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Analysis of the value of dynamic computed tomography (CT) examination in the diagnosis of early lung cancer.

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Keywords: CT dynamic enhancement scan; early stage; diagnostic value; blood flow.

Abstract. Early diagnosis and treatment are vital to improving lung cancer patients' quality of life and survival rate. This study aimed to investigate the value of dynamic enhanced scanning examination by computed tomography (CT) in early lung cancer diagnosis. One hundred and twenty patients with isolated lung nodules were selected to analyze this diagnostic method, using pathological diagnostic results of cancer as the gold standard. Of the 120 patients with isolated pulmonary nodules, the diagnosis was confirmed by pathological examination in 96 patients with early lung cancer (adenocarcinoma of the lung) and 24 patients with benign lung lesions. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of CT dynamic enhancement scans for the diagnosis of early-stage lung cancer were 93.75%, 83.33%, 91.67%, 95.74%, and 76.92%, respectively. Early-stage lung cancer had significantly less blood volume and a noticeably shorter mean time to passage than benign lung lesions ($p<0.01$). Blood flow and surface permeability were higher in early-stage lung cancer than in benign lung lesions ($p<0.05$). The areas under the receiver operating characteristic (ROC) curves for blood volume, blood flow, surface permeability, and mean time to passage for the diagnosis of early-stage lung cancer were 0.737, 0.724, 0.779, and 0.946, respectively. In conclusion, CT dynamic enhancement scan has good application value in diagnosing early lung cancer and is worth promoting in clinical practice.

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Análisis del valor del escaneo dinámico realzado por tomografía computarizada (TC) en el diagnóstico de cáncer de pulmón temprano.

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Palabras clave: tomografía computarizada (TC) de realce dinámico; etapa temprana; cáncer de pulmón; valor de diagnóstico; flujo sanguíneo.

Resumen. El diagnóstico y tratamiento tempranos son vitales para mejorar la calidad de vida y la tasa de supervivencia de los pacientes con cáncer de pulmón. Este estudio tuvo como objetivo investigar el valor del examen de escaneo dinámico realzado por tomografía computarizada (TC) en el diagnóstico de cáncer de pulmón temprano. Ciento veinte pacientes con nódulos pulmonares aislados fueron seleccionados para analizar este método diagnóstico, utilizando los resultados del diagnóstico patológico de cáncer como el estándar de oro. De los 120 pacientes con nódulos pulmonares aislados, el diagnóstico fue confirmado mediante un examen patológico en 96 pacientes con cáncer de pulmón temprano (adenocarcinoma de pulmón) y 24 pacientes con lesiones pulmonares benignas. La sensibilidad, la especificidad, la precisión, el valor predictivo positivo y el valor predictivo negativo de las tomografías computarizadas de realce dinámico para el diagnóstico de cáncer de pulmón en etapa inicial fueron respectivamente del 93,75%, 83,33%, 91,67%, 95,74% y 76,92%. El cáncer de pulmón en etapa temprana tuvo un volumen de sangre de modo significativo menor y un tiempo medio notablemente más corto hasta el paso que las lesiones pulmonares benignas ($p<0,01$). El flujo sanguíneo y la permeabilidad de la superficie fueron mayores en el cáncer de pulmón en etapa temprana que en las lesiones pulmonares benignas ($p<0,05$). Las áreas bajo las curvas ROC (Característica Operativa del Receptor) para el volumen de sangre, el flujo sanguíneo, la permeabilidad de la superficie y el tiempo medio hasta el paso para el diagnóstico de cáncer de pulmón en etapa temprana fueron respectivamente 0,737, 0,724, 0,779 y 0,946. En conclusión, la tomografía computarizada de realce dinámico tiene un buen valor de aplicación diagnóstico temprano del cáncer de pulmón y vale la pena promoverla en la práctica clínica.

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INTRODUCTION

Lung cancer originates from the bronchial mucosa epithelium, and its incidence gradually increases. The early clinical symptoms of lung cancer are not obvious, and about 2/3 of lung cancer patients are at an advanced stage (stage III or IV) [1]. Aggressive radiotherapy, chemotherapy, or surgery can cure and extend the survival time of patients with early-stage lung cancer. However, patients with intermediate to advanced lung cancer have poor outcomes, high mortality rates, and a significantly lower quality of life [2].

