Original Article

Prognostic value of ^{18}F-FDG PET/CT tumor metabolic parameters and Ki-67 in pre-treatment diffuse large B-cell lymphoma

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Background: Diffuse large B-cell lymphoma (DLBCL) is a highly aggressive lymphoma. Rituximab-based conventional chemotherapy still leads to drug resistance or relapse in 30–40% of patients. Therefore, early identification of high-risk patients and accurate assessment of prognosis are very important for clinical decision-making. The aim of this study is to investigate the value of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) of tumor metabolic, clinical and biological parameters in the prognostic risk stratification of DLBCL before treatment.

Methods: We retrospectively collected clinical data on 63 patients with newly diagnosed DLBCL admitted to Shanxi Bethune Hospital during the period from November 2016 to April 2020 who underwent ^{18}F-FDG PET/CT prior to treatment in a cohort study. Metabolic, clinical, and biological parameters were analyzed by Cox regression. Kaplan-Meier curves of patient survival were compared by the log-rank test.

Results: The median follow-up was 21 months. The 2-year progression-free survival (PFS) was 47.62%, and the overall survival (OS) was 53.97%. The subtype, double expression, Ann Abor stage, NCCN-IPI score, Ki-67, maximum standardized uptake value (SUV_{max}), bulk volume glycolysis (BVG), total lesion glycolysis (TLG), total metabolic tumor volume (TMTV) were the influencing factors for PFS and OS (P<0.050) in univariate analysis. BVG (PFS: HR =6.62, P<0.001; OS: HR =3.53, P=0.029), TLG (PFS: HR =8.56, P<0.001; OS: HR =5.20, P=0.004), TMTV (PFS: HR =12.02, P=0.001; OS: HR =5.05, P=0.033) and Ki-67 were found to be independent prognostic risk stratification parameters affecting PFS and OS by multivariate regression analysis. The 2-year PFS and OS rates for patients with high BVG (≥288.00 cm^3), TLG (≥1,854.00 cm^3), TMTV (≥103.00 cm^3), and Ki-67 (≥85%) were 20% and 28.57%, 9.68% and 22.58%, 20.51%, and 30.77%, and 25% and 33.33%, respectively; and the 2-year PFS and OS rates for patients with low BVG (<288.00 cm^3), TLG (<1,854.00 cm^3), TMTV (<103.00 cm^3), and Ki-67 (<85%) patients were 82.14% and 85.71%, 84.37% and 84.37%, 91.67% and 91.67%, and 61.54% and 66.67%, respectively. Patients with high BVG, TLG, TMTV, and Ki-67 had a worse 2-year PFS as well as OS rate (Ki-67: P=0.0018/P=0.0025; P<0.0001 for the rest of the groups).

Conclusions: Our findings suggest that BVG, TLG, TMTV, and Ki-67 are independent prognostic indicators for survival in patients with pre-treatment DLBCL, especially BVG, which is a novel prognostic indicator that has to be validated in future research.

Keywords: Diffuse large B-cell lymphoma (DLBCL); ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT); prognosis

Submitted May 19, 2023. Accepted for publication Oct 19, 2023. Published online Nov 30, 2023.
doi: 10.21037/qims-23-702
View this article at: https://dx.doi.org/10.21037/qims-23-702

Introduction

Diffuse large B-cell lymphoma (DLBCL) is a prevalent lymphoma, contributing to about one-third of non-Hodgkin's lymphomas (NHL) (1). Although the combination of rituximab (R) and cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) in the chemotherapy regimen of diffuse large B patients have increased patient curability (2), drug resistance or relapse still occurs in about 30–40% of patients (3). Therefore, the prognosis should be accurately evaluated before conventional treatment, and the high-risk patients should be identified early. It is of great value in determining clinical treatment options.

The international prognostic index (IPI) (4), the subsequent revision of IPI (5), and the emergence of National Comprehensive Cancer Network IPI (NCCN-IPI) (6) in recent years have provided risk stratification for NHL. However, adverse outcomes have yet to be found in a sufficient number of patients (7). Other prognostic factors, such as the germinal center B-cell (GCB) and non-GCB (8) or dual expression (DE) of MYC and BCL2 (9,10) and Ki-67 (11), have been recently identified, but their value in guiding treatment decisions is still debatable. Therefore, new strategies are urgently needed to better evaluate the prognosis of DLBCL.

