Lung Cancer 84 (2014) 236–241

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

High resolution CT in differentiating minimally invasive component in early lung adenocarcinoma☆

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ARTICLE INFO

Article history:
Received 1 September 2013
Received in revised form 13 January 2014
Accepted 12 February 2014

Keywords:
Lung cancer
Atypical adenomatous hyperplasia
Adenocarcinoma in situ
Minimally invasive adenocarcinoma
High-resolution CT
Preinvasive lesion

ABSTRACT

Objectives: To analyze high-resolution computed tomography (HRCT) appearances of early lung adenocarcinoma and evaluate HRCT in the differentiation of minimally invasive component in early lung adenocarcinoma.
Materials and methods: HRCT appearances of 140 nodules (less than 2 cm in diameter) of early lung adenocarcinoma were reviewed retrospectively. All these nodules were proven by surgery and pathology including 60 nodules of minimally invasive adenocarcinoma (MIA) and 80 nodules of preinvasive lesion (PL). HRCT features of two groups of lung nodules, including shape, margin, pattern, diameter, diameter of solid component, vascular changes, air bronchogram, vacuole, pleural indentation and multiplicity were analyzed and compared using univariate logistic regression analysis. Attenuation values of pure ground-glass nodule, pure ground-glass component and solid component of mixed ground-glass nodule were compared by using unpaired *t*-test or Wilcoxon rank-sum test.
Results: The statistically significant differences were found in shape, margin, pattern, diameter, diameter of solid component, pulmonary vein changes, air bronchogram and pleural indentation (Odds ratio [OR] = 3.115 [P = 0.001], OR = 3.754 [P = 0.011], OR = 9.815 [P = 0.000], OR = 1.306 [P = 0.000], OR = 1.361 [P = 0.031], OR = 6.971 [P = 0.000], OR = 6.167 [P = 0.000], OR = 2.296 [P = 0.027], respectively). The statistically significant difference was also found in attenuation value of solid component (t = 3.702, P = 0.000). By multivariate logistic analysis, attenuation value of solid component was significantly associated with MIA (OR = 1.005, P = 0.032). MIA was more often a larger, lobulated or irregular, mixed ground-glass nodule with a solid component larger than 5 mm, and higher attenuation values. In addition, MIA often had an abnormality in pulmonary vein, air bronchogram and pleural indentation.
Conclusions: HRCT can demonstrate the morphological features of early lung adenocarcinoma and identify minimally invasive component.

1. Introduction

CT screening for lung cancer has been shown to reduce obviously lung cancer mortality in a recent randomized controlled trial [1]. Consequently in the near future, it will become a routine program of physical examination and detect a large number of small or micro lung nodules which pose a diagnostic challenge to radiologists. Among the lung nodules found by screening CT in high risk population, 1% of them are malignant and most of them are lung adenocarcinomas which often appear as ground-glass nodules (GGN) [2]. On high-resolution computed tomography (HRCT), GGN appears as a hazy nodular increased attenuation of lung, with preservation of bronchial and vascular margins. As is known that GGN is a non-specific finding and can be a variety of benign or malignant disorders [3–7]. Therefore, CT characterization of GGN keeps a long-term focus of attention. Recently, an international multidisciplinary classification is developed to address advances in oncology, molecular biology, pathology, radiology, and surgery of lung adenocarcinoma [8]. According to the new classification, lung adenocarcinoma is divided into preinvasive lesions (PL) including atypical adenomatous hyperplasia (AAH) and adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma

☆ Grants from National Natural Science Foundation of China (81171340) and Science and Technology Commission of Shanghai (10411956800).
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http://dx.doi.org/10.1016/j.lungcan.2014.02.008
0169-5002/

Table 1
HRCT morphologic features of lung MIA and PL.

Morphologic features	MIA (n = 60)	PL (n = 80)	Odds ratio[a]	P-value	95% CI
Shape			3.115	0.001	1.552–6.254
Round/oval	24 (40)	54 (67)			
Lobulated/irregular	36 (60)	26 (33)			
Margin	14 (23)	6 (7)	3.754	0.011	1.347–10.459
Pattern			9.815	0.000	4.314–22.330
PGGN	10 (17)	53 (66)			
MGGN	50 (83)	27 (34)			
Diameter[b]	13.0 ± 4.1	9.6 ± 3.0	1.306	0.000	1.169–1.460
Diameter of solid component[b]	6.0 ± 2.2	5.0 ± 1.6	1.361	0.031	1.209–1.800
Abnormal pulmonary vein	37 (62)	15 (19)	6.971	0.000	3.242–14.989
Abnormal pulmonary artery	17 (28)	14 (17)	1.864	0.130	0.833–4.168
Air bronchogram	20 (33)	6 (7)	6.167	0.000	2.291–16.597
Vacuole	8 (13)	5 (6)	2.308	0.162	0.715–7.450
Pleural indentation	24 (40)	18 (22)	2.296	0.027	1.100–1.995
Multiplicity	20 (33)	27 (34)	0.981	0.959	0.483–1.995

MIA = minimally invasive adenocarcinoma, PL = preinvasive lesions, PGGN = pure ground-glass nodule, MGGN = mixed ground-glass nodule.
[a] Computed using the preinvasive lesions as the reference group. The numbers in parentheses represent percentages.
[b] Mean ± S.D.

