Original Article

Development of predictive models for assessing the progression and invasiveness of satellite lesions in patients with multiple pulmonary ground glass nodules

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Background: Currently, the appropriate treatment of satellite lesions is still controversial. With this study, we aimed to construct a set of nomograms to determine the characteristics of satellite lesions in patients with multiple pulmonary ground glass nodules (MPGGNs) and propose a reference for the management of satellite lesions.

Methods: We retrospectively analyzed patients with MPGGNs who had undergone multiple rounds of surgical resection of primary and satellite lesions, including pathologic examinations after surgical resection.

Results: A total of 125 lesions from 105 patients were included in the analysis; 85 lesions were advanced and 40 lesions were not advanced. Among them, 55 invasive pulmonary adenocarcinomas (IPA) and 70 noninvasive pulmonary adenocarcinomas were identified. After the final regression analysis, the patients' age, satellite lesion location, consolidation tumor ratio (CTR), lesion border clarity, and lesion diameter were used to predict satellite lesion progression. Patients' gender, satellite lesion location, lesion diameter, and computed tomography (CT) attenuation values were used to predict the invasiveness of the satellite lesion. The constructed nomograms showed strong discrimination with concordance indices (C indices) of 0.816 and 0.823, respectively.

Conclusions: We developed a set of nomograms that can predict the risk of advanced or invasive satellite lesions in patients with MPGGNs. The area under the receiver operating characteristic (ROC) curve (AUC), the C-index, and the calibration curve suggest that the nomogram may be useful in the clinical setting. This model has the potential to help clinicians make treatment recommendations for the remaining lesions while treating the primary lesion in patients with MPGGNs.

Keywords: Multiple pulmonary ground glass nodules (MPGGNs); nomogram; invasive pulmonary adenocarcinoma (IPA)

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Introduction

The widespread use of computed tomography (CT) has increased the detection rate of ground-glass nodules (GGNs); therefore, more patients are now being diagnosed with multiple pulmonary GGNs (MPGGNs).

A dilemma in understanding synchronous multiple lung tumors involves is whether multiple pulmonary nodules are either intrapulmonary metastases or independent tumors; studies investigating the clonal nature of tumors and tumor heterogeneity may help to find an answer to this question (1). It is believed that most of these tumors are multifocal, independent cancers (2-4). However, it is difficult for pathologists to distinguish the various pathological cancer types during preoperative examination using endobronchial biopsy, fine-needle aspiration, or other methods (5). Treatment options for different MPGGNs may vary widely, as criteria for the selection of lesions to be treated have not yet been developed; moreover, the appropriate type of local treatment and the treatment of remaining or new satellite nodules after initial local treatment are still unclear. There is currently no predictive model that can effectively discriminate whether satellite nodules should be removed along with the main lesion when treating MPGGNs, or whether they should be removed in the future.

In patients with multiple pulmonary nodules, the decision to treat the main lesion is often complicated by hesitation regarding treatment of the remaining lesions. Our aim is focusing on the changes of satellite nodules after primary lesion resection to propose a reference treatment plan for satellite lesion management.

Highlight box

Key findings

- A set of nomograms that could predict the risk of advanced or invasive satellite lesions in patients with multiple pulmonary ground glass nodules (MPGGNs).

What is known and what is new?

- Treatment options for different MPGGNs can vary widely.
- The models have the potential to help clinicians make treatment recommendations for the remaining lesions while managing the primary lesion in patients with MPGGNs.

What is the implication, and what should change now?

- We focused on the changes of satellite nodules after primary lesion resection to help patients with multiple pulmonary nodules. Moving forward, the management of the remaining lesions in these patients will be more decisive and swifter.

In this study, nomograms examined whether the satellite lesions will progress in the future or are invasive adenocarcinomas to study the characteristics of satellite lesions after primary lesion resection among patients with MPGGNs. We present this article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1162/rc).

Methods

Patients

Between April 2015 and December 2021, we retrospectively analyzed patients in the First Affiliated Hospital, Zhejiang University School of Medicine with MPGGNs (all of whom were pathologically confirmed as malignant lesions) who underwent multiple rounds of resection of primary and satellite lesion by thoracic surgery. Some patients underwent multiple rounds of surgery within a short period of time, but not because of the satellite lesions had progressed. When a patient has multiple pulmonary nodules, the nodule requiring surgical resection is considered the primary lesion and the remaining nodules are deemed to be satellite lesions. When multiple nodules were removed for the first time, the nodule with the largest diameter and greatest degree of solidity was designated as the primary lesion.

