Original Investigations

Pleural Invasion by Peripheral Lung Cancer:

Prediction with Three-Dimensional CT

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Rationale and Objectives: To evaluate the clinical utility of three-dimensional (3D) computed tomography (CT) for predicting pleural invasion by peripheral lung cancer.

Materials and Methods: CT findings (tumor size, vertical diameter, length and area of the interface between tumor and the pleura, ratios of length and area [R_{area}] of interface between tumor and the pleura to tumor size, angle between the tumor and adjacent pleura, presence or absence of pleural thickening, and originally developed 3D pleural patterns) in 201 consecutive patients with lung cancer of ≤3 cm in contact with pleural surface were correlated with pathologic findings. Logistic modeling was used for determining the significant factors for prediction of pleural invasion, and receiver operating characteristic (ROC) curves were used for investigating diagnostic capability of significant factors, resulting in a recommendation to the optimal criteria for predicting pleural invasion and to the optimal threshold for differentiating parietal from visceral invasion.

Results: Sixty-one (30%) of the 201 patients had pathologically verified pleural invasion. Logistic modeling revealed that the 3D pleural pattern was the only significant factor ($P < .001$; relative risk of 7.34). Among every combination of the 3D patterns, skirt-like pattern showed the highest accuracy of 77% for predicting pleural invasion. In differentiating parietal from visceral pleural invasion, ROC analysis revealed that R_{area} was optimal for differentiating parietal from visceral pleural invasion, and the highest accuracy of 77% was obtained with a cut-off value of 13.4 for this criterion.

Conclusions: Computer-aided 3D CT analysis of the pleura was useful for predicting pleural invasion.

Key Words: 3D CT; pleural invasion; lung cancer; computer-aided diagnosis.

The anatomic extent of disease as expressed by the tumor, node, and metastasis staging system is the most important prognostic factor for lung cancer. Presence of visceral pleural invasion by lung cancer increases T staging from T1 to T2, and the presence of parietal pleural invasion upstages it from T2 to T3, when the tumor is <3 cm in size (1). Therefore, prognosis of patients with T1-sized (≤3 cm) lung cancer depends on the presence or absence of pleural invasion and the depth of invasion of the pleura (2). Five-year survival rates are reported to worsen from 86% (for patients with no pleural invasion) to 62%–70% (for patients with visceral pleural invasion) and then to 57% (for patients with parietal pleural invasion) for non–small cell lung cancer (NSCLC) (3).

Computed tomography (CT) is currently the imaging method of choice in staging of lung cancer. However, a well-known limitation of conventional CT is the diagnosis of pleural invasion by peripheral lung cancer. Sensitivity in diagnosing invasion of the parietal pleura or chest wall based on two-dimensional (2D) CT is reported to range from 38% to 89.7% and specificity from 40% to 96% (4,5). However, the visceral pleural invasion is difficult to diagnose with CT and has not been assessed in detail, especially in patients with T1-sized lung cancer. Thin-section spiral CT allows continuous data collection and provides uninterrupted volume data that can be reconstructed to produce three-dimensional (3D) images, which have been reported to be superior to 2D CT in the assessment of pleural invasion by lung cancer (6).

The objective of this study was to evaluate the value of 3D CT in diagnosing pleural invasion and differentiating parietal from visceral pleural invasion by T1-sized peripheral lung cancer.

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MATERIALS AND METHODS

This retrospective study was approved by our institutional review board and written informed consent was obtained from all participants for the use of thin-section CT data.

Patients

Between January 2007 and December 2012, 1003 patients with peripheral lung cancer of ≤3 cm underwent thin-section CT examinations before surgery and subsequent surgical resection of lung cancer. Of these, 422 tumors in 422 patients and 380 tumors in 380 patients were excluded from the present study because the former tumors were remote from the pleura and had no pleural tag on thin-section CT images (lung window setting), and the latter ones were also remote from the pleura but had pleural tags only. A pleural tag was defined as a linear strand originating from the nodule surface and reaching the pleural surface. Thus, 201 consecutive patients (126 men and 75 women; age, 66.7years ± 9.3 [mean ± standard deviation, SD]) with tumors in contact with pleura were included in this series. In our institute, the following nodules were recommended surgical resection with or without preceding biopsy procedures (depending on the size of the nodules): mixed ground-glass opacity nodules of ≥5 mm that are stable in size or show interim growth; solid nodules of ≥5 mm that show interim growth. The median interval time between thin-section CT and surgery was 14 days (range, 1–30 days).

