Prognostic Stratification of Baseline Total Metabolic Tumor Volume on PET/CT Combined with MYC/Bcl-2 Dual Expression in Patients with Primary Gastrointestinal Diffuse Large B-Cell Lymphoma

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Abstract

Purpose: The aim of the present study was to explore whether pretreatment total metabolic tumor volume (TMTV) combined with MYC/BCL-2 dual expression (DE) would improve the prognostic stratification of patients who were newly diagnosed with primary gastrointestinal diffuse large B-cell lymphoma (PGI-DLBCL).

Materials and methods: Eighty-three patients between March 2011 and November 2019, diagnosed with PGI-DLBCL prior to treatment, were included in this retrospective study. Baseline TMTV on PET/CT scans were calculated automatically using the boundaries of voxels presenting a SUVmax≥2.5. Expression of MYC/BCL-2 were detected at protein levels via immunohistochemistry（IHC）. The distributions of Progression-free survival (PFS) and overall survival (OS) rates were estimated using the Kaplan-Meier method and differences were compared using a log-rank test followed by multivariate analysis using the Cox proportional hazards model.

Results: TMTV and DE were significantly associated with a worse PFS and OS. Multivariate analysis revealed that TMTV (HR=6.090, P<0.001) and DE (HR=2.761, P=0.021) were each independent predictors of PFS, whereas TMTV (HR=9.512, P<0.001) was the only independent predictor of OS. A monogram comprised of TMTV and DE expression identified four groups with very different outcomes: (PFS:χ^2=32.178, P<0.001; OS:χ^2=23.091, P<0.001): low-risk group (low TMTV and non-DE, 46 patients); low-intermediate risk group (low TMTV and DE, 16 the patients); high-intermediate risk group (high TMTV and non-DE, 12 patients); and high-risk group (high TMTV and DE patients, 9 patients).

Conclusions: TMTV and DE independently predicted survival outcomes in PGI-DLBCL patients. Furthermore, our findings suggest that combination of TMTV and DE may further improve the ability of clinicians to stratify patients in terms of differential prognoses.

Introduction

Extranodal non-Hodgkin's lymphoma occurs most commonly in the gastrointestinal (GI) tract, which accounts up to 5-20 % of all cases, [1] and recently its incidence has been increasing in the world.[2] The most frequent site of GI lymphoma is the stomach, followed by the small intestine and ileocecal region.[3] Histopathologically, primary GI lymphoma is mainly represented by diffuse large B cell lymphoma (DLBCL). Currently, the optimal treatment strategy for primary GI diffuse large B-cell lymphoma (PGI-DLBCL) remain controversial.[4] For example, surgery is the first-line therapy for the management of primary gastric DLBCL. However, chemotherapy (CHOP or R-CHOP) alone or followed by radiotherapy were reported to produce similar or better results than surgical resection.[5-6] Besides, surgical resection of the primary mass is also a topic of debate in primary intestinal DLBCL because surgery is associated with otherwise avoidable complications and well response to chemotherapy alone were reported in some studies. [7-8] Actually, it is difficult to make single treatment recommendation for all PGI-DLBCL due to the nature of heterogeneity in this group of tumors. Therefore, an accurate prognostic assessment is urgently needed for patients with PGI-DLBCL to better evaluate the effectiveness of administered treatments and to further risk-stratify patients.

It has been validated that ^{18}F-FDG PET/CT is a promising tool for prognostic assessment and management in PGI-DLBCL when interpreted using volume-based PET parameters, or total lesion glycolysis (TLG).[9-12] Additionally, there is growing interest in dual expression lymphomas (dual expressers, DE), defined as the dual expression of two oncogene proteins (i.e., MYC/BCL-2) based on immunohistochemistry（IHC）.[13] Previous studies have shown that DE is a reliable predictor of prognosis in patients with PGI-DLBCL treated with a standard dose of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP)[14]. However, published research on the prognostic value of TMTV combined with DE for improving stratification of PGI-DLBCL patients is still lacking. Hence, the aim of the present study was to explore the prognostic capacity of combination of pretreatment TMTV and DE in improving risk stratification in PGI-DLBCL patients.

Patients And Methods

Patients

Patients recently diagnosed with PGI-DLBCL who underwent pretreatment whole-body ^{18}F-FDG PET/CT between March 2011 and November 2019 were included in this retrospective study. To be included, patients were required to be treated with R-CHOP-like or CHOP-like regimens with a curative intent and had to be free of any concurrent diseases that precluded the protocol treatment. Patients were excluded if they were treated by surgical operation. Patients who had a previous malignancy, chemotherapy, radiotherapy, pregnancy (lactation), or diabetes mellitus with a fasting blood glucose level greater than 150 mg/dL were excluded from this study (Firgue 1). Clinical parameters (sex, age, B symptoms, Eastern Cooperative Oncology Group performance status ECOG PS , IPI score, lactate dehydrogenase LDH level, the modified Ann Arbor stage) were determined from the medical records. Approval was obtained from the Ethics Committee of Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School. All of the subjects signed a written consent form.

