GENERAL THORACIC SURGERY

THE CURRENT ROLE OF MEDIASTINOSCOPY IN THE EVALUATION OF THORACIC DISEASE

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Objective: **Mediastinoscopy is a common procedure used for the diagnosis of thoracic disease and the staging of lung cancer. We sought to determine the current role of mediastinoscopy in the evaluation of thoracic disease.** ***Methods:*** **We conducted a retrospective review of all mediastinoscopies performed by members of our service between January 1988 and September 1998.** ***Results:*** **We performed mediastinoscopies on 2137 patients. A total of 1745 patients underwent mediastinoscopy for known or suspected lung cancer. In 422 of these procedures, N2 or N3 disease was identified; only 28 of these patients underwent resection. The remaining 1323 had no evidence of metastatic disease. In these patients 947 had lung cancer. Only 76 of the patients with lung cancer were found to have N2 disease at exploration. Among the 1323 patients with a negative mediastinoscopy result, 52 underwent resection of a nonbronchogenic malignancy, and 217 had resection of a benign lesion. A total of 392 patients underwent mediastinoscopy for the evaluation of mediastinal adenopathy in the absence of any identifiable pulmonary lesion. Of these, 161 had a nonbronchogenic malignancy, 209 had benign disease, and 25 had no diagnosis established; mediastinoscopy established a definitive diagnosis in 93.6% of patients. In the entire group of 2137 patients, there were 4 perioperative deaths and 12 complications. Only one death was directly attributed to mediastinoscopy. No deaths or complications occurred in patients undergoing mediastinoscopy for benign disease.** ***Conclusions:*** **Mediastinoscopy is a highly effective and safe procedure. We believe that mediastinoscopy should currently be used routinely in the diagnosis and staging of thoracic diseases. (J Thorac Cardiovasc Surg 1999;118:894-9)**

Mediastinoscopy is a common procedure used for the diagnosis of thoracic disease and the staging of lung cancer. Since its introduction by Carlens[1] in 1959, mediastinoscopy has become the standard to which all other methods of evaluating the mediastinum are compared. The efficacy of mediastinoscopy in the preoperative staging of bronchogenic carcinoma is well established, with a procedural sensitivity of greater than 90% and specificity of 100%.[2-4] Similarly, mediastinoscopy has been shown to be efficacious in the diagnosis of mediastinal disease other than bronchogenic carcinoma, with an ability to establish a diagnosis in greater than 90% of cases.[5,6] However, mediastinoscopy continues to be a subject of debate among thoracic surgeons. Although some surgeons consider the procedure essential in the evaluation of the mediastinum for lung cancer, as well as for other conditions, others view the procedure as overly invasive, with a comparatively high rate of morbidity and occasional mortality. The advent of continuously improving noninvasive imaging studies, such as positron emission tomography (PET), have added to the debate.

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Table I. *Histologic diagnosis of 217 patients who underwent resection of what proved to be a benign lesion after mediastinoscopy*

Diagnosis	*No.*
Hamartoma	56
Caseating granuloma	47
Noncaseating granuloma	41
Organized pneumonia	22
Histoplasmosis	13
Other	38

Table II. *Pathologic diagnosis of 161 patients in whom mediastinoscopy revealed nonbronchogenic cancer*

Diagnosis	*No.*
Non-Hodgkin's lymphoma	81
Hodgkin's lymphoma	28
Melanoma	10
Sarcoma	9
Other	33

We conducted a retrospective study of all mediastinoscopies performed at our institution over a 10-year period to determine the safety, efficacy, and the current role of mediastinoscopy in the evaluation of thoracic disease.

Methods

This study is a retrospective, chart-computer database review of all mediastinoscopies performed between January 1988 and September 1998 on the Thoracic Surgical Service of the Barnes-Jewish Hospital. The techniques used are well described elsewhere.[7,8]

During the study period, mediastinoscopy was performed on 2137 patients. These consisted of 1956 cervical mediastinoscopies, 68 anterior mediastinotomies, and 113 combined procedures. We did not perform extended cervical mediastinoscopy, as described by Ginsberg and colleagues,[9] on any patient. Nineteen patients underwent repeat mediastinoscopy; for purposes of simplicity, the second mediastinoscopy was not used in the tabulation of data in this study. All data were entered into a previously established computer database. This database was then used to delineate the indication(s) for, the results of, as well as the complications of, all mediastinoscopies performed by members of our service during the study period. When indicated, patient records were reviewed to clarify and/or confirm database findings.

