Prognostic value of pretransplantation positron emission tomography using fluorine 18-fluorodeoxyglucose in patients with aggressive lymphoma treated with high-dose chemotherapy and stem cell transplantation

Karoline Spaepen, Sigrid Stroobants, Patrick Dupont, Peter Vandenberghe, Johan Maertens, Guy Bormans, José Thomas, Jan Balzarini, Christine De Wolf-Peeters, Luc Mortelmans, and Gregor Verhoef

The study assessed the prognostic value of fluorine 18-fluorodeoxyglucose positron emission tomography ([^{18}F]FDG-PET) after salvage chemotherapy before high-dose chemotherapy with stem cell transplantation (HDT/SCT) in patients with induction failure or relapsing chemosensitive lymphoma. Retrospective analysis of the clinical and conventional imaging data of 60 patients scheduled for HDT/SCT was performed in parallel with the analysis of the [^{18}F]FDG-PET results. To determine the ability of [^{18}F]FDG-PET to predict clinical outcome, PET images were reread without knowledge of conventional imaging and clinical history. Presence or absence of abnormal [^{18}F]FDG uptake was related to progression-free survival (PFS) and overall survival (OS) using Kaplan-Meier survival analysis. Thirty patients showed a negative [^{18}F]FDG-PET scan before HDT/SCT; 25 of those remained in complete remission, with a median follow-up of 1510 days. Two patients died due to a treatment-related mortality but without evidence of recurrent disease at that time (228-462 days). Only 3 patients had a relapse (median PFS, 1083 days) after a negative [^{18}F]FDG-PET scan. Persistent abnormal [^{18}F]FDG uptake was seen in 30 patients and 26 progressed (median PFS, 402 days); of these 26, 16 died from progressive disease (median OS, 408 days). Four patients are still in complete remission after a positive scan. Comparison between groups indicated a statistically significant association between [^{18}F]FDG-PET findings and PFS ($P < .000001$) and OS ($P < .00002$). [^{18}F]FDG-PET has an important prognostic role in the pretransplantation evaluation of patients with lymphoma and enlarges the concept of chemosensitivity used to select patients for HDT/SCT. (Blood. 2003;102:53-59)

Introduction

Depending on the histology and risk factors, 30% to 75% of patients with advanced Hodgkin disease (HD) and aggressive non-Hodgkin lymphoma (NHL) can be cured with front-line treatment.[1,2] However, patients who do not achieve complete remission (CR) at the end of first-line treatment or who have a relapse after CR have a poor prognosis regardless of any further conventional treatment.[3] Compared with standard chemotherapy, treatment with high-dose chemotherapy combined with stem cell transplantation (HDT/SCT) increases progression-free survival (PFS) and overall survival (OS), especially in lymphoma patients still chemosensitive to treatment.[4,5] The international consensus conference on high-dose therapy with hematopoietic SCT in aggressive NHL[6] recommended HDT/SCT as the treatment of choice for patients with chemosensitive first or subsequent relapse based on the randomized prospective Parma trial[5] as well as for patients with induction failure. Chemosensitivity and response to treatment are currently assessed on the basis of clinical, radiologic, and pathologic (bone marrow) criteria. X-ray computed tomography (CT) remains the standard for evaluation of nodal disease. However, defining response criteria based on conventional radiographic characteristics remains difficult because lymphoma patients treated with chemotherapy often present with residual masses of uncertain significance. These residual masses may consist of fibrotic tissue or viable tumor and CT cannot differentiate between active tumor and fibrosis.[7] Fluorine 18-fluorodeoxyglucose positron emission tomography ([^{18}F]FDG-PET), using increased glycolysis to differentiate between fibrosis and active tumor, was first reported by Paul[8] as a functional imaging technique for the detection of lymphomas. [^{18}F]FDG-PET has been demonstrated to be more precise than conventional radiologic imaging techniques for restaging after chemotherapy.[9] Several groups, including our own, have reported the important prognostic value of [^{18}F]FDG-PET during and after chemotherapy to identify patients who require further intensified chemotherapy.[10-12] However, the value of [^{18}F]FDG-PET to predict clinical outcome after HDT/SCT has yet to be established because only a few papers have been published regarding this issue.[13,14] In the present study, we assessed the prognostic value of a pretransplantation [^{18}F]FDG-PET scan in patients with chemosensitive lymphoma, treated with salvage chemotherapy before HDT/SCT. If only patients with a negative scan can achieve a long-term CR after HDT/SCT, selection of patients who may benefit from this toxic treatment based on

From the Departments of Nuclear Medicine, Oncology, Hematology, and Pathology, UZ Gasthuisberg, Leuven, Belgium; and Rega Institute, Katholieke Universiteit, Leuven, Belgium.