Therefore, early detection and treatment are the keys to improving lung cancer

patients' survival rate and quality of life. In clinical practice, the diagnosis of early-stage lung cancer depends mainly on imaging data.

With the more frequent usage of imaging techniques, more research concentrated on detecting pulmonary nodules using computed tomography (CT). CT enhancement peaks and associated parameters are obtained from CT dynamic enhancement scans and analyzed for their diagnostic efficacy [3]. Due to the aggressive nature of malignant tumors during the growth period, their morphological features and enhancement modes are commonly used for early diagnosis of pulmonary nodules in the clinical practice.

Also, a series of radiomic studies based on tissue analysis of lung nodules have been considered for better interpretation of morphological heterogeneity and irregular proliferation of tumor cells than using traditional CT images [4,5]. It was confirmed that CT dynamic enhancement detection has considerable value for identifying malignant and benign nodules [6]. Wang and Shan[7] reported that dynamic enhanced CT scanning showed the ability to differentiate pulmonary inflammatory pseudotumor, pulmonary tuberculosis, and lung cancer, representing its diagnostic value.

The blood supply in lung cancer is markedly different from benign lesions due to tumor angiogenesis, and the change in tissue density after contrast injection is marked. Some studies reported that malignant nodules have higher blood flow, volume, and mean transit time [8–10]. Nevertheless, a study showed that malignant lesions had lower blood volume and mean transit time [11]. In addition, the results of a meta-analysis showed that blood volume is the best indicator and marker for describing the blood supply, while permeability surface has a high specificity in quantifying the vascular permeability [4].

However, these studies focused on the high stages of lung cancer. Therefore, investigation of CT parameters in early lung cancer patients is necessary.

In this study, the value of dynamic CT-enhanced scanning examination in the diagnosis of early lung cancer was investigated.

MATERIALS AND METHODS

Subjects and study design

Patients with isolated pulmonary nodules who attended our hospital from January 2017 to December 2020 were selected. Inclusion criteria included that all patients were pathologically confirmed, aged >18 years, without lymph node enlargement, and underwent CT dynamic enhancement scans. Exclusion criteria were that the quality of the images was suboptimal and that the patient had a combination of other malignancies. According to the inclusion and exclusion criteria, 96 patients with isolated pulmonary nodules were included in this study, of whom 68 were males and 28 were females. Their ages ranged from 34 to 71 years, with a mean age of (52.04 ± 5.12) years.

CT dynamic enhancement scan

All patients underwent CT dynamic enhancement scans and pathological examinations. A SOMATOM Definition AS multi-layer spiral CT machine from Siemens, Germany, was employed as the CT dynamic enhancement scanning equipment. A volume of 65 mL of iopamidol injected into the patient's elbow vein at a flow rate of 3 mL/s. Patients were instructed to fast before the examination and adopt the correct breathing method for the iodine allergy test. The patient's lung lesion and a surrounding area of approximately 6 mm were scanned at 20, 80, 140, 200, and 260 s after the contrast injection, and the CT perfusion parameters were calculated.

Observation indicators

The diagnostic value of CT dynamic enhancement scans for early lung cancer was analyzed using pathological findings as the gold standard, including sensitivity, specificity, accuracy, and positive and negative

predictive values. CT dynamic enhancement scans were performed for patients with early lung cancer, whose diagnosis was confirmed by a histological study on the sample removed by biopsy through bronchoscopy.

CT perfusion parameters, which included blood flow, volume, surface permeability, and mean time to passage, were compared between patients with early-stage lung cancer and benign lung nodules. Based on the Patlak analysis method, reflux can be calculated from the maximum slope of the tissue concentration-time curve or its peak height normalized to the arterial input function. According to this theoretical model, the exchange between blood and tissue can be well described by a Patlak diagram, which shows the tissue-to-blood concentration ratio versus the AUC (area under the curve) ratio of the blood-to-blood concentration curve. For different time values, if the data fits this theoretical model, the graph will be a line with a slope equal to the blood vacuum per unit volume (permeability) and an interval equal to the relative blood volume of the tissue.