We set the interval between surgeries to at least 1 year to exclude this effect; in addition, GGNs do not tend to increase rapidly in size in the short term. The exclusion criteria were as follows: (I) on CT, the main or satellite lesion was solid before resection of the main lesion; (II) the diameter of the main or satellite lesion was ≥3 cm before resection of the main lesion, as seen on CT; (III) the satellite lesion was a new nodule and was not present at resection of the main lesion; and (IV) CT imaging was either incomplete or absent. 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 (6). The endpoints of this study: satellite lesion progresses or is invasive adenocarcinomas.

Management of MPGGN

Treatment recommendations for MPGGNs are heavily influenced by individual physicians (7). The general principle of the surgical resection of MPGGNs is to remove the suspected malignant lesion. The extent of surgical resection is usually determined based on the tumor stage, postoperative

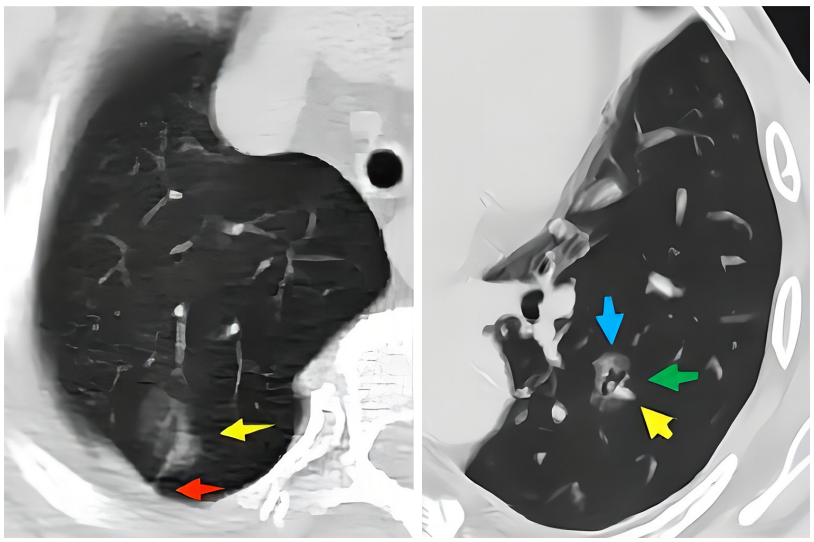

Figure 1 CT images showing vascular through (yellow arrows), pleural indentation sign (red arrow), lobulation sign (blue arrow), and bubble sign (green arrow). CT, computed tomography.

lung function estimates, preoperative comorbidities, and tumor location. In addition, when multiple primary lesions are removed, the distribution of the lesion is an important consideration; nodes located on the same side are removed simultaneously in one operation if they meet the guidelines/indications for surgery. By contrast, nodes belonging to different sides and satellite nodes with high-risk manifestations are removed in stages; whether on the same side or contralateral side, satellite nodes with a low location or slow progression are considered for surgery with caution and are usually initially observed by follow-up; further treatment is considered based on the follow-up results.

Radiation analysis

CT images were acquired with a 16-row CT scanner (Brilliance; Philips Medical Systems, Cleveland, OH, USA). The window plane for the lung was 600 Hounsfield units (HU) with a window width of 1,500 HU, and the window plane for the mediastinum was 30 HU with a window width of 400 HU. The CT scan parameters were as follows: Tube voltage 120 kV, tube current automatic modulation, collimation 0.625 mm, matrix 512×512, layer thickness 1.0–1.25 mm). Diameter, location, high-risk features, and CT attenuation values of the lesions were evaluated. High-risk features included border (clear, blurred), shape (regular, irregular), lobulation sign, pleural indentation sign, bubble sign, air bronchus sign, and penetrating vessel (*Figure 1*). The longest diameter of the nodule at the entire level was considered the lesion diameter. In terms of the lesion border, >75% of the circumference was defined as clear if a clear demarcation was noted between the lesion and surrounding lung parenchyma; otherwise, the border was defined as blurred. Linear or small plaques between the nodule and localized pleura were considered signs of pleural indentation. Bubble sign: clearly defined air density or cavities within the nodule. Air bronchus sign: bronchial shadowing is seen in areas of increased density. Penetrating vessel: with blood vessel penetration. Lobulation sign: due to the different growth rates, the nodules have multiple curved projections in profile. The consolidation tumor ratio (CTR) was defined as the ratio of the maximum consolidation diameter on high-resolution CT (HRCT) scan divided by the maximum tumor diameter in the lung window (8), and the measurements were averaged 3 times. The location of the satellite lesion is the lobe of the lung where the nodule is located. CT Images were used for the final preoperative evaluation of the primary lesions to understand the need for surgery. The definition of follow-up time is duration from the resection of the primary lesion to the resection to the satellite lesion.

