Correlation between the Size of the Solid Component on Thin-Section CT and the Invasive Component on Pathology in Small Lung Adenocarcinomas Manifesting as Ground-Glass Nodules

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Introduction: We aimed to evaluate the correlation between the size of the solid component on thin-section computed tomography (CT) and invasive component on pathology in small lung adenocarcinomas manifesting as subsolid nodules.

Methods: Fifty-nine subsolid nodules in 58 patients were evaluated. The maximum diameters of subsolid nodules and the solid component on CT were measured by two radiologists in three-dimensional (3D) and two-dimensional (2D) planes using in-house software. In addition, the maximum diameters of the tumor and invasive component were measured on pathology by two pathologists. CT measurements were compared with pathologic measurements.

Results: There was a strong correlation between the size of the solid component on CT and invasive component on pathology, as well as the size of subsolid nodules and the tumor size (r = 0.82–0.87 for 3D measurement, 0.72–0.88 for 2D measurement; $p < 0.0001$). The size of subsolid nodules in 3D and 2D measurements was significantly larger than tumor size ($p < 0.0001$). In regard to measurement of the solid component, 3D measurements tended to be larger than the size of the invasive component whereas 2D measurement tended to be similar to the size of the invasive component. By applying a size criteria of solid component that was 3 mm or lesser in maximum diameter, preinvasive and minimally invasive adenocarcinoma was predicted with a specificity of 100% (28 of 28).

Conclusion: We found a significant correlation between the size of the solid component on thin-section CT and the invasive component on pathology.

Key Words: Subsolid nodule, Lung adenocarcinoma, Minimally invasive adenocarcinoma.

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Recently, a new classification of lung adenocarcinomas was proposed by the International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society.[1] In this classification, new concepts of adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA) were introduced. On the basis of the size of the invasive component and pathologic features, lung adenocarcinomas are now classified into four categories—preinvasive lesions, MIA, invasive adenocarcinoma, and variants of invasive adenocarcinoma. AIS and atypical adenomatous hyperplasia fall under the category of preinvasive lesions for lung adenocarcinoma. With preinvasive lesions and MIA, patients will have 100% or near-100% disease-specific survival, respectively, if completely resected. Furthermore, previously published data have shown that patients with preinvasive lesions or MIA may undergo less extensive surgery such as sublobar resection.[2–9] However, to date, it is hard to make a diagnosis of preinvasive lesions or MIA with frozen biopsy specimens, as the invasive component should be precisely evaluated using the entire pathologic sampling. Thus, if preoperative imaging is able to predict the invasive component of adenocarcinomas, it will have great clinical value in determining the extent of surgical resection as well as the patient's prognosis.

"Subsolid nodule" is a more comprehensive term than "part-solid nodule." *Subsolid nodule* refers to both pure ground-glass nodule (GGN) and part-solid GGN, as a category separated from purely solid nodule. *Part-solid GGN* indicates the nodule that has both ground-glass and solid components.[10] In subsolid nodules, many previous reports have demonstrated that ground-glass opacity (GGO) components represent the lepidic growth and that solid components are frequently related with invasion[11–23] and also note that computed tomography (CT) plays an important role in the management of subsolid nodules.[10] It has also been suggested that the T staging in the Tumor Node Metastasis classification should be adjusted radiologically by measuring the solid component of subsolid nodules[1] and that the management of subsolid nodules should be based on the size of subsolid nodules and the solid component.[10] The comparison of radiologic–pathologic tumor measurements conducted in several other cancers has demonstrated that radiologic measurement significantly corresponded with pathologic tumor size and may be valuable in treatment planning.[24–29] To our knowledge, however, no previous study has provided and directly correlated the measurement data between the solid component of subsolid nodules on thin-section CT and the invasive component on pathologic exams.

Therefore, the purpose of our study was to evaluate the correlation between the size of the solid component on thin-section CT and the invasive component on pathology in small lung adenocarcinomas and preinvasive lesions manifesting as subsolid nodules.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of our institution, and written informed consent was waived for all patients in this retrospective study.