Statistical analysis

The SPSS 22.0 was used for the statistical analysis of the data. The measurement data were expressed as mean ± standard deviation (x ± SD), and the t-test was used for comparison between groups. The statistical data were expressed as the number of cases and the rate (%), and the $\chi 2$ test was used for comparison between groups. The diagnostic value of the perfusion parameters was assessed using the receiver operating characteristic (ROC) curve. The difference was considered statistically significant at $p<0.05$.

RESULTS

Pathological findings

Among 120 patients with isolated lung nodules, 96 patients were diagnosed with early-stage lung cancer (adenocarcinoma of the lung) by pathological examination. Twenty-five patients of those were classified as stage 0 of TNM (Tumor-Node-Metastasis) staging system, 44 patients were classified as stage I A, and 27 patients were classified as stage I B. There were 24 patients with benign lung lesions, including 11 with pneumonia and 13 with tuberculosis (Table 1).

Demographic of patients

Out of 21 patients in TNM stage 0M, 17 patients were men, and eight were women. Also, out of 44 patients in TNM stage I A, 30 were men, and 14 were women; out of 27 patients in TNM stage I B, 21 were men, and six were women. There were no significant differences in terms of gender in the three stages of the disease.

The average age of patients in TNM stage 0M was 54.05 ± 6.4 years. Moreover, the average age of patients in TNM stage I A and TNM stage I B stages were 52.03 ± 3.1 and 55 ± 4.2, respectively, and the patients of the three stages were significantly different in terms of average age ($p \leq 0.03$) (Table 2).

Diagnostic value of CT dynamic enhancement scans for early-stage lung cancer

The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of CT dynamic enhancement scans for the diagnosis of early-stage lung cancer were 93.75% (90/96), 83.33% (20/24),

Table 1
Pathological findings

	Early-stage lung cancer			Benign lung lesions	
	TNM stage 0	TNM stage I A	TNM stage I B	pneumonia	tuberculosis
Cases	25	44	27	11	13

Table 2
Characteristics of the three groups with different pathological findings.

Characteristics	TNM stage 0M	TNM stage I A	TNM stage I B	p-value
Gender				
Male	17	30	21	0.07*
Female	8	14	6	
Age (y)	54.05 ± 6.4	52.03 ± 3.1	55 ± 4.2	0.03**

*p-value calculated based on chi-square, ** p-value calculated based on One-way ANOVA.

91.67% (110/120), 95.74% (90/94) and 76.92% (20/26), respectively.

Comparison of parameters of early-stage lung cancer and benign lung lesions

The blood volume of early-stage lung cancer was significantly lower than that of benign lung lesions, and the mean time to passage was significantly shorter than that of benign lung lesions, and all differences were statistically significant ($p<0.01$). Both blood flow and surface permeability were higher in early-stage lung cancer than in benign lung lesions, and the differences were statistically significant ($p<0.05$). There were no statistically significant differences in lesion size and proportion of solid nodules when comparing early-stage lung cancer and benign lung lesions ($p>0.05$) (Fig. 1).

Comparison of CT perfusion parameters for early-stage lung cancer at different TNM stages

The differences in blood flow, surface permeability, and mean time to passage were not statistically significant when comparing patients with TNM stage 0, stage IA and stage IB early-stage lung cancer ($p>0.05$) (Fig. 2).

Diagnostic efficacy of CT perfusion parameters for early-stage lung cancer

The areas under the ROC curves of blood volume, blood flow, surface permeability, and mean time to passage for the diagnosis of early-stage lung cancer were 0.737, 0.724, 0.779, and 0.946, respectively. Surface permeability had the highest sensitivity of 92.5% for diagnosing early-stage lung cancer and the highest specificity of 99.5% for diagnosing early-stage lung cancer by mean time to passage (Table 3).

