Technology in Cancer Research & Treatment
Volume 20: 1–9

DOI: 10.1177/15330338211056478
journals.sagepub.com/home/tct
SAGE

Post-transplantation Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography in Patients with Lymphoblastic Lymphoma is an Independent Prognostic Factor with an Impact on Progression-Free Survival but not Overall Survival

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Abstract

Purpose: In the present study, we mainly aimed to evaluate the prognostic value of 2-deoxy-2-[^{18}F]fluoro-D-glucose ([^{18}F]F-FDG) positron emission tomography (PET)/computed tomography (CT) after allogeneic stem cell transplantation (allo-SCT) in lymphoblastic lymphoma (LBL) patients using Deauville Scores (DS). **Materials and Methods:** A total of 63 LBL patients who benefited from ^{18}F-FDG PET-CT after allo-SCT in our institution between April 2010 and August 2020 were enrolled in this retrospective study. These above-mentioned patients were divided into two groups based on the Deauville criteria. Diagnostic efficiency of ^{18}F-FDG PET/CT and integrated CT in detecting lymphoma were calculated. Consistencies were evaluated by comparing 18F-FDG PET/CT and integrated CT results through kappa coefficient. Kaplan-Meier method was used in survival analysis, and the log-rank method was adopted in comparisons. Prognostic factor analysis was performed by the Cox regression model. **Results:** The sensitivity, specificity, positive predictive value, negative predictive value, accuracy of post-SCT ^{18}F-FDG PET-CT were 100%(12/12), 92.2%(47/51), 75.0%(12/16), 100%(47/47) and 93.7%(59/63). The consistency of 18F-FDG PET-CT and integrated CT was moderate(Kappa = .702, $P < .001$). Positive post-SCT 18F-FDG PET-CT was associated with lower progression-free survival (PFS) but not overall survival (OS) ($p = .000$ and $p = .056$, respectively). The 3-year PFS of the PET-positive group and PET-negative group was 18.8% and 70.2%, respectively. Multivariate analysis showed that post-SCT PET-CT findings was an independent prognostic factor for PFS ($p = .000$; HR, 3.957; 95%CI, 1.839-8.514). Other factors independently affecting PFS were sex ($p = .018$; HR, 2.588; 95% CI, 1.181 − 5.670) and lactate dehydrogenase (LDH) ($p = .005$; HR, 3.246; 95% CI, 1.419 − 7.426). However, none of the above-mentioned factors were associated with OS. **Conclusions:** Collectively, we found that 18F-FDG PET-CT after allo-SCT was a strong indicator for PFS, but not OS, which might provide important evidence for the selection of subsequent treatment regimen for LBL patients. Trial registration number: ChiCTR2100046709.

Keywords

lymphoblastic lymphoma, allogeneic hematopoietic stem cell transplantation, ^{18}F-FDG PET/CT, prognosis, deauville score

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Introduction

Lymphoblastic lymphoma (LBL), including B-(B-LBL) or T-cell lineage (T-LBL), is a relatively rare disease,[1] accounting for approximately 8% of all lymphoid malignancies. The 5-year survival is related to age, and younger patients have a higher survival rate according to a European study.[2]

Hematopoietic stem cell transplantation (HSCT) plays a very important role in the treatment of lymphoma.[3,4] Patients with adverse prognostic features assessed by post-induction computed tomography (CT) or positron emission tomography (PET) and minimal residual disease (MRD) analysis should be considered for high-dose chemotherapy and stem cell transplantation (SCT).[2] Available data suggest that intensive consolidation therapy followed by ASCT or allogeneic SCT (allo-SCT) may improve the long-term prognosis, while which group of patients may benefit from SCT remains largely unclear.[5-9] Due to the lack of a convincing prognostic model for LBL, monitoring of PET may be useful for assessing the role of SCT.

Fluorine-18 fluorodeoxyglucose PET-CT (^{18}F-FDG PET-CT) has become an important tool to evaluate the prognosis of lymphoma since PET-CT is incorporated into The National Cancer Institute-sponsored international consensus response criteria for lymphoma guidelines in 2007.[10-12] Although opinions remain controversial, most previous studies have shown that the pre-SCT PET-CT status is strongly associated with outcomes.[12-23] However, it is still an open question whether ^{18}F-FDG PET-CT after allo-SCT can be useful for prognostic evaluation. In the present study, we evaluated the prognostic value of ^{18}F-FDG PET-CT after allo-SCT in LBL patients using Deauville Scores (DS).

Materials and Methods

Patients

This study was approved by the medical ethics committee of the First Hospital Affiliated to Soochow University. Institutional databases were reviewed to identify lymphoma patients who met the inclusion criteria as follows: pathologically confirmed as lymphoblastic lymphoma, allo-SCT between April 2010 and August 2020 in our institution, and ^{18}F-FDG PET/CT within 1 year after allo-SCT. Patients who were lost during follow-up were excluded. Finally, 63 patients were enrolled, and the data on these patients were analyzed. Status at transplant before allo-SCT and relapse or disease progression after allo-SCT was determined according to the International Working Group standard criteria.[10-11,24] This study was approved by the institutional review board of our hospital. Because the trial was a retrospective study, written informed consent for this study was waived by the ethics committee, and no personal information was disclosed. Trial registration number: ChiCTR2100046709.

FDG-PET Imaging

The PET/CT images were acquired on a GE DiscoverySTE16 PET/CT. All patients had blood glucose levels<11 mmol/L before injection. The patients were intravenously injected with ^{18}F-FDG (4.07-5.18 MBq/kg). Image acquisition for the whole-body PET scan started approximately 60 min after injection. Patients were imaged from the skull base to mid-thigh (approximately 2 min per bed position, with an average of 7-10 bed positions per scan). Spiral CT was performed with the following parameters for attenuation correction: 3.5 mm/slice, 140 kV, 120 mA, and free breathing.