PET/CT Scanning Protocol

All of the patients underwent whole-body ^{18}F-FDG PET/CT on a combined Gemini GXL PET/CT scanner with a 16-slice CT component (Philips Corp, Netherlands). After 6 h of fasting (no oral or intravenous fluids containing sugar or dextrose), 185–370 MBq of ^{18}F-FDG (5.18 MBq/kg) was

administered intravenously. Each patient's blood glucose level was checked immediately before ^{18}F-FDG administration. Each patient was weighed for determination of the standardized uptake value (SUV) prior to each scan. Whole-body PET/CT scans were started 60 min following radiopharmaceutical injection. Emission data were acquired for 2 min in each bed position. CT acquisition data were used for attenuation correction, and corrected PET images were reconstructed using ordered-subset expectation maximization (OSEM). The acquired images from the PET and CT scans were sent for image registration and fusion using Syntegra software.

Imaging Analysis

PET/CT images were read by two physicians specializing in nuclear medicine. These physicians were blind to any patient information or to any of the patient's clinical conditions. Results were determined by a consensus between the two physicians. Images were reviewed using volume-viewer software on a dedicated workstation (Compassview 5.0, Philips Corp, the Netherland) to calculate SUV and MTV. Regions of interest (ROIs) were placed manually to cover the lesion, and the maximum SUV (SUVmax) value was recorded for each lesion. For each PET dataset, the SUVmax was defined as the highest SUV among all of the hypermetabolic tumor foci. MTV was determined by drawing a circular ROI fully encasing all involved lesions in axial, coronal, and sagittal PET/CT images. Then, the boundaries of voxels with SUV exceeding 2.5 were produced automatically. Normal organs and false-positive lesions—such as inflammation, infection or other benign FDG-avid lesions based on histopathological reports or other imaging modalities—were subtracted. The TMTV was obtained by summing the MTV of all lesions. TLG was calculated as the sum of all MTV × SUV (mean of lesions) in each patient. SUVmax values were obtained and corrected for body weight using the following standard formula: mean ROI activity (MBq/mL)/[injected dose (MBq)/body weight (kg)] .

Immunohistochemistry

All of the patient biopsy specimens were retrospectively analyzed independently by a pathologist. Formalin-fixed paraffin-embedded (FFPE) 3-μm sections were placed on adhesive-coated slides. IHC for BCL-2 and MYC expression was performed as described previously.[15] If 30% or more of the tumor cells were stained with the antibody, the samples were judged as positive.

Statistical Methods

Progression-free survival (PFS) and overall survival (OS) were chosen as the end points to evaluate the prognoses of PGI-DLBCL patients. PFS was defined as the interval between the date of diagnosis and the date of first relapse, progression, death from any cause, or last follow-up. OS was defined as the interval from the date of diagnosis until the time of death from any cause or last follow-up. The distributions of PFS and OS rates were estimated using the Kaplan-Meier method, and the survival curves were compared by a log-rank test. For the significant PET and clinical variables in univariate analysis, multivariate analysis using the Cox proportional hazards model was performed to assess the potential independent effects on PFS and OS. Receiver-operating-characteristic (ROC) curves were constructed to estimate the accuracies in predicting ideal cut-off values for SUVmax ,TMTV and TLG. All of the statistical analyses were performed using SPSS 22.0, and a P value less than 0.05 was considered to be statistically significant.

Results

Patient Characteristics and Treatment Results

The clinical characteristics of the 83 patients (46 women and 37 men) included in this study are summarized in Table 1. The median patient age was 42 years (range 19–83 years). The average SUVmax,TMTV and TLG of the primary tumors was 18.3 (4.7–46.8) ,415.7 (4.8–4323.6) cm^3 and 5466 (7.8-20955.2). After a median follow-up of 30 months (range, 3–96 months), 22 patients had disease relapse or progression and 14 patients died.

Clinical characteristics of patients in relation to TMTV

Table 1 shows the differences in clinical characteristics between the dichotomized TMTV groups. A Pearson's chi-square test showed that the IPI score and the modified Ann Arbor stage were significantly associated with TMTV. Patients with high TMTV usually possessed the following characteristics: elevated LDH levels, high IPI scores, and stage III/IV.

Survival analysis for TMTV and MYC/BCL-2 expression

The mean PFS was 66.5 mo (95% CI: 54.6–78.4 mo, range: 1–96 mo), and the mean OS was 79.6 mo (95% CI: 71.8–87.5 mo, range: 3–96 mo). The PFS and OS estimates for all of the patients were 73.5% and 83.1%, respectively. ROC curve analysis was used to calculate the accuracies of the ideal cut-off values to distinguish the low SUVmax group from the high SUVmax group, as well the low TMTV group from the high TMTV group. The ideal cut-off values for SUVmax,TMTV and TLG were 25.6,415.0 cm^3 and 2918.3, respectively. Additionally, 25 out of 83 cases (30.1%) demonstrated MYC/BCL-2 dual expression. (Figure 2-3) Univariate analysis showed that high TMTV and DE were significantly correlated with both inferior PFS (P<0.001, P=0.001; Fig. 4) and OS (P<0.001, P=0.047; Fig. 4). The univariate analyses are shown in Table 3. Multivariate analysis revealed that TMTV (HR=6.090, P<0.001) and DE (HR=2.761, P=0.021) were each independent predictors of PFS, whereas TMTV (HR=9.512, P<0.001) was the only independent predictor of OS. (Table 3).

