Patterns of Lymphadenopathy in Thoracic Malignancies

Amita Sharma, FRCR, Panos Fidias, MD, L. Anne Hayman, MD, Susanne L. Loomis, MS, Katherine H. Taber, PhD and Suzanne L. Aquino, MD

From the Departments of Radiology (A.S., S.L.L., S.L.A.) and Medicine (P.F.), Massachusetts General Hospital, Harvard Medical School, 55 Fruit St, Founders 202, Boston, MA 02114; and the Department of Radiology and Herbert J. Frensley Center for Imaging Research, Baylor College of Medicine, Houston, Tex (L.A.H., K.H.T.). Presented as an education exhibit at the 2002 RSNA scientific assembly. Received March 19, 2003; revision requested April 29; final revision received November 6; accepted November 7. Address correspondence to A.S. (e-mail: asharma2@partners.org).

Introduction

The accurate classification of nodal involvement in a patient with malignancy is important. Computed tomography (CT) is the primary modality for imaging malignancy in the chest. It is used in staging the disease, planning treatment, evaluating response, and estimating prognosis. Knowledge of the drainage pathways of different malignancies is extremely useful as it directs the radiologist to the relevant nodal stations. Radiologists should therefore be aware of the criteria for evaluating mediastinal lymphadenopathy, the sites of the thoracic lymph nodes, and the limitations of CT.

Nodal tissue is present within the mediastinum and is often seen at chest CT. It is mainly situated around the distal trachea, carina, and main bronchi (1).
Autopsy studies and CT studies confirm that the average sizes of normal lymph nodes vary depending on their region (2–4). The majority of CT studies record the short-axis diameter of a lymph node, as this is the most reproducible measurement (3). Low paratracheal and subcarinal nodes can measure up to 11 mm in short-axis diameter. Nodes in the superior mediastinum and high paratracheal space are generally smaller and measure up to 7 mm. Normal right hilar and periesophageal nodes can be up to 10 mm in diameter, and left hilar and periesophageal nodes can be up to 7 mm in short-axis diameter. To simplify measurements, a lymph node in the paratracheal, hilar, subcarinal, paraesophageal, paraaortic, or subaortic region is generally considered enlarged if the short-axis diameter is greater than or equal to 10 mm (3,5).

There are very few data on the size of thoracic lymph nodes outside the mediastinum. Peridiaphragmatic nodes are considered abnormal if greater than 5 mm in short-axis diameter (6). No size criteria are available for internal mammary, retrocrural, and extrapleural nodes, and detection of these nodes should be considered abnormal.

There are limitations to use of size criteria to determine the presence or absence of nodal metastases, since metastases occur in normal-sized nodes and nodal enlargement can be secondary to benign conditions such as granulomatous disease (7).

Evaluation of the mediastinum for the presence of metastatic nodal disease with fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) involves assessment of metabolic activity rather than node size. FDG PET has been shown to reflect metastatic involvement more accurately than CT (8,9). The poor anatomic resolution of FDG PET may be overcome with CT and FDG PET fusion imaging, whereby the site of increased uptake at FDG PET can be accurately defined with CT.

The International Lymph Node Classification and the International System for Staging Lung Cancer adopted by the American Joint Committee on Cancer (AJCC) and the Union Internationale Contre le Cancer (UICC) have defined the lymph node stations in the hila and mediastinum that are relevant to the staging of lung cancer (10). These stations can be applied to tumors of the breast, esophagus, and pleura and to lymphomas. However, additional lymph node regions in the thorax that are not included in this nomenclature can also be involved by tumor metastases.

This article describes the normal drainage pathways of the lung, breast, esophagus, and pleura. The sites of nodal metastases and their relevance in staging are presented with clinical radiologic examples. The role and limitations of imaging techniques, especially CT, are evaluated.

## Lung Cancer

The lungs have a rich lymphatic supply that consists of a pleural and parenchymal network (11). The pleural lymphatics course over the parietal and visceral pleural surfaces and drain into the medial aspect of the lung near the hilum, where they anastomose with the parenchymal lymphatics. The parenchymal lymphatics are located in the interlobular septa and bronchovascular bundles. Multiple lymphatic channels anastomose with each other before draining sequentially into the intralobular, interlobular, lobar, and finally the hilar nodes. The entire lymphatic system clears interstitial fluid from the lungs and removes foreign particles and antigens. This pathway is also responsible for the spread of tumor from the lung to the hilum and subsequently into the mediastinum.

The hilar nodes drain into the mediastinum, but the mediastinal pathways are variable and are related to the lobe of origin of the pulmonary lymphatics. Studies of lung cancer in various lobes confirm that nodal pathways are largely dependent on the lobe origin of the tumor (Fig 1) (12,13). Most parenchymal tumors drain to the hilar nodes before reaching the
mediastinum. Lesions of the right upper lobe predominantly then drain into the right paratracheal and anterior mediastinal nodes. Right middle and lower lobe tumors predominantly drain into the subcarinal nodes and subsequently into the right paratracheal and anterior mediastinal nodes. Left upper lobe tumors drain to the subaortic and paraaortic nodes, and left lower lobe tumors drain to the subcarinal and subaortic nodes.