^{18}F-deoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) has become a routine tool for staging, restaging, and monitoring the development of lymphomas (12,13). In recent years, the value of PET/CT metabolic indicators in predicting the risk of lymphoma has attracted a growing amount of attention due to advancements in software programs and image-processing techniques. The metabolic parameters of maximum standardized uptake value (SUV_{max}), total metabolic tumor volume (TMTV) and total lesion glycolysis (TLG) are increasingly being used in tumor prognostic studies (14,15). However, metabolic parameters as pre-treatment predictors in DLBCL are less well studied, and their results are inconsistent (16-20). Consequently, additional studies are required to assess the predictive value of PET/CT metabolic parameters for risk stratification of pre-treatment DLBCL.

Lymphomatous lesions greater than 6 to 10 cm have been regarded as worse prognostic factors (21,22), but their value in DLBCL remains uncertain. It has been reported that 3D measurement of the metabolic bulk volume (MBV) in ^{18}F-FDG PET/CT may be associated with poor prognosis (23). However, bulk volume glycolysis (BVG), which combines the volume and metabolic parameters of the largest lesion on PET/CT images is more representative of or close to the actual tumor burden. Yet, it has not been researched to the best of our knowledge.

The purpose of this study is to investigate the prognostic value of ^{18}F-FDG PET/CT of tumor metabolic, clinical, and biological parameters in pre-treatment DLBCL. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-702/rc).

Methods

Patients

We retrospectively analyzed 63 patients with DLBCL admitted to Shanxi Bethune Hospital during the period from November 2016 to April 2020 in a cohort study. Inclusion criteria were: (I) newly diagnosed adult DLBCL; (II) PET/CT examination prior to the therapy; and (III) R-CHOP and similar therapeutic regimens; exclusion criteria were: patients with central nerve lymphoma or secondary tumors, history of surgery, chemotherapy, radiotherapy, or incomplete follow-up or therapy (*Figure 1*). The following indicators were collected from medical records: age, gender, NCCN-IPI level, Ann Abor stage, DLBCL subtypes (GCB and non-GCB) (24), DE of BCL2 and MYC protein, and Ki-67. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Shanxi Bethune Hospital (No. YXLL-2022-146) and

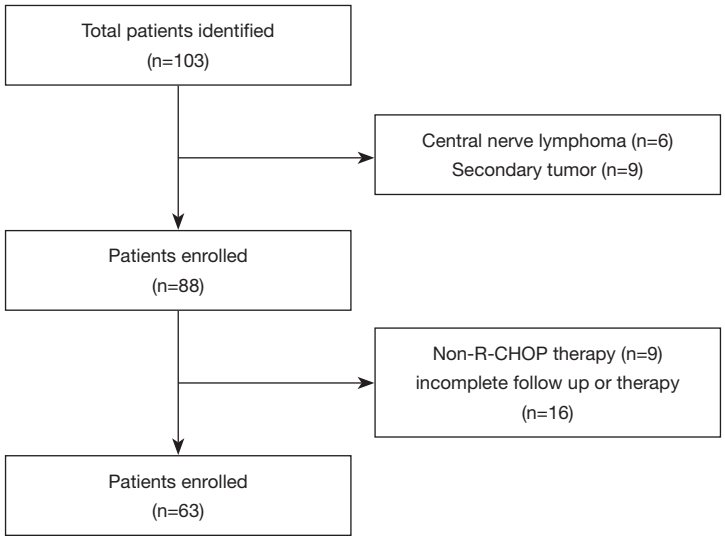

Figure 1 Flow chart of patient selection.

informed consent was taken from all the patients.

Image acquisition and analysis

All images were acquired using a PET/CT scanner [Discovery VCT 64 (GE Healthcare, Milwaukee, Wisconsin, USA)]. Patients were required to fast for at least 6 h and have a blood glucose level of less than 200 mg/dL prior to drug injection. After intravenous ^{18}F-FDG (4.44 MBq/kg), patients were instructed to rest for 50–60 min before the examination. PET reconstructed images based on CT attenuation correction and ordered subset expectation maximum (OSEM) algorithm.

