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Comparison of the Brock Model and LU-RADS in Differentiating Benign and Malignant Subsolid Pulmonary Nodules

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Abstract: *Background* The Lung Imaging Reporting and Data System (LU-RADS) and the Brock model are commonly utilized tools in clinical practice for evaluating pulmonary nodules. However, both LU-RADS and the Brock model have yet to be validated and compared specifically in subsolid pulmonary nodules (SSN). Therefor, the objective of this study was to compare the perfomance of the Brock model and LU-RADS in differentiating between malignant and benign SSN. *Methods* The study retrospectively analyzed the clinical data of patients diagnosed with SSN who underwent surgical resection and received pathological confirmation between January 2018 and December 2022. Based on the pathological results, the patients were categorized into two groups: benign SSN and malignant SSN. The clinical data of these groups were subjected to statistical analysis. The probability of malignancy in SSN was determined using the Brock model. Additionally, the LU-RADS category of SSN was independently determined by two radiologists. Receiver operating characteristic (ROC) curves were constructed for both the Brock model and LU-RADS, and the area under the curve (AUC) was calculated. *Results* A total of 133 patients with SSN were included in the study. The malignant SSN group, specifically LU-RADS category 4A and 4B, exhibited a higher prevalence compared to the benign SSN group (56 vs 4, $P<0.05$). Furthermore, the probability of malignancy in the malignant SSN group was significantly greater than that in the benign SSN group (0.21 vs 0.06, $P<0.05$). The Brock model demonstrated a strong correlation with LU-RADS (r=0.75, $P<0.01$) and exhibited comparable diagnostic performance in identifying lung cancer in patients with SSN (Brock vs LU-RADS, AUC: 0.83 vs 0.78, $P=0.16$). Subgroup analysis revealed that the Brock model displayed superior diagnostic accuracy in identifying malignancy in mixed ground glass nodules (Brock vs LU-RADS, AUC: 0.92 vs 0.85, $P=0.03$). However, both models demonstrated similar lower performance in detecting malignancy in pure ground glass nodules (Brock vs LU-RADS, AUC: 0.59 vs 0.55, $P=0.66$). *Conclusion* The Brock model demonstrated superior efficacy in distinguishing between malignant and benign mixed ground glass nodules, as compared to the LU-RADS. However, both the Brock model and LU-RADS exhibited limited efficacy in distinguishing between malignant and benign pure ground glass nodules.

Keywords: Subsolid Pulmonary Nodules, Predictive Model, LU-RADS, Malignant Nodule

1. Introduction

Lung cancer is a prevalent form of cancer that is frequently diagnosed and is the leading cause of cancer-related mortality in males, as well as the third most commonly diagnosed cancer and second most common cause of cancer-related death in females worldwide [1]. The implementation of low-dose computed tomography (LDCT) screening has been shown to decrease lung cancer mortality by 20% [2]. As LDCT screening becomes more widely utilized, there has been a gradual increase in the identification of pulmonary nodules. These nodules can be categorized as either solid or

subsolid pulmonary nodules (SSN) based on their appearance on CT scans, SSN is observed on CT scans as either mixed ground glass nodules (mGGN) or pure ground-glass nodules (pGGN), depending on the presence or absence of a solid component within the hazy lesion that does not obscure underlying bronchial structures or pulmonary vessels [3]. In recent years, SSN has garnered growing interest among clinicians due to its higher likelihood of malignancy compared to solid nodules [4].

The Lung Imaging Reporting and Data System (LU-RADS), developed by the American College of Radiology, serves as a standardized approach for interpreting and reporting CT studies of pulmonary nodules. It is considered one of the guidelines for managing pulmonary nodules [5]. The National Lung Screening Trial demonstrated that low-dose computed tomography (LDCT) has a high rate of false positive findings for pulmonary nodules, but this rate can be reduced by incorporating LU-RADS into the evaluation process [6]. In addition to LU-RADS, there is a growing interest in utilizing predictive models, such as the Mayo model [7], Veterans Association model [8], and Brock model [9], to enhance the assessment of pulmonary nodules. Among them, the Brock model exhibited superior accuracy in assessing the probability of malignancy in pulmonary nodules when compared to other models [10]. However, both LU-RADS and the Brock model have yet to be validated and compared specifically in SSN. Therefor, the objective of this study was to compare the perfomance of the Brock model and LU-RADS in differentiating between malignant and benign SSN.

