Role of Thoracoscopic Lymph Node Staging for Lung and Esophageal Cancer

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By Mark J. Krasna, MD

Staging is extremely important in determining the proper treatment of patients with thoracic malignancies. Staging groups can be used to predict outcome after cancer treatment and allocate patients to appropriate treatment.

Introduction

Staging of thoracic malignancies is of the utmost importance to the proper treatment of patients with thoracic malignancies. The 1988 American Joint Committee on Cancer Staging (AJCC) criteria defined the tumor, node, metastasis (TNM) staging for lung and esophageal carcinoma [1,2]. These staging criteria are based on survival statistics, which allow the stage groups to be used to predict outcome after cancer treatment. In addition, the definitive staging of patients with thoracic malignancies correctly allocates patients to treatment regimens appropriate for their disease stage. This enables adjuvant and neoadjuvant treatment to be given to patients who will truly derive the greatest benefit and in whom it will be worthwhile to undertake the possible risks and side effects of such treatment.

Thoracoscopy is an excellent means for staging intrathoracic malignancies. Thoracoscopy affords an excellent view of the entire thoracic cavity, including the mediastinum, and thus, is a good tool for biopsy of mediastinal lymph nodes. Thoracoscopic evaluation of the pleural cavity can clearly show invasion of the chest wall by intrathoracic malignancies. It also permits evaluation of the entire parietal pleural surface and the visceral pleural surface of the lung.

Importance of Lymph Node Staging

Lung Cancer
The modern lung cancer staging system was described by Naruke and Mountain [3,4]. The clinical importance of this system is its ability to successfully predict the outcome of patients on the basis of TNM staging. Most important is the distinction between hilar and mediastinal lymph node involvement in these patients (Figures 1 and 2). Not only has this staging system proven to be a useful prognosticator, but treatment strategies based on the presence or absence of mediastinal lymph node involvement have proven to be important in managing patients with lung cancer [5]. Although Whittesey [6] described the usefulness of the CT scan in predicting lymph node invasion in 1988, this noninvasive tool still remains only approximately 85% accurate in predicting malignant lymph nodes when lymph nodes are > 1.5 cm in size.

Esophageal Cancer
Lymph node stage is an important independent prognostic indicator in esophageal carcinoma (Figures and 4), as noted by Ellis et al [7]. Skinner et al [8] stressed the importance of node stage and recommended extended resection for esophageal cancer depending on operative lymph node staging. Akiyama et al [9] found that the pattern of lymph node spread in esophageal cancer showed metastasis to at least one thoracic node station in almost all cases. Metastasis to distant lymph nodes was not uncommon in their series. Preoperative staging of thoracic lymph node stations would be likely to reflect the actual lymph node status, provided that all lymph node stations could be assessed prior to surgery. Preoperative staging of esophageal cancer may allow us to allocate adjuvant therapy to patients in whom it would be most beneficial.

Surgical Staging Procedures
The classic approaches to mediastinal lymph node sampling include a variety of invasive techniques. Mediastinoscopy, described by Harken et al [10] in 1954 and popularized by Carlens [11] in 1959, is the standard tool for mediastinal lymph node biopsy. One limitation of this technique is the difficulty in sampling the aortopulmonary window and left para-aortic lymph nodes. Although extended transcervical mediastinoscopic biopsy of the aortopulmonary window is possible, it is a relatively complicated procedure [12]. Also, biopsy of subcranial lymph nodes may be difficult, especially when nodes are inferior and posterior. Lastly, mediastinoscopy also is not useful for biopsying masses in the anterior mediastinum, as this region is inaccessible to the mediastinoscope. The Chamberlain procedure (parasternal anterior mediastinotomy) provides an excellent approach to lymph node biopsy of the anterior mediastinum [13]. It is particularly useful for biopsy of the aortopulmonary window and para-aortic lymph nodes on the left but can also access lymph nodes or mediastinal masses on the right. The mediastinoscope can be inserted into the pleural space at the same sitting to further stage local disease. Desauliers et al described a combination of mediastinoscopy, pleuroscopy, and bimanual palpation to document lymph node involvement in the mediastinum [14]. The disadvantages of the Chamberlain procedure include the frequent requirement for rib resection, with resultant pain, longer hospital stay for recuperation, and a more disfiguring cosmetic result, compared with mediastinoscopy. Although proven in lung cancer, only recently has the importance of mediastinal lymph nodes been clarified in patients with esophageal cancer. In 1993, the initial results with thoracoscopic staging of esophageal cancer were reported. Although thoracic nodes were correctly staged in all patients, celiac nodes were missed in two patients [15]. Since then, routine thoracoscopic and laparoscopic lymph node staging has been used in patients with esophageal carcinoma with excellent results. Although as yet, there is no consensus regarding the role of surgical staging in patients with esophageal cancer, the results of pilot trials in which patients were treated with neoadjuvant therapy promise an important future role for this new technique in separating advanced esophageal cancer from local disease.

