Impact of Pretransplantation F-18-fluorodeoxy Glucose-Positron Emission Tomography Status on Outcomes after Allogeneic Hematopoietic Cell Transplantation for Non-Hodgkin Lymphoma

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Abstract

Assessment with ^{18}F-fluorodeoxy glucose (FDG)—positron emission tomography (PET) before hematopoietic cell transplantation (HCT) for lymphoma may be prognostic for outcomes. Patients with chemotherapy-sensitive non—Hodgkin lymphoma (NHL) undergoing allogeneic HCT reported to the Center of International Blood and Marrow Transplantation Registry between 2007 and 2012 were included. Pre-HCT PET status (positive versus negative) was determined by the reporting transplantation centers. We analyzed 336 patients; median age was 55 years and 60% were males. Follicular lymphoma (n = 104) was more common than large cell (n = 85), mantle cell (n = 69), and mature natural killer or T cell lymphoma (n = 78); two thirds of the cohort received reduced-intensity conditioning; one half had unrelated donor grafts. Patients underwent PET scanning a median of 1 month (range, .07 to 2.83 months) before HCT; 159 were PET positive and 177 were PET negative. At 3 years, relapse/progression, progression-free survival (PFS), and overall survival (OS) in PET-positive versus PET-negative groups were 40% versus 26%; P = .007; 43% versus 47%; P = .47; and 58% versus 60%; P = .73, respectively. On multivariate analysis, a positive pretransplantation PET was associated with an increased risk of relapse/progression (risk ratio [RR], 1.86; P = .001) but was not associated with worse OS (RR, 1.29, 95% confidence interval [CI], .96 to 1.7; P = .08), PFS (RR, 1.32; 95% CI, .95 to 1.84; P = .10), or nonrelapse mortality (RR, .75; 95% CI, .48 to 1.18; P = .22). PET status conferred no influence on graft-versus-host disease. A positive PET scan before HCT is associated with increased relapse risk but should not be interpreted as a barrier to a successful allograft. PET status does not appear to predict survival after allogeneic HCT for NHL.

Keywords

Non-Hodgkin lymphoma; Allogeneic transplantation; Positron emission tomography

Introduction

Allogeneic hematopoietic cell transplantation (HCT) can provide long-term survival for patients with various subtypes of lymphoma; however, relapse remains the predominant cause of treatment failure [1-4]. The use of ^{18}F-fluorodeoxy glucose (FDG)-positron emission tomography (PET) after front-line or salvage chemotherapy is a valuable prognostic tool to assess the depth of remission before autologous HCT [5-9]. FDG-PET scan metabolic positivity is associated with a higher post-autograft relapse risk and worse survival in patients with diffuse large B cell lymphoma (DLBCL) and Hodgkin lymphoma (HL) [5,9]. However, it is unclear whether FDG-PET before allogeneic HCT can be reliably used to predict post-transplantation outcomes among non-Hodgkin lymphoma (NHL) patients. Several single-institution studies have found conflicting data on relapse and long-term survival among allogeneic HCT recipients according to pretransplantation PET status; however, these studies were based on smaller cohorts of patients (58 to 88 patients) and often included patients with both HL and NHL [10-13]. We conducted a retrospective, multicenter, registry-based analysis of a large cohort of NHL patients to determine whether FDG-PET performed before allogeneic HCT can be used to predict post-transplantation outcomes.

Patients and Methods

Data Sources

The Center of International Blood and Marrow Transplantation Registry (CIBMTR) is a working group of more than 450 transplantation centers worldwide that contribute detailed data on HCTs longitudinally with yearly follow-up to a statistical center at the Medical College of Wisconsin. Centers report HCTs consecutively, with compliance monitored by on-site audits. The study was performed in compliance with federal regulations and the institutional review board of the Medical College of Wisconsin.