2. Materials and Methods

2.1. Patients

Between January 2018 and December 2022, a retrospective review was conducted on the database of patients with SSN who underwent surgical resection and received pathological confirmation at The First Affiliated Hospital of Hunan Traditional Chinese Medicine College. The inclusion criteria were as follows: (1) SSN with maximum diameter less than 30 mm; (2) presence of a definitive pathological diagnosis; (3) presence of a solitary pulmonary nodule. Patients were excluded from the study if their maximum diameter exceeded 30 mm and/or if their CT scans indicated the presence of atelectasis, enlarged hila, pleural effusion, lymphadenopathy, or metastatic disease [11].

2.2. Data Collection

All patients underwent preoperative thin-section CT scans. Based on the pathological results, the patients were categorized into two groups: benign SSN and malignant SSN. Their clinical data, including age, sex, history of smoking, family history of lung cancer, emphysema, and previous malignancy, were collected and analyzed. Nodule characteristics, such as maximum nodule diameter, margin characteristics (spiculation, lobulation, pleural indentation, vascular convergence sign, vacuole sign), nodule types, location, and LU-RADS category of SSN (was independently determined by two radiologists according to the LU-RADS version 1.1 [5]), were also assessed. The malignancy probability of SSN was determined through the utilization of the Brock model, obtained from the official website of Brock University (www.brocku.ca/cancerpredictionresearch).

2.3. Statisical Analysis

The analysis was conducted using MedCalc software (v.19.6.4). Measurement data that followed a normal distribution were reported as mean ± standard deviation (SD) and statistical significance was determined using either *t*-test or *t'*-test. Non-normally distributed data were presented as median and inter-quartile range (IQR) and analyzed using the *Mann-Whitney U* test. Enumeration data were expressed as percentages and analyzed using either the *chi-square* test or *Fisher exact* test. The correlation between LU-RADS and the Brock model was assessed using the *Spearman* correlation test. The LU-RADS category and the malignant probability determined by the Brock model were compared to the postoperative pathological findings. Sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio were calculated. Receiver operating characteristic (ROC) curves were plotted for both the LU-RADS category and the Brock model, and the area under the curves (AUC) was calculated. The AUC values were compared using the *DeLong* test. A significance level of $P<0.05$ was used to determine statistical significance.

3. Results

3.1. Patient and Nodule Description

A total of 133 patients diagnosed with SSN were included in this study. The age range of all participants varied from 21 to 74 years, with a mean (SD) age of 52.45 years (±12.80). Among the participants, 76.69% were female and 12.03% were either current or former smokers. Fourteen patients (10.53%) had a history of previous malignancy or a family history of cancer. Thirty-nine patients (29.32%) presented with pGGN, while 94 patients (70.68%) had mGGN. Furthermore, 90 nodules (67.67%) were located in the upper lobe. The median maximum nodule diameter was determined to be 12.0mm (IQR, 8.98-16.20mm).

A total of 42 nodules (31.58%) were assigned to category 2, while 31 nodules (23.31%) were categorized as category 3. Additionally, 30 nodules (22.56%) fell into category 4A, and another 30 nodules (22.56%) were classified as category 4B. Among the patients, 92 (69.17%) were pathologically confirmed to have malignant nodules, consisting of 29 cases of microinvasive adenocarcinoma and 63 cases of invasive adenocarcinoma. Conversely, 41 patients (30.83%) were confirmed to have benign nodules, including 2 cases of inflammatory lesion, 2 cases of atypical adenomatous hyperplasia, and 37 cases of adenocarcinoma in situ.

