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Thin-section CT of the mediastinum in preoperative N-staging of non-small cell lung cancer: Comparison with FDG PET

Atsushi Nambu[a,*], Satoshi Kato[a], Utaroh Motosugi[a], Tsutomu Araki[a], Hideto Okuwaki[b], Keiichi Nishikawa[c], Akitoshi Saito[a], Keiko Matsumoto[a], Tomoaki Ichikawa[a]

[a] Department of Radiology, University of Yamanashi, Shimokawato, Chuo-shi, Yamanashi Prefecture, Japan
[b] Second Department of Surgery, University of Yamanashi, Japan
[c] Second Department of Internal Medicine, University of Yamanashi, Japan

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ABSTRACT

Purpose: To compare diagnostic capability of preoperative N-staging of lung cancer between thin-section CT of the mediastinum and FDG PET, and 5 mm slice thickness CT.
Materials and methods: The subjects were 34 patients with lung carcinoma who were examined by both CT and PET, and subsequently underwent surgery between May 2005 and January 2007. CT was carried out with a 16 detector row helical CT scanner. The raw data were reconstructed into 5 mm slice thickness and 1 mm slice thickness (thin-section CT). A total of 251 lymph node stations were retrospectively assessed for the presence of lymph node metastasis with thin-section CT, 5 mm CT and PET. In the interpretations of thin-section CT and 5 mm CT, we employed multi-criteria as follows: nodular calcification and intranodal fat as benign criteria, and short-axis diameter more than 10 mm (size criterion), focal low density other than fat, surrounding fat infiltration and convex margin in hilar lymph nodes, as malignant criteria. On PET, maximum standardized uptake value (SUVmax) of 2.5 or more was used as the criterion of malignancy. Sensitivity and specificity were compared between these examinations using McNemar test.
Results: Sensitivities and specificities of thin-section CT, 5 mm CT and PET were 25%, 25%, 25%, and 97%, 94%, 98%, respectively. The statistical analysis revealed that the specificity of 5 mm CT was significantly lower than those of thin-section CT ($p = 0.039$) and PET ($p = 0.006$), while no difference was present between thin-section CT and PET.
Conclusion: Thin-section CT of the mediastinum using multiple criteria was comparable to PET in preoperative N-staging of lung cancer.

1. Introduction

The evaluation of hilar and mediastinal lymph nodes (N-staging) is critical in the management of lung cancer as it affects the choice of treatment; surgery is usually not appropriate for advanced disease with lymph node metastasis to the contralateral mediastinum or distant metastasis, while surgery should be performed in limited disease unless inoperable. CT has been used for this purpose for a long time. However, its sensitivity and specificity for N-staging were unsatisfactorily low, ranging from 33 to 77% and from 53 to 96%, respectively [1–6].

Fluorine-18-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) has recently emerged as a new modality of choice in the evaluation of lung cancer, including N-staging, and already has become widely used in medical practice [1,3–9]. Many reports suggested that FDG-PET was superior to CT in N-staging of lung cancer [1,5,6]. However, it is also well known that there are a significant number of false-positive and false-negative findings in FDG-PET [3,10–12].

On the other hand, recent development of multidetector row CT has enabled us to easily obtain thin-section CT by reconstructing raw data without rescanning, which does not require extra radiation exposure and has an appropriate timing of contrast enhancement. We thought that the inferiority of CT in N-staging was mainly due to limitation of simple size criterion (i.e. a lymph node more than 10 mm in short-axis diameter is metastatic.) disregarding other appearances of lymph node. Detailed observation of lymph nodes on thin-section CT images of the mediastinum with additional multi-criteria may improve accuracy of N-staging of lung cancer, as in thin-section CT of the lung, which has been already proved to be useful by many data and has become routine in the assessment of focal or diffuse pulmonary parenchymal disease.

* Corresponding author at: Department of Radiology, University of Yamanashi, Shimokawato 1110, Chuo-shi, Yamanashi Prefecture, 409-3898 Japan.
Tel.: +81 55 273 1111; fax: +81 55 273 6744.
E-mail address: nambu-a@gray.plala.or.jp (A. Nambu).

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In this study, we compared conventional 5 mm slice CT with thin-section CT of the mediastinum and PET to evaluate whether employment of thin-section CT of the mediastinum is clinically useful in the preoperative assessment of N-staging of lung cancer. Thereafter, we also tried to find out the reasons why CT and PET yield false-negative findings by correlating the pathological specimens of resected lymph nodes that contained metastasis with the results of interpretation of PET and CT.

2. Methods

2.1. Subjects

Our institutional review board did not require its approval for a retrospective study obtained with routine clinical data, including PET, CT and their reconstruction. Informed consent was not required either.

