Original Article

Changing trends of invasive mediastinal evaluation in India: A questionnaire-based survey

ABSTRACT

Background: The utilization of mediastinoscopy for mediastinal staging or evaluation has been on the wane, because of the increasing use of methods such as endoscopic ultrasound (EUS)/endobronchial ultrasound (EBUS). The choice of one modality over the other is based on individual preferences, expertise, cost, and the disease in question.

Objectives: This study was aimed at assessing the changing trends in the practice of mediastinoscopy and endoscopic techniques across India.

Materials and Methods: This online, questionnaire-based survey was conducted at the Malabar Cancer Center, Kerala, India, between September 2019 and January 2020. Surgical oncologists, thoracic surgeons, and pulmonologists treating patients with lung cancer in the National Cancer Grid, India-affiliated institutions were enrolled. A total of 20 questions directed at determining the experience of the healthcare professionals, type of institutions where they practiced, the volume of patients with lung cancers being treated by them, and the temporal changes in the utility of mediastinoscopy and EBUS/EUS over the past 2 years were included in the questionnaire. The survey was conducted using Google Forms. Descriptive and inferential statistics were used for data analysis. A $P < 0.05$ was considered statistically significant.

Results: A total of 347 clinicians were invited to participate in the survey, of which 70 responded. A total of 62 (88.6%) respondents recommended invasive mediastinal staging in patients with lung cancer with positive mediastinal nodes on positron emission tomography (PET). In addition, 39 (55.7%) respondents believed that invasive staging is required even in those with a negative mediastinum on PET; 58 (82.9%) respondents were of the opinion that EBUS is the investigation of choice for suspicious mediastinal nodes, while 8 (11.4%) preferred mediastinoscopy.

Conclusion: Endoscopic techniques have superseded mediastinoscopy for invasive mediastinal evaluation across the country.

Keywords: Endobronchial ultrasound, invasive mediastinal evaluation, video mediastinoscopy, EUS, EBUS, mediastinoscopy

INTRODUCTION

The need for mediastinal staging as a part of the diagnostic workup for patients with lung cancer cannot be overemphasized. The presence of mediastinal lymph nodes alters the disease stage and prognosis, thereby resulting in a change in the treatment recommendations. In patients with positive mediastinal lymph nodes, a non-surgical approach or the use of systemic therapy is preferred in many centers.[1-3]

Conventional mediastinoscopy is considered the workhorse for invasive mediastinal evaluation. With the addition of minimally invasive techniques, such as endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound (EUS) to

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the diagnostic armamentarium, the use of mediastinoscopy has been on the wane. Nevertheless, mediastinoscopy is still useful in staging the mediastinum after neoadjuvant chemotherapy or in the setting of negative EBUS/EUS results.[4,5] It is also used as a first-line investigation when EBUS and EUS are unavailable.

In the presence of mediastinal lymphadenopathy due to malignant (lung cancer, metastatic deposits, or lymphoma) and non-malignant conditions (tuberculosis or other granulomatous diseases), invasive mediastinal evaluation is essential for the diagnosis and accurate staging of the disease.[6,7] A corollary of this is that the confirmation of an absence of malignancy in the mediastinum can alter both, the stage and intent of treatment.

There exist differences of opinion among the healthcare workers about the choice of a single modality for mediastinal staging. The choice of one modality over the other depends on individual preferences, expertise, cost, and the disease in question. As both mediastinoscopy and EBUS/EUS have their own advantages and pitfalls, variability in their usage is not uncommon. Therefore, we initiated an online questionnaire-based survey to assess the changing trends in the utility of mediastinoscopy and endoscopic techniques across the country.

MATERIALS AND METHODS

General study details

This online, questionnaire-based survey was conducted at Malabar Cancer Center which is a tertiary cancer center under the Government of Kerala between September 2019 and January 2020. Doctors treating patients with lung cancer in the National Cancer Grid (NCG)-affiliated institutions across India were invited to take part in the survey. The study was approved by the institutional review board and institutional ethics committee on August 27, 2019 (bearing no. 1617) (the study protocol is attached as supplementary appendix 1). The need for written informed consent was waived. The study was not registered with a public clinical trials registry, like the Clinical Trials Registry-India. No funding was obtained for conducting this research. The study was conducted according to the ethical guidelines outlined in the Declaration of Helsinki and the Indian Council of Medical Research guidelines for ethical research.

