

# The Possible Value of Mediastinoscopy in Staging Hodgkin's Disease<sup>1</sup>

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## Summary

The historical, anatomical, and technical aspects of mediastinoscopy are reviewed. The indications for its use, as well as the attendant low morbidity and minimal mortality, are presented. Extension of these indications to include patients with Hodgkin's disease has been examined through our personal experience, from questionnaires sent to leading thoracic surgeons and to directors of lymphoma treatment centers, and by review of the literature.

Only a small percentage of mediastinoscopies are performed to determine the presence of lymphoma or Hodgkin's disease. The procedure does not appear to be as helpful in staging, if applied on a routine basis, as exploratory laparotomy. It may be helpful, however, in determining the cause of recurrent mediastinal enlargement in patients with previously treated Hodgkin's disease.

## Introduction

The first mediastinotomies were performed at the end of the 19th century as therapeutic attempts to treat mediastinitis, which at that time was a frequent and uniformly fatal complication of deep-seated neck infections. According to Palva (13), Heidenbain reported the first successful collar mediastinoscopy in 1899. During World War I, Marschik of the Viennese School introduced the concept of prophylactic mediastinotomy in the management of neck and mediastinal war injuries (13).

The first diagnostic approach to the mediastinum was advocated by Daniels (4) in a study of scalene fat pad biopsies reported in 1949. Lateral mediastinoscopy as an approach to the superior mediastinum was used by Harken *et al.* (6) in the early 1950's. This approach represented a logical extension of the scalene fat pad biopsy of Daniels wherein, following excision of the fat pad, blunt digital dissection was used to explore the upper mediastinum. Abnormal tissue could be directly visualized or biopsied with a laryngoscope introduced into the area of digital dissection. Although the complications from this approach among a large series of cases were few and all were nonfatal, this technique never gained popular acceptance.

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The technique of mediastinoscopy which has been almost uniformly adopted by thoracic surgeons today is that of midline mediastinoscopy as used by Carlens (2) in 1959. As this method utilizes the anterior surface of the trachea as a guide, it is by no means a blind exploration and lessens injury to the great vessels in the neck and pleura, which, in the past, was felt to be a serious possible hazard of lateral mediastinoscopy [although Harken's series of cases (6) testified to the contrary]. Certainly, the extent of mediastinal exploration is greater through the midline approach, for it allows visualization of the entire width of the upper mediastinum, at least to the level of the carina. It has been accepted with great enthusiasm as a valuable diagnostic tool in European centers for almost a decade and has regained a rapidly growing popularity in the United States over the past 5 years.

## Anatomy

A thorough knowledge of the anatomy of the mediastinum is mandatory for the surgeon performing mediastinoscopy, for damage to any of the many vital structures contained therein may lead to acute and/or delayed catastrophe, particularly if such injuries go unrecognized. Although most standard anatomy texts cover this anatomy adequately, a very detailed, explicit, and well-illustrated dissertation on this region is contained in the textbook of mediastinoscopy by Jepsen (8).

Of particular interest to the mediastinoscopist is the superior mediastinum, for it is this region to which mediastinoscopy is generally limited. The thoracic outlet is the upper limit of the superior mediastinum. Laterally, it is bounded by the mediastinal (parietal) pleura. The anterior and posterior boundaries are, respectively, the manubrium sterni and upper 4 thoracic vertebrae. The inferior boundary is at the level of the tracheal bifurcation. The most anteriorly located structures are the thymic remnant, innominate veins, and proximal superior vena cava. Interposed between these structures and the anterior surface of the trachea are the aortic arch and its 3 branches. At the level of the sternal notch, the vagi are located lateral to the innominate and left common carotid vessels and hence are protected from possible damage through a midline approach. Within the upper thorax, they occupy a more posterolateral location with respect to the arch vessels. The phrenic nerves are found near the lateral mediastinal boundaries throughout their course in the upper

mediastinum. The esophagus, thoracic duct, and recurrent nerves are well protected by virtue of their posterior relationships to the trachea.