Patients

We included adults undergoing first allogeneic HCT for a histologically proven diagnosis of follicular lymphoma (FL), DLBCL, mantle cell lymphoma (MCL), or mature T cell or natural killer (NK) cell neoplasm between 2007 and 2012. Eligible histological subtypes were restricted to either routinely FDG-avid lymphomas or subtypes where expected FDG avidity rates ranged from 80% to 100% [14,15]. Patients not responding (ie, not achieving a complete or partial remission [CR or PR]) to the last line of therapy (n = 104), with an untreated relapse (n = 50) before allogeneic HCT, or undergoing ex vivo graft manipulation (n = 4) or post-transplantation cyclophosphamide (n = 1) were excluded. We identified 998 potential cases and contacted transplantation centers for additional information about availability, date, and status of the last FDG-PET scan performed before allogeneic HCT (Supplemental Appendix Figure). Among the 815 (81.2%) responses received, 367 patients

met the eligibility criteria of the protocol, including the final designation of FDG-PET status as assessed by the local radiology team in individual centers. Cases where the interval between the FDG-PET scan and day 0 of allogeneic HCT was > 3 months were excluded (n = 31).

Definitions

The CIBMTR form defines *CR* after the last line of therapy before HCT as complete resolution of all known disease on radiographic (computerized tomography [CT] scan) assessments. *PR* required ≥ 50% reduction in the greatest diameter of all sites of known disease and no new sites of disease. Pre-HCT PET scan status determination (positive scan versus negative scan) was performed by the reporting transplantation center according to routinely used criteria at individual centers.

Conditioning regimens were categorized by intensity using established consensus criteria [16]. Previously established criteria for categorizing the degree of HLA matching were used for unrelated donor transplantations [17]. Well-matched patients had either no identified HLA mismatching and informative data at 4 loci or allele matching at HLA-A, -B, and -DRB1 (6/6). Partially matched pairs had a defined, single-locus mismatch, and/or missing HLA data. Mismatched cases had ≥ 2 allele or antigen mismatches.

Study Endpoints

Primary outcomes were relapse/progression and progression-free survival (PFS); secondary outcomes were nonrelapse mortality (NRM) and overall survival (OS). *NRM* was defined as death without evidence of lymphoma relapse; relapse/progression was defined as progressive lymphoma after HCT or lymphoma recurrence after a CR; NRM was considered a competing risk. For PFS, treatment failure occurred at the time of relapse or death from any cause. Patients alive without evidence of disease relapse were censored at last follow-up. *OS* was defined as the interval from the date of transplantation to the date of death or last follow-up. *Acute graft-versus-host disease* (GVHD) was defined and graded based on the pattern and severity of organ involvement using established criteria [18]. *Chronic GVHD* was defined as the development of any evidence of chronic GVHD based on clinical criteria [19].

Statistical Analysis

Probabilities of PFS and OS were calculated using the Kaplan-Meier estimator. Probabilities of NRM and lymphoma relapse were calculated using cumulative incidence curves to account for competing risks. Patient-, disease-, and transplantation-related factors were compared between PET-positive and PET-negative groups using the chi-square test for categorical variables and the Wilcoxon sample test for continuous variables. Associations among patient-, disease-, and transplantation-related variables and outcomes of interest were evaluated using multivariate Cox proportional hazards regression. A stepwise selection multivariate model was built to identify covariates that influenced outcomes. Covariates with a $P < .05$ were considered significant. The proportionality assumption for Cox regression was tested by adding a time-dependent covariate for each risk factor and each outcome. Covariates violating the proportional hazards assumption were stratified in the

Cox regression model. Results are expressed as relative risk (RR) or the relative rate of occurrence of the event.

Variables considered in multivariate analysis included positive or negative PET status (the main effect) and clinical factors listed in Tables 1 and 2 (denoted by an asterisk sign). Potential interactions among the main effect and all significant covariates were tested. CR versus PR and bulky disease (≥5 cm) at HCT were not included in multivariate analysis owing to the strong correlation of CR with PET-negative status and presence of bulky disease with PET-positive status.

