Journal of Interventional Medicine 3 (2020) 89–92

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Journal of Interventional Medicine

journal homepage: www.keaipublishing.com/cn/journals/journal-of-interventional-medicine/

Clinicopathologic characteristics of pulmonary ground glass opacity located preoperatively using a Hook-wire guidewire

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ARTICLE INFO

Keywords:
CT guidance
Hook-wire localization
Ground glass opacity
Imaging
Pathology

ABSTRACT

Objective: To evaluate the relationship between the clinical and imaging features of ground glass opacity (GGO) localized using a preoperative Hook-wire guidewire and postoperative pathology.

Method: Preoperative Hook-wire guidewire localization was performed in 83 patients with GGO less than 2 cm, and their clinical data, imaging data, and postoperative pathology findings were retrospectively analyzed. The images were classified as pure GGO (pGGO) or mixed GGO (mGGO). The relationship between clinical and imaging features and postoperative pathology was analyzed.

Result: The 83 cases were colocalized, and the success rate of the guidewire positioning was 100%. Complications included pneumothorax (19.2% [16/83]) and the incidence of minor bleeding (30.2 [25/83]). Forty-seven patients had mGGO and 36 had pGGO. Among the 47 cases of mGGO, 18 (38.3%) were invasive adenocarcinoma (IAC), 18 (38.3%) were microinvasive adenocarcinoma (MIA), 8 (17.0%) were adenocarcinoma in situ (AIS), 2 (4.3%) were atypical adenomatous hyperplasia (AAH), and 1 (2.1%) was benign. Among the 36 cases of pGGO, 6 (16.7%) were IAC, 13 (36.1%) were MIA, 8 (22.2%) were AIS, 2 (5.6%) were AAH, and 7 (19.4%) cases were benign lesions. A significantly higher proportion of patients with IAC had mGGO than pGGO (21.7% vs. 7.2%, respectively; $p = 0.004$). Among patients with mGGO, a higher proportion of them had a nodule diameter of $\geq$1 cm than those with a diameter of $<$1 cm (25.5% vs. 12.8%, respectively; $p = 0.003$). There was no significant difference in age, location distribution, or pathological type.

Conclusion: Preoperative CT-guided Hook-wire guidewire positioning was safe with minor complications. A significantly higher proportion of patients with IAC had mGGO than pGGO. Patients with mGGO and a nodule diameter $\geq$1 cm require active treatment.

1. Introduction

The detection of asymptomatic ground glass opacity (GGO) has increased in recent years through low-dose thin-slice spiral computed tomography (CT) screening. GGO is defined as a slightly dense, low-density nodule in the lung that does not mask nonspecific imaging of the same layer of blood vessels and bronchioles.[1] The pathological basis of GGO-like lesions is localized thickening of the alveolar wall, collapse of the alveolar space, reduced air volume in the alveolar space, and filling of fluid or cellular material.[2] GGO includes a wide variety of pathological types including benign nodules such as focal interstitial fibrosis, inflammatory lesions, hemorrhage, and malignant nodules.[3,4]

In 2011, the International Association for the Study of Lung Cancer, the American Thoracic Society, and the European Respiratory Society jointly published a new classification system for lung adenocarcinoma. Minimally invasive adenocarcinoma (MIA) and adenocarcinoma in situ (AIS) were introduced for the first time, and the concept of bronchioloalveolar carcinoma was abolished. The new classification system subdivides GGO into pathologically preinvasive lesions, including atypical adenomatous hyperplasia (AAH) and AIS, and divides invasive lesions into MIA and invasive adenocarcinoma (IAC).[5] Previous studies have reported that preoperative CT imaging findings are associated with pathological features and postoperative prognosis.[6,7] Some studies reported that GGO lesion size, lobulation signs, Burr signs, vacuole signs, and other signs suggest the nature of GGO-like lesions,[8] but the conclusions regarding the correlation between clinicopathological data and GGO pathology remain inconsistent.[9–11] The transition from AAH to MIA follows a continuously changing natural course. The 5-year survival rate

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https://doi.org/10.1016/j.jimed.2020.03.006

Available online 30 March 2020

of patients with AAH and MIA is reportedly almost 100%; however, the long-term survival rate of patients with IAC remains low.[12] Therefore, the early identification of such patients using clinical, imaging, and pathological analyses of GGO lesions is particularly important for the clinical management of GGO.