**Figure 1a.** Diagrams of the axial anatomy of the chest show the lymph nodes and drainage pathways for lung cancer in different lobes of the lung. All tumors drain to the interlobar and hilar nodes. The separate drainage pathways for tumors of the right upper lobe (black nodes), middle lobe (dark gray nodes), right lower lobe (striped nodes), left upper lobe (crosshatched nodes), and left lower lobe (dotted nodes) are shown. The corresponding American Thoracic Society (ATS) stations are labeled. **E** = esophagus, **TD** = thoracic duct. (a) Diagram shows the left paratracheal nodes (LPTN) (ATS station 2L) and right paratracheal nodes (RPTN) (ATS station 2R). **LBCV** = left brachiocephalic vein, **LCCA** = left common carotid artery, **LSCA** = left subclavian artery, **RBCA** = right brachiocephalic artery, **RBCV** = right brachiocephalic vein, **Tr** = trachea. (b) Diagram shows the left paratracheal nodes (LPTN) (ATS station 4L), right paratracheal nodes (RPTN) (ATS station 4R), and subaortic nodes (SAN) (ATS station 5). **AA** = ascending aorta, **Ao** = aorta, **SVC** = superior vena cava, **Tr** = trachea. (c) Diagram shows the hilar nodes (HN) (ATS station 10), interlobar nodes (ILN) (ATS station 11), lobar nodes (LN) (ATS station 12), and subcarinal nodes (SCN) (ATS station 7). **Ao** = aorta, **BI** = bronchus intermedius, **LMB** = left main bronchus, **LPA** = left pulmonary artery, **LULB** = left upper lobe bronchus, **PA** = pulmonary artery, **RPA** = right pulmonary artery, **SPV** = superior pulmonary vein, **SVC** = superior vena cava. (d) Diagram shows the left inferior pulmonary ligament node (LIPLN) (ATS station 9) and right inferior pulmonary ligament node (RIPLN) (ATS station 9). **Ao** = aorta, **CS** = coronary sinus, **ECF** = epicardial fat, **LV** = left ventricle, **RA** = right atrium, **RV** = right ventricle.
Figure 1b. Diagrams of the axial anatomy of the chest show the lysmph nodes and drainage pathways for lung cancer in different lobes of the lung. All tumors drain to the interlobar and hilar nodes. The separate drainage pathways for tumors of the right upper lobe (black nodes), middle lobe (dark gray nodes), right lower lobe (striped nodes), left upper lobe (crosshatched nodes), and left lower lobe (dotted nodes) are shown. The corresponding American Thoracic Society (ATS) stations are labeled. E = esophagus, TD = thoracic duct. (a) Diagram shows the left paratracheal nodes (LPTN) (ATS station 2L) and right paratracheal nodes (RPTN) (ATS station 2R). LBCV = left brachiocephalic vein, LCCA = left common carotid artery, LSCA = left subclavian artery, RBCA = right brachiocephalic artery, RBCV = right brachiocephalic vein, Tr = trachea. (b) Diagram shows the left paratracheal nodes (LPTN) (ATS station 4L), right paratracheal nodes (RPTN) (ATS station 4R), and subaortic nodes (SAN) (ATS station 5). AA = ascending aorta, Ao = aorta, SVC = superior vena cava, Tr = trachea. (c) Diagram shows the hilar nodes (HN) (ATS station 10), interlobar nodes (ILN) (ATS station 11), lobar nodes (LN) (ATS station 12), and subcarinal nodes (SCN) (ATS station 7). Ao = aorta, BI = bronchus intermedius, LMB = left main bronchus, LPA = left pulmonary artery, LULB = left upper lobe bronchus, PA = pulmonary artery, RPA = right pulmonary artery, SPV = superior pulmonary vein, SVC = superior vena cava. (d) Diagram shows the left inferior pulmonary ligament node (LIPLN) (ATS station 9) and right inferior pulmonary ligament node (RIPLN) (ATS station 9). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, LV = left ventricle, RA = right atrium, RV = right ventricle.

Figure 1c. Diagrams of the axial anatomy of the chest show the lymph nodes and drainage pathways for lung cancer in different lobes of the lung. All tumors drain to the interlobar and hilar nodes. The separate drainage pathways for tumors of the right upper lobe (black nodes), middle lobe (dark gray nodes), right lower lobe (striped nodes), left upper lobe (crosshatched nodes), and left lower lobe (dotted nodes) are shown. The corresponding American Thoracic Society (ATS) stations are labeled. E = esophagus, TD = thoracic duct. (a) Diagram shows the left paratracheal nodes (LPTN) (ATS station 2L) and right paratracheal nodes (RPTN) (ATS station 2R). LBCV = left brachiocephalic vein, LCCA = left common carotid artery, LSCA = left subclavian artery, RBCA = right brachiocephalic artery, RBCV = right brachiocephalic vein, Tr = trachea. (b) Diagram shows the left paratracheal nodes (LPTN) (ATS station 4L), right paratracheal nodes (RPTN) (ATS station 4R), and subaortic nodes (SAN) (ATS station 5). AA = ascending aorta, Ao = aorta, SVC = superior vena cava, Tr = trachea.
However, mediastinal metastases may occur through direct lymphatic drainage that
bypasses the hilar nodes (13, 14). This is most commonly seen in the upper lobes. In rare instances, a direct connection may exist between the pulmonary segments and the thoracic duct, enabling direct passage of tumor into the systemic circulation without mediastinal node involvement (15).

In a patient with lung cancer, the nodal status determines surgical resectability. The TNM classification system for lung cancer (Table 1) (16) defines N1 disease as involvement of ipsilateral peribronchial, hilar, or intrapulmonary nodes (Fig 2). N1 nodes lie within the pleural reflection and correspond to ATS stations 10–14 (10). Cases of N1 disease are considered surgically resectable in the absence of mediastinal invasion by tumor, a malignant pleural effusion, satellite nodules, or metastases. Ipsilateral mediastinal or subcarinal node involvement is classified as N2 disease (Fig 3). These nodes lie outside the pleural reflection and correspond to ATS stations 1–9 (10). These cases may be amenable to surgery, but treatment also involves chemotherapy and irradiation. Contralateral mediastinal or hilar node involvement and disease in the supraclavicular nodes are classified as N3 disease (Fig 4). This is advanced disease, and patients are not surgical candidates.

