Title page

Title Prognostic role of PET scanning before and after reduced intensity allogeneic stem cell transplant for lymphoma

Short title PET in reduced-intensity allografting for lymphoma

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Abstract

Allogeneic SCT is an established therapy for patients with relapsed lymphoma, but the role of PET scanning pre- and post- allogeneic SCT is uncertain. We investigated whether pre-transplant PET status predicted outcome following allogeneic SCT, and whether PET surveillance post-transplantation provided additional information compared to CT scanning. Eighty consecutive patients with lymphoma who received a reduced intensity allogeneic SCT were entered onto a prospective trial. PET and CT scans were performed pre-transplant and up to 36 months post-transplant. Forty two patients were PET positive prior to transplant. Pre-transplant PET status had no significant impact on either relapse rate or overall survival. Thirty-four relapses were observed, of which 17 were PET positive with a normal CT scan at relapse. DLI were administered in 26 episodes of relapse, and were guided by PET alone in 14 patients. These findings suggest that in contrast to autologous SCT, pre-transplant PET status is not predictive of relapse and survival following allogeneic SCT for lymphoma. Post-transplant surveillance by PET detected relapse before CT in half of episodes, often allowing earlier administration of DLI in patients with recurrent lymphoma, and permitted withholding of potentially harmful DLI in those with PET negative masses on CT scans.
Introduction

High-dose chemotherapy followed by allogeneic stem cell transplantation (SCT) has become an established approach in the management of selected patients with relapsed lymphoma often after the failure of autologous SCT.\(^1\) More recently, reduced-intensity allogeneic SCT has been shown to be effective in the treatment of patients with lymphoma but with less toxicity than standard myeloablative allogeneic SCT.\(^2\)\(^-\)\(^4\)

Reduced intensity regimens rely on immunosuppression of the recipient to allow allogeneic engraftment, and then harness the alloreactivity of the donor T-cells against any residual lymphoma cells (graft-versus-lymphoma, GVL, effect). Donor T-cells may be administered either on the day of transplant (T-cell replete graft) or many months following a T-cell depleted graft (or indeed a T-cell *replete* graft) as a donor lymphocyte infusion (DLI).

A number of published series in both autologous and reduced-intensity allogeneic SCT suggest that satisfactory outcomes are largely confined to those patients who show a response to salvage therapy prior to the transplant.\(^5\)\(^-\)\(^9\) In recent years, assessment of response to therapy has been improved by the use of fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography (PET). Several studies have shown that the results of autologous SCT are poor in patients with a positive pre-transplant PET scan, even if they have had a response using conventional computed tomography (CT) criteria.\(^10\)\(^-\)\(^12\) It is not known whether a positive PET scan immediately prior to a reduced intensity *allogeneic* SCT is associated with a similarly poor outcome.
Following reduced intensity allogeneic SCT, the GVL effect may be augmented by the administration of DLI, typically at the first sign of disease persistence or relapse, when it may re-induce remission.\textsuperscript{13} Consequently patients who have undergone reduced intensity allogeneic transplantation for lymphoma may require close monitoring post-transplant to detect persistent or recurrent disease at an early stage, when DLI might be most effective. PET scanning may therefore be of value following allogeneic SCT by providing early evidence of recurrent lymphoma. A small retrospective analysis of patients at our centre who underwent PET imaging for possible relapse following allogeneic transplant found that administration of DLI was influenced by PET in 9 of 15 patients.\textsuperscript{14} There are, however, no prospective data on the utility of PET in this setting.

This prospective study aimed to investigate: 1) whether the pre-transplant PET status was predictive of outcome in patients undergoing reduced intensity allogeneic SCT for lymphoma, and 2) whether post-transplant PET imaging would lead to earlier detection of relapse when compared to standard CT scans, thereby potentially allowing earlier use of adoptive immunotherapy.
Methods

Study population

All patients being considered for allogeneic transplantation for lymphoma that are typically FDG-avid were eligible for entry to the study, and were treated at University College London Hospital and the Royal Free Hospital, which together comprise a single, integrated academic transplant unit. Approval for the study was provided by the Multi-centre Research Ethics Committee and all patients gave written, informed consent in accordance with the Declaration of Helsinki.