Herein, we discuss the clinical manifestations of GGO-type lesions and the relationship between imaging findings and postoperative pathology through a retrospective analysis of 83 cases of Hook-wire localization.

2. Materials and method

2.1. Clinical data

A retrospective analysis was performed of the medical history of 83 patients (27 men, 56 women; age range, 23–79 years; median age, 55 years) with surgically resected lung GGO by preoperative CT-guided Hook-wire localization between December 2015 and September 2017 in Tianjin Medical University Cancer Hospital. The mean GGO lesion size was 1.59 ± 0.54 cm (range, 0.4–2.5 cm).

Depending on whether the GGO lesion was accompanied by a solid component that accounted for lesion density, GGO was divided into pure GGO (pGGO) and mixed GGO (mGGO). According to the evaluation criteria, the CT images were evaluated by two experienced deputy chief physicians for a double-blind review and consensus. Different window widths and levels were adjusted on the picture archiving and communication system, and multiplanar reconstruction was performed. Furthermore, GGO size, classification, and distribution position details were recorded.

2.2. Guidewire positioning surgery

With guidance from the preoperative CT scan, the appropriate puncture position was selected according to lesion location and patient comfort. The CT scan parameter setting was designed according to lesion size. The laser was positioned on the surface of the selected puncture level to place the fence-shaped metal-positioning ruler. The puncture point was selected to introduce the puncture needle after administering local anesthesia and to observe the relative spatial positioning relationship between the needle tip and the lesion. After the puncture, the needle reached the target lesion. If the position was satisfactory, the guidewire was released and the puncture needle was pulled outward. The guidewire was then fixed inside the lesion.

2.3. Surgical resection and pathological analysis

Thoracoscopic resection was performed according to the guidewire position, and the postoperative tissue specimens were sent to pathology department; experienced physicians divided the lesions into preinfiltration lesions (AAH or AIS) and invasive lesions (MIA or IAC) by referencing the new standard proposed by the International Association for the Study of Lung Cancer/American Thoracic Society/Europe Respiratory Society in 2011. Pathological observation and specimen analyses were performed to obtain pathological reports.

2.4. Statistical analysis

Data analysis was performed using SPSS 22.0 software. The data including lesion size, sex, age, and nodule site and the pathological results were analyzed using Fisher's exact probability method. $p < 0.05$ was considered to indicate statistical significance.

3. Results

The clinical data of the 83 cases were collected. The success rate of guidewire positioning was 100%. No localization needles were removed before the operation. The main complications were pneumothorax and bleeding at the puncture site (19.2% and 30.2%, respectively). No serious complications occurred (Fig. 1).

Of the 83 cases of GGO lesions, 36 were pGGO and 47 were mGGO. Postoperative pathology confirmed 31 cases of MIA, 24 cases of IAC, 16 cases of AIS, 4 cases of AAH, and 8 cases of benign lesions. The lesions were distributed in the lung as follows: 59 in the upper lobe (70.8%), 3 in the right middle lobe (3.6%), and 21 in the lower lobe (25.2%). There were 26 cases of mGGO <1 cm (31.3%) and 21 cases of mGGO ≥ 1 cm (25.3%). There were 23 cases of pGGO <1 cm (27.7%) and 13 cases of pGGO ≥ 1 cm (15.7%) (Table 1). There were significantly more invasive lesions in the patients of the mGGO group, especially among those with IAC, than in those of the pGGO group (21.7% vs. 7.2%, $p = 0.004$) (Table 2).

Further analysis of the mGGO patient group revealed no significant differences between subgroups in age, sex, or pathological type. A significantly higher proportion of patients with IAC had nodule diameter ≥1 cm than those with that of >1 cm (25.5% vs. 12.8%, $p = 0.003$). Regarding lesion location, although there were more lesions in the upper and middle levels in patients with IAC than in patients with MIA (72.3% vs. 27.7%), there were no significant differences between subgroups in lesion distribution or pathological classification (Tables 3 and 4).