Participants

Surgical oncologists, thoracic surgeons, and pulmonologists treating patients with lung cancer in the NCG-affiliated institutions were invited to participate in the survey.

Variables

Our primary objective was to assess the change in trends in the utility of mediastinoscopy and endoscopic techniques across the country.

Study methodology

A total of 20 questions were included in the questionnaire [Table 1]. The online survey was conducted using Google Forms. The questions were directed at determining the experience of the healthcare professionals, type of institutions where they practiced, the volume of patients with lung cancers being treated by them, and the temporal changes in the utility of mediastinoscopy and EBUS/EUS over the past 2 years. In addition, a few practically oriented and conceptual questions about the need and type of invasive mediastinal evaluation in the setting of lung cancer or mediastinal adenopathy from non-pulmonary cancers and tuberculosis were also included. The database was locked, and the responses were analyzed on June 30, 2020.

Statistical analysis

Data were analyzed using the IBM Statistical Package for the Social Sciences for Windows, Version 20.0. (Armonk, NY, USA: IBM Corp.). Descriptive and inferential statistics were used for data analysis. Chi-square test and Fisher's exact test were used to determine the association between the various factors. A $P < 0.05$ was considered statistically significant.

RESULTS

A total of 347 clinicians were invited to participate in the survey. Of these, 70 responded to the questionnaire. Respondents included 64 oncologists, 3 thoracic surgeons, and 3 pulmonologists. Relative proportions of the various responses to all the questions included in the survey are depicted in Table 1. A total of 59 (84.3%) respondents were affiliated to academic institutions; 25 (35.8%) respondents had more than 5 years of work experience and were affiliated to hospitals where more than 10 patients underwent a mediastinoscopy per month. In addition, 21 (30%) respondents were involved in the evaluation and treatment of more than 10 patients with lung cancer every month in their day-to-day practice. The availability of mediastinoscopy and EBUS/EUS, as per the responses, was 52.9% and 60%, respectively. A total of 10 (27.03%) respondents with access to mediastinoscopy reported an upward trend in its utilization over the past 2 years. Moreover, 10 (17.24%) of the respondents who had suggested that EBUS/EUS should be the first investigation for invasive mediastinal evaluation also reported an increase in the use of mediastinoscopy during the same time period. With regard to EBUS/EUS, 36 (85.71%) respondents with access to the facility reported an increase in its utilization.

Table 1: Questionnaire used for the nationwide survey on the changing trends in invasive mediastinal evaluation

