



# The Solid Volume Ratio is Better Than the Consolidation Tumor Ratio in Predicting the Malignant Pathological Features of cT1 Lung Adenocarcinoma

Yu Liu<sup>1,\*</sup> Ning Jiang<sup>2,\*</sup> Zhiqiang Zou<sup>1</sup> Hongxiu Liu<sup>3</sup> Chuanhang Zang<sup>4</sup> Jia Gu<sup>5</sup> Ning Xin<sup>1</sup>

<sup>1</sup>Department of Thoracic Surgery, PLA 960th Hospital, Jinan, China

<sup>2</sup>Department of Thoracic Surgery, The Second Hospital of Shandong University, Jinan, China

<sup>3</sup>Department of Medical Imaging, PLA 960th Hospital, Jinan, China

<sup>4</sup>Department of Thoracic Surgery, PLA 964th Hospital, Changchun, China

<sup>5</sup>Department of Pathology, PLA 960th Hospital, Jinan, China

Address for correspondence Ning Xin, MS, Department of Thoracic Surgery, PLA 960th Hospital, Jinan, China  
(e-mail: xinning1112@163.com).

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## Abstract

**Background** More effective methods are urgently needed for predicting the pathological grade and lymph node metastasis of cT1-stage lung adenocarcinoma.

**Methods** We analyzed the relationships between CT quantitative parameters (including three-dimensional parameters) and pathological grade and lymph node metastasis in cT1-stage lung adenocarcinoma patients of our center between January 2015 and December 2023.

**Results** A total of 343 patients were included, of which there were 233 males and 110 females, aged  $61.8 \pm 9.4$  (30–82) years. The area under the receiver operating characteristic (ROC) curve for predicting the pathological grade of lung adenocarcinoma using the consolidation–tumor ratio (CTR) and the solid volume ratio (SVR) were 0.761 and 0.777, respectively. The areas under the ROC curves (AUCs) for predicting lymph node metastasis were 0.804 and 0.873, respectively. Multivariate logistic regression analysis suggested that the SVR was an independent predictor of highly malignant lung adenocarcinoma pathology, while the SVR and pathological grade were independent predictors of lymph node metastasis. The sensitivity of predicting the pathological grading of lung adenocarcinoma based on SVR  $>5\%$  was 97.2%, with a negative predictive value of 96%. The sensitivity of predicting lymph node metastasis based on SVR  $>47.1\%$  was 97.3%, and the negative predictive value was 99.5%.

**Conclusion** The SVR has greater diagnostic value than the CTR in the preoperative prediction of pathologic grade and lymph node metastasis in stage cT1-stage lung adenocarcinoma patients, and the SVR may replace the diameter and CTR as better criteria for guiding surgical implementation.

## Keywords

- ▶ lung adenocarcinoma
- ▶ predictive factor
- ▶ lymph node metastasis
- ▶ pathological grading

\* These authors contributed equally to this article.

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## Introduction

There are still many controversies regarding the surgical resection range, lymph node dissection method, clinical prognosis, and postoperative intervention methods for T1-stage lung adenocarcinoma. Since 2002, the Japan Clinical Oncology Group has been conducting a series of studies on T1-stage lung adenocarcinoma,<sup>1–3</sup> selecting nodule diameter and the consolidation–tumor ratio (CTR) as grading criteria for different extents of pulmonary resection. However, there is still controversy over whether the CTR and tumor diameter are related to the prognosis of patients with partial solid non-small cell lung cancer.<sup>4–6</sup> Kim et al's<sup>7</sup> study revealed that the CTR is not an independent predictor of prognosis for patients with cT1N0M0-stage lung adenocarcinoma, neither in the entire population nor in partial solid nodules. Ye and his colleagues<sup>8</sup> reported that the CTR, solid partial diameter, and tumor size are not independent predictors of prognosis for partially solid lung adenocarcinoma patients. In addition, a considerable portion of solid lung nodules have an irregular or scattered distribution of solid parts, which has strong subjectivity and uncertainty in selecting the optimal CT plane. Even the tumor length and CTR measured by the same expert have poor reproducibility. Therefore, using only diameter and CTR as the layering standard is not the optimal approach. With the application of various lung nodule analysis software, such as Lung VCAR, Syngo, In house, and Advanced Lung Analysis,<sup>9,10</sup> we could measure the three-dimensional composition information of tumor size, shape, and density more accurately, comprehensively, and conveniently. Therefore, we analyzed the CT data and postoperative pathological information of T1-stage lung adenocarcinoma patients who underwent lung cancer resection at the 960th Hospital of the People's Liberation Army to identify better predictive indicators for surgical implementation.