All serial scans were evaluated by two interpreters blinded to all clinical information. The above-mentioned patients were divided into two groups using the Deauville 5-point scale as indicated by Lugano's recommendations in lymphoma.[11,25] The Deauville 5-point scale as follows: 1.No uptake 2.Uptake $\leq$ mediastinum 3.Uptake > mediastinum but $\leq$ liver 4.Uptake moderately higher than liver 5.Uptake markedly higher than liver (>2 times liver SUVmax) and/or new lesions. At the level with the highest FDG uptake in the lesion, a 1 cm diameter VOI was used to measure the SUVmax in the lesion. Liver maximum standardised uptake values (SUVmax) were measured using an automatic 3 cm-diameter volume of interest (VOI) set in the right liver lobe, avoiding liver lesions in the case of focal liver involvement. SUVmax in the mediastinum were measured using an 1-cm diameter VOI set in the descending thoracic aorta. DS 4 or 5 that could not be attributed to a physiologic or inflammatory cause was divided into the positive group, while DS<4 was the negative group for comparison. According to the CT-Based Response on the Lugano Classification, target nodes/nodal masses must regress to $\leq$ 1.5 cm in longest transverse diameter of a lesion (LDi) were defined as negative CT result. Target nodes/nodal masses still > 1.5 cm in LDi or/and a new node>1.5 cm in any axis or a minimum of 1 cm in LDi of new extra-nodal lesions were defined as positive CT result. In case of a discrepancy in response score between the two observers, an independent panel of PET readers made the final decision.

Statistical Analysis

^{18}F-FDG PET/CT results were compared with the results from pathological examination, clinical long-term follow-up($\geq$6 months) and conventional imaging. Diagnostic efficiency of ^{18}F-FDG PET/CT and integrated CT in detecting lymphoma were calculated. IBM SPSS Statistics (Version 26.0) was used for all statistical analyses. Consistencies were evaluated by comparing ^{18}F-FDG PET/CT and integrated CT results through kappa coefficient. Overall survival (OS) was defined as the time from day 0 of allo-SCT to death or last follow-up for survivors. Progression-free survival (PFS) was defined as the time from day 0 of allo-SCT to the date of progression/relapse, death, or last follow-up without evidence of relapse or disease progression. PFS and OS of the patients were

estimated by the Kaplan–Meier method and compared using the log-rank test. Prognostic factor analysis was performed by the Cox regression model.

Characteristics considered for univariate analysis were gender (male vs female), age (< 18 years vs ≥18 years), type of lymphoma (B-LBL vs T-LBL), Ann Arbor stage (I-II vs III-IV), extranodal lesions (<2 vs ≥2), mediastinal mass (negative vs positive), central nervous system (CNS) involvement (negative vs positive), bone marrow (BM) involvement (negative vs positive), lactate dehydrogenase (LDH)[≤ versus > upper laboratory limit (ULN)], Eastern Cooperative Oncology Group performance status (ECOG PS)(<2 vs ≥2), conditioning regimen (BuCy vs TBI/Cy vs others), previous lines of treatment (= 1 vs ≥2), disease status at transplant (complete remission and partial response vs stable disease and progressive disease), donor type (HLA identical sibling vs HLA haploidentical sibling vs unrelated), and DS for PET-CT (DS<4 vs DS ≥ 4) after transplant. Factors significantly associated with PFS or OS in the univariate analysis were analyzed by multivariate analysis. All tests were two-sided, and $P < .05$ was considered statistically significant.

Results

Patient Characteristics

Between April 2010 and December 2019, 63 patients fulfilled the above-mentioned inclusion criteria, including 44 males and 19 females. Moreover, 17 of the 63 patients also underwent a pre-transplant ^{18}F-FDG PET-CT scan. The median age of the cohort was 22 years old (range 9-51). Five B-LBL patients and 58 T-LBL patients were included. Most patients received Hyper-CVAD (fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone) as the first-line therapy. If no complete remission was achieved, some second-line regiments were allowed, such as VDLP (vincristine, daunorubicin, L-asparaginase and prednisone) and irradiation. 24 patients received allo-SCT as the consolidation therapy after the first-line treatment, and 39 patients with recurrent or refractory lymphoma received allo-SCT as the salvage consolidation therapy. The median follow-up time was 20 months (range, 4-69). Table 1 lists the patient characteristics.

Table 1. Patient characteristics (N = 63).

Characteristics	No.
Sex	
Male	44
Female	19
Age (range)	22 (9-51)
Type of lymphoma	
B- LBL	5
T- LBL	58
Median follow-up, month (range)	20 (4-69)
Number of previous treatments	
1	24
≥2	39
Ann Arbor stage	
I-II	9
III-IV	54
Mediastinal mass	
negtive	34
positive	29
CNS involvement	
negtive	61
positive	2
BM involvement	
negtive	23
positive	40
Extranodal lesions	
<2	20
≥2	43
LDH	
≤ULN	48
>ULN	15
ECOG PS	
<2	54
≥2	9
Conditioning regimen	
BuCy	37
TBI	23
others	3
Status at SCT	
CR + PR	54
SD + PD	9
Donor type	
HLA identical sibling	12
HLA haploidentical sibling	37
Unrelated	14
PET-CT results	
negative (DS < 4)	47
Positive (DS = 4 or 5)	16

LBL, Lymphoblastic lymphoma; BM, bone marrow; CNS, central nervous system; SCT, stem cell transplantation; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ULN, upper laboratory limit; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; DS, Deauville score; PET, positron emission tomography; CT, computed tomography.