Pathological and genetic descriptions

According to the World Health Organization (WHO) classification, adenocarcinomas and their precursors

are classified as pre-invasive lesions [including atypical adenomatous hyperplasia (AAH) and carcinoma in situ (AIS)], minimally invasive adenocarcinomas (MIA), and invasive adenocarcinomas (IAC) (9). This study was conducted in accordance with the principles outlined in the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of the First Affiliated Hospital, Zhejiang University School of Medicine (No. 2022-984) and individual consent for this retrospective analysis was waived.

Statistical analysis

Linearity assumptions for continuous variables were analyzed with the Student's *t*-test, rank sum tests for non-conformity to normal distribution, and chi-square tests for categorical variables. Statistical analyses and graphs were performed with the software SPSS 22.0 (IBM Corp., Armonk, NY, USA) and R 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria) and the statistical package RMS. For all analyses, P<0.05 was considered statistically significant.

Results

Patient characteristics

After searching our database for the exclusion criteria, we identified 105 patients with MPGGNs who underwent operations; accordingly, a total of 125 nodules were resected, and all of the patients were followed up at our institution. The median follow-up time was 720 days (355–2,112 days). *Table 1* shows the clinical and radiological characteristics of the patients based on the progression of their satellite lesions, whereas *Table 2* shows the clinical and radiological characteristics of the patients based on whether their satellite lesions were invasive or not.

Logistic regression analysis of satellite lesion progression

Univariate logistic regression analysis revealed that age ≥58 years [odds ratio (OR): 3.96, 95% confidence interval (CI): 1.74–8.97, P<0.001], CTR ≥50% (OR: 2.67, 95% CI: 1.16–6.13, P=0.02), belonged to part solid GGN (PSGGN) (OR: 2.31, 95% CI: 1.00–5.33, P=0.05) with clear borders (OR: 0.13, 95% CI: 0.04–0.47, P<0.001) and with a penetrating vessel (OR: 2.54, 95% CI: 1.04–6.18, P=0.04) were risk factors for lesion progression. Multifactorial analysis revealed that older age (OR: 5.12, 95% CI: 1.48–17.77, P=0.01), satellite lesion location (P=0.03), larger CTR (OR: 4.79, 95% CI: 1.19–19.37, P=0.03), and clear borders (OR: 0.14, 95% CI: 0.03–0.68, P=0.02) were risk factors for lesion progression (*Table 3*).

Nomogram of the probability of progression of satellite lesions

We included the 4 factors that were significant in the multifactorial analysis in the construction of a nomogram for predicting progression of satellite lesions and incorporated the size which is a common clinical risk predictor to construct a nomogram for predicting satellite lesion progression (*Figure 2*). The total lesion progression score was calculated based on patient's age, satellite lesion location, CTR, lesion border clarity, and lesion size. The values of each of these variables were assigned a score on the point scale axis. The total score could be easily calculated by summing each score; In addition, by projecting the total score to a lower total score scale, we could estimate the probability of progression of the satellite lesion. Based on a area under the receiver operating characteristic (ROC) curve (AUC) analysis, the nomogram was found to have good differentiation (*Figure 3*). The AUC was 0.799 (95% CI: 0.722–0.875), and the concordance index (C-index) was 0.823 (95% CI: 0.749–0.895). The calibration curves of the nomogram are shown in *Figure 4*.

Logistic regression analysis for satellite lesion invasiveness

Based on the logistic regression analysis results, the larger size (OR: 1.35, 95% CI: 1.17–1.57, P<0.001), the larger CT attenuation value (OR: 2.86, 95% CI: 1.41–5.79, P<0.001), belonging to PSGGN (OR: 3.22, 95% CI: 1.52–6.84, P<0.001) with regular shape (OR: 0.38, 95% CI: 0.15–0.98, P=0.05), no lobulation sign (OR: 11.75, 95% CI: 1.42–97.03, P=0.02), pleural indentation sign (OR: 2.98, 95% CI: 1.04–8.54, P=0.04), and penetrating vessel (OR: 2.84, 95% CI: 1.37–5.92, P=0.01), and a larger primary lesion diameter (OR: 1.11, 95% CI: 1.04–1.19, P<0.001) were risk factors for lesion invasiveness. In addition, the multifactorial analysis revealed that female (OR: 0.25, 95% CI: 0.07–0.83, P=0.02), location of satellite lesions (P=0.05), and larger size (OR: 1.34, 95% CI: 1.09–1.63, P=0.05) were risk factors for lesion invasiveness (*Table 4*).

