Predictive Value of One-Dimensional Mean Computed Tomography Value of Ground-Glass Opacity on High-Resolution Images for the Possibility of Future Change

Masaya Tamura, MD,, Yosuke Shimizu, MD,* Toru Yamamoto, MD,† Jun Yoshikawa, MD,† and Yasuo Hashizume, MD**

Objectives: The purpose of this study was to evaluate the relationship between clinical and radiological findings and the progression of ground-glass opacity (GGO) and to identify risk factors that predict the outcome of pure GGO lesions.

Methods: A retrospective study was conducted on 63 nodules of pure GGO. Clinical characteristics, the largest diameter, shape, and marginal characteristics, and one-dimensional mean computed tomography (m-CT) value of the GGO lesions were evaluated. During follow-up, 12 GGO lesions increased in size, and 17 appeared as solid portion. These 29 lesions were classified as growth group, and the remaining 34 lesions as stable group.

Results: The m-CT values were -634.9 ± 15.3 and -712.1 ± 14.1 HU for the growth and stable groups, respectively. The growth group was strongly associated with high m-CT values ($p = 0.0007$) and a history of lung cancer ($p = 0.0389$), whereas association with smoking habits and the shape of the GGO nodules was marginal. The m-CT values and a history of lung cancer were independent predictors for future changes in GGO lesions ($p = 0.0023$ and $p = 0.0129$, respectively). Sixteen of 18 lesions (88.9%) in patients without a history of lung cancer and with low m-CT values showed no nodule changes.

Conclusions: The m-CT value of GGO lesions is a risk factor associated with their future change. The interval of follow-up CT scanning or treatment policy should be determined considering the m-CT value.

Key Words: Ground-glass opacity, Radiological features, Mean computed tomography

(*J Thorac Oncol*. 2014;9: 469–472)

With recent advancement in diagnostic imaging technologies, ground-glass opacity (GGO) lesions are increasingly detected on high-resolution computed tomography (HRCT) scans.[1,2] GGO is defined as a shadow that is completely occupied by a hazy increased attenuation of the lung, with preservation of the bronchial and vascular lesion margins when assessed with HRCT.[3] Many radiological studies of small lung adenocarcinomas have demonstrated a strong correlation between CT findings and pathological features, but few have demonstrated the outcome of pure GGO lesions in patients in whom some lesions are not resected and then followed by CT scans. Therefore, the appropriate treatment strategies for small tumors displaying GGO remain controversial. The objectives of this study were to determine the relationship between the clinical and radiological findings and the progress of GGO to predict the outcome of pure GGO lesions.

PATIENTS AND METHODS

Patients

This study was approved by our hospital's internal review board. Between October 2008 and October 2012, a total 63 nodules with GGO in consecutive 53 patients were followed up. Patients with localized and pure GGO without any solid component were included in this study, and those with GGO with a solid component were excluded. Medical records were retrospectively reviewed to investigate the clinical characteristics, GGO features, histopathological results, and follow-up outcomes. All patients were followed up in accordance with the follow-up criteria for lung cancer CT screening guideline.[4]

Image Acquisition and Analysis

CT scans were performed from the lung apex to base during breath holding at mid-inspiration by using a CT scanner with a section thickness of 2 mm (Asteion 4, Toshiba, Tokyo, Japan). Two radiologists with 19 and 10 years of experience in general radiology independently viewed these images and subjectively classified the nodules. Pure GGO was defined as a shadow completely occupied by a hazy increased attenuation of the lung, with preservation of the bronchial and vascular margins of the lesion with no solid regions on HRCT. The longest diameters of the GGO lesions were measured, and the shapes were classified as round and others (oval or polygonal). The marginal characteristics were classified as smooth and others (lobulated and speculated). Maximum diameter and one-dimensional mean CT (m-CT) value of this diameter were measured using a computer graphics support

Departments of *Surgery and †Radiology, Fukui Prefectural Hospital, Fukui, Japan.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Masaya Tamura, MD, Department of Surgery, Fukui Prefectural Hospital, Yotsui 2-8-1, Fukui, Fukui 910–8526, Japan. E-mail: masatamu2007@yahoo.co.jp

ISSN: 1556-0864/14/0904-0469

system (Synapse PACS, Fujifilm, Tokyo, Japan). The shape of the region of interest was standardized for each patient and configured by freehand drawing. The interobserver variation was corrected by calculating the mean value of two observers.

