Received: 25 Mar 2025 | **Accepted:** 02 Jun 2025 **Genel Tıp Derg. Volume** 35/**Issue** 3 (June), 535-543
DOI: 10.54005/geneltip.1665515

ORIGINAL ARTICLE

The Role of Malignancy Risk Scores in Assessing Cancer Risk in Pure Ground-Glass and Part-Solid Nodules

Saf Buzlu Cam ve Subsolid Nodüllerin Kanser Riskinin Değerlendirilmesinde Malignite Risk Skorlarının Rolü

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How to cite ?

Gurz S, Temel NG, Sullu Y, Sayit Tanrivermis A, Gurz Alper A, Sengul A. The Role of Malignancy Risk Scores in Assessing Cancer Risk in Pure Ground-Glass and Part-Solid Nodules. Genel Tıp Derg. 2025;35 (3): 535-543

ABSTRACT

Aim: This study aimed to evaluate the effectiveness of commonly used malignancy risk prediction models in assessing the likelihood of malignancy in pure ground-glass opacities (pGGNs) and part-solid pulmonary nodules (PSNs) among patients with solitary pulmonary nodules (SPN).
Methods: Between January 2021 and June 2024, 75 patients undergoing the uniportal video-assisted thoracoscopic (U-VATS) segmentectomy due to SPNs were retrospectively reviewed. Of these, 32 patients undergoing segmentectomy for radiologically defined pGGN or PSNs were included in the study. Demographic data, smoking history, nodule characteristics, and surgical details were collected. Malignancy risk scores were calculated separately using the Mayo Clinic, Brock, Bayesian, and Herder models. These scores were then compared with the final histopathological results.
Results: The mean age of the included patients was 62.89±10.53 years (range: 35–80), with a male-to-female ratio of 17:15. The smoking prevalence was 50%, with a history of malignancy present in 8 patients and a family history of lung cancer in 3 patients. The prevalence of chronic immune-mediated diseases was 43.8%. The mean radiological nodule size was 13.04±5.14 mm (range: 6–26 mm). Among the nodules, 59.4% (n=19) were pGGNs, and 40.6% (n=13) were PSNs. The median malignancy risk scores were 11.95% (IQR: 15.7) for the Mayo Clinic model, 9.77% (IQR: 18.15) for the Brock model, 13% (IQR: 36.25) for the Bayesian model, and 12.1% (IQR: 14.58) for Herder model. The overall malignancy rate was 93.8%, with invasive adenocarcinoma (37.5%) and adenocarcinoma in situ (28.1%) being the most common histopathological subtypes. The median chest tube removal time was 2 days (IQR: 1), and the median length of hospital stay was 3 days (IQR: 2). No postoperative mortality was observed.
Conclusions: Our findings suggest that the widely used risk prediction models are insufficient in accurately identifying early-stage lung adenocarcinoma in patients with pGGN and PSNs. Incorporating additional patient-related factors, such as chronic immune-mediated conditions, into multivariate analyses may enhance the predictive accuracy of malignancy-risk assessments in SPN.

Keywords: Ground-glass nodule, risk prediction models, segmentectomy, subsolid nodule.