Question	Options	Number of responses	Result (%)
Years of experience	<2	70	12 (17.1)
	2-5		33 (47.1)
	>5		25 (35.8)
Type of hospital	Government	70	15 (21.4)
	Private		37 (52.9)
	Semi-government		18 (25.7)
Type of institution	Academic	70	59 (84.3)
	Non-academic		11 (15.7)
Number of new cases of lung cancer evaluated per month	0-2	70	27 (38.6)
	3-10		22 (31.4)
	11-25		11 (15.7)
	> 25		10 (14.3)
Number of cases of suspicious mediastinal adenopathies evaluated per month	0-2	70	31 (44.3)
	3-5		19 (27.1)
	6-10		10 (14.3)
	>10		10 (14.3)
Is mediastinoscopy available at your institution?	Yes	70	37 (52.9)
	No		33 (47.1)
Is EBUS/EUS available at your institution?	Yes	70	42 (60.0)
	No		28 (40.0)
Who performs EBUS/EUS at your institution?	Pulmonologist	42/70	24 (57.1)
	Radiologist		1 (2.4)
	Oncologist		2 (4.8)
	Combination		15 (35.7)
Number of patients who underwent a mediastinoscopy over the past 2 years	<10	36/70	11 (30.56)
	10-25		8 (22.22)
	25-50		3 (8.33)
	>50		14 (38.89)
Change in the trend in mediastinoscopy usage over the past 2 years	Increasing	37/70	10 (27.03)
	Decreasing		18 (48.65)
	Stable		3 (8.11)
	Unable to comment		6 (16.22)
Change in the trend of EBUS usage over the past 2 years	Increasing	42/70	36 (85.71)
	Decreasing		0 (0.0)
	Stable		2 (4.76)
	Unable to comment		4 (9.52)
Is invasive mediastinal staging necessary in those with suspicious mediastinal lymph nodes?	Yes	70	62 (88.6)
	No		8 (11.4)
In case of PET-negative mediastinum, is there a need for further invasive staging?	Yes	70	39 (55.7)
	No		19 (27.1)
	Maybe		12 (17.1)
If your response is "yes"/"maybe" to the above question, what should be used to stage such patients?	EBUS/EUS	51/70	23 (45.1)
	Mediastinoscopy		8 (15.7)
	Both		20 (39.2)
What should be the first investigation for mediastinal evaluation according to you?	EBUS/EUS	70	58 (82.9)
	Mediastinoscopy		8 (11.4)
	Both		4 (5.7)
Is there a need for mediastinoscopy for confirmation of suspicious mediastinal nodes? (%)	<5	70	16 (22.8)
	5-10		25 (35.7)
	11-25		22 (31.4)
	>25		7 (10.0)
What is the cost of mediastinoscopy at your institution? (in ₹)	<20,000	37/70	17 (45.94)
	20-50,000		12 (32.43)
	>50,000		8 (21.62)

Contd...

Table 1: Contd...

Question	Options	Number of responses	Result (%)
What is the cost of EBUS/EUS at your institution? (in ₹)	<20,000	42/70	22 (52.38)
	20-50,000		19 (45.24)
	>50,000		1 (2.38)
What is the incidence of Koch's infection/granulomas in your practice? (%)	<1	70	3 (4.3)
	1-10		31 (44.3)
	10-20		24 (34.3)
	>20		12 (17.1)

EUS: Endoscopic ultrasound, EBUS: Endobronchial ultrasound, PET: Positron emission tomography

Most respondents agreed that invasive staging is mandatory for suspicious mediastinal nodes detected on imaging. A total of 62 (88.6%) respondents recommended invasive mediastinal staging in patients with lung cancer with positive mediastinal nodes detected on PET imaging, and 39 (55.7%) believed that invasive staging was necessary even in those with a negative mediastinum on PET imaging but deemed to be at high risk of metastasis to the mediastinal nodes. According to 58 (82.9%) respondents, EBUS was the investigation of choice for suspicious mediastinal lymph nodes. Those who had an EBUS/EUS facility available at their institution confirmed its use for mediastinal evaluation ($P = 0.003$). Respondents from institutions where a large number of patients underwent mediastinoscopy every year also favored EBUS/EUS as the first choice for invasive mediastinal evaluation ($P = 0.084$). The majority of the respondents suggested the use of mediastinoscopy as a confirmatory tool following a negative or an inconclusive EBUS/EUS report.

A significant correlation of each of the following variables, namely the number of new lung cancer cases evaluated per month, the number of suspicious mediastinal nodes evaluated every month, and the incidence of Koch's infection/granulomas in one's professional practice, with the availability of mediastinoscopy and change in the trend of mediastinoscopy usage, was observed [Table 2].

DISCUSSION

This survey confirms that minimally invasive mediastinal staging has superseded conventional mediastinoscopy as the first choice for invasive mediastinal evaluation in patients with lung cancer as well as for the evaluation of suspected mediastinal lymphadenopathy arising from non-pulmonary cancers and non-cancerous causes. However, we observed a significant variation in practice across the country which is largely related to the availability of equipment and expertise and to a smaller extent to individual preferences, procedural cost, and other practical issues. The overwhelmingly higher response to the survey from clinicians practicing in academic institutions suggests the possibility of higher compliance to invasive mediastinal evaluation in academic institutions compared to private settings. Those treating a greater number of patients with lung cancers and evaluating more cases of suspected mediastinal adenopathy tend to have more access to mediastinoscopy, thus leading to an increased detection of Koch's infection/granulomas. Majority of the respondents were of the opinion that invasive mediastinal evaluation was required in a PET-positive mediastinum in patients with lung cancer, with many supporting its use even in cases of a PET-negative mediastinum. This suggests that, regardless of the PET findings, the mediastinum needs to be staged invasively.