Survival analysis for TMTV combined with MYC/BCL-2 expression

TMTV combined with DE expression identified four groups with very different outcomes: (PFS:χ^2=32.178, P<0.001; OS:χ^2=23.091, P<0.001): low-risk group (low TMTV and non-DE, 46 patients); low-intermediate risk group (low TMTV and DE, 16 the patients); high-intermediate risk group (high TMTV and non-DE, 12 patients); and high-risk group (high TMTV and DE patients, 9 patients). (Fig. 5 and Table 4).

Survival curves generated by Kaplan-Meier analysis are used to display the differences among these 4 risk groups by the monogram, which showed a stronger ability to reveal further discrimination among subgroups compared with IPI. (Table 4)

Discussion

The volumetric imaging parameters of ^{18}F-FDG PET/CT have been shown to be useful not only in the prognostic evaluation of patients with DLBCL, [16] but also in other types of lymphomas such as Hodgkin lymphoma [17] and peripheral T-cell lymphoma.[18] In the present study, we assessed the prognostic value of ^{18}FDG PET/CT volume-based PET parameters (TMTV) prior to pretreatment in patients with PGI-DLBCL. The results indicated that patients with a TMTV greater than 415.0 cm^3 had lower survival and that TMTV was an independent predictor of survival outcomes after multivariate analysis. This finding is consistent with the results of Song et al.[12] In the study of Song et al, TMTV was a valid prognostic indicator of survival for Ann Arbor Stage IE/IIE patients greater than 160.1 cm^3 with PGI-DLBCL. The discrepancy between the optimal thresholds in this previous study compared to those in our present study may be partially explained by the different stages of patients included; Stage I/II patients were included in the study by Song et al, while Stage I–IV patients were included in our present study. In addition, SUV is currently a popular semiquantitative, easy-to-calculate index of the FDG metabolic rate. However, TMTV, as a volume metric quantitatively presenting total tumor burden, has been found to be a better predictor than SUVmax for survival in our present study and in the study by Song et al.[12] These results support TMTV as a useful volumetric imaging parameter for developing better treatment plans by providing more accurate prognostic information.

In recent years, with the progress of molecular genetic research, it has been shown that molecular heterogeneity of tumors is directly correlated with treatment responses and prognoses and is crucial for allowing the possibility of individualized risk-adapted therapy .[19] A series of studies have shown that DLBCL patients with concurrent expression of MYC and BCL2 proteins have a significantly poorer survival outcome.[20-22] In the current study, DE accounted for 30.8% of PGI-DLBCL patients which is consistent with the results of PGI-DLBCL patients reported by Xia et al(30%) [14] but was higher in all of the DLBCL patients (21%) included in Johnson et al,[23] suggesting that concurrent expression of MYC and BCL-2 is more frequently found in PGI-DLBCL patients. Moreover, our present study, as well as that of Xia et al,[14] indicated that PGI-DLBCL patients with DE have significantly poorer survival outcomes. In our present study, BCL2 protein expression alone did not significantly predict PFS or OS, which is contrast to the findings of Cakmak et al .[24] The reason for this discrepancy may be explained by the different IHC-sample positive criteria, in which 30% of cells were stained with the antibody in our study while only 10% of cells were stained in Cakmak et al. In our present study, MYC and BCL-2 expression determined via IHC—as a convenient, rapid and low-cost method to detect protein expression—was found to have clinical significance in predicting prognoses in PGI-DLBCL patients.

PGI-DLBCL, characterized as highly heterogeneous, has been treated with various modalities in the past, but optimal treatment strategies have remained controversial. The IPI has been the most widely used metric for determining prognoses among patients with DLBCL since it was first published in 1993. However, because of the addition of rituximab (R) to conventional CHOP or CHOP-like regimens, the capacity of the IPI model to discriminate between risk groups has been questioned in the rituximab era.[25-26] Moreover,the combination of molecular and imaging characteristics at diagnosis has been demonstrated to improve DLBCL patient stratification in several studies.[27-28] Accordingly, the desire for more efficient risk stratification urged us to further assess a monogram comprised with TMTV and DE performance as prognostic indicators in patients with PGI-DLBCL. In present study, our results suggest that the monogram (PFS:χ^2=32.178, P<0.001; OS:χ^2=23.091, P<0.001) could yield a better stratification than IPI (PFS:χ^2=8.738, P=0.003; OS:χ^2=8.216, P=0.004) for PGI-DLBCL patients. Taken together, TMTV combined with DE could be better for risk stratification and selecting patients for tailor treatments.

This single-institution retrospective study was constrained by several limitations. The differences in thresholds used for delineating tumors when calculate TMTV may have resulted in inconsistencies among our results. An isocontour threshold of Liver SUVmean + SD × 2.00 and a fixed threshold of 42% of the intratumoral SUVmax were chosen by Mixue Rosj Gallicchio et al., respectively .[29] Although the limits of different tumor-delineation techniques have been reported , [30] most of these studies have shown that, independent of the segmentation approach used, a higher TMTV in DLBCL patients is more strongly associated with a higher risk of unfavorable survival outcomes compared to that of SUVmax.[16,30] Additionally, because of the limited number of patients in our present study, a selection bias may have confounded the analysis of our results. Therefore, a prospective clinical trial with a larger sample size of PGI-DLBCL patients is needed to provide a more reliable prediction of survival in such patients.