ÖZ

Amaç: Bu çalışmanın amacı, soliter pulmoner nodüllerin (SPN) malignite risklerini belirlemede kullanılan risk skorlarının, pür buzlu cam (pGGNs) ve kısmi-solid nodüllerde (PSNs) etkinliğini değerlendirmek.
Gereç ve Yöntemler: Ocak 2021 ile Haziran 2024 tarihleri arasında SPN nedeniyle uniportal video-torakoskopik segmentektomi uygulanan 75 hasta retrospektif olarak incelendi. pGGNs ve PSNs nedeniyle segmentektomi uygulanan 32 hasta çalışmaya dahil edildi. Demografik verileri, tütün kullanımları, nodul özellikleri ve uygulanan cerrahi tedaviye ait veriler kayıt edildi. Nodullerin risk skorları Mayo Clinic, Brock, Bayesian ve Herder Modelleri kullanılarak ayrı ayrı belirlendi. Histopatolojik sonuçlarla karşılaştırıldı.
Bulgular: Çalışmaya dahil edilen hastaların yaş ortalaması 62,89±10,53(35-80) ve erkek kadın oranı 17/15 idi. Sigara kullanım oranı %50'di. Malignite özgeçmişi 8 hastada, akciğer kanseri soygeçmişi 3 hastada mevcuttu. İmmun-yanıtlı hastalık oranı %43,8 idi. Radyolojik olarak ortalama 13,04±5,14(6-26) mm olan nodüllerin %59,4(n=19)'ü pGGNs, %40,6(n=13) PSNs lezyonlardı. Nodullerin risk skorlamasında Mayo Clinic Modeline göre ortanca değer %11,95 (IQR: 15,7), Brock Modeline göre ortanca değer %9,77 (IQR: 18,15), Bayesian Modeline göre ortanca değer %13 (IQR: 36,25) ve Herder Modeline göre ortanca değer %12,1 (IQR: 14,58) idi. Malignite oranı %93,8 olan çalışmada en sık tespit edilen histopatolojik subtipler Invazif Adenokarsinom (%37,5) ve Insitu Adenokarsinomdu (28,1). Ortanca tüp çekme süresi 2 (IQR:1), hastanede yatış süresi 3 (IQR:2) gündü. Mortalite görülmedi.
Sonuçlar: Çalışmamız, SPN'lerde malignite riskini belirlemede yaygın olarak kullanılan modellerin, pGGNs ve PSNs'de gelişen erken evre akciğer adenokanser riskini tespit etmede, yetersiz olduğunu göstermiştir. Riskleri belirlemede, immün-yanıtlı hastalıklar gibi, hastaya ait farklı faktörlerinde değerlendirmeye dahil edilerek multivaryans analizlerin daha değerli olacağı görüşüne varıldı.

Anahtar Kelimeler: Buzlu cam nodul, kısmi-solid nodul, risk skorları, segmentektomi.

Introduction

In recent years, the increasing adoption of minimally invasive pulmonary segmentectomy has prompted a shift in the clinical approach to the surveillance of pulmonary nodules. Notably, the JCOG0802 and JCOG0804 trials conducted by the Japan Clinical Oncology Group have provided compelling evidence that pure ground-glass opacities (pGGNs) and part-solid nodules (PSNs) harbor a high likelihood of being early-stage adenocarcinomas, underscoring the need for timely and accurate risk stratification (1, 2). In these studies, evaluations were made based on the radiological characteristics of the nodules, while the

Peer-Review: Double anonymized - Two External
Plagiarism Checks: Yes - intihal.net
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Selcuk University Press
Genel Tıp Dergisi | e-ISSN: 2602-3741
https://dergipark.org.tr/tr/pub/geneltip
https://yayinevi.selcuk.edu.tr/

clinical features of the included patients were not assessed.

Solitary pulmonary nodules (SPN) are commonly detected on chest computed tomography scans, and their etiologies range from benign conditions to malignant pathologies (3). Therefore, several guidelines have been developed to guide the clinical approach to pulmonary nodules based on risk factors at the time of detection. These guidelines aim to characterize nodules and identify patterns of behavior. In this way, standardized protocols for follow-up, diagnosis, and treatment can be established in clinical practice. Among these, the most widely used is the Fleischner Society guideline, specifically addressing the management of SPN (4, 5). These guidelines classify patients into low- and high-risk categories based on clinical and radiological features. For individuals with small nodules and low predicted risk, routine follow-up may not be necessary, whereas larger nodules in high-risk patients warrant further diagnostic evaluation and consideration of treatment (4). In addition, both the American College of Chest Physicians (ACCP) and the British Thoracic Society (BTS) recommend the use of risk prediction models to estimate the probability of malignancy in pulmonary nodules (6, 7). These models estimate the probability of malignancy by integrating both radiological features of the nodule and patient-specific clinical characteristics. Among the prediction models recommended by current guidelines and widely used in clinical practice are the Brock, Mayo Clinic, Herder, and Bayesian models. Each of these models was developed using datasets differing in terms of population size, inclusion and exclusion criteria for nodules and patients, and the underlying prevalence of lung cancer (8-11). The reliability of these SPN risk prediction models in the context of pGGNs and PSNs remains uncertain. In this study, we aimed to evaluate the effectiveness of commonly used lung cancer prediction models in estimating malignancy risk in pGGNs and PSNs among patients undergoing anatomical pulmonary segmentectomy.