**Technique of Mediastinoscopy**

The technique of mediastinoscopy is relatively simple and straightforward. The critical factors in performance of the examination are: (a) a thorough knowledge of the regional anatomy; (b) appreciation of the gravity of such an exploration and a constant awareness of the potential hazards; (c) gentle manipulation of all structures; (d) positive identification of tissue prior to biopsy; and (e) diligence in sterile technique.

Endotracheal general anesthesia is routinely used for mediastinoscopy. Muscle relaxation and positive pressure breathing are important in the prevention of air emboli and mediastinal emphysema among those cases in which problems in technique occur. In all cases, the surgeon should be prepared to proceed immediately with a thoracotomy if necessary.

The patient is placed supine. The neck is hyperextended and the anesthesiologist is positioned at the patient's side to allow the surgeon access to the head of the table for manipulation of the scope. The dissection down to the incision of the pretracheal fascia is identical to that used in routine tracheotomy. If this dissection is contained in the midline, the only significant vascular structures encountered are the inferior thyroid veins and thyroidea ima branches, usually of aberrant origin. Following incision in the pretracheal fascia, the index finger is cautiously introduced into the mediastinum along the anterior surface of the trachea. If the finger is in the proper distal fascial plane, the loose areolar tissue of the mediastinum can easily be bluntly dissected down to below the level of tracheal bifurcation. In creating this plane, the

aortic arch and innominate artery are appreciated as prominent anterior pulsations. These vessels protect the great veins located anteriorly from injury. This technique of neck dissection, mediastinal palpation, mediastinoscopy, and mediastinoscopic biopsy have been presented in detail (8, 13).

**Complications**

The complications generally encountered are those previously alluded to and are predominantly related to occurrence of pneumothorax, mediastinal hemorrhage, subcutaneous emphysema, and wound infection. Atelectasis, however, is a complication of mediastinoscopy which probably occurs in 20 to 30% of cases. Certainly, this incidence can be lowered by awareness of this potential complication and the use of vigorous pulmonary toilet in the postoperative period. Most complications are self-limited and easily managed. As surgeons have gained greater experience with judicious performance of the examination, operative complications after mediastinoscopy have occurred less frequently. Today mortality from mediastinoscopy is practically nil (14).

An abundance of data has accumulated to confirm the safety of mediastinoscopy. Among numerous thoracic surgeons who have collected large series of cases in which mediastinoscopy has been performed, the operative and postoperative morbidity is low.

Ashbaugh (1) reviewed 9543 patients with mediastinoscopy with 9 deaths (0.09%) and 149 complications (1.5%). Specifically, there was hemorrhage in 48, pneumothorax in 43, recurrent nerve injury in 22, infection in 12, tumor implantation in wound in 8, phrenic nerve injury in 3, esophageal injury in 1, chylothorax in 1, air embolism in 1, and transient hemiparesis in 1.

From responses to questionnaires sent to a number of thoracic surgeons (Table 1) who have gained experience with

Table 1  
Response to questionnaire sent to thoracic surgeons to determine usefulness of mediastinoscopy in Hodgkin's disease

Surgeons polled	Question <sup>a</sup>									
	1	2	3	4a	4b	4c	5a	5b	6	7
		(%)							(%)	(%)
Ferguson	3	5	3	0	3	0	No		0	0
Pearson	10	2	12	0	0	0	Yes	1	1.9	0
Trinkle	0								3	0.02
Provan	0	0			0	0	0	0	10	0
Dineen	4	2	4	0	0	0	No		1	0
Takaro	0	0	0	0			0		7	0.7

<sup>a</sup>Questions asked in following order:

1. What is the number of patients in your series who had the histological diagnosis of Hodgkin's disease made from biopsy material obtained by mediastinoscopy?
2. This represents what percentage of all positive mediastinoscopies?
3. Of these cases, how many were previously undiagnosed?
4. (a) In how many patients have you been able to establish mediastinal involvement in Hodgkin's disease by mediastinoscopy among patients with previously proven Hodgkin's disease? (b) Of these cases, how many had X-ray evidence of mediastinal or pleural involvement by Hodgkin's disease? (c) How many had normal X-rays?
5. Do you have cases of proven Hodgkin's disease involving the mediastinum in which mediastinoscopy did *not* yield a positive biopsy (e.g., false negatives) (a)? If so, how many (b)?
6. What is your morbidity rate from mediastinoscopy?
7. What is your mortality rate from mediastinoscopy?

mediastinoscopy, as well as our own experience with 25 such operations, we conclude that the morbidity rate is in the range of 2 to 10%.

**Experience in Other Diseases**

The technique of mediastinoscopy as described by Carlens (2) in 1959 is an accurate method of exploration and biopsy of the superior mediastinum. Over the past decade, it has gained primary importance in the diagnosis of many intrathoracic and systemic diseases, as well as in the assessment of resectability in bronchogenic carcinoma. The enthusiasm that has been shared among thoracic surgeons of European centers since the inception of mediastinoscopy has rapidly grown in this country over the past several years. This is not surprising when one considers the major contributions that have occurred through its use. Probably the most significant of these relates to the changing concept of surgical management of bronchogenic carcinoma. Prior to the use of mediastinoscopy, all patients who were considered medically operable and without evidence of extrathoracic extension of bronchogenic carcinoma were subjected to thoracotomy. An alarmingly high percentage of such patients either proved to have unresectable lesions or demonstrated early recurrence of tumor following attempted resection. Such discouraging results indicated the futility of surgery in many patients with lung cancer (2, 13, 16).

In recent years, many centers have adopted mediastinoscopy as a routine part of the evaluation of all patients with proven or suspected bronchogenic carcinoma. Among large series in which mediastinoscopy has been so utilized, it has proven to be an invaluable tool in determining the extent and prognosis of intrapulmonary cancer, and it has become possible to establish, with a high degree of accuracy, which patients have cancers so limited that pulmonary resection offers a realistic possibility of encompassing all of the tumor and, hence, potential curability (3, 8, 16).

The results have been repeatedly confirmed in many large medical centers and demonstrate that in 30 to 40% of patients previously considered operable, mediastinoscopy will confirm that the tumor has extended into the mediastinum and beyond the limits of curability. These 30 to 40% of patients are therefore spared from unnecessary exploratory thoracotomy (15). In contrast, patients who do not show tumor extension into the mediastinum at the time of mediastinoscopy have better than a 95% chance of having a resectable lesion (15).

**Experience in Lymphoma and Hodgkin's Disease**

Since mediastinoscopy has become established as a safe and valid method of definitive diagnosis in a variety of pathological processes involving the mediastinum, the indications for its use have been extended.

**Our Experience in Lymphoma and Hodgkin's Disease.** At the University of Chicago, this has included its possible role in the evaluation and staging of Hodgkin's disease. Unlike many systemic cancers, Hodgkin's disease is now proving to be rather unique in that among some of its histological variants, long-term remissions or cures in significant numbers have been

achieved through the use of megavoltage radiation, chemotherapy, or both (17, 19). Since such long-term cures have been undoubtedly the results of precise definition of the extent of the tumor in conjunction with adequate radiotherapy to these areas, a staging of Hodgkin's disease through the use of numerous examinations, including exploratory laparotomy, have become accepted medical practice (17, 18).

In our experience at the University of Chicago over the past 1.5 years, we have encountered 2 patients in whom we were able to determine the presence or absence of mediastinal involvement by Hodgkin's disease by the use of mediastinoscopy and open mediastinal biopsy. These case histories are presented.