TMTV and DE identified a subset of PGI-DLBCL patients with poor survival outcomes. Furthermore, our findings suggest that TMTV combined with DE may assist clinicians in more accurately stratifying PGI-DLBCL patients and providing them with more risk-tailored therapies.

Declarations

Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.Informed consent was obtained from all individual participants included in the study.
Consent for publication: Written informed consent for publication was obtained from all participants.

Availability of data and material: The datasets generated and analysed during the current study are available in the Nanjing Drum Tower Hospital, the Affiliated Hospital of Nanjing University Medical School

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: Chong Jiang participated in the design of the study, carried out analysis and interpretation of data, and drafted the manuscript; final approval of the version to be published and agree to be accountable for all aspects of the work. Yue Teng participated in the design of the study, carried out acquisition of data, and helped to draft the manuscript; final approval of the version to be published and agree to be accountable for all aspects of the work. Jieyu Chen ,Zhong Zheng and Zhen Wang involved in image analysis,participate in the discussion of the result of the part and final approval of the version to be published. Zhengyang Zhou,Chongyang Ding and Jingyan Xu gave conception and design of the study, participated in the image analysis, participate in the discussion of the results analysis, approved the final submittion.

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Tables

Table 1. Demographics and Clinical Characteristics of the Study Population.

Characteristic	Value
Sex,Female/Male	46/37
Age (years) *	42 (19-83)
≤60 years/>60 years	45/38
Primary site,stomach/ intestinal	51/32
LDH,normal/ higher than normal	54/29
B symptoms,no/yes	51/32
ECOG PS, 0-1/≥2	69/14
Modified Ann Abor stage†, I-II/III-IV	51/32
No. of extranodal sites, 1/≥ 2	70/13
IPI,0-2/3-5	66/17
0-1	40
2	26
3	13
4-5	4
Bulky Disease, no/yes	58/25
Pathological type ,GCB/non-GCB	36/47
MYC expression,-/+	43/40
BCL-2 expression,-/+	46/37
MYC/BCL-2 dual expression,-/+	58/25
SUVmax	18.3 (4.7–46.8)
TMTV (cm^3)	415.7 (4.8–4323.6)
TLG	5466 (7.8-20955.2)

Abbreviations: F, female; M, male; LDH, lactate dehydrogenase; ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; GCB, germinal center B-cell; SUVmax, maximum standardized uptake value;TMTV, total metabolic tumor volume; TLG, total lesion glycolysis.

†The Musshoff modified Ann Arbor stage;

-/+:negative/positive;

*median (range).

Table 2. Comparison of TMTV and MYC/BCL-2 dual expression with patient clinical data.

Patient Data	No. of patients (n = 83)	TMTV			TLG		
		Low (n = 62)	High (n = 21)	P value*	Negative (n=58)	Positive (n=25)	P value*
Sex, F/M	46/37	35/27	11/10	0.803	34/24	12/13	0.472
Age,≤60 />60	45/38	34/28	11/10	1.000	30/28	15/10	0.632
Primary site, stomach /intestinal	51/32	42/20	9/12	0.068	39/19	12/13	0.140
LDH level, normal/elevate	54/29	47/15	7/14	0.001	37/21	17/8	0.805
B symptoms, no/yes	51/32	40/22	11/10	0.437	38/20	13/12	0.326
ECOG PS, 0-1/≥2	69/14	52/10	14/7	0.119	47/11	19/6	0.767
Modified Ann Abor stage†, I-II/III-IV	62/21	46/16	5/16	<0.001	43/15	8/17	<0.001
No. of extranodal sites, 1/≥ 2	70/13	53/9	17/4	0.730	50/8	20/5	0.518
IPI Score,0-2/3-5	66/17	53/9	13/8	0.030	50/8	16/9	0.036
Bulky Disease, no/yes	58/25	44/18	14/7	0.785	40/18	18/17	1.000
Pathological type, GCB/non-GCB	36/47	28/34	8/13	0.619	26/32	10/15	0.810
MYC, -/+	43/40	32/30	11/10	1.000	29/29	14/11	0.641
BCL-2, -/+	46/37	37/25	9/12	0.211	35/23	11/14	0.229
DE, -/+	58/25	46/16	12/9	0.173	43/15	15/10	0.206

Abbreviations: LDH, lactate dehydrogenase; ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; GCB, germinal center B-cell; TMTV, total metabolic tumor volume; TLG, total lesion glycolysis.

†The Musshoff modified Ann Arbor stage;

-/+:negative/positive

*P < 0.05.

Table 3. Univariate and multivariate analysis of factors predictive of progression-free survival and overall survival.