(MIA), and invasive adenocarcinoma (IA). MIA, a new concept and an intermediate phase from PL to IA, grows into IA rapidly. The prompt resection of lung MIA will prevent it developing into IA or happening lymphatic and distant metastasis, which will markedly reduce patient's survival rate. In contrast, patient with PL can be followed up and resected in no hurry to rule out possible benign lesions. Not only will overtreatment be avoided, but no poorer prognosis will happen. Therefore, it has an important significance preoperatively identifying the minimally invasive component of early lung adenocarcinoma and differentiating MIA from PL. To our knowledge up to date, however, no similar HRCT study has been performed. The present study attempted to discriminate MIA from PL by analyzing retrospectively HRCT features of 80 PL and 60 MIA.

2. Materials and methods

2.1. Patients

The institutional review boards of our hospitals approved this retrospective study and informed consent was waived. From September 2011 to January 2013, HRCT of 131 patients with 140 GGN less than 2 cm was reviewed. All the nodules underwent a surgical resection and were pathologically proven to be MIA or PL (60 MIA, and 80 PL, including 12 AAH and 68 AIS). Among them, fifty-six patients had single MIA, one had 2 MIA, one had 1 MIA with 1 AIS and 1 AAH, one had 1 MIA and 1 AAH. Sixty-one patients had single AIS, one had 3 AIS and 1 AAH, one had 2 AIS, one had 1 AIS and 1 AAH, eight had single AAH. Thirty-one patients were men and 100 were women. Their age ranged from 25 to 75 (average, 53.6 ± 10.0) years old. Patients with MIA or PL were 25–75 (average, 54.1 ± 10.7) and 27–70 (average, 53.2 ± 9.5) years old, respectively, with no significant difference. All patients had neither lymphatic or pleural invasion nor distant metastasis.

2.2. CT screening

CT scans were obtained with a 64-detector row scanner (Brilliance, Philips, Clevland, USA) using the unenhanced helical technique at the end of inspiration during one breath hold. The scanning parameters of routine CT were as follows: detector collimation, 64 mm × 0.625 mm; pitch, 1.08; section thickness and interval, 5.0 and 5.0 mm; 5–7 s scan time; matrix, 512 × 512; FOV, 400 mm; 120 kVp and 250 mA. When a lung nodule was found, a HRCT target scan followed with following, parameters: collimation, 64 mm × 0.625 mm; pitch, 0.64; section thickness and interval, 1.0 and 1.0 mm; 1–3 s scan time; matrix, 1024 × 1024; FOV, 180 mm; 120 kVp and 300 mA. The reconstruction algorithms for routine CT and targeted HRCT scans were "standard" and "sharp" respectively.

2.3. Evaluation of CT features

Two radiologists (Y.Z, J.W.Q, with 4 and 29 years of experience in chest imaging, respectively), who did not know the histologic result of GGN, assessed CT images on both mediastinal (width, 350 HU; level, 40 HU) and lung (width, 1450 HU; level, −520 HU) windows, respectively. Decisions on CT findings were reached by consensus. HRCT findings of each nodule were analyzed as follows: (1) shape (round or oval, lobulated or irregular), (2) margin (speculated, smooth), (3) pattern (pure ground-glass nodule, PGGN or mixed ground-glass nodule, MGGN), (4) diameter (the largest diameter on axial, sagittal and coronal sections), (5) diameter of solid component (the largest diameter on three-dimensional section), (6) air bronchogram, (7) vascular changes (dilated, rigid, convergent and tortuous; only one time was recorded if more than one changes found; we traced the vessel from nodule to hilum to determine its source of pulmonary or bronchial, and artery or vein), (8) pleural indentation, (9) vacuole, (10) multiplicity (if there were two or more GGN in an individual), (11) CT value (attenuation values of PGGN and pure ground-glass and solid component of MGGN, these measurements were performed three times with the biggest area of interest, and mean value was recorded).

2.4. Pathologic evaluation

The surgically resected specimens were fixed in 10% formalin, embedded in paraffin, sectioned with a microtome, and stained with hematoxylin and eosin (H & E). Histopathological analysis of nodule was performed and was classified according to the 2011 international multidisciplinary classification of lung adenocarcinoma by two experienced lung pathologists in consensus.

2.5. Statistical analysis

HRCT features of two groups of lung nodules, including shape, margin, pattern, diameter, diameter of solid component, vascular changes, air bronchogram, vacuole, pleural indentation and multiplicity were analyzed and compared by using univariate logistic regression analysis. Attenuation values of PGGN, pure ground-glass and solid components of MGGN were compared by using unpaired t-test or Wilcoxon rank-sum test. The variable with statistically significant difference was brought into multivariate