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Reprints: Luc Mortelmans, Department of Nuclear Medicine, University Hospital Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium; e-mail: luc.mortelmans@uz.kuleuven.ac.be.

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[18F]FDG-PET may be more precise than based on CT alone and definitions of response could include [18F]FDG-PET results in their criteria.

Patients, materials, and methods

Patient selection

Between January 1996 and June 2001, the PET patient database of our department was matched with the SCT database of our hospital regardless of any criteria other than being on the 2 lists. Of the 142 lymphoma patients who recieved transplants who had [18F]FDG-PET for various reasons, 60 were eligible for the study based on the following inclusion criteria: patients with histologic proven NHL or HD with induction failure (defined as progression during induction treatment or within 90 days after the end of treatment) or first/subsequent relapse, sensitivity to conventional-dose salvage chemotherapy based on conventional diagnostic methods (CDMs), a follow-up of at least 1 year, and an [18F]FDG-PET scan in addition to CDM at restaging between salvage therapy and HDT/SCT performed within an interval of at least 3 weeks after the last chemotherapy or last irradiation and not more than 8 weeks prior to HDT/SCT.

Front-line therapy

According to departmental trials at that time, patients with HD had received either the MOPP/ABV (mechlorethamine, Oncovin [vincristine sulfate], procarbazine, prednisone, Adriamycin [doxorubicin], bleomycin, vinblastine) hybrid regimen or the Stanford V regime.[15] Patients with NHL had received either CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or CHVmP/BV (cyclophosphamide, doxorubicin, teniposide, prednisone, bleomycin, vincristine).

Salvage therapy and conditioning regimen

After documented progression or relapse, patients received either VIM-DHAP (etoposide, ifosfamide, methotrexate-dexamethasone, cytarabine, cisplatin) or dexa-BEAM (dexamethasone, carmustine, etoposide, cytarabine, mephalan) as salvage treatment. Involved-field radiotherapy after salvage therapy was applied in patients with initial bulky disease or residual masses on CT. The conditioning regimen used for all patients was BEAM (carmustine, etoposide, cytarabine, mephalan).

SCT

Autologous SCT was performed in 54 patients and allogeneic SCT in 6 patients.

Staging procedures

Before salvage chemotherapy, the extent of disease was assessed by CDM. CDM consisted of a clinical examination, laboratory screening, chest x-ray, CT of the thorax and abdomen, ultrasound, bone marrow biopsy, and, if indicated, magnetic resonance imaging (MRI). Restaging was also performed after the end of salvage therapy and after HDT/SCT. The results of conventional diagnostic tests and follow-up were drawn from the patient's records. Patient's remission status was assessed using recently reported standardized guidelines.[16]

[18F]FDG-PET imaging

All patients had at least one [18F]FDG-PET scan between salvage chemotherapy and before HDT/SCT. In addition, baseline [18F]FDG-PET scans before chemotherapy were available in 56 patients and follow-up [18F]FDG-PET scans after SCT in all patients. Whole-body [18F]FDG-PET scans were performed with a CTI Siemens ECAT 931 tomograph (Siemens-CTI, Knoxville, TN). All patients fasted for at least 6 hours before [18F]FDG-PET scanning and the serum glucose level was measured before scanning. All patients had a glucose level less than 120 mg/dL and no patient had diabetes. A dose of 10-15 mCi (370-555 MBq) [18F]FDG was administered intravenously as a bolus. Patients received a diuretic to minimize image artifacts due to urinary stasis and were kept well hydrated. Between injection and scanning, patients were asked to lie still to avoid muscular [18F]FDG uptake. A whole-body acquisition was performed 60 minutes after injection and consisted of 10 non-overlapping bed positions, during 4 minutes per bed position so that the total effective field of view extended from the head to the upper part of the thighs. To keep time for the patients in the scanner short, no attenuation correction was performed. The images were iteratively reconstructed.[17] For the purpose of this study, the baseline and posttreatment [18F]FDG-PET scan from each patient was reviewed in batch by 2 experienced nuclear medicine physicians (K.S. and S.S.), who were blinded to all clinical, radiologic, and follow-up data. All scans were scored either as positive or negative. Negative was defined as having no evidence of disease. Positive was defined as any focal or diffuse area of increased activity in a location incompatible with normal anatomy and suspect for residual disease.