Results

The study population was comprised of 1237 men and 900 women, with a median age of 65 years. Of the 2137 patients who underwent mediastinoscopy, 1745 (81.7%) had mediastinoscopies performed for known or suspected lung cancer or in the presence of an undiagnosed parenchymal pulmonary lesion. Of these 1745, mediastinoscopies revealed N2 or N3 disease (evidence of tumor in mediastinal nodes) in 422 (24%), whereas in the remaining 1323, mediastinoscopy revealed no evidence of metastatic disease.

Of the 422 patients in whom mediastinoscopy revealed N2 or N3 disease, only 28 (6.6%) underwent thoracotomy with resection. The indications for resection in these 28 patients included participation in a neoadjuvant protocol (12 patients), as well as limited disease (eg, only one node; 7 patients).

Of the 1323 patients in whom mediastinoscopy revealed no evidence of tumor in the mediastinum, 1216 underwent thoracotomy with exploration; the remaining 107 patients were deemed unsuitable for thoracotomy with a possible resection, mostly because of medical comorbidities. Of the 1216 patients who underwent thoracotomy, 947 (77.9%) were proven to have lung cancer. Of these 947, only 76 (8.0%) were found to have N2 disease at exploration. Of these 76 patients, 70 (92.1%) underwent some type of resection; the remaining 6 patients were explored but did not undergo resection. This group of 76 patients included 9 in whom mediastinoscopy revealed no evidence of metastatic disease on frozen section but in whom permanent pathology revealed metastatic disease in the same mediastinal lymph nodes (ie, false-negative results). The majority of the remaining patients in this group had metastatic disease in nodes that were inaccessible to standard cervical mediastinoscopy (eg, subaortic nodes in 25 patients, posterior subcarinal nodes in 26 patients, and pulmonary ligament nodes in 5 patients).

Among the 1216 patients in whom mediastinoscopy revealed no evidence of tumor in the mediastinum and who underwent thoracotomy, 52 (4.3%) underwent resection of a nonbronchogenic malignancy; metastatic colon cancer was the most common diagnosis (12 patients). Resection of what proved to be a benign lesion was carried out in 217 (17.8%) of these 1216 patients. Table I shows the diagnosis established in these resections.

Of the 2137 patients, 392 underwent mediastinoscopy for the evaluation of mediastinal adenopathy in the absence of any identifiable parenchymal or endobronchial pulmonary lesions. In this group of patients, a definitive diagnosis was established in 367

Table III. *Pathologic diagnosis of 206 patients in whom mediastinoscopy revealed a benign disease process*

Diagnosis	*No.*
Noncaseating granuloma	130
Follicular-reactive hyperplasia	20
Caseating granuloma	16
Anthracosis	11
Other	29

Table IV. *Cause of death in 4 patients who underwent mediastinoscopy*

Cause of death	*No.*
Aortic laceration	1
Stroke	1
Cardiac arrest	1
Undetermined (do not resuscitate)	1

(93.6%). These 392 patients consisted of 161 patients with nonbronchogenic cancer, 206 patients with a benign disease process, and 25 patients in whom a diagnosis was not established. Table II shows the diagnosis established in those patients with nonbronchogenic cancer. Table III shows the diagnosis established in those patients with a benign disease process.

In the entire group of 2137 patients, there were 4 perioperative deaths; only 1 (0.05%) was directly attributable to mediastinoscopy. Also among the entire group, there were 12 (0.6%) complications associated with mediastinoscopy. Table IV lists the causes of death, and Table V lists the complications. No deaths or complications occurred in any patient in whom mediastinoscopy was carried out for what proved to be a benign process.

