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Prognostic Value of Semi-Quantitative 18F-FDG PET/CT Parameters in Hodgkin's Lymphoma

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Abstract: *Objective:* To assess the prognostic value of maximum standardized uptake value (SUV_{max}), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) determined by 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET/CT) imaging in Hodgkin's lymphoma patients. *Methods:* A total of 148 Hodgkin's lymphoma patients diagnosed with lymph node biopsy from October 2014 to October 2015 were retrospectively analyzed followed by categorizing into good (125 cases) and poor (23 cases) prognosis groups. The chi-squared test was used to analyze the clinicopathological characteristics of Hodgkin's lymphoma patients with the semi-quantitative 18F-FDG PET/CT parameters; the Spearman method was used to analyze the correlation between the semi-quantitative parameters and clinicopathological features of Hodgkin's lymphoma; receiver operating characteristic curve was used to analyze the predictive value of the semi-quantitative parameters for poor prognosis of Hodgkin's lymphoma patients. *Results:* Mean SUV_{max}, MTV, and TLG of the 148 cases of Hodgkin's lymphoma were 7.26 ± 2.38, 12.46 ± 3.14 cm^3, and 76.83 ± 18.56 g, respectively. Significant variations in the Ann Arbor stage and clinical classification were observed with different levels of semi-quantitative parameters ($P < 0.05$). The semi-quantitative parameters were not correlated with age and gender ($P > 0.05$) but positively correlated with Ann Arbor stage and clinical classification ($P < 0.05$). These parameters in the poor prognosis group were higher than those in the good prognosis group ($P < 0.05$). The area under the curve (AUC) of SUV_{max}, MTV, and TLG in predicting the poor prognosis group was 0.881, 0.875, and 0.838, with cut-off values of 7.264, 12.898 cm^3, and 74.580g, as well as specificity of 88.8%, 84.0%, and 78.4%, and sensitivity of 87.0%, 87.0%, and 78.3%, respectively; the AUC of the combined prediction was 0.986, with a specificity of 97.6% and sensitivity of 86.3%. *Conclusion:* The semi-quantitative 18F-FDG PET/CT parameters provide valuable insights for Hodgkin's lymphoma prognosis assessment.

Keywords: Hodgkin's lymphoma; 18F-fluorodeoxyglucose positron emission tomography-computed tomography; Maximum standardized uptake value; Metabolic tumor volume; Total lesion glycolysis; Prognosis

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1. Introduction

Lymphoma is primarily classified into Hodgkin's and non-Hodgkin's lymphoma, representing malignant tumors affecting lymph nodes or lymphoid tissue [1]. Hodgkin's lymphoma constitutes a group of severe blood system diseases. Currently, its diagnosis mainly relies on pathological findings, laboratory tests, and imaging studies [2]. While comprehensive treatments, including chemotherapy and radiotherapy, have led to high long-term remission rates for Hodgkin's lymphoma patients, some patients remain susceptible to relapse, eventually resulting in fatal outcomes [3]. Therefore, it is necessary to identify effective indicators and parameters for guiding treatment decisions and determining prognosis.

Among the diagnostic tools available, 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET/CT) imaging stands out as a common molecular functional imaging technique that has been applied in various diseases, including lymphoma. It plays a pivotal role in diagnosing and assessing the prognosis of different malignant tumors and has significant implications for clinical staging [4,5]. The semi-quantitative parameters of 18F-FDG PET/CT imaging lesions mainly encompass maximum standardized uptake value (SUV_{max}), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) [6]. Nevertheless, the current utility of SUV_{max}, MTV, and TLG values obtained through 18F-FDG PET/CT imaging in predicting the prognosis of Hodgkin's lymphoma patients warrants further investigation.

Hence, this study aims to explore the correlation between SUV_{max}, MTV, and TLG values and the clinicopathological characteristics of Hodgkin's lymphoma patients, as well as their predictive value in assessing the prognosis of these patients. The objective is to provide valuable insights into the prediction of Hodgkin's lymphoma patients' prognosis through the development of reliable new metrics.

2. Materials and Methods

2.1. General information

A retrospective analysis of 18F-FDG PET/CT scans was conducted from October 2014 to October 2015. During this period, 148 patients were diagnosed with Hodgkin's lymphoma through PET/CT imaging and lymph node biopsy. These patients had an age range of 19–56 years, with an average age of 44.84 ± 8.72 years. Of the total, 91 were male, and 57 were female.