## Methods

### Patient Eligibility Criteria

This retrospective study included 956 T1-stage lung cancer patients who underwent lung cancer resection at our center between January 2015 and December 2023. The inclusion criteria were as follows: (1) plain scan multiple-slice spiral CT DICOM images within 2 weeks prior to surgery; (2) partial or pure solid nodules with a diameter less than 3 cm in the solid portion (if multiple pulmonary nodules were present, the largest nodule in the solid portion was taken as the research object); (3) standardized lymph node dissection or sampling procedures; and (4) all nodules confirmed by surgical pathology as primary lung adenocarcinoma. The exclusion criteria were as follows: (1) preoperative imaging with suspected lymph node or organ metastasis; (2) patients who had undergone preoperative treatments such as chemotherapy, radiation therapy, targeted therapy, and immunotherapy; (3) the postoperative pathological type was a preinvasive lesion or contains other pathological components, such as adenosquamous cell carcinoma, adenoid cystic carcinoma, and mucoepidermoid carcinoma; and (4)

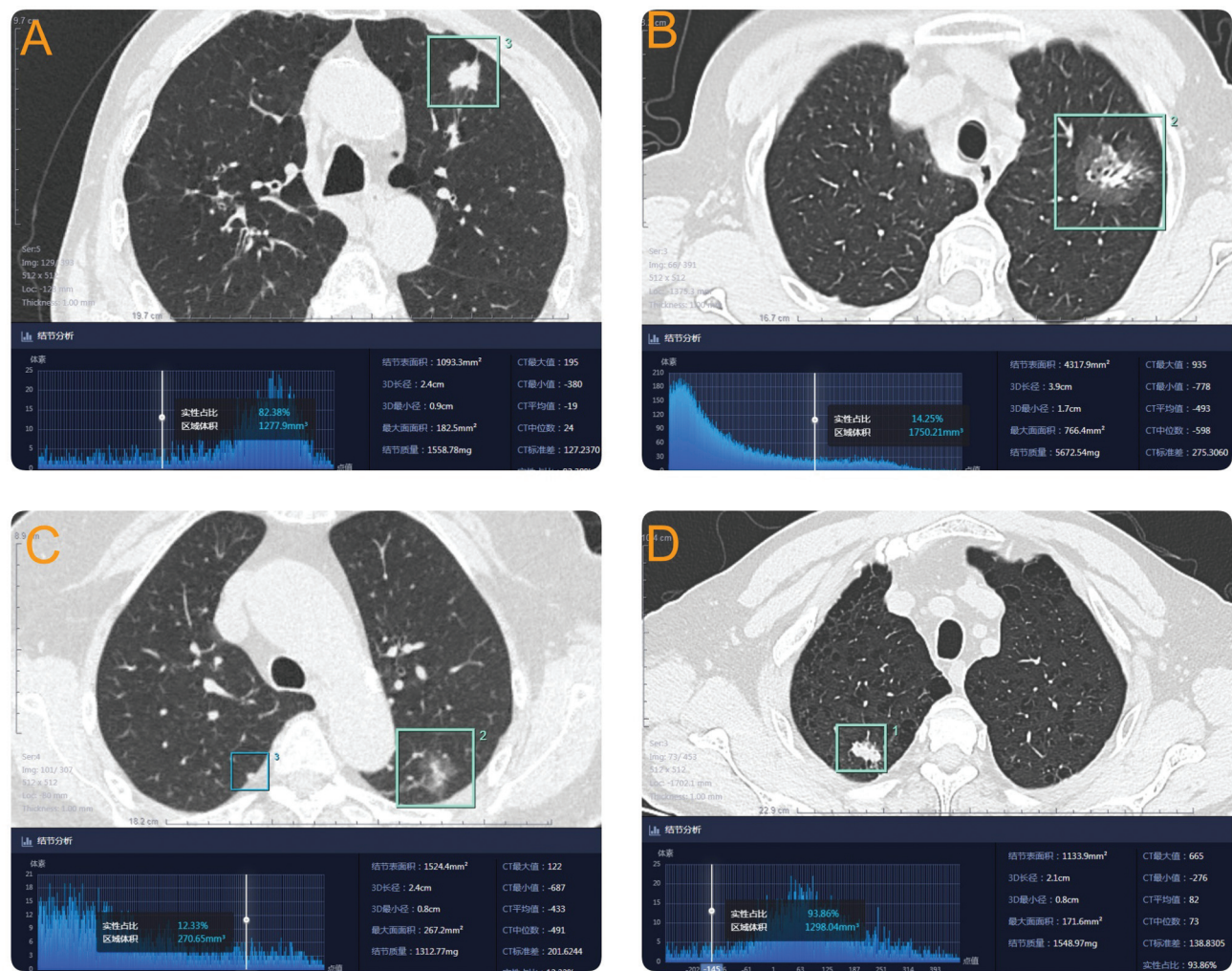
the clinical, imaging, and pathological data were not complete or accurate enough. This study was reviewed and approved by the Ethics Committee of the 960th Hospital of the People's Liberation Army (approval number S2023-025).