Mediastinoscopy is considered the gold standard for the evaluation of the mediastinum.[8,9] Through standard mediastinoscopy, nodes from stations 2R, 2L, 4R, 4L, 7, and 10 are sampled. With extended mediastinoscopy, stations 5 and 6 can also be accessed; however, the availability of expertise for the extended procedure is rare. With the development of minimally invasive tools such as EBUS-TBNA and EUS, more nodal stations can be accessed for sampling, thus increasing the sensitivity of the evaluation. However, the role of conventional mediastinoscopy in staging has been debated.[10-12] A decreasing use of mediastinoscopy after the advent of EBUS/EUS has been reported by several international studies.[13,14] However, data on the usage of mediastinoscopy reported from India are limited to small case series, studies, and review articles.[15-18] Contrary to mediastinoscopy, the use of EBUS/EUS for mediastinal evaluation in cancerous and granulomatous conditions in a large volume of patients has been extensively reported in the Indian medical literature.[19-25] This could be indicative of the growing acceptance and enthusiasm for these minimally invasive techniques among the healthcare professionals, as well as the recent increase in the utilization of invasive mediastinal evaluation, in general, at least in the major healthcare centers.[26] A number of review articles comparing mediastinoscopy and EBUS for invasive mediastinal evaluation have favored the use of the latter as the investigation of choice. One such study from a reputed tertiary cancer center showed positive mediastinal nodes on mediastinoscopy/mediastinal dissection in 9 out

Table 2: Correlation of the number of new lung cancer cases, number of suspicious mediastinal adenopathy, and the incidence of Koch's infection/granulomas in one's professional practice, with the availability and usage of mediastinoscopy

Variable	Parameters	*P*
Number of new lung cancer cases evaluated per month	Number of suspicious mediastinal adenopathies evaluated per month	<0.001
	Availability of mediastinoscopy	<0.001
	Mediastinoscopy usage	<0.001
	Type of hospital	<0.001
	Increase in the trend of mediastinoscopy usage	0.002
Number of suspicious mediastinal adenopathy evaluated per month	Availability of mediastinoscopy	0.001
	Mediastinoscopy usage	<0.001
	Type of hospital	0.003
	Increase in the trend of mediastinoscopy usage	0.058
	PET positive mediastinal evaluation	0.057
Incidence of Koch's infection/granulomas in one's clinical practice	Mediastinoscopy usage	0.024

PET: Positron emission tomography

of 65 patients after false-negative reports for EBUS-guided fine-needle aspiration cytology. In five cases, the nodes were subcentimeter sized and showed low uptake on the PET scan and were missed on EBUS. Therefore, the authors concluded that mediastinoscopy remains an integral part of invasive mediastinal evaluation along with endosonographic techniques.[27]

The overall low response or compliance to the online survey, despite repeated reminders, suggests the possibility that most oncologists and pulmonologists were not performing invasive mediastinal evaluation in their routine practice and/or had not been exposed to the procedure. Only 25 (35.8%) respondents were associated with hospitals where a substantial number of invasive mediastinal evaluations were being performed, of which 12 belonged to a single large institution. This highlights the scarcity of expertise and facilities available for mediastinal evaluation in healthcare centers across the country, even among those who are members of the NCG. The technical complexity of mediastinoscopy is partly responsible for this. The majority of those who perform a significant number of mediastinoscopy procedures treat a larger number of patients with lung cancer. Such professionals are also involved in evaluating a significantly greater number of suspected mediastinal lymph nodes arising from non-pulmonary cancers and non-cancerous causes. However, it is not possible to assess whether the converse is true, just based on the results of this survey.