Role of Thoracoscopy

Lung Cancer
For patients with lung cancer, thoracoscopy is an excellent tool to augment other noninvasive and minimally invasive staging procedures. T3 lesions with suspicious direct spread to the chest wall can be evaluated prior to formal resection. Similarly, in patients who have suspicious T4 lesions with questionable mediastinal invasion, thoracoscopy can differentiate between abutment of the mediastinal pleura and mediastinal invasion by tumor. Thus, thoracoscopy can help avoid unnecessary thoracotomy in high-risk patients in whom one would want to avoid an unnecessary chest wall incision.

Thoracoscopy is also useful for evaluating primary tumor status in patients with pleural effusions. In those with suspicious T4 lesions, thoracoscopy may be useful in finding and evaluating malignant invasion of the pleura or a malignant pleural effusion. It can help determine the presence of pleural implants or invasion of the pericardium, the vagus, phrenic, or recurrent laryngeal nerves. Again, thoracoscopy can help avoid an unnecessary thoracotomy for attempted resection in the patient who is found to have gross disease spread.

Thoracoscopy is a particularly useful tool in evaluating mediastinal lymph nodes. It is used as a complement to standard cervical mediastinoscopy in evaluation of levels 2 through 11 mediastinal and hilar lymph nodes. Although mediastinoscopy is excellent for evaluating the upper and lower paratracheal nodes (American Thoracic Society [ATS] levels 2 through 4), evaluation of the subcranial nodes (level 7) or aortopulmonary and periaortic lymph nodes (ATS levels 5 and 6) is either difficult or impossible by standard techniques. We no longer perform the Chamberlain procedure (parasternal mediastinotomy) to evaluate the aortopulmonary window but instead use thoracoscopy to assess this area [16]. Thoracoscopy is especially helpful in patients who have lymph nodes in the aortopulmonary window that are > 1 cm or patients who have left-sided lung tumors in whom cervical mediastinoscopy does not show positive mediastinal lymph nodes.

Levels 8 and 9 paraesophageal and inferior pulmonary ligament lymph nodes are also considered N2 mediastinal lymph nodes according to the staging criteria. Despite this, the preoperative staging of these lymph node stations is almost never accomplished due to the inaccessibility of this region to cervical mediastinoscopy. Thoracoscopy is a useful tool to biopsy these stations preoperatively when they are enlarged. Thoracoscopy may help establish whether these stations are actually of the same
prognostic importance as are other mediastinal (N2) lymph nodes. Some surgeons have even suggested the use of routine thoracoscopic evaluation of the pleural cavity prior to all thoracotomies for lung cancer resection. The rationale behind this approach is to rule out previously unsuspected T4 lesions in patients who would otherwise undergo an unnecessary thoracotomy. At present, other than serving as a very useful training tool, there is no clear advantage of this technique in routine cases.

**Esophageal Cancer**

Despite aggressive surgical treatment of esophageal cancer, high perioperative morbidity and mortality are typical. Despite attempts at using combination therapy with chemotherapy, radiation therapy, and surgical resection in patients with esophageal cancer, 5-year survival rates have been disappointingly low [17-19]. If a subgroup of patients with a relatively good prognosis could be selected, survival rates with combination therapy and even standard surgical therapy might be significantly improved.

If it were possible to achieve accurate preoperative staging in esophageal cancer, patients could be separated prospectively into those likely to have residual local or lymphatic disease and those in whom complete resection is likely to be attainable. This would enable the physician to allocate modalities, such as adjuvant chemotherapy and radiation therapy, to the appropriate patient populations who would derive the greatest benefit, and thus, would limit the morbidity associated with these treatments.