### Instrument and Parameters

An Aquilion ONE 320-row spiral CT machine (Toshiba, Japan) was used for a nonenhanced CT scan. The scanning parameters were as follows: tube voltage of 120 kV and a tube current of 50 to 150 mA; beam pitch, 0.516 to 0.98; slice thickness, 5 mm; matrix, 512 × 512. The imaging data were reconstructed into 0.625-mm and/or 1-mm slice thickness with a soft-tissue algorithm used for the mediastinal window image and a lung algorithm for the lung window image. After anonymous processing of the two-dimensional image data, the original DICOM image (lung window image) was imported into pulmonary nodule CT image-assisted detection software (artificial intelligence target reconstruction of pulmonary nodules) to automatically analyze the following CT quantitative parameters of pulmonary nodules, with a nodule solidity threshold of –145 Hounsfield unit (HU).

### Observation Indicators

General information: age, sex, smoking history, cancer antigen status, tumor location, and surgical method. Pathological information: pathological type, pathological subtype (classified according to the 2020 World Health Organization histological subtype classification criteria for lung adenocarcinoma and the proportion of each subtype), vascular invasion, pleural invasion, air cavity dissemination, and lymph node metastasis status were recorded. CT quantitative parameters (–Fig. 1) included the maximum diameter of the tumor, maximum diameter of the solid part, total volume of the nodule, volume of the solid part, average CT value (HU value) of the nodule, average CT value of the solid part, nodule mass, and mass of the solid part of the lung nodule, and the CTR and solid volume ratio (SVR) were calculated. The CTR was defined as the ratio of the maximum solid diameter of the tumor to the maximum diameter of the tumor in the lung window on high resolution spiral CT.<sup>11</sup> The nodule mass formula was  $M = V \times (A + 1,000) / 1,000$ , where  $M$  was the body mass of the sub-solid nodules (SSN) in mg,  $V$  was the volume of the SSN in mm<sup>3</sup>, and  $A$  was the three-dimensional average CT value of the SSN in HU. The 2020 The International Association for the Study of Lung Cancer (IASLC) pathological new grading system<sup>12</sup> divides lung adenocarcinoma into three levels—level 1 was highly differentiated: the adherent growth type was dominant, and the high-grade pattern (solid, micropapillary, or complex glandular type) did not exceed 20%; grade 2 was moderately differentiated: mainly acinar or papillary, and the high-grade pattern did not exceed 20%; and level 3 was poorly differentiated: with 20% or more high-level patterns. In this study, pathological malignancies were divided into low-grade and highly malignant groups, with the low-grade malignancy group corresponding to IASLC grading system levels 1 and 2 and the highly malignant group corresponding to IASLC grading system level 3.



**Fig. 1** (A–D The four images correspond to the three-dimensional quantitative parameters obtained from spiral CT analysis of different lung cancer patients using the “InferVision” imaging-assisted detection software. Taking (A) as an example: the total volume of the nodule is 1,277.9 mm<sup>3</sup>, the volume of the solid part is 1,052.7 mm<sup>3</sup>, the average CT value of the nodule is –19 HU, the nodule mass is 1,558.78 mg, and the mass of the solid part of the lung nodule could be calculated by using nodule mass formula:  $M = V \cdot (A + 1000) / 1000$ . HU, Hounsfield unit.

Statistical Methods

SPSS 25.0 statistical software was used for statistical analysis of the data. The normality test (Kolmogorov-Smirnov test), was performed on quantitative data and data that conformed to or approximated a normal distribution were measured as the mean ± standard deviation ( $\bar{x} \pm s$ ). Two independent sample *t*-tests were used for intergroup mean comparisons. If the data showed a skewed distribution, the data were measured as the median (interquartile range; *M* [P25, P75]), and the median between groups was compared using the Mann–Whitney U test (nonparametric test). If the data showed a normal distribution, Pearson correlation analysis was used. Receiver operating characteristic (ROC) curves were drawn for quantitative data, and the optimal cutoff value was determined. In the multivariate analysis, variables with statistical significance (*p* < 0.1) according to univariate analysis were included in the multivariate logistic regression model. For the bilateral test, *p* < 0.05 indicated a statistically significant difference.

