

Mediastinal Staging Prior to Surgical Resection

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Documenting the anatomic extent of lung cancer before surgical resection has value in therapeutic decision-making. In the past, documenting mediastinal disease spared the patient the morbidity of an exploratory thoracotomy.¹ Currently, the presence of stage IIIA lung cancer is an indication for neoadjuvant chemoradiation therapy.² In the future, it is likely that tissue biopsies will be used for biomarkers staging,³ tissue typing for oncogenic mutations,⁴ and/or drug sensitivity testing.⁵

The pathophysiologic assumption in cancer staging is that the progressive growth of the primary tumor eventually leads to the embolic spread of metastatic cells to the lymphatic system and subsequently to the blood circulation. This predictable sequence of tumor progression has led to staging systems designed to provide consistent descriptions of the anatomic extent of cancers at specific times in their clinical progression. Denoix and colleagues first advocated the “TNM” classification in the 1940s.⁶ In 1986, the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) adopted a common TNM staging system.⁷ In 1997, this staging system was reconciled with the 1983 American Thoracic Society statement on clinical staging.⁸ The current staging system is based on the relative size and extent of the primary tumor (T), the absence, presence, and extent of regional lymph node involvement (N), and the absence or presence of distance metastases (M). The present TNM staging system has been universally adopted as the basis for therapeutic comparisons worldwide.

In potentially operable lung cancer, a description of the anatomic extent of the cancer depends on the size of the tumor (T) and the involvement of regional or mediastinal lymph nodes (N). Clinical T stage is typically assessed by chest CT scans. T2 tumors are greater than 3 cm, involve a large bronchus (>2 cm from the carina), or are associated with atelectasis.⁹ The survival of clinically staged patients with T2N0 disease is only 75% at 1 year and 40% at 5 years.⁸ The survival of pathologically staged patients with T2N0 disease is 90% at 1 year and 60% at 5 years.⁸ The disappointing survival of these early-stage (stage IB) lung

cancer patients suggests two conclusions: (1) we do a poor job of characterizing the extent of malignant disease, and (2) we do a particularly poor job of clinical staging.

Recent attempts to improve the sensitivity of all cancer staging have focused on lymphatic mapping. Clinical and experimental evidence of sentinel node mapping in breast cancer and melanoma suggest that (1) lymph drainage patterns are predictable; (2) lymph node drainage follows a sequential pattern; and (3) lymph nodes filter and entrap tumor cells. In lung cancer, the lymphatic map developed by Naruke and coworkers and adopted by the AJCC has demonstrated an even more predictable pattern of lymphatic drainage than is seen in trunkal malignancies.^{10,11} The success of the lymph node map likely reflects the defined hilar and mediastinal lymphatic anatomy as well as the unidirectional lymph flow along the thoracic duct. Attempts to replace tissue biopsies with noninvasive staging have been plagued with a consistent 10% error rate regardless of the technique employed.

The mapping of mediastinal lymph nodes can be performed by using a mediastinoscopic or thoracoscopic procedure. Cervical mediastinoscopy provides access to the paratracheal (levels 2R, 2L, 4R, and 4L) and subcarinal lymph nodes (level 7). The lymph nodes in the aortopulmonary window (levels 5 and 6) are accessible through an anterior mediastinotomy—a procedure commonly referred to as an anterior or parasternal mediastinoscopy.

Biopsies of mediastinal lymph nodes can also be performed by thoracoscopy. In the right hemithorax, thoracoscopic staging provides access to the right paratracheal nodes (level 4R), inferior pulmonary ligament nodes (level 9), and subcarinal nodes (level 7). In the left hemithorax, thoracoscopy provides access to the aortopulmonary (AP) window nodes (level 5 and 6) and posterior hilar nodes.

Surgical Procedure

Mediastinoscopy is performed by using a general anesthetic. At our institution, mediastinoscopy is performed as an ambulatory procedure in patients with suspected mediastinal disease. Patients suspected of having no mediastinal malignancy are typically staged by a combination of preoperative PET/CT scanning and intraoperative thoracoscopic staging to confirm the absence of mediastinal malignancy.

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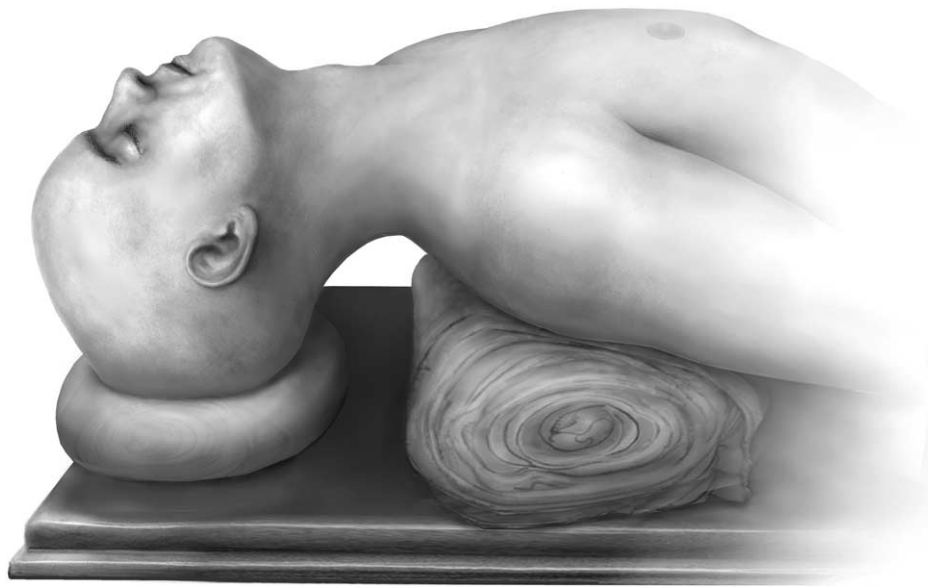


Figure 1 The patient is positioned for mediastinoscopy in the supine position so that the head extends just beyond the end of the operating table. A roll is placed under the shoulders to facilitate extension of the neck. The head is in the midline position and is stabilized by using a circular cushion. Intravenous tubing and monitoring lines are placed to one side to facilitate surgical access to the patient's head and neck. The suprasternal notch is palpated to identify a potentially ectatic innominate artery. The supraclavicular regions are palpated because previously unrecognized lymph nodes may be identified in this position.