The clinical and imaging characteristics of malignant and

benign SSN are presented in Table 1. It was observed that patients with malignant SSN were significantly older compared to those with benign SSN (P<0.01). Furthermore, malignant SSN exhibited a higher prevalence of margin characteristics such as spiculation (41 vs 7, P<0.01), lobulation (44 vs 11, P=0.02), and pleural indentation (30 vs 2, P<0.01) when compared to benign SSN. The median maximum diameter of malignant SSN was found to be significantly larger compared to that of benign SSN (13.20 mm vs 8.80 mm, P<0.01). The dominant nodule type in the malignant SSN group was mGGN, accounting for 77.17% of cases. Additionally, the malignant SSN group exhibited a higher number of LU-RADS category 4 nodules compared to the benign SSN group (56 vs 4, P<0.01). Furthermore, the calculated malignant probability using the Brock model was significantly higher in the malignant SSN group compared to the benign group (0.21 vs 0.06, P<0.01).

Table 1. *Clinical and CT characteristics of the patients with subsolid pulmonary nodules.*

Variables	Benign SSN (n=41)	Malignant SSN (n=92)	*P* value
Age (yr)	44.00 (38.75-55.25)	56.50 (47.50-65.00)	<0.01
Gender (Female,%)	33 (80.49)	69 (75.00)	0.49
Smoking history (%)	3 (7.32)	13 (14.13)	0.27
History of cancer (%)	5 (12.20)	9 (9.78)	0.68
Upper lobe (%)	28 (68.29)	62 (67.39)	0.92
Spiculation (%)	7 (17.07)	41 (44.57)	<0.01
Lobulation (%)	11 (26.83)	44 (47.83)	0.02
Pleural indentation (%)	2 (4.88)	30 (32.61)	<0.01
Vascular convergence sign (%)	13 (31.71)	46 (50.00)	0.05
Vacuole sign (%)	6 (14.63)	26 (28.26)	0.09
Maximum nodule diameter (mm)	8.80 (6.98-10.85)	13.20 (10.30-19.00)	<0.01
Nodule types (%)			0.01
pGGN	18 (43.90)	21 (22.83)	
mGGN	23 (56.10)	71 (77.17)	
LU-RADS category (%)			<0.01
2	23 (56.10)	19 (20.65)	
3	14 (34.15)	17 (18.48)	
4A	3 (7.31)	27 (29.35)	
4B	1 (2.44)	29 (31.52)	
Probability from the Brock model	0.06 (0.03-0.08)	0.21 (0.09-0.44)	<0.01

3.2. Correlation Analysis Between LU-RADS and Brock Model

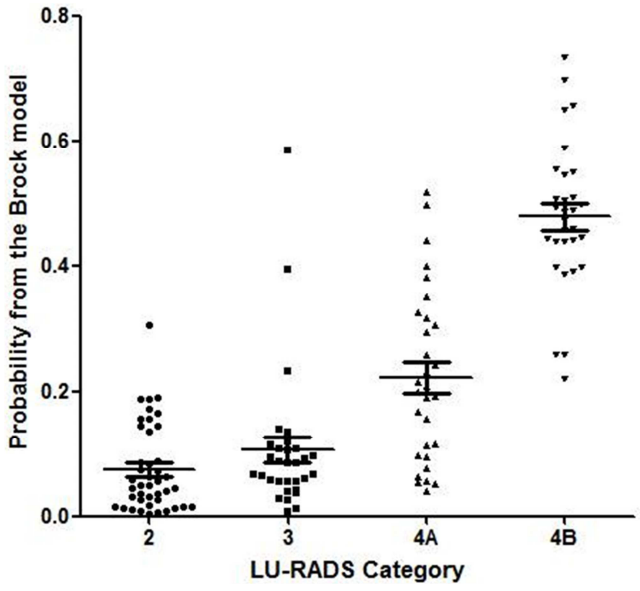

Figure 1. *Comparison of malignant probability among different LU-RADS categories of SSN.*

The *Spearman* correlation test demonstrated a positive correlation (r=0.75, P<0.01) between LU-RADS and the Brock model. The calculated malignant probabilities, as determined by the Brock model, for LU-RADS categories 2, 3, 4A, and 4B were 0.07±0.06, 0.11±0.11, 0.22±0.14, and 0.48±0.12, respectively. Notably, there was a significant difference among the LU-RADS categories in terms of malignant probabilities (P<0.01) (see Figure 1).

