Reliability of positron emission tomography–computed tomography in identification of mediastinal lymph node status in patients with non–small cell lung cancer

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Objective: The involvement of mediastinal lymph nodes is a very important prognostic factor in patients with potentially resectable non–small cell lung cancer. Our aim in this study was to investigate the value of positron emission tomographic–computed tomographic scanning in staging lung cancer, especially for mediastinal lymph node evaluation, and to determine whether this could decrease the need for mediastinoscopy.

Methods: Seventy-eight patients with non–small cell lung cancer who were potential candidates for surgical resection and admitted to the thoracic surgery unit of our hospital from March 2006 to June 2008 joined this prospective study. Positron emission tomographic–computed tomographic scanning was performed as part of the prospective studies used to diagnose or stage the tumors. All 78 patients underwent tissue sampling of mediastinal lymph nodes to compare these with imaging results. The diagnostic efficacy of the computed tomographic and positron emission tomographic–computed tomographic scans compared with histopathologic findings were calculated with sensitivity, specificity, positive and negative predictive values, and accuracy.

Results: Final histology was available on 397 lymph node stations (N1, N2, and N3) sampled from 78 patients during mediastinoscopy or surgical intervention. Sensitivity, specificity, and positive and negative predictive values of mediastinal lymph node involvement in patients undergoing thoracic computed tomographic scanning were 45.4%, 80.5%, 27.7%, and 90%, respectively. The accuracy of computed tomographic scanning was 75.6%. The sensitivity, specificity, and positive and negative predictive values of mediastinal lymph node involvement in patients undergoing positron emission tomographic–computed tomographic scanning were 81.8%, 89.5%, 56.2%, and 96.7%, respectively.

Conclusion: There is a need for mediastinoscopy in positron emission tomographic–computed tomographic scanning–positive mediastinal lymph nodes, but it might not be necessary for positron emission tomographic–computed tomographic scanning–negative lymph nodes.

The involvement of mediastinal lymph nodes (MLNs) is an important prognostic factor in patients with potentially resectable non–small cell lung cancer (NSCLC). The appropriate treatment of patients with NSCLC is based on accurate staging. Various diagnostic tools are used for preoperative staging of NSCLC, including chest radiography, computed tomography (CT), magnetic resonance imaging, bronchoscopy, thoracoscopy, mediastinoscopy, endobronchial and endoscopic ultrasound-guided fine-needle aspiration biopsy, and positron emission tomography (PET). PET scanning with [18F]-2-fluoro-2-deoxy-D-glucose (FDG) imaging has shown substantial promise during the past decade in helping with the noninvasive preoperative staging of lung cancer.[1] If there are no distant metastases, the status of the MLNs is critical. Resection is not considered in patients with lung cancer if there is MLN involvement. In these patients neoadjuvant treatment is recommended before surgical intervention.[2]

Although PET scanning might accurately accomplish lymph node staging in patients with lung cancer, mediastinoscopy is often used for deciding unresectability pertaining to the presence of N2/N3 disease. PET scanning is reported to be more effective than CT scanning in lymph node staging; however, efficacy increases further when results from both methods are combined.[3,4]

Our aim in the present study was to evaluate the need for such routine invasive sampling procedures in all cases to confirm the findings of PET–CT scanning. The question was whether PET–CT scanning was reliable for staging in patients with NSCLC and whether it could decrease the need for mediastinoscopy.

MATERIALS AND METHODS

Patient Population

Seventy-eight consecutive patients with NSCLC who were potential candidates for surgical resection and were admitted to the thoracic surgery unit of our hospital from March 2006 to June 2008 joined this prospective study.

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Abbreviations and Acronyms

CT	= computed tomography
EBUS–FNA	= endobronchial ultrasound-guided fine-needle aspiration
EUS–FNA	= endoscopic ultrasound-guided fine-needle aspiration
FDG	= [18F]-2-fluoro-2-deoxy-D-glucose
FNA	= fine-needle aspiration
MLN	= mediastinal lymph node
NSCLC	= non–small cell lung cancer
PET	= positron emission tomography
SUV	= standardized uptake value

After approval by the institution's ethics committee, oral and written informed consent was obtained from all the subjects. All patients were included in this prospective study, excluding (1) patients with evidence of metastatic disease, except for those with solitary brain or adrenal metastasis; (2) patients who had not undergone PET–CT scanning as part of their preoperative evaluation or who had undergone FDG–PET scanning in another center; and (3) patients with diabetes mellitus whose blood glucose levels could not be controlled and brought to normal values. Because the patients found to have N2 disease before neoadjuvant therapy were included, we did not include patients receiving neoadjuvant treatment in this study. Complete blood counts and blood chemistry tests, chest radiographs, thoracic CT scans, PET-CT scans, pulmonary function tests, and, if clinically indicated, bone scans and cranial magnetic resonance imaging were performed in all cases. PET–CT scans were performed as part of the prospective studies used to assess the utility of PET–CT scanning in diagnosing or staging tumors. The positive findings on PET–CT and CT scans were labeled to identify the involved lymph node station. Definitive diagnosis was established based on the histopathologic findings of lymph node sampling in mediastinoscopy or biopsy during the surgical procedure. If a mediastinoscopy was performed, histologic evaluation of the specimens was performed with a frozen section. If N2 disease was present, definitive resection was not performed at that time. These patients received neoadjuvant therapy.