The patient is prepped from the chin to the upper abdomen so that any inadvertent arterial injury can be addressed through a median sternotomy. The surgical drapes are only suspended by the intravenous tubing and monitoring lines on one side of the patient's head.

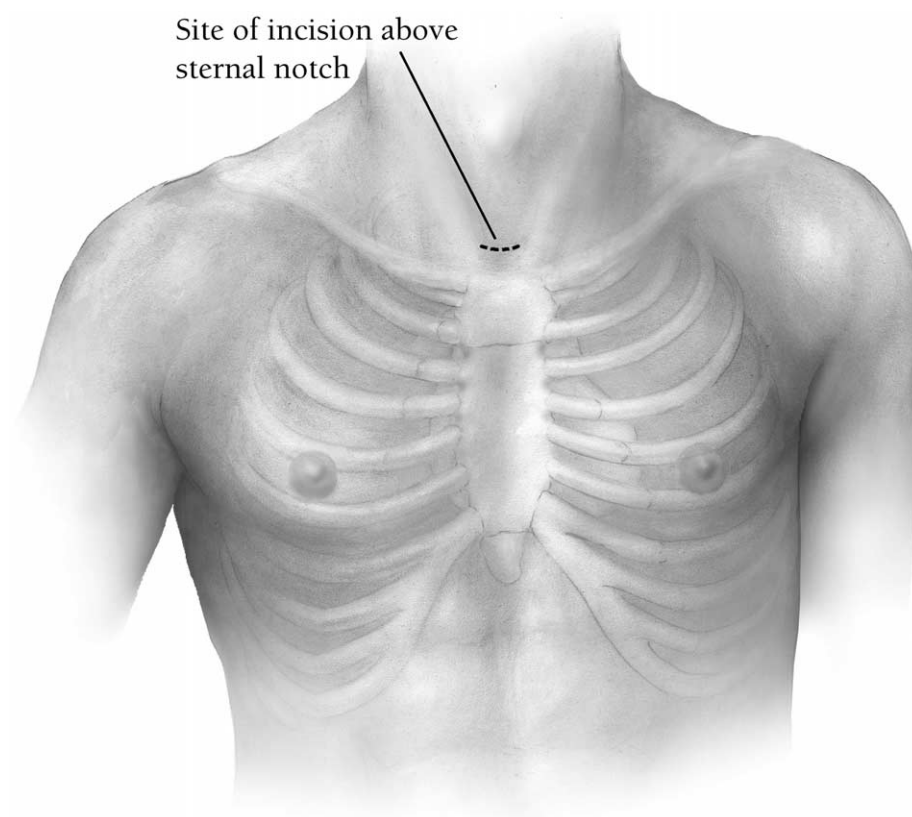


Figure 2 The cervical mediastinoscopy incision is made in the suprasternal notch 1 fingerbreadth above the manubrium. The horizontal incision is approximately 1 fingerbreadth in length and is placed in Langer's lines to minimize scarring. The horizontal dissection is continued through the platysma. The dissection is then continued vertically between the strap muscles. Because of the significant mobility of the strap muscles and veins in the neck, there is little need to ligate or cauterize vessels in this dissection. If vessels are cauterized during this dissection, adequate hemostasis can be assessed by an end inspiratory hold maneuver that approximates the venous pressure during postoperative coughing or valsalva maneuvers.

The most important step in the cervical dissection is the definition of the pretracheal fascia. The pretracheal space, an avascular potential space between the pretracheal fascia and the anterior trachea, is the conduit for the safe passage of the mediastinoscope. A relatively small hole in the pretracheal fascia can be expanded sufficiently to admit a finger by mobilizing the pretracheal fascia laterally as well as inferiorly within the neck. Attempts to blindly mobilize the pretracheal fascia in the mediastinum—particularly the blind spreading of the Metzenbaum scissors within the mediastinum—risks injury to an ectatic or atherosclerotic innominate artery. Repair of these posterior wall injuries of the innominate artery typically require a median sternotomy. Similarly, an excessively large hole in the pretracheal fascia may complicate the insertion of the mediastinoscope and may even lose access to the pretracheal space.