On an advanced workstation (GE ADW 4.6), CT and PET images were displayed independently and in infusion mode in axial, coronal, and sagittal planes. Abnormal lesions were determined by consensus between two experienced nuclear medicine physicians who were blinded to patient outcomes. PET/CT tumor metabolic parameters were calculated using PETVCAR software (GE ADW 4.6). The boundaries of the tumor were automatically generated using the 41% threshold recommended by the European Association of Nuclear Medicine (25). SUV_{max} and MTV were calculated using the software. BVG was defined as the metabolic value of the lesion with the largest volume on ^{18}F-FDG PET/CT (MTV × SUV_{mean} of the largest lesion). TLG was the sum of MTV × SUV_{mean} of all lesions.

Statistical analysis

All statistical analyses were performed using Statistical Package for the Social Sciences Version 26.0 software (SPSS Inc., Chicago, IL, USA) and R 4.0.5 software. The definition of progression-free survival (PFS) was the time between the date of diagnosis and the first relapse, progression, mortality from any cause, or the date of the last follow-up. Overall survival (OS) was defined as the duration between the date of diagnosis and the date of mortality from any cause or last follow-up. Optimal cut off values for SUV_{max}, BVG, TMTV, TLG, and Ki-67 were sought and evaluated by receiver operating characteristic (ROC) curves. PET metabolic, clinical, and biological parameters that significantly affected prognosis in the univariate regression statistical analysis were subsequently included in the multivariate statistical analysis. The Kaplan-Meier survival curve evaluated the survival status of patients, and the comparison between groups was performed by log-rank test. $P<0.05$ was considered statistically significant.

Results

Patient characteristics

The clinical, biological, and metabolic parameters of the 63 enrolled participants (24 women and 39 men) are summarized in *Table 1*. The median age of the participants

Table 1 Patient characteristics

Characteristic	Value (n=63)
Age (years)	
Mean (SD)	62.86 (13.75)
Median (P_{25}, P_{75})	66.00 (55.00, 71.00)
>60, n (%)	40 (63.49)
≤60, n (%)	23 (36.51)
Sex, n (%)	
Male	39 (61.90)
Female	24 (38.10)
Subtype, n (%)	
GCB	20 (31.75)
Non-GCB	43 (68.25)
Double expression, n (%)	
Yes	25 (39.68)
No	38 (58.73)
Ann-Abor stage, n (%)	
I–II	22 (34.92)
III–IV	41 (65.08)
NCCN-IPI score, n (%)	
0–3	24 (38.10)
≥4	39 (61.90)
SUVmax (g/mL)	
Mean (SD)	23.51 (11.32)
Median (P_{25}, P_{75})	23.25 (14.28, 32.40)
BVG (cm^3)	
Mean (SD)	1,683.57 (2,611.56)
Median (P_{25}, P_{75})	392.00 (64.00, 1,718.00)
TLG (cm^3)	
Mean (SD)	3,888.76 (4,753.77)
Median (P_{25}, P_{75})	1,749.00 (168.00, 7,658.00)
TMTV (cm^3)	
Mean (SD)	376.48 (577.17)
Median (P_{25}, P_{75})	152.00 (17.00, 470.00)
Ki-67 (%)	
Mean (SD)	74.68 (15.73)
Median (P_{25}, P_{75})	80.00 (60.00, 90.00)

GCB, germinal center B-cell; SD, standard deviation; NCCN-IPI, National Comprehensive Cancer Network International Prognostic Index; SUVmax, standardized maximum uptake value; BVG, bulk volume glycolysis; TLG, total lesion glycolysis; TMTV, total tumor metabolic volume.

was 66 years (range, 28–87 years). At a median follow-up of 21 months (range, 3–87 months), 33 patients experienced disease progression, and 29 died. The 2-year PFS and OS were 47.62% and 53.97%, respectively.

ROC analysis

The best cut-off values of SUVmax, BVG, TMTV, TLG, and Ki-67 for PFS were 19.41 g/mL, 288.00 cm^3, 103.00 cm^3, 1,854.00 cm^3, and 85%, respectively, based on the analysis of the ROC curves. For clinicians, the OS of a patient is more important, and hence the OS cut-off values were selected for subsequent analysis (Table S1).