Materials and Methods

This retrospective study was approved by the Clinical Research Ethics Committee of Ondokuz Mayis University (Approval number: 2025/66; date: 12 February 2025). Written informed consent was obtained from all patients before surgery. All procedures involving human participants were conducted under the Declaration of Helsinki (as revised in 2013). Patient data were anonymized to ensure confidentiality and protect personal privacy.

The Study Population

Between January 2021 and June 2024, a total of 75 patients undergoing the uniportal video-assisted thoracoscopic (U-VATS) segmentectomy for SPN were retrospectively assessed. Among them, 32 patients undergoing segmentectomy specifically for pGGNs and PSNs were included in the final analysis. All nodules were followed according to the Fleischner Society guidelines and were surgically resected due to high suspicion of malignancy. The inclusion and exclusion criteria of the study are summarized in Figure 1.

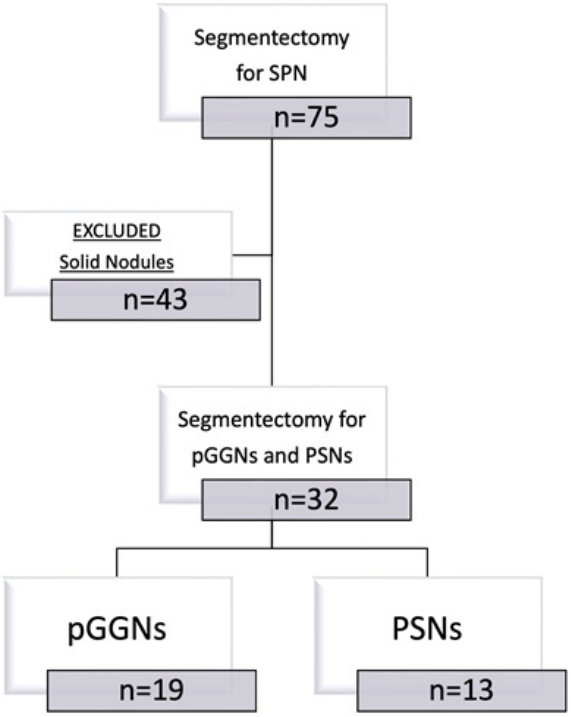

Figure 1. Flowchart of the study.(pGGNs: Pure ground-glass opacity, PSNs: Part-solid nodule)

The probability of malignancy for each pulmonary nodule was calculated using four established lung cancer prediction models: Mayo Clinic, Brock, Bayesian, and Herder. The variables used in these models are listed in Table 1. For this purpose, clinical, demographic, and radiological characteristics of the patients and nodules were collected. The recorded data included age, sex, body mass index (BMI), smoking history, history of extrapulmonary and/or primary lung cancer, family history of lung cancer, chronic obstructive pulmonary disease (COPD), chronic immune-mediated diseases, and preoperative symptoms.

Table 1. Evaluation parameters of the Mayo Clinic, Brock, Bayesian, and Herder malignancy prediction models

Evaluation Factors	Mayo Clinic	Brock	Bayesian	Herder
Age (years)	(+)	(+)	(+)	(+)
Sex		(+)		
Smoking	(+)		(+)	(+)
History of cancer (extra-thoracic)	(+)		(+)	(+)
Family history of lung cancer		(+)		
Emphysema in CT		(+)		
Nodule size	(+)	(+)	(+)	(+)
Nodule morphology	(+)	(+)	(+)	(+)
Nodule type (pGGN, PSN, Solid)		(+)		
Lobe localization	(+)	(+)	(+)	(+)
Number of nodules		(+)		
PET-CT (FDG uptake)			(+)	
PET-CT (degree of FDG uptake)				(+)

CT: Computerized tomography, FDG: Fluorodeoxyglucose, pGGN: Pure ground-glass opacity, PSN: Part-solid nodule

The radiological features of each nodule were evaluated by an experienced thoracic radiologist using images retrieved from the hospital's imaging archive system. Recorded nodule characteristics included maximum diameter, attenuation, lobar and segmental location, peripheral or central positioning, presence of speculation, and the consolidation-to-tumor (C/T) ratio. For patients with serial imaging, nodule growth was assessed. Preoperative F-18 fluorodeoxyglucose uptake on positron emission tomography (PET) was evaluated for each patient. In addition, three-dimensional reconstructions of thoracic computed tomography images were used to identify the segmental location of the nodules and the associated bronchovascular structures.

