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Diagnostic Value of 64-Slice CT Dual Perfusion Parameters Combined with Serum VEGF in Lymph Node Metastasis of Lung Cancer

Guoliang Shi [1,*], Hongyu Mao [1]

[1.] Radiology Department, Deqing County People's Hospital, Wukang Town, Deqing County, 313299 Huzhou, Zhejiang, China

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* **Correspondence**

Guoliang Shi

Radiology Department, Deqing County People's Hospital, Wukang Town, Deqing County, 313299 Huzhou, Zhejiang, China

E-mail: sgl_sg@126.com

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Abstract

Background: Our study is engineered to explore the diagnostic value of 64-slice computed tomography (CT) dual perfusion parameters combined with serum vascular endothelial growth factor (VEGF) in lymph node metastasis of lung cancer. **Methods:** The clinical data of 80 patients with suspected lymph node metastasis of lung cancer admitted to our hospital from December 2021 to December 2022 were retrospectively analyzed. According to the pathological examination results, 43 patients with lymph node metastasis of lung cancer were assigned into the metastasis group, and 37 patients with non-metastatic lung cancer lymph nodes were assigned into the non-metastasis group. Blood perfusion parameters and serum VEGF level in the two groups were collected and compared with the results of pathological examination. The diagnostic value of 64-slice CT dual perfusion parameters combined with serum VEGF was analyzed using the area under the receiver operating characteristic (ROC) curves (AUC). **Results:** In this study, the bronchial arterial blood flow (BAF) and VEGF in metastasis group were significantly higher than those in non-metastasis group ($p < 0.05$), yet perfusion index (PI) was obviously lower than that in non-metastasis group ($p < 0.05$). The AUC values of BAF, PI, VEGF and their combination in the diagnosis of lymph node metastasis in lung cancer were 0.809, 0.794, 0.770 and 0.886, respectively. AUC value of combined detection was higher than that of single detection ($p < 0.05$). Accuracy rates of BAF, PI and VEGF detection were 36.25%, 46.25%, and 30.00%, respectively. BAF and VEGF were positively correlated with lymph node metastasis of lung cancer ($p < 0.05$), whilst PI was negatively correlated with lymph node metastasis of lung cancer ($p < 0.05$). **Conclusion:** 64-slice CT dual perfusion parameters combined with serum VEGF have good diagnostic value for lymph node metastasis of lung cancer. Also, BAF and VEGF may be positively correlated with lymph node metastasis of lung cancer, while PI is negatively correlated with lymph node metastasis of lung cancer.

1 Introduction

Lung cancer is a common malignant tumor, with about 85% of lung cancer belonging to non-small cell lung cancer, showing a high morbidity and mortality [1-3]. The treatment plan for lung cancer patients needs to be formulated based on lymph node metastasis. If the accuracy of evaluation is low based on the metastasis, it will directly affect the treatment effect, to some extent, leading to a decrease in patients' survival rate and various complications [4,5]. Therefore, lymph node metastasis in lung cancer patients needs to be accurately evaluated before treatment, which is of great significance for formulating reasonable treatment plans and improving the prognosis of the patients.

Pathological examination is the gold standard for clinical diagnosis of lymph node metastasis of lung cancer, which is diagnosed by extracting and analyzing lung tissue. However, it is difficult to be widely used in clinical practice due to its complex operation and great harm to patients [6]. In recent years, electronic computed tomography (CT) examination is one of effective methods for early detection of lung cancer. Notably, 64-slice CT mainly scans the human chest through computers to obtain dual perfusion parameters, diagnose, and differentiate. It has minimal trauma to patients, with simple operation and clear imaging, which is commonly used in clinical diagnosis of gastric cancer, cervical cancer and lung cancer [7-10]. In present study, the diagnostic value of dual perfusion parameters in the lymph node metastasis of lung cancer is further explored.

In recent years, vascular endothelial growth factor (VEGF) has gradually been applied to clinical diagnosis. Studies have shown that the level of VEGF can reflect the vascular density of the lesion and is related to the degree of tumor deterioration [11,12]. Furthermore, numerous studies have pointed out that VEGF is highly expressed in lung cancer tissues and metastatic lymph nodes [13-15]. These evidences suggest that high VEGF level may be considered as a diagnostic marker for lymph node metastasis in lung cancer. Nevertheless, since existing diagnostic methods for lymph node metastasis of lung cancer are limited, how to improve the diagnostic efficiency is the current focus.