Univariate and multivariate analyses of prognostic risk factors

Univariate analysis showed that double expression subtype, NCCN-IPI score, Ann-Abor stage, Ki-67, SUV_{max}, BVG, TLG, and TMTV were predictive factors for PFS and OS (P<0.05) (*Table 2*). Statistical analysis of Spearman's rank correlation showed that BVG, TLG, and TMTV were correlated with each other (P<0.001) (Table S2). Therefore, the univariate significant SUV_{max}, BVG, TLG, and TMTV were analyzed separately using multivariate Cox regression analysis (*Table 3*). The results revealed that BVG (PFS: HR =6.62, 95% CI: 2.50–17.56, P<0.001; OS: HR =3.53, 95% CI: 1.13–11.01, P=0.029), TLG (PFS: HR =8.56, 95% CI: 3.18–23.03, P<0.001; OS: HR =5.20, 95% CI: 1.71–15.76, P=0.004), TMTV (PFS: HR =12.02, 95% CI: 2.72–53.13, P=0.001; OS: HR =5.05, 95% CI: 1.14–22.40, P=0.033) and Ki-67 were found to be independent prognostic risk stratification parameters affecting PFS and OS by multivariate regression analysis.

Survival status analysis

The optimal cut-off values of BVG, TLG, TMTV, and Ki-67 were analyzed by Kaplan-Meier curves and compared using log-rank tests. The 2-year PFS and OS rates for patients with high BVG (≥288.00 cm^3, n=35) were 20% and 28.57%, respectively, compared with low BVG (<288.00 cm^3, n=28) 82.14% and 85.71% (c^2=25.3/c^2=22.7, both P<0.0001). The 2-year PFS and OS rates for patients with high TLG (≥1,854.00 cm^3, n=31) were 9.68% and 22.58%, respectively, compared with 84.37% and 84.37% for low TLG (<1,854.00 cm^3, n=32) (c^2=45.2/c^2=30.0, both P<0.0001). The 2-year PFS and OS rates for patients with

Table 2 Univariate Cox proportional hazard regression analysis

Characteristic	N	PFS		OS	
		HR (95% CI)	P value	HR (95% CI)	P value
Age (≤60/>60 years)	23/40	2.64 (1.14–6.08)	0.023	2.12 (0.90–4.97)	0.085
Sex (male/female)	39/24	1.04 (0.51–2.11)	0.924	1.23 (0.59–2.58)	0.582
Subtype (non-GCB/GCB)	43/20	0.21 (0.08–0.61)	0.004	0.25 (0.09-0.73)	0.011
Double expression (no/yes)	38/25	2.70 (1.35–5.38)	0.005	2.85 (1.36–5.96)	0.005
Ann Abor stage (I–II/III–IV)	22/41	8.72 (2.65–28.68)	<0.001	10.20 (2.42–42.98)	0.002
NCCN-IPI score (0–3/≥4)	24/39	9.68 (2.94–31.90)	<0.001	29.18 (3.94–216.24)	0.001
Ki-67 (<85%/≥85%)	39/24	2.83 (1.42–5.64)	0.003	2.96 (1.42–6.18)	0.004
SUVmax (<19.41/≥19.41 g/mL)	23/40	2.43 (1.09–5.39)	0.030	3.32 (1.34–8.22)	0.009
BVG (<288.00/≥288.00 cm^3)	28/35	8.03 (3.07–21.04)	<0.001	8.96 (3.06–26.22)	<0.001
TLG (<1,854.00/≥1,854.00 cm^3)	32/31	13.96 (5.26–37.00)	<0.001	10.32 (3.79–28.14)	<0.001
TMTV (<103.00/≥103.00 cm^3)	24/39	18.23 (4.33–76.83)	<0.001	14.49 (3.40–61.69)	<0.001

PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; GCB, germinal centre B cells; Double expression, dual expression of MYC and BCL2; NCCN-IPI, National Comprehensive Cancer Network International Prognostic Index; SUVmax, maximum standardised uptake value; BVG, metabolic volume; TLG, total lesion glycation; TMTV, total metabolic tumor volume.

high TMTV (≥103.00 cm^3, n=39) were 20.51% and 30.77%, respectively, compared with low TMTV (<103.00 cm^3, n=24), 91.67% and 91.67% (c^2=29.6/c^2=25.1, both P<0.0001). The 2-year PFS and OS rates for patients with high Ki-67 (≥85%, n=24) were 25% and 33.33%, respectively, compared with patients with low Ki-67 (<85%, n=39) were 61.54% and 66.67% (c^2=9.7/c^2=9.2, P=0.0018, P=0.0025, *Figure 2*).