Definitions of Malignant Findings

Lesion size was defined as the maximal diameter on HRCT and an increase in diameter of more than 2 mm, or an emerging solid portion was defined as a malignant radiological finding. We defined these lesions as *growth* group and others as *stable* group. The lesions that had a history of previous lung cancer were followed up by the surgeons and those that were discovered as part of CT screening were followed up by the pulmonologists. Radiologists and physicians performed careful and close monitoring to determine whether GGO lesions had any malignant radiological findings. Histological findings of adenocarcinoma were classified according to the criteria of the World Health Organization.[5]

Statistical Analysis

All data regarding continuous variables are expressed as mean ± SD. Significant differences were assessed using the *t* test for continuous variables, and the χ^2 test for categorical variables. Analyses were performed using the SAS software package (SAS Institute, Inc., Cary, NC). A p value less than 0.05 was considered statistically significant.

RESULTS

Patient characteristics and GGO features are summarized in Table 1. A total 63 lesions were detected in 53 patients. Of these, one lesion was detected in 46 patients, two in four, and three in three. The mean age at diagnosis was 70.8 ± 9.3 years (range, 40–87 years). Twenty-three lesions were found in men and 40 in women. The mean size of GGO lesions at initial detection was 11.4 ± 4.2 mm (range, 3.8–19.6 mm). Thirty-nine patients (61.9%) had no history of smoking. Twenty-four lesions had a history of previous lung cancer, and 39 were discovered as part of CT screening. The average follow-up period for all patients was 26.1 ± 4.6 months. During the follow-up, 12 GGO lesions increased in size and 17 appeared as solid portion. These 29 lesions were classified as the growth group and the remaining 34 lesions as the stable group. During the follow-up period, 45 lesions were resected and pathologically diagnosed as adenocarcinoma in situ (AIS; 38 lesions), minimally invasive adenocarcinoma (5), and invasive adenocarcinoma (papillary predominant; 2). m-CT values were −634.9 ± 15.3 HU in the growth group and −712.1 ± 14.1 HU in the stable group (p = 0.0005) (Fig. 1). Prediction of the GGO change was attempted based on the m-CT value, and receiver operating characteristics curve analysis was performed to determine the appropriate cutoff value. The maximum sensitivity and specificity were obtained at a cutoff value of −677 HU. The mean interval from the first detection of GGO to the last observation was 28.6 ± 4.5 months for the growth group and 24.2 ± 4.0 months for the stable group (p = 0.3366). Table 2 shows the comparison of clinico–radiological data between lesions in the stable group and those in growth groups. The growth group was strongly associated with a high CT attenuation value (p = 0.0007) and the growth group was associated with a history of lung cancer (p = 0.0389), whereas smoking habit and the shape of GGO nodules were marginally significant (p = 0.0632 and p = 0.0725, respectively). Table 3 shows the results of multivariate analysis for predictors of changes in GGO lesions. m-CT value and a history of lung cancer were independent predictors (p = 0.0023 and p = 0.0129, respectively). A comparative distribution of the m-CT values between with and without a history of lung cancer is presented in Figure 2. Sixteen of 18 lesions (88.9%) in those without a history of lung cancer and with low m-CT values showed no change during the follow-up.

TABLE 1. Clinical Characteristics of Patients and 63 GGO Lesions

Characteristics	n
No. of patients	53
Total no. of GGO lesions	63
No. of GGO lesions per patient	
1	46
2	4
3	3
Age at diagnosis (yrs, mean ± SD)	70.8 ± 9.3 (40–87)
Male:female	23:40
History of smoking	
Nonsmoker	42
Smoker	21
History of previous lung cancer	
No	39
Yes	24
Size of GGO lesions (mm: mean ± SD [range])	11.4 ± 4.2 (3.8–19.6)

GGO, ground-glass opacity.

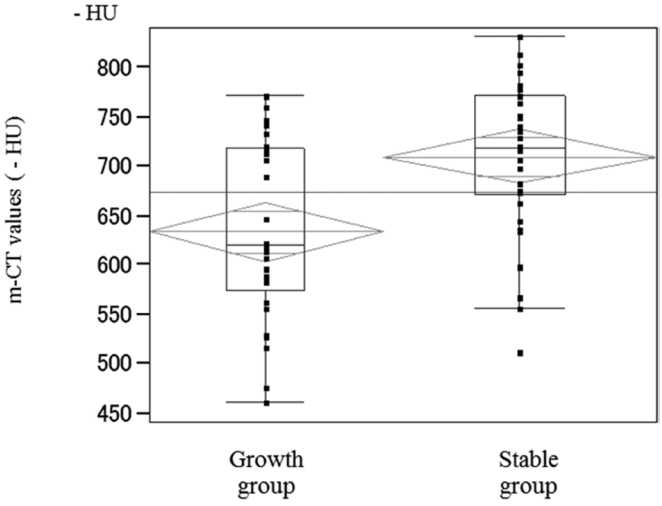

FIGURE 1. Comparison of the mean CT values between the growth and stable groups.