Although surgery for esophageal carcinoma achieves the best immediate palliation currently available for dysphagia, many esophageal carcinoma lesions are found at the time of surgery to be full thickness (T3, T4) or to involve lymph nodes (N1). Mediastinal invasion by an esophageal carcinoma precludes a safe resection. The pathologic stage differs from the clinical stage in up to two-thirds of cases showing full-thickness tumors or lymphatic spread. Surgical staging thus may identify those individuals who are candidates for aggressive palliative or nonsurgical treatment regimens and avoid unnecessary surgical resections.

Huang and Sun have shown that, among patients with esophageal carcinoma, the 5-year survival rate in patients without lymph node metastases was 45%, as compared with 13% in those with lymph node spread. Likewise, when more than five nodes were involved, the survival rate was 0%, as opposed to 15% when fewer than five nodes were involved [20]. Hagen et al [21] have recently claimed an improved survival benefit for patients with complete lymphadenectomy associated with esophagectomy for distal third and gastroesophageal junction tumors. In 1986 Dagnini et al [22] described the routine use of laparoscopy before undertaking esophagectomy for esophageal cancer. Of 369 patients, intra-abdominal metastases were noted in 14% and celiac lymph node metastases in 9.7%.

In 1977 Murray et al [23] described the use of mediastinoscopy and "mini-laparotomy" in patients with esophageal cancer. In their series of 30 patients, 5 had positive lymph nodes at mediastinoscopy and 16 had positive nodes at mini-laparotomy. This finding supports the use of an operative staging tool to differentiate localized from advanced esophageal cancer.

**Thoracoscopy Techniques**

The operating room set-up for thoracoscopy involves placing the patient in the standard lateral decubitus position for thoracotomy (Figure 5). One television monitor is placed over the patient's head and a second video monitor is positioned over the patient's legs. The video cable, light source, cautery, irrigation and suction, hard copy/camera, and VCR are placed behind the first assistant. This set-up allows the surgeon and first assistant to visualize the same field equally, without the occasional confusion "mirror image" that can occur with video screens.

The patient is intubated with a double-lumen endotracheal tube. This allows for collapse of the ipsilateral lung, which is of paramount importance to achieve good exposure. The first incision is made along the posterior axillary line in the sixth intercostal space, and a trocar is inserted. Two additional incisions are made at the fifth intercostal space anterior axillary line and at the seventh or eighth intercostal space anterior axillary line (Figures 6 and 7). This three-pronged approach allows for clear visualization of the entire thoracic cavity. The technique also permits the different devices all to work on a location at the base of an "upside-down pyramid."

During the procedure, 0° and 30° fiberoptic telescopes should be available. We find it is often helpful to use carbon dioxide insufflation in these patients, as this allows the lung to be compressed. Currently, we have the pleural pressure set at 10 mm or less Hg and flow at < 2.5 L/min. This level has been found to facilitate exposure without causing complications to a small nubbin [24]. Together
with manipulating the position of the bed, exposure is facilitated, allowing the lung to be easily moved out of the way.

We currently employ three 12-mm trocars. Specially designed retractors and lung clamps have been developed, which are atraumatic. A thoracotomy tray should always be available in the room. A thorough exploratory thoracoscopic should be done to systematically assess the entire chest.

Anteriorly, the pericardium, phrenic nerve, and internal mammary vessels are identified. Superiorly, the subclavian vessels and the cupula of the pleura are inspected. Posteriorly, the aorta, vagus, esophagus, and periaortic lymph nodes are inspected. Finally, the inferior chest cavity is examined, specifically, the diaphragm and inferior pulmonary ligament and any lymph nodes in this region. In this fashion, any enlarged node can be identified and evidence of pleural metastases or direct spread can be found (Figures 8A and 8B).

**Right-Sided Thoracoscopic Staging of Esophageal Cancer**

The mediastinal pleura overlying the proximal esophagus is elevated just lateral to the posterior edge of the trachea. Using an endoshears with an electrocautery attachment, the pleura is incised from the level of the subclavian vessels (Figure 9). All fat and any obvious lymph nodes in this region are removed for sampling. In addition to electrocautery, an endoclips is used to achieve hemostasis. The azygos vein itself is then mobilized to access lymph nodes underneath (Figure 10). If this is difficult, the azygos vein can be divided using an Endogia vascular stapler. Level 10 lymph nodes in the subazygos region are easily sampled. By retracting the lung anteriorly after grasping the superior segment of the right lower lobe, the subcarinal space can be identified.