Variable	No. of patients (n = 83)	Univariate analysis						Multivariate analysis					
		Progression-free survival			Overall survival			Progression-free survival			Overall survival		
		HR	95% CI	P value*	HR	95% CI	P value*	HR	95% CI	P value*	HR	95% CI	P value*
Sex, F/M	46/37	2.241	0.935-5.370	0.070	2.445	0.819-7.303	0.109						
Age,≤60 />60	45/38	1.301	0.551-3.068	0.548	1.427	0.499-4.083	0.507						
Primary site, stomach /intestinal	51/32	3.210	1.339-7.697	0.009	1.772	0.619-5.073	0.286						
LDH level, normal/elevate	54/29	1.711	0.726-4.037	0.220	1.877	0.657-5.360	0.240						
B symptoms, no/yes	51/32	1.219	0.520-2.857	0.649	2.232	0.805-6.703	0.119						
ECOG PS, 0-1/ ≥2	66/17	2.317	0.930-5.770	0.071	2.906	0.973-8.678	0.056						
Modified Ann Abor stage†, I-II/III-IV	51/32	3.428	1.430-8.215	0.006	3.412	1.139-10.225	0.028						
No. of extranodal sites, 1/≥ 2	70/13	2.911	1.180-7.178	0.020	3.356	1.122-10.037	0.030						
IPI Score,0-2/3,4	58/25	3.142	1.351-7.306	0.008	2.600	0.911-7.419	0.074						
Bulky disease, no/yes	58/25	1.358	0.569-3.240	0.490	1.809	0.627-5.219	0.273						
Pathological type, GCB/non-GCB	36/47	1.520	0.617-3.745	0.362	1.301	0.435-3.891	0.638						
MYC, -/+	43/40	2.363	0.984-5.673	0.054	2.258	0.752-6.777	0.146						
BCL-2, -/+	46/37	1.671	0.720-3.881	0.232	1.748	0.606-5.041	0.302						
DE, -/+	58/25	3.594	1.543-8.368	0.003	2.775	0.966-7.973	0.058	2.761	1.163-6.556	0.021	-	-	-
SUVmax, low/high	66/17	2.079	0.838-5.157	0.114	1.633	0.512-5.210	0.407						
TMTV, low/high	62/21	7.058	2.942-16.931	<0.001	9.512	2.967-30.495	<0.001	6.090	2.503-14.817	<0.001	9.512	2.967-30.495	<0.001
TLG, low/high	58/25	5.841	2.370-14.395	<0.001	6.679	2.092-21.323	0.001						

Abbreviations: CI, confidence interval; SE, standard error; HR, hazard ratio;LDH, lactate dehydrogenase; ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; GCB, germinal center B-cell;TMTV, total metabolic tumor volume; TLG, total lesion glycolysis.

†The Musshoff modified Ann Arbor stage;

*P < 0.05.

Table 4. Comparing the NCCN-IPI with the monogram based on TMTV and DE.

Risk Factors	Risk Stratification	No. of patients (n=83)	Progression-free survival			Overall survival		
			Number of events	Survival (%)	χ^2 (P value*)	Number of events	Survival (%)	χ^2 (P value*)
IPI	Low	40	5	87.5	8.738	3	92.5	8.216
	Low-intermediate	26	10	61.5	0.003	6	76.9	0.004
	High-intermediate	13	4	69.2		2	84.6	
	High	4	3	25.0		3	25.0	
Monogram	Low	46	4	91.3	32.178 <0.001	3	93.5	23.091
	Low-intermediate	16	4	75.0		1	93.8	<0.001
	High-intermediate	12	6	50.0		4	66.7	
	High	9	8	11.1		6	33.3	

*P < 0.05.