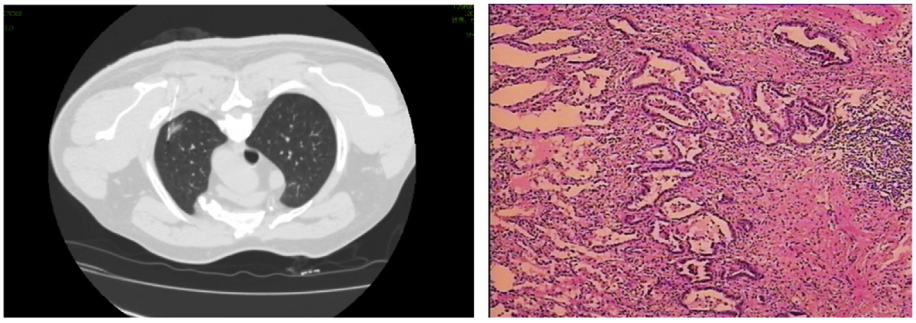
Further, there were no significant differences in age, sex, or pathological type among patients with pGGO, and a significantly higher proportion of patients with AIS had lesion diameter <1 cm than those with lesion diameter ≥1 cm (16.7% vs. 0%, $p = 0.014$). There were no significant differences between subgroups in lesion distribution or pathological classification, but the number of lesions in the upper and middle levels was higher in patients with IAC than in those with MIA (77.8% vs. 21.2%) (Tables 5 and 6).

4. Discussion

There are different pathological types of GGO lesions, including benign lesions such as inflammatory lesions, old hemorrhages, and some malignant nodules. The current pathological classification divides lung adenocarcinoma into preinvasive (AAH and AIS) and invasive lesions (MIA and IAC).[5] Most studies evaluated the predictive value of CT features for differentiating between two lesions and postoperative pathology, but the conclusions of these studies were inconsistent.[9,13] This may be related to the number of cases included and the observation indicators selected for the statistical stratification analysis.

The specimens included in our study were pathologically confirmed by postoperative pathology, and the relationships among age, sex, nodule diameter, and pathological type in the mGGO and pGGO groups were compared by a retrospective stratification analysis of GGO lesions according to the latest pathological types. In a previous retrospective analysis of GGO lesions by pathological type, the 5-year postoperative survival rates of AAH, AIS, and MIA were 95.1%, while the IAC survival rate was only 87.6%.[14] This may be because IAC is associated with a higher probability of lymph node metastasis and vascular invasion.[15] One study[11] reported that most round GGO lesions with rough edges were microinvasive carcinoma and mixed-density ground glass nodules with burrs on the edge, whereas those with pleural indentation signs were invasive carcinoma. Regarding pathological behavior, the lesions that invaded the lymphatic vessels, blood vessels, or pleura appeared as partially solid nodules on CT.[16] In our study, the pathological subsets of the mGGO and pGGO lesions were compared and analyzed, and there were more invasive lesions in the mGGO group than in the pGGO group. The proportion of patients with IAC was significantly higher in the mGGO group than in the pGGO group (21.7% vs. 7.2%, $p = 0.004$). As there is a high proportion of IAC patients with mGGO, active measures should be taken during clinical treatment.

Some studies have reported that the diameter of invasive lesions in mGGO nodules was significantly larger than that of preinvasive lesions (AAH and AIS).[17] Lesion size is a factor that determines the degree of



a b

Fig. 1. A 49-year-old woman underwent imaging. a: mGGO in the left lung upper lobe, approximately 1.5 × 0.8 cm in size with Hook-wire positioning before the operation. b: pathological result: invasive adenocarcinoma.

Table 1
Clinicopathological features of patients with GGO.

Feature		mGGO	pGGO
Age (years)	≥55	24 (28.9%)	17 (20.5%)
	<55	23 (27.7%)	19 (22.9%)
Sex	Male	12 (14.4%)	15 (18.1%)
	Female	35 (42.2%)	21 (25.3%)
Opacity size (cm)	≥1.0	21 (25.3%)	13 (15.7%)
	<1.0	26 (31.3%)	23 (27.7%)
Location in the lung	upper lobe	33 (39.6%)	26 (31.2%)
	middle lobe	1 (1.2%)	2 (2.4%)
	lower lobe	13 (15.6%)	8 (9.6%)
Pathology type	AIS	8 (9.6%)	8 (9.6%)
	MIA	18 (21.7%)	13 (15.7%)
	IAC	18 (21.7%)	6 (7.2%)
	AAH	2 (2.4%)	2 (2.4%)
	Benign condition	1 (1.2%)	7 (8.4%)

AAH, atypical adenomatous hyperplasia; AIS, adenocarcinoma in situ; GGO, ground glass opacity; IAC, invasive adenocarcinoma; mGGO, mixed ground glass opacity; MIA, microinvasive adenocarcinoma; pGGO, pure ground glass opacity.