Eighty patients were recruited (55 male; median age at transplant was 44.1 years, range 19 – 67 years) and these were a median of 45.6 (range 10 – 84) months post-transplant at the time of analysis in May 2009. The diagnoses were follicular lymphoma (n=30), Hodgkin lymphoma (n=22), diffuse large B cell lymphoma (n=7), transformed follicular lymphoma (n=6), mantle cell lymphoma (n=11), and peripheral T-cell lymphoma (n=4). Forty-three patients underwent HLA-matched sibling donor transplantation, and 37 patients underwent matched unrelated donor transplantation.

Study design and timing of scans

An observational, prospective study design was followed. Imaging was performed pre-transplant, then at 3-, 6-, 9-, 15-, 24- and 36-months post reduced intensity SCT. At each time point, patients underwent both conventional CT scanning and fused PET-CT scanning. Pre-transplant, conventional CT was used to determine chemosensitivity and
suitability to proceed to transplant. Concomitant pre-transplant PET was not used in the decision to proceed to transplant. Following transplant, patients were eligible to receive DLI +/- chemotherapy if there was evidence of relapse, assessed either clinically, by CT or by PET.

**Conditioning regimen and clinical follow-up**

Seventy-eight patients were conditioned using alemtuzumab, fludarabine and melphalan, and 2 received alemtuzumab, carmustine, cytarabine, etoposide and melphalan. Unmanipulated peripheral blood stem cells were returned on day 0. Cyclosporine A was administered as immunosuppression and continued for 3 months post-SCT. Patients were assessed clinically for the presence of graft-versus-host disease (GVHD), infective complications, and evidence of relapse. Lineage-specific chimerism was assessed routinely every 3 months.

**Fused PET-CT**

PET was performed using the GE Advance PET scanner and the GE Light-speed multi-slice spiral CT (GE Medical Systems, Milwaukee, WI, USA). The Light-speed CT acquires four 5-mm slices at 140 kV with 80 mAs and a large pitch of 6 (30 mm of table travel per gantry rotation). The CT and the PET studies were acquired during normal quiet breathing. Images were acquired 60 min after the injection of 370 MBq of FDG. The CT acquisition took 20–30 s and the PET acquisition, 25–30 min (five to six bed positions with an acquisition time of 5 min per position). PET data were reconstructed
using iterative reconstruction [ordered subsets expectation maximization (OSEM)], and CT was used for attenuation correction of the PET images.

PET scans were assessed visually by a core team of experienced nuclear medicine physicians within our institution, in keeping with the most recent Consensus recommendations and reported as ‘positive’ (suggestive of residual or recurrent lymphoma) or ‘negative’ (suggestive of remission from lymphoma).

**CT**

CT was performed with intravenous contrast using a 64-multi-detector row CT scanner and covered from base of neck to pelvis. CT appearances were reported as ‘complete remission’ (CR), ‘relapse/progression’, or ‘residual abnormality’. The latter category combined the standard response criteria ‘partial response’ and ‘stable disease’, on the grounds that either would prompt further investigation in the post-transplant setting.

**Definitions**

Chemotherapy sensitivity was defined as the achievement of at least partial remission (a reduction in nodal bulk of at least 50% using standard CT volume criteria).

Primary progression of lymphoma was defined as the persistence of lymphoma at 3 months and at 6 months post-transplant, whether detected clinically, or by the presence of PET-positivity, or the presence of progression on CT. Relapse was defined as the development of new findings on physical examination, new positivity on PET, and/or
evidence of relapse/progression on CT, that were in keeping with the recurrence of lymphoma, in a patient previously in documented remission, and death occurring after relapse was always ascribed to disease. Progression-free survival (PFS) was defined as survival in continuous remission from transplant until the time of analysis. Current progression-free survival (cPFS) was defined as survival in remission at the time of analysis, and included patients in continuous remission since transplant, and those who relapsed after transplant but re-achieved remission following further therapy.

Post-transplant DLI administration

Patients with relapse/progression had immunosuppression withdrawn and received DLI, unless they had on-going GVHD. Escalating doses, ranging from $10^6$ to $10^8$ T-cells/kg, were used, according to our published regimen. DLI were withheld in patients with stable CT abnormalities who had a normal PET scan and full donor chimerism.