3.3. Comparison of the Diagnostic Performance of LU-RADS with Brock Model

The Brock model and LU-RADS demonstrated comparable performance in the diagnosis of lung cancer for the SSN, as evidenced by their respective AUC values of 0.83±0.03 and 0.78±0.04 (P=0.16). Subgroup analysis further revealed that both models exhibited similar lower performance in detecting malignancy from the pGGN, with AUC values of 0.59±0.09 and 0.55±0.03 for Brock and LU-RADS, respectively (P=0.66). Additionally, the Brock model exhibited higher performance in diagnosing malignancy for the mGGN compared to LU-RADS, with AUC values of 0.92±0.03 and 0.85±0.04, respectively (P=0.03) (see Figure 2).

The sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and Youden index of both the Brock model and LU-RADS for distinguishing malignant from benign mGGN are presented in Table 2. The Brock model exhibited higher sensitivity, specificity, and positive likelihood ratio compared to LU-RADS, while the negative likelihood ratio was lower for the Brock model in comparison to LU-RADS.

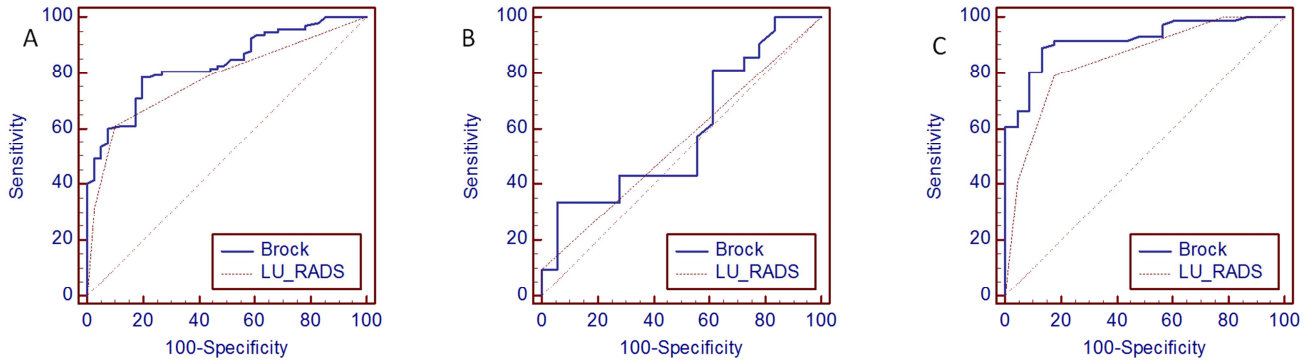

Figure 2. *Receiver operating characteristic (ROC) curves of the Brock model and LU-RADS. A: Brock model and LU-RADS had a comparable performance in diagnosing lung cancer for the SSN (Brock vs LU-RADS, AUC± 1.96 SE: 0.83±0.03 vs 0.78±0.04, p=0.16). B: Brock model and LU-RADS had a similar lower performance in the detection of malignancy from the pGGN (Brock vs LU-RADS, AUC± 1.96 SE: 0.59±0.09 vs 0.55±0.03, p=0.66). C: Brock model had a higher performance in diagnosing maligancy for the mGGN than LU-RADS (Brock vs LU-RADS, AUC± 1.96 SE: 0.92±0.03 vs 0.85±0.04, p=0.03). AUC : area under curve; SE: standard error.*

Table 2. *Comparison of Brock model and LU-RADS category for distinguishing malignant from the mGGN.*

	Sensitivity	Specificity	+LR	-LR	Youden index	Cutoff	AUC	*P* value
Brock model	88.73	86.96	6.80	0.13	0.76	0.09	0.92	<0.01
LU-RADS category	78.87	82.61	4.54	0.26	0.61	3	0.85	<0.01

AUC: area under curve; +LR: positive likelihood ratio; -LR: negative likelihood ratio.