FDG PET-CT Results and Outcomes After Allo-SCT

A total of 63 LBL patients underwent post-SCT ^{18}F-FDG PET-CT, of whom 12(19.0%) were demonstrated to be lymphoma by biopsy or follow-up imaging. The sensitivity, specificity, positive predictive value, negative predictive value, accuracy of post-SCT ^{18}F-FDG PET-CT and integrated CT were 100%(12/12), 92.2%(47/51), 75.0%(12/16), 100%(47/47), 93.7%(59/63) and 91.7%(11/12)、76.5%(39/51)、47.8%(11/23)、97.5%(39/40)、79.4%(50/63), respectively. The consistency of ^{18}F-FDG PET-CT and integrated CT was moderate(Kappa = .702, $P < .001$). Among the 12 patients with true positive PET/CT results, tumor restaging was up-regulated in 2 patients and down-regulated in 1 patient compared with integrated CT. Besides, 15 patients with positive integrated CT results but negative post-SCT PET results were demonstrated to be a benign process but rather lymphoma by biopsy or follow-up imaging.

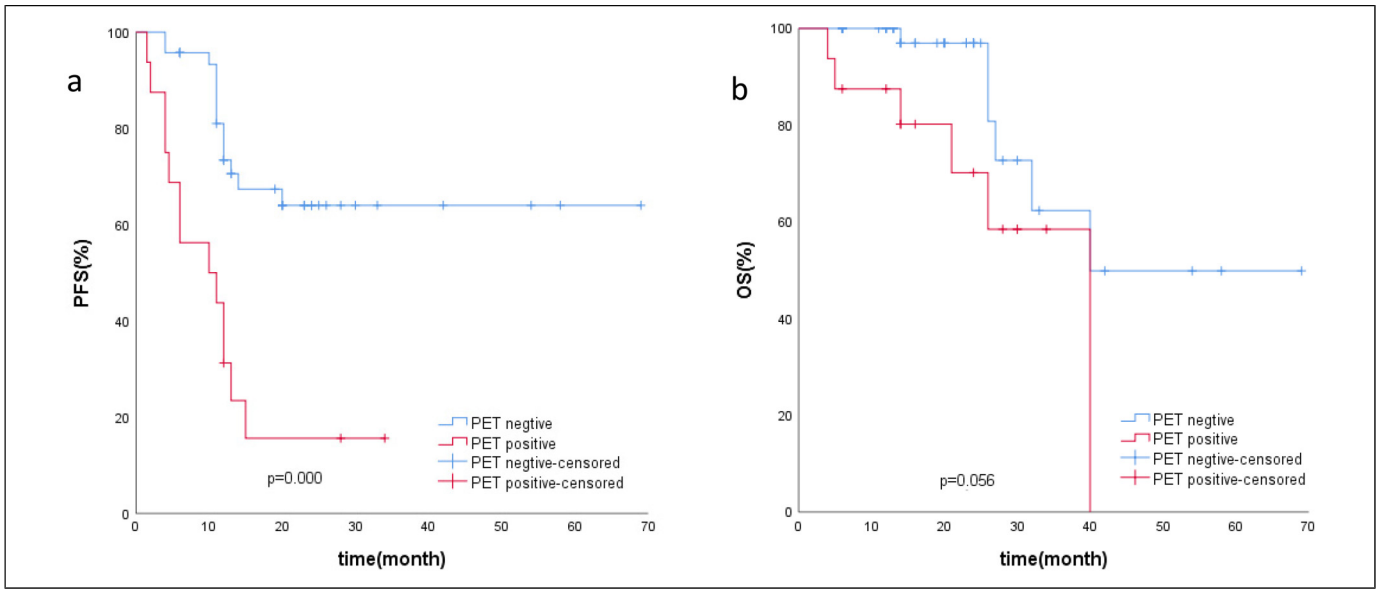

Figure 1. Kaplan-Meier analysis of PFS (a) and OS (b) for LBL patients with [18F]F-FDG PET-CT findings after allo-SCT.

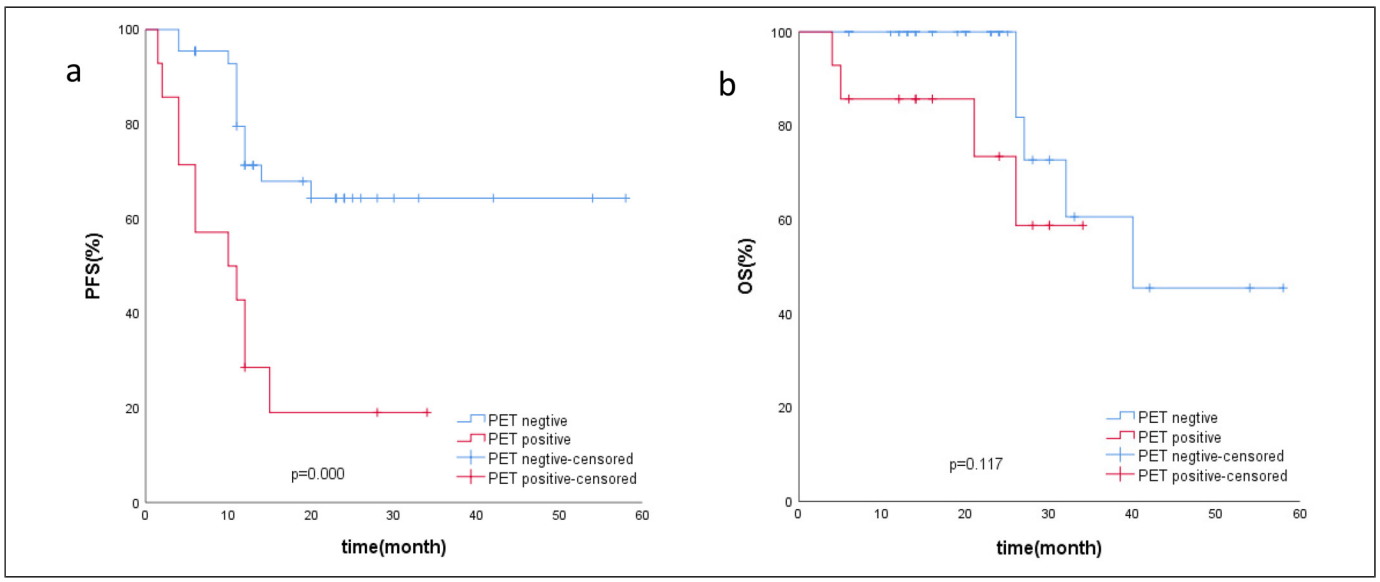

Figure 2. Kaplan-Meier analysis of PFS (a) and OS (b) for T-LBL patients with [18F]F-FDG PET-CT findings after allo-SCT.