All patients underwent anatomical pulmonary segmentectomy via UVATS under general anesthesia. Intraoperative details including the resected segment, type of segmentectomy performed, histopathological diagnosis of the nodule, number of lymph nodes removed, intraoperative and postoperative complications, chest tube removal time, and length of hospital stay were recorded. Systematic mediastinal lymph node dissection was performed in all patients, including stations 4R, 4L, 7, 10, and 11, under the ESTS guidelines.

Statistical Analysis

The results were analyzed using Statistical Package for the Social Sciences Statistics software, version 24.0 for Windows (IBM Corp., Armonk, NY, USA). Data were presented as mean ± standard deviation (SD), as median (interquartile range: IQR) as frequency (%). The Shapiro–Wilk test was used to analyze the normal distribution assumption of the quantitative outcomes. Data were analyzed by the Mann-Whitney test for non-normal data. The frequencies were compared, using the Pearson Chi-square, Continuity Correction Chi-square, and Fisher Exact test. A p-value of <.05 was considered statistically significant.

Results

A total of 32 patients undergoing segmentectomy due to pGGNs and PSNs were included in the study. Demographic characteristics and nodule-related features of the patients are presented in Table 2.

Table 2. Analysis of variables related to demographic and nodule characteristics

Variables	Total (n=32)
Age, year, mean±SD	62.2±11.1
Sex, % (n)	
Male	53.1 (17)
Female	46.9 (15)
BMI, mean±SD	26.9±3.8
Smoking, % (n)	
Non-smoker	50 (16)
Smoker	9.4 (3)
Ex-smoker	40.6 (13)
History of lung cancer, % (n)	12.5 (4)
History of COPD, % (n)	18.75 (6)
Extrathoracic malignancy, % (n)	28.1 (9)
Family history of lung cancer, % (n)	9.4 (3)
Chronic inflammatory disease, % (n)	43.8 (14)
Nodule Type, % (n)	
pGGNs	59.4 (19)
PSNs	40.6 (13)
Nodule Size, mm, mean±SD	12.7±5.0
Localization, % (n)	
Upper Lobe	59.4 (19)
Lower Lobe	40.6 (13)
Follow-up Time, month, median (IQR)	12.5 (18)

COPD: Chronic obstructive pulmonary disease, pGGNs: Pure ground-glass opacities, PSNs: Part-solid nodules, SD: Standard deviation

The mean age was 62.2±11.1 years, and 53.1% (n=17) of the patients were male, while 46.9% (n=15) were female. The mean body mass index (BMI) was calculated as 26.9±3.8. Among the patients, 50% (n=16) had never smoked, 9.4% (n=3) were current smokers, and 40.6% (n=13) were former smokers. A history of lung cancer was present in 12.5% (n=4), chronic obstructive pulmonary disease (COPD) in 18.75% (n=6), extrapulmonary malignancy in 28.1% (n=9), and a family history of lung cancer in 9.4% (n=3). Chronic immune-mediated diseases were identified in 43.8% (n=14) of the patients, and their distribution is shown in Table 3.

Table 3. Distribution of chronic-immune responsive diseases of patients included in the study

Chronic Immune-Mediated Diseases	Total (n=32) % (n)
Burger Disease	6.3 (2)
Hypothyroidism	6.3 (2)
Guatr	6.3 (2)
Hashimoto Thyroiditis	3.1 (1)
Parathyroid Adenoma	3.1 (1)
Psoriasis	3.1 (1)
Nephropathy	3.1 (1)
Ankylosing Spondylitis	3.1 (1)
Rheumatoid Arthritis	6.3 (2)
HIV	3.1 (1)

HIV: Human immunodeficiency virus

Radiologically, 59.4% (n=19) of the nodules were classified as pGGNs, while 40.6% (n=13) were PSNs. The mean nodule diameter was 12.7±5.0 mm. In terms of localization, 59.4% (n=19) of the nodules were located in the upper lobe and 40.6% (n=13) in the lower lobe. The median follow-up duration was 12.5 months, ranging from three to 108 months.