Predictive nomogram construction for assessing the satellite lesion invasion probability

We used three factors (patient sex, satellite lesion location,

Table 1 The clinical and radiological characteristics of patients grouped by satellite lesion progression

Variables	Total	Advance	Non-advance	P value
Sex				0.886
Male	21	14	7	
Female	104	71	33	
Age, years, mean ± SD	57.19±10.03	58.45±10.09	54.53±9.46	0.041
Smoking history				0.409
No	119	80	39	
Yes	6	5	1	
Location†				0.104
Right upper lobe	30	17	13	
Right middle lobe	8	3	5	
Right lower lobe	18	12	6	
Left upper lobe	42	32	10	
Left lower lobe	27	21	6	
Pathology†				<0.001
AAH	13	6	7	
AIS	3	1	2	
MIA	54	30	24	
IAC	55	48	7	
CTR‡				0.019
<50%	75	45	30	
≥50%	50	40	10	
Type of nodules‡				0.046
PGGN	78	48	30	
PSGGN	47	37	10	
Border clear‡				<0.001
No	35	32	3	
Yes	90	53	37	
Bubble sign‡				0.037
No	84	52	32	
Yes	41	33	8	
Size of the primary lesion, mm, median (IQR)	13.1 (9.9–17.8)	14.1 (10.7–19.4)	11.1 (9.2–16.3)	0.042
Size of the satellite lesion, mm, median (IQR)	9.7 (7.9–13.45)	11.7 (9.0–14.75)	7.9 (5.93–9.58)	<0.001

†, the characteristics of satellite lesions; ‡, the CT feature of the satellite lesion. CT is the last surgical evaluation of the primary lesion before surgery. SD, standard deviation; AAH, atypical adenomatous hyperplasia; AIS, carcinoma in situ; MIA, minimally invasive adenocarcinomas; IAC, invasive adenocarcinomas; CTR, consolidation tumor ratio; PSGGN, part-solid ground glass nodule; PGGN, pure ground glass nodule; IQR, interquartile range; CT, computed tomography.

Table 2 The clinical and radiological characteristics of the patients grouped by whether the satellite lesions were invasive or not

Variables	Total	IPA	Non-IPA	P value
Age, years, median [IQR]	57 [52–63]	60 [54–66]	55 [50.75–63]	0.033
Size†, mm, median (IQR)	7.8 (5.6–9.85)	9.6 (6.8–11.9)	6.6 (5.43–8.23)	<0.001
CT attenuation†, HU, median (IQR)	−577.7 (−682.65 to −436.23)	−531.3 (−652.67 to −410.94)	−593.25 (−699.06 to −492.25)	0.034
CTR†				0.066
<50%	75	28	47	
≥50%	50	27	23	
Type of nodules†				0.002
PGGN	78	26	52	
PSGGN	47	29	18	
Shape regular†				0.041
No	22	14	8	
Yes	103	41	62	
Lobulation sign†				0.005
Yes	116	47	69	
No	9	8	1	
Pleural indentation sign†				0.036
No	107	43	64	
Yes	18	12	6	
Vessel through†				0.005
No	61	19	42	
Yes	64	36	28	
Size of the primary lesion, mm, mean ± SD	14.48±5.68	16.23±0.81	13.11±13.10	0.002

†, the CT feature of the satellite lesion. CT is the last surgical evaluation of the primary lesion before surgery. IPA, Invasive pulmonary adenocarcinoma; IQR, interquartile range; CT, computed tomography; HU, Hounsfield units; CTR, consolidation tumor ratio; PGGN, pure ground glass nodule; PSGGN, part-solid ground glass nodule.

and lesion size) that were significant in the multifactorial analysis, as well as the CT attenuation value (which is the common clinical risk predictor), to construct a nomogram to predict satellite lesion invasiveness (*Figure 5*). Based on the ROC analysis findings, the nomogram had good discrimination (*Figure 6*). The AUC was 0.816 (95% CI: 0.742–0.890), and the C-index was 0.816 (95% CI: 0.742–0.889). The calibration curve of the nomogram is shown in *Figure 7*.