The mediastinal pleura is next incised from the azygos vein to the subcarinal region and finally to the inferior pulmonary vein. The paraesophageal groove is dissected, and biopsies of all nodes are taken using hemoclips for hemostasis. The lung retractor is moved to the upper incision, and the lower lobe is grasped and retracted superiorly. The inferior pulmonary ligament is then divided using an endoshears with electrocautery. Once the inferior pulmonary vein is visualized, the dissection is complete, and level 9 lymph nodes are biopsied using cautery and/or hemoclips for hemostasis.

The chest is irrigated and examined for hemostasis or air leak from retraction. A single 24-French chest tube is placed posteriorly and secured with 2-0 silk sutures. The remaining incisions are closed with a 3-0 vicryl subcutaneous and subcuticular suture.

**Left-Sided Thoracoscopic Lymph Node Biopsy**

After the chest is entered, inspection of the aortopulmonary window will identify level 5 and 6 lymph nodes. The rest of the hemithorax is examined for evidence of gross esophageal tumor extension or metastatic disease to the lung.

A biopsy grasper is used to elevate the mediastinal pleura overlying the lymph nodes (Figure 11), and a bipolar electrocautery probe or monopolar cautery scissors is used to incise the pleura. The incision is continued up to the apex of the triangle formed by the phrenic and vagus nerves. Inferiorly, the pleura is incised over the left main pulmonary artery. Lymph nodes in this region are mobilized, and the vascular pedicle is ligated with an endoscopic clip applier. The nodes are removed, and the area is irrigated with a saline solution. Once hemostasis is assured and no air leaks are noted, a chest tube is left, and the incisions are closed as described above.

**Laparoscopy Technique**

**Celiac Axis and Perigastric Lymph Node Sampling**

The patient is placed in the supine position, with the surgeon standing on the patient's left. Both monitors are placed at the head of the table. The abdomen is prepared and draped for a standard laparotomy. The procedure is begun with three operating ports (all 12 mm in diameter), although a fourth port may be necessary in the left upper quadrant for retraction of the stomach and placement of tension on the hepatogastric ligament, or lesser omentum (Figure 12). An angled laparoscope (30° or greater) is helpful for exposure of the operative field. We have recently begun using an operating scope for the laparoscopic staging procedure to allow four instruments to be used with three trocars.

After thorough exploration of the peritoneal cavity, the surface of the liver is inspected, and gross abnormalities are biopsied and sent for frozen section. The liver is retracted with an expandable fan retractor, and the lesser sac is entered using sharp dissection through the lesser omentum, just to the right of the esophagus. The dissection is carried cranial toward the right crus of the diaphragm. Most of this dissection may be performed with electrocautery, but clips may occasionally be necessary. When very large vessels are seen in this area, we use an Endogia stapler with a vascular load (2.5-mm). Lymph nodes identified along the lesser curve are biopsied. Pulsations from the right gastric artery are visible caudally, and division of the omentum may stop at this point. Exposure of
the celiac axis is achieved by elevating the lesser curve of the stomach near the gastroesophageal junction. The left gastric artery is identified by its pulsation as it projects straight up from the celiac axis and enters the posterior wall of the stomach (Figures 13), and small lymph nodes can usually be found.

After completion of lymph node sampling, the field is irrigated and the area is inspected for hemostasis. In cachectic patients, we generally place a laparoscopic jejunostomy immediately before terminating the procedure. A mediport for chemotherapy can also be placed at this time.

**Results**

**Lung Cancer**
We used thoracoscopy to stage lung cancer in nine patients (Table 1). Mediastinal lymph node sampling was performed in five patients, and in four, the evaluation was correct. Patients with positive IIIA or IIIB disease were referred for neoadjuvant chemoradiation. Despite negative cervical mediastinoscopy and thoracoscopy assessment of the level 7 node, one patient was found to have a positive lymph node in the subcarinal space at resection. One patient underwent preoperative thoracoscopy to rule out N3 as well as T4 disease in the contralateral space. Three patients underwent thoracoscopic evaluation of direct tumor spread and were shown to have T4 disease with mediastinal invasion. In all of these patients, an unnecessary thoracotomy was avoided [25].

There were no deaths. One patient developed staphylococcal empyema, which was treated by intravenous antibiotics and chest tube drainage. The mean duration of chest tube drainage was 1.8 days, and the mean duration of hospital stay was 2.3 days.