Discussion

In this study, we focused on the prognostic value of PET/CT-derived tumor metabolic, clinical, and biological parameters in risk stratification of DLBCL before treatment. We found that BVG, TLG, TMTV, and Ki-67 were found to be independent prognostic risk stratification parameters affecting PFS and OS. To the best of our knowledge, the predictive value of BVG has not been investigated, and these indicators can help clinicians identify high-risk patients early, which is very important for clinical treatment decision-making.

The maximum transverse diameter (MTD) of the largest lesion is considered to be a factor of poor prognosis (21,22,26). However, MTD is a single-dimensional measure, and the MTD cutoff range of 6 to 10 cm in previous studies does not completely represent the tumor burden of the largest lesion, so the results are debatable (16,23,27). In this study, we attempted to incorporate the BVG of the largest lesion, which combines the three-dimensional measured volume of the largest lesion with metabolic values and more accurately reflects the tumor load of large lesions. The present study showed that BVG were found to be independent prognostic risk stratification parameters affecting PFS and OS. Elevated levels of BVG (≥288.00 cm^3) correlated with a poorer prognosis and were more difficult to treat compared with low BVG (<288.00 cm^3). The relationship between chemotherapy outcomes and pretreatment tumor volume in patients with DLBCL was investigated by Tout *et al.* (28). They found that as tumor volume increased, it increased the difficulty in chemotherapeutic drug penetration, which may have contributed to the poor prognosis observed in this study.

SUV_{max} is a widely used metabolic index to reflect tumor invasiveness. Wu *et al.* discovered that SUV_{max} could be used to guide DLBCL risk stratification (29), whereas Xie *et al.* rejected this claim (30). In our study, TLG and TMTV but not SUV_{max} were found to be independent prognostic risk stratification parameters affecting PFS and OS; patients with high TLG (≥1,854.00 cm^3) and high TMTV (≥103.00 cm^3) had a poorer prognosis than those with low TLG and low TMTV. This result is consistent with the findings of prior research (31,32). Jiang *et al.* discovered that TLG ≥1,852 cm^3 was associated with an adverse prognosis (8,33), and our

Table 3 Multivariate Cox proportional hazard regression analysis

Characteristic	N	PFS		OS	
		HR (95% CI)	P value	HR (95% CI)	P value
Model 1					
SUVmax (<19.41/≥19.41 g/mL)	23/40	0.82 (0.30–2.22)	0.693	1.58 (0.56–4.46)	0.392
NCCN-IPI score (0–3/≥4)	24/39	4.77 (1.36–16.65)	0.014	18.97 (2.48–145.40)	0.005
Ki-67 (<85%/≥85%)	39/24	2.81 (1.39–5.66)	0.004	3.71 (1.72–8.03)	0.001
Ann-Abor stage (I–II/III–IV)	22/41	3.84 (1.01–13.35)	0.035	–	–
Model 2					
BVG (<288.00/≥288.00 cm^3)	28/35	6.62 (2.50–17.56)	<0.001	3.53 (1.13–11.01)	0.029
NCCN-IPI score (0–3/≥4)	24/39	–	–	9.25 (1.10–77.74)	0.040
Ki-67 (<85%/≥85%)	39/24	2.57 (1.27–5.20)	0.008	3.45 (1.56–7.63)	0.0002
Ann-Abor stage (I–II/III–IV)	22/41	6.50 (1.96–21.53)	0.002	–	–
Subtype (non-GCB/GCB)	43/20	–	–	3.27 (1.01–10.45)	0.046
Model 3					
TLG (<1,854.00/≥1,854.00 cm^3)	32/31	8.56 (3.18–23.03)	<0.001	5.20 (1.71–15.76)	0.004
NCCN-IPI score (0–3/≥4)	24/39	–	–	12.53 (1.63–96.39)	0.015
Ki-67 (<85%/≥85%)	39/24	2.13 (1.05–4.33)	0.036	3.39 (1.56–7.39)	0.002
Ann-Abor stage (I–II/III–IV)	22/41	4.80 (1.42–16.21)	0.012	4.38 (1.02–18.86)	0.047
Model 4					
TMTV (<103.00/≥103.00 cm^3)	24/39	12.02 (2.72–53.13)	0.001	5.05 (1.14–22.40)	0.033
NCCN-IPI score (0–3/≥4)	24/39	–	–	12.16 (1.57–94.01)	0.017
Ki-67 (<85%/≥85%)	39/24	3.11 (1.53–6.32)	0.002	4.18 (1.89–9.27)	<0.001
Subtype (non-GCB/GCB)	43/20	–	–	3.77 (1.15–12.36)	0.029

