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Research article

Effect of computed tomography window settings and reconstruction plane on 8th edition T-stage classification in patients with lung adenocarcinoma manifesting as a subsolid nodule

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ABSTRACT

Purpose: To assess the effect of window settings and reconstruction plane on clinical T-stage determined by solid portion size within subsolid nodules (SSNs), based on 8th-edition TNM standards.

Materials and methods: This retrospective study included 247 SSNs from 221 patients who underwent surgery for lung adenocarcinomas between Feb 2012 and Oct 2015. Two radiologists independently measured the diameter of the solid portion on axial, coronal, and sagittal planes using lung- and mediastinal-window. The largest diameter among the measurements on the three planes was referred to as multiplanar measurement. Inter-reader agreement as well as the correlation between the CT and pathologic measurements were calculated using intra-class correlation coefficients (ICCs). The proportions of disagreement in clinical T-stage on different measurement methods were measured. The κ values for agreement between clinical- and pathological T-stage were measured.

Results: Inter-reader agreement was moderate-to-excellent (ICC confidence interval [CI] range, 0.51–0.92) in lung-window, while it was good-to-excellent (0.77–0.95) in mediastinal-window. The correlation between the CT and pathologic measurements was good-to-excellent (ICC CI range, 0.63–0.82) in lung-window and fair-to-good (0.25–0.78) in mediastinal-window. The proportions of disagreement between clinical T-stages using mediastinal- and lung-window were 32.0%–41.7% and 33.6%–49.0% with axial and multiplanar measurement, respectively. Multiplanar measurement resulted in upstaging in 12.6%–15.8% and 19.0%–24.3% of cases with mediastinal- and lung-window, respectively, when compared with axial measurement alone. The κ values for agreement between clinical T-stage and pathological T-stage ranged from 0.53 to 0.69.

Conclusions: Mediastinal-window was a more stable method in the aspect of the inter-reader agreement, but the correlation between the CT and pathologic measurement was better in lung-window. The clinical T-stage varied in up to one-half of the cases according to the window setting, and multiplanar measurement resulted in up-staging in up to one-fourth of the cases.

1. Introduction

For patients with subsolid nodules (SSNs), accurate clinical staging is important for determining the extent of surgical resection pre-operatively and predicting prognosis [1]. Clinical stage can be obtained in virtually all patients who undergo CT imaging, even before surgical resection [2]. Furthermore, due to the shrinkage after formalin fixation in resected specimen, CT measurement of the solid component may better represent the in-vivo state of the invasive component than pathologic measurement in some cases [3].

The 8th edition of the tumor, node, and metastasis (TNM) staging of lung cancers states that the clinical T-stage should be based on the size of its solid portion within SSNs [1]. In T_1 lung adenocarcinomas manifesting as SSNs, clinical T-stage is sub-categorized into the five

Abbreviations: SSN, subsolid nodule; CI, confidence interval; ICC, intra class correlation coefficients; OR, odds ratio

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categories as cT_{is}, cT_{1mi}, cT_{1a}, cT_{1b}, and cT_{1c} according to the diameter of solid portion. For clinical T-staging, the 8th edition TNM staging guideline suggests measuring the single largest dimension of the solid portion in lung or intermediate window settings [1]. However, it still leaves which window setting is the best method for measuring the solid component as research questions [1]. If the lesions are aligned along a craniocaudal axis, multiplanar reconstructions in the coronal and sagittal plane are recommended for obtaining a more accurate assessment of nodule size. However, measuring the solid portion in the three reconstruction planes increases reading times, when compared with that in the axial plane. To our knowledge, the difference between the clinical T-stage according to the reconstruction plane or window settings in patients with SSNs has never been investigated.

The present study aimed to assess the effect of window settings and reconstruction plane on clinical T-stage determined by solid portion size within SSNs, based on 8th edition TNM standards.

2. Materials and methods

This retrospective study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (a tertiary referral center), which waived the requirement for informed consent.

2.1. Case selection

We searched the medical records of our institution from February 2012 to October 2015, as storage of thin-section imaging data (slice thickness of 2 mm or less) began during this period. Our search identified 882 patients who had undergone an operation for lung adenocarcinoma. Among them, 273 patients had tumors manifesting as SSNs. A total of 52 patients were excluded on the basis of the following criteria: (1) CT unavailable for thin-section reconstruction (n = 44), (2) nodules with impossible histopathological matching (n = 5), nodules evaluated with suboptimal protocols (coronary CT angiogram [n = 1], and low-dose screening CT [n = 2]), and (3) interval between CT and surgery of more than 90 days (n = 1). A final total of 221 patients (99 men, mean age: 62.2 years, age range: 35–83 years; 122 women, mean age: 62.5 years, age range: 39–84 years) were included in the present study. Nodules were identified by a second-year radiology resident (H.A.) after reviewing surgical records and CT images and confirmed by a chest radiologist (K.W.L.) with 20 years of experience. For patients with multiple SSNs, only nodules with pathological confirmation were selected. A total of 203 patients had single SSNs, while 12 patients had two, five patients had three, and one patient had five, resulting in a total of 247 SSNs for analysis.

