
Peer Review File

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Reviewer A

This study retrospectively evaluated the clinical/radiological/pathological findings of multiple pulmonary ground class nodules which had been surgically resected. From the results, the authors established quantitative nomograms to predict the satellite lesion characteristics in patients with multiple pulmonary ground glass nodules. This manuscript is well-written and the findings may be useful for clinicians. I have some comments:

Major:

1. Please describe the endpoints of this study in the method section.

Reply 1: We have modified our text as advised. (see page 4, line 110-111)

Changes in the text: The endpoints of this study: satellite lesion progresses or is invasive adenocarcinomas.

2. Line 176-177 What is the definition of median follow-up time? Duration from the resection of the primary lesion to the resection to the satellite lesion? Clinical follow-up duration after the resection to the satellite lesion? Additionally, please describe the range of the follow-up time.

Reply 2: The definition of median follow-up time is duration from the resection of the primary lesion to the resection to the satellite lesion. We have added the data about the range of the follow-up time in the text. (see page 5-6, line 153-154; page 6, line 182)

Changes in the text: The definition of follow-up time is duration from the resection of the primary lesion to the resection to the satellite lesion. (355-2112)

3. Line 178, “progression of their satellite lesions,” Table 1 “Advance” and “Non-advance.” What are the definitions and how did you categorize? Please describe them in the method section. Additionally, please describe the minimal duration for categorizing “Advance” and “Non-advance.”

Reply 3: Nodule progression was defined as follows: (I) an increase in nodule diameter of ≥ 2 mm, and (II) the appearance of new solid components visible at CT. This definition is described in the Method section. Progression and Advance are the same

definitions, just different words. The classification criteria are by definition. Some patients underwent multiple rounds of surgery within a short period of time, but not because of the satellite lesions had progressed. So we set the interval between surgeries to at least 1 year to exclude this effect. It seems pointless to describe the minimal duration for categorizing.

4. Table 1 and Table 2. The variables should be unified. Why did the author evaluate based on “boarder clear” and “bubble sign” in the Table 1, and “shape regular,” “lobulation sign,” “pleural indentation sign,” and “vessel through” in the Table 2?

Reply 4: Because of limited space, we only selected the results of some meaningful variables and put them in the table.

5. The size of the satellite lesion on chest CT may be important. Why did not the authors analyze it in Table 1, Table 3, and Table 4. Similarly, please add the data on the size of the primary lesions to Table 3.

Reply 5: We have added the data on the tables as advised.

6. Table 2. After time passes, the “Non-IPA” may change to “IPA.” Were there any differences between the follow-up periods of IPA and non-IPA?

Reply 6: Your idea makes sense. However, this article does not address the study of time variables. We will add this factor in subsequent studies.

Minor

1. Table 1. Change “PGGO, PSGGO” to “PGGN, PSGGN.”

Reply 1: We have modified the tables as advised.

2. All Tables: Please describe all abbreviations in the bottom of each Table. (AAH, AIS, MIA, , IAC, IPA, PGGN, PSGGN, etc)

Reply 2: We describe all abbreviations of Tables in the text. (see page14,line441-450)

Reviewer B

Interesting topic. Some difficulties for clinical application. Not very explored topic.

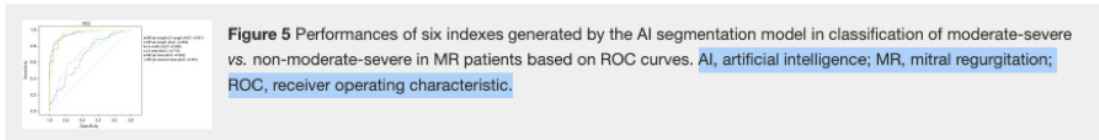
Reviewer C

Congratulations for your work. This paper is really interesting just for the merging of radiologic and histologic aspects of multiple GGOs.

Reviewer D

- ALL abbreviations** used in each table/figure or table/figure description **should be defined** in a footnote below the corresponding table/figure. **Please check carefully and revise.** Such as: CTR (in figure 2); SD, AAH, AIS, MIA, IAC, IPA (in table 1), etc.

Example:



Reply: we have accomplished the text as revised.

2. Table 1

- Please indicate the unit.