Inclusion criteria:

(1) Patients who met the diagnostic criteria and were clinically diagnosed with Hodgkin's lymphoma [7].
(2) Patients were newly diagnosed, and their case data were complete.
(3) No radiotherapy or chemotherapy had been administered before the 18F-FDG PET/CT imaging examination.
(4) This study received approval from the hospital's clinical research ethics committee, and all research subjects participated voluntarily.

Exclusion criteria:

(1) Individuals with infectious diseases and other tumors.
(2) The time interval between 18F-FDG PET/CT imaging examination and biopsy exceeded 2 hours.
(3) Pregnant or lactating women.

Patient data were collected and organized, primarily including gender, age, Ann Arbor stage, and clinical classification.

2.2. 18F-FDG PET/CT imaging and image analysis

The VCT64 PET/CT scanner produced by GE Company of the United States was employed for imaging

analysis. The imaging agent, 18F-FDG, was supplied by the PET Center of the Department of Nuclear Medicine at the First Affiliated Hospital of Xinjiang Medical University, with a radiochemical purity exceeding 95%. To prepare for the examination, subjects refrained from eating or drinking for at least 6 hours and ensured fasting blood sugar was below 7.8 mmol/L. 18F-FDG was administered intravenously through the cubital vein based on body weight. Following the injection, patients rested in a dark, warm, and quiet environment for 50 minutes.

A standard PET/CT scan (from the middle of the femur to the top of the skull) was conducted after emptying the bladder. If necessary, lower limbs or sole scans were added. The CT slice thickness was 3.75 mm, with an acquisition voltage of 140 kV. PET imaging was performed in 3D, collecting a total of 5 to 7 beds, with each bed scanned for 3 to 4 minutes. Two experienced imaging physicians jointly analyzed PET/CT images to assess lesion size, location, density, shape, and FDG metabolism. The densest accumulation area among the largest lymph nodes in the body was selected, and an appropriate area of interest was placed to avoid adjacent blood vessels, necrotic areas, and lesion edges, followed by measuring its SUV_{max}, mean standardized uptake value (SUV_{mean}), MTV value, and TLG were calculated using the equation $TLG = SUV_{mean} \times MTV$.

2.3. Treatment and follow-up

All patients underwent 6 courses of first-line BEACOPP regimen (bleomycin + etoposide + doxorubicin/adriamycin + cyclophosphamide + vincristine/oncovin + procarbazine + prednisone) or ABVD regimen (doxorubicin/adriamycin + bleomycin + vinblastine + dacarbazine/DTIC) chemotherapy, and 29 cases received radiotherapy following chemotherapy. Patients with Hodgkin's lymphoma were followed up for 5 years through telephone, home visits, and outpatient visits, with the follow-up period ending in October 2020. Tumor recurrence or death was determined based on imaging examinations, histopathological examinations, and follow-up results. Based on the prognosis, 148 Hodgkin's lymphoma patients were categorized into a good prognosis group (125 cases) and a poor prognosis group (23 cases).

2.4. Statistical analysis

Statistical analysis was performed using SPSS 23.0. Measurement data, following a normal distribution, were expressed as mean ± standard deviation (SD). The *t*-test compared data between two groups. Count data were expressed as [*n* (%)] and compared using the χ^2 test. Spearman's method analyzed the correlation between SUV_{max}, MTV, TLG, and clinical pathological characteristics in Hodgkin's lymphoma patients. Receiver operator characteristic (ROC) curves assessed the predictive value of SUV_{max}, MTV, and TLG for poor prognosis in Hodgkin's lymphoma patients. A *P*-value less than 0.05 indicated statistical significance.

3. Results

3.1. 18F-FDG PET/CT manifestations in patients with Hodgkin's lymphoma

Patients with Hodgkin's lymphoma exhibited increased FDG metabolism in the enlarged lymph nodes at the corresponding site, as shown in **Figure 1**.