Discussion

The treatment of MPGGNs remains controversial. In an attempt to assist clinicians in making treatment recommendations for patients with MPGGNs, in this study, we created simple and intuitive charts for a statistical prediction model that quantifies the risk of satellite nodule progression versus invasiveness. We identified 5 predictors of satellite lesion progression (age, satellite lesion location, CTR, border clarity, and lesion size) and 4 satellite lesion invasiveness predictors (sex, satellite lesion location, lesion size, and CT attenuation value). Importantly, the predictive ability of our nomogram for patients with MPGGNs was optimally discriminative and well-calibrated in terms of the AUC, C-index, and calibration curve. When patients and physicians treat the primary lesion, they can refer to

Table 3 Logistic regression analysis of satellite lesion progression

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age		<0.001		0.01
<58 years	Reference		Reference	
≥58 years	3.96 (1.74–8.97)		5.12 (1.48–17.77)	
Smoking history		0.42		0.08
No	Reference		Reference	
Yes	2.44 (0.28–21.58)		22.30 (0.67–739.16)	
Location†		0.13		0.03
Right upper lobe	0.37 (0.12–1.19)	0.10	0.30 (0.06–1.50)	0.14
Right middle lobe	0.17 (0.03–0.93)	0.04	0.19 (0.02–2.00)	0.17
Right lower lobe	0.57 (0.15–2.17)	0.41	1.82 (0.31–10.74)	0.51
Left upper lobe	0.91 (0.29–2.89)	0.88	2.62 (0.57–11.97)	0.22
Left lower lobe	Reference		Reference	
CTR‡		0.02		0.03
<50%	Reference		Reference	
≥50%	2.67 (1.16–6.13)		4.79 (1.19–19.37)	
Type of nodules‡		0.05		0.98
PGGN	Reference		Reference	
PSGGN	2.31 (1.00–5.33)		1.02 (0.25–4.11)	
Border clear‡		<0.001		0.02
No	Reference		Reference	
Yes	0.13 (0.04–0.47)		0.14 (0.03–0.68)	
Bubble sign‡		0.04		0.18
No	Reference		Reference	
Yes	2.54 (1.04–6.18)		2.19 (0.69–6.98)	
Size of the primary lesion	1.06 (0.99–1.14)	0.10	1.08 (0.97–1.20)	0.18
Size of the satellite lesion	1.08 (0.98–1.20)	0.13	0.98 (0.82–1.18)	0.86

†, the characteristics of satellite lesions; ‡, the CT feature of the satellite lesion. CT is the last surgical evaluation of the primary lesion before surgery. OR, odds ratio; CI, confidence interval; CTR, consolidation tumor ratio; PGGN, pure ground glass nodule; PSGGN, part-solid ground glass nodule; CT, computed tomography.

our model to decide whether to treat the satellite lesions simultaneously.

We compared the differences between progressive and nonprogressive satellite lesions and found significant differences in terms of the patient's age, pathologic findings, CTR, nodule type, presence of clear borders, Bubble sign, and primary lesion size. Regarding the results of multivariate analysis, we found that older age, the satellite