Table 2
Subgroup analysis between GGO imaging finding and pathology.

	AAH	AIS	MIA	IAC	Benign condition
mGGO	2 (2.4%)	8 (9.6%)	18 (21.7%)	18 (21.7%)	1 (1.2%)
pGGO	2 (2.4%)	8 (9.6%)	13 (15.7%)	6 (7.2%)	7 (8.4%)
χ^2	2.000	1.753	3.785	8.229	
P	0.236	0.253	0.088	0.004#	

AAH, atypical adenomatous hyperplasia; AIS, adenocarcinoma in situ; GGO, ground glass opacity; mGGO, mixed ground glass opacity; pGGO, pure ground glass opacity; IAC, invasive adenocarcinoma; MIA, microinvasive adenocarcinoma.
Compared with benign condition: *P < 0.05; #P < 0.01.

malignancy. The larger a lesion is, the worse is its nature. One study[9] reported that the positive predictive value of invasive cancer was higher if there is a microvascular sign and the nodule diameter >1 cm in mGGO. Another study[18] considered a nodule size of 1.05 cm as the threshold between preinvasive and invasive lesions. Our pathological analyses also considered 1-cm size as a factor for determining whether GGO lesions have invasive components, and the result was consistent with that of the previous meta-analysis on GGO lesions.[19] Further analysis of the relationship between pathological subclass and sex, age, or nodule diameter of patients with mGGO revealed that a significantly higher proportion of patients with IAC had nodule diameter ≥1 cm than patients with IAC and nodule diameter <1 cm (25.5% vs. 12.8%, p = 0.003). Among cases of mGGO, a diameter ≥1 cm could significantly predict IAC, and there were no significant differences in age, sex, or pathological type between IAC and MIA.

According to the National Comprehensive Care Network recommendation of subsolid pulmonary nodules,[20] for nodules ≥6 mm and solid components <6 mm, a low-dose CT scan should be performed within 6 months; if it continues to be stable, then an annual screening can be adopted. If the clinical, imaging and PET findings suggest lung cancer, then biopsy or surgical resection is required. Otherwise, if the nodules are mildly suggestive of lung cancer, then low-dose CT should be performed within 3 months. Lee [21] conducted a study of 272 pGGO specimens and found that when a pure GGO was greater than 15 mm in diameter with nodularity or had high pixel attenuation (>-472 HU), the nodules were more likely to be IAC. Our study showed a significantly higher proportion of AIS and MIA lesions in pGGO that were smaller than 1 cm and that there were no significant differences in age, sex, or pathological type in the pGGO patient group. Previous studies have reported significant prognostic differences between histological subtypes[14]: patients with AIS and MIA had better overall survival and relapse-free survival than those with IAC. The differences in prognosis may be due to the differences in pathological invasion behavior between lesion types. Compared to those with IAC, patients with AIS had earlier tumor T stages and lower incidences of lymphatic and pleural infiltration. MIA does not invade the lymphatic vessels, blood vessels, or pleura; further, there is no necrosis in the lesion, and the prognosis is very good [22]. Lymph node metastasis was not detected in any of the patients with AIS or MIA. The prognosis of patients with IAC was relatively poor. For mGGO lesions with a diameter greater than 1 cm, an MDT should be recommended.

In summary, preoperative CT-guided Hook-wire guidewire positioning is a safe and effective method. There exists a certain relationship

Table 3
Clinical characteristics of patients with mGGO and pathological analysis.