A total of 34 patients with lung carcinoma were enrolled into this study. They were examined by both CT and PET, and subsequently underwent surgery between May 2005 and January 2007. CT of the chest and upper abdomen was routinely performed for patients with lung carcinoma in our institution. Also almost routinely performed was integrated PET in patients with lung carcinoma. However, in patients with lung carcinoma showing pure focal ground-glass opacity on thin-section CT, which was highly suggestive of bronchioloalveolar carcinoma, PET was not done as bronchioloalveolar carcinoma was well known not to uptake FDG and was not considered to metastasize to lymph nodes or other organs. Additionally, patients with distant metastasis or lymph node metastasis to the contralateral mediastinum (i.e. N3) were not eligible for surgery in our institution. Therefore, these patients were not included in this study. There were 23 men and 11 women, ranging in age from 47 to 83 years with an average of 69 years. The pathological subtypes of resected lung carcinomas are summarized in Table 1. The nodal stations were classified according to the American Thoracic Society lymph node map.

2.2. Methods of examinations

2.2.1. CT examination

CT was carried out with Aquilion (Toshiba Medical Systems), a 16 detector row helical CT scanner in all cases within 1 month before the surgery. The scan parameters were as follows: 1 mm detector row, electric current of 120–380 mA (automatic exposure control employed), peak voltage of 120 kVp, X-ray tube rotation time of 0.5 s, 1 mm collimation and a slice pitch of 15. Contrast material (Omnipaque 300, 100 ml, Daiichi-Sankyo, Tokyo, Japan) was used in all cases and was intravenously injected at the rate of 1.5 ml/s. The scans were started 70 s after the initiation of the contrast material injection. Raw data were reconstructed in the following two settings: 5 mm slice thickness images of the whole chest with a FOV (field of view) encompassing the entire thorax, which was routine chest CT in our institution, and 1 mm slice thickness images with a smaller FOV, targeting to the mediastinum and pulmonary hila. The latter was defined as thin-section CT of the mediastinum in this study.

Table 1
Pathologic subtypes of the lung carcinomas.

Subtype	Number of cases
Adenocarcinoma	23
Adenocarcinoma with mixed subtypes	17
Bronchioloalveolar carcinoma	2
Mucinous colloid adenocarcinoma	1
Solid carcinoma with mucin	1
Papillary type	1
Acinar type	1
Squamous cell carcinoma	8
Large cell carcinoma	1
Pleomorphic carcinoma	1
Mucoepidermoid carcinoma	1

2.2.2. FDG PET examination

FDG PET was carried out with Biograph LSO DUO (Siemens, Germany) in all cases within 1 month before the surgery. This was an integrated PET/CT machine, but the CT was mainly used to localize the anatomical locations of lymph nodes or primary tumors and its findings were not considered in the interpretation of FDG PET because of its suboptimal quality compared with the detailed CT examination above. All patients fasted for at least 6 h before FDG PET. After confirmation of a normal blood glucose level (less than 150 mg/dl) in peripheral blood, the patients received an intravenous injection of 3.0 MBq/kg of FDG and thereafter rested for 60 min before scanning.

The CT scanning in PET/CT was performed from the head to the pelvis with the following parameters: electric current of 200–300 mA, peak voltage of 120–140 kvp, X-ray tube rotation time of 0.5 s, a slice pitch of 9, and slice thickness of 2.5 mm. No contrast material was used. Immediately after this CT scanning, PET was performed with the same field of view. The acquisition time for PET was 2 min per table position. The CT data were converted from 512×512 matrices to 128×128 matrices to match the PET data, by which the images of both examinations could be fused. PET data were reconstructed with an ordered subsets expectation maximization algorithm and attenuation correction was done with the CT data. Coregistered images were displayed by e-soft-PET software (Siemens, Germany).

Maximum standardized uptake value (SUVmax) of lymph node stations was calculated by the following formula in all cases. A three dimensional acquisition was used to calculate the SUVmax.

$$\text{SUVmax} = \frac{\text{maximum tissue concentration (MBq/g)}}{\text{injected dose (MBq)/body weight (g)}}$$

The maximum tissue concentration was represented by the counts per second of the voxel showing the maximum radioactivity in the volume of interest encompassing the tumor divided by the volume of the voxel (milliliters).

2.3. Methods of image interpretation and analysis

2.3.1. CT interpretation

We used multi-criteria for the evaluation of lymph nodes on CT as follows: nodular calcification [6,8,9] and intranodal fat tissue as benign criteria, and short-axis diameter more than 10 mm (size criterion), focal low density other than fat suggesting necrosis [6,13], surrounding fat infiltration suggesting extrafascial extension [13], and convex margin to the surrounding pulmonary parenchyma in hilar lymph nodes [14], as malignant criteria. These criteria were used in the previous reports except for intranodal fat. Intranodal fat is considered to be a normal architecture seen in the hilum of a lymph node or aging change and is generally used as an indicator of benignancy of a lymph node in diagnostic imaging. Although some authors modified the size criterion (i.e. changing the cutoff value of size in some nodal stations) in some reports [6,15,16], we used 10 mm as the cutoff value in all nodal stations in this study. The presence of convex margin in hilar lymph nodes was evaluated by using lung window setting according to the original report [14]. If malignant and benign criteria were coexistent in one lymph node, it was regarded as benign in this study because such cases were exclusively seen as a combination of more than 10 mm in short-axis diameter (size criterion) and intranodal calcification or fat, which were empirically more likely to be benign.