Model 1 included age, subtype, double expression, Ann Abor stage, NCCN-IPI score, Ki-67 and SUVmax; Model 2 included age, subtype, double expression, Ann Abor stage, NCCN-IPI score, Ki-67 and BVG; Model 3 included age, subtype, double expression, Ann Abor stage, NCCN-IPI score, Ki-67 and TLG; Model 4 included age, subtype, double expression, Ann Abor stage, NCCN-IPI score, Ki-67 and TMTV. – indicates that the indicator did not enter the model. PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; SUVmax, standardized maximum uptake value; NCCN-IPI, National Comprehensive Cancer Network international prognostic index; BVG, bulk volume glycolysis; GCB, germinal center B-cell; TLG, total lesion glycolysis, TMTV, total metabolic tumor volume.

study had a similar cut-off value for TLG (≥1,854.00 cm^3). However, previous studies only included one of these, and did not consider the correlation between TLG and TMTV (8,33). The advantage of this study is that multivariate regression model was developed separately for each of the associated indicators, and the indicator correction was more comprehensive at the level of available data. TMTV and TLG reflect the total body tumor load from a three-dimensional perspective, whereas SUV_{max} only reflects the highest metabolic pixel value in the tumor, therefore, TMTV and TLG can be more effective indicators for prognostic assessment in DLBCL.

Ki-67 is a pathologic indicator of cell proliferation, and studies on its prognostic stratification value have been divergent in recent years (34); Huber *et al.* retrospectively analyzed 58 cases of DLBCL, and they found that OS was significantly worse in those with high Ki-67 (>70%) than low Ki-67 (≤70%), but PFS was not significantly different (11). Gaudio *et al.* found that Ki-67 expression was more than 80% correlated with OS and PFS (35).