The post-SCT ^{18}F-FDG PET-CT was positive for 16 patients (25.4%).Positive post-SCT ^{18}F-FDG PET-CT was associated with a lower PFS (p = .000), but not OS (p = .056) (Figure 1A, B). Moreover, the 3-year PFS of the PET-positive group and PET-negative group was 18.8% and 70.2%, respectively. For 58 T-LBL patients, positive post-ASCT ^{18}F-FDG PET-CT was associated with a lower PFS but not OS (p = .000 and p = .117, respectively) (Figure 2A, B). For 17 LBL patients who underwent ^{18}F-FDG PET-CT before transplantation, a positive pre-SCT PET-CT result was associated with a lower PFS and OS (p = .000 and p = .027, respectively).Besides, according to Ulaner's research, benign FDG avid ≤1.5 cm lymph nodes can mimic malignancy after allo-SCT.[26] Therefore, of the seven patients with suggestive foci in lymph nodes only, three patients with FDG avid ≤1.5 cm lymph nodes were reclassified into the PET-CT "negative" group. Patients with parenchymal suggestive foci or FDG avid >1.5 cm lymph nodes were reclassified into the PET-CT "positive" group. There was no statistically significant change. The PET-CT "positive" group was associated with a lower PFS (p = .000), but not OS (p = .116) (Figure 3A, B).

Univariate and Multivariate Analyses

Factors significantly associated with PFS or OS in univariate analysis (Table 2) were analyzed by multivariate analysis (Table 3). Post-SCT PET-CT finding was significantly associated with PFS

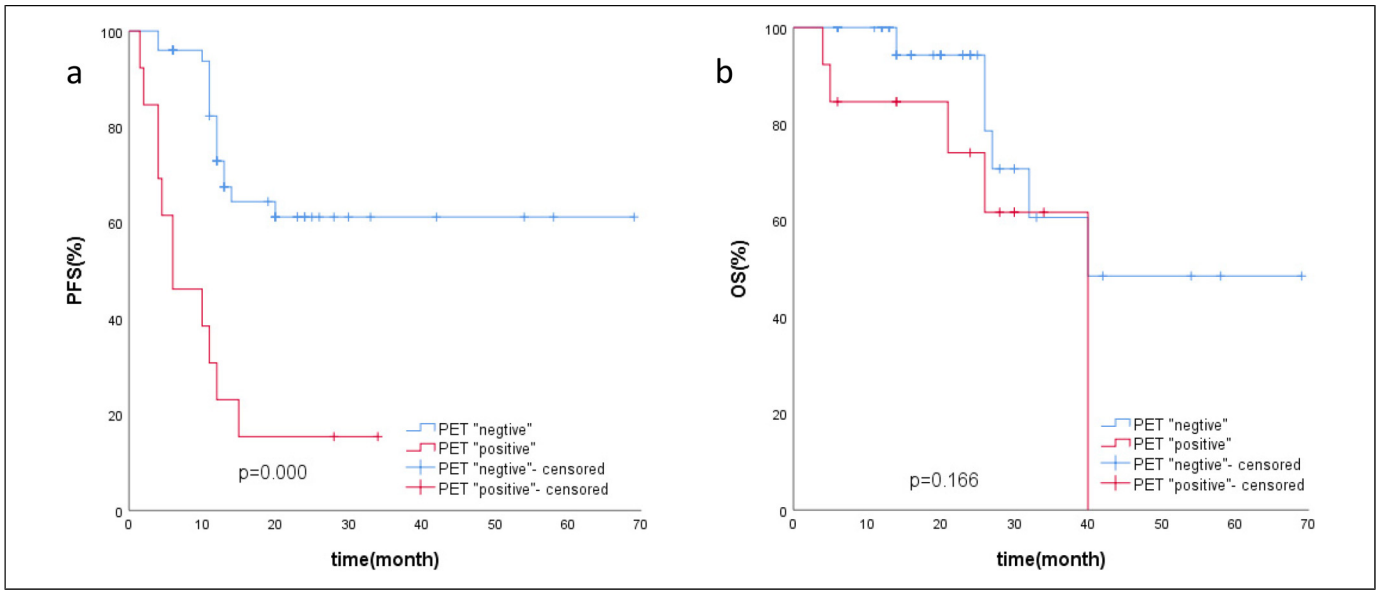

Figure 3. Patients with FDG avid ≤1.5 cm lymph nodes were reclassified into PET-CT "negative" group. Patients with parenchymal suggestive foci or FDG avid >1.5 cm lymph nodes were reclassified into PET-CT "positive" group. Kaplan-Meier analysis of PFS (a) and OS (b) for the two groups of LBL patients.

(p = .000; HR, 3.957; 95%CI, 1.839-8.514). Meanwhile, the multivariate analysis also showed that sex and LDH were associated with PFS (p = .018; HR, 2.588; 95% CI, 1.181 − 5.670, and p = .005; HR, 3.246; 95% CI, 1.419 − 7.426). However, none of the above-mentioned factors were associated with OS.