Figures

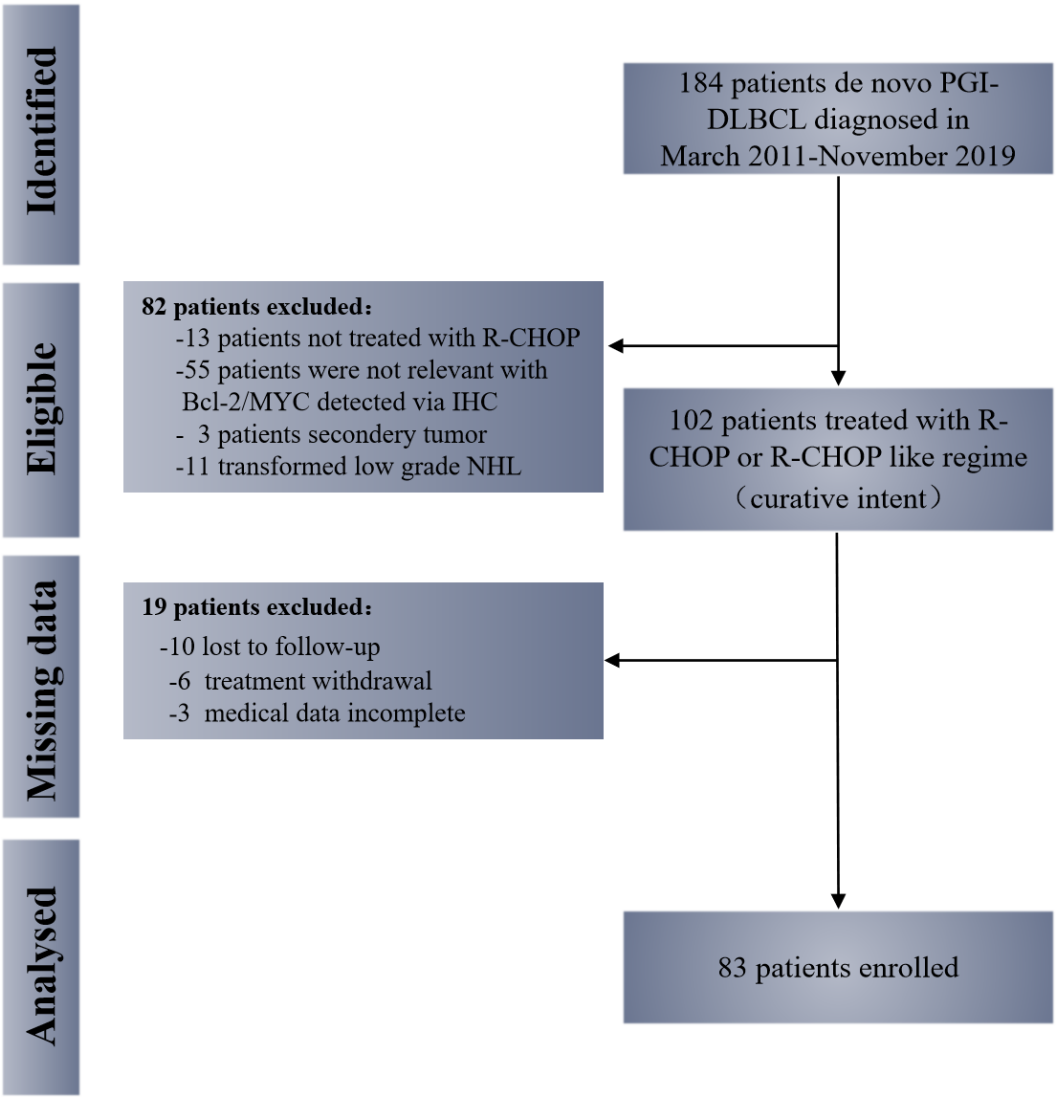

Figure 1

Flow chart of patient selection

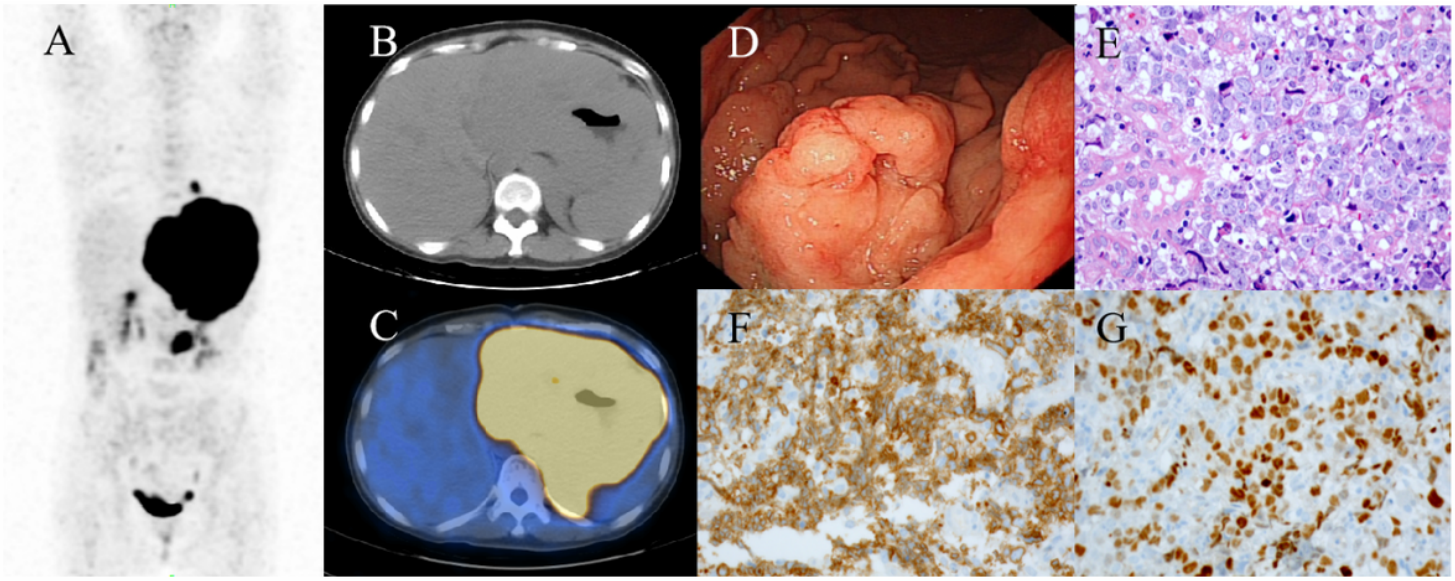

Figure 2

A 45-year-old man diagnosed with primary gastric DLBCL. (A)maximum-intensity projection (MIP) images with (B) CT images fused with (C) axial PET images show irregular thickening of the gastric wall with FDG uptake (SUVmax=21.5,TMTV: 3642.2). (D) Endoscopic images of protruding, multiply irregular surface in stomach. (E) Diffuse large B-cell lymphoma in a stomach biopsy (H&E, 20×). (F) MYC expression is positive in tumor cells (IHC,20×); (G) Bcl-2 expression is positive in tumor cells (IHC,20×). The patient relapsed in 8 months and died in 11 monthes after the completion of 6 cycles R-CHOP therapy.