*Case 1.* A 68-year-old man was admitted to the University of Chicago in 1970 for further evaluation of an enlarging mediastinal mass in conjunction with pleural effusion. In 1968, the diagnosis of lymphosarcoma, lymphocytic type, had been established by axillary node biopsy at an outside hospital. Without adequate staging, he had received several modalities of therapy, including 4000 R to the upper abdomen through inverted Y-ports. In conjunction with this therapy, he had received a course of i.v. nitrogen mustard in addition to cyclophosphamide p.o. Symptoms at the time of his readmission in October 1970 included progressive dyspnea, weakness, and productive cough. Sputums for culture and cytology, as well as bronchial brushings and bronchoscopy, failed to reveal the nature of his pulmonary lesions. In an attempt to delineate the nature of his pulmonary mass, left scalene node biopsy and mediastinoscopy were undertaken. The only gross abnormality at mediastinoscopy was a tortuous and dilated innominate artery. This was in conjunction with extensive mediastinal fibrosis secondary to radiation therapy. Nevertheless, no tumor mass was visualized within the mediastinum. A histological diagnosis, therefore, was not confirmed by mediastinoscopy. Over the next several months, he had protracted difficulty with cardiac failure and arrhythmias, which ultimately led to his demise in February 1971.

*Case 2.* A 27-year-old man had the diagnosis of nodular sclerosing Hodgkin's disease confirmed by right supraclavicular lymph node biopsy in 1959. He received 550 R to the mediastinum and neck via an Orthovoltage 250-kV machine. Following this treatment, his chest film was normal. In 1961 he again demonstrated widening of the mediastinum. With the presumptive diagnosis of recurrent Hodgkin's disease, he received 750 R to the mediastinum with the use of <sup>60</sup>Co. Subsequently, slight left hilar enlargement persisted, but the patient was totally asymptomatic and remained so until the spring of 1970 when he developed weight loss, easy fatigability, abdominal cramps, and pruritus. Chest X-ray this time showed marked widening of the upper mediastinum. He was hospitalized at the University of Chicago where a battery of diagnostic tests including inferior venacavagram, lymphangiogram, and liver function tests were all normal. There were no physical findings at this time. In June 1970, he underwent a staging laparotomy. No evidence of Hodgkin's disease was present. Shortly after recovery from laparotomy, he underwent mediastinoscopy for evaluation of the mediastinal mass. The mediastinal mass, although not

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accessible to the mediastinoscopy, was appreciated and, in an attempt to establish a histological diagnosis, mediastinal exploration was approached through the right parasternal area, resecting the bed of the 2nd costal cartilage. With this approach, the mediastinum was entered extrapleurally. A large, firm, fixed mediastinal mass which surrounded the aorta posteriorly was visualized and biopsied. This proved to be nodular sclerosing Hodgkin's disease. Consequently, the patient was staged as IIB and treated with radiation to the cervical and mediastinal regions as well as to the axilla. The initial port included the entire mediastinal mass at 200 R a day with a total dosage of 4000 R. Subsequent follow-up has shown the patient to be in good health.

**Surgeons Polled.** In an attempt to gain more information, we sent questionnaires to a number of thoracic surgeons (Table 1) who have had wide experience with mediastinoscopy. We were surprised to find that most of these investigators had little, if any, experience with the diagnosis of Hodgkin's disease by mediastinoscopy. Dineen and coworkers (Table 1) at the Yale University Medical Center, however, established a protocol for the evaluation of Hodgkin's disease by mediastinoscopy and pneumomediastinoscopy in 1967. They accumulated 4 patients in whom they were able to establish the diagnosis of Hodgkin's disease by mediastinoscopy. Pearson (Table 1) reports 10 such patients in whom mediastinoscopy established the diagnosis of Hodgkin's disease not made otherwise. Other reports which we have encountered (Table 1) mention only 1 or 2 cases in which mediastinoscopy was valuable in establishing the diagnosis of Hodgkin's disease or in proving mediastinal involvement.