Statistical analysis

The aim of this study was to evaluate the role of [18F]FDG-PET before HDT/SCT in predicting PFS and OS. PFS was defined as the time interval from the date of entry into the salvage protocol until the first objective evidence of relapse/progression or date of last follow-up. OS was calculated from the date of entry into the salvage protocol until lymphoma-related death. Survival curves were calculated by Kaplan-Meier survival analysis and comparison between groups was performed by the log-rank test. Multivariate analysis by proportional hazard (Cox) regression was performed to evaluate the significance of the International Prognostic Index (IPI)[18] for NHL, respectively, the prognostic score[19] for HD, and [18F]FDG-PET findings on PFS and OS.

Results

Thirty-seven men and 23 women who underwent an [18F]FDG-PET scan before HDT/SCT were included in the study. The median age was 37 years (range, 12-65 years). Nineteen patients had HD and 41 had NHL. The indication for HDT/SCT was induction failure in 28 patients, first chemosensitive relapse in 22 patients, and second chemosensitive relapse in 10 patients. All patients were staged at progression or relapse according to the Ann Arbor clinical stage; histology of biopsies was classified according to the Revised American Lymphoma classification[20] and the IPI for NHL and a prognostic score for HD were calculated. Table 1 shows the characteristics of the 60 patients.

Of the 60 scans performed before HDT/SCT, 30 scans showed residual abnormal FDG uptake, and 30 scans were considered negative. According to these findings, patients were divided into 2 groups. The results of the pretransplantation [18F]FDG-PET scan and the restaging according to CDM are shown in Figure 1.

PET-positive cases before HDT/SCT

In the group of 30 positive pretransplantation scans, 26 patients experienced relapse after HDT/SCT. The median PFS was 402 days (range, 104-1666 days). Specifications with regard to histology, sex, age, stage, prognostic factors, and prior treatment are listed in Table 1. Although all patients were categorized as chemosensitive to salvage chemotherapy based on CDM, 12 patients in this group achieved a partial response before HDT/SCT. But in the remaining 14 patients, CDM showed no evidence for residual lymphoma and only [18F]FDG-PET was positive for residual disease. During further treatment, 16 patients (2 HD and 14 NHL) died of progressive disease (median OS, 480 days; range, 208-1086 days), 6 patients

Table 1. Patient characteristics

	Patients, n = 60			
	PET−, n = 30		PET+, n = 30	
Clinical outcome	CR, n = 27	Relapse, n = 3	CR, n = 4	Relapse, n = 26
Age, y, median (range)	38 (15-65)	32 (17-47)	36 (35-56)	34.5 (12-62)
Sex, M/F	16/11	2/1	3/1	16/10
Status				
Primary refractory disease	14	1	2	11
First relapse	9	1	1	11
Second relapse	4	1	1	4
Stage at progression or relapse				
I	3	0	0	2
II	12	2	3	12
III	3	0	0	6
IV	9	1	1	6
B symptoms at progression, yes/no	12/15	1/2	1/3	9/17
Histology				
HD, nodular sclerosis	7	0	2	7
HD, mixed cellularity	2	0	0	0
HD, lymphocyte predominant	0	1	0	0
NHL, diffuse large B-cell lymphoma	11	1	1	9
NHL, anaplastic large B-cell lymphoma	3	1	1	7
NHL, mantle-cell lymphoma	4	0	0	3
Prognostic score				
HD, score 0	1	0	1	4
HD, score 1	3	0	1	2
HD, score 2	4	1	0	1
HD, score 3	0	0	0	0
HD, score 4	1	0	0	0
NHL, low	10	2	1	13
NHL, low-intermediate	4	0	1	4
NHL, high-intermediate	2	0	0	2
NHL, high	2	0	0	0
Frontline therapy				
CHOP	13	1	2	17
MOPP-ABV	6	1	1	4
CHVmP-BV	4	1	0	3
Stanford	4	0	1	2
Salvage therapy				
VIM-DHAP	23	2	1	18
dexa-BEAM	4	1	3	8
Transplantation				
Autologous	25	3	4	22
Allogeneic	2	0	0	4

(2 HD and 4 NHL) are still under treatment, and 4 patients (3 HD and 1 NHL) achieved a CR after additional HDT/SCT.