Discussion

Cure rates for pediatric, adolescent, and young adult patients with LBL have been dramatically improved. However, there are still important challenges, including the identification of prognostic factors.[27,28] There are still poor outcomes for patients who show chemotherapy resistance or relapse. HSCT is considered the optimal option for LBL. Allo-HCT can produce long-term disease control via the graft-versus-lymphoma effect.[29-32] In the present study, we aimed to evaluate the prognostic value of 18F-FDG PET-CT after allo-SCT in LBL patients using DS. For all 63 LBL patients, positive post-SCT 18F-FDG PET-CT was associated with a lower PFS, but not OS. The 3-year PFS of the PET-positive group and PET-negative group was 70.2% and 18.8%, respectively. Multivariate analysis showed that sex, LDH, and post-SCT PET-CT findings were associated with PFS. However, none of the above-mentioned factors were associated with OS.

T-LBL patients, compared with B-LBL patients, have a younger age, and a higher rate of mediastinal tumors or BM involvement. Lymph nodes and extranodal sites, such as the skin, bone, and soft tissue, are more frequently involved in B-LBL.[33,34] In our study cohort, the majority of T-LBL patients presented with BM involvement (39/58) or a mediastinal mass (29/58), while 0/5 B-LBL patients had a mediastinal mass, and 4/5 B-LBL patients had BM involvement.

Very few previous studies have investigated the role of PET imaging after allo-SCT. A meta-analysis about the role of 18F-FDG PET in prognosis evaluation of lymphoma shows that the combined HR for PFS is 4.61 for the post-SCT PET scan,[35] while it includes both auto- and allo-SCT. Bouard L's research has demonstrated that FDG PET-CT positivity after allo-SCT appears to be highly predictive of relapse and LFS in lymphoma patients.[36] A recent study has shown that post-SCT PET is not predictive for OS in T-LBL patients, while it is strongly associated with PFS.[17] Our study presented similar results. For LBL patients, positive post-SCT 18F-FDG PET-CT was associated with a lower PFS, but not OS. The results suggested that although post-SCT 18F-FDG PET-CT result did not affect the ability to predict the long-term outcome, it might be useful for guiding subsequent clinical treatment decisions. Meanwhile, our study suggested that PET could be used to evaluate the prognosis of LBL before transplantation, which is still controversial according to previous conclusions.[17-23]

Previous studies have shown several possible prognostic factors for LBL. For European patients diagnosed between 2000 to 2007, the 5-year survival is bad in the old patients (65 years or more; 8.6%) and good in children (0-14 years; 90%). The prognosis is intermediate in adolescents and young adults (15-24 years) and adults (25-64 years), and the 5-year survival is 60% and 39%, respectively.[1] In the German Multicentre Trials for Adult Acute Lymphoblastic Leukemia study (GMALL) series on T-LBL, elevated LDH is the only significant prognostic factor for survival.[37] This study has also suggested an equivalence between CR and PET-negative CRu, which may be informative eliminating the need for intensification of chemotherapy or mediastinal irradiation.[38] Some

Table 2. Univariate Cox hazard analysis of risk factors for PFS and OS.

	PFS		OS	
Variables	HR (95%CI)	p	HR (95%CI)	p
Sex				
male				
female	2.238 (1.051-4.768)	0.037*	1.556 (0.496-4.887)	0.449
Age				
≤18 years				
>18 years	0.448 (0.199-1.010)	0.053	0.521 (0.159-1.707)	0.281
Type of lymphoma				
B-LBL				
T-LBL	0.725 (0.218-2.415)	0.601	0.488 (0.124-1.918)	0.304
Ann Arbor Stage				
I-II				
III-IV	1.093 (0.376-3.175)	0.871	0.537 (0.158-1.820)	0.318
Extranodal lesions				
<2				
≥2	2.173(0.870-5.432)	0.097	0.928 (0.289-2.977)	0.900
Mediastinal mass				
negative				
Positive	0.845(0.393-1.818)	0.667	0.611 (0.182-2.054)	0.426
CNS involvement				
negative				
Positive	0.046(0.000-119.188)	0.442	0.930 (0.117-7.395)	0.946
BM involvement				
negative				
Positive	2.338(0.981-5.570)	0.055	2.332 (0.649-8.371)	0.194
LDH				
≤ULN				
>ULN	2.905 (1.323-6.378)	0.008*	2.598 (0.801-8.427)	0.112
ECOG PS				
<2				
≥2	3.541 (1.481-8.470)	0.004*	0.039 (0.000-134.752)	0.435
Conditioning regimen				
BuCy		0.128		0.324
TBI	1.968 (0.895-4.330)	0.092	2.013 (0.555-7.303)	0.287
others	3.207(0.716-14.354)	0.128	3.508 (0.620-19.864)	0.156
Number of previous treatments				
1				
≥2	1.841 (0.777-4.362)	0.166	1.133(0.339-3.785)	0.839
Status at SCT				
CR + PR				
SD + PD	1.195(0.451-3.166)	0.720	2.474(0.769-7.962)	0.129
Donor type				
HLA identical sibling		0.281		0.316
HLA haploidentical sibling	2.684(0.780-9.239)	0.118	1.512 (0.393-5.819)	0.548
Unrelated	2.610(0.674-10.115)	0.165	0.311 (0.032-3.016)	0.314
PET-CT results				
negative (DS < 4)				
Positive (DS = 4 or 5)	4.238 (1.979-9.079)	0.000*	2.818 (0.897-8.860)	0.076

*p < .05

LBL, Lymphoblastic lymphoma; BM, bone marrow; CNS, central nervous system; SCT, stem cell transplantation; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ULN, upper laboratory limit; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; DS, Deauville score; PET, positron emission tomography; CT, computed tomography.

studies have demonstrated that post-SCT 18F-FDG PET/CT may be a strong prognostic factor of PFS in T-LBL patients.[17,39] Other prognostic factors have been proposed, such as the presence or absence of BM or CNS involvement, Ann Arbor stage IV, and MRD.[39-41] In our present study, univariate and multivariate analyses showed that sex, LDH, and post-SCT PET-CT findings were associated with PFS, while none of the above-mentioned factors were associated with OS. Our data might provide additional evidence for establishing a prognostic model for LBL.