Surgical findings are presented in Table 4. Simple segmentectomy was performed in 31.3% (n=10) of the cases, while complex segmentectomy was applied in 68.8% (n=22). Among the resected segments, the most frequently targeted area was segment S6, accounting for 25% (n=8) of the procedures. This was followed by segment S2 with 18.8% (n=6). Segmentectomy involving S1 and S1/2 was performed in 12.5% (n=4) each. Other segments included S1/2–6 and S1/2/3a (each 3.1%, n=1), S3 (9.4%, n=3), and S4/5, S7, S8/9, and S10 (each 3.1%, n=1), as well as S9/10 (6.3%, n=2).

The median number of lymph node stations evaluated was 4 (IQR: 2.75), and the mean number of lymph nodes retrieved was 4.6±3.0. Postoperative outcomes showed a median chest tube removal time of 2 days (IQR: 1), and a median hospital stay of 3 days (IQR: 3).

Histopathological examination revealed that invasive adenocarcinoma was the most commonly identified malignant pathology, observed in 37.5% (n=12) of patients. This was followed by adenocarcinoma in situ (AIS) in 28.1% (n=9) and minimally invasive adenocarcinoma (MIA) in 9.4% (n=3). Other histopathological diagnoses included squamous cell carcinoma (SCC) in 9.4% (n=3), neuroendocrine tumor (NET) in 3.1% (n=1), metastatic tumors in 6.3% (n=2), and benign lesions in 6.3% (n=2).

Table 4. Evaluation of surgical outcomes and parameters

Variables	Total (n=32)
Segmentectomy Type, % (n)	
Simple	31.3 (10)
Complex	68.8 (22)
Segment, % (n)	
S1	12.5 (4)
S1/2	12.5 (4)
S1/2-6	3.1 (1)
S1/2/3a	3.1 (1)
S2	18.8 (6)
S3	9.4 (3)
S4/5	3.1 (1)
S6	25.0 (8)
S7	3.1 (1)
S8/9	3.1 (1)
S10	3.1 (1)
S9/10	6.3 (2)
Lymph Node Number, mean±SD	4.6±3.0
Lymph Node Station, median (IQR)	4 (3)
Tube Removal, day, median (IQR)	2 (1)
Hospital Stay, day, median (IQR)	3 (3)

IQR: Interquartile range

According to pathological tumor (pT) staging, the most frequently observed stage was pT1a in 34.4% (n=11) of cases. This was followed by pT is (in situ) in 25% (n=8), pT1b in 18.8% (n=6), pT1mi (minimally invasive) in 9.4% (n=3), pT2 in 6.3% (n=2), and both pT3 and pT4 in 3.1% (n=1) each. The mean tumor size was measured as 11.3 ± 4.5 mm. The distribution of histopathological findings is summarized in Table 5.

Table 5. Distribution of variables related to histopathological data

Variables	% (n)
Pathology	
Adenocarcinoma in situ	28.1 (9)
Minimally Invasive Adenocarcinoma	9.4 (3)
Invasive Adenocarcinoma	37.5 (12)
Squamous Cell Carcinoma	9.4 (3)
Carcinoid Tumor	3.1 (1)
Metastasis	6.3 (2)
Benign Pathology	6.3 (2)
pT Size, mm, mean±SD	11.3±4.5
pT Stage	
Tis	25.0 (8)
T1mi	9.4 (3)
T1a	34.4 (11)
T1b	18.8 (6)
T2	6.3 (2)
T3	3.1 (1)
T4	3.1 (1)

pT: Pathological tumor, SD: Standard deviation

A comparison of clinicopathological features between the pGGNs and PSNs groups is presented in Table 6. The mean radiological nodule size was larger in the PSNs group compared to the pGGNs group, although the difference did not reach statistical significance. The mean nodule diameter was 11.6 ± 3.8 mm (95% CI: 9.74–13.42) in the pGGNs group and 14.2 ± 6.2 mm (95% CI: 10.50–17.96) in the PSNs group (p=0.255). Regarding follow-up duration, the pGGNs group had a median follow-up of 18 months (IQR:15), whereas the PSNs group had 9 months (IQR:21). This difference was also not statistically significant (p=0.146).