Results

Patients Characteristics

We examined data on 336 eligible patients from 81 reporting centers (Tables 1 and 2). Median age was 55 years (range, 18 to 71); 60% were males. FL (n = 104) was more common than DLBCL (n = 85), MCL (n = 69), and mature NK or T cell (n = 78) lymphomas. Patients underwent FDG-PET scanning a median of 1 month (range, .07 to 2.83 months) before allografting; 159 were FDG-PET positive (FDG-PET+) and 177 FDG-PET negative (FDG-PET−). As expected, there were differences in disease characteristics between FDG-PET+ and FDG-PET− groups (Table 1). FDG-PET+ patients more often had FL (38% versus 25%), ≥3 lines of prior therapy (70% versus 58%), extranodal disease before HCT (36% versus 11%), marrow involvement before HCT (14% versus 5%), and bulky disease before HCT (10% versus 1%) compared with the FDG-PET− cohort. Pretransplantation radiation was administered for 20% of FDG-PET+ patients and 24% of FDG-PET – patients before PET imaging. The interval from diagnosis to transplantation was similar (median 28 versus 26 months). In addition, similar proportions of patients in both groups received rituximab-containing conditioning (25% versus 19%) and peritransplantation antithymocyte globulin/alemtuzumab (26% versus 27%), and only a few had radiation (2% versus 1%) after transplantation (Table 2). For the entire cohort, most patients received reduced-intensity (RIC) or nonmyeloablative conditioning. Less than 25% had a prior autologous HCT, with DLBCL being the most common histology (undergoing an autologous transplantation previously) in both PET groups (FDG-PET+ 46% and FDG-PET – 37%; $P = .44$) and similar distribution of other histologies. There was no significant difference between the FDG-PET+ and FDG-PET− cohorts in graft and donor type (Table 2). Median follow-up of survivors was 48 months (12 to 82 months; PET+ group) and 49 months (range, 3 to 75 months; PET– group).

NRM and GVHD

The cumulative incidence of NRM at 1 year was 14% (95% confidence interval [CI], 9% to 20%] in FDG-PET+ and 19% (95% CI, 13% to 25%; $P = .23$) in FDG-PET− groups (Table 3, Figure 1A). The respective figures at 3 years were 17% versus 27% ($P = .03$). On multivariate analysis, FDG-PET status was not predictive of NRM risk (Table 4). Unrelated donor (RR, 3.59; 95% CI, 1.96 to 6.58; $P < .0001$) and cord blood (RR, 2.69; 95% CI, 1.2 to 6.03; $P = .01$) HCT were associated with increased NRM risk (Table 4). The cumulative

incidences of grade II to IV acute GVHD at day 100 (26% and 27%) and chronic GVHD at 1 year (43% versus 43%) were not significantly different between the 2 cohorts (Table 3).

Relapse/Progression

The cumulative incidence of relapse at 1 year of PET+ patients was higher than that of the PET– group (32% versus 17%; *P* = .002) (Table 3) and the relapse difference persisted at 3 years (40% versus 26%; *P* = .007) (Figure 1B). On multivariate analysis, a positive pretransplantation PET scan was associated with increased the risk of relapse by almost 2-fold (RR, 1.86; 95% CI, 1.26 to 2.74; *P* = .002) (Table 4). Whereas higher relapse risk with PET+ status was seen in all histological subtypes (3-year cumulative incidence rates: DLBCL, 51% versus 34%; *P* = .10; MCL, 54% versus 27%, *P* = .025; NK/T lymphoma, 44% versus 24%; *P* = .07); the trend was negligible in patients with FL (22% versus 17%, *P* = .50). Other clinical factors independently prognostic of relapse risk were lymphoma histology other than FL (RR, 1.88 to 2.36 for different subsets) and prior autologous transplantation (RR, 1.73; *P* = .01) and use of bone marrow grafts (RR, 3.0) (Table 4). The median time to relapse in PET– and PET+ groups were 10 months (range, 1 to 50) and 4 months (range, .1 to 51), respectively.