Herein, we compared the 64-slice CT dual perfusion parameters and serum VEGF level with the results of pathological examination, so as to explore the correlation between them and lymph node metastasis of lung cancer, and provide reference and guidance for evaluating lymph node metastasis.

2 Patients and methods

2.1 General data

The clinical data of 80 patients with suspected lymph node metastasis of lung cancer admitted to our hospital from December 2021 to December 2022 were retrospectively analyzed. According to the pathological examination results, 43 patients with lymph node metastasis of lung cancer were assigned into the metastasis group, and 37 patients with non-metastatic lung cancer lymph nodes were allocated into the non-metastasis group. There was no statistically significant difference in gender, age, and disease type between the two groups of patients (p < 0.05), which however were comparable. The results were displayed in Table 1.

2.2 Inclusion and exclusion criteria

2.2.1 Inclusion criteria

(1) Patients were diagnosed with lung cancer by pathological examination, with lymphadenopathy and pain. (2) Patients did not undergo chemotherapy, radiotherapy, and targeted therapy before CT examination. (3) All patients underwent 64-slice CT examination. (4) The expected survival period of the patients was more than 3 months.

Table 1 Comparison of general data between the two groups.

Groups	Cases	Gender (cases)		Age (years old)	Disease type (cases)	
		Male	Female		Squamous cell carcinoma	Adenocarcinoma
Metastasis group	43	28	15	63.53 ± 8.41	13	30
Non-metastasis group	37	25	12	65.89 ± 9.01	10	27
X^2/t		0.053		1.210	0.100	
p		0.817		0.230	0.752	

2.2.2 Exclusion criteria

(1) Patients with other malignant tumors. (2) Patient was allergic to iodine contrast agents. (3) Patients with serious blood diseases, such as leukemia, lymphoma, and multiple myeloma. (4) Patients with lung disease, including severe lung infection and emphysema. (5) Patients with dysfunction in vital organs such as heart, liver, and kidneys. (6) Patients with mental disorders and poor compliance. (7) Patients with incomplete clinical data.

2.3 Methods

64-slice spiral CT machine from Siemens (Munich, Germany) was used in the two groups. Before the examination, metal objects from the chest were removed, and professional medical staff guided the patients in breathing exercises such as holding their breath or slowing down their breath. During the examination, the patients were placed in a supine position, holding their breath while scanning. Low dose conventional plain scan was performed on the chest to locate the lesion site, and then the perfusion scanning range was determined. The scanning parameters were set to tube current of 345 mA, tube voltage of 130 kV, detector width of 64.00 mm × 0.625 mm, pitch of 1.50, layer thickness of 3.0 mm, reconstructed slice thickness of 3 mm, a cycle of 1 second, scanning field of view of 250 mm, matrix of 512 × 512, and a total scanning time of 30 seconds. Dual-phase CT enhanced scanning of venous phase and arterial phase was performed from thoracic inlet to the lung base. 90 mL of iohexol (Zhejiang Tianrui Pharmacentical Industry Co., Ltd.; National Medical Products Administration (NMPA) approval No.: H20103185; 50 mL:15 g) was injected via the anterior elbow vein at a rate of 3.0 mL/seconds. The scanning parameters of CT enhanced scan were the same as those of the plain scanning. On the basis of plain scanning to determine the location of the lesion, 8 planes above and below the largest diameter of the lesion were selected to implement CT perfusion scanning. 0.5 mL/kg of iohexol was injected via the median elbow vein at a rate of 3.0 mL/seconds, and 20 mL of saline was injected at the same rate. Then single-level dynamic CT scan was performed for 1 second/week at a rate of 4 layers/second, with a scanning interval of 0.8 second, a layer thickness of 5 mm, a delayed start of scanning of 5 seconds, a tube current of 60 mA, and a tube voltage of 120 kV. Image processing: The scan data were analyzed and processed for respiratory motion artifact using body tumor perfusion software to obtain CT perfusion pseudo-color image and to collect bronchial arterial blood flow (BAF) and perfusion index (PI). 64-slice CT dual perfusion parameters and serum VEGF level were collected from both groups and compared with pathological examination results.

2.3.1 Serum indicator testing

In both groups, 5 mL of fasting peripheral venous blood was drawn in the early morning, left to stand at room temperature for 30-60 min. Then the blood was centrifuged at 3000 r/min for 10 min, and the serum was separated and stored at -20 °C for measurement. According to the manual of human VEGF detection kit

(E-EL-H0111c, Elabscience, Houston, TX, USA), the VEGF level was measured using enzyme-linked immunosorbent assay, which was detected by a microplate reader (VLBL0TD2, Thermo Fisher Scientific, Waltham, MA, USA).