Table 3. Multivariate analysis of risks factors for PFS.

	PFS	
Variables	HR (95%CI)	P value
Sex		
male		
female	2.588(1.181-5.670)	0.018*
LDH		
≤ULN		
>ULN	3.246(1.419-7.426)	0.005*
ECOG PS		
<2		
≥2	-	0.094
PET-CT results		
negative (DS < 4)		
Positive (DS = 4 or 5)	3.957 (1.839-8.514)	0.000*

*p < .05.
ULN, upper laboratory limit; ECOG PS, Eastern Cooperative Oncology Group performance status; DS, Deauville score; PET, positron emission tomography; CT, computed tomography.

Previous studies have shown FDG-PET/CT was more sensitive and specific than CT for detecting residual disease post therapy for lymphoma[42] but a high false-positive rate.[43] Our study presented similar results. Besides small lympomatous lesions may be overlooked as it is below the PET resolution. In recent years, a number of new promising diagnostic methods have been developed. Recent studies showed assessment for minimal/measurable residual disease (MRD) is a powerful prognostic factor in lymphoblastic leukemia/lymphoma, with higher levels of MRD associated with worse prognosis.[44-45] The novel PET tracer Ga-pentixafor, which targets the C-X-C chemokine receptor 4 (CXCR4), maybe helpful for differential diagnosis of lymphoma.[46] 18F-FDG PET/MR has comparable accuracy in detection of disease sites and added benefit of radiation dose -reduction compared to FDG PET/CT.[47-48] Recently Xu Zhang et al. demonstrated PET/MR can provide better treatment evaluation of CNS Lymphoma than either PET/CT or MRI,[49] which made PET/MRI a very promising tool for future lymphoma imaging. But if these methods could be a part of convincing prognostic model for LBL is still an open question.

There were several limitations in our current study, which resulted in non-standardized treatment and timing of follow-up examinations. Furthermore, some cases lacked biopsy specimens to document the presence or absence of malignancy, when the 18F-FDG PET/CT showed positive results after allo-SCT.

Taken together, we found that the positive result of 18F-FDG PET-CT after allo-SCT was associated with a lower PFS, but not OS. Sex, LDH, and post-SCT PET-CT findings were associated with PFS, but not OS, in univariate and multivariate analyses. Collectively, our current data provided valuable insights into the prognostic value of 18F-FDG PET-CT after allo-SCT, and might guide the following treatment regimen for LBL patients.

Ethical Approval Statement

This study was approved by the institutional review board of the First Affiliated Hospital of Soochow University. Trial registration number: ChiCTR2100046709. Because the trial was a retrospective study, written informed consent for this study was waived by the ethics committee, and no personal information was disclosed.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The present study was supported by the National Natural Science Foundation of China (grant no. 81601522), Medical Youth Talent Project of Jiangsu Province (grant no. QNRC2016749), Gusu Health Talent Program (grant no. GSWS2020013), Suzhou People's Livelihood Science and Technology Project (grant no. SYS2019038), and Project of State Key Laboratory of Radiation Medicine and Protection, Soochow University, (No. GZK1202127).

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References

1. Gatta G, Capocaccia R, Botta L, et al. Burden and centralised treatment in Europe of rare tumours: results of RARECAREnet-a population-based study [published correction appears in Lancet Oncol. 2017 Aug;18(8):e433]. *Lancet Oncol.* 2017;18(8):1022-1039. doi:10.1016/S1470-2045(17)30445-X
2. Cortelazzo S, Ferreri A, Hoelzer D, Ponzoni M. Lymphoblastic lymphoma. *Crit Rev Oncol Hematol*. 2017;113:304-317. doi:10.1016/j.critrevonc.2017.03.020
3. Shankland KR, Armitage JO, Hancock BW. Non-Hodgkin lymphoma. *Lancet*. 2012;380(9844):848-857. doi:10.1016/S0140-6736(12)60605-9
4. Shanbhag S, Ambinder RF. Hodgkin lymphoma: a review and update on recent progress. *CA Cancer J Clin*. 2018;68(2):116-132. doi:10.3322/caac.214385
5. Burroughs LM, O'Donnell PV, Sandmaier BM, et al. Comparison of outcomes of HLA-matched related, unrelated, or HLA-haploidentical related hematopoietic cell transplantation following nonmyeloablative conditioning for relapsed or refractory Hodgkin lymphoma. *Biol Blood Marrow Transplant*. 2008;14-(11):1279-1287. doi:10.1016/j.bbmt.2008.08.014
6. Thomson KJ, Peggs KS, Smith P, et al. Superiority of reduced-intensity allogeneic transplantation over conventional treatment for relapse of Hodgkin's Lymphoma following autologous stem cell transplantation. *Bone Marrow Transplant*. 2008;41(9):765-770. doi:10.1038/sj.bmt.1705977
7. Rashidi A, Ebadi M, Cashen AF. Allogeneic hematopoietic stem cell transplantation in Hodgkin lymphoma: a systematic review and meta-analysis. *Bone Marrow Transplant*. 2016;51(4):521-528. doi:10.1038/bmt.2015.332
8. Devetten MP, Hari PN, Carreras J, et al. Unrelated donor reduced-intensity allogeneic hematopoietic stem cell

transplantation for relapsed and refractory hodgkin lymphoma. *Biol Blood Marrow Transplant*. 2009;15(1):109-117. doi:10.1016/j.bbmt.2008.11.011