2.2. Image acquisition

Images were obtained using 64- and 256-slice CT scanners (Brilliance 64 and iCT; Philips Medical Systems, Cleveland, Ohio). Nodules were evaluated with the following scanning protocols: high-resolution CT (n = 150), and contrast-enhanced CT (n = 97). All CT images were obtained with a tube voltage of 120 kVp, using automatic tube current modulation (Dose Right Index of 18 with maximal tube current time product of 160 mAs) at a pitch value of 0.984. For contrast-enhanced CT, 80 mL of non-ionic contrast media (Iomeron 350; Bracco UK, Ltd., High Wycombe, UK) was injected at a rate of 2 mL/s, followed by infusion of 20 mL of normal saline at the same rate. The trigger point was set at the time when the attenuation coefficient within the ascending aorta exceeded 150 Hounsfield Units. CT image acquisition began 28 s after the trigger point. All CT scans were obtained with patients in the supine position, in a fully inspiratory state, with a gantry rotation time of 0.5 s. Images were reconstructed using a filtered back-projection algorithm with a sharp convolution kernel (kernel D for high-resolution CT, and kernel YA for contrast-enhanced CT).

2.3. CT scan assessment

All CT slices containing each nodule were reconstructed in axial, coronal, and sagittal planes by a radiology resident (H.A.), with the section thickness of 1 mm (n = 165) or 2 mm (n = 82). Independent measurements were performed by two chest radiologists (Reader 1, K.H.L., and Reader 2, J.K., with 4 and 2 years of experience after board certification, respectively). The readers measured the long diameters of the ground-glass and solid portions on the representative image in which each component exhibited the largest diameter in the axial plane with lung-window settings (level -600 HU; width 1500 HU), respectively. They also measured the solid portion using mediastinal-window settings (level 30 HU; width 400 HU) on the representative image where it showed the largest diameter. Measurements were obtained in the same manner for the coronal and sagittal planes. The largest diameter among the measurements on the three planes was referred to as multiplanar measurement. When a nodule contained multiple solid portions, readers measured the size of the single largest solid portion. Electronic caliper on a PACS workstation was used for measurement. The results were rounded off to the nearest tenth in units of centimeters. Reader 1 repeated the measurement after three months. The readers were blinded to both radiology and pathology reports, and the reading order was randomized for each reader and session.

2.4. Pathological assessment

After being inflated and fixed using 10% buffered formalin, the specimens involving the whole tumor were cut at 3 mm interval along the longest tumor dimension, embedded in paraffin, and stained with hematoxylin and eosin. All sections containing the tumor were microscopically examined. Diagnoses were based on 2015 WHO classification criteria [4]. The three-dimensional sizes of the whole tumor, as well as the invasive components, were recorded by a pulmonary pathologist (J.H.C.) with 19 years of experience. When multiple invasive foci were present, the size of invasion was calculated as the summated percentage of invasive components multiplied by total tumor size, following the 2015 WHO classification of lung tumors.

2.5. Clinical and pathological T-stage classification

Clinical and pathological T-stages were assigned based on the sizes of the solid portion on CT images and those of the invasive components upon pathological examination, respectively, according to the eighth edition of TNM-staging classification for lung cancer [1,5].

2.6. Statistical analysis

For assessment of intra- and inter-reader agreement, intra-class correlation coefficients (ICCs) were used. The proportions of disagreement between clinical T-stages based on different measurement methods were measured with 95% confidence intervals (CIs).

For correlation between CT and pathological measurements, ICCs were used. Bland-Altman plots with 95% CIs were applied for the comparison of CT and pathological measurements. The agreement between clinical and pathological T-stage was assessed via the proportion of agreement and weighted κ-statistics. The proportion of agreement between the clinical and pathological T-stages depending on different measurement settings was compared using a generalized linear mixed model, considering clustered nature of data by nodules. To adjust the effect of heterogeneous CT protocols, the use of contrast enhancement and section thickness also entered as input variables.

The correlation as determined using ICCs and κ-statistics was interpreted as follows: 0–0.20, poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; and 0.81–1.00, excellent. Data were analyzed using MedCalc 14.8.1 (MedCalc Software, Mariakerke, Belgium) and Stata 14 (Stata Inc, College Station, Tex). A difference with a *P* value of