3.2. Comparison of clinicopathological characteristics in Hodgkin's lymphoma patients with different SUV_{max}, MTV, and TLG levels

The SUV_{max}, MTV, and TLG of the 148 Hodgkin's lymphoma patients were 7.26 ± 2.38, 12.46 ± 3.14 cm^3, and 76.83 ± 18.56 g, respectively. There were 76 patients with high SUV_{max} levels and 72 patients with low SUV_{max} levels. Additionally, there were 74 patients with high MTV levels and 74 patients with low MTV levels, as well as 73 patients with high TLG levels and 75 patients with low TLG levels. The clinicopathological

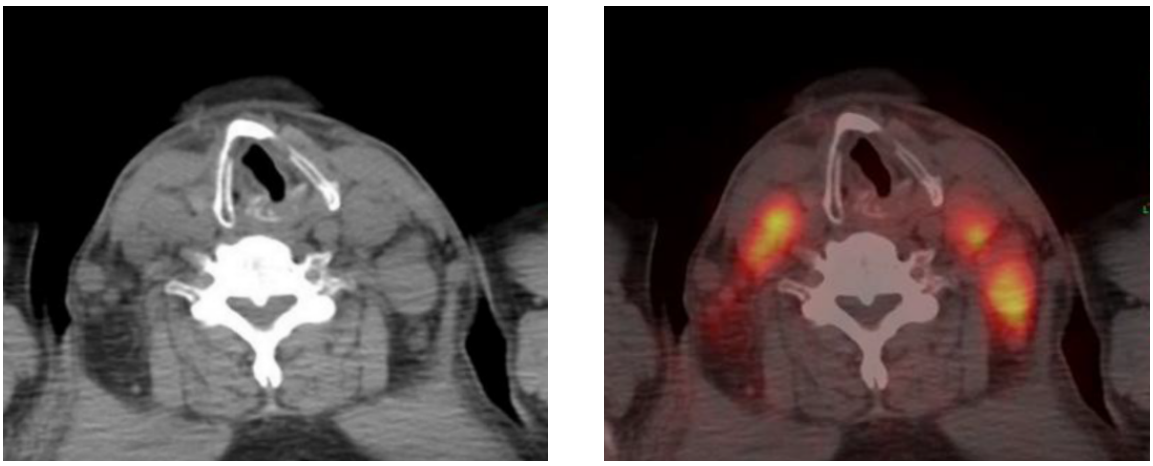

Figure 1. 18F-FDG PET/CT performance of patients with Hodgkin's lymphoma (**left**: CT imaging; **right**: PET imaging)

characteristics of Hodgkin's lymphoma patients with different SUV_{max}, MTV, and TLG levels were analyzed and compared. The results revealed no statistically significant differences in age and gender among Hodgkin's lymphoma patients with varying SUV_{max}, MTV, and TLG levels ($P > 0.05$). However, when comparing Ann Arbor staging and clinical classification of Hodgkin's lymphoma patients with different SUV_{max}, MTV, and TLG levels, statistically significant differences were observed ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of clinicopathological characteristics in Hodgkin's lymphoma patients with different SUV_{max}, MTV, and TLG levels [*n* (%)]

Group	*n*	Age		Gender		Ann Arbor staging		Clinical classification	
		≤ 45 (*n* = 86)	> 45 (*n* = 62)	Male (*n* = 91)	Female (*n* = 57)	I/IIA (*n* = 94)	IIB/IVB (*n* = 54)	Classic type (*n* = 119)	Nodular lymphocyte-predominant type (*n* = 29)
SUV_{max} high level	76	48 (63.16)	28 (36.84)	50 (65.79)	26 (34.21)	28 (36.84)	48 (63.16)	70 (92.11)	6 (7.89)
SUV_{max} low level	72	38 (52.78)	34 (47.22)	41 (56.94)	31 (43.06)	66 (91.67)	6 (8.33)	49 (68.06)	23 (31.94)
χ^2	-	1.637		1.221		47.955		13.573	
P	-	0.201		0.269		0.000		0.000	
MTV high level	74	44 (59.46)	30 (40.54)	45 (60.81)	29 (39.19)	28 (37.84)	46 (62.16)	68 (91.89)	6 (8.11)
MTV low level	74	42 (56.76)	32 (43.24)	46 (62.16)	28 (37.84)	66 (89.19)	8 (10.81)	51 (68.92)	23 (31.08)
χ^2	-	0.111		0.029		42.102		12.394	
P	-	0.739		0.866		0.000		0.000	
TLG high level	73	45 (61.64)	28 (38.36)	41 (56.16)	32 (43.94)	26 (35.62)	47 (64.38)	69 (94.52)	4 (5.48)
TLG low level	75	41 (54.67)	34 (45.33)	50 (66.67)	25 (33.33)	68 (90.67)	7 (9.33)	50 (66.67)	25(33.33)
χ^2	-	0.740		1.723		48.377		18.217	
P	-	0.390		0.189		0.000		0.000	