Selection of Cases

We retrospectively reviewed the medical records of all patients who had undergone surgical resection for small lung adenocarcinomas and preinvasive lesions that manifested as subsolid nodules on CT at our hospital between August 2005 and June 2011. We defined small adenocarcinomas as measuring 3 cm or lesser on the basis of pathologic report. All the tumors had T stage of T1 or lower in our study population. There was a total of 141 eligible patients for whom pathology slides were available. Among them, we excluded 83 patients based on our exclusion criteria defined as follows: (1) time between CT and surgery of more than 4 weeks ($n = 11$) and (2) patients who were considered to have inappropriate CT images for subsolid nodule analysis (section thickness > 1.25 mm, CT images scanned at outside hospitals or reconstructed with different algorithms; $n = 72$). Finally, a total of 58 patients (19 men and 39 women) (median age, 61 years; range, 26–85 years) were included in our study. Surgical procedures included wedge resection in 13 patients and lobectomy in 45 patients. The mean time ± standard deviation between CT and surgery was 14.2 ± 12.5 days.

Through the surgical records and transverse CT images, one chest radiologist (JMG) with 21 years of experience reading chest CT images and one radiology resident in her fourth year of training (KHL) identified the location of corresponding subsolid nodules on CT images by consensus. Images were displayed by using a lung window setting with a center of −700 HU and a width of 1500 HU. When there were multiple subsolid nodules per patient, only subsolid nodules with pathologic confirmation of lung adenocarcinomas were selected based on surgical records. All patients had a single subsolid nodule with pathologic confirmation, except one patient who had two subsolid nodules with pathologic proof. Finally, a total of 59 subsolid nodules were selected in 58 patients for image analysis. The study population and subsolid nodules enrolled in our study partly overlap with those of our previous reports from our department.[30,31] However, the methodology is totally different from that of prior studies.

Image Acquisition

CT images were obtained using one of the following four CT scanners; Sensation 16 (Siemens Medical Solutions, Forchheim, Germany), Somatom Definition (Siemens Medical Solutions, Forchheim, Germany), LightSpeed Ultra (GE Healthcare, Milwaukee, WI), or Brilliance 64 (Philips Medical Systems, Best, The Netherlands). As all data were collected retrospectively, a variety of scanning protocols were used, including CT with ($n = 35$) or without ($n = 23$) intravenous contrast material, and CT with standard-dose ($n = 45$) or low-dose techniques ($n = 13$). Tube current ranged from 200 to 400 mAs for standard-dose techniques and 20 to 40 mAs for low-dose techniques, with tube voltage of 120 kV for all scans. In all patients, CT images were reconstructed using the high-frequency algorithm with a section thickness of 1.25 mm or 1 mm. The image matrix size ranged from 512 × 512 pixels. The field of view was optimized for the size of the patients and ranged from 300 to 350 mm.

Assessment of CT Scans

For the 59 subsolid nodules, two radiologists (Reader 1: a radiology resident (KHL); Reader 2: a chest radiologist (JYW), with 5 years of experience) independently drew the borders of subsolid nodules as well as the solid component and saved them as regions of interest files by using in-house software. On the basis of the regions of interest of subsolid nodules drawn by radiologists for the whole boundary of subsolid nodules and their solid components, the program automatically calculated the maximum diameter in both (three-dimensionsal) 3D and (two-dimensional) 2D planes and showed the axis of the maximum diameter of subsolid nodules. Two readers then reviewed the measurement results and axes of the maximum diameter generated by the program in all cases and were allowed to adjust the measurements by manually drawing the maximum diameter if the generated results were deemed unacceptable because of long spiculations of subsolid nodules in a few cases.

To assess intrareader variability, Reader 1 outlined the boundary of the subsolid nodules as well as the solid component on the CT scans over two sessions (Fig. 1): in the first session, she drew a border around all involved CT sections that contained subsolid nodules to obtain both 3D and 2D measurement data, and in the second session, she only outlined the border of the subsolid nodules and the solid component on the representative CT image with the largest long diameter of subsolid nodules. For cases in which the slice of the maximum dimension of the solid portion was different from that of the maximum dimension of subsolid nodule, she drew a border around the solid component on the slice of