2.4 Statistical methods

Statistical analysis was performed using SPSS 20.0, and count data were expressed as cases (%) and compared using X^2 test. Measurement data were expressed as mean ± standard deviation. Comparison between two groups was performed using the independent samples t-test, and the diagnostic value of 64-slice CT dual perfusion parameters combined with serum VEGF was analyzed using the area under the receiver operating characteristic (ROC) curves (AUC). Correlation between 64-slice CT dual perfusion parameters combined with serum VEGF and lymph node metastasis of lung cancer was analyzed by Pearson's method. Difference was considered to be statistically significant at $p < 0.05$.

3 Results

3.1 Comparison of blood flow perfusion parameters and serum VEGF level between the two groups

The bronchial arterial blood flow (BAF) and VEGF levels in metastasis group were significantly higher than those in non-metastasis group ($p < 0.05$), and perfusion index (PI) level in metastasis group was obviously lower than that in non-metastasis group ($p < 0.05$). The results were shown in Table 2.

3.2 ROC analysis of 64-slice CT dual perfusion parameters, serum VEGF, and their combined diagnosis

The AUC values of BAF, PI, VEGF and their combination in the diagnosis of lymph node metastasis in lung cancer were 0.809, 0.794, 0.770 and 0.886, respectively. AUC value of combined detection was higher than that of single detection ($p < 0.05$). The results were exhibited in Table 3.

Table 2 Comparison of blood flow perfusion parameters and serum VEGF level between the two groups (mean ± standard deviation).

Groups	Cases	BAF [mL/(min·100 mL)]	PI	VEGF (pg/mL)
Metastasis group	43	65.23 ± 7.55	0.37 ± 0.05	179.28 ± 14.98
Non-metastasis group	37	55.23 ± 8.00	0.47 ± 0.10	166.29 ± 7.05
t		5.744	5.442	4.829
p		0.000	0.000	0.000

Table 3 Diagnostic value of ROC analysis on various parameters.

Indicators	AUC	Specificity	Sensibility	p	Optimal cutoff value	95% CI
BAF	0.809	0.676	0.744	0.000	61.485	0.714-0.904
PI	0.794	0.676	0.860	0.000	0.415	0.693-0.896
VEGF	0.770	0.676	0.721	0.000	175.920	0.666-0.874
Combined diagnosis	0.886	0.757	0.837	0.000	0.518	0.816-0.956

3.3 Comparison of 64-slice CT dual perfusion parameters and serum VEGF with pathological examination results

36 cases in the metastasis group and 44 cases in the non-metastatic group were detected to be positive for BAF. 49 cases in the metastatic group and 31 cases in the non-metastatic group were determined to be positive for PI. 26 cases in the metastasis group and 54 cases in the non-metastatic group were evaluated to be positive for VEGF. Accuracy rates of BAF, PI and VEGF detection were 36.25%, 46.25%, and 30.00%, respectively. The results were exhibited in Table 4-6.

3.4 Correlation between 64-slice CT dual perfusion parameters and serum VEGF with lymph node metastasis in lung cancer

BAF and VEGF were positively correlated with lymph node metastasis of lung cancer ($\rho < 0.05$), and PI was negatively correlated with lymph node metastasis of lung cancer ($\rho < 0.05$). The results were exhibited in Table 7.

Table 4 Comparison of BAF and pathological examination results (cases).

BAF	Pathological examination results		Total
	Metastasis group	Non-metastatic group	
Metastasis group	29	7	36
Non-metastatic group	14	30	44
Total	43	37	80
Accuracy rates		36.25%	

Table 5 Comparison of PI and pathological examination results (cases).

PI	Pathological examination results		Total
	Metastasis group	Non-metastatic group	
Metastasis group	37	12	49
Non-metastatic group	6	25	31
Total	43	37	80
Accuracy rates		46.25%	

Table 6 Comparison of VEGF and pathological examination results (cases).

VEGF	Pathological examination results		Total
	Metastasis group	Non-metastatic group	
Metastasis group	24	2	26
Non-metastatic group	19	35	54
Total	43	37	80
Accuracy rates		30.00%	

Table 7 Correlation between 64-slice CT dual perfusion parameters and serum VEGF with lymph node metastasis in lung cancer.