PFS and OS

At a median follow-up of 4 years (range, .25 to 6.8), FDG-PET status before allograft did not affect survival. Three-year PFS and OS for PET+ and PET– groups were similar at 43% (95% CI, 36% to 51%) versus 47% (95% CI, 40% to 55%); *P* = .47 and 58% (50% to 65%) versus 60%; (95% CI, 52% to 67%); P = .73, respectively (Figure 1C,D). On multivariate analysis, FDG-PET+ status was not associated with increased risk of therapy failure (ie, inferior PFS; RR, 1.29; 95% CI, .96 to 1.74; *P* = .08) or mortality (ie, inferior OS; RR, 1.32; 95% CI, .94 to 1.84; *P* = .10). Factors significantly associated with therapy failure (donor type, stem cell source, and lymphoma subgroup) and mortality (donor type, stem cell source, lymphoma subgroup, and conditioning intensity) are summarized in Table 4.

Causes of Death

In the FDG-PET+ group, 75 patients died. The most common causes of death were primary disease (55%) followed by GVHD (19%), organ failure (8%), and infection (8%). FDG-PET − patients (n = 73) died most often of primary disease (36%), GVHD (25%), organ failure (18%), and infections (8%) (Table 5).

Discussion

In our multicenter retrospective analysis of 336 patients, the largest cohort studied for the association between FDG-PET status and allogeneic HCT outcomes to our knowledge, we found that patients with residual lymphoma, as detected by FDG uptake on PET imaging, had a modestly increased risk of disease relapse after transplantation. Long-term survival, however, was similar for all lymphoma patients receiving allogeneic HCT in our cohort regardless of PET status.

Our results showed a link between a positive FDG-PET scan and clinical factors before transplantation, including extranodal involvement, presence of bulky disease, marrow involvement, and more prior lines of therapy, suggesting biologic differences in the compared PET status groups. Whereas 3-year NRM appeared to be higher in PET– patients compared with PET+ patients on univariate analysis, the difference, which is partially attributable to competing risk of early progressive disease in PET+ patients, was not confirmed after adjusting for potential confounding factors in multivariate analysis. It is important to highlight that all patients included in the current study were chemosensitive by CT criteria and, regardless of metabolic depth of remission immediately before transplantation, allogeneic HCT yielded 3-year survival close to 60%. Our results suggest that in NHL patients demonstrating chemosensitive disease by conventional radiographic criteria, a FDG-PET (at least as clinically applied in individual centers across the world) is not predictive of post-allogeneic HCT survival outcomes. Disease control long-term benefits from graft-versus-lymphoma (GVL) responses and the availability of effective salvage therapies in the case of post-allogeneic HCT relapse of NHL. The GVL effect in our series is further implied by improved survival using peripheral blood compared with marrow graft source.

We recognize that variations in PET techniques and interpretation among centers in different countries exist and evolve over time. In general, PET/CT interpretation guidelines from the International Harmonization Project in Lymphoma recommend using visual assessment of residual mass (positive versus negative) with mediastinal blood pool activity or background activity as the reference [20]. We collected additional supplemental data from centers and utilized the pre-HCT PET status as determined by the reporting transplantation center using their institutional practice and criteria. This strategy allowed us to examine the utility of pre-allograft PET scan, as practiced and utilized in the “real-world.” Whether our observations would be applicable to PET images interpreted centrally or by using standardized 5-point scale criteria is not known and likely beyond the scope of a registry analysis [20,21]. This limitation highlights the future need to use standardized 3- or 5-point scale PET imaging in forthcoming studies [14]. It is also important to highpoint that the Deauville criteria were published in late 2009 and nearly one half of the subjects included in our analysis underwent transplantation before the availability of these guidelines. Until future prospective studies are conducted in NHL histological subsets using standardized PET imaging methods, our analysis provides clinically relevant insights on the predictive value of PET after allograft for patients with NHL.