Table 6. Comparison of Clinicopathological Characteristics Between pGGNs and PSNs Groups

	pGGNs Group (n=19)	PSNs Group (n=13)	p
Nodule Size, mean±SD	11.6±3.8 (95% CI: 9.74-13.42)	14.2±6.2 (95% CI:10.50-17.96)	0.255
Follow-up Time, median	18 (IQR: 15)	9 (IQR: 21)	0.146
Malignancy Risk Score, median			
Mayo-Clinic	11.4 (IQR: 12.6)	12.9 (IQR: 30.6)	0.490
Brock	8.4 (IQR: 16)	12.9 (IQR: 24.3)	0.084
Bayesian	7 (IQR: 29)	18 (IQR: 73.5)	0.111
Herder	11.9 (IQR: 11.8)	12.9 (IQR: 29.2)	0.409
Tumor size, mean±SD	9.8±4.1 (95% CI: 7.9-11.8)	13.4±4.2 (95% CI: 10.8-15.9)	0.019
Lymph Node Number, mean±SD	3.7±2.6 (95% CI: 2.4-4.9)	5.9±3.2 (95% CI: 3.9-7.8)	0.049
Lymph Node Station, median	3 (IQR: 3)	4 (IQR: 2)	0.144

IQR: Interquartile range, pGGNs: Pure ground-glass opacities, PSNs: Part-solid nodules, SD: Standard deviation

When malignancy risk scores were analyzed, the median score according to the Mayo Clinic model was 11.4 (IQR:12.6) in the pGGNs group and 12.9 (IQR:30.6) in the PSNs group; however, this difference was not statistically significant (p=0.490). According to the Brock model, the median score was 8.4 (IQR:16) in the pGGNs group and 12.9 (IQR:24.3) in the PSNs group, showing a trend toward significance (p=0.084). The Bayesian model did not demonstrate a statistically significant difference in malignancy scores between the PSNs and the pGGNs (7 vs. 18, p=0.111). Similarly, the Herder model did not demonstrate a statistically significant difference between the groups (p=0.409).

From a histopathological perspective, tumor size was significantly larger in the PSNs group compared to the pGGNs group. The mean tumor diameter was 9.8 ± 4.1 mm (95% CI: 7.9–11.8) in the pGGNs group and 13.4 ± 4.2 mm (95% CI: 10.8–15.9) in the PSNs group (p=0.019). Lymph node analysis revealed that more lymph nodes were removed in the PSNs group. The mean number of dissected lymph nodes was 3.7 ± 2.6 in the pGGNs group and 5.9 ± 3.2 in the PSNs group, with a statistically significant difference (p=0.049). The median number of lymph node stations removed was 3 (IQR:3) in the pGGNs group and 4 (IQR:2) in the PSNs group, but this difference was not statistically significant (p=0.144).

Discussion

In this study, the role of malignancy risk prediction models in estimating the likelihood of adenocarcinoma in pGGNs and PSNs was evaluated. Among the 32 patients undergoing segmentectomy, 59.4% had pGGNs and 40.6% had PSNs. PSNs were found to be significantly larger, and a greater number of lymph nodes were removed in this group; however, no significant differences were observed between the groups in terms of malignancy-risk scores. Only the Bayesian model demonstrated a significantly higher risk score in PSNs. Invasive adenocarcinoma was the most frequently observed malignant pathology (37.5%), and tumor size was significantly larger in the PSNs group. These findings suggest that currently used malignancy risk models may be insufficient for accurately stratifying oncologic risk in pGGNs and PSNs, indicating a need for more sensitive and specific predictive tools.