9. Aljurf M, Zaidi SZ. Chemotherapy and hematopoietic stem cell transplantation for adult T-cell lymphoblastic lymphoma: current status and controversies. *Biol Blood Marrow Transplant*. 2005;11-(10):739-754. doi:10.1016/j.bbmt.2005.07.001
10. Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. *J Clin Oncol*. 2007;25(5):579-586. doi:10.1200/JCO.2006.09.2403
11. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol*. 2014;32(27):3059-3068. doi:10.1200/JCO.2013.54.8800
12. Younes A, Hilden P, Coiffier B, et al. International working group consensus response evaluation criteria in lymphoma (RECIL 2017). *Ann Oncol*. 2017;28(7):1436-1447. doi:10.1093/annonc/mdx097
13. Yam C, Landsburg DJ, Nead KT, et al. Autologous stem cell transplantation in first complete remission may not extend progression-free survival in patients with peripheral T cell lymphomas. *Am J Hematol*. 2016;91(7):672-676. doi:10.1002/ajh.24372
14. Moskowitz CH, Yahalom J, Zelenetz AD, et al. High-dose chemoradiotherapy for relapsed or refractory Hodgkin lymphoma and the significance of pre-transplant functional imaging. *Br J Haematol*. 2010;148(6):890-897. doi:10.1111/j.1365-2141.2009.08037.x
15. Moskowitz CH, Matasar MJ, Zelenetz AD, et al. Normalization of pre-ASCT, FDG-PET imaging with second-line, non-cross-resistant, chemotherapy programs improves event-free survival in patients with Hodgkin lymphoma. *Blood*. 2012;119-(7):1665-1670. doi:10.1182/blood-2011-10-388058
16. Alcantara M, Dupuis J, Mareschal S, et al. PET/CT before autologous stem cell transplantation predicts outcome in refractory/relapsed follicular lymphoma. *Eur J Nucl Med Mol Imaging*. 2015;42(2):215-221. doi:10.1007/s00259-014-2896-2
17. Sun N, Qiao W, Xing Y, Wang T, Yang J, Zhao J. Prognostic value of 18F-FDG PET/CT in T-lymphoblastic lymphoma before and after hematopoietic stem cell transplantation. *Clin Transl Oncol*. 2021;23(8):1571-1576. doi:10.1007/s12094-021-02551-7
18. Lambert JR, Bomanji JB, Peggs KS, et al. Prognostic role of PET scanning before and after reduced-intensity allogeneic stem cell transplantation for lymphoma. *Blood*. 2010;115(14):2763-2768. doi:10.1182/blood-2009-11-255182
19. Ulaner GA, Goldman DA, Sauter CS, et al. Prognostic value of FDG PET/CT before allogeneic and autologous stem cell transplantation for aggressive lymphoma. *Radiology*. 2015;277-(2):518-526. doi:10.1148/radiol.2015142556
20. Bachanova V, Burns LJ, Ahn KW, et al. Impact of pretransplantation (18)F-fluorodeoxy glucose-positron emission tomography Status on outcomes after allogeneic hematopoietic cell transplantation for Non-Hodgkin lymphoma. *Biol Blood Marrow Transplant*. 2015;21(9):1605-1611. doi:10.1016/j.bbmt.2015.05.007
21. Kletter K, Kalhs P. (18)F-deoxyglucose PET: useful in the management of patients with stem cell transplantation for lymphoma? *Expert Rev Hematol*. 2010;3(4):405-410. doi:10.1586/ehm.10.35
22. Reyal Y, Kayani I, Bloor AJC, et al. Impact of pretransplantation (18)F-fluorodeoxyglucose-positron emission tomography on survival outcomes after T cell-depleted allogeneic transplantation for Hodgkin lymphoma. *Biol Blood Marrow Transplant*. 2016;22-(7):1234-1241. doi:10.1016/j.bbmt.2016.03.034
23. Sauter CS, Lechner L, Scordo M, et al. Pretransplantation fluorine-18-deoxyglucose–positron emission tomography scan lacks prognostic value in chemosensitive B cell non-Hodgkin lymphoma patients undergoing nonmyeloablative allogeneic stem cell transplantation. *Biol Blood Marrow Transplant*. 2014;20(6):881-884. doi:10.1016/j.bbmt.2014.02.009
24. Cheson BD, Horning SJ, Coiffier B, et al. Report of an international workshop to standardize response criteria for non-Hodgkin's Lymphomas. NCI sponsored international working group [published correction appears in J Clin Oncol 2000 Jun;18(11):2351]. *J Clin Oncol.* 1999;17(4):1244. doi:10.1200/JCO.1999.17.4.1244
25. Barrington SF, Mikhaeel NG, Kostakoglu L, et al. Role of imaging in the staging and response assessment of lymphoma: consensus of the international conference on malignant lymphomas imaging working group [published correction appears in J Clin Oncol. 2016 Jul 20;34(21):2562]. *J Clin Oncol*. 2014;32-(27):30483058. doi:10.1200/JCO.2013.53.5229
26. Ulaner GA, Lilienstein J, Gönen M, Maragulia J, Moskowitz CH, Zelenetz AD. False-Positive [18F]fluorodeoxyglucose-avid lymph nodes on positron emission tomography-computed tomography after allogeneic but not autologous stem-cell transplantation in patients with lymphoma. *J Clin Oncol*. 2014;32(1):51-56. doi:10.1200/JCO.2013.50.8044
27. Candoni A, Lazzarotto D, Ferrara F, et al. Nelarabine as salvage therapy and bridge to allogeneic stem cell transplant in 118 adult patients with relapsed/refractory T-cell acute lymphoblastic leukemia/lymphoma. A CAMPUS ALL study. *Am J Hematol*. 2020;95(12):1466-1472. doi:10.1002/ajh.25957
28. Burkhardt B, Hermiston ML. Lymphoblastic lymphoma in children and adolescents: review of current challenges and future opportunities. *Br J Haematol*. 2019;185(6):1158-1170. doi:10.1111/bjh.15793
29. Wang J, Duan X, Yang L, et al. Comparison of survival between autologous and allogeneic stem cell transplantation in patients with relapsed or refractory B-cell Non-hodgkin lymphoma: a meta-analysis. *Cell Transplant*. 2020;29:963689720975397. doi:10.1177/0963689720975397
30. Mehta-Shah N, Teja S, Yu T, et al. Successful Treatment of Mature T-Cell Lymphoma with Allogeneic Stem Cell Transplantation: The Largest Multicenter Retrospective Analysis[C]. 59th Annual Meeting and Exposition (December 9-12, 2017). 2017. https://www.researchgate.net/publication/320774655_Successful_Treatment_of_Mature_TCell_Lymphoma_with_Allogeneic_Stem_Cell_Transplantation_The_Largest_Multicenter_Retrospective_Analysis
31. Wulf G, Hasenkamp J, Jung W, et al. Allogeneic stem cell transplantation for patients with relapsed or refractory T-cell

lymphoma: efficacy of lymphoma-directed conditioning against advanced disease. *Bone Marrow Transplant*. 2019;54(6):877-884. doi:10.1038/s41409-018-0360-9