Statistical analysis

Continuous variables are presented using mean (SD) and categorical variables using $n$ (%). Baseline characteristics between PET negative and PET positive patients were compared using t-tests or Fisher’s exact test as appropriate. There were five time-to-event outcomes of interest: overall survival (OS, primary endpoint), relapse, PFS, cPFS and non-relapse mortality, assessed at the start of May 2009. Survival distributions for overall survival, PFS and cPFS were estimated using Kaplan-Meier curves, and differences between the PET negative and positive groups tested using the Log-rank test. Relapse and non-relapse mortality events were analysed using cumulative
incidence estimates.\textsuperscript{19} A Cox proportional hazards model was used to estimate the hazard ratio for differences between the groups. McNemar's test was used to assess agreement between PET and CT results. A p value of <0.05 was considered statistically significant. Data analysis was performed by JRL, KSP and MR, and all authors had access to primary clinical data.
Results

PET and CT concordance pre-reduced intensity SCT

Seventy-eight of 80 patients were assessed to have chemosensitive lymphoma by CT criteria. Thirty-eight patients were PET negative and 42 were PET positive. Using CT criteria alone, 29 of 80 patients were in complete remission (CR). There were no significant differences in patient characteristics between the PET negative and PET positive groups (table 1). Concordance between pre-transplant PET and CT was 69%, with 8 patients who were PET positive and CT negative, and 17 who were PET negative and CT positive (p=0.072) (table 2).

Relationship between pre-transplant PET and survival

At the time of analysis, 54 patients were still alive and 26 had died (table 3). There were 12 (31.6%) deaths in the PET negative group and 14 (33.3%) in the PET positive group, with no significant difference in survival between the two groups (HR 1.08 95% CI (0.50, 2.33) p=0.851, figure 1A). There was also no difference in non-relapse mortality between the two groups (HR 1.04, 95% CI (0.40, 2.69) p=0.939, figure 1B).

Relationship between pre-transplant PET and primary progression and relapse

Of the 80 patients, 7 fulfilled the criteria for primary progression, of whom 4 died of lymphoma, 2 entered remission following the administration of DLI, and one remains
alive but with evidence of ongoing disease. A further 21 patients relapsed during follow-up.

In total, 15 of the 28 patients diagnosed with primary progression or relapse were PET positive pre-transplant. Overall, the rate of primary progression and relapse combined was not significantly different in those who were PET positive compared to those who were PET negative pre-transplant (HR 1.14 95% CI (0.54, 2.41) p=0.714, figure 1C). Similarly there was no difference in the PFS and cPFS between the 2 groups (HR 1.12 95% CI (0.62, 2.02), p= 0. 703; and HR 1.15 95% CI (0.57, 2.30), p=0.699, respectively; figures 1D and 1E).

**PET and CT results and chimerism analysis at relapse**

Thirty-four episodes of progression / relapse were observed in 28 different patients (4 patients relapsed twice and one relapsed 3 times). In 17 of these episodes the diagnosis was made using PET alone, as they were judged to be negative on CT: in 16 of these, the relapse was at a site documented to be involved by lymphoma pre-transplant, whereas in one the relapse was at a new site. In 2 of these 17 episodes, relapsed / progressive lymphoma was proven histologically. In the remaining 15 episodes, the presence of residual or relapsed lymphoma was diagnosed on the basis of persistently abnormal FDG uptake (at least 2 consecutive scans), in nodal areas documented to be involved by lymphoma prior to transplant, and biopsy was not attempted for the following reasons: in 7 episodes, the PET positivity affected anatomical locations not readily amenable to biopsy (retroperitoneal or mediastinal); in 2 episodes, the persistently abnormal FDG uptake was so marked and so extensive
(above and below the diaphragm) that it was felt unlikely to be due to anything other than relapse; and in the other 6 episodes, the PET positivity was confined to a single nodal group, but persisted for at least 6 months without any apparent infective or inflammatory cause.

There were 13 relapse episodes where both CT and PET were positive, and 4 where both were initially negative (McNemar's test p value <0.001). Of the 4 patients whose relapse was first identified clinically, one was beyond 3 years, one relapsed intracranially, one had an isolated cutaneous relapse (not detected on the most recent imaging performed 4 months earlier), and the fourth developed new supraclavicular lymphadenopathy just a few days before his next imaging was due (his PET and CT scans 3 months earlier demonstrated complete remission).

Peripheral blood chimerism showed a full donor pattern in 13 of the 34 episodes of progression/relapse, mixed donor/recipient in 16 episodes, and was unknown in 5 episodes.

Nineteen patients had residual abnormalities on CT post-transplant, with a normal simultaneous PET. None of these patients received anti-lymphomatous therapy for the abnormal CT appearances. After a median follow-up of 36 months, 13 of them remained in continuous remission; of the 6 who relapsed, the site of relapse was within the region of CT abnormality in 4, and distant from it in 2.
Administration of DLI

Thirty-nine doses of DLI were administered for 26 episodes of relapse/primary progression, to 22 different patients. Of these 39 doses, 32 were collected by steady-state leucopheresis (for 19 patients), and 7 (for 3 patients) were collected following hematopoietic growth factor stimulation. In 16 of the 26 episodes, chemotherapy, rituximab or radiotherapy (or a combination of these) was also administered, and in a further case (of cutaneous relapse) an excision biopsy was performed.