Results

Summary of the General Data

There were 956 lung cancer surgical patients in our center from January 2015 to December 2023, including 343 patients who met the abovementioned inclusion criteria (► **Table 1**), 166 males and 177 females, aged 61.8 ± 9.4 (30–82) years. A total of 171 cases (49.9%) underwent lobectomy (including combined segmental or wedge resection), 85 cases (24.8%) underwent segmental resection, and 87 cases (25.4%) underwent wedge resection (pure ground glass nodules less than 2 cm and located outside one-third of the lungs).

Statistical Analysis of Pathological Grade and Lymph Node Metastasis Status in Lung Adenocarcinoma Patients

Univariate analysis (using *t*-tests and Mann–Whitney U tests) revealed that (► **Table 2**) the maximum diameter of the solid part, CTR, total volume of the nodule, solid part

**Table 1** General clinical information

| Items                                                        | Mean (95% CI) or proportion |
|--------------------------------------------------------------|-----------------------------|
| Age (years)                                                  | 61.83 ± 9.378 (30–82)       |
| Gender (number)                                              |                             |
| Male                                                         | 166 (48.4%)                 |
| Female                                                       | 177 (51.6%)                 |
| Removal range (number)                                       |                             |
| Lobectomy (including combined segmental or wedge resection)  | 171 (49.9%)                 |
| Pulmonary segmentectomy (including combined wedge resection) | 85 (24.8%)                  |
| Wedge resection                                              | 87 (25.4%)                  |
| Number of lymph node dissection groups (groups)              | 2.83 ± 1.867 (0–7)          |
| Number of lymph node dissection (number)                     | 8.88 ± 7.819 (0–40)         |
| Lymph node metastasis status (number)                        |                             |
| Lymph node metastasis                                        | 37 (10.8%)                  |
| N1 <sup>a</sup> positive                                     | 30 (8.7%)                   |
| N2 <sup>b</sup> positive                                     | 20 (5.8%)                   |

<sup>a</sup>N1 positive, N1 lymph node positive only.

<sup>b</sup>N2 positive, N2 lymph node positive, accompanying N1 positive or not.

volume, SVR, average CT value of the nodule, average CT value of the solid part, total mass of the nodule, solid part mass, Carcinoembryonic antigen (CEA), and pleural invasion were significantly correlated with the pathological grade of lung adenocarcinoma. The maximum diameter of the nodules, maximum diameter of the solid parts, CTR, total volume of the nodules, solid part volume, SVR, average CT value of the nodules, average CT value of the solid parts, total mass of the nodules, solid part mass, CEA, and pleural invasion were significantly correlated with lymph node metastasis. Multivariate analysis (logistic regression analysis) suggested that the SVR was an independent predictor of highly malignant lung adenocarcinoma pathology (►Table 3), while the SVR and pathological grade are independent predictors of lymph node metastasis (►Table 4).

#### Comparison of Pathological Grading Prediction Parameters for Lung Adenocarcinoma

The areas under the ROC curve (AUCs) of the CTR, average CT value of nodules, and SVR for predicting the pathological grade of lung adenocarcinoma were 0.761, 0.768, and 0.777, respectively (►Fig. 2A and ►Tables 5 and 6). By analyzing coordinates on the ROC curve, we could work out that using an SVR >5% as the standard, the sensitivity for predicting the pathological grade of lung adenocarcinoma was 97.2%, and the negative predictive value was 96%. The sensitivity of predicting the pathological grade of lung adenocarcinoma patients with a CTR >0.45 was 95.5%, and the negative predictive value was 91.5%. The sensitivity of predicting the pathological grade of lung adenocarcinoma based on the average CT value of nodules > –470 was 95.5%, and the negative predictive value was 91.8%.

#### Comparison of Predictive Parameters for Lymph Node Metastasis

The AUCs of the CTR, average CT value of nodules, and SVR for predicting lymph node metastasis were 0.804, 0.858, and 0.873, respectively (►Fig. 2B and ►Tables 5 and 6). The sensitivity of predicting lymph node metastasis based on SVR >47.1% was 97.3%, and the negative predictive value was 99.5%. The sensitivity of predicting lymph node metastasis based on CTR >0.67 was 97.3%, with a negative predictive value of 99.3%. The sensitivity of predicting lymph node metastasis based on CT values > –211 was 97.3%, and the negative predictive value was 98.9%.