**TABLE 1. Nodal Staging in Lung Cancer according to the AJCC TNM Classification**

---

**Figure 2.** Adenocarcinoma of the left upper lobe in a 60-year-old woman. CT scan shows a 3-cm-diameter left hilar node (ATS station 10) (arrow). At lobectomy, this node contained tumor tissue, whereas all other nodes were negative. This finding corresponds to N1 disease.
CT is the most useful preoperative, noninvasive method of assessing for thoracic lymphadenopathy. However, nodal size cannot be used reliably to indicate metastatic involvement (7). McLoud et al (7) reported that 13% of nodes measuring less than 1 cm in evaluated patients with lung cancer were metastatic. Although the prevalence of metastatic disease increased with nodal size, one-third of nodes 2–4 cm in diameter were hyperplastic and did not contain metastases. A metaanalysis of 20 studies evaluated the accuracy of mediastinal staging for lung cancer with CT (5). Toloza et al (5) reported a pooled sensitivity for CT of 0.57 (95% confidence interval, 0.49–0.66) and specificity of 0.82 (95% confidence interval, 0.77–0.86). The overall positive predictive value and negative predictive value were 0.56 (range, 0.26–0.84) and 0.83 (range, 0.63–0.93), respectively.

The role of chest CT is to allow identification of enlarged lymph nodes and document their exact location so that an appropriate method for biopsy may be chosen, such as mediastinoscopy or fine-needle aspiration via a transbronchial, transesophageal, or transthoracic route.

Distinction between the different nodal stations around the right tracheobronchial angle can be difficult at CT, as the parietal pleural reflection is not visible (17). N1 nodes are within the confines of the pleural reflection and are therefore intrapulmonary. N2 nodes are outside the pleural reflection and are therefore mediastinal. The pleural reflection begins at the origin of the right upper lobe bronchus. Lymph nodes proximal to this bronchus should be considered mediastinal in location.
Magnetic resonance (MR) imaging is essentially equivalent to CT in staging, although Crisci et al (18) found that the administration of gadolinium contrast material improved staging accuracy. MR imaging is superior to CT in the evaluation of superior sulcus tumors for invasion of the brachial plexus or vertebral bodies.

FDG PET has shown significant improvement in radiologic staging of lung cancer. A metaanalysis of 18 studies (5) demonstrated a pooled sensitivity of 0.84 (95% confidence interval, 0.78–0.89) and specificity of 0.89 (95% confidence interval, 0.83–0.93). The overall positive predictive value and negative predictive value were 0.79 (range, 0.40–1.00) and 0.93 (range, 0.75–1.00), respectively. Because false-positive uptake of FDG can be seen with inflammatory and granulomatous diseases involving the lymph nodes, pathologic confirmation of mediastinal nodal involvement should be undertaken when there is increased uptake in mediastinal lymph nodes (5).

Breast Cancer

The breast and overlying skin are derived from the ectoderm and act as a single functional unit (19–21). The lymphatic drainage of the breast occurs through three principal routes: the axillary, transpectoral, and internal mammary pathways (22). According to Sappey (23), the skin, nipple, lactiferous tubules, and surrounding parenchyma drain into the subareolar plexus, which divides into medial and lateral trunks. The medial trunk receives lymph from the inferior breast. The lateral trunk receives lymph from the superior breast. These two trunks drain into the lower axillary lymph nodes (Fig 5). Studies by Tanis et al (20) also describe a direct route to the axilla, which may bypass the subareolar plexus.

Figure 5a. Axial diagrams show the main drainage pathways (black nodes) of breast cancer to the axillary, internal mammary, and supraclavicular lymph nodes. E = esophagus, Tr = trachea. (a) Diagram shows the axillary nodes (AN), anterior scalene/supravclavicular nodes (ASSCN), and pectoral nodes (PN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJ = left jugular vein, RCCA = right common carotid artery, RJ = right jugular vein. (b) Diagram shows the axillary nodes (AN), pectoral nodes (PN), and subclavian chain nodes (SCCN). LCCA = left common carotid artery, LJSCC = left juguloussubclavian confluence, LSCA = left subclavian artery, LSCV = left subclavian vein, RBCA = right brachiocephalic artery, RJSCC = right juguloussubclavian confluence, RSCV = right subclavian vein, TD = thoracic duct. (c) Diagram shows the axillary nodes (AN), internal mammary/retromamribial nodes (IMRNN), and pectoral nodes (PN). LBCV = left brachiocephalic vein, LCCA = left common carotid artery, LSCA = left subclavian artery, RBCA = right brachiocephalic artery, RBCV = right brachiocephalic vein, TD = thoracic duct.
The axillary lymph nodes are divided into three levels with respect to their position relative to the pectoralis minor muscle (16) (Fig 6). Level I nodes, or low axillary nodes, lie lateral to the...
The **lymphatics** that drain the medial breast perforate the pectoral and intercostal muscles and enter the internal mammary **lymph nodes** (Fig 8). The internal mammary **nodes** and **lymphatics** lie in the intercostal spaces along the margins of the sternum and are usually present from the fifth intercostal space to the clavicles. Rarely, the breast parenchyma may drain directly into the supraclavicular **nodes**. When tumor obstructs normal **lymphatic** flow, collateral pathways open. These include contralateral internal mammary and **mediastinal lymphatics**. Spread through the rectus abdominus muscle sheath to the subdiaphragmatic and subperitoneal plexus may lead to spread to the liver and retroperitoneal **nodes**.
In patients with breast cancer, lymph node status is one of the most important prognostic factors (16). The TNM staging system for breast cancer (Table 2) classifies mobile axillary nodes as N1. The confirmation of N1 disease requires chemotherapy and/or hormone therapy in addition to surgery. Axillary nodes that are fixed to each other or to adjacent structures are classified as N2. The confirmation of N2 disease requires chemotherapy and radiation therapy in addition to surgery. Further subdivisions depend on the number of positive axillary nodes. Isolated ipsilateral internal mammary nodal disease is defined as N2. If both the axillary and internal mammary nodes are involved, this is defined as N3 (16). Disease involving infraclavicular and supraclavicular nodes is also defined as N3. Preoperative chemotherapy is necessary in cases of N3 disease.