Patients with resectable disease on mediastinoscopy underwent further operative procedures. Three patients underwent transcarinal sleeve pneumonectomy, 16 underwent pneumonectomy (invasion of the left atrium, main pulmonary artery, carina, distal trachea, and proximal main bronchus, with some major fissure invasion), 4 underwent bilobectomy, 2 underwent sleeve lobectomy, and 46 underwent lobectomy. One patient was identified as unresectable (M1) during thoracotomy. Six patients did not undergo thoracotomy because of positive results on mediastinoscopy. One patient given a positive diagnosis after mediastinoscopy underwent resection as a result of drainage to the pleural space caused by tumor necrosis and hemoptysis.

Multistation nodal mediastinal sampling was performed, with removal of levels 2, 4, 7, 8, and 9 on the right side. For left-sided tumors, lymph nodes at levels 5 and 6 were dissected also. However, nonpalpable station 2L could not be removed in some patients. Hilar lymph nodes were also dissected.

Preoperative staging of the mediastinum with PET–CT scanning was compared with conventional preoperative staging with chest CT scanning; the accuracy of each study was assessed against the pathology results obtained by means of mediastinoscopy or MLN dissection at the time of thoracotomy. All patients underwent tissue sampling of MLNs to compare sampling results with imaging results.

Thoracic CT Scanning

CT examinations were performed by using a helical CT scanner (Brilliance 6; Philips Medical Systems, Cleveland, Ohio). Images (7.5 mm thick) were obtained with sections after intravenous injection of 60 to 100 mL of contrast material (Ultravist 300; Bayer Schering Pharma, Berlin, Germany). The images were read by a radiologist before obtaining a PET–CT scan. The CT scan reader was blinded to the results of the reference tests. MLNs were considered positive if they were larger than 10 mm in their short-axis diameters.

PET–CT Scanning

Whole-body PET–CT scanning was performed with Siemens Biograph 2 PET-CT system (Siemens, Munich, Germany). A whole-body acquisition was performed immediately 1 hour after intravenous administration of FDG (11–16 mCi), and images were obtained from the vertex to the upper thigh region. High-quality images were acquired, and semiquantitative measurements of glucose metabolism were obtained. All patients fasted for at least 4 hours before imaging, their fasting blood glucose levels were within the normal range, and none received insulin to return blood glucose to normal levels. The standardized uptake values (SUVs) of hilar lymph nodes and MLNs were determined from the transverse views by the nuclear medicine physician blinded to results of reference tests. Coronal–sagittal images and their correlation with CT scans were used when the exact location was uncertain. Regions of interest were drawn on the images, and semiquantitative SUV measurements were defined as the regional tissue radioactivity concentration normalized for injected dose and body weight. Results of PET–CT scans were considered positive in the mediastinum and hilar area that was separate from the primary mass if the SUV in patients suspected to have lymph node metastases was greater than 2.5.

Mediastinoscopy

Mediastinoscopy was performed according to the following criteria: (1) ipsilateral or contralateral MLNs with a diameter of greater than 10 mm in the short axis on the chest CT scan; (2) MLN uptake on the PET–CT scan; (3) a histopathology of adenocarcinoma on bronchoscopy or transthoracic biopsy; (4) central tumors (tumor involving hilar structures, such as the main bronchus, distal trachea, and main pulmonary artery; visible by means of bronchoscopy; or both), even if N2 disease was not detected in radiologic examinations; and (5) high-risk surgical candidacy. Mediastinoscopy was not performed in patients excluded from these criteria or found to have N2 disease by means of transbronchial fine-needle aspiration.

In mediastinoscopy biopsy specimens were taken from nodal stations, with 4L, 4R, and 7 being the most commonly sampled. All lymph node stations observed on PET–CT scans were sampled by means of mediastinoscopy. Video-assisted thoracoscopy was performed in patients with positivity of lymph nodes at station 5, as well when the cervical mediastinoscopy result was negative. In patients with clinical stage I or II NSCLC and without the above criteria based on PET–CT and CT scanning, mediastinoscopy was not performed, but multinodal mediastinal sampling at the time of thoracotomy was performed.

If metastasis of NSCLC to the MLNs was detected at the time of mediastinoscopy, then lung resection was not performed, and patients were referred to neoadjuvant therapy. If the MLNs were negative for metastasis, we continued the procedure with thoracotomy and resection with mediastinal lymphadenectomy.

Statistical Analysis

CT and PET–CT findings were compared with histopathologic findings in the lymph node stations undergoing biopsy, resection, or both to determine their diagnostic capabilities. The diagnostic efficacy of the CT and PET–CT scans was calculated with sensitivity, specificity, positive and negative predictive values, and accuracy. True positivity and true negativity were assessed based on the presence of N2 disease in patients with NSCLC.

RESULTS

There were 73 male and 5 female patients (age range, 44–79 years; mean age, 61.3 years) in the study.