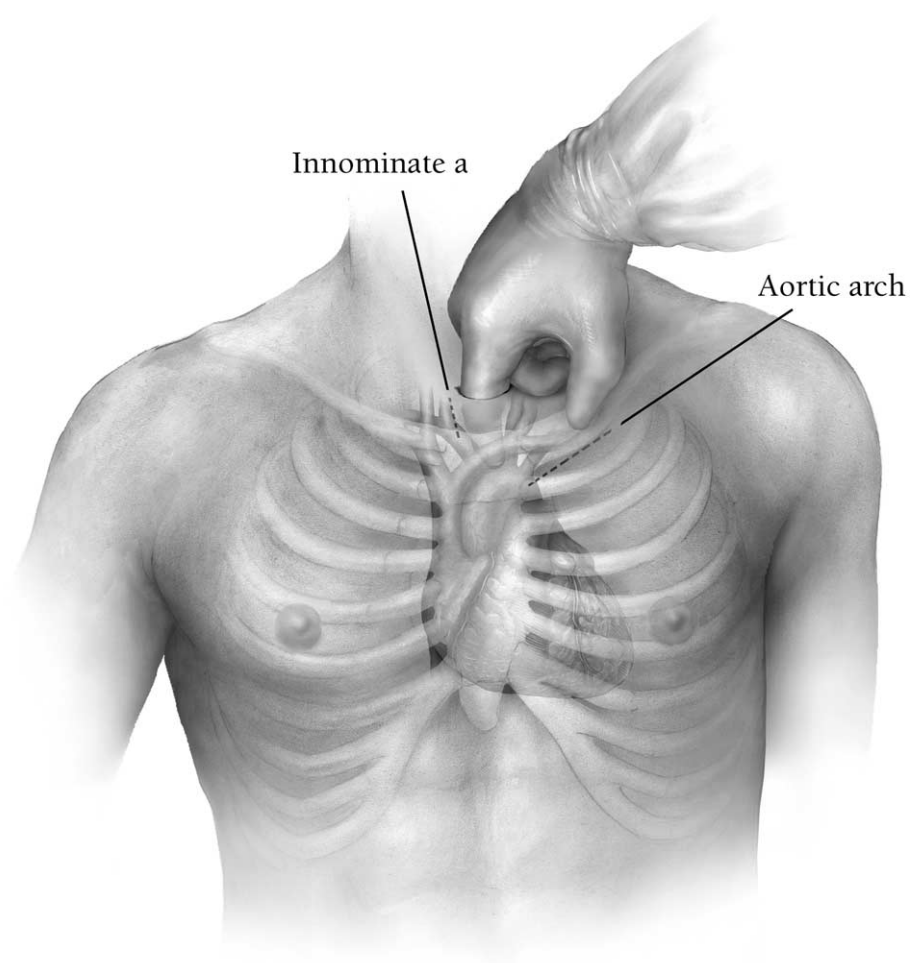


Figure 3 When the pretracheal fascia has been sufficiently mobilized, the operating table is lowered and the surgeon's index finger is inserted between the pretracheal fascia and the tracheal cartilages. This pretracheal "space" is developed by blunt digital dissection. The initial dissection is begun on the anterolateral aspect of the trachea to avoid the innominate artery. The broad dissection plane is gradually extended to both sides of the trachea, between the innominate artery and the trachea, and as far distally as possible. In almost all patients, the surgeon's index finger should extend distal to the innominate artery.

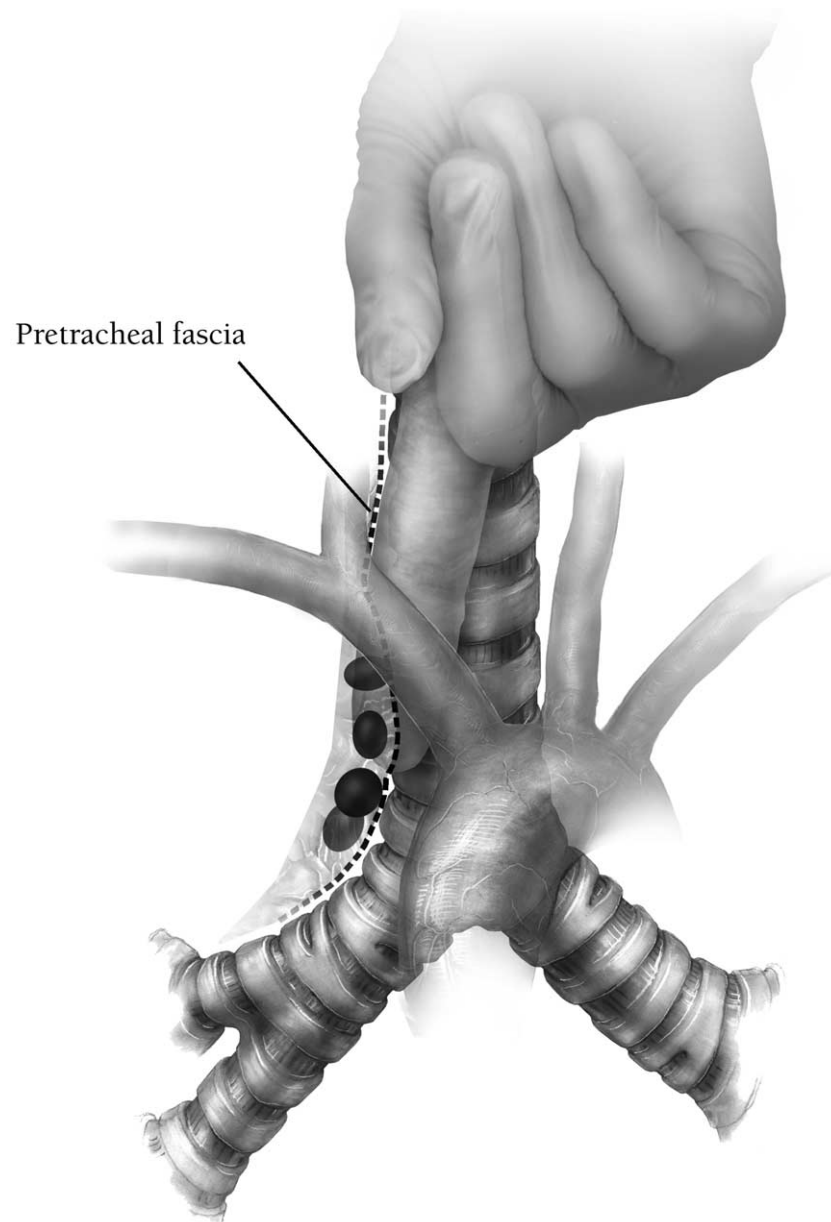


Figure 4 The lower right paratracheal lymph nodes (level 4R) are located at the distal extent of the surgeon's finger and external to the pretracheal fascia. The surgeon's finger is used to penetrate the pretracheal fascia and facilitate exposure of the lower paratracheal lymph nodes during subsequent mediastinoscopic examination. Digital palpation of the lower right paratracheal lymph nodes is a critical step in the procedure. Pathologic nodes are often better appreciated by palpation than by visual inspection.