3.3. Correlation between SUV_{max}, MTV, TLG, and clinicopathological characteristics in Hodgkin's lymphoma patients

Analysis using the Spearman method (**Table 2**) indicated that SUV_{max}, MTV, and TLG had no correlation with age and gender ($P > 0.05$), but were positively correlated with Ann Arbor stage and clinical classification ($P < 0.05$).

Table 2. Correlation between SUV_{max}, MTV, TLG, and clinicopathological characteristics in Hodgkin's lymphoma patients

Index		Age	Gender	Ann Arbor staging	Clinical classification
SUV_{max}	*r*	0.105	0.091	0.569	0.303
	P	0.203	0.272	0.000	0.000
MTV	*r*	0.027	0.014	0.533	0.289
	P	0.741	0.867	0.000	0.000
TLG	*r*	0.071	0.108	0.572	0.351
	P	0.393	0.192	0.000	0.000

3.4. Comparison of SUV_{max}, MTV, and TLG values in different prognostic groups of Hodgkin's lymphoma

Table 3 shows that SUV_{max}, MTV, and TLG values in the poor prognosis group were significantly higher than those in the good prognosis group ($P < 0.05$).

Table 3. Comparison of SUV_{max}, MTV, and TLG values in different prognostic groups of Hodgkin's lymphoma (mean ± SD)

Group	Number of examples	SUV_{max}	MTV (cm^3)	TLG (g)
Good prognosis group	125	6.24 ± 1.28	9.78 ± 2.82	60.22 ± 19.75
Poor prognosis group	23	8.05 ± 1.63	14.97 ± 4.71	92.54 ± 23.68
t		5.960	7.199	6.986
P		0.000	0.000	0.000

3.5. Predictive value of SUV_{max}, MTV, and TLG for poor prognosis in Hodgkin's lymphoma patients

ROC curves were plotted using SUV_{max}, MTV, and TLG as test variables for Hodgkin's lymphoma patients (**Figure 2**). The results indicated that SUV_{max}, MTV, and TLG had an area under the curve (AUC) of 0.881 (95% CI: 0.778–0.985), 0.875 (95% CI: 0.791–0.959), and 0.838 (95% CI: 0.743–0.933), respectively. The null hypothesis (AUC = 0.5) was rejected with a significance level of $P = 0.000$. The cutoff values of SUV_{max}, MTV, and TLG were 7.264, 12.898 cm^3, and 74.580 g, with specificities of 88.8%, 84.0%, and 78.4%, and sensitivities of 87.0%, 87.0%, and 78.3%, respectively. When the three variables were combined, the AUC reached 0.986 (95% CI: 0.965–1.000), with a specificity of 97.6% and a sensitivity of 86.3%.

4. Discussions

Hodgkin's lymphoma is characterized by atypical cell morphology in the bone marrow and lymph nodes, typically manifesting as painless lymphadenopathy [8]. It frequently occurs in cervical and mediastinal lymph nodes and can extend to other regional lymph nodes. In advanced stages, it may affect the liver, bone marrow, spleen, and more [9]. While advancements in diagnostic and treatment technologies, including targeted therapies, new chemotherapy drugs, radiotherapy, and liver cell transplantation, have significantly improved the 5-year survival rate of Hodgkin's lymphoma patients, some individuals still face poor prognoses [10]. Therefore, accurately assessing prognosis, developing personalized treatment plans, and reducing treatment risks remain