Discussion

The role of mediastinoscopy in the evaluation of thoracic disease continues to be a subject of some debate. The advent of various noninvasive or minimally invasive techniques for evaluating the mediastinum has led to a number of studies carried out in an attempt to compare these various techniques with mediastinoscopy. Several studies have compared computed tomography (CT) to mediastinoscopy in the accurate staging of bronchogenic carcinoma.[2,4,10-15] CT alone does not seem to obviate the need for mediastinoscopy. Even if mediastinal adenopathy is noted on CT, a tissue diagnosis must still be obtained because a normal-appearing mediastinum on CT may yet harbor metastatic disease (13% of cases in our own experience, unpublished data). Mediastinoscopy has also been compared with other techniques.[16-18] These studies continue to support the routine use of mediastinoscopy in the preoperative staging of patients with bronchogenic carcinoma.

Table V. *Complications in 12 patients who underwent mediastinoscopy*

Complication	*No.*
Arrhythmia	6
Pulmonary artery laceration	1
Esophageal perforation	1
Excessive bleeding	1
Intravenous fluid extravasation	1
Pneumothorax	1
Hypotension	1

Recently, PET has been used in the staging of bronchogenic carcinoma. PET in addition to CT has been found to be superior to CT alone in the evaluation of mediastinal lymph node status in non–small-cell lung cancer.[19,20] A study by Vansteenkiste and colleagues[21] found a high negative predictive value of mediastinal PET and suggested that PET could substantially reduce the need for mediastinoscopy. However, further studies comparing PET with mediastinoscopy are needed to form definitive conclusions regarding this relatively new modality and to determine the role that PET may come to play in the preoperative staging of bronchogenic carcinoma. A study by the clinical oncology group of the American College of Surgeons will be undertaken in an attempt to evaluate PET in this role.

We routinely perform mediastinoscopy in patients with a presumptive or known diagnosis of lung cancer who are being considered for resection. In highly selected cases, such as a biopsy-proven peripheral squamous cancer with mediastinal lymph nodes of less than 1 cm on CT scan, we may proceed directly to resection. The frequency with which our service performs mediastinoscopy has resulted in a great degree of comfort with the technique. The frequent application of mediastinoscopy by members of our service has also allowed us to standardize our technique, with particular emphasis on meticulous dissection and biopsy. These facts have widened our application of mediastinoscopy, and we currently perform mediastinoscopy for the evaluation of mediastinal adenopathy in a variety of disease processes.

Our practice is to obtain biopsy specimens from each node station sampled. We have not used needle aspiration cytology from nodes visualized at mediastinoscopy. Recently, we have used transbronchial

needle aspiration in selected cases. However, the sampling error with this technique has been impressive.

Our data supports the use of mediastinoscopy in the preoperative staging of bronchogenic carcinoma. In those patients in whom mediastinoscopy was carried out for this purpose, mediastinoscopy had a sensitivity of 85.2% in the accurate staging of N2 or N3 disease; this figure is consistent with those found in other reports.[3,16,18] It should be noted, however, that most mediastinal lymph nodes found to be positive at the time of thoracotomy were inaccessible to mediastinoscopy (eg, subaortic nodes in 25 patients). We do not routinely sample subaortic nodes in patients with left upper lobe lesions because we have previously demonstrated the reasonable outcome for patients with resected positive subaortic nodes who had a negative mediastinoscopy.[22] In patients with enlarged subaortic nodes on CT scan, we routinely perform anterior mediastinotomy before resection. We do not use extended cervical mediastinoscopy in such cases because we believe that this procedure presents added risk when used infrequently.

In this series a total of 392 patients underwent mediastinoscopy in an effort to diagnose mediastinal adenopathy in the absence of any identifiable parenchymal or endobronchial pulmonary lesion. Mediastinoscopy established a diagnosis in 93.6% of these patients, indicating the efficacy and applicability of mediastinoscopy for such an indication. Of these patients, a majority (206) proved to have a benign process on pathologic examination. This is consistent with data found in other reports.[5,6] For these patients with a diagnosis of benign disease, mediastinoscopy may well obviate the need for any further evaluation.

We observed a low rate of morbidity and mortality (0.6% and 0.2%, respectively). These numbers are consistent with previously reported results from large series.[3,23] As may be seen in Table III, only one death was directly attributable to mediastinoscopy (an aortic tear in a patient in whom there was infiltration of tumor into the aorta). The remaining deaths occurred in patients with widely metastatic disease who simply required a tissue diagnosis; all 3 patients died of conditions that existed at the time of mediastinoscopy, such as diffuse brain metastases, which led to a fatal stroke in one patient. Furthermore, only 2 complications necessitated an additional operation (a pulmonary artery laceration and an esophageal perforation). In both cases the operation was used to simultaneously manage the complication and to resect the lung cancer. The right upper lobe pulmonary artery laceration was recognized immediately, bleeding was controlled with packing, and the patient underwent an uneventful thoracotomy with lobectomy. The esophageal perforation was suspected in the recovery room after the patient complained of severe chest pain. A contrast swallow demonstrated the leak. The patient then underwent immediate thoracotomy with repair of the perforation and simultaneous lobectomy. The postoperative course in both patients was uneventful. It should be noted, however, that the rate of morbidity may be somewhat higher because we were unable to document some minor complications (eg, recurrent nerve injuries and wound infections) due to lack of long-term follow-up.

Given its safety and efficacy, our experience with mediastinoscopy suggests that it should currently be used routinely in the diagnosis and staging of thoracic disease.

REFERENCES

1. Carlens EL. Mediastinoscopy: a method for inspection and tissue biopsy in the superior mediastinum. Dis Chest 1959;36:343-52.
2. Van Schil PEY, Van Hee RHGG, Schools ELG. The value of mediastinoscopy in preoperative staging of bronchogenic carcinoma. J Thorac Cardiovasc Surg 1989;97:240-4.
3. Luke WP, Pearson FG, Todd TPU, et al. Prospective evaluation of mediastinoscopy for assessment of carcinoma of the lung. J Thorac Cardiovasc Surg 1986;91:53-6.
4. Gdeedo A, Van Schill P, Corthouts B, et al. Prospective evaluation of computed tomography and mediastinoscopy in mediastinal lymph node staging. Eur Respir J 1997;10:1547-51.
5. Forse RA, Dutton JW, Munro DD. Mediastinoscopy for diagnosing diseases of the lung other than primary carcinoma. Can J Surg 1978;21:438-40.
6. Porte H, Roumilhac D, Eraldi L, et al. The role of mediastinoscopy in the diagnosis of mediastinal lymphadenopathy. Eur J Cardiothorac Surg 1998;13:196-9.
7. Kirschner, PA. Cervical mediastinoscopy. Chest Surg Clin N Am 1196;6:1-20.
8. Pearson, FG. Mediastinoscopy: a method of biopsy in the superior mediastinum. J Thorac Cardiovasc Surg 1965;49:11-21.
9. Ginsberg RJ, Rice TW, Goldberg M, et al. Extended cervical mediastinoscopy: a single staging procedure for bronchogenic carcinoma of the left upper lobe. J Thorac Cardiovasc Surg 1987; 94:673-8.
10. Funatsu T, Matsubara Y, Hatakenaka R, et al. The role of mediastinoscopic biopsy in preoperative assessment of lung cancer. J Thorac Cardiovasc Surg 1992;104:1688-95.
11. De Leyn P, Vansteenkiste J, Cuypers P, et al. Role of cervical mediastinoscopy in staging of non-small cell lung cancer without enlarged mediastinal lymph nodes on CT scan. Eur J Cardiothorac Surg 1997;12:706-12.
12. Staples CA, Muller NL, Miller RR, et al. Mediastinal nodes in bronchogenic carcinoma: comparison between CT and mediastinoscopy. Radiology 1988;167:367-72.
13. Richey HM, Matthews JI, Helsel RA, et al. Thoracic CT scanning in the staging of bronchogenic carcinoma. Chest 1984;85:218-21.
14. Afita T, Kuramitsu T, Kawamura M, et al. Bronchogenic carcino-

ma: incidence of metastases to normal sized lymph nodes. Thorax 1995;50:1267-9.
15. McLoud TC, Bourgouin PM, Greenberg RW, et al. Bronchogenic carcinoma: analysis of staging in the mediastinum with CT by correlative lymph node mapping and sampling. Radiology 1992; 182:319-23.
16. Gossot D, Toledo L, Fritsch S, et al. Mediastinoscopy vs. thoracoscopy for mediastinal biopsy: results of a prospective nonrandomized study. Chest 1996;110:1328-31.
17. Rendina EA, Venuta F, De Giacomo T, et al. Comparative merits of thoracoscopy, mediastinoscopy, and mediastinotomy for mediastinal biopsy. Ann Thorac Surg 1994;57:992-5.
18. Patterson GA, Ginsberg RJ, Poon PY, et al. A prospective evaluation of magnetic resonance imaging, computed tomography, and mediastinoscopy in the preoperative assessment of mediastinal node status in bronchogenic carcinoma. J Thorac Cardiovasc Surg 1987;94:679-84.
19. Steinert HC, Hauser M, Allemann F, et al. Non-small cell lung cancer: nodal staging with FDG-PET versus CT with correlative lymph node mapping and sampling. Radiology 1997;202:441-6.
20. Sasaki M, Ichiya Y, Kuwabara Y, et al. The usefulness of FDG positron emission tomography for the detection of mediastinal lymph node metastases in patients with non-small cell lung cancer: a comparative study with X-ray computed tomography. Eur J Nucl Med 1996;23:741-7.
21. Vansteenkiste JF, Stroonbants SG, De Leyn PR, et al. Lymph node staging in non-small cell lung cancer with FDG-PET scan: a prospective study on 690 lymph node stations from 68 patients. J Clin Oncol 1998;16:2142-9.
22. Patterson GA, Piazza D, Pearson FG, et al. Significance of metastatic disease in subaortic lymph nodes. Ann Thorac Surg 1987;43:155-9.
23. Puhakka HJ. Complications of mediastinoscopy. J Laryngol Otol 1989;103:312-5.

Discussion

Dr Douglas E. Wood *(Seattle, Wash).* Dr Hammoud, I congratulate you and your colleagues at Washington University for an outstanding review of the modern utility, efficacy, and safety of mediastinoscopy. Your group has been pioneers and leaders in several areas of thoracic surgery, and it is especially meaningful to hear your insights on the current utility of an old-fashioned procedure like mediastinoscopy. The controversies about mediastinoscopy arise regarding its routine use in lung cancer staging. Many thoracic surgeons perform only selective mediastinoscopies for central tumors or enlarged mediastinal lymph nodes. Their argument is that CT staging of the mediastinum is accurate, that mediastinoscopy adds risk and unnecessary morbidity, and that mediastinoscopy does not change therapy (ie, resectability in radiologically occult N2 or N3 disease).

Your review of over 1700 mediastinoscopies for suspected lung cancer strongly supports your own practice of routine surgical assessment of the mediastinal lymph nodes before thoracotomy. The sensitivity and specificity of CT scanning for mediastinal lymph nodes are each approximately 65%. Your article reports a CT false-negative rate of 13%, which closely corresponds with the data from Seely and colleagues in Vancouver that showed a 15% false-negative rate even in peripheral T1 tumors.

You have shown that in experienced hands the mortality and morbidity rates of mediastinoscopy are extremely low (0.05% and 0.6%, respectively). Perhaps most importantly in this series, a positive mediastinoscopy result prevented a primary thoracotomy in 96% of patients. Clearly this information changed the planned therapy at your institution. Even radiologically occult but mediastinoscopically detectable lymph node involvement is a marker of systemic disease, which is best treated by multimodality protocols that include surgery or even by nonsurgical therapy alone.

Dr Hammoud, I have 3 questions for you. First, some surgeons believe that it is necessary to perform mediastinoscopy at a separate sitting from the thoracotomy because of concerns regarding the unreliability of the frozen section diagnosis. Clearly this adds to the expense and inefficiency of mediastinoscopy, favoring its selective use. You reported an extremely low false-negative rate at frozen section, which I calculated to be under 1%. What is your own routine for the sequence of mediastinoscopy? Is it usually performed within an operative sequence leading to thoracotomy or as a separate outpatient procedure?

Second, frequently surgeons report mediastinoscopy biopsy specimens from only one lymph node station, which questions the thoroughness of mediastinoscopic exploration. Do you have data regarding the average number of lymph node stations undergoing biopsy in your patients with lung cancer that we may use as a standard in lung cancer staging?

Finally, has the improvement in staging accuracy by combined CT and PET imaging changed your own practice of routine mediastinoscopy, or do you think that it will have an impact in the next few years?

I enjoyed your article and agree with your conclusions. Thank you for the privilege of the discussion.

Dr Hammoud. Dr Wood, thank you for those insightful comments, and I will attempt to answer your questions.

Regarding the first question, there is no doubt that mediastinoscopy is heavily dependent on a good pathology department and a timely manner in which they can report results. Our routine at Washington University is to perform mediastinoscopy at the same sitting as a thoracotomy as part of one procedure. We know that we have experienced pathologists who can give us an accurate, as well as a timely, turnaround on the results, and therefore we make it a routine of ours to perform a bronchoscopy, mediastinoscopy, and then proceed to thoracotomy if those are negative.

Regarding your second question about the average number of lymph nodes, unfortunately I do not know the exact number, but I can tell you that it would be my guess that it is in excess of 5 based on the data that I looked at and the number of lymph node stations that are reported for each mediastinoscopy in the database. It is certainly not 1 or 2.

As to your third question regarding CT and PET scanning, I have obviously reviewed the data in the literature, and it is interesting to note that one of the talks later on this afternoon reports on PET scanning for such a purpose. We have

reviewed our own data, as well as other data in the literature, with CT scanning and done the same with PET scanning, and it really has not changed our practice, mainly because most of the data that is reported demonstrate the inferiority of those techniques either alone or in combination compared with mediastinoscopy for the evaluation of the mediastinum. Therefore I do not think we are at the stage yet where any of those modalities either alone or in combination will deter us from performing mediastinoscopy.

Dr Benedict D. T. Daly *(Boston, Mass).* I would just like to congratulate the authors on a very important paper.

I would like to point out that one of the things that they have not emphasized but that I think should be emphasized is that the false-negative rate for mediastinoscopy is significant. And what is important and not stressed in the conclusions is that systematic lymph node sampling or systematic lymph node dissection must be performed at the time of thoracotomy.

Dr Hammoud. I think we are fortunate at our institution in that our pathologists are extremely good, and they are used to looking at mediastinal lymph nodes. Therefore our reported false-negative rate is actually pretty low.

Dr Steven J. Mentzer *(Boston, Mass).* You only performed 68 anterior mediastinoscopy procedures. Do you use thoracoscopy to evaluate the aorticopulmonary window?

Dr Hammoud. Not routinely.

Dr Mentzer. For left upper lobe lesions?

Dr Hammoud. No.

Dr Thomas R. J. Todd *(Toronto, Ontario, Canada).* I noticed in your abstract, and I am not sure whether you detailed it in your slides, that there were 74 patients who were found to have N2 disease at thoracotomy who had a negative mediastinoscopy result. Interestingly enough, your 5-year survival rate for the group of 24% parallels the rate for those patients who had N2 disease at mediastinoscopy, which is in contradistinction to the original report that Griffith Pearson summarized when he was looking at N2 disease at thoracotomy versus mediastinoscopy. Why do you think your N2 disease at thoracotomy did not do better?

Dr Hammoud. We re-reviewed that information, and I actually did not include it in the final manuscript, but our belief is that we are looking at a different subgroup of patients. These patients are much more highly selected than those in the group reported from the Toronto group by Dr Pearson. About the only thing that we can come up with is that we have a greater selection of patients who we selected for resection.

Dr G. Alexander Patterson *(St Louis, Mo).* It may simply be a reflection of better neoadjuvant chemotherapy or chemoradiation, neither of which were routinely used in the early days of Dr Pearson's prior report. I suspect that may have something to do with the different observations we have made.