

Management of Multiple Pure Ground-Glass Opacity Lesions in Patients with Bronchioloalveolar Carcinoma

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Introduction: The objective of this study was to evaluate the clinical characteristics and long-term outcome of multiple pure ground-glass opacity (GGO) lesions detected in patients undergoing pulmonary resection for bronchioloalveolar carcinoma (BAC).

Methods: Between January 2000 and December 2007, 73 patients underwent pulmonary resection for BAC. Of those, 23 patients had multiple pure GGOs on their preoperative computed tomography (CT) scans. Eighty-nine GGO lesions were detected with a median number of 3 (range, 2–11) per patient. Resection included wedge resection in 12 patients, lobectomy in 7, lobectomy with wedge resection in 3, and bilobectomy in 1. Five patients had all GGOs lesions resected (group I), whereas 18 had some of the GGO lesions resected and the remaining lesions followed by serial CT scans (group II). Median follow-up was 40.3 months.

Results: No late death occurred during the follow-up period. In group I, four patients had no recurrences and one patient developed a new lesion that was resected and found to be adenocarcinoma. In group II, GGO lesions either did not change in size ($n = 15$) or disappeared ($n = 3$) in all patients. No GGO lesions increased in size or developed a solid component during the follow-up period.

Conclusions: When multiple pure GGO lesions in patients with BAC remained without surgical resection, there was no change in their size or features during follow-up. When it is not feasible to resect all GGO lesions in patients with multifocal BAC, close follow-up using CT scans represents an alternative to surgical resection.

Keywords: Ground-glass opacity, Bronchioloalveolar carcinoma, Follow-up, Surgical resection.

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With recent advances in diagnostic imaging modalities, pure ground-glass opacity (GGO) lesions have been increasingly detected on high-resolution computed tomogra-

phy (HRCT) scans.^{1–4} The correlation between the radiologic findings of GGO lesions and their pathologic diagnosis has been extensively studied.^{5–12} As GGO is a nonspecific finding, it can be caused by various diseases such as inflammation, fibrosis, or neoplasm.⁵ In particular, with respect to pure GGO, the possibility of nonmucinous bronchioloalveolar carcinoma (BAC) cannot be excluded. Indeed, BAC usually appears as multiple pure GGO lesions. Previous genetic research on BAC using a novel strategy for clonality determination indicates that these tumors are mostly multifocal, independent cancers.¹³ Accordingly, in patients with multiple pure GGO lesions on HRCT scans, when one of the lesions is pathologically confirmed as BAC, the remaining lesions may have the same pathology (i.e., multifocal BAC).

When a GGO lesion is located deep in the hilum or multiple lesions are scattered in different lobes in patients with multifocal BAC, it can be difficult to resect them all. Yet, it has also not been determined whether these lesions should be resected or followed by serial computed tomography (CT) scans. Few reports have demonstrated the fate of pure GGO lesions in cases where some are not resected and then followed by CT scans. The objectives of this study were to (1) evaluate the clinical characteristics and long-term outcome of multiple pure GGO lesions detected in patients undergoing pulmonary resection for BAC and (2) report the fate and follow-up outcome of unresected, residual GGO lesions.

PATIENTS AND METHODS

Between January 2000 and December 2007, 2361 patients underwent pulmonary resection for non-small cell lung cancer at our institution. Pathologic examinations revealed that among these, 73 patients had BAC according to the recently revised World Health Organization classification of lung tumors.¹⁴ Of these, 23 patients had multiple pure GGO lesions on preoperative CT scans and were included in the study population. Patients who had single GGO lesion were excluded. Patients who had GGO lesions with a solid component (“mixed GGO”) were excluded. Patients who had adenocarcinoma with BAC features were also excluded. Medical records were retrospectively reviewed to investigate the clinical characteristics, GGO features, histopathologic results, and follow-up outcomes. This study was reviewed and approved by the Institutional Review Board of Samsung Medical Center.

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In patients with multiple pure GGO lesions, we tried to resect pure GGO lesions larger than 10 mm regardless of the location. For pure GGO lesions smaller than 10 mm, if the extent of resection was expected to be greater than lobectomy due to the central location or if there were multiple lesions scattered throughout multiple lobes, we decided not to resect such lesions and instead closely follow them using serial CT scans. No patients underwent percutaneous fine needle aspiration or transbronchial biopsy via bronchoscopy.