Pulmonary segmentectomy has gained increasing popularity in recent years. One of the landmark studies contributing to this shift was conducted by Saji et al., demonstrating that segmentectomy provided superior survival compared to lobectomy in patients with solitary pulmonary nodules smaller than 2 cm (1). Similarly, Altorki et al. suggested that sublobar resection could be considered a standard surgical approach for solitary pulmonary nodules smaller than 2 cm (12). The motivation behind these studies is closely linked to advancements in imaging technologies and minimally invasive surgical techniques. These technological developments have significantly improved the detection rates of early-stage lung cancer, particularly in carefully selected patient groups. In this study, pGGNs and PSNs were identified using multislice computed tomography (CT) imaging. Based on these images, three-dimensional reconstruction technology was used to visualize the anatomical segments containing the nodules, allowing for surgical resection to be performed under the oncologic principles.

Risk prediction models are recommended and routinely used by pulmonologists in the evaluation of SPN. According to the ACCP guidelines, surgical resection is recommended for any pGGNs showing growth or development of a solid component, pGGNs larger than 10 mm, PSNs larger than 8 mm with a growth tendency, or PSNs larger than 15 mm that have not been followed radiologically (6). Similarly, the Fleischner Society recommends surgical resection for pGGNs that develop a solid component, PSNs with growing solid components, and persistent PSNs with solid components larger than 6 mm (4). These guidelines recommend surveillance rather than immediate intervention for other pGGNs and PSNs not meeting the criteria for high-risk lesions, due to their relatively low probability of malignancy. Moreover, risk prediction models provide malignancy estimates not only based on radiological findings but also by incorporating various demographic and clinical factors, including age, sex, history of other malignancies, chronic lung disease, smoking duration, and family history of lung cancer (13). The Mayo Clinic model is a widely used clinical prediction tool developed to estimate the probability of malignancy in SPN. It is based on the original study published by Swensen et al. in 1997, which laid the foundation for the model (14). The Mayo Clinic model primarily evaluates factors such as age, smoking history, history of extrathoracic cancer, and radiologic characteristics including nodule size, morphology, and number. In contrast, the Brock model—also known as the PanCan model—was developed by Brock University (Canada) and the Pan-Canadian Early Detection of Lung Cancer Study group to estimate the malignancy risk of screen-detected pulmonary nodules and to help reduce unnecessary invasive procedures (15). Unlike the Mayo Clinic model, the Brock model incorporates additional variables such as female sex, family history of lung cancer, and the presence of emphysema on CT, as these factors have been shown to increase malignancy risk. It also includes nodule type and nodule count as radiological variables in its logistic regression framework. The Bayesian model, on the other hand, is fundamentally based on the Mayo Clinic model but extends it by incorporating PET/CT findings—specifically the presence or absence of FDG uptake—using a Bayesian probability approach (16). The integration of PET data into the risk calculation has improved the predictive accuracy of the model, particularly for nodules classified as having an intermediate risk. Distinctively, Herder et al. revised the Bayesian model in 2005 by incorporating the degree of FDG uptake observed on PET-CT and suggested that this addition significantly enhanced the model's performance (17). In clinical practice, these models stratify malignancy risk as follows: <5% as low risk (follow-up recommended), 5–65% as intermediate risk (PET/CT or biopsy may be considered), and >65% as high risk (surgical resection or biopsy may be planned). This classification aims to reduce unnecessary invasive procedures while increasing the rates of early detection and treatment of lung cancer through more accurate risk prediction. Chen et al. quantitatively evaluated the diagnostic performance of the Brock model for estimating malignancy risk in pulmonary nodules through a systematic review and meta-analysis (18). The authors concluded that while the Brock model is useful in estimating malignancy risk in pulmonary nodules, it has certain limitations in clinical practice and may require additional assessment in some cases. Similarly, Papalampidou et al. conducted a comparable evaluation of the Mayo Clinic model and suggested that it may be more applicable in specific patient populations, such as smokers and individuals from non-Asian regions (19). Similarly, Nomenoglu et al. reported comparable findings in a large-scale study conducted in the Turkish population, where only the Brock model demonstrated significant discriminative ability in ground-glass nodules. These findings highlight the need for recalibration of current risk models, particularly for nodules with minimal or absent solid components (20). In our study, consistent with previous reports, we found that pGGNs and PSNs that underwent segmentectomy were predominantly malignant—particularly with adenocarcinoma histology—even though their predicted risk scores generally fell within the low to intermediate range. Risk scores calculated using the standard prediction models did not show statistically significant differences between the pGGNs and PSNs groups, except for the Bayesian model, identifying a higher malignancy risk in the PSNs group.