| TABLE 2. Nodal Staging in Breast Cancer according to the AJCC TNM Classification |

In patients with small tumors and clinically negative axillae, preoperative sentinel node imaging is useful in limiting the extent of surgical intervention (24–26). This node can be imaged by injecting technetium-99m radiocolloid or blue dye into or adjacent to the tumor (21). The first draining axillary node or sentinel node is identified and resected. If this node is free of tumor, further dissection is not performed.

CT does not currently have a role in the preoperative staging of every patient with newly diagnosed breast cancer. The sensitivity of CT for axillary metastases is reported as only 50%–60% (27, 28). CT is used in the assessment of a patient with a large tumor or with palpable, fixed axillary nodes, where there is high suspicion of occult metastatic disease.

Improved accuracy has been achieved by using thin-section CT in patients lying prone (29). CT identification of the sentinel lymph node has also shown good correlation with dye- and gamma probe–guided sentinel lymph node biopsy (30). This is defined at CT as the most inferior lymph node adjacent to the lateral thoracic vessels.
The lymphomas are a diverse group of neoplastic disorders. They are divided into Hodgkin disease (characterized by the presence of Reed-Sternberg cells) and non-Hodgkin lymphoma. Further subdivisions depend on the histologic type. A number of pathologic classifications have been described. The most updated and widely used classification is the combined Revised European-American Classification of Lymphoid Neoplasms (REAL)/World Health Organization Classification of Lymphoid Neoplasms (31).

More than 80% of patients with Hodgkin disease have intrathoracic involvement at initial presentation (32). In the thorax, Hodgkin disease most frequently involves the anterior mediastinal and paratracheal regions (Fig 9) and tends to spread to contiguous nodal groups. The subcarinal, peridiaphragmatic, periesophageal, and internal mammary nodes are involved in decreasing order of frequency. In most patients, two or more nodal groups are involved at initial presentation. Isolated hilar involvement is rare and should suggest an alternative diagnosis.

**Figure 9a.** Axial diagrams show the main intrathoracic drainage pathways (black nodes) for lymphoma. E = esophagus, TD = thoracic duct. (a) Diagram shows the internal mammary/retromanubrial nodes (IMRMN), left bronchomediastinal trunk node (LBMTN), left paratracheal node (LPTN), preaortocarotid node (PACN), periesophageal/posterior mediastinum nodes (PEPMN), right brachiocephalic angle node (RBCAN), right phrenic node (RPN), and right paratracheal nodes (RPTN). LBCV = left brachiocephalic vein, LCCA = left common carotid artery, LSCA = left subclavian artery, RBCA = right brachiocephalic artery, RBCV = right brachiocephalic vein, Tr = trachea. (b) Diagram shows the internal mammary nodes (IMN), left phrenic node (LPN), periesophageal/posterior mediastinum nodes (PEPMN), right phrenic node (RPN), and right paratracheal nodes (RPTN). AA = aortic arch, LBCV = left brachiocephalic vein, RBCV = right brachiocephalic vein, Tr = trachea. (c) Diagram shows the extrapleural nodes (EPN), internal mammary nodes (IMN), lobar node (LN), left phrenic node (LPN), periesophageal/posterior mediastinum nodes (PEPMN), subcarinal node (SCN), and segmental node (SN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava. (d) Diagram shows the pericardial fat nodes (PCFN) and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, LV = left ventricle, PCF = pericardial fat, RA = right atrium, RV = right ventricle. (e) Diagram shows the anterior peridiaphragmatic...
Figure 9b. Axial diagrams show the main intrathoracic drainage pathways (black nodes) for lymphoma. E = esophagus, TD = thoracic duct. (a) Diagram shows the internal mammary/retromanubrial nodes (IMRMN), left bronchomediastinal trunk node (LBMTN), left paratracheal node (LPTN), preaortocarotid node (PACN), periesophageal/posterior mediastinum nodes (PEPMN), right brachiophecalic angle node (RBCAN), right phrenic node (RPN), and right paratracheal nodes (RPTN). LBCV = left brachiocephalic vein, LCCA = left common carotid artery, LSCA = left subclavian artery, RBCA = right brachiophecalic artery, RBCV = right brachiophecalic vein, Tr = trachea. (b) Diagram shows the internal mammary nodes (IMN), left phrenic node (LPN), periesophageal/posterior mediastinum nodes (PEPMN), right phrenic node (RPN), and right paratracheal nodes (RPTN). AA = aortic arch, LBCV = left brachiocephalic vein, RBCV = right brachiophecalic vein, Tr = trachea. (c) Diagram shows the extrapleural nodes (EPN), internal mammary nodes (IMN), lobar node (LN), left phrenic node (LPN), periesophageal/posterior mediastinum nodes (PEPMN), subcarinal node (SCN), and segmental node (SN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava. (d) Diagram shows the pericardial fat nodes (PCFN) and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, LV = left ventricle, PCF = pericardial fat, RA = right atrium, RV = right ventricle. (e) Diagram shows the anterior peridiaphragmatic nodes (APDN), extrapleural nodes (EPN), gastrohepatic ligament/celiac nodes (GHLCN), and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta.
Figure 9c. Axial diagrams show the main intrathoracic drainage pathways (black nodes) for lymphoma. E = esophagus, TD = thoracic duct. (a) Diagram shows the internal mammary/retromanubrial nodes (IMRMN), left bronchomediastinal trunk node (LBMTN), left paratracheal node (LPTN), preaortocarotid node (PACN), periesophageal/posterior mediastinum nodes (PEPMN), right brachiocephalic angle node (RBCAN), right phrenic node (RPN), and right paratracheal nodes (RPTN). LBCV = left brachiocephalic vein, LCCA = left common carotid artery, LSCA = left subclavian artery, RBCA = right brachiocephalic artery, RBCV = right brachiocephalic vein, Tr = trachea. (b) Diagram shows the internal mammary nodes (IMN), left phrenic node (LPN), periesophageal/posterior mediastinum nodes (PEPMN), right phrenic node (RPN), and right paratracheal nodes (RPTN). AA = aortic arch, LBCV = left brachiocephalic vein, RBCV = right brachiocephalic vein, Tr = trachea. (c) Diagram shows the extrapleural nodes (EPN), internal mammary nodes (IMN), lobar node (LN), left phrenic node (LPN), periesophageal/posterior mediastinum nodes (PEPMN), subcarinal node (SCN), and segmental node (SN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava. (d) Diagram shows the pericardial fat nodes (PCFN) and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, LV = left ventricle, PCF = pericardial fat, RA = right atrium, RV = right ventricle. (e) Diagram shows the anterior peridiaphragmatic nodes (APDN), extrapleural nodes (EPN), gastrohepatic ligament/celiac nodes (GHLCN), and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta.