4. Discussion

The findings of our study indicate that both the Brock model and LU-RADS exhibit a high predictive value when it comes to differentiating between benign and malignant SSN. Additionally, the Brock model demonstrates superiority over LU-RADS in accurately distinguishing malignant mGGN from benign cases.

The malignancy prediction model has been found to be a highly effective and accurate diagnostic tool for distinguishing between malignant and benign pulmonary nodules [12]. Several clinical guidelines for pulmonary nodules recommend the utilization of malignancy prediction models [11, 13, 14]. The Brock model, developed using data from the Pan-Canadian Early Detection of Lung Cancer Study and employing multivariate logistic regression, demonstrated strong predictive ability in external validation sets with an area under the curve (AUC) of 0.970 [9]. The model parameters encompassed various factors such as age, gender, family history of tumor, spiculation, nodule diameter, nodule type, upper lobe nodules, nodule number, and the presence of emphysema. Notably, the Brock model is the pioneering predictive model that incorporates the types of nodules, namely solid nodules, ground-glass nodules (GGN), and part-solid nodules. The current study revealed significant disparities in age, maximum nodule diameter, spiculation, and mGGN between the malignant and benign SSN groups, which are also encompassed within the Brock model. Consequently, the malignancy probability calculated by the Brock model exhibited a significantly higher value in the malignant SSN group compared to the benign group. This observation potentially elucidates the strong discriminatory ability of the Brock model in distinguishing between malignant and benign mGGN, as evidenced by an AUC value of 0.92.

The LU-RADS classification system has gained significant acceptance among clinicians as a dependable instrument for assessing and monitoring pulmonary nodules [15]. Within this system, nodules falling under category 2 are typically considered benign, with a malignant probability of less than 1%. Category 3 nodules are deemed probably benign, with a low likelihood of developing into lung cancer (1-2%). Nodules categorized as 4A are suspiciously malignant (5-15%), while those falling under category 4B are highly suspicious of malignancy (>15%) [5]. Given the similar probabilities and management of malignancy between category 4B and 4X nodules, this study includes them together for analysis. Our findings indicate that the malignant SSN group exhibited a higher prevalence of LU-RADS category 4 compared to the benign SSN group. This observation aligns with the significantly larger median maximum diameter of malignant SSN in comparison to benign SSN, as well as the predominance of mGGN nodule type in the malignant SSN group. These results can be attributed to the fact that LU-RADS classification primarily relies on nodule size and type. Furthermore, a notable correlation was observed between the LU-RADS and Brock model.

In this study, we conducted a comparative analysis between the Brock model and LU-RADS to assess their respective abilities in distinguishing benign and malignant SSN. The findings demonstrated that both the Brock model and LU-RADS exhibited a commendable diagnostic performance for lung cancer in SSN cases, with no significant statistical disparity observed between them (AUC: 0.83 vs 0.78, *P*=0.16). However, the Brock model exhibited superior performance in diagnosing malignancy for the mGGN compared to LU-RADS,

as evidenced by a higher AUC value of 0.92 compared to 0.85 (P=0.03). Furthermore, the Brock model demonstrated better diagnostic sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio when compared to LU-RADS. Similar findings have been documented by M. M. Hammer *et al* [16]. Previous research has indeed indicated that LU-RADS has underestimated the risk of lung cancer associated with pulmonary nodules [17, 18]. This discrepancy may be attributed to the absence of patient-specific clinical characteristics, such as age, cancer history, and smoking history, within the LU-RADS framework. Importantly, both the Brock model and LU-RADS exhibited limited efficacy in distinguishing between malignant and benign pGGN. These outcomes imply that the differentiation of benign and malignant pGGN poses a greater challenge, further research is warranted.

This study is not without limitations, including a small sample size, the inclusion of patients with SSN undergoing surgical resection, selection bias, and being a single-center retrospective study. Consequently, the findings of this study necessitate further validation through a larger sample size and a multi-center prospective study.

5. Conclusion

The Brock model demonstrated superior efficacy in distinguishing between malignant and benign mixed ground glass nodules, as compared to the LU-RADS. However, both the Brock model and LU-RADS exhibited limited efficacy in distinguishing between malignant and benign pure ground glass nodules.

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