Current published data contain limited and contrasting findings on the predictive value of FDG-PET imaging. Dodero et al. reviewed 80 patients (34 with high-grade NHL and 46 with HL) before RIC allogeneic HCT [10]. PET positivity predicted survival, but over one half of the patients had HL, a disease where PET-CT provides the most reliable assessment of chemosensitivity and possibly weaker GVL effects [22,23]. Our cohort appears more homogenous, as HL patients were not included. A study from the University College London that reported outcomes of 88 patients with predominantly indolent NHL treated with alemtuzumab-containing RIC conditioning and risk-adapted post-HCT donor lymphocyte infusion showed a lack of difference in relapse and similar PFS between PET+ patients versus PET– groups; however, persistence of PET activity after transplantation most often

predicted imminent relapse and reduced PFS [11-13]. More recent single-institution studies from the University of Minnesota and Memorial Sloan Kettering used Deauville score PET interpretation in their cohorts (78 and 58 NHL allograft recipients, respectively) who were chemosensitive by CT criteria and found no difference in event-free survival or OS between FDG-PET positive (Deauville 4, 5) and FDG-PET negative (Deauville 1 to 3) patients [12,13]. It is important to highlight that most aforementioned series studying PET in allogeneic HCT, including ours, comprised predominantly indolent NHL histologies, whereas publication on autologous HCT [5,8,9] included predominantly aggressive histologies. Biologic differences inherent to histologic subtypes clearly impact on predictive utility of PET; however, more data will be needed to assess implications of pretransplantation functional imaging in specific histologic subsets.

Our results provide potentially useful clinical information for interpreting the prognostic meaning of FDG-PET imaging results in the setting of allogeneic HCT. For example, whereas PET negativity leads to a lower risk of relapse, PET positivity may guide decisions about post-transplantation interventions to reduce relapse. Importantly, a positive PET scan should not be interpreted as a barrier to a successful allograft. It is a potentially modifiable variable affecting early relapse and, unlike histology or prior autograft, can be targeted by pre- or peritransplantation strategies [24,25]. Our study also highlights the need to standardize interpretation of PET scans and examine the utility of the Deauville scoring system in NHL and within the context of allogeneic HCT [14,26].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

1. Patients with non-Hodgkin lymphoma and positive positron emission tomography scan before allogeneic hematopoietic cell transplantation are at higher risk of relapse.
2. In chemosensitive non—Hodgkin lymphoma patients by computed tomography criteria, positron emission tomography scan does impact allogeneic hematopoietic cell transplantation outcomes.

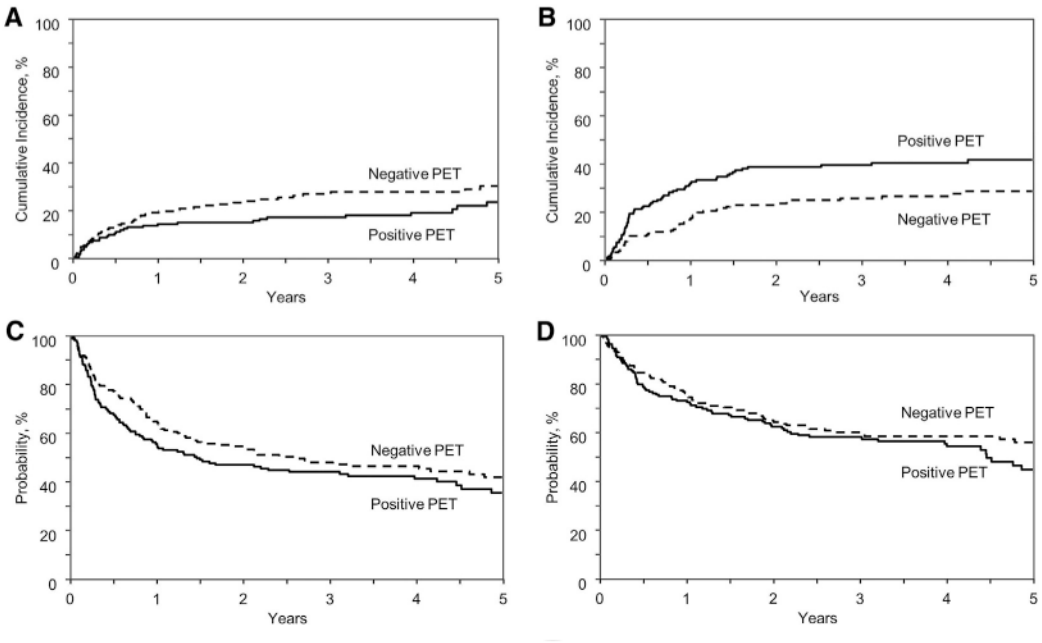

Figure 1.
Cumulative incidence of NRM (A) and relapse (B) and Kaplan-Meyer estimates of PFS (C) and OS (D).