Figure 9d. Axial diagrams show the main intrathoracic drainage pathways (black nodes) for lymphoma. E = esophagus, TD = thoracic duct. (a) Diagram shows the internal mammary/retromanubrial nodes (IMRMN), left bronchomediastinal trunk node (LBMTN), left paratracheal node (LPTN), preaortocarotid node (PACN), periesophageal/posterior mediastinum nodes (PEPMN), right brachiocephalic angle node (RBCAN), right phrenic node (RPN), and right paratracheal nodes (RPTN). LBCV = left brachiocephalic vein, LCCA = left common carotid artery, LSCA = left subclavian artery, RBCA = right brachiocephalic artery, RBCV = right brachiocephalic vein, Tr = trachea. (b) Diagram shows the internal mammary nodes (IMN), left phrenic node (LPN), periesophageal/posterior

mediastinum nodes (PEPMN), right phrenic node (RPN), and right paraatracheal nodes (RPTN). AA = aortic arch, LBCV = left brachiocephalic vein, RBCV = right brachiocephalic vein, Tr = trachea. (c) Diagram shows the extrapleural nodes (EPN), internal mammary nodes (IMN), lobar node (LN), left phrenic node (LPN), periesophageal/posterior mediastinum nodes (PEPMN), subcarinal node (SCN), and segmental node (SN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava. (d) Diagram shows the pericardial fat nodes (PCFN) and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, LV = left ventricle, PCF = pericardial fat, RA = right atrium, RV = right ventricle. (e) Diagram shows the anterior perilidiafragmatic nodes (APDN), extrapleural nodes (EPN), gastrohepatic ligament/celiac nodes (GHLCN), and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta.
Diagram shows the anterior peridiaphragmatic nodes (APDN), extrapleural nodes (EPN), gastrohepatic ligament/celiac nodes (GHLCN), and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta.

Non-Hodgkin lymphoma is a more heterogeneous group of diseases, and thoracic involvement is present in up to 45% of cases (33). It is difficult to differentiate Hodgkin disease from non-Hodgkin lymphoma on the basis of nodal distribution alone. The paratracheal and anterior mediastinal nodes are still the most common sites of involvement for non-Hodgkin lymphoma (Fig 10). Other common sites, in decreasing order of frequency, are the subcarinal, hilar (Fig 10), posterior mediastinal (paraaortic, paravertebral, and retrocrural), and pericardial nodes (33).
Figure 10c. Non-Hodgkin lymphoma in a 66-year-old man. (a) CT scan obtained at the level of the great vessels shows bilateral axillary, right paratracheal (white arrow), left internal mammary (black arrow), and anterior mediastinal (arrowhead) nodes. (b) CT scan obtained at the level of the main pulmonary artery shows a left internal mammary node. Right hilar (arrow) and subcarinal (arrowhead) lymphadenopathy and bilateral pleural effusions are also present. (c) CT scan obtained at the level of the interventricular septum shows enlarged pericardial fat nodes (black arrow). Soft tissue in the extrapleural space (white arrows) and bilateral pleural effusions are also present.

Histopathologic classification and tumor size are the most important prognostic factors for non-Hodgkin lymphoma. In both Hodgkin disease and non-Hodgkin lymphoma, single-station nodal disease is defined as stage 1. Multiple nodes confined to one body area such as the chest are defined as stage 2, and disease on both sides of the diaphragm is defined as stage 3. Visceral involvement is regarded as stage 4. The grade and bulk of tumor determine whether treatment is with chemotherapy, radiation therapy, or a combination. Accurate description of the extent of disease is important for radiation therapy planning. Large mediastinal adenopathy or bulky disease is defined as the presence of a mediastinal mass greater than 10 cm in transverse diameter or greater than one-third of the thoracic diameter (measured at the level of the diaphragm). Large mediastinal adenopathy is associated with an increased risk of relapse and therefore requires both chemotherapy and radiation therapy, regardless of tumor grade (16).