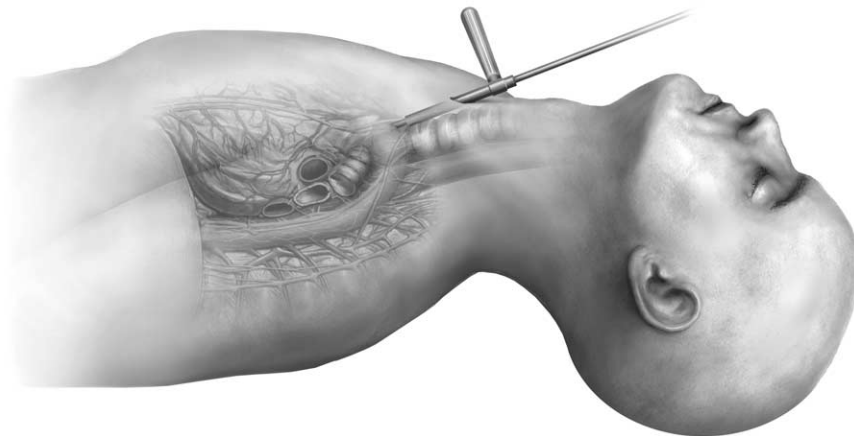


Figure 5 The surgeon's finger is withdrawn and the mediastinoscope is introduced into the pretracheal space. Some surgeons raise the operating table and stand when performing the mediastinoscopy, while other surgeons sit on a stool for the procedure. An advantage of sitting, in addition to comfort, is that the surgeon can readily reassess the mediastinum by palpation without changing the operating table position. The beveled end of the mediastinoscope is used to retract the soft tissue of the neck and pretracheal fascia. Rotation of the mediastinoscope during insertion often facilitates visualization of the pretracheal fascia and the anterior wall of the trachea. The mediastinoscope is inserted along the axis of the trachea: approximately a 30 degree angle relative to the sternum.

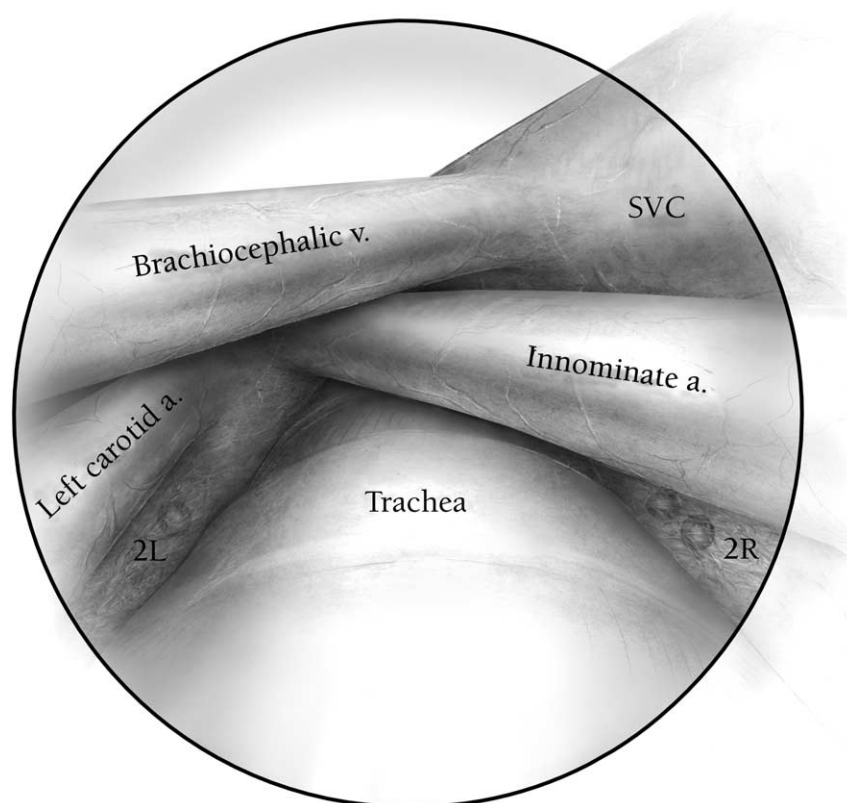


Figure 6 The initial view of the mediastinum is the innominate artery apposed to the anterior wall of the trachea. The importance of an intact pretracheal fascia is apparent in this step: the pretracheal fascia provides a potential space for passing the mediastinoscope distal to the artery. Although rarely involved with metastatic cancer, the upper paratracheal lymph nodes (2R and 2L) are accessible at this level of the dissection.

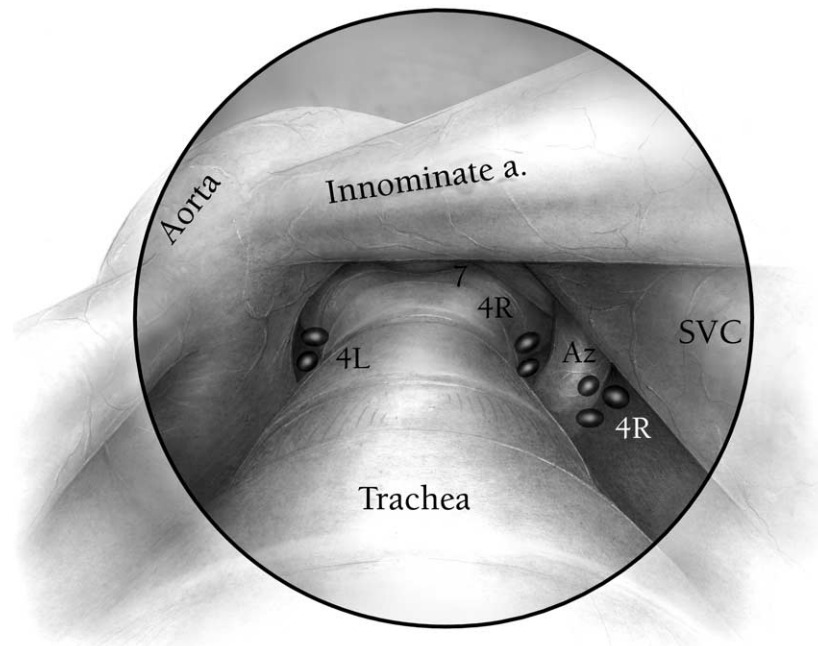


Figure 7 The right lower paratracheal lymph nodes are typically more anterior (retrocaval) than is usually depicted in schematic diagrams. Since digital palpation has defined the area, dissection can be performed without the concern of an arterial injury. The dissection is typically performed with the tip of a suction handle or occasionally with biopsy forceps. Right lower paratracheal lymph nodes should be circumferentially dissected. The azygos vein, constrained by surrounding pretracheal fascia, can be virtually indistinguishable from an anthracotic lymph node. Injury to the azygos vein is rarely controllable through the mediastinoscopy incision. In the event of an azygos vein injury, the mediastinum should be packed, the patient repositioned, and a right thoracotomy performed to facilitate exposure of the azygos vein and superior vena cava. Although azygos vein injuries can be repaired through a median sternotomy, exposure of the medial aspect of the azygos vein is limited and manipulation of the superior vena cava may result in extension of the injury.