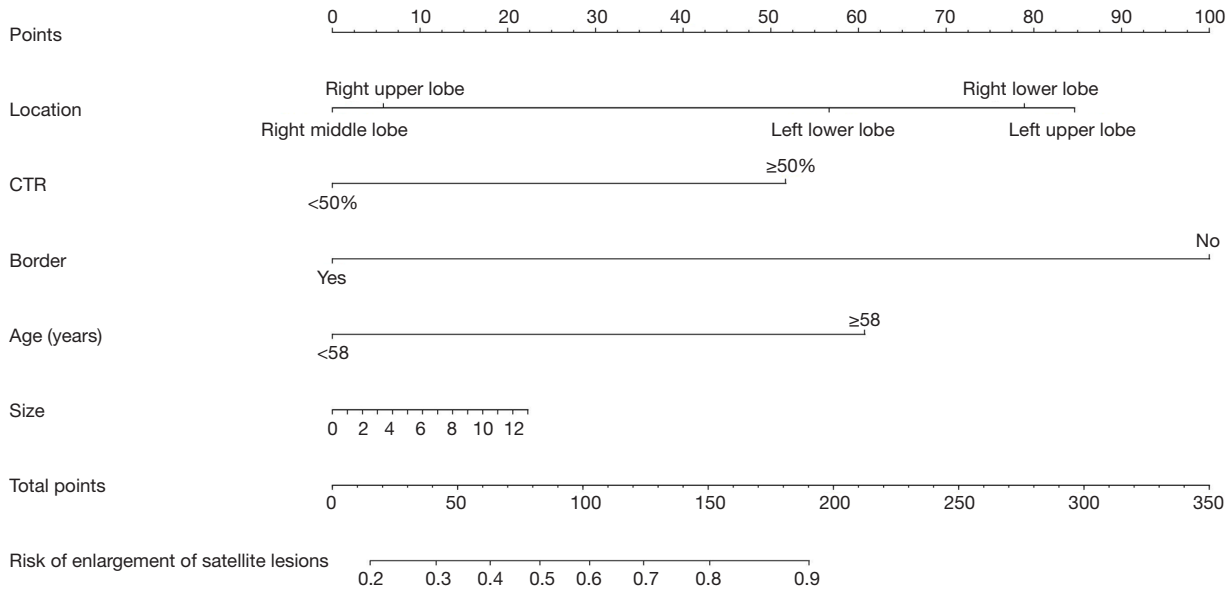

Figure 2 The Nomogram forms a score to indicate the likelihood of progression of a satellite nodule based on its location, CTR, border, age, and size. Nodule size scoring criteria: 0, 0.4 cm; 1, >0.4–0.6 cm; 2, >0.6–0.8 cm; 3, >0.8–1 cm; 4, >1–1.2 cm; 5, >1.2–1.4 cm; 6, >1.4–1.6 cm; 7, >1.6–1.8 cm; 8, >1.8–2 cm; 9, >2–2.2 cm; 10, >2.2–2.4 cm; 11, >2.4–2.6 cm; 12, >2.6–2.8 cm; 13, >2.8–3 cm. CTR, consolidation tumor ratio.

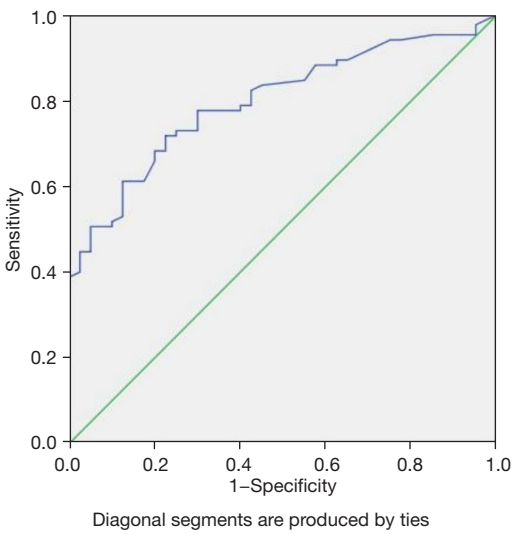

Figure 3 The area under the ROC curve. Blue line, nomogram; green line, reference line; ROC, receiver operating characteristic.

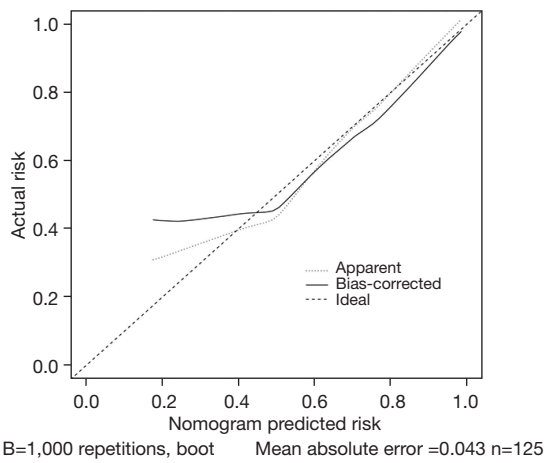

Figure 4 The calibration curves of the nomogram. A portion of the calibration curves are very close to the ideal curve, representing good predictability of the nomogram.

lesion location, a larger CTR, and unclear borders were risk factors for satellite lesion progression. Previous study 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). Sato *et al.* (11) found no significant differences in the incidence of the growth of multiple GGNs and single GGNs at ≥36 months. In study 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).

Upon comparing invasive adenocarcinoma with non-

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)	
Location†		0.27		0.05
Right upper lobe	0.53 (0.18–1.51)	0.23	0.10 (0.02–0.56)	0.08
Right middle lobe	0.10 (0.01–0.92)	0.04	0.01 (0.00–0.31)	0.08
Right lower lobe	0.44 (0.13–1.48)	0.18	0.15 (0.03–0.93)	0.04
Left upper lobe	0.52 (0.19–1.38)	0.19	0.25 (0.06–1.00)	0.05
Left lower lobe	Reference		Reference	
Size‡	1.35 (1.17–1.57)	<0.001	1.34 (1.09–1.63)	0.05
CT attenuation‡		<0.001		0.89
<–500 HU	Reference		Reference	
–500 to –200 HU	Reference		Reference	
>–200 HU	2.86 (1.41–5.79)		1.09 (0.31–3.78)	
Type of nodules‡		<0.001		0.33
PGGN	Reference		Reference	
PSGGN	3.22 (1.52–6.84)		1.91 (0.52–7.03)	
Shape regular‡		0.05		0.93
No	Reference		Reference	
Yes	0.38 (0.15–0.98)		0.93 (0.21–4.23)	
Lobulation sign‡		0.02		0.36
Yes	Reference		Reference	
No	11.75 (1.42–97.03)		3.33 (0.25–4.23)	
Pleural indentation sign‡		0.04		0.45
No	Reference		Reference	
Yes	2.98 (1.04–8.54)		0.55 (0.11–2.64)	
Vessel through‡		0.01		0.14
No	Reference		Reference	
Yes	2.84 (1.37–5.92)		2.34 (0.75–7.27)	
Size of the primary lesion	1.11 (1.04–1.19)	<0.001	1.07 (0.97–1.18)	0.16
Size of the satellite lesion	1.35 (1.17–1.57)	<0.001	1.34 (1.09–1.63)	0.05