<u>Size of the satellite lesion,</u>	9.7 (7.9, 13.45)	11.7 (9.0, 14.75)	7.9 (5.93, 9.58)	0
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*, the characteristics of satellite lesions; #, the CT feature of the satellite lesion. CT is the

- This review comment is not addressed. Please revise.

Minor↓

- Table 1. Change “PGGO, PSGGO” to “PGGN, PSGGN.”

Reply 1: We have modified the tables as advised.↓

↵

Type of nodules#
PGGO
PSGGO

Reply: we have accomplished the text as revised.

3. Table 3

Please confirm if the description “unclear borders” match table 3.

202 1.00–5.33, P=0.05) with unclear borders (OR: 0.13, 95% CI: 0.04–0.47, P=0.00) and
 203 with a penetrating vessel (OR: 2.54, 95% CI: 1.04–6.18, P=0.04) were risk factors for
 206 1.19–19.37, P=0.03), and unclear borders (OR: 0.14, 95% CI: 0.03–0.68, P=0.02)

Border clear#		0.00	
No	Reference		Reference
Yes	0.13 (0.04–0.47)		0.14 (0.03–0.68)

Reply: we have accomplished the text as revised.

4. Table 4

a. Please check if “PGGO, PSGGO” in table 4 should also be “PGGN, PSGGN.”

Type of nodules#	
PGGP	Re:
PSGGO	3.2

b. Please confirm which one is correct.

229 P=0.00), belonging to **MPGGN** (OR: 3.22, 95% CI: 1.52–6.84, P=0.00)

Type of nodules#		0.00
PGGP	Reference	
PSGGO	3.22 (1.52–6.84)	

c. Please confirm if the description “irregular shape” match table 4.

229 P=0.00), belonging to **MPGGN** (OR: 3.22, 95% CI: 1.52–6.84, P=0.00) with irregular
 230 shape (OR: 0.38, 95% CI: 0.15–0.98, P=0.05), no lobulation sign (OR: 11.75, 95% CI:
 231 1.42–97.03, P=0.02), neural indentation sign (OR: 2.98, 95% CI: 1.04–8.54, P=0.04)

Shape regular#		0.05	
No	Reference		Reference
Yes	0.38 (0.15–0.98)		0.93 (0.21–4.23)

d. The description does not match table 4.

234 invasiveness. In addition, the multifactorial analysis revealed that male (OR: 0.25, 95%
235 CI: 0.07–0.83, P=0.02), location of satellite lesions (P=0.05), and larger size (OR: 1.34,

Table 4 Logistic regression analysis of the invasiveness of satellite lesions

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P	OR (95% CI)	P
Sex		0.08		0.02
Male	Reference		Reference	
Female	0.42 (0.16–1.09)		0.25 (0.07–0.83)	

Reply: we have accomplished the text as revised.

5. Please have a final double-check for all the details/accuracy of data including tables, and figures.

Reply: we have checked the text as revised.

6. Patient's source

Please also indicate the source of patients in “##Patients”.

97 ##Patients

98

99 Between April 2015 and December 2021, we retrospectively analyzed patients with
100 MPGGNs (all of whom were pathologically confirmed as malignant lesions) who
101 underwent multiple rounds of resection of primary and satellite lesion by thoracic
Reply: we have accomplished the text as revised.

7. Please unify the wording.

169 2013). The study was approved by institutional ethics board of the First Affiliated
170 Hospital of Zhejiang University School of Medicine (No. 2022984) and individual
171 consent for this retrospective analysis was waived.

366 was approved by the Ethics Committee of the First Affiliated Hospital, Zhejiang
367 University, School of Medicine (No. 2022-984) and individual consent for this

Reply: we have accomplished the text as revised.

8. Please confirm if more studies should be cited in below sentence. Please revise “studies” to “a study” or to give more than one citation.

*Please note that the references should be cited in order of their appearance in the text.

Previous studies investigating residual nodules after resection of non-small cell lung cancer showed that a large GGN size, the presence of PS GGNs, and a smoking history increased the probability of nodule growth (10).

In *studies* assessing single nodules, an age ≥ 65 years, history of lung cancer, initial nodule size of ≥ 8 mm, presence of a solid component, and bronchial inflation were considered independent risk factors for subsequent nodule growth (6).

Reply: we have accomplished the text as revised.