In our study, a relatively high prevalence of chronic immune-mediated diseases was observed. Previous literature has explored the potential impact of such conditions on lung cancer development, with important analyses conducted to better understand the underlying mechanisms. Brooks et al. reported an increased risk of lung cancer in patients with both rheumatoid arthritis and interstitial lung disease and emphasized the need for enhanced screening efforts

in these patient populations (21). In a comprehensive review, Lee et al. examined the relationship between chronic inflammation and lung cancer, providing detailed insights into the mechanisms by which smoking contributes to carcinogenesis. However, they also emphasized that in non-smoker populations, chronic inflammation may serve as a key underlying mechanism in the development of lung cancer (22). Similarly, Nakano-Narusawa et al. reported that chronic inflammation significantly contributes to pulmonary carcinogenesis, and suggested that suppressing inflammation may play a role in limiting cancer progression (23). Therefore, incorporating chronic immune-mediated diseases into regression analyses of models used to assess the risk of pGGNs and PSNs may enhance their predictive accuracy.

An increasing global incidence of adenocarcinoma has been demonstrated (24). In their meta-analysis on subsolid nodules, AlShammari et al. reported that invasive adenocarcinoma was identified in 20% of pGGNs smaller than 30 mm (25). Cho et al. demonstrated that the risk of invasive adenocarcinoma increases with nodule size in pGGNs (26). Consistently, Lee et al. showed that pGGNs progressing to invasive adenocarcinoma had larger diameters compared to those that developed into minimally invasive adenocarcinoma (27). Many studies evaluating the risk of invasive adenocarcinoma development in PSNs have focused on assessing the consolidation-to-tumor ratio (C/T) and tumor doubling time (1, 28, 29). However, in a meta-analysis conducted by Liang et al., 49.23% of stable PSNs and 81.01% of PSNs that exhibited growth were identified as invasive adenocarcinomas in the included studies (30). The timing of surgical intervention for pGGNs and PSNs, when assessed in conjunction with all these characteristics, is directly associated with patient survival. Compared to solid nodules, pGGNs, and PSNs are associated with significantly better survival outcomes (31). In our study, the histopathological features of pGGNs and PSNs were evaluated, and a significant proportion of these nodules were identified as adenocarcinomas. Although no significant difference was found between the two groups in terms of radiological nodule size, the pathological tumor size was significantly larger in the PSNs group. These findings highlight the importance of surgical resection in selected patients with pGGNs to enable the detection of disease at smaller tumor sizes.

This study has several limitations. First, its retrospective and single-center design may introduce selection bias and limit the generalizability of the findings. Second, the relatively small sample size may have reduced the statistical power of subgroup analyses, particularly between the pGGNs and PSNs groups. Third, all histopathological evaluations were conducted at a single center, which may have led to interpretative variability—especially in the classification of borderline lesions such as AIS, MIA, and invasive adenocarcinoma. Additionally, the relatively short median follow-up duration of 12 months may have missed late malignant transformations in slow-growing nodules. Lastly, interobserver variability in radiological assessments—including the measurement of solid components and nodule margins—may have influenced both risk score calculations and the interpretation of outcomes. Furthermore, this study included only pathologically confirmed nodules that underwent surgical resection, and therefore may reflect a high-risk cohort, introducing selection bias due to exclusion of nodules that regressed or disappeared during follow-up.

In conclusion, the findings of studies recommending pulmonary segmentectomy as a standard treatment for nodules smaller than 2 cm have highlighted the high malignancy risk particularly associated with pGGNs and PSNs. Our study demonstrated that widely used prediction models for estimating malignancy risk in SPN may be insufficient in detecting early-stage lung adenocarcinoma, especially in pGGNs and PSNs cases. It is therefore suggested that future multicenter, prospective studies incorporating multivariate analyses—including patient-related factors such as chronic immune-mediated diseases—would provide more accurate and clinically valuable risk stratification.

Conflict of Interests: The authors have no conflict of interest to declare.

Financial support: This study received no funding.

Acknowledgment: A version of this study was presented as an oral presentation at the Turkish Thoracic Society 2024 Fall Symposium in Konya, November 2-3, 2024

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