†, the characteristics of satellite lesions; ‡, the CT feature of the satellite lesion. CT is the last surgical evaluation of the primary lesion before surgery. OR, odds ratio; CI, confidence interval; CT, computed tomography; HU, Hounsfield units; PGGN, pure ground glass nodule; PSGGN, part-solid ground glass nodule.

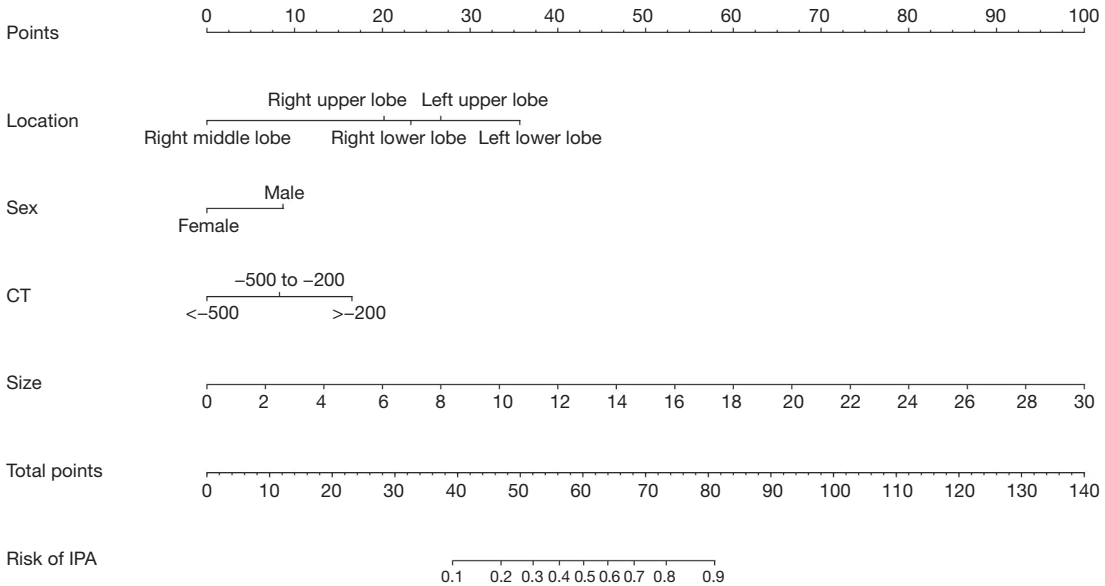

Figure 5 The Nomogram forms a score to indicate the likelihood of IPA of a satellite nodule based on its location, sex, CT and size. Size, mm; CT, HU. CT, computed tomography; IPA, invasive pulmonary adenocarcinoma; HU, Hounsfield units.

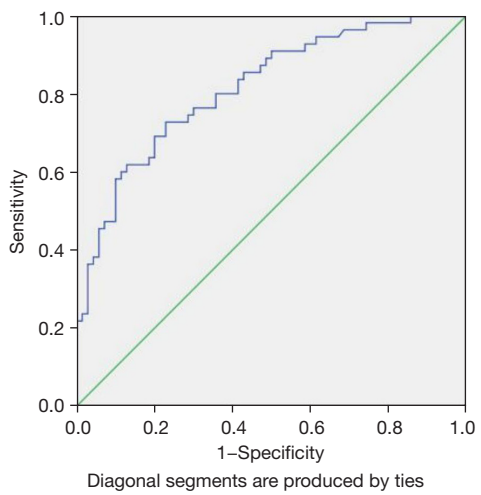

Figure 6 The area under the ROC curve. Blue line, Nomogram. Green line, reference line. ROC, receiver operating characteristic.