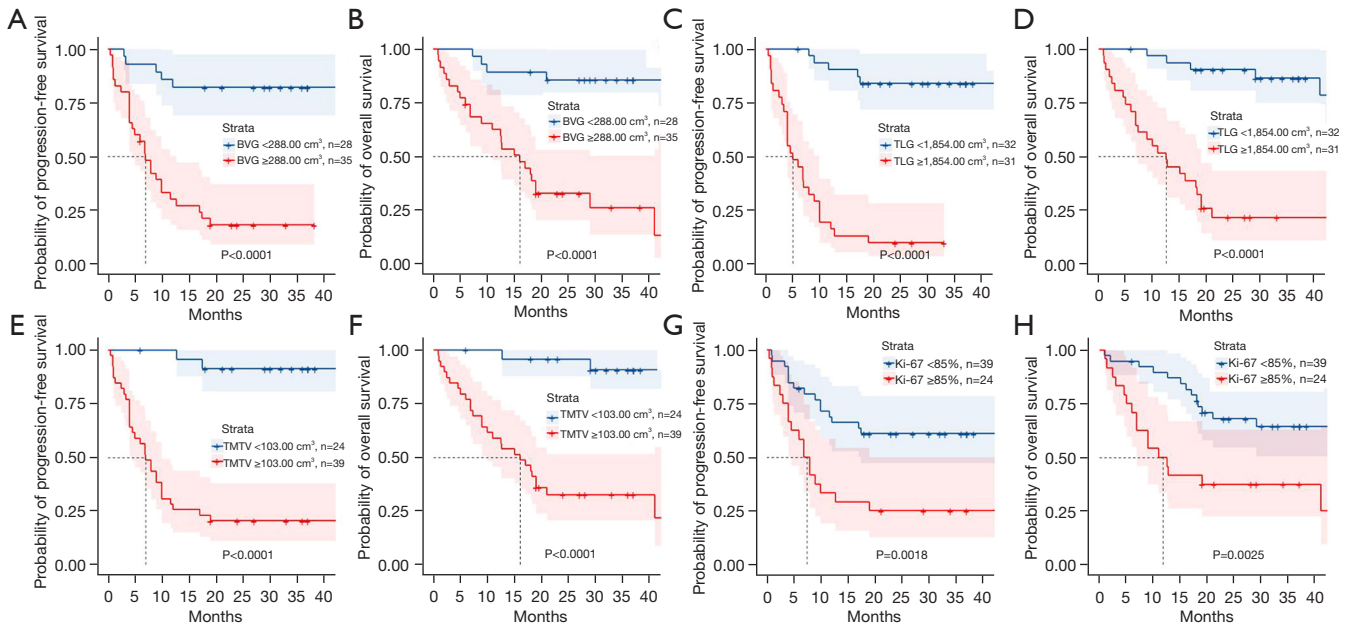

Figure 2 Kaplan-Meier curves for PFS and OS based on BVG, TLG, TMTV and Ki-67 in all patients. (A) PFS in relation to BVG; (B) OS in relation to BVG; (C) PFS in relation to TLG; (D) OS in relation to TLG; (E) PFS in relation to TMTV; (F) OS in relation to TMTV; (G) PFS in relation to Ki-67; (H) OS in relation to Ki-67. PFS, progression-free survival; OS, overall survival; BVG, bulk volume glycolysis; TLG, total lesion glycolysis; TMTV, total metabolic tumor volume.

In accordance with the findings of Gaudio *et al.* (35) our findings indicated that Ki-67 was an independent prognostic risk stratification indicator affecting PFS and OS. However, the cut-off values were marginally different, and we found that patients in the Ki-67 (≥85%) group had worse 2-year PFS as well as OS than those in Ki-67 (<85%) group.

Some studies have reported separately that other clinical and biological parameters such as IPI score ≥4, non-GCB cell origin subtype, and dual MYC and BCL2 protein expression are likely correlated with worse survival outcomes (11,36); but the results of this study found that they were associated with PFS and OS in a univariate regression analysis, and a multifactorial regression analysis did not demonstrate independent prognostic value; thus, further studies with larger groups are warranted.

The limitations of this study stem from its retrospective nature, the need to expand the sample size, and the lack of standardization of thresholds for describing tumors, which may have contributed to inconsistent results. We used the criteria recommended by the European Association of Nuclear Medicine as there was better inter-observer agreement (25).

Conclusions

Our study demonstrates that the PET/CT tumor metabolic parameters BVG, TLG, TMTV, and Ki-67 are independent prognostic risk stratification indicators affecting PFS and OS. These indicators can help clinicians identify high-risk patients early and guide intensive treatment and clinical trials. In particular, BVG, a novel prognostic indicator, requires confirmation through prospective studies.

Acknowledgments

We would like to acknowledge the hard and dedicated work of all the staff that implemented the intervention and evaluation components of the study.

Funding: This work was supported by the Shanxi Provincial External Expert Studio.

Footnote

Reporting Checklist: The authors have completed the

STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-23-702/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-702/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Shanxi Bethune Hospital (No. YXLL-2022-146) and informed consent was taken from all the patients.

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Cite this article as: Geng H, Lian K, Zhang W. Prognostic value of ^{18}F-FDG PET/CT tumor metabolic parameters and Ki-67 in pre-treatment diffuse large B-cell lymphoma. Quant Imaging Med Surg 2024;14(1):325-334. doi: 10.21037/qims-23-702

Supplementary

Table S1 Cut-off value by ROC analysis

Characteristic	AUC	Cut-off value	Sensitivity, %	Specificity, %	N > cut-off value
Ki-67 (%)	0.740	85	55.17	76.47	24 (38.10)
SUVmax (g/mL)	0.726	19.41	79.31	50.00	40 (63.49)
BVG (cm^3)	0.965	288.00	86.21	70.59	35 (55.56)
TLG (cm^3)	0.932	1,854.00	82.76	79.41	31 (49.21)
TMTV (cm^3)	0.919	103.00	93.10	64.71	39 (61.90)

ROC, receiver operating characteristic; AUC, area under the curve; SUVmax, maximum standardised uptake value; BVG, metabolic volume; TLG, total lesion glycation; TMTV, total metabolic tumor volume.

Table S2 Spearman rank correlation analysis

Characteristic	ρ_s	P value
SUVmax-BVG	0.564	<0.001
SUVmax-TLG	0.493	<0.001
SUVmax-TMTV	0.305	0.038
BVG-TLG	0.877	<0.001
BVG-TMTV	0.749	<0.001
TLG-TMTV	0.902	<0.001

SUVmax, maximum standardised uptake value; BVG, metabolic volume; TLG, total lesion glycation; TMTV, total metabolic tumor volume.

https://dx.doi.org/10.21037/qims-23-702