More distally, lymph nodes are readily identified at the tracheobronchial angle. These lymph nodes are within the pretracheal fascia. Defined as 10R lymph nodes in the original AJCC classification,⁷ these lymph nodes have been reclassified as level 4R¹² despite their distinct anatomic location. The right tracheobronchial angle lymph nodes represent a transition between N1 and N2 lymph nodes and are likely an early site mediastinal metastatic disease.

Dissection at the right tracheobronchial angle should remain lateral to the mainstem bronchus. Dissection that strays anterior to the bronchus may injure the first pulmonary arterial branch to the right upper lobe (truncus anterior artery). A traction injury to the artery may also occur if there is bulky disease in this location. A potential consideration in video-assisted resections is that a delay of several weeks after thorough dissection of the lymph nodes in the tracheobronchial angle may result in adhesions to the truncus anterior artery.

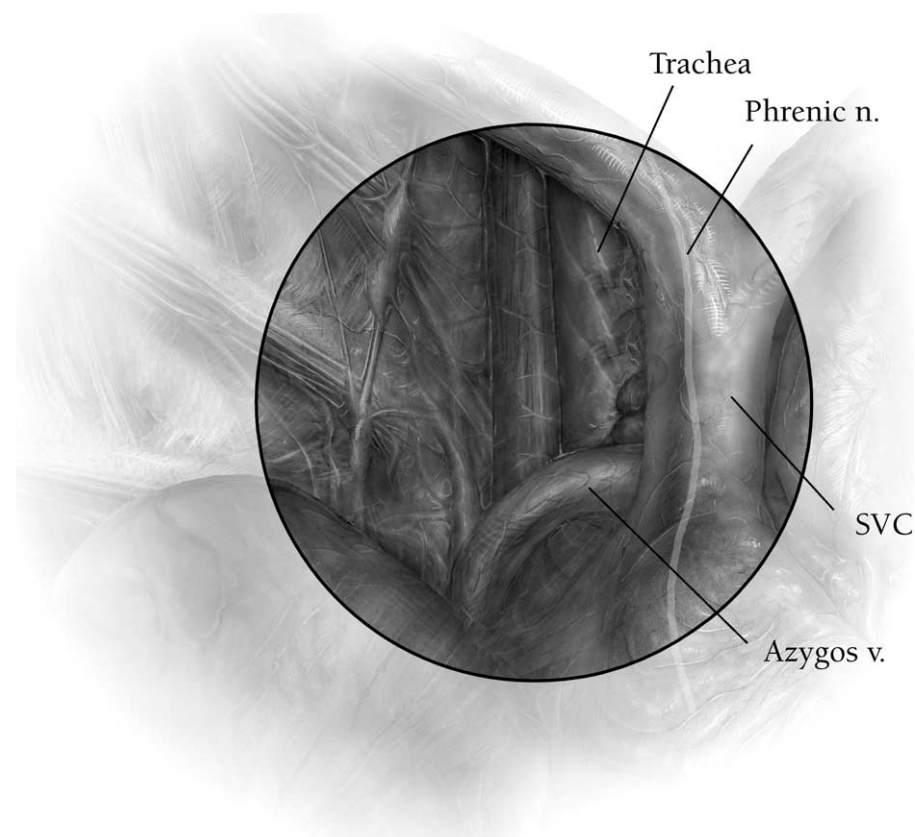


Figure 8 An alternative approach to sampling the lower right paratracheal lymph nodes is video thoracoscopy. Thoracoscopic staging requires single lung ventilation. The procedure can be performed through two access ports; typically these can be placed in the 3rd and 7th interspace in the anterior axillary line. The thoracoscope is inserted through the 7th interspace access port and the lung is reflected caudad exposing the supra-azygos mediastinal pleura. The superior vena cava is reflected anteriorly exposing the retrocaval lymph nodes. A rounded instrument, such as a ring forceps, can be useful to extract the nodal tissue in the retrocaval location. On occasion, a lower lobe tumor will have an isolated inferior pulmonary ligament lymph node. These level 9 lymph nodes are uniquely accessible by thoracoscopy.