Even though invasive mediastinal evaluation is generally accepted as a standard procedure before attempting curative resection of lung cancer, there are several clinicians who argue against the routine use of invasive mediastinal evaluation in all patients with lung cancer. This controversy should be understood in light of the fact that there are two approaches followed in different centers of the country for patients with lung cancer with positive N2 nodes, as the international guidelines also vary. Some centers follow routine chemoradiation in all patients with proven N2 nodes, whereas others offer surgical treatment in selected patients with a similar stage. In centers that use the former approach, routine invasive mediastinal evaluation is mandatory in all patients with non-small-cell lung cancer (NSCLC) with suspected N2 nodes on imaging. Contrarily, in centers that follow the surgical approach, if the patient is considered a suitable candidate for adjuvant chemotherapy by virtue of the radiological extent of the primary disease with no suspected N2 or N1 nodes, neoadjuvant chemotherapy may be readily offered, as chemotherapy in both the neoadjuvant and adjuvant settings has been found to be useful in improving the survival and the magnitude of benefit seems to be comparable.[28-30] Nevertheless, in the prevailing scenario, the case for routine mediastinal evaluation in NSCLC appears to be significantly weakened.

However, patients with positive N2 nodes in multiple ipsilateral stations or in the contralateral mediastinum are generally offered non-surgical treatment, and hence, if such a situation is suspected based on the imaging findings, invasive mediastinal evaluation is indicated. Studies have shown that positive N2 nodes are present in about a quarter of the patients with positive N1 nodes (cN1) detected on PET computed tomography. In addition, up to 40% of the patients with positive mediastinal lymph nodes have them at multiple or N3 stations (contralateral mediastinum).[31] Moreover, in patients with cN1, video mediastinoscopy offers significantly increased sensitivity compared to endosonography.[27,32]

Our study is limited by its small sample size. Moreover, only a small proportion of respondents treated a high volume of patients with lung cancers and had access to invasive mediastinal evaluation, which is likely to affect the generalization of the results.

CONCLUSION

Currently, the expertise of clinicians treating patients with lung cancer in invasive mediastinal staging, particularly using mediastinoscopy, is highly limited, and endoscopic techniques have superseded cervical mediastinoscopy for invasive mediastinal evaluation in India. Therefore, concerted efforts are required for improving the knowledge and implementation of invasive mediastinal staging in clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY APPENDIX

Supplementary Appendix 1: Study protocol

An online survey to assess changing trends in utility of mediastinoscopy in India

BACKGROUND AND LITERATURE REVIEW

Mediastinoscopy is an important tool and the gold standard for evaluating the mediastinal lymph nodes in lung cancers and other malignancies. It has been a valid tool for the oncologist for the last 50 years.[1] In standard mediastinoscopy, we are able to sample nodes from pretracheal, right and left upper and lower paratracheal, and subcarinal nodes. If the imaging shows suspicious nodes in the mediastinum, mediastinoscopic evaluation provides vital information and hence influences important treatment decisions. Over the last 30 years, after newer imaging modalities became available, the role of mediastinoscopy has evolved.[2,3] However, mediastinoscopy is not a commonly performed investigation as the expertise with this procedure is scarce. Mediastinoscopy is also associated with potential morbidity and mortality.[4] Complications related to mediastinoscopy include recurrent laryngeal nerve palsy, others being pneumothorax, bleeding from main pulmonary vessels.[1,4,5]

Recently, endobronchial ultrasound (EBUS)-guided fine-needle aspiration cytology/biopsy has been shown to have comparable accuracy to mediastinoscopy in the evaluation of mediastinal nodes. Subsequently, the number of mediastinoscopy performed has come down worldwide. However, mediastinoscopy is still performed in patients who have negative endoscopic evaluation due to higher false negativity of EBUS. It is also valuable in cases where lymphoma is suspected. Hence, maintaining the expertise for mediastinoscopy is important for the thoracic oncologist.

The survey aims to study these changing trends in the use of cervical mediastinoscopy for evaluation of mediastinal nodes in context of pulmonary and nonpulmonary cancers.

