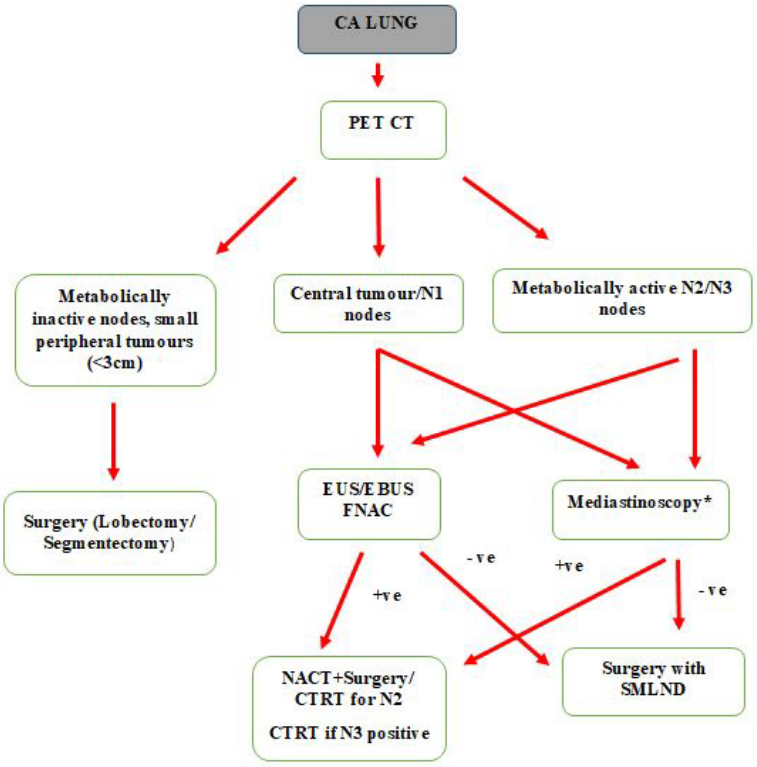

Fig. 2. Algorithm on the management of mediastinal nodes in lung cancer

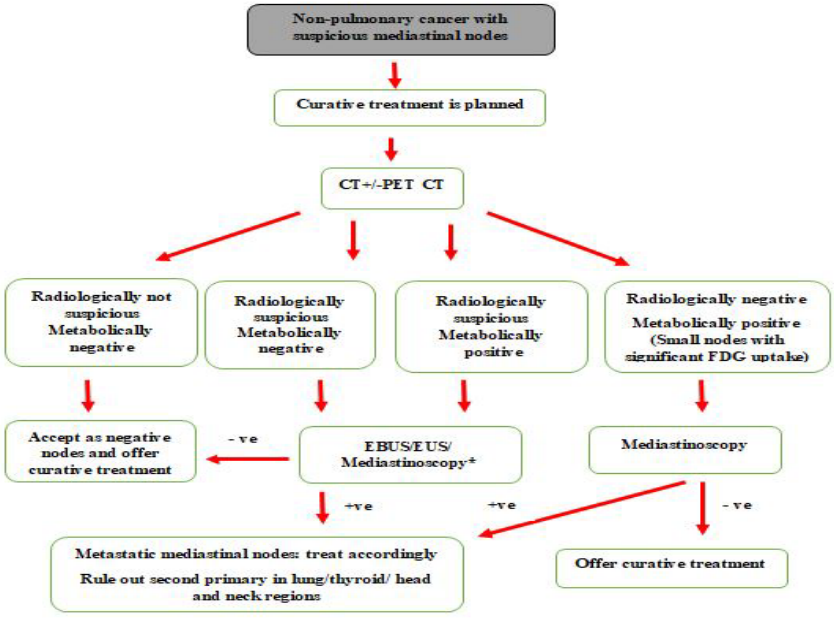

Fig. 3. Algorithm on the management of suspicious mediastinal nodes in non-pulmonary cancers

Our experience showed that only 50% of the patients with metabolically active nodes in PET scan had pathologically positive nodes in the mediastinum, whereas one out of four patients with negative PET scan had a positive nodes in the mediastinum. All mediastinoscopy results influenced treatment decision in our series, stressing the importance of invasive mediastinal evaluation in radiologically suspected mediastinal metastasis.

LIMITATIONS OF THE STUDY

Our study includes small number of patients and hence, it is not possible to evaluate the false positivity and false negativity of PET scan or mediastinoscopy.

CONCLUSION

Mediastinoscopy is a valuable tool in the armamentarium of thoracic oncologist to evaluate mediastinal nodes and mediastinal masses which cannot be approached or characterized by image guided biopsy. Following the advent of EBUS-TBNA and EUS guided FNA techniques, the number of mediastinoscopies performed for mediastinal evaluation/staging have reduced. However, there may be some situations where mediastinoscopy

is still indicated as a problem solving tool. Hence it is important for the thoracic surgical oncologists to retain the skill for performing mediastinoscopy and train the residents in the procedure. Centralized training programs may be helpful for this goal.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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