Only 4 patients with a positive pretransplantation scan achieved a CR after HDT/SCT and sustained a CR after a median follow-up of 1326 days (range, 790-1902 days). Two men with NHL (anaplastic large B cell, IPI low-intermediate; diffuse large B-cell, IPI low) were treated with dexa-BEAM for induction failure after CHOP. Both pretransplantation [18F]FDG-PET scans were positive for residual pathologic FDG uptake in the parahilar region but showed a CR on CDM. These 2 patients suffered from neutropenic fever with positive hemocultures 1 to 2 weeks before the pretransplantation scan, which could explain the false-positive result. After HDT/SCT, the [18F]FDG-PET scans became negative.

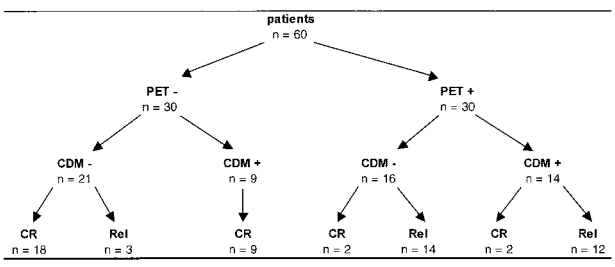

Figure 1. Clinical outcome according to the results of [18F]FDG-PET findings before HDT/SCT. PET indicates positron emission topography; CDM, conventional diagnostic methods; CR, complete remission; and Rel, relapse.

The 2 other patients suffered from nodular sclerosis HD. One 35-year-old woman received VIM-DHAP for a late relapse (prognostic score, 0) and one 37-year-old man received dexa-BEAM for a second relapse (prognostic score, 1). After salvage treatment, [18F]FDG-PET as well as CT were positive for residual disease in the mediastinal region. Neither patient had infectious parameters at that moment but did receive irradiation prior to the [18F]FDG-PET scan. After HDT/SCT, the residual mass remained present on the CT, but all follow-up [18F]FDG-PET scans were negative.

An example of a positive pretransplantation [18F]FDG-PET study in a patient who had a relapse after HDT/SCT is shown in Figure 2, and a false-positive pretransplantation [18F]FDG-PET study is shown in Figure 3. PFS and OS for the total group of

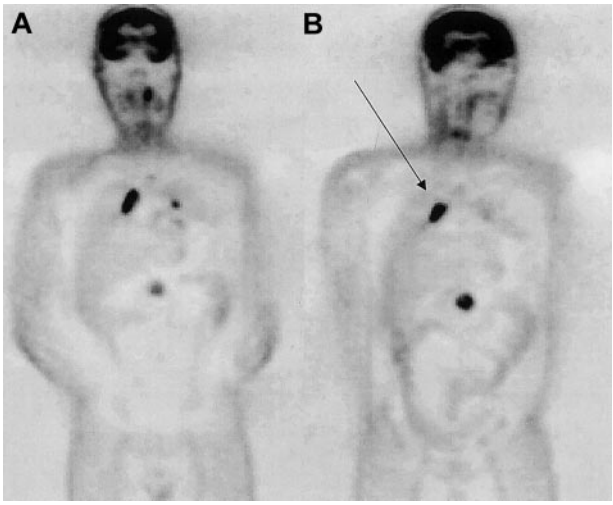

Figure 2. Example of a positive study. Pretransplantation [^{18}F]FDG-PET scan in a patient with diffuse large B-cell lymphoma showed intense residual [^{18}F]FDG uptake (arrow). After HDT/SCT, the patient had a relapse and died of progressive lymphoma (PFS, 104 days; OS, 314 days). (A) Scan before the start of treatment; (B) Scan before transplantation.

PET-positive patients were calculated by Kaplan-Meier survival analysis and are shown in Figures 4 and 5.

PET-negative cases before HDT/SCT

Of the 30 patients with a negative pretransplantation [^{18}F]FDG-PET scan, 25 are still in CR after a median follow-up of 1510 days (range, 377-2155 days). According to CDM, 16 of these patients achieved a CR and 9 patients had only a partial response.

Two patients (anaplastic large B cell, IPI low-intermediate; diffuse large B-cell, IPI low) died after achieving CR following HDT/SCT. One patient died from a cardiac arrest and the other from late septic shock due to a fungal infection. Because postmortem anatomic-pathologic investigation showed no evidence for residual lymphoma, both patients were censored in the analysis at the time of their death (426 days and 228 days).