Recurrent disease is common in the pericardial and internal mammary lymph nodes, as these are usually not included in the radiation field. Involvement of the posterior mediastinal lymph nodes is associated with pleural, retrocrural, and retroperitoneal disease (Fig 10). Nodal disease can also occur in the extrapleural space, especially in patients with non-Hodgkin lymphoma (34). There is often an associated pleural effusion secondary to malignancy or obstruction of the pleural lymphatics. Lymph node calcification before treatment is unusual (0.84% of cases) but has been associated with aggressive Hodgkin disease or non-Hodgkin lymphoma (35). After treatment, diseased lymph nodes may show irregular or eggshell calcifications at CT.

Esophageal Carcinoma

The esophagus is divided into cervical and thoracic portions. The cervical esophagus begins at the level of the lower margin of the cricoid cartilage and ends at the thoracic inlet. The thoracic esophagus extends from the thoracic inlet to the gastroesophageal junction and is divided into three regions (36). The upper thoracic portion extends from the thoracic inlet (at the level of the suprasternal notch) to the carina. The midthoracic portion extends from the carina to just above the gastroesophageal junction. The lower esophagus includes the intraabdominal esophagus and the gastroesophageal junction.

The esophageal lymphatics form an uninterrupted dense submucosal plexus around the esophagus (37,38). In general, the lymphatics of the upper two-thirds of the esophagus drain cephalad. The lymphatics of the lower one-third drain caudally toward the abdomen. Esophageal lymphatics also directly communicate with the neighboring thoracic duct at
multiple levels. As a result of this extensive drainage system, skip metastases are common, whereby nodal disease appears at remote sites with no intervening nodal involvement (37). Nodal spread of tumors from the upper and middle esophagus often involves paratracheal lymph nodes. The most frequent sites of nodal spread for lower esophageal cancers are the lymph nodes of the lesser curvature and left gastric artery (gastrohepatic ligament nodes).

Nodal spread of esophageal tumors may be extensive at initial clinical presentation (Fig 11). The TNM staging system for esophageal cancer (Table 3) reflects the bidirectional longitudinal lymphatic flow along the esophagus. It is essential to evaluate the entire thorax from the thoracic inlet to the upper abdomen (Fig 12) in all patients with esophageal carcinoma because the detection and confirmation of regional nodal disease necessitates the addition of chemoradiation treatment to surgery. The specific regional nodes for tumors of the cervical esophagus include the supraclavicular, internal jugular, upper and lower cervical, and periesophageal nodes. Regional nodes for tumors of the thoracic esophagus are the paratracheal, periesophageal, and subcarinal nodes (below the azygos vein). For gastroesophageal junction tumors, the regional nodes include nodes adjacent to the diaphragm, pericardium, left gastric artery (gastrohepatic ligament), and celiac artery (16). For all intrathoracic esophageal tumors, supraclavicular and celiac axis nodal involvement is classified as distant metastatic disease (16) and precludes surgery.

Figure 11a. Axial diagrams show the regional drainage pathways (black nodes) for esophageal cancer. Supraclavicular nodes are considered regional nodes (N1) for tumors that originate at the cervical esophagus but represent distant disease (M1) for intrathoracic esophageal tumors. E = esophagus. (a) Diagram shows the anterior scalene/supraclavicular nodes (ASSCN) and periesophageal/posterior mediastinum nodes (PEPMN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJV = left internal jugular vein, RCCA = right common carotid artery, RJV = right internal jugular vein, Tr = trachea. (b) Diagram shows the periesophageal/posterior mediastinum nodes (PEPMN) and right paratracheal nodes (RPTN). AA = aortic arch, LBCV = left brachiocephalic vein, RBCV = right brachiocephalic vein, TD = thoracic duct, Tr = trachea. (c) Diagram shows the periesophageal/posterior mediastinum nodes (PEPMN) and subcarinal node (SCN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava, TD = thoracic duct. (d) Diagram shows the gastrohepatic ligament/celiac nodes (GHLCN) and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta, TD = thoracic duct.
Figure 11b. Axial diagrams show the regional drainage pathways (black nodes) for esophageal cancer. Supraclavicular nodes are considered regional nodes (N1) for tumors that originate at the cervical esophagus but represent distant disease (M1) for intrathoracic esophageal tumors. E = esophagus. (a) Diagram shows the anterior scalene supraclavicular nodes (ASSCN) and periesophageal posterior mediastinum nodes (PEPMN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJ = left internal jugular vein, RCCA = right common carotid artery, RJ = right internal jugular vein, Tr = trachea. (b) Diagram shows the periesophageal posterior mediastinum nodes (PEPMN) and right paratracheal nodes (RPTN). AA = aortic arch, LBCV = left brachiocephalic vein, RBCV = right brachiocephalic vein, TD = thoracic duct, Tr = trachea. (c) Diagram shows the periesophageal posterior mediastinum nodes (PEPMN) and subcarinal node (SCN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava, TD = thoracic duct. (d) Diagram shows the gastrohepatic ligament/celiac nodes (GHL) and periesophageal posterior mediastinum nodes (PEPMN). Ao = aorta, TD = thoracic duct.