Table 1

Patient and Disease Characteristics

Variable	FDG-PET−	FDG-PET+	*P* Value
No. of patients	177	159	
Age at transplantation, yr*			.950
Median (range)	54 (19-71)	55 (18-70)	
Karnofsky score before HCT*			.054
<90%	45 (25)	48 (30)	
≥90%	128 (72)	100 (63)	
Missing	4 (2)	11 (7)	
Sex*			.571
Male	110 (62)	94 (59)	
Female	67 (38)	65 (41)	
Histology*			.009
FL	44 (25)	60 (38)	
DLBCL†	41 (23)	44 (28)	
MCL	41 (23)	28 (18)	
Mature T cell and NK cell neoplasm‡	51 (29)	27 (17)	
No. of prior chemotherapy lines*			.025
1-2	68 (43)	44 (30)	
≥3	92 (58)	102 (70)	
Missing	17	13	
Disease status before transplantation§			<.001
CR//	147 (83)	6 (4)//	
PR	30 (17)	153 (96)	
Extranodal involvement before transplantation*			<.001
No	154 (87)	99 (62)	
Yes	20 (11)	58 (36)	
Unknown	3 (2)	2 (1)	
Bulky disease before transplantation (nodal)			<.001
<5 cm	8 (5)	68 (43)	
≥5 cm	1 (1)	16 (10)	
No nodal involvement before transplantation	153 (86)	33 (21)	
Missing	15 (8)	42 (26)	
BM involvement before transplantation			<.001
No	12 (7)	35 (22)	
Yes	8 (5)	22 (14)	
Unknown	157 (89)	102 (64)	
Symptoms at diagnosis			.328
A	84 (47)	72 (45)	

Variable	FDG-PET−	FDG-PET+	*P* Value
B	59 (33)	46 (29)	
Missing	34 (19)	41 (26)	
Elevated LDH before transplantation*	43 (26)	47 (33)	.179
Missing	11	16	
Interval from diagnosis to transplantation (range), mo*	26 (3-208)	28 (4-352)	.320
Interval from FDG-PET to transplantation (range), mo	1 (.20-2.80)	1 (.07-2.83)	.595
Prior autologous transplantation* 41 (23)		28 (18)	.208
Time from autoHCT to alloHCT, (range) mo	24 (7-133)	21 (7-66)	.447
≤12	8 (5)	5 (3)	
>12	33 (19)	23 (14)	

BM indicates bone marrow; LDH, lactate dehydrogenase; auto, autologous; allo, allogeneic.

*Variables considered in multivariate analysis.

†Thirty-two transformed patients were included (32 out of 85 DLBCL).

‡FDG-PET−: mycosis fungoides (n = 1), anaplastic large T cell (n = 12),peripheral T cell (n = 9), angioimmunoblastic T cell (n = 9), adult T cellleukemia/lymphoma (n = 3), extranodal NK/T cell (n = 4), other NK (n = 9),hepatosplenic gamma delta T-cell (n = 2), subcutaneous panniculitis T-cell(n = 2); FDG-PET+: peripheral T cell (n = 10), angioimmunoblastic T cell(n = 7), extranodal NK/T cell (n = 2), other NK cell (n = 4), subcutaneouspanniculitis T cell (n = 2), anaplastic large T cell (n = 2).

§Disease status: FDG-PET−: CR (CR1 = 40 and CR2+ = 107), PR (PIF sensitive = 14 and REL sensitive = 16); FDG-PET+: CR (CR1 = 1 and CR2+ = 5), PR (PIF sensitive = 54 and REL sensitive = 99).

//FDG-PET/CT reports of 6 patients who were in CR by CT criteria but with PET+ scans were reviewed. In all patients, CR by CT criteria was confirmed. All cases had metabolic activity in nonenlarged lymph nodes.