In 14 of the 26 episodes of relapse treated with DLI +/- chemotherapy, the relapse was diagnosed solely on the basis of an abnormal PET, and 13 of these 14 patients achieved CR. In the remaining 12 episodes (where there was both CT and PET evidence of relapse, \(n=9\); or the diagnosis was clinical, \(n=3\)) CR was attained in 7 cases. In total therefore, in 20 of the 26 episodes of relapse/primary progression, administration of DLI +/- chemotherapy resulted in CR within 6 months of administration.

PET positivity due to infective or inflammatory causes

There were 11 instances of PET positivity due to infective or inflammatory causes, of a total of 475 PET scans performed (2%). Three of these demonstrated increased pulmonary FDG uptake and patients underwent tissue biopsy: in 2 cases an infectious agent was identified (one fungal infection, one tuberculosis), and in the third a non-specific inflammatory appearance was observed histologically. A fourth patient had abnormal mediastinal lymph node uptake on PET (and lymphadenopathy on CT) which
was found on biopsy to be due to sarcoidosis. Patient 5 had femoral FDG avidity which was histologically proven to be due to bone remodelling at a site previously treated with radiotherapy. In the other 6 cases, the FDG avidity was observed in cervical lymph nodes in patients who were documented to be suffering from an upper-respiratory tract infection at the time, and the abnormalities resolved spontaneously after their respiratory symptoms improved. In every case, spontaneous normalisation of PET appearances was documented on subsequent scans in the absence of any anti-lymphomatous treatment.

Chimerism status and incidence of graft-versus-host disease (GVHD)

There was no significant difference in the proportion of patients who showed full donor chimerism at 6 months between the PET negative pre-transplant group and the PET-positive pre-transplant group (12/38 vs. 13/42, \( p = 1.000 \)).

The rate of clinically significant GVHD (i.e. grade II-IV acute, or any chronic) occurring prior to DLI administration was similar for patients who were PET negative and those who were PET positive pre-transplant (10/38 vs. 12/42, \( p = 0.638 \)). However the rate of clinically significant GVHD was significantly lower in the evaluable patients who relapsed compared to those who did not (4/28 vs. 18/52, \( p = 0.018 \)).

In total, DLI were administered for 26 episodes of relapse: of these, 10 were complicated by GVHD (including 2 grade II-IV acute, 2 limited chronic, and 5 extensive chronic). Of the 14 episodes of DLI administered for PET positivity alone, 4 were complicated by GVHD, of which none were grade II-IV acute, 2 were limited chronic,
and 1 was extensive chronic. In the latter case, DLI administration had been prompted by two consecutive PET scans showing extensive FDG uptake, above and below the diaphragm, with progression between the two scans. Administration of DLI resulted in a rapid improvement in PET appearances, but was followed by extensive chronic GVHD, manifest as arthritis.
Discussion

The present study is the first prospective examination of the role of PET imaging in allogeneic stem-cell transplantation. Our data indicate that in patients with chemo-sensitive lymphoma, PET status prior to transplant had no significant effect on OS, PFS, cPFS, and relapse/progression rate. However, following allogeneic SCT, surveillance with PET imaging did add clinically useful information to that provided by CT.

The observation that pre-transplant PET status did not predict outcome following reduced intensity allogeneic SCT contrasts with the findings of most published studies which have investigated the role of PET prior to autologous transplantation.\textsuperscript{10-12} Each of these studies indicated that OS and PFS in patients with metabolic evidence of residual lymphoma pre-autologous SCT was significantly worse than in patients with negative PET scans pre-transplant. By comparison, with a median follow-up of nearly 45 months, neither group had reached median OS in our study. It is possible that the relatively small number of patients in some histological sub-groups obscured a genuine correlation between pre-transplant PET status and outcome in certain types of lymphoma, but, overall, our data suggest that reduced intensity SCT may surmount the unfavourable prognostic effects of a positive PET pre-transplant. This is in keeping with the conclusion of a small retrospective study which investigated the prognostic role of PET imaging prior to \textit{myeloablative} allogeneic transplantation,\textsuperscript{20} and is of considerable clinical significance: patients with chemo-sensitive relapsed lymphoma who are PET-
positive after salvage chemotherapy should not be excluded from reduced intensity SCT.