32. Schmitz N, Lenz G, Stelljes M. Allogeneic hematopoietic stem cell transplantation for T-cell lymphomas. *Blood*. 2018;132-(3):245-253. doi:10.1182/blood-2018-01-791335
33. Ellin F, Jerkeman M, Hagberg H, Relander T. Treatment outcome in T-cell lymphoblastic lymphoma in adults - a population-based study from the Swedish lymphoma registry. *Acta Oncol*. 2014;53-(7):927-934. doi:10.3109/0284186X.2014.889850
34. Maitra A, McKenna RW, Weinberg AG, Schneider NR, Kroft SH. Precursor B-cell lymphoblastic lymphoma. A study of nine cases lacking blood and bone marrow involvement and review of the literature. *Am J Clin Pathol*. 2001;115(6):868-875. doi:10.1309/Q5GV-3K00-WAC6-BBUB
35. Wang C, Li P, Wu S, et al. The role of fluorine-18 fluorodeoxyglucose PET in prognosis evaluation for stem cell transplantation of lymphoma: a systematic review and meta-analysis. *Nucl Med Commun*. 2016;37(4):338-347. doi:10.1097/MNM.0000000000000468
36. Bouard L, Bodet-Milin C, Bailly C, et al. Deauville scores 4 or 5 assessed by fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography early post-allotransplant Is highly predictive of relapse in lymphoma patients. *Biol Blood Marrow Transplant*. 2019;25(5):906-911. doi:10.1016/j.bbmt.2018.11.019
37. Hoelzer D, Gökbuget N, Digel W, et al. Outcome of adult patients with T-lymphoblastic lymphoma treated according to protocols for acute lymphoblastic leukemia. *Blood*. 2002;99(12):4379-4385. doi:10.1182/blood-2002-01-0110
38. Gökbuget N, Wolf A, Stelljes M, et al. Favorable outcome in a large cohort of prospectively treated adult patients with T-lymphoblastic lymphoma (T-LBL) despite slowly evolving complete remission assessed by conventional radiography. *Blood*. 2014;124(21):370. doi:10.1182/blood.V124.21.370.370
39. Lepretre S, Touzart A, Vermeulin T, et al. Pediatric-Like acute lymphoblastic leukemia therapy in adults With lymphoblastic lymphoma: the GRAALL-LYSA LL03 study. *J Clin Oncol*. 2016;34(6):572-580. doi:10.1200/JCO.2015.61.5385
40. Bassan R, Spinelli O, Oldani E, et al. Improved risk classification for risk-specific therapy based on the molecular study of minimal residual disease (MRD) in adult acute lymphoblastic leukemia (ALL). *Blood*. 2009;113(18):4153-4162. doi:10.1182/blood-2008-11-185132
41. Thomas DA, O'Brien S, Cortes J, et al. Outcome with the hyper-CVAD regimens in lymphoblastic lymphoma. *Blood*. 2004;104(6):1624-1630. doi:10.1182/blood-2003-12-4428
42. Karls S, Shah H, Jacene H. PET/CT for lymphoma post-therapy response assessment in other lymphomas, response assessment for autologous stem cell transplant, and lymphoma follow-up. *Semin Nucl Med*. 2018;48(1):37-49. doi:10.1053/j.semnuclmed.2017.09.004
43. Adams HJA, Kwee TC. Proportion of false-positive lesions at interim and end-of-treatment FDG-PET in lymphoma as determined by histology: systematic review and meta-analysis. *Eur J Radiol*. 2016;85-(11):1963-1970. doi:10.1016/j.ejrad.2016.08.011
44. Borowitz MJ, Wood BL, Devidas M, et al. Prognostic significance of minimal residual disease in high risk B-ALL: a report from Children's Oncology group study AALL0232. *Blood*. 2015;126(8):964-971.
45. DiGiuseppe JA, Wood BL. Applications of flow cytometric immunophenotyping in the diagnosis and posttreatment monitoring of B and T lymphoblastic leukemia/lymphoma. *Cytometry B Clin Cytom*. 2019;96(4):256-265.
46. Starzer AM, Berghoff AS, Traub-Weidinger T, et al. Assessment of central nervous system lymphoma based on CXCR4 expression In vivo using 68Ga-pentixafor PET/MRI. *Clin Nucl Med*. 2021;46(1):16-20. doi:10.1097/RLU.0000000000003404
47. Platzek I. (18)F-fluorodeoxyglucose PET/MR imaging in lymphoma. *PET Clin*. 2016;11(4):363-373. doi:10.1016/j.cpet.2016.05.001
48. Afaq A, Fraioli F, Sidhu H, et al. Comparison of PET/MRI With PET/CT in the evaluation of disease Status in lymphoma. *Clin Nucl Med*. 2017;42(1):e1-e7. doi:10.1097/RLU.0000000000001344
49. Zhang X, Zhou C, Yuan J, Fan W. High-resolution 18F-FDG PET/MR offers better treatment evaluation than PET/CT or MRI in CNS lymphoma. *Jpn J Clin Oncol*. 2021;51(5):842-843. doi:10.1093/jjco/hyaa217