#### Discussion

Postoperative pathological findings of lymph node metastasis lead to poor prognosis in patients with T1-stage lung adenocarcinoma.<sup>13</sup> In addition, for T1-stage lung adenocarcinoma, highly invasive components such as micropapillary components, solid subtypes, or complex acinar components are independent risk factors for lymph node metastasis and early recurrence and metastasis.<sup>14–16</sup> Preoperative prediction of pathological subtypes and lymph node metastasis is crucial for developing surgical or comprehensive treatment plans. The analysis results of this study indicated that in some solid lung nodules smaller than 3 cm, the average CT value and SVR had greater predictive power for predicting the pathological grade and lymph node metastasis of lung adenocarcinoma than the CTR, of which the SVR had the highest accuracy. Multivariate analysis indicated that the SVR was an independent predictor of highly malignant lung adenocarcinoma pathology, while the SVR and pathological

Table 2 Univariate analysis of pathological malignancy and lymph node metastasis

| Items                               | Pathological grading   |                      |  | Lymph node metastasis |          |  | t, Z or X <sup>2</sup> | p-Value | Lymph node metastasis   |                      | t, Z or X <sup>2</sup> | p-Value |
|-------------------------------------|------------------------|----------------------|--|-----------------------|----------|--|------------------------|---------|-------------------------|----------------------|------------------------|---------|
|                                     | Negative               | Positive             |  | Negative              | Positive |  |                        |         | Negative                | Positive             |                        |         |
| Age                                 | 61.64 ± 9.064          | 62.27 ± 10.066       |  | -0.581                | 0.562    |  |                        |         | 61.95 ± 9.374           | 60.86 ± 9.487        | 0.665                  | 0.507   |
| Gender                              |                        |                      |  | 2.101                 | 0.147    |  |                        |         |                         |                      | 0.145                  | 0.703   |
| Male                                | 108                    | 58                   |  | -                     |          |  |                        |         | 147                     | 19                   | -                      |         |
| Female                              | 128                    | 49                   |  | -                     |          |  |                        |         | 159                     | 18                   | -                      |         |
| Smoking                             |                        |                      |  | 4.725                 | 0.030    |  |                        |         |                         |                      | 0.181                  | 0.671   |
| No                                  | 163                    | 61                   |  | -                     |          |  |                        |         | 201                     | 23                   | -                      |         |
| Yes                                 | 73                     | 46                   |  | -                     |          |  |                        |         | 105                     | 14                   | -                      |         |
| Pleural invasion                    |                        |                      |  | 6.248                 | 0.012    |  |                        |         |                         |                      | 7.841                  | 0.005   |
| Negative                            | 167                    | 61                   |  | -                     |          |  |                        |         | 211                     | 17                   | -                      |         |
| Positive                            | 69                     | 46                   |  | -                     |          |  |                        |         | 95                      | 20                   | -                      |         |
| CEA                                 |                        |                      |  | 15.439                | 0.000    |  |                        |         |                         |                      | 7.478                  | 0.006   |
| Negative                            | 217                    | 82                   |  | -                     |          |  |                        |         | 272                     | 27                   | -                      |         |
| Positive                            | 19                     | 25                   |  | -                     |          |  |                        |         | 34                      | 10                   | -                      |         |
| Maximum diameter of the nodule      | 21 (15-26)             | 22 (18-27)           |  | -1.350                | 0.177    |  |                        |         | 20.3 (15, 26)           | 27 (21, 29)          | -4.089                 | 0.000   |
| Maximum diameter of the solid part  | 13 (7.08, 19)          | 18.5 (14, 25)        |  | -5.858                | 0.000    |  |                        |         | 13.25 (8.00, 19.12)     | 25 (19, 28)          | -6.870                 | 0.000   |
| CTR <sup>a</sup>                    | 0.666 (0.4286, 0.8925) | 1 (0.78, 1)          |  | -7.828                | 0.000    |  |                        |         | 0.7236 (0.4650, 0.9622) | 1 (0.9354, 1)        | -6.018                 | 0.000   |
| Total volume of nodules             | 2,240 (953.4-4,203)    | 2,946 (1,446, 4,856) |  | -1.863                | 0.062    |  |                        |         | 2,256 (998, 4,161)      | 4,664 (3,097, 6,900) | -4.455                 | 0.000   |
| Solid part volume                   | 417.6 (100, 1,618)     | 1,968 (721, 3,459)   |  | -6.49                 | 0.000    |  |                        |         | 539 (136, 1,933)        | 3,459 (2,360, 5,895) | -7.221                 | 0.000   |
| SVR <sup>b</sup>                    | 24.32 (6.63, 55.8)     | 75.94 (47.31, 94.00) |  | -8.213                | 0.000    |  |                        |         | 32.93 (8.94, 66.53)     | 94 (75.68, 100)      | -7.414                 | 0.000   |
| Overall CT value                    | -322 (-465, -131)      | -57 (-198, 19)       |  | -7.968                | 0.000    |  |                        |         | -259.5 (-443.5, -87.75) | 16 (-69.5, -39)      | -7.123                 | 0.000   |
| CT value of the solid part          | -83.5 (-127.5, -10)    | 20 (-35, 29)         |  | -7.844                | 0.000    |  |                        |         | -59.83 (-122, 12)       | 25 (14.5, 43.0)      | -6.948                 | 0.000   |
| Mass of nodule                      | 1,378 (649, 3,102)     | 2,713 (1,227, 4,714) |  | -4.019                | 0.220    |  |                        |         | 1,512 (668, 3,130)      | 3,899 (2,922, 7,099) | -5.929                 | 0.003   |
| Mass of solid portion of the nodule | 24.3 (6.63, 55.8)      | 2,071 (627, 3,552)   |  | -6.582                | 0.000    |  |                        |         | 514.8 (117.8, 1,929.4)  | 3,597 (2,302, 5,952) | -7.230                 | 0.000   |
| Pathological malignancy             |                        |                      |  |                       |          |  |                        |         |                         |                      | 43.017                 | 0.000   |
| Low degree                          | -                      |                      |  |                       |          |  |                        |         | 228                     | 8                    | -                      |         |
| High degree                         | -                      |                      |  |                       |          |  |                        |         | 78                      | 29                   | -                      |         |