**Esophageal Cancer**
We performed thoracoscopic lymph node staging in 46 patients with biopsy-proven carcinoma of the esophagus between June 1992 and June 1995 [26]. Laparoscopic lymph node staging was done in the last 20 patients as well. Thoracoscopic staging was aborted in three patients due to adhesions. Thoracic lymph node stage was N0 in 40 patients and N1 in 3; celiac nodes were negative in 14 patients and positive in 6.

Esophageal resection was performed in 31 patients after thoracoscopy, 18 of whom also underwent laparoscopy. Thoracoscopic-laparoscopic lymph node staging showed N0 lymph node status in 29 patients and N1 in 2 patients (Figure 14). Of the 29 N0 patients, 2 (7%) were found at resection to have paraesophageal lymph node involvement (N1) and were thus understaged by thoracoscopy-laparoscopy. Thoracoscopic-laparoscopic lymph node staging was accurate, therefore, in detecting the presence of thoracic lymph node involvement in 29/31 cases (93%).

Laparoscopic staging found negative celiac nodes in 13 patients and positive nodes in 5 patients. After esophagectomy, final pathology of the 13 N0 patients was N0 in 12 and positive lymph node in 1 patient. Thus, laparoscopic staging was accurate in detecting lymph node metastases in 17/18 patients (94%). Of the patients who underwent laparoscopic staging, 5 had unsuspected celiac axis nodal involvement missed by standard noninvasive techniques. After preoperative chemotherapy plus radiotherapy, 3% of thoracic nodes and 17% of celiac nodes were downstaged.

**Discussion**
Thoracoscopy is a useful technique that complements cervical mediastinoscopy in the definitive surgical staging of lung cancer. Cervical mediastinoscopy remains the standard surgical staging tool for patients with N2 and N3 non-small-cell lung cancer [27]. Obtaining definitive pathologic diagnosis of the status of the mediastinal lymph nodes allows for accurate determination of prognosis and allocation of patients to adjuvant therapy protocols prior to resection.

Thoracoscopy is also useful for ruling out resection on the basis of invasion of mediastinal structures (T4 tumors). This procedure can thus avoid unnecessary thoracotomies in patients who may have advanced locoregional disease, which would preclude a complete resection [28]. Although we did miss the correct T stage in one patient, we have recently advocated exploring the intrapericardial vessels using thoracoscopy to more accurately stage these patients.

Many noninvasive tests are currently used in the preoperative evaluation of esophageal cancer, although their usefulness in lymph node staging is limited (Figure 14). Reports in the literature have not shown preoperative noninvasive lymph node staging to be particularly successful. CT and MRI have proved unreliable as predictors for lymph node involvement in esophageal cancer [29]. Although esophageal ultrasound (EUS) was useful in determining T status in patients with esophageal cancer in one study, EUS correctly assessed lymph node status preoperatively in fewer than 70% of patients in this series [30].
Preoperative thoracoscopic-laparoscopic lymph node staging may be as useful in esophageal cancer staging as cervical mediastinoscopy has proved to be in lung cancer staging. If thoracoscopy shows local spread of disease, this may avoid unnecessary resection in patients with T4 disease. A prospective multi-institutional pilot trial [31] utilizing thoracoscopy and laparoscopy in patients with esophageal cancer has been completed, and a prospective multi-institutional trial (CALGB 9380) is now underway to evaluate the role of this staging procedure in esophageal cancer.

**Conclusions**

Thoracoscopic surgery appears to be highly effective in intrathoracic TNM staging for lung cancer, and can be used in conjunction with cervical mediastinoscopy for this purpose. Thoracoscopy is well tolerated, and patients who undergo this minimally invasive technique generally can be discharged the next day. Although we routinely insert chest tubes in these patients, it is possible that tubes may not be needed at all in patients with no bleeding or parenchymal disease. Pain and discomfort are minimal with the operation. Not only can patients be discharged home early, but also they generally can return to work as early as 7 to 10 days after surgery.

In developing this new technique as a standard staging tool for intrathoracic malignancies, thoracoscopic staging must be correlated with both the preoperative assessment using radiographic means and the final biopsy diagnosis made at the time of thoracotomy. This will standardize the technique and determine its overall efficacy. A careful analysis of preoperative lymph node status may prove to be a helpful tool in allocating patients to adjuvant chemotherapy or radiation therapy. Thus far, thoracoscopy has proved very useful and easy to perform technically. If prospective studies of staging esophageal cancer confirm our findings to date, in the future thoracoscopic-laparoscopic lymph node staging can be incorporated into multimodality protocols to allocate therapy to node-positive patients.

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