Figure 11c. Axial diagrams show the regional drainage pathways (black nodes) for esophageal cancer. Supraclavicular nodes are considered regional nodes (N1) for tumors that originate at the cervical esophagus but represent distant disease (M1) for intrathoracic esophageal tumors. E = esophagus. (a) Diagram shows the anterior scalene supraclavicular nodes (ASSCN) and periesophageal posterior mediastinum nodes (PEPMN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJ = left internal jugular vein, RCCA = right common carotid artery, RJ = right internal jugular vein, Tr = trachea. (b) Diagram shows the periesophageal posterior mediastinum nodes (PEPMN) and right paratracheal nodes (RPTN). AA = aortic arch, LBCV = left brachiocephalic vein, RBCV = right brachiocephalic vein, TD = thoracic duct, Tr = trachea. (c) Diagram shows the periesophageal posterior mediastinum nodes (PEPMN) and subcarinal node (SCN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava, TD = thoracic duct. (d) Diagram shows the gastrohepatic ligament/celiac nodes (GHL) and periesophageal posterior mediastinum nodes (PEPMN). Ao = aorta, TD = thoracic duct.
**Figure 11d.** Axial diagrams show the regional drainage pathways (black nodes) for esophageal cancer. Supraclavicular nodes are considered regional nodes (N1) for tumors that originate at the cervical esophagus but represent distant disease (M1) for intrathoracic esophageal tumors. E = esophagus. (a) Diagram shows the anterior scalene/supraclavicular nodes (ASSCN) and periesophageal/posterior mediastinum nodes (PEPMN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJV = left internal jugular vein, RCCA = right common carotid artery, RJV = right internal jugular vein, Tr = trachea. (b) Diagram shows the periesophageal/posterior mediastinum nodes (PEPMN) and right paratracheal nodes (RPTN). AA = aortic arch, LBCV = left brachiocephalic vein, RBCV = right brachiocephalic vein, TD = thoracic duct, Tr = trachea. (c) Diagram shows the periesophageal/posterior mediastinum nodes (PEPMN) and subcarinal node (SCN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava, TD = thoracic duct. (d) Diagram shows the gastrohepatic ligament/celiac nodes (GHLCN) and periesophageal/posterior mediastinum nodes (PEPMN). Ao = aorta, TD = thoracic duct.

**TABLE 3. Nodal Staging in Esophageal Cancer according to the AJCC TNM Classification**

**Figure 12.** Lower esophageal carcinoma in a 71-year-old man. CT scan obtained at the level of the falciform ligament shows several gastrohepatic ligament nodes (arrow), which contained tumor tissue. These nodes are defined as distant disease for intrathoracic esophageal tumors but as regional nodes for tumors that originate at the gastroesophageal junction.
Studies of normal lymph node size have found that normal paraesophageal nodes measure up to 1 cm in diameter (3). However, more recent data suggest that this is an overestimation. Schroder et al (39) performed a histopathologic study of lymphadenectomy specimens from patients with esophageal carcinoma. They analyzed a total of 1,196 lymph nodes, of which 129 (10.8%) were malignant, and found no significant correlation between lymph node size and the frequency of nodal metastases. The average size of nonmetastatic nodes was 5 mm. The average size of metastatic lymph nodes was 6.7 mm, and only 12% of metastatic nodes were greater than 10 mm in diameter. Dhar et al (40) reported that patients with metastatic lymph nodes smaller than 10 mm in long-axis diameter had significantly better overall and cancer-specific survival than patients with metastatic lymph nodes larger than 10 mm in diameter at histopathologic analysis following surgical resection.

Endoluminal ultrasound has improved accuracy in assessment of local lymph node metastases when compared with CT (80% compared with 51%) (41). However, patients suspected of having distant metastases are better assessed with CT of the thorax and abdomen (41).

**Malignant Pleural Mesothelioma**

Malignant pleural mesothelioma arises in the parietal and diaphragmatic pleura. The natural spread of mesothelioma is to the lungs through the visceral pleura and by local extension into the chest wall and diaphragm (42).

The anterior pleural lymphatics drain into the internal mammary lymph nodes in the upper and middle thorax (Fig 13) and the peridiaphragmatic lymph nodes in the lower thorax. The posterior pleural lymphatics drain into the extrapleural lymph nodes, which lie in the paraspinal extrapleural fat adjacent to the rib heads (Fig 14) (43).

**Figure 13a.** Axial diagrams show the main regional drainage pathways (black nodes) for malignant mesothelioma. E = esophagus. (a) Diagram shows the anterior scalene/supraclavicular nodes (ASSCN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJN = left internal jugular vein, RCCA = right common carotid artery, RJV = right internal jugular vein, Tr = trachea. (b) Diagram shows the extrapleural nodes (EPN), internal mammary nodes (IMN), lobar node (LN), subcarinal node (SCN), and segmental node (SN). GA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava, TD = thoracic duct. (c) Diagram shows the pericardial fat nodes (PCFN). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, LV = left ventricle, PCF = pericardial fat, RA = right atrium, RV = right ventricle, TD = thoracic duct. (d) Diagram shows the anterior peridiaphragmatic nodes (APDN) and extrapleural nodes (EPN). Ao = aorta.
Figure 13b. Axial diagrams show the main regional drainage pathways (black nodes) for malignant mesothelioma. $E$ = esophagus. (a) Diagram shows the anterior scalene/supraclavicular nodes (ASSCN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJV = left internal jugular vein, RCCA = right common carotid artery, RJV = right internal jugular vein, $Tr$ = trachea. (b) Diagram shows the extrapleural nodes (EPN), internal mammary nodes (IMN), lobar node (LN), aortic node (SCN), and segmental node (SN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava, $TD$ = thoracic duct. (c) Diagram shows the pericardial fat nodes (PCFN). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, LV = left ventricle, PCF = pericardial fat, RA = right atrium, RV = right ventricle, $TD$ = thoracic duct. (d) Diagram shows the anterior peridiaphragmatic nodes (APDN) and extrapleural nodes (EPN). Ao = aorta.