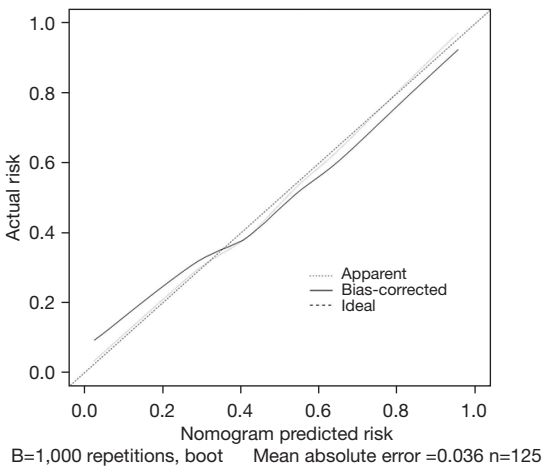

Figure 7 The calibration curves. The full calibration curves closely fit the ideal curves, representing good predictability of the Nomogram.

invasive adenocarcinoma, significant differences were found in age, size of satellite lesions, CT attenuation values, nodule type, clear borders, Lobulation sign, Pleural indentation sign, Penetrating vessel, and main lesion size. Regarding the multivariate analysis results, female sex, the satellite lesion location, and a larger lesion size were considered risk factors for lesion invasiveness. Previous studies have used CTR and maximum tumor size to predict tumor invasiveness and prognosis (12-14); however, a recent study reported conflicting perceptions of CTR and maximum tumor size (15). Mean CT attenuation values have also been used to predict tumor invasiveness (16-18). It has been shown that larger diameter and PSGGNs are the high-risk factors of satellite lesions (10,19), which is consistent with our findings.

Although several predictive models have been previously

established to evaluate the malignancy and growth of pulmonary nodules (20-22), only a few nomograms have been established for patients with MPGGNs. To the best of our knowledge, these studies were the first to establish quantitative nomograms to predict the satellite lesion characteristics among patients with MPGGNs. Compared with previous studies (10,11,19), our sample of MPGGNs is relatively large, and each satellite lesion has a clear pathological finding; this is one of the highlights of this study. In addition, because of the larger sample and known pathologic findings, we were able to study the changing characteristics of satellite lesions rather than just describing their outcome. When we included only the results with significance in the multifactorial analysis in the nomogram, the C indices for predicting the progression of the satellite lesion and invasive models were 0.822 (95% CI: 0.748–0.895) and 0.791 (95% CI: 0.713–0.870), respectively, which still represents good discriminatory power.

In their basic treatment criteria for MPGGNs, Shimada *et al.* (23) concluded that residual satellite lesions should be considered for local treatment, preferably second-stage surgical excision, because most lesions are likely to be invasive carcinomas. However, their study found that although >50% of patients with MPGGNs had residual satellite lesions that were not treated locally during the follow-up period, no significant prognostic impacts of treatment completion or residual lesion progression were noted (19,23). The average volume doubling time (VDT) of GGNs is 769–1,005 days (24-26). Thus, follow-up without resection of the satellite lesion may be a reasonable approach. The range of future satellite lesion progression in the literature is 0–46.0% (19,27,28). For satellite lesions that may remain stable in the long term, we may be able to preserve more of the patient's lung tissue by conducting an observational follow-up of the primary lesion at the time of resection.

The relationship between multiple intrapulmonary nodules as primary tumors or intrapulmonary metastases is currently unclear. However, in this work, data related to the primary lesion, such as the primary lesion size, were significant in the analysis between satellite lesion groups analysis and the univariate analysis; the authors believe that this may provide a clue for understanding the relationship. In the future, a larger sample number will hopefully be available to help understand these relationships. The appearance of new lesions during the follow-up period is an independent predictor of satellite lesion progression (23), the development of a pure GGN into a part-solid nodule or the development of a new solid component during follow-up indicates a higher risk of invasive adenocarcinoma (29). This study aimed to make predictions based on satellite lesion characteristics that occurred concurrently with the primary lesion; thus, dynamic variables, such as the follow-up duration, were not considered in this study. Future studies could be conducted to provide greater research value.

Conclusions

In summary, we have developed a new set of nomograms to predict the risk of progression of the satellite lesion and the invasiveness of the lesion in patients with MPGGNs. The constructed nomograms are easy to use, highly accurate, and well-calibrated. These charts can help clinicians to make individualized predictions for satellite lesion regression in patients and provide assistance to patients in terms of MPGGN treatment.

Limitations

First, we only reviewed the records of patients who underwent resection of both the primary and satellite lesions of MPGGNs. Patients who did not undergo resection were excluded and the study was selective. Second, our predictive model was retrospective and in a single center. Further data collection, in collaboration with multicenter institutions, may improve this model for future use.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1162/rc

Data Sharing Statement: Available at https://jtd.amegroups.

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-1162/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine (No. 2022-984) and individual consent for this retrospective analysis was waived.

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