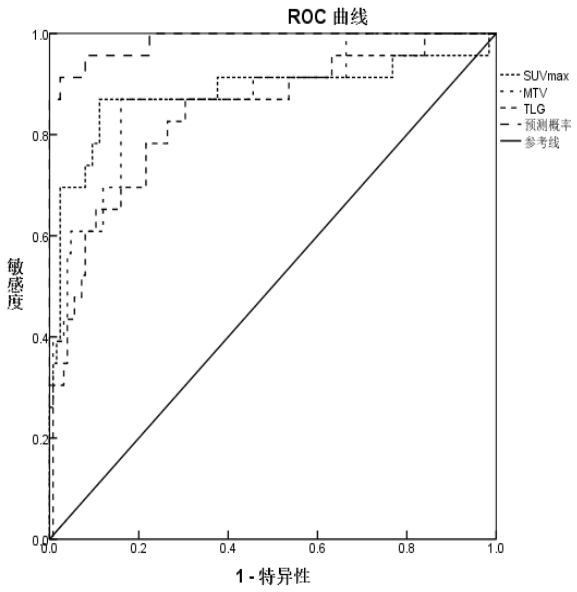

Figure 2. Predictive value of SUV_{max}, MTV, and TLG for poor prognosis in Hodgkin's lymphoma patients

challenges in Hodgkin's lymphoma diagnosis and treatment.

In comparison to traditional imaging methods, PET/CT is a cutting-edge molecular imaging technology that combines anatomy and function. During the examination, CT offers structural and anatomical information about lesions, while PET provides details about their metabolic and functional characteristics. These aspects complement each other [11]. The commonly used glucose metabolism imaging agent, 18F-FDG, leverages variations in glucose metabolism levels between normal and tumor cells. Tumor cells, being more metabolically active, accumulate larger amounts of 18-FDG. PET/CT scans provide clear visualization of tumor location, size, shape, and radioactive distribution [12,13]. Research has shown that SUV_{max}, a metabolic parameter derived from PET/CT imaging, can indirectly indicate tumor cell proliferation based on FDG metabolism levels. MTV represents the tumor volume with higher glucose metabolism, and TLG reflects the tumor load [14].

In this study, SUV_{max}, MTV, and TLG were all significantly correlated with the Ann Arbor stage and clinical classification of Hodgkin's lymphoma. These findings suggest that higher levels of FDG metabolism and tumor cell volume correspond to increased tumor cell proliferation activity, resulting in accelerated growth and a higher likelihood of distant metastasis. This is consistent with the study by Li *et al*. [15], which found similar relationships between these parameters and pathological features such as the Ann Arbor stage and maximum length diameter of primary mediastinal large B-cell lymphoma. Moreover, the results of this study indicated that patients with poor prognosis in Hodgkin's lymphoma tend to exhibit higher levels of SUV_{max}, MTV, and TLG. This reinforces the notion that elevated SUV_{max}, MTV, and TLG correspond to accelerated sugar metabolism, cell division, and an increased degree of malignancy, all of which are unfavorable for patient prognosis. This study further shows that all three parameters detected by 18F-FDG PET/CT imaging hold predictive value for the prognosis of Hodgkin's lymphoma, with SUV_{max} exhibiting the highest predictive value (AUC = 0.881). Notably, combining all three parameters significantly improves specificity.

Wang *et al*. similarly emphasized the importance of 18F-FDG PET/CT in evaluating and predicting the prognosis of Hodgkin's lymphoma patients before autologous stem cell transplantation [16], aligning with

the findings of this study. This suggests that SUV_{max}, MTV, and TLG can be used collectively as reference indicators to predict the poor prognosis of Hodgkin's lymphoma patients. When clinical 18F-FDG PET/CT imaging reveals $SUV_{max} > 7.264$, MTV > 12.898 cm^3, and TLG > 74.580 g, it may indicate a poor prognosis for the patient.

In conclusion, the semi-quantitative parameters, SUV_{max}, MTV, and TLG, derived from 18F-FDG PET/CT imaging, exhibit significant correlations with Ann Arbor staging and clinical classification in Hodgkin's lymphoma patients. Elevated SUV_{max}, MTV, and TLG values are associated with poor prognosis. These parameters hold promise for predicting and evaluating the prognosis of Hodgkin's lymphoma patients. Clinically, they can serve as valuable reference indicators for identifying patients at risk of a poor prognosis. However, it is important to note that this study is retrospective and based on a relatively small number of cases. Additionally, the application of 18F-FDG PET/CT in Hodgkin's lymphoma may have certain limitations due to inconsistent evaluation standards, thus necessitating further research to determine its clinical value.

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Disclosure statement

The authors declare no conflict of interest.

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