Table 2
Transplantation and Treatment Characteristics

Variable	FDG-PET−	FDG-PET+	*P* Value
No. of patients	177	159	
Donor type*			.402
Cord blood	27 (15)	26 (16)	
HLA-identical siblings	65 (37)	57 (36)	
Unrelated well matched	59 (33)	57 (36)	
Unrelated partially matched	17 (10)	17 (11)	
Unrelated matching missing	9 (5)	2 (1)	
Graft type*			.331
Bone marrow	7 (4)	12 (8)	
Peripheral blood	143 (81)	121 (76)	
Cord blood	27 (15)	26 (16)	
Conditioning intensity*			.814
Myeloablative	50 (28)	40 (25)	
Cyclophosphamide + TBI	30 (17)	19 (12)	
Busulfan + fludarabine	10 (6)	7 (4)	
Other/busulfan + cyclophosphamide	5/4 (4/2)	6/8 (4/5)	
Reduced intensity	70 (40)	66 (42)	
TBI + other	14 (9)	5 (4)	
Fludarabine + melphalan	18 (10)	21 (13)	
Melphalan ± others†	16 (9)	9 (6)	
Busulfan + others	20 (12)	27 (17)	
Nonmyeloablative	57 (32)	53 (33)	
Fludarabine + cyclophosphamide + TBI	17 (10)	20 (13)	
Fludarabine + cyclophosphamide or TBI	37 (21)	33 (20)	
Radiation ± ATG	6 (3)	2 (1)	
Radiation before HCT*			.094
No	134 (76)	127 (80)	
Yes	43 (24)	32 (20)	
Rituximab at conditioning*			.189
Yes	34 (19)	40 (25)	
No	143 (81)	119 (75)	
Donor-recipient CMV status*			.336
Positive donor	25 (14)	17 (11)	
Positive recipient	88 (49)	81 (51)	
Donor-recipient negative	42 (24)	40 (25)	
Missing	22 (12)	21 (13)	
Year of transplantation			.125
2007-2008	84 (47)	66 (42)	

Variable	FDG-PET−	FDG-PET+	*P* Value
2009-2010	57 (32)	68 (43)	
2011-2012	36 (20)	25 (16)	
ATG/alemtuzumab*			.434
ATG alone	36 (20)	30 (19)	
Alemtuzumab alone	12 (7)	11 (7)	
GVHD prophylaxis*			.325
Tacrolimus + MMF ± others	48 (27)	29 (18)	
Tacrolimus + MTX ± others (except MMF)	58 (33)	66 (42)	
Tacrolimus + others (except MTX, MMF)	12 (7)	17 (10)	
CSA + MMF ± others (except tacro)	31 (18)	24 (15)	
CSA + MTX ± others (except tacro, MMF)	9 (5)	10 (6)	
CSA + others (except tacro, MTX, MMF)	5 (3)	3 (2)	
Other GVHD prophylaxis‡	14 (8)	10 (6)	
Planned post-transplantation radiation	1 (1)	3 (2)	
Median follow-up of survivors, mo	49 (3-75)	48 (12-82)	

TBI indicates total body irradiation; ATG, antithymocyte globulin; CMV, cytomegalovirus; MMF, mycophenolate mofetil; CsA, cyclosporine; MTX, methotrexate.

Data presented are n (%), unless otherwise indicated.

*Variables considered in multivariate analysis.

†Negative PET: Ara-C + VP16 + melphalan+nitro (n = 9), melphalan alone (n = 2); Positive PET: Ara-C + VP16 + melphalan + nitro (n = 5), Ara-C + VP16 + melphalan + nitro + Velcade (n = 2), melphalan alone (n = 1), melphalan + clorabine (n = 1).

‡MTX + MMF = 1, KGF + MTX = 1, MAB + MMF + Campath = 2, MTX + Siro = 1, not specified = 19.