Figure 13c. Axial diagrams show the main regional drainage pathways (black nodes) for malignant mesothelioma. $E$ = esophagus. (a) Diagram shows the anterior scalene/supraclavicular nodes (ASSCN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJV = left internal jugular vein, RCCA = right common carotid artery, RJV = right internal jugular vein, $Tr$ = trachea. (b) Diagram shows the extrapleural nodes (EPN), internal mammary nodes (IMN), lobar node (LN), subcarinal node (SCN), and segmental node (SN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, PA = pulmonary artery, RMB = right main bronchus, RPA = right pulmonary artery, SVC = superior vena cava, $TD$ = thoracic duct. (c) Diagram shows the pericardial fat nodes (PCFN). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, LV = left ventricle, PCF = pericardial fat, RA = right atrium, RV = right ventricle, $TD$ = thoracic duct. (d) Diagram shows the anterior peridiaphragmatic nodes (APDN) and extrapleural nodes (EPN). Ao = aorta.
Figure 13d. Axial diagrams show the main regional drainage pathways (black nodes) for malignant mesothelioma. \(E\) = esophagus. (a) Diagram shows the anterior scalene/supraclavicular nodes (ASSCN). ASM = anterior scalene muscle, LCCA = left common carotid artery, LJV = left internal jugular vein, RCCA = right common carotid artery, RJV = right internal jugular vein, \(Tr\) = trachea. (b) Diagram shows the extrapleural nodes (EPN), internal mammary nodes (IMN), lobar node (LN), subcarinal node (SCN), and segmental node (SN). AA = ascending aorta, Ao = aorta, LMB = left main bronchus, \(PA\) = pulmonary artery, \(RMB\) = right main bronchus, \(RPA\) = right pulmonary artery, SVC = superior vena cava, \(TD\) = thoracic duct. (c) Diagram shows the pericardial fat nodes (PCFN). Ao = aorta, CS = coronary sinus, ECF = epicardial fat, \(LV\) = left ventricle, \(PCF\) = pericardial fat, \(RA\) = right atrium, \(RV\) = right ventricle, \(TD\) = thoracic duct. (d) Diagram shows the anterior peridiaphragmatic nodes (APDN) and extrapleural nodes (EPN). Ao = aorta.

Figure 14a. Malignant mesothelioma in a 56-year-old man. (a) CT scan obtained at the level of the left atrium shows a 4-mm-diameter lymph node in the left extrapleural space (arrow). (b) CT scan obtained at the level of the clavicles shows a 2-cm-diameter left supraclavicular node (arrow), which was confirmed to be metastatic. This finding is defined as N3 disease. (c) CT scan obtained at the level of the interventricular septum shows a cluster of enhancing left peridiaphragmatic nodes (arrow). Note the irregular, enhancing, nodular pleural thickening and the loculated pleural effusion.

Figure 14b. Malignant mesothelioma in a 56-year-old man. (a) CT scan obtained at the level of the left atrium shows a 4-mm-diameter lymph node in the left extrapleural space (arrow). (b) CT scan obtained at the level of the clavicles shows a 2-cm-diameter left supraclavicular node (arrow), which was confirmed to be metastatic. This finding is defined as N3 disease. (c) CT scan obtained at the level of the interventricular septum shows a cluster of enhancing left peridiaphragmatic nodes (arrow). Note the irregular, enhancing, nodular pleural thickening and the loculated pleural effusion.
The diaphragm, which is commonly involved in mesothelioma, has a rich lymphatic network that communicates between the thorax and peritoneum. The anterior and lateral diaphragm lymphatics drain into the internal mammary and anterior peridiaphragmatic lymph nodes. The posterior diaphragm lymphatics drain into the paraaortic lymph nodes and nodes of the posterior mediastinum. Posterior mediastinal lymphatics drain superiorly and communicate with the middle mediastinum lymphatics. They may also drain inferiorly and involve the lymphatics of the gastrohepatic ligament and celiac axis (44).

A TNM staging system for malignant mesothelioma (Table 4) has been proposed by the International Mesothelioma Interest Group (45). N1 disease includes involvement of ipsilateral hilar or bronchopulmonary nodes (lobar, interlobar, and segmental nodes). N2 disease includes subcarinal and ipsilateral mediastinal nodes, including the internal mammary nodes. N3 disease includes contralateral mediastinal or internal mammary nodes and all supraclavicular nodes (Fig 14). The staging system is of limited value, as most patients present with advanced disease. However, there is a subset of patients who benefit from surgery and follow-up chemotherapy (46). These patients have epithelial histology and no evidence of extrapleural nodes, defined as mediastinal or peridiaphragmatic nodes (Fig 14a). Detection of these lymph nodes at CT would influence the care of this patient group.

**Conclusions**

There are different lymphatic drainage pathways within the thorax that are relevant in the staging of lung cancer, breast cancer, lymphoma, esophageal cancer, and malignant mesothelioma. It is important to carefully evaluate the specific nodal stations that drain the thoracic structures from which a primary tumor originates in order to properly search for metastatic spread. Owing to the limitations of size criteria in predicting nodal status, pathologic...
confirmation is essential for true staging. CT is useful for guiding the surgeon or interventionalist to the most appropriate approach for nodal sampling. FDG PET, particularly when fused with CT, has a growing role in detecting the presence of disease in lymph nodes that appear normal at CT alone. However, the role of radiologic imaging extends beyond initial staging and interventional guidance and includes posttreatment assessment and the detection of recurrent disease. Therefore, it is essential, at all levels of cancer imaging, to identify the relevant lymph node regions and relate them to the primary tumor.

References


44. Souilamas R, Hidden G, Riquet M. Mediastinal lymphatic efferents from the diaphragm. Surg Radiol Anat 2001; 23:159-162. [CrossRef][Medline]