Thin-Section CT

A 16-slice CT scanner (Aquilion 16; Toshiba, Tokyo, Japan) was performed during a single breath hold with (n = 153) or without (n = 48) intravenous contrast agent. Technical parameters of CT scans were 120 kVp, 100–150 mA, 0.5 s/rotation, and 16 × 0.5 mm collimation. Axial images of 1.0 mm thickness with 0.5 mm spacing were reconstructed with a matrix of 512 × 512 and a field of view of 350 × 350 mm. The spatial resolution for reconstruction images was 0.7, 0.7, and 1.0 mm on x-axis, y-axis, and z-axis, respectively. The conventional 2D CT images and the 3D CT reconstruction images were reviewed independently by two observers (B.J. and S.T., with 8-year and 30-year experience in chest radiology, respectively) blinded to the pathologic diagnoses. The final findings for the analyses were determined by consensus of the two observers for categorical data, and averaged values were used for continuous data.

Nodule size (the maximum dimensions on transverse CT images), vertical diameter (the greatest craniocaudal dimensions of a nodule on coronal or sagittal images), the length (the greatest contact length on transverse, coronal, or sagittal CT images) and the area (Fig 1) of the interface between the tumor and the pleura, and the ratios of length (R_{length}) and the area (R_{area}) of the interface between tumor and the pleura to tumor size were assessed. We manually drew the interface between the tumor and the pleura and measured the distance (Figs 1a,b). The ratio of this distance to tumor size was defined as R_{length}. Next, we calculated the volume of all the voxels that comprise the interface, and the volume was divided by a voxel size of y-axis of CT images (Fig 1c). This value was defined as the area of the interface, and the ratio of the area to tumor size was defined as R_{area} in our study. Although both ends of the interface were determined on a CT image of lung window setting, when a part of the interface was difficult to identify, we used different window settings such as mediastinal window setting. In addition, the angle (acute or obtuse) between the tumor and the adjacent pleura (if either of the both sides showed an obtuse angle, this nodule was regarded as having an obtuse angle), and presence or absence of pleural thickening was assessed. The presence or absence of pleural thickening was evaluated on CT images with mediastinum window setting (level, 40 HU; width, 350 HU), and the other analyses on 2D CT images were made on the CT images with lung window setting (level, −600 HU; width, 1200 HU).

A software package (AZE VirtualPlace, Tokyo, Japan) was used for 3D reconstruction in each case. The 3D reconstruction was done with a volume-rendering algorithm. Initially, the effect of threshold level on the appearance of 3D images was evaluated qualitatively in each case. The optimal threshold values (between −470 HU and −540 HU) were chosen on axial images to best visualize the adjacent pleura and the tumor, and only the pixels of higher than the threshold values were visualized on 3D rendering images. All pixels of the other CT attenuation values were automatically removed, leaving only the tumor, pulmonary vessels, pleura, and the chest wall. If necessary, adjacent bronchi and vessels were manually removed, and the opacity was adjusted for optimal visualization of the 3D rendering images. This process required 3 minutes ± 35 seconds (mean ± SD) per case. Thus, the pleural morphology adjacent to the tumor were assessed and classified in reference to 3D rendering images.

Pleural Patterns on 3D CT

The 3D CT rendering images of the pleura were classified into four patterns (Fig 2) according to the presence or absence of adjacent pleural morphologic changes, presence or absence of indrawn pleura toward tumor, and presence or absence of wrinkling of the indrawn pleura as the following: flat pattern (Fig 2a), flat pleura without any morphologic changes in the adjacent pleura; waving pattern (Fig 2b), wrinkled pleura without pleural indrawn thickening toward tumor; rectangular solid pattern (Fig 2c), indrawn pleural thickening toward tumor, and its shape resembles rectangular solid but not associated with pleural wrinkling of the indrawn pleura. Therefore, the indrawn pleura has broad and narrow sides; skirt-like pattern (Fig 2d), indrawn pleural thickening toward tumor associated with pleural wrinkling of the indrawn pleura. Indrawn pleura looks similar on lateral views of different angles.