DISCUSSION

Diagnostic imaging is critical for the detection and staging of lung cancer. Standard clinical imaging examinations are conventional chest scans and dynamic enhancement CT [12]. Performing a plain chest examination on a patient usually requires a continuous change of position to ensure that the examination is completed. However, it can worsen the patient's lung pain, leading to poor compliance. Therefore, in practice, this option is not chosen for most patients [13] The CT dynamic enhancement scanning technique with non-overlapping images allows for precise detection of small early lesions, timely detection of enlarged mediastinal lymph nodes, and determination of the extent of tumor invasion of the pleura and surrounding blood vessels, leading to the correct staging of lung cancer [14]. In addition, relevant studies have shown that dynamic CT-enhanced scanning techniques can be used as an effective adjunctive diagnostic tool for early lung cancer in clinical practice [15].

The results of this study showed that the sensitivity, specificity, accuracy, and positive and negative predictive values of CT dynamic enhancement scans for the diagnosis of malignant lesions were all at a high level. This

is because the imaging features in the early diagnosis of lung cancer are manifested by lobar signs, burr signs, vascular collection signs, and bronchial inflation signs, which are absent in patients with benign nodules. These phenomena allow the identification of benign and malignant nodules and can improve the accuracy of diagnosis of early-stage lung cancer. The lobar sign is caused by the lack of clear cut and heterogeneity of the tumor margins, which is caused by restricted growth [16].

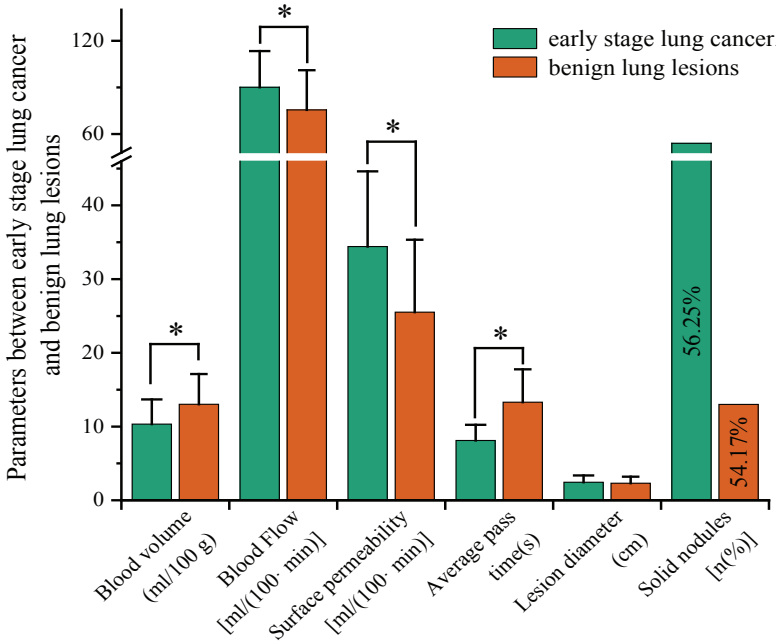

Fig. 1. Comparison of parameters between early-stage lung cancer and benign lung lesions *p<0.05.