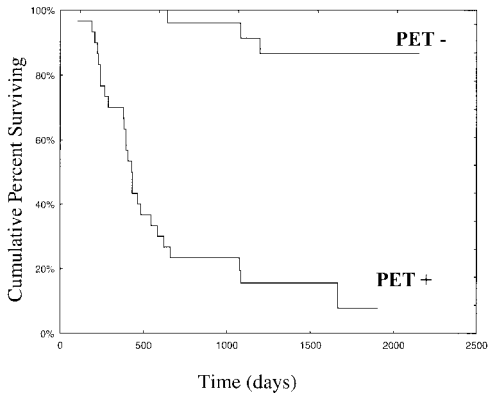

Figure 4. Kaplan-Meier PFS curve. Kaplan-Meier estimate of PFS in 30 patients with a positive pretransplantation [^{18}F]FDG-PET scan compared with 30 patients with a negative pretransplantation [^{18}F]FDG-PET scan.

The remaining 3 patients with a negative pretransplantation [^{18}F]FDG-PET scan had a relapse after HDT/SCT. All 3 patients were also restaged as complete responders by CDM at the time of transplantation. One patient (HD, mixed cellularity, prognostic score 2) who received VIM-DHAP for a first relapse was in CR after HDT/SCT for 1083 days. During that time, all [^{18}F]FDG-PET results remained negative. The late relapse was first suspected by [^{18}F]FDG-PET and biopsy taken at the FDG-positive site was positive for HD. However, the biopsy showed no mixed cellularity but paragranuloma. Because this is a low-grade form of lymphoma, a "watch and wait" policy was followed with still stable disease for the moment. The second patient who had a relapse after a negative pretransplantation [^{18}F]FDG-PET scan was a 47-year-old woman with NHL (diffuse large B cell lymphoma, IPI low) who had received VIM-DHAP for induction failure. This patient had a relapse after 1200 days documented by a splenectomy. The spleen was positive for a low-grade follicular lymphoma and not for a diffuse large B-cell lymphoma. During additional therapy, this patient died (OS, 1482 days) due to septic multiorgan failure. The third patient (NHL, anaplastic large B cell, IPI low) had a second late relapse and received dexa-BEAM as salvage chemotherapy.

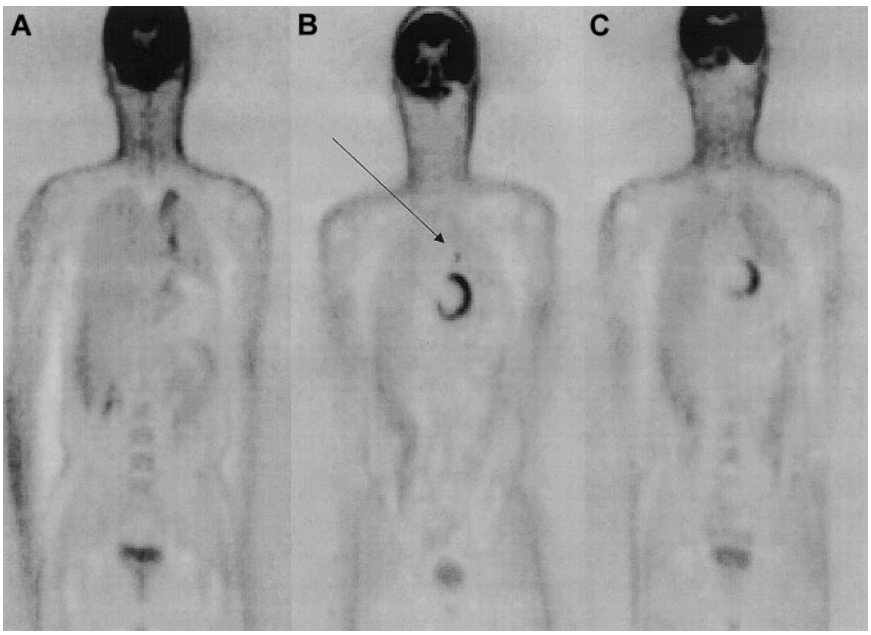

Figure 3. Example of a false-positive study. Pretransplantation [^{18}F]FDG-PET scan in a patient with nodular sclerosis HD showed residual [^{18}F]FDG uptake parahilar after radiotherapy (arrow). After HDT/SCT, the patient remained in CR (follow-up, 1464 days). (A) Scan before the start of treatment; (B) scan before transplantation; (C) scan after transplantation.