Indicators	Lymph node metastasis in lung cancer	
	r	p
BAF	0.655	0.000
PI	-0.555	0.000
VEGF	0.369	0.025

4 Discussion

To improve the accuracy of diagnosing lymph node metastasis of lung cancer, this article explored the diagnostic efficacy of 64-slice CT dual perfusion parameters combined with serum VEGF in lymph node metastasis of lung cancer. The results showed that 64-slice CT dual perfusion parameters combined with serum VEGF had good diagnostic value for lymph node metastasis of lung cancer.

BAF and PI are commonly used as indicators to reflect the blood flow status and hemodynamics of the lungs, which are influenced by blood flow, oxygen consumption, and permeability at the lesion site [16-18]. The more severe progression of lung cancer (for example, lymph node metastasis) indicates the higher permeability, which causes an increase in BAF and a decrease in PI [19,20]. Similarly, our data support these findings. Yet, the correlation between 64-slice CT dual perfusion parameters (BAF and PI) and lymph node metastasis of lung cancer is still unclear. In this study, it is an outstanding finding that BAF is positively correlated with lymph node metastasis of lung cancer, while PI was negatively correlated with lymph node metastasis of lung cancer. These evidences suggest that the 64-slice CT dual perfusion parameters of BAF and PI may be served as the diagnostic indicators of lymph node metastasis in lung cancer.

Reportedly, VEGF can be produced by tumor cells and can stimulate the proliferation and migration of vascular endothelial cells, affecting tumor growth and diffusion. The higher level of VEGF suggests a higher risk of lymph node metastasis in lung cancer [21,22]. Similar results are obtained in this study that VEGF level is higher in lung cancer patients with lymph node metastasis than that in lung cancer patients without lymph node metastasis. Moreover, existing report has delineated that the expression of VEGF is significantly related to the lymph node metastasis of lung cancer [12]. Our data reveal that VEGF is positively correlated with lymph node metastasis of lung cancer. Above findings indicate that VEGF may be served as the diagnostic indicator of lymph node metastasis in lung cancer.

As previously mentioned, 64-slice spiral CT can judge the blood supply status of pulmonary bronchial circulation and pulmonary circulation according to the collected data through enhanced scanning of the lesion tissue, analyze the local tissue blood flow perfusion, calculate the average transit time and permeability, and obtain the perfusion parameters of BAF and PI, thereby effectively reflecting the lymph node metastasis [23]. Furthermore, VEGF can promote the generation of lymphatic vessel, inhibit immune cells, enhance local and systemic immune suppression of cancer, and regulate epithelial mesenchymal transformation-mediated growth of tumor cells [24]. Positive VEGF indicates lymph node metastasis, reflects stages and progression of lung cancer to some extent, and provides diagnostic value for lymph node metastasis of lung cancer [25-27], which is consistent with the findings of this study. Combined with these findings, it is indicated that the combination of 64-slice CT dual perfusion parameters and serum VEGF may be used for the diagnosis of lymph node metastasis in lung cancer. In our study, 64-slice CT dual perfusion parameters combined with serum VEGF can effectively analyze the blood flow of the body tissue and lesion site, determine the progression of the disease, and improve the diagnostic efficiency.

On the other hand, pathological examination is one of common methods to diagnose the stage of lung cancer [28]. Yet, compared with the result of pathological examination, the diagnostic accuracies of 64-slice CT dual perfusion parameters and serum VEGF in lymph node metastasis of lung cancer are unclear. Hence, we carried out pathological examination, 64-slice CT

examination, and serum VEGF detection for all patients with suspected lymph node metastasis of lung cancer and compared the diagnostic accuracy of different indicators. It was calculated that the detection accuracy of BAF, PI, and VEGF was high, indicating that they were highly feasible to diagnose lymph node metastasis of lung cancer. Notably, the application value of combined diagnosis was higher than that of a single diagnostic indicator, which reduced the missed diagnosis rate of lymph node metastasis in lung cancer.

However, the research results in this study are not sufficient to represent the situation of all patients due to the limited sample size and review time. The diagnostic value of 64-slice CT dual perfusion parameters combined with serum VEGF still needs further experiments, exploration, and verification to improve relevant theoretical research.

In conclusion, 64-slice CT dual perfusion parameters combined with serum VEGF have good diagnostic value for lymph node metastasis of lung cancer. Also, BAF and VEGF may be positively correlated with lymph node metastasis of lung cancer, while PI is negatively correlated with lymph node metastasis of lung cancer.

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Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization, G.S.; Data curation, H.M.; Formal analysis, G.S.; Methodology, H.M.; Writing-original draft, G.S.; Writing-review and editing, H.M. All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee, and the patients were informed and consented.

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Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

Supplementary Material

Not applicable.

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