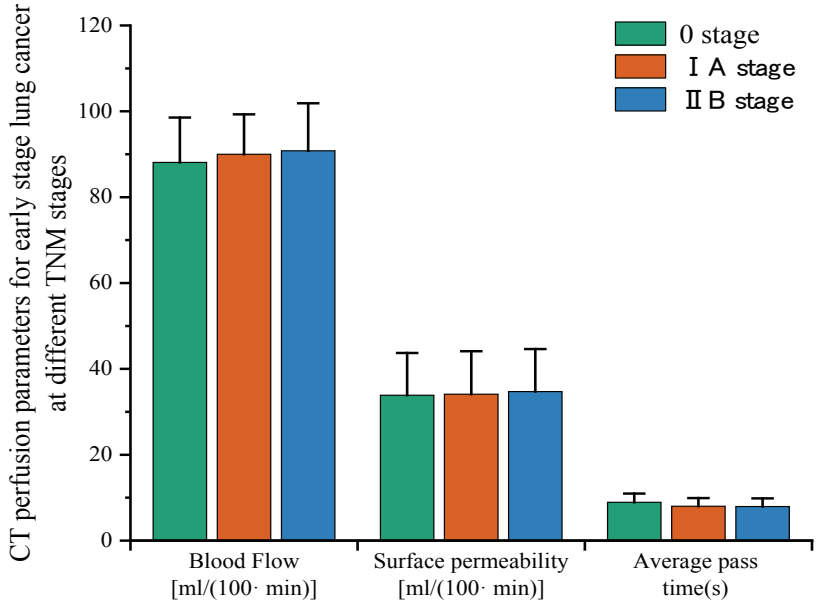

Fig. 2. Comparison of CT perfusion parameters for early-stage lung cancer at different TNM stages.

Table 3
Diagnostic efficacy of CT perfusion parameters for early-stage lung cancer.

Parameters	Area under the curve	95%CI	Optimal cut-off value	Sensitivity (%)	Specificity (%)
Blood volume	0.74	0.60~0.88	13.15	85.0	65.0
Blood Flow	0.72	0.60~0.85	72.11	81.3	60.0
Surface permeability	0.78	0.66~0.89	27.27	92.5	50.0
Average pass time	0.95	0.89~0.99	10.64	85.0	99.5

Most tumor cells grow invasively along the alveolar wall and lymphatic vessels, resulting in localized venous stasis and burr. However, signs of pneumonia may also be present in pneumonic nodules, which can lead to misdiagnosis. The CT dynamic enhancement scan examination method is simple, quick, and has non-invasive characteristics, which can detect the whole range and location of lung lesions with clear images and high diagnostic accuracy, indicating that CT dynamic enhancement scan can be used for the diagnosis of lung cancer to effectively reduce the misdiagnosis rate and improve the diagnostic efficiency.

If the differential diagnosis cannot be made based on the imaging features of early lung cancer, the diagnosis can be accomplished by blood flow parameters. The results of this study showed that early-stage lung cancer had significantly less blood volume, significantly shorter mean time to passage, and higher blood flow and surface permeability than benign lung lesions. In contrast, the differences in blood volume, blood flow, surface permeability, and mean time to passage were not statistically significant when comparing patients with early-stage lung cancer at different TNM stages. These results suggest that CT flow parameters can be used clinically to differentiate between benign and malignant lung lesions but are of less diagnostic value for clinical TNM staging, which is caused by the lymphatic return and lymphatic volume of malignant lesions. During a CT dynamic enhancement scan, the patient's lymphatic reflux slows, and the lymphatic volume decreases, affecting contrast flow due to lymphatic lesions in clinical malignancies. In contrast, the endothelial space of the capillaries widens, and there are various inter endothelial channels, which leads to a loss of basement membrane and, therefore, a high blood flow in the vessels.

Some studies have found that CT perfusion parameters such as blood volume, blood flow, surface permeability, and passage time during CT dynamic enhancement scans are of high diagnostic value for early lung cancer [17,18]. However, fewer studies have separately accounted for their sensitivity and specificity. In this study, we found that the mean time to passage was of high diagnostic value for early-stage lung cancer by plotting ROC curves.

In conclusion, CT dynamic enhancement scan has high application value in diagnosing early lung cancer and is worthy of clinical promotion. However, the number of cases included in this study was small, and there is a need to expand the sample size in future studies to eliminate statistical errors. In addition, it is necessary to further analyze the intrinsic association between peak CT enhancement and lung cancer pathogenesis in conjunction with some immunohistochemical indicators to elucidate the adjunctive clinical significance of CT dynamic enhancement scanning technology.

Limitation

One of the limitations of the study is that it was conducted in a single hospital. Therefore, it is recommended to carry out

similar studies in several hospitals or medical centers in the future.

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Competing Interests

The authors declared that they have no competing interests.

Authors' Contribution

LS, LW and JL contributed to the conception of the study; LS, XX and JL performed the experiment; LW contributed significantly to the analysis and manuscript preparation; LS and JL performed the data analyses and wrote the manuscript; XX helped perform the analysis with constructive discussions.

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