The difference between our findings and those from studies examining autologous transplantation implies that either the conditioning regimen, or the GVL effect of the transplant and subsequent DLI, abrogates the negative effects of low-level persistent disease (as evidenced by PET positivity) pre-transplant. Of the 10 episodes of relapse treated with DLI alone, CR was achieved within 6 months in 9 patients. This strongly suggests the presence of a GVL effect in this context and is consistent with previous observations from our centre. The inverse association between the presence of clinically significant GVHD and relapse also points to the presence of a GVL effect.

Any GVL effect is most likely to be effective in the presence of relatively low disease burden, and consequently relapse should ideally be detected early to maximise its benefit. We observed that post-transplant PET surveillance detected 17 relapses (half of all episodes) which were not apparent on simultaneous CT scans. Further, of the 26 relapses treated with DLI +/- chemotherapy, PET alone directed therapy in 14 episodes. Early intervention, facilitated by PET scanning, may have contributed to the encouraging outcomes seen. By contrast, no relapses were detected on CT that were not evident on PET. Taken together, this might imply that where available, routine post-transplant surveillance with PET alone may be the preferred strategy.

The 11 instances of PET positivity due to inflammatory or infective causes demonstrate the importance of interpreting the findings from one imaging modality together with
those from others and the clinical scenario. For example, the 6 cases with FDG-avid cervical nodes in the presence of an upper-respiratory tract infection allowed watchful waiting instead of intervention.

The low rate of histological confirmation of relapse in our study (only three were biopsy-proven, largely due to anatomical difficulties) raises the possibility that some of the cases of relapse diagnosed solely on the basis of a positive PET were actually false-positives. We think this is unlikely, because of the following: in the majority of cases the FDG-avid lymph nodes were at the site of previous disease; there was no concurrent clinical suggestion of an infective or inflammatory cause; and in all the patients these changes either resolved following anti-lymphomatous therapy, or progressed to overt relapse. Furthermore, administration of DLI in this situation appears relatively safe – of the 14 episodes of DLI administration guided by PET positivity alone, only one resulted in extensive chronic GVHD, and in this case the PET appearances on repeated scans were highly suspicious of relapsed lymphoma. Therefore, whilst administration of DLI solely on the basis of PET abnormalities may theoretically risk overtreatment, with the potential to cause unnecessary GVHD, the observed rate of clinically significant GVHD was low, and we believe was more than compensated by the likely benefit of treating relapses early with relatively low T-cell doses of DLI.

The characterisation of residual post-therapy masses is a common problem in the management of patients with lymphoid malignancies. The findings of this study indicate that PET is a valuable tool in this situation: only a small minority of the patients with residual PET-negative abnormalities on CT relapsed at the site of these abnormalities.
This suggests that some patients with a negative PET and stable abnormalities on CT can simply be observed without compromising their outcome.

It is possible that by increasing the scanning interval after the first 9 months post-transplant we might have diminished the potential benefit of using a sensitive imaging modality such as PET. However, the schedule was based on our prior experience of the timing of relapse in similar patients, and it is notable that in this study 22 of the 34 relapses occurred within 9 months of transplantation. Further, of the 12 later relapses, it is likely than 7 would not have been diagnosed earlier by the use of more frequent routine scans between 9 and 36 months, since 4 were detected less than 3 months following a scheduled scan (either clinically or on additional imaging requested in view of equivocal abnormalities on the scheduled scan) and 3 occurred after 36 months. Therefore routine imaging of all 80 patients every 3 months for 3 years would have resulted in earlier detection of, at most, 5 relapses and it is unlikely that such a surveillance schedule could be justified. It should also be noted that in all 5 cases therapy resulted in remission within 6 months.

In conclusion, a positive pre-transplant PET scan does not preclude a successful long-term outcome in patients with chemosensitive lymphoma. PET is a valuable imaging modality in the post-transplant management of such patients and detected relapse before CT in half of episodes, often allowing earlier administration of DLI. It should therefore be considered in the routine surveillance of patients following reduced intensity allogeneic SCT for lymphoma.
Acknowledgments

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Authorship contributions

JRL performed data collection and analysis, and wrote the paper. JBB and PJE reviewed patient imaging, wrote the paper, and designed the study. KSP performed data collection & analysis, wrote the paper and participated in patient management. KJT, RKC, AKF, PDK, ECM, AHG & DCL performed data collection, participated in patient management, and revised the paper. MR performed data analysis and wrote the paper. SM participated in patient management, wrote the paper and designed the study.