All patients were regularly evaluated by CT scans every 3 months for the first 2 years after surgery, and then every 6 months thereafter regardless of whether or not all GGO lesions were resected. Descriptive statistics were used to summarize patient characteristics and outcomes. The normally distributed, continuous data were expressed as mean \pm SD. Categorical data were expressed as counts and proportions. Significance was defined as a *p* value less than 0.05.

RESULTS

Clinical Findings

Patient characteristics and GGO features are summarized in Table 1. There were 11 men (48%) and 12 women (52%), with a mean age of 57.2 ± 9.3 years (range, 38–78 years). Fifteen patients (65%) had no history of smoking. No patients had a history of malignancy except for one who had a colon cancer. A total of 89 GGO lesions were detected in 23 patients, and the median number of GGO lesions per patient was 3 (range, 2–11). The median size of GGO lesions was 5 mm (range, 3–40). The mean diameter of the resected GGO lesions was 9 mm, whereas the mean diameter of those that were followed with imaging studies was 5 mm. GGO lesions

were detected bilaterally in 13 patients (57%) and unilaterally in 10 (43%). Typical images of CT scans are shown in Figure 1.

Operative Procedures

Operative procedures are listed in Table 2. Preoperative percutaneous CT-guided marking using a hook wire was performed in 16 patients (70%). Procedures were done using video-assisted thoracic surgery in 16 patients (70%). Wedge resection was performed in 12 patients (52%), lobectomy in 7 (30%), lobectomy with wedge resection in 3 (13%) and bilobectomy in 1 (4%). Of the 11 patients who had a lobectomy or bilobectomy, 8 underwent conversion from wedge resection to lobectomy because the possibility of adenocarcinoma could not be ruled out based on the intraoperative frozen section alone. Two patients underwent lobectomy for a deeply-located lesion and one for multiple lesions in a lobe. In all patients who underwent lobectomy or bilobectomy, systematic mediastinal lymph node dissection was done. Five patients (22%) had all GGO lesions resected, whereas 18 patients (78%) had some GGO lesions resected and the remaining lesions followed by serial CT scans.

Early Outcomes

No early mortality or morbidity occurred during the postoperative period. The mean duration of hospital stay was 5.3 ± 2.8 days (range, 2–14 days). Thirty-nine GGO lesions were resected, and the pathologic diagnoses included nonmucinous BAC in 26 lesions, atypical adenomatous hyperplasia in 10, anthracofibrosis in 2, and mucinous BAC in 1. All the 11 patients who underwent a mediastinal lymph node dissection had N0 disease.

Late Outcomes

The median follow-up duration was 40.3 months (range, 22–110 months). No late death occurred during the follow-up period, and no patients developed a local recurrence or distant metastasis. Of the five patients who had all GGO lesions resected, four (80%) had no recurrences, whereas one (20%) developed a new lesion 49 months after the initial operation. The patient, who had undergone a bilobectomy for multifocal BAC, received a wedge resection for the newly developed lesion, which turned out to be adenocarcinoma. In the 18 patients who had some GGO lesions resected and the remaining lesions followed by CT scans, the residual lesions either did not change in size ($n = 15$, 83%) or disappeared ($n = 3$, 17%) in all patients. No GGO lesions increased in size or developed a solid component during the follow-up period. Patient demographics and follow-up outcomes are presented in Table 3.

DISCUSSION

GGO is a radiographic finding defined as hazy, increased attenuation of the lung with preservation of bronchial and vascular margins.⁵ GGO features arise from a replacing growth pattern along the alveolar wall.⁵ Because the pathology of GGO may be a neoplasm such as BAC or early-stage adenocarcinoma, many authors have investigated the correlation of radiologic findings with pathologic diagnosis.^{5–12} When GGO lesions are substantially large (e.g., >10 mm) or

TABLE 1. Clinical Characteristics and GGO Features

Characteristics	
No. of patients (<i>n</i>)	23
Age at operation (yr, mean \pm SD)	57.2 \pm 9.3 (38–78)
Male:female	11:12
History of smoking (<i>n</i>)	
Nonsmoker	15
Current smoker	7
Exsmoker	1
History of previous malignancy (<i>n</i>)	
No	22
Yes	1 ^a
Total no. of GGO lesions (<i>n</i>)	89
No. of GGO lesions per patient, <i>n</i> , median (range)	3 (2–11)
2	7
3	6
4	6
>5	4
Size of GGO lesions, mm, median (range)	5 (3–40)
Location (<i>n</i>)	
Bilateral	13
Unilateral	10

^a Had a history of colon cancer.

GGO = ground-glass opacity.

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