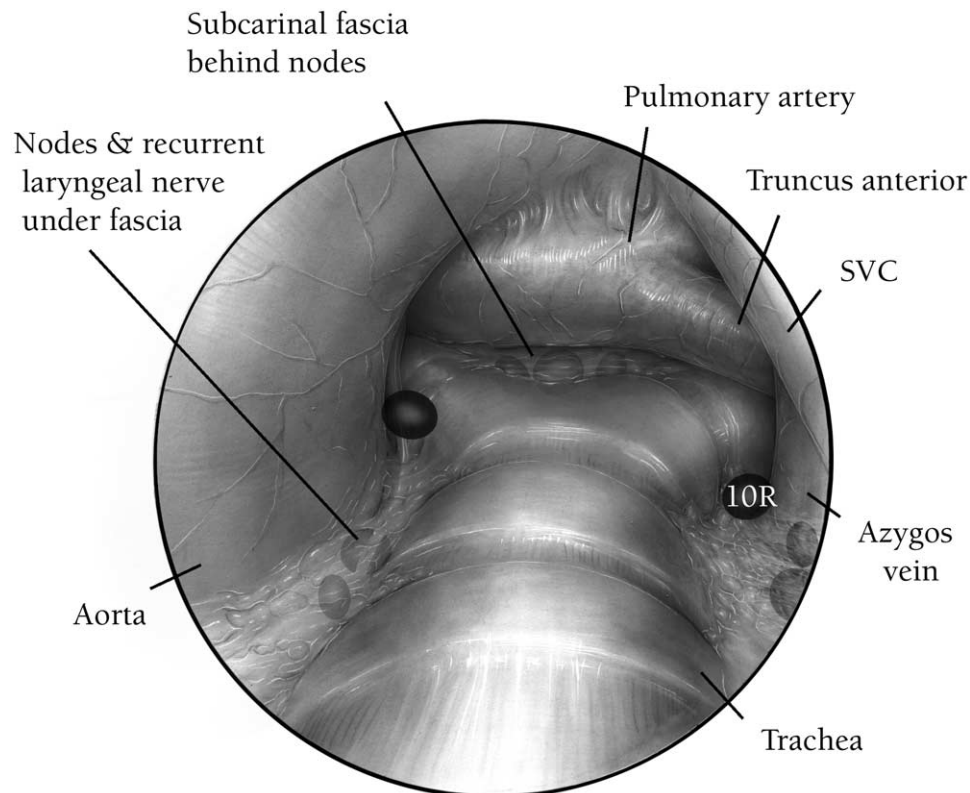


Figure 9 An early site of embolic spread from middle and lower lobe malignancies is the subcarinal space (level 7).¹³ The subcarinal space is difficult to evaluate by conventional CT scanning and its retrocardiac location compromises evaluation by PET scanning.

Dissection that is carried down to the level of the subcarinal space frequently reveals anterior tracheal lymph nodes. A note of caution is that these lymph nodes may be associated with an anterior bronchial artery in 5% of the patients.¹⁴ The true subcarinal space, however, lies below the subcarinal fascia. Dissection of this fascial plane is required to expose pathologic lymph nodes. Particularly with substantial adenopathy, lymph nodes may be extruded from the subcarinal space facilitating biopsies, limiting the necessity of extensive dissection.

In contrast to other lymph node levels, circumferential dissection of the subcarinal (level 7) lymph nodes is not advisable in the subcarinal space because of the potential for arterial bleeding. Excessive dissection in the subcarinal space may result in bleeding that appears to originate deep within the subcarinal space. Direct pressure may be required for 10 minutes or more to obtain hemostasis. This can be accomplished by using vaginal packing gauze and a biopsy forceps to apply direct pressure. The biopsy forceps is used in preference to a standard packing forceps to facilitate visualization and direct pressure on the bleeding site. In general, bleeding is less severe in patients with significant aortic atherosclerotic disease and more severe in patients with chronic infections such as bronchiectasis.

The left paratracheal lymph nodes are dissected to identify contralateral (stage IIIB) nodal involvement from a right lung cancer or ipsilateral (stage IIIA) nodal involvement from a left lung cancer. On the left side of the trachea, the pretracheal fascia inserts into the lateral trachea. The insertion of the pretracheal fascia is progressively more anterior near the carina. This fascia must be dissected to expose the underlying left lower paratracheal (level 4L) lymph nodes. The left lower paratracheal lymph nodes are often a pair of nodes straddling the left recurrent laryngeal nerve.

The left recurrent nerve courses cephalad over the left mainstem bronchus and along the tracheoesophageal groove. Although the mechanism of postoperative recurrent nerve paralysis is often unclear, excessive dissection should be avoided to minimize ischemic injury and electrocautery should not be used near the recurrent nerve to avoid thermal injury.

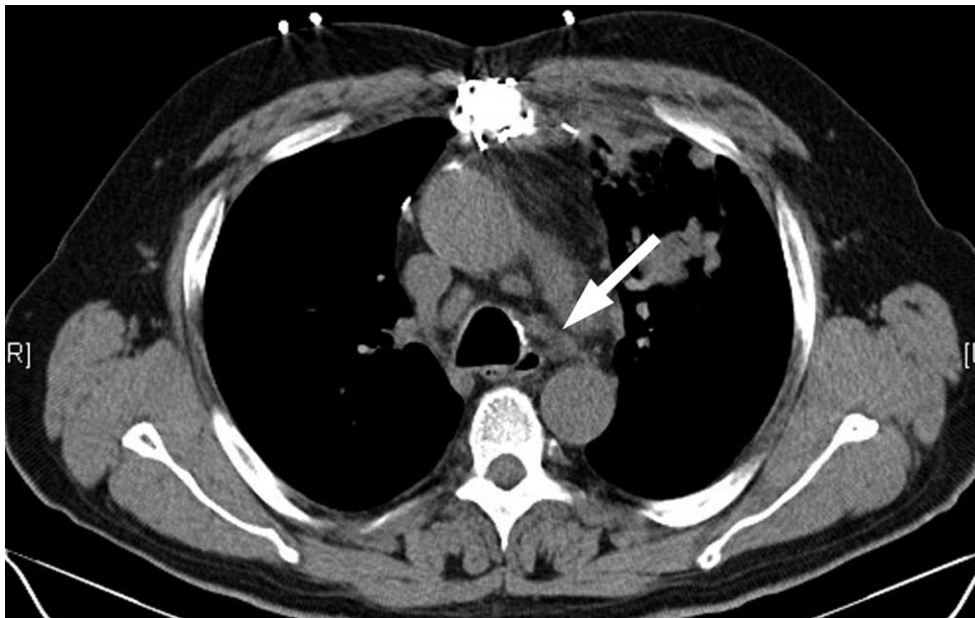


Figure 10 The distal left lower paratracheal 4L lymph nodes (formerly 10L) are found on the lateral aspect of the left mainstem bronchus just distal to the left tracheobronchial angle. As the left pulmonary artery lies anterior to the left mainstem bronchus, the lateral dissection can be extended several centimeters along the lateral border of the bronchus. This dissection is only limited by the aortic arch. If the lymph nodes at the left tracheobronchial angle are visible by chest CT scanning, these lymph nodes are typically positive on biopsy (Fig 10, arrow).