Table 3

Univariate Analysis*

Outcomes	FDG-PET−	FDG-PET+	*P* Value
	Cumulative Incidence (CI)		
Acute GVHD (grade II-IV)			
100 Days	26 (20-33)	27 (21-34)	.874
Chronic GVHD			
1 Year	43 (36-51)	43 (36-51)	.997
3 Years	52 (44-59)	54 (46-62)	.717
NRM			
1 Year	19 (13-25)	14 (9-20)	.236
3 Years	27 (20-34)	17 (11-23)	**.031**
Relapse/progression			
1 Year	17 (12-23)	32 (25-40)	**.002**
3 Years	26 (19-33)	40 (32-48)	**.007**
PFS			
1 Year	64 (57-71)	54 (46-62)	.064
3 Years	47 (40-55)	43 (36-51)	.472
OS			
1 Year	75 (68-81)	72 (65-79)	.581
3 Years	60 (52-67)	58 (50-65)	.731

*Probabilities of acute GVHD, chronic GVHD, treatment-related mortality, and relapse were calculated using the cumulative incidence estimate. PFS and OS were calculated using the Kaplan-Meier product limit estimate. *P* values reflect point-wise comparison at defined times.

Table 4

Multivariate Analysis

Factor	N	RR (95% CI)	*P* Value
NRM			
Main effect			
FDG-PET−	177	1	
FDG-PET+	156	.754 (.479-1.185)	.2202
Donor type			
HLA-identical sibling	120	1	
Cord blood	53	2.691 (1.2-6.032)	.0162
Unrelated	160	3.595 (1.964-6.583)	<.0001
Stem cell source			
Bone marrow	18	1	
Peripheral blood	262	.33 (.16-.67)	.0025
Relapse/progression			
Main effect			
FDG-PET−	177	1	
FDG-PET+	156	1.862 (1.263-2.745)	.0017
Histology			
FL	104	1	
DLBCL	82	2.365 (1.378-4.059)	.0018
MCL	69	2.122 (1.209-3.726)	.0088
T and NK neoplasm	78	1.882 (1.051-3.369)	.0333
Prior auto transplantation			
Yes	66	1	
No	267	.578 (.38-.881)	.0109
Therapy failure (PFS)			
Main effect			
FDG-PET−	177	1	
FDG-PET+	156	1.297 (.966-1.741)	.0833
Donor type			
HLA-identical sibling	120	1	
Cord blood	53	1.896 (1.228-2.929)	.0039
Unrelated	160	1.521 (1.083-2.136)	.0155
Stem cell source			
Bone marrow	18	1	
Peripheral blood	262	.54 (.3-.5)	.03
Histology			
FL	104	1	
DLBCL	82	2.094 (1.401-3.131)	.0003
MCL	69	1.873 (1.23-2.853)	.0035
T and NK neoplasm	78	1.548 (.995-2.408)	.0527

Factor	N	RR (95% CI)	*P* Value
Mortality (OS)			
Main effect			
FDG-PET−	177	1	
FDG-PET+	159	1.321 (.946-1.844)	.1028
Donor type			
HLA-identical sibling	122	1	
Cord blood	53	2.098 (1.266-3.476)	.004
Unrelated	161	2.064 (1.379-3.09)	.0004
Stem cell source			
Bone marrow	18	1	
Peripheral blood	262	.38 (.21-.67)	.0008
Histology			
FL	104	1	
DLBCL	85	2.393 (1.489-3.846)	.0003
MCL	69	1.844 (1.118-3.041)	.0166
T and NK neoplasm	78	1.706 (1.01-2.883)	.0458
Conditioning regimen			
Myeloablative	90	1	
Non-myeloablative/RIC	246	.642 (0.447-0.921)	.0161

Table 5

Causes of Death

Cause of Death	FDG-PET−	FDG-PET+
Total no. of deaths	73	75
Primary disease	26 (36)	41 (55)
Infection	6 (8)	6 (8)
Idiopathic pneumonia syndrome	0	3 (4)
GVHD	17 (23)	14 (19)
Organ failure	13 (18)	6 (8)
Second malignancy	3 (4)	3 (4)
Hemorrhage	0	1 (1)
Severe platelet transfusion reaction	1 (1)	0
Not specified	7 (10)	1 (1)

Data presented are n (%).