<sup>a</sup>CTR, consolidation-tumor ratio.  
<sup>b</sup>SVR, solid volume ratio.

**Table 3** Multivariate regression analysis of pathological grading of lung adenocarcinoma

| Risk factors     | B      | p-Value | OR (95% CI)          |
|------------------|--------|---------|----------------------|
| CTR <sup>a</sup> | 1.042  | 0.312   | 2.834 (0.376–21.356) |
| Overall CT value | −0.002 | 0.530   | 0.998 (0.993–1.004)  |
| SVR <sup>b</sup> | 0.036  | 0.018   | 1.036 (1.006–1.068)  |
| CEA positive     | 0.000  | 0.968   | 1.000 (0.977–1.022)  |
| Pleural invasion | −0.055 | 0.842   | 0.946 (0.549–1.630)  |
| Constant         | −3.716 | 0.021   | 0.024                |

<sup>a</sup>CTR, consolidation–tumor ratio.<sup>b</sup>SVR, solid volume ratio.**Table 4** Multivariate regression analysis of pathological grading of lymph node metastasis

| Risk factors         | B      | p-Value | OR (95% CI)           |
|----------------------|--------|---------|-----------------------|
| CTR <sup>a</sup>     | −0.073 | 0.976   | 0.930 (0.008–105.785) |
| Overall CT value     | −0.003 | 0.656   | 0.997 (0.985–1.009)   |
| SVR <sup>b</sup>     | 0.061  | 0.041   | 1.063 (1.003–1.127)   |
| Pathological grading | −1.401 | 0.002   | 0.246 (0.099–0.611)   |
| CEA positive         | −0.171 | 0.721   | 0.843 (0.330–2.155)   |
| Pleural invasion     | −0.247 | 0.553   | 0.781 (0.345–1.767)   |
| Constant             | −5.461 | 0.135   | 0.004                 |

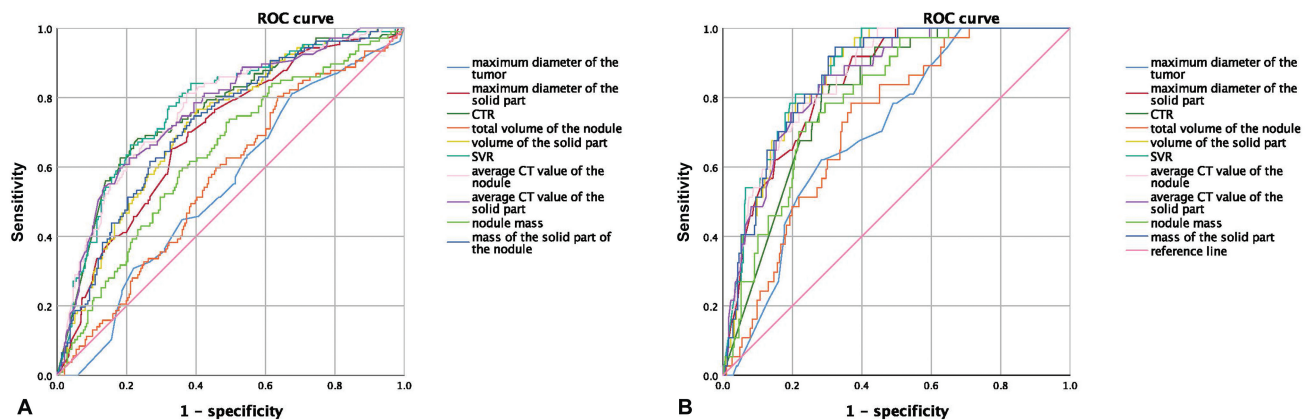
<sup>a</sup>CTR, consolidation–tumor ratio.<sup>b</sup>SVR, solid volume ratio.

malignancy grade were independent predictors of lymph node metastasis.