Conflict of Interest Disclosures

There are no conflicts of interest to disclose.
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6. Robinson SP, Goldstone AH, Mackinnon S, et al. Chemoresistant or aggressive lymphoma predicts for a poor outcome following reduced-intensity allogeneic progenitor cell transplantation: an analysis from the Lymphoma Working Party of
the European Group for Blood and Bone Marrow Transplantation. Blood. 2002;100(13):4310-4316.


# Tables

**Table 1:** Baseline and transplant related characteristics according to pre-transplant PET status

<table>
<thead>
<tr>
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<th>PET negative (n=38)</th>
<th>PET positive (n=42)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Age at transplant</td>
<td>46.7 (10.6)</td>
<td>42.1 (12.9)</td>
<td>0.085</td>
</tr>
<tr>
<td>Male</td>
<td>27 (71.1)</td>
<td>28 (66.7)</td>
<td>0.810</td>
</tr>
<tr>
<td>GVHD (pre-DLI)</td>
<td>10 (26.3)</td>
<td>12 (28.6)</td>
<td>0.638</td>
</tr>
<tr>
<td>Full donor chimerism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(6 months post-SCT)</td>
<td>12 (31.6)</td>
<td>13 (31.0)</td>
<td>1.000</td>
</tr>
<tr>
<td>Lymphoma subtype</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Follicular</td>
<td>14 (36.8)</td>
<td>16 (38.1)</td>
<td>0.387</td>
</tr>
<tr>
<td>Hodgkin</td>
<td>8 (21.1)</td>
<td>14 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Mantle cell</td>
<td>5 (13.2)</td>
<td>6 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Diffuse large B-cell</td>
<td>6 (15.8)</td>
<td>1 (2.4)</td>
<td></td>
</tr>
<tr>
<td>Transformed follicular</td>
<td>3 (7.9)</td>
<td>3 (7.1)</td>
<td></td>
</tr>
<tr>
<td>Peripheral T-cell</td>
<td>2 (5.3)</td>
<td>2 (4.8)</td>
<td></td>
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<tr>
<td>Donor type</td>
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<td></td>
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<tr>
<td>Matched</td>
<td>13 (34.2)</td>
<td>16 (38.1)</td>
<td>0.761</td>
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<tr>
<td>Mismatched</td>
<td>3 (7.9)</td>
<td>5 (11.9)</td>
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<tr>
<td>Sibling</td>
<td>22 (57.9)</td>
<td>21 (50.0)</td>
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Table 2: Indication for transplantation according to PET and CT status pre-transplant

<table>
<thead>
<tr>
<th>Subtype</th>
<th>PET negative (n=38)</th>
<th>PET positive (n=42)</th>
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<tbody>
<tr>
<td></td>
<td>CT positive (n=17)</td>
<td>CT negative (n=21)</td>
</tr>
<tr>
<td>Follicular lymphoma*</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Mantle cell lymphoma</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Transformed follicular</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Peripheral T-cell lymphoma</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*14 patients with follicular lymphoma were PET-negative pre-transplant. Of these 3 had evidence of FDG-avid disease at some stage prior to transplant (but were rendered PET-negative immediately pre-transplant by salvage chemotherapy). A further 3 patients relapsed with FDG-avid disease post-transplant. It is therefore possible that up to 8 patients with FL did not have FDG-avid disease.
Table 3: Cause of death according to PET status pre-transplant

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>PET negative</th>
<th>PET positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Disease progression</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Graft-versus-host disease</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Encephalomyelitis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Accidental</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pneumonitis</td>
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<td>0</td>
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Figure legends

Figure 1. Survival estimates of outcome following reduced-intensity allogeneic SCT according to pre-transplant PET status. All lymphoma subtypes are shown (percentages on the graphs indicate 3-year rates for each outcome). (A) Overall survival. (B) Non-relapse mortality. (C) Relapse and primary progression. (D) Progression-free survival. (E) Current progression-free survival.
Figure 1

(A) Overall survival

(B) Non-relapse mortality
Figure 1 (cont.)

(C) Relapse and primary progression

(D) Progression-free survival
Figure 1 (cont.)

(E) Current progression-free survival

PET negative pre-SCT
PET positive pre-SCT

Survival

Months since SCT

66%
62%
Prognostic role of PET scanning before and after reduced intensity allogeneic stem cell transplant for lymphoma