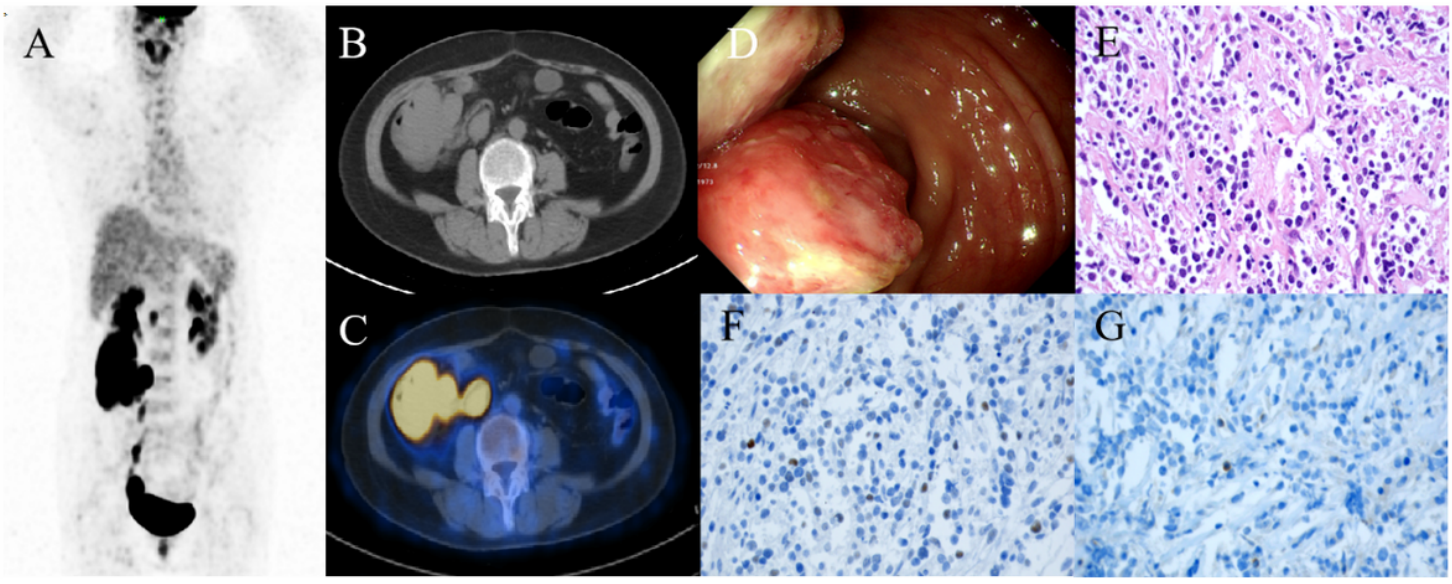

Figure 3

A 58-year-old man diagnosed with primary ileocecal DLBCL. (A)maximum-intensity projection (MIP) images with (B) CT images fused with (C) axial PET images show irregular thickening of the intestinal wall with FDG uptake (SUVmax=15.4,TMTV: 429.7). (D) Endoscopic images of protruding surface in ileocecal region. (E) Diffuse large B-cell lymphoma in a biopsy (H&E, 20×). (F) MYC expression is negative in tumor cells (IHC,20×); (G) Bcl-2 expression is negative in tumor cells (IHC,20×). The patient remains completed released after the completion of 6 cycles R-CHOP therapy.