For some solid nodules, in pathological examination, the infiltrating part usually corresponds to the solid part on imaging. The size of the solid portion of a nodule was closely related to its invasiveness.<sup>17–19</sup> Therefore, the eighth edition of the IASLC guidelines only uses solid components to determine the T stage for some solid nodules.<sup>20</sup> The statistical analysis of this study also revealed that there was no

significant correlation between the total length or volume of nodules and the pathological grade or lymph node metastasis status of lung adenocarcinoma; on the contrary, the solid part and the total tumor size or volume can better reflect the degree of tumor invasion.

Regarding the equivalence of using two-dimensional measurements or three-dimensional volume analysis to diagnose lung cancer, the UK Lung Screening Test<sup>21</sup> divided lung nodule volume into four categories, and the results



**Fig. 2** (A) The areas under the ROC curve of CTR, average CT value of nodules, and SVR for predicting pathological grading of lung adenocarcinoma were 0.761, 0.768, and 0.777, respectively. (B) The areas under the ROC curve of CTR, average CT value of nodules, and SVR for predicting lymph node metastasis were 0.804, 0.858, and 0.873, respectively. CTR, consolidation–tumor ratio; ROC, receiver operating characteristic; SVR, solid volume ratio.

**Table 5** Comparison of diagnostic efficacy (area under the receiver operating characteristic curve) of different CT quantitative parameters

|                                    | Pathological grading | Lymph node metastasis |
|------------------------------------|----------------------|-----------------------|
| Maximum diameter of the tumor      | 0.545                | 0.705                 |
| Maximum diameter of the solid part | 0.697                | 0.845                 |
| CTR <sup>a</sup>                   | 0.761                | 0.804                 |
| Total volume of the nodule         | 0.568                | 0.724                 |
| Volume of the solid part           | 0.719                | 0.863                 |
| SVR <sup>b</sup>                   | 0.777                | 0.873                 |
| Average CT value of the nodule     | 0.768                | 0.858                 |
| Average CT value of solid part     | 0.764                | 0.850                 |
| Nodule mass                        | 0.638                | 0.798                 |
| Mass of the solid part             | 0.722                | 0.864                 |

<sup>a</sup>CTR, consolidation–tumor ratio.

<sup>b</sup>SVR, solid volume ratio.

**Table 6** Sensitivity and specificity corresponding to different diagnostic criteria

|                                    | Pathological grading   |             |             | Lymph node metastasis    |             |             |
|------------------------------------|------------------------|-------------|-------------|--------------------------|-------------|-------------|
|                                    | Diagnostic criteria    | Sensitivity | Specificity | Diagnostic criteria      | Sensitivity | Specificity |
| Maximum diameter of the tumor      | 11 mm                  | 95.3%       | 4.2%        | 18 mm                    | 94.6%       | 35.3%       |
| Maximum diameter of the solid part | 7 mm                   | 95.3%       | 19.1%       | 15 mm                    | 97.3%       | 53.6%       |
| CTR <sup>a</sup>                   | 0.45                   | 95.3%       | 27.5%       | 0.67                     | 97.3%       | 46.1%       |
| Total volume of the nodule         | 389 mm <sup>3</sup>    | 95.3%       | 4.7%        | 1,408 mm <sup>3</sup>    | 97.3%       | 36.3%       |
| Volume of the solid part           | 134 mm <sup>3</sup>    | 95.3%       | 28.8%       | 995 mm <sup>3</sup>      | 97.3%       | 62.1%       |
| SVR <sup>b</sup>                   | 5.0%                   | 97.2%       | 20.8%       | 47.1%                    | 97.3%       | 60.5%       |
| Average CT value of the nodule     | −470 HU                | 95.3%       | 23.3%       | −211 HU                  | 97.3%       | 56.5%       |
| Average CT value of solid part     | −130 HU                | 96.3%       | 22.0%       | −52 HU                   | 97.3%       | 51.3%       |
| Nodule mass                        | 415 HU·mm <sup>3</sup> | 95.3%       | 13.1%       | 1,477 HU·mm <sup>3</sup> | 97.3%       | 49%         |
| Mass of the solid part             | 100 HU·mm <sup>3</sup> | 95.3%       | 26.3%       | 836 HU·mm <sup>3</sup>   | 97.3%       | 59.5%       |

Abbreviation: HU, Hounsfield unit.

<sup>a</sup>CTR, consolidation–tumor ratio.

