学 位 論 文 の 要 旨

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学 位 論 文 名	Radiographic and Pathological Analysis of Small Lung Adenocarcinoma Using the New IASLC Classification
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論 文 内 容 の 要 旨

INTRODUCTION

Adenocarcinoma is the most common histologic type of small-sized lung cancer. We classified tumors of size ≤ 20 mm as air-containing or solid-density type based on the percentage reduction of maximum tumor size on the mediastinal window image compared with the area on the lung window image on thin-section computed tomography (TS-CT): ≥ 50% was classified as air-containing type and < 50% was classified as solid-density type. Several studies reported an excellent prognosis in the air-containing type, with 5-year survival of approximately 100%. In the International Association for the Study of Lung Cancer (IASLC) / American Thoracic Society (ATS) / European Respiratory Society (ERS) Classification of Lung Adenocarcinoma (termed the new IASLC classification), Travis et al. defined new classifications for lung adenocarcinoma, as follows: adenocarcinoma in situ (AIS, ≤ 30 mm) (formerly termed bronchioloalveolar carcinoma [BAC]); minimally invasive adenocarcinoma (MIA, ≤ 30 mm lepidic growth predominant adenocarcinoma with ≤ 5 mm invasion); and invasive adenocarcinoma (including lepidic predominant with > 5 mm invasion, acinar, papillary, micropapillary, or solid predominant). Five-year survival of AIS was reported 100% and of MIA was reported approximately 100%. The aim of the present study was to determine whether TS-CT findings were good indicators of noninvasive carcinoma of the lung and to clarify the correlation between CT image findings and the new IASLC classification.

MATERIALS AND METHODS

We retrospectively reviewed the TS-CT findings and pathologic specimens of 300 lesions in 295 consecutive patients who underwent surgical resection for peripheral adenocarcinoma ≤ 20 mm in size. This study was approved by our institutional review board after confirmation of informed consent by the patients for us to review their records and images. Enhanced CT scans were obtained serially from the thoracic inlet to the lung bases during one breath hold. Two sets of images were processed: one set each with mediastinal window settings and lung window settings. All CT images were reviewed by three pulmonologists. A tumor was defined as air-containing type if the ratio (disappearance rate) of the maximum dimension of the tumor on mediastinal windows to the maximum dimension of the tumor on lung windows was ≤ 50%, and defined as solid-density type if the value was > 50%. We applied the following formula to calculate disappearance rate: Disappearance rate = (tumor size on lung windows – tumor size on mediastinal windows) / (tumor size on lung windows) × 100. Tumors were classified as air-containing or solid-density type on the basis of the disappearance rate. Evaluation of the preoperative CT images (on lung windows) was based on the presence or absence of air bronchogram, vascular involvement, pleural tag, notch, and spiculation. Tumors were further evaluated in terms of the following pathologic factors: pathologic stage (TNM system). We also evaluated the pathologic subtypes of the tumors as defined by new IASLC classification for resection specimens. Logistic regression analysis was used to investigate correlations between the presence of CT imaging findings and pathological classification.

RESULTS AND DISCUSSION

There were 300 lesions in 295 patients, and the median age was 66 years. On the basis of CT findings on lung windows and on mediastinal windows, 142 tumors were air-containing type and 158 were solid-density type. According to the new IASLC classification, 144 tumors were AIS, 52 were MIA, and 104 were invasive adenocarcinoma. Regarding pathological TNM stage, 268 tumors were Stage IA and 32 were stage IB or greater (all lesions were solid-density type). Of the cases of AIS, 114 (79.2%) were air-containing type and 30 (20.8%) were solid-density type. Of the cases of MIA, 28 (53.8%) were air-containing type and 24 (46.2%) were solid-density type. Of the cases of invasive adenocarcinoma, 0 (0.0%) were air-containing type and 104 (100.0%) were solid-density type. The chi-square test revealed that the incidence of solid-density lesions in invasive adenocarcinoma was significantly higher than AIS and MIA($P < 0.001$). In cases of AIS, median disappearance rate was 84.5%. Pleural tag were found in 80 (55.6%) and notch in 28 (19.4%). In cases of MIA, median disappearance rate was 50.0%. Pleural tag were found in 38 (73.1%) and notch in 22 (42.3%). In cases of invasive

adenocarcinoma, median disappearance rate was 13.3%. Pleural tag were found in 82 (78.9%) and notch in 78 (75.0%). Analysis of correlation between CT findings and pathological classification revealed the presence of notch and pleural tag as a significant factor in invasive adenocarcinoma, and air bronchogram as a significant factor in AIS and MIA.

We examined correlations between CT scan findings and the new IASLC classification. Our results revealed that all tumors determined as air-containing type on CT were AIS or MIA, but not invasive adenocarcinoma. The air-containing type is previously noted to have an excellent prognosis, with approximately 100% 5-year survival, but the solid-density type has poor prognosis. Because pathological invasive size can be differentiated on CT based on the disappearance rate, we consider that disappearance rate should be regarded as a prognostic factor. In addition, logistic regression analysis of correlation of the CT imaging findings and the new IASLC classification indicated that a lesion was likely to be invasive adenocarcinoma if notch was seen. Many investigators have reported a correlation between CT scan findings and pathologic findings. Areas of ground glass opacity (GGO) reflect a growth pattern where tumor cells have replaced alveolar lining cells, as in lepidic growth; in contrast, areas of consolidation mainly represent the foci of fibrosis or tumors of a solid growth pattern. Accordingly, in the present study, AIS and MIA were classified as air-containing type because large areas had predominately lepidic growth. In contrast, invasive adenocarcinoma was classified as solid-density type because large areas had predominately acinar, papillary, or solid growth. Solid-density type AIS (30 lesions) showed foci of fibrosis or mucinous adenocarcinoma. The percentage of the area of consolidation or GGO relative to tumor size indicates the existence or non-existence of invasion.

The present study found that all air-containing type tumors of size $\leq$ 20 mm showed predominantly lepidic growth with invasion size $\leq$ 5 mm. Based on the CT findings and pathological review, it appears likely that the air-containing type has good prognosis. We consider that application of this method will improve the accuracy of diagnosis for small lung adenocarcinomas.

CONCLUSION

This is the first report showing the correlation between CT image findings and the new IASLC classification. Disappearance rate should be regarded as a prognostic factor. Lung adenocarcinomas of size $\leq$ 20 mm that were classified as air-containing type on TS-CT were found pathologically to be AIS or MIA, but not invasive adenocarcinoma. The presence of notch and pleural tag were a significant factor in predicting invasive adenocarcinoma.