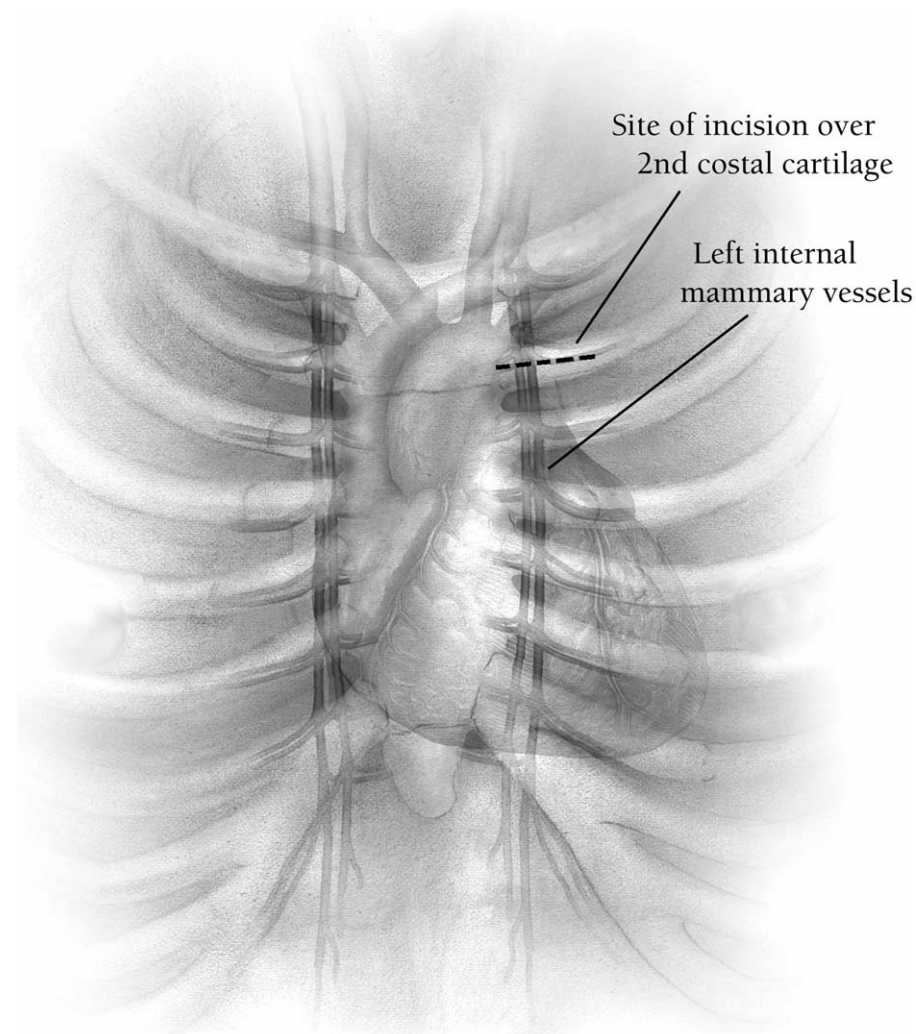


Figure 11 Tumors in the left upper lobe preferentially metastasize to the aortopulmonary lymph nodes. These lymph nodes can be sampled by anterior mediastinoscopy or video thoracoscopy. Contraindications to anterior mediastinoscopy include a significant mediastinal shift or cardiac revascularization procedures. In contrast to thoracoscopic staging of the AP window, anterior mediastinoscopy is performed within the mediastinal pleura.

The patient is positioned in the supine position identical to the cervical mediastinoscopy position. The operating table may be placed in slight reverse Trendelenburg. The head is in the midline position and is stabilized by using a circular cushion. A 1-fingerbreadth-wide incision is made over the second intercostal space or the second intercostal cartilage. Removal of the costal cartilage may lessen the risk of postoperative costochondritis and leaves a cosmetically acceptable incision. At this level, the internal thoracic (mammary) artery lies within 1 cm of the lateral sternal border. The internal thoracic fascia medial to the internal thoracic artery is dissected to facilitate access to the retrosternal space. An index finger can be used to sweep the artery laterally to provide access to the anterior mediastinum. Should injury to the artery occur during this maneuver, bleeding is readily controlled with digital pressure.

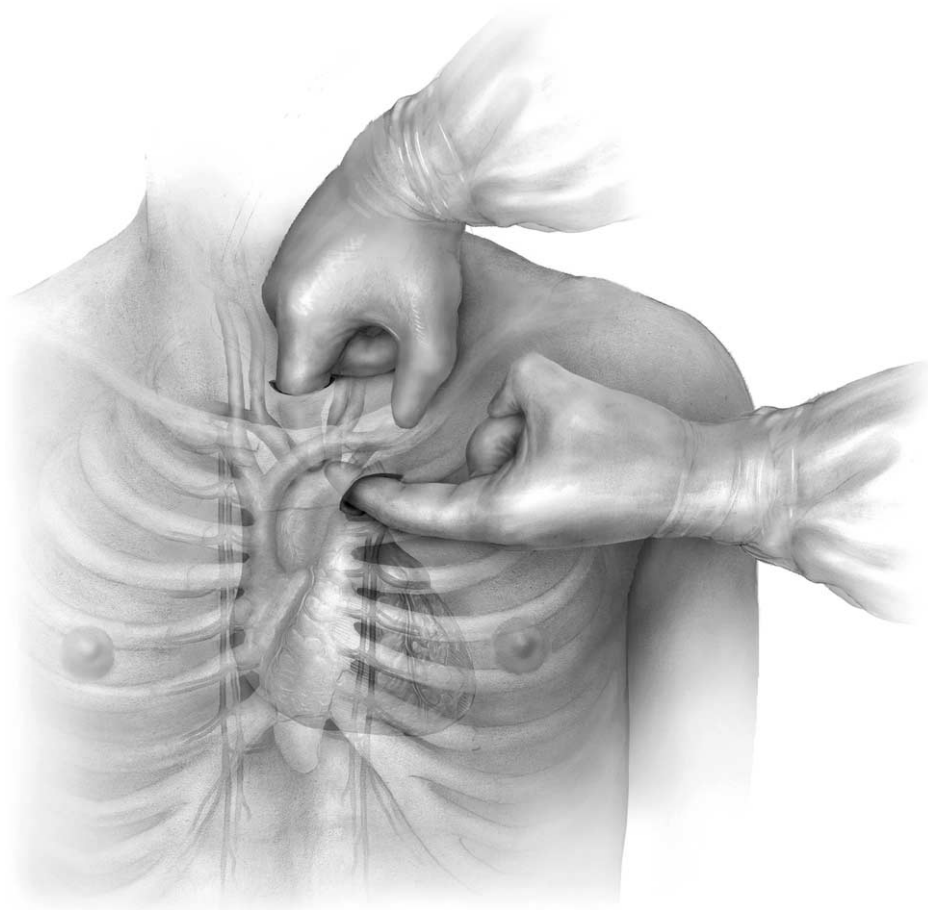


Figure 12 The aortic arch is readily identified within the extrapleural mediastinum. The surgeon's index finger is advanced along the lateral border of the aortic arch to the base of the innominate artery. At this level, the phrenic and vagus nerves define a parallel course over the lateral aspect of the aortic arch. These nerves are palpated as a ridge or "bowstring" on the aortic arch. The preaortic (level 6) lymph nodes are generally found straddling the nerves near the base of the innominate artery. Because of the limited visualization from mediastinal fat, pathologic lymph nodes are initially palpated and the mediastinoscope is introduced subsequently to facilitate biopsy of the lymph nodes.