<sup>b</sup>SVR, solid volume ratio.

showed that volume analysis was superior to two-dimensional analysis. Yanagawa et al<sup>22</sup> performed computer-assisted volume measurements on preoperative thin-layer CT scans of stage 1 lung adenocarcinoma patients and reported that solid portion volumes greater than 1.5 cm<sup>3</sup> or solid portion proportions greater than 63% were found to be independent risk factors for recurrence or death of stage 1 lung adenocarcinoma patients. Kitazawa et al<sup>23</sup> studied 96 patients with less than 2 cm of ground-glass nodule and reported that the three-dimensional average CT value was an important parameter for predicting infiltration, and the results were better than the two-dimensional average CT value. Wu et al<sup>24</sup> conducted a multicenter study, dividing ground glass nodules into solid and ground glass components through 3D reconstruction, measuring their 3D volume and

CT values, respectively, and establishing a predictive infiltration model, obtaining good diagnostic effect. However, previous studies have mainly analyzed the diagnostic value of three-dimensional CT quantitative parameters for the invasive status of lung cancer patients, and there is no research on their predictive value for the pathological grade or lymph node metastasis status of lung adenocarcinoma patients. In this study, multiple CT quantitative parameters, such as the CTR, solid-to-volume ratio (SVR), and average CT value of the nodules, were included. The analysis results indicated that three-dimensional parameters had better predictive performance than two-dimensional parameters in predicting the pathological grade and lymph node metastasis of lung adenocarcinoma. The AUCs for the CTR and SVR for predicting the pathological grade of lung adenocarcinoma were

0.761 and 0.777, respectively, and the AUCs for predicting lymph node metastasis were 0.804 and 0.873, respectively. In addition, univariate and multivariate analyses incorporating multiple clinical factors, such as age, sex, smoking history, and cancer-associated antigens, suggested that the SVR is an independent predictor of highly malignant lung adenocarcinoma pathology, while the SVR and pathological malignancy grade are independent predictors of lymph node metastasis. This finding suggested that the SVR has greater clinical value for predicting pathological grade and lymph node metastasis in lung adenocarcinoma patients.

From a clinical application perspective, we focused more on the high sensitivity of prediction methods to reduce missed diagnoses. Based on the results of this study, with an SVR >5% as the standard, the sensitivity of predicting the pathological grade of lung adenocarcinoma was 97.2%, and the negative predictive value was 96%. According to the above criteria, 97.2% of highly malignant lung adenocarcinomas could be screened out, and 96% of patients who tested negative had low-grade malignancies. Therefore, for T1-stage lung adenocarcinoma patients who meet the SVR <5% standard, subpulmonary lobectomy could be chosen. The sensitivity of predicting lymph node metastasis based on an SVR >47.1% was 97.3%, with a negative predictive value of 99.5%. According to the above criteria, 97.3% of lung adenocarcinomas with lymph node metastasis can be screened, and 99.5% of lung adenocarcinoma-negative patients have no lymph node metastasis. Therefore, T1-stage lung adenocarcinoma patients who meet the SVR <47.1% standard could be exempted from lymph node dissection or sampling.

Previous studies have used three-dimensional quantitative parameters of pulmonary nodules, such as volume, CT value, volume doubling time, and mass doubling time,<sup>23,25</sup> to predict tumor invasiveness. This study was the first to use these parameters to predict the pathological grade and lymph node metastasis of lung adenocarcinoma, and the corresponding thresholds obtained have high sensitivity and negative predictive value. According to the above volume ratio standards, unnecessary lobectomy and lymph node dissection might be avoided for some patients, which would be of important clinical significance.

### Study Limitations

First, this single-center study included a limited number of patients and has certain representative significance. In the future, multicenter studies will be conducted to increase the number of cases and expand the representativeness of this study. In addition, there is currently no unified standard for the segmentation methods and thresholds of real parts in clinical applications, and there is an urgent need to conduct more prospective studies to establish a unified threshold for solid part segmentation. Finally, due to the short follow-up time of the patients in this study, the prognostic significance of the above imaging parameters could not be analyzed. We will release corresponding follow-up data within the next 2 to 3 years.

## Conclusion

The proportion of solid volume is an independent predictive factor for the pathological grade and lymph node metastasis of T1-stage lung adenocarcinoma. The proportion of solid volume may replace the CTR as a better predictive indicator for the pathological grade and lymph node metastasis of T1-stage lung adenocarcinoma.

### Data Availability Statement

All authors had full access to the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

### Authors' Contribution

Conceptualization, Y.L., N.X., and N.J. Methodology, Y.L. and N.X. Investigation, J.G. Formal analysis, Y.L. and N.X. Resources, Y.L., H.L., C.Z. Writing—original draft, Y.L. and N.J. Writing—review and editing, N.X. Visualization, Y.L. Supervision, Z.Z.

### Conflict of Interest

None declared.

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