Research question

What are the changing trends, if any, in the utility of mediastinoscopy for evaluation of suspicious mediastinal nodes in the context of pulmonary and nonpulmonary malignancies?

Aim of the study

To assess, via an online survey, the changing trends in the utility of mediastinoscopy for evaluation of suspicious mediastinal nodes across India.

Objectives

1. To assess the current status of mediastinoscopy for evaluation of mediastinal nodes in lung cancer and in nonpulmonary cancers
2. To indirectly assess the burden of lung cancers and nonpulmonary cancers (with suspicious mediastinal nodes) across India
3. To understand the changing trends of mediastinoscopy usage over the years.

MATERIALS AND METHODS

Study setting

Institutes/centers in the National Cancer Grid (NCG) catering to cancer patients.

Study design

An online web-based survey.

Study population

Doctors involved in care of lung cancer patients and those patients with mediastinal nodes.

Inclusion criteria/population

1. Surgical oncologists, thoracic surgeons, and pulmonologists involved in the care of cancer patients
2. NCG centers which treat cancer patients.

Exclusion criteria

None.

Study period

July to August 2019.

Data collection and data management

An online survey will be conducted among oncologists/thoracic surgeons/pulmonologists across all centers in The NCG. Questions will be directed at current practice and changing trends in the utility of mediastinoscopy. The results of the survey will be analyzed using appropriate statistical tools.

Ethics considerations

- The permission from the institutional review board/institutional scientific committee will be obtained for the study
- The process of data collection will not pose any risk or harm to the subjects as no kind of intervention or any interference with treatment is undertaken in this study
- Data confidentiality: The names of the patients will not be entered anywhere in the study.

Dissemination of results

The results will be published in peer-reviewed national and international journals and conferences, increasing the body of knowledge and informing the larger scientific/medical body.

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QUESTIONNAIRE

Questionnaire 1: Survey Questionnaire

1. Institution: .....
2. Designation: .....
3. Years of experience: <2 years, 2–5 years, >5 years
4. Type of hospital: Government, private, semi-government (autonomous)
5. Type of hospital: Academic institute, nonacademic institute
6. Number of new cases of CA lung being evaluated every month: 0–2 cases, 3–10, 11–25, >25
7. Number of new cases of mediastinal adenopathy being evaluated every month (including those due to lung cancer): 0–2 cases, 3–5, 6–10, >10
8. Is mediastinoscopy available at your institute?: Yes/No
9. Is endobronchial ultrasound/endoscopic ultrasound (EBUS/EUS) available at your institute?: Yes/No
10. If yes, who performs EBUS/EUS?: Oncologist, pulmonologist, radiologist, combination of above
11. Number of mediastinoscopies performed over the last 2 years: <10, 11–25, 25–50, >50
12. Is there a change in the utility of mediastinoscopy over the last 5 years? Increasing, decreasing, stable, unable to comment
13. Do you think invasive mediastinal staging is still recommended in patients with suspicious mediastinal nodes on radiological ± functional imaging? Yes/No
14. For positron emission tomography-negative mediastinal nodes, do you still stage them? Yes/No
15. If yes, how do you stage?: EBUS, EUS/mediastinoscopy/both
16. If a patient of mediastinal adenopathy comes to you, which investigation would you offer first: EBUS/EUS or mediastinoscopy? .....
17. Please mention the reason for the above answer: .....
18. What % of patients subjected to EBUS/EUS do need mediastinoscopy for problem solving? <5%, 5%–10%, 11%–25%, >25%
19. What is the approximate cost of mediastinoscopy at your institute? <Rs. 20,000, Rs. 20,000–50,000, >Rs. 50,000?
20. What is the approximate cost of EBUS/EUS at your institute? <Rs. 20,000, Rs. 20,000–50,000, >Rs. 50,000?
21. What is the incidence of finding Koch's/benign granulomas in patients with suspicious mediastinal adenopathy in your practice? <1%, 1%–10%, 10%–20%, >20%
22. Additional comments if any: .....