Aortopulmonary lymph nodes are palpated by sliding the index finger caudad toward the pulmonary artery. Because of the relative compliance and variable orientation of the pulmonary artery, dissection with the suction handle without a palpable target is inadvisable. Large, soft, and sessile lymph nodes are often found intimately opposed to the main pulmonary artery. The normal level 5 lymph nodes is often large; size alone is not an indication of malignancy.

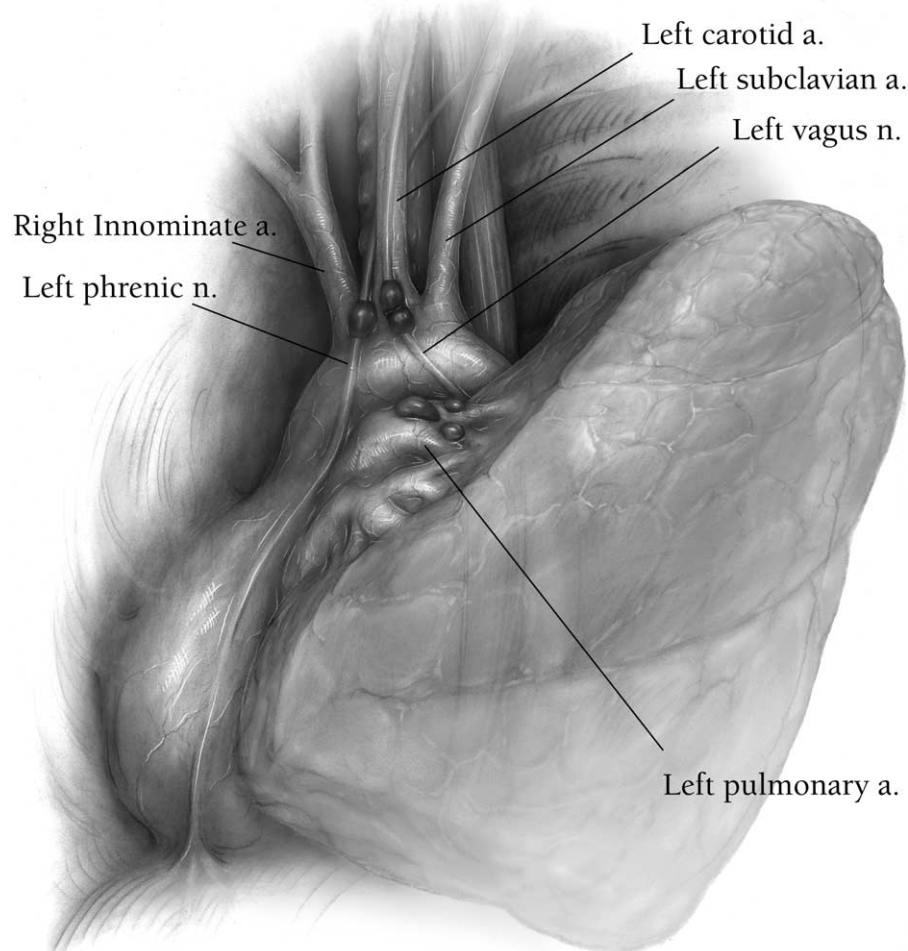


Figure 13 An alternative approach to sampling the AP window is video thoracoscopy. As noted previously, thoracoscopy requires general anesthesia and single lung ventilation. The approach is similar to the right side: 3rd and 7th interspace access ports. The lung is reflected posteriorly using an endoscopic Kitner inserted next to the thoracoscope. Posterior rotation of the operating table also facilitates exposure of the hilum. The phrenic nerve is traced to the level 6 lymph nodes at the base of the innominate artery. Thoracoscopy has the advantage of clear visualization of the level 5 lymph node as well as the lymph nodes in the posterior hilum juxtaposed to the mainstem bronchus.

In cases requiring both paratracheal and AP window staging, cervical and anterior mediastinoscopy are performed. Bimanual palpation permits a thorough appreciation of the aortic arch and the thin fascial plane that separates the cervical from preaortic dissections. It is this fascial plane, at the base of the "V" formed by the innominate and carotid arteries, that is dissected in an extended cervical mediastinoscopy.¹⁵ Because of the traction of the mediastinoscope on the aorta, this procedure is contraindicated in patients with atherosclerotic aortic disease.

Summary

In our current conception of cancer, lymph nodes represent a pivotal transition between a primary tumor treated by surgical therapy alone and metastatic disease treated by an evolving combination of multimodality therapy. Invasive mediastinal staging provides an opportunity for pre-resectional histologic examination of these pivotal lymph nodes. The disadvantages of mediastinoscopy is that it requires general anesthesia and, in many cases, a delay in surgical resection. The advantages of mediastinoscopy are that it is safe and effective.¹⁶ In patients with suspected mediastinal lung cancer (stage III), mediastinoscopy provides lymph node staging and histologic confirmation of tumor type. In these selected patients, we perform sufficiently extensive mediastinal sampling that it is impractical to examine the entire specimen by frozen section. The price of a thorough examination of the lymph nodes is that the therapeutic resection may be delayed a week; nonetheless, the mediastinoscopy is low risk and can be performed as an outpatient procedure. In appropriately selected patients, invasive mediastinal staging provides important histologic information with minimal morbidity.

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