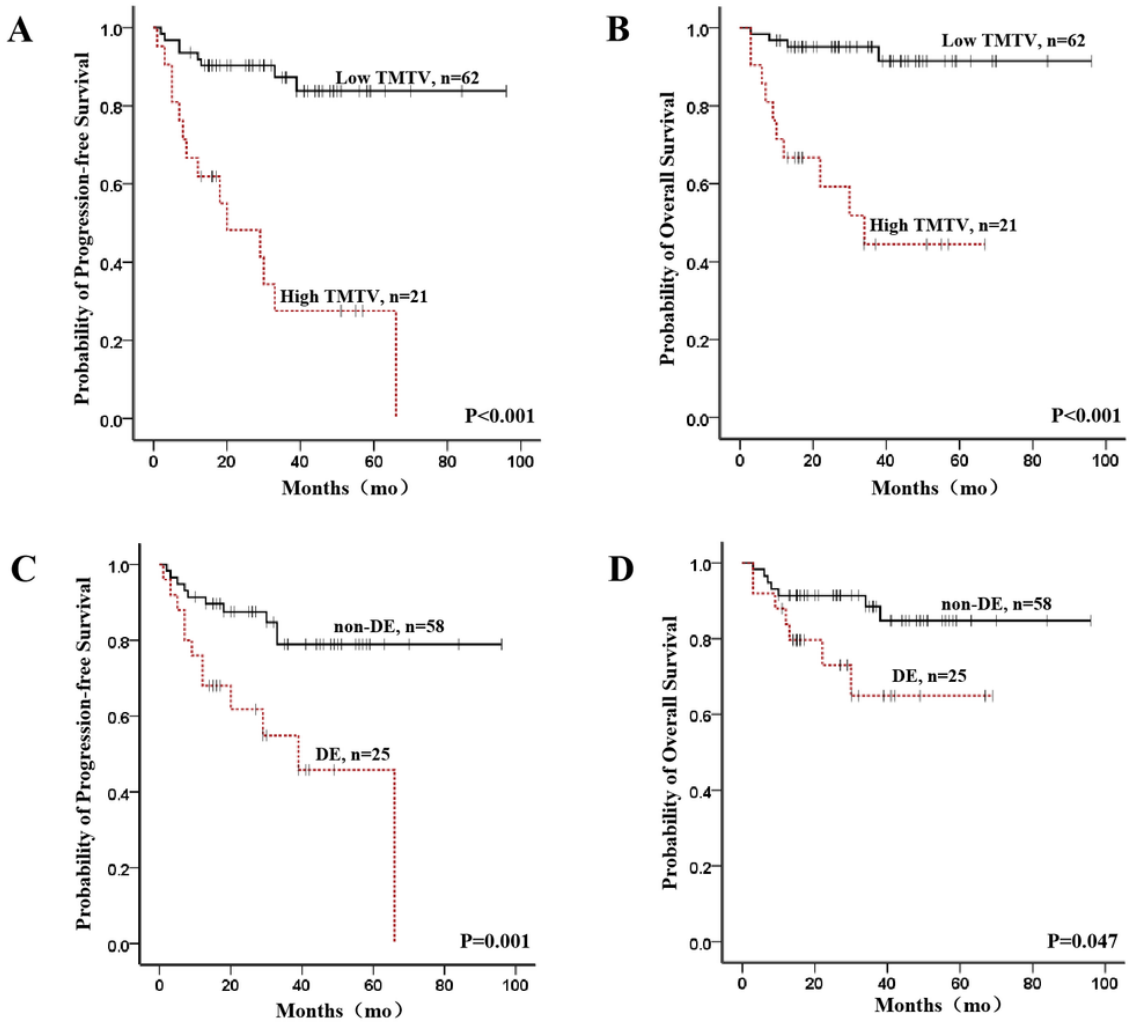

Figure 4

Progression-free survival (PFS) and overall survival (OS) in PGI-DLBCL patients according to TMTV (A, B) and MYC/BCL-2 dual expression (C, D).

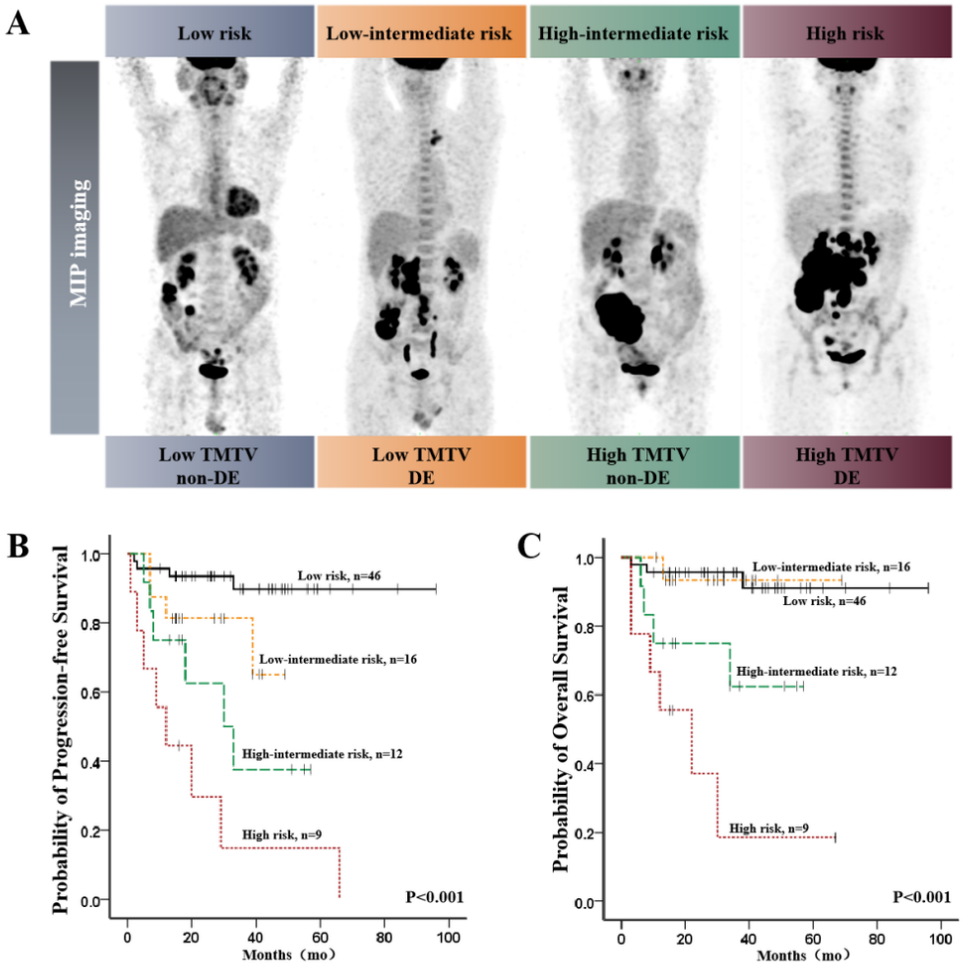

Figure 5

A. Illustration of the monogram using maximal intensity projection on FDG-PET images. B. Kaplan–Meier curve of overall survival (PFS) according to the monogram. C. Kaplan–Meier curve of overall survival (OS) according to the monogram.