		AAH	AIS	MIA	IAC	Benign condition	χ^2	P
Age (years)	≥55	0	6 (12.8%)	6 (12.8%)	12 (25.5%)	0	8.983	0.062
	<55	2 (4.2%)	2 (4.2%)	12 (25.5%)	6 (12.8%)	1 (2.1%)		
Sex	Male	1 (2.1%)	1 (2.1%)	4 (8.4%)	5 (10.6%)	1 (2.1%)	4.412	0.353
	Female	1 (2.1%)	7 (14.9%)	14 (29.8%)	13 (27.7%)	0		
Opacity size (cm)	≥1.0	1 (2.1%)	1 (2.1%)	4 (8.4%)	14 (29.8%)	1 (2.1%)	16.263	0.003#
	<1.0	1 (2.1%)	7 (14.9%)	14 (29.8%)	4 (8.4%)	0		

AAH, atypical adenomatous hyperplasia; AIS, adenocarcinoma in situ; GIAC, invasive adenocarcinoma; MIA, microinvasive adenocarcinoma; mGGO, mixed ground glass opacity.
Compared with benign condition: *P < 0.05; #P < 0.01.

Table 4
Clinical characteristics of patients with pGGO and pathological analysis.

		AAH	AIS	MIA	IAC	Benign condition	χ^2	*P*
Age (years)	≥55	1 (2.8%)	3 (8.3%)	8 (22.2%)	4 (11.1%)	1 (2.8%)	5.336	0.225
	<55	1 (2.8%)	5 (13.9%)	5 (13.9%)	2 (5.6%)	6 (16.7%)		
Sex	Male	1 (2.8%)	2 (5.6%)	5 (13.9%)	2 (5.6%)	5 (13.9%)	3.749	0.441
	Female	1 (2.8%)	6 (16.7%)	8 (22.2%)	4 (11.1%)	2 (5.6%)		
Opacity size (cm)	≥1.0	1 (2.8%)	0	6 (16.7%)	5 (13.9%)	1 (2.8%)	12.502	0.014*
	<1.0	1 (2.8%)	8 (22.2%)	7 (19.4%)	1 (2.8%)	6 (16.7%)		

AAH, atypical adenomatous hyperplasia; AIS, adenocarcinoma in situ; IAC, invasive adenocarcinoma; MIA, microinvasive adenocarcinoma; pGGO, pure ground glass opacity.
Compared with benign condition: *P < 0.05; #P < 0.01.

Table 5
Distribution and pathological analysis of mGGO lesions.

	AIS	MIA	IAC	Benign condition	χ^2	P
Upper and middle lobe	7 (14.9%)	15 (31.9%)	11 (23.4%)	1 (0.02%)	5.422	0.143
Lower lobe	1 (0.02%)	3 (0.06%)	7 (14.9%)	2 (0.04%)		

AIS, adenocarcinoma in situ; IAC, invasive adenocarcinoma; mGGO, mixed ground glass opacity; MIA, microinvasive adenocarcinoma.

Table 6
Distribution and pathological analysis of pGGO lesions.

	AIS	MIA	IAC	Benign condition	χ^2	P
Upper and middle lobe	6 (16.7%)	11 (30.6%)	5 (13.9%)	6 (16.7%)	1.137	0.768
Lower lobe	2 (0.06%)	2 (0.06%)	1 (0.03%)	3 (0.08%)		

AIS, adenocarcinoma in situ; IAC, invasive adenocarcinoma; MIA, microinvasive adenocarcinoma; pGGO, pure ground glass opacity.

between GGO imaging findings and pathological manifestations. Moreover, mGGO lesions are more invasive than pGGO lesions. In particular, the proportion of patients with IAC was significantly higher in the mGGO group than in the pGGO group. A further analysis of the mGGO patient group revealed a significantly higher number of patients with IAC who had lesion diameter ≥1 cm, but age, sex, and location were not good prognostic factors for invasive lesions. Patients with mGGO nodules with diameters ≥1 cm require MDT discussion to make management decisions.

As expected, there are some limitations to our study including selection bias (inherent to a retrospective study) and the limited number of cases included in this study. Hence, further studies should be performed in the future.

Ethical approval

The study was approved by the ethics committee of Tianjin Medical University Cancer Institute and Hospital. All clinical practices and observations were conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from each patient before the study was conducted.

Patient consent

Written informed consent was obtained from patients for publication of these case reports and any accompanying images.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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