**Lymphoma Centers Polled.** In further attempting to delineate the experience of others with this technique in lymphoma and Hodgkin's disease, we asked 6 directors of lymphoma centers about their experience and they informally answered that they had none. The centers consulted included the National Cancer Institute, M. D. Anderson Hospital and Tumor Institute, Roswell Park Memorial Institute, Memorial Hospital for Cancer and Allied Diseases, University of Southern California, and Stanford University.

**Literature.** Goswitz and Klassen (5) found the diagnosis of mediastinal lymphoma positive in only 7 of 20 patients suspected to have lymphoma and subjected to limited thoracotomy. The yield is not much higher with

mediastinoscopy, but of course mediastinoscopy is a more benign procedure.

Lincoln and Provan (10) found that the lowest yield (33%) of positive biopsies was when mediastinoscopy was done in patients with cancer. This increased to 80% when benign disease was being considered. Table 2 summarizes 9 series (7-12, 14, 16, 20) of mediastinoscopy carried out in 1309 patients. Twenty-five cases of lymphoma were proven by this technique; 10 cases could not be substantiated. In reviewing the 556 cases examined by Jepsen (8), there were only 2 proven lymphomas, 2 proven Hodgkin's disease cases, and 3 negative diagnoses in patients with lymphoma or Hodgkin's disease.

Musshoff, Wolfart, and their colleagues at the University of Freiburg have performed over 400 mediastinoscopies (K. Musshoff, personal communication, June 23, 1971). In most instances, the procedure was performed as a diagnostic approach to mediastinal tumors. Fifteen cases of previously unsuspected Hodgkin's disease were diagnosed by the mediastinoscopy procedure. There was minimal morbidity and no mortality.

### Discussion

At this point in time, insufficient data have been accumulated to evaluate critically the possible role of mediastinoscopy in the staging of Hodgkin's disease. It seems reasonable, however, to state that since the staging of Hodgkin's disease is indeed critical and since exploratory laparotomy has become an integral part in the staging of Hodgkin's disease, the use of mediastinoscopy in conjunction with exploratory laparotomy in evaluating Hodgkin's disease would seem quite practical *only* if the mediastinum were not to be included in the Maltese cross. Since this is usually done, the usefulness of mediastinoscopy might be found only in the undiagnosed mediastinal mass, before or after the establishment of Hodgkin's disease elsewhere. Especially in the previously treated patient (Case 1), mediastinoscopy might prevent a thoracotomy or a blind course of radiotherapy by ruling out recurrence.

Mediastinoscopy cannot be compared to laparotomy in terms of diagnostic and therapeutic usefulness. In

Table 2  
Literature review of mediastinoscopy for lymphoma and Hodgkin's disease

Author	Year	Total mediastinoscopies	Lymphoma		Hodgkin's disease	
			Proven	Disproven	Proven	Disproven
Nohl-Oser (12)	1965	100		1	4	2
Jepsen (8)	1966	556	2	2	2	1
Nielsen and Olsen (11)	1966	223	2			
Hosie and Ford (7)	1967	42			4	
Kirschner (9)	1967	50			3	1
Trinkle <i>et al.</i> (16)	1968	155	1	3		
Ward <i>et al.</i> (20)	1969	46	1			
Pinkham and Torgerson (14)	1969	117	3			
Lincoln and Provan (10)	1970	20	3			
Totals		1309	12	6	13	4

mediastinoscopy only the top of the mediastinum can be well explored. In contrast, laparotomy permits biopsy of lymph nodes suspected to be abnormal by inferior venacavography or lymphangiography, biopsy of lymph nodes considered abnormal by inspection and often located lateral to standard radiation fields (*i.e.*, porta hepatis, mesenteric, splenic pedicle), removal of spleen, and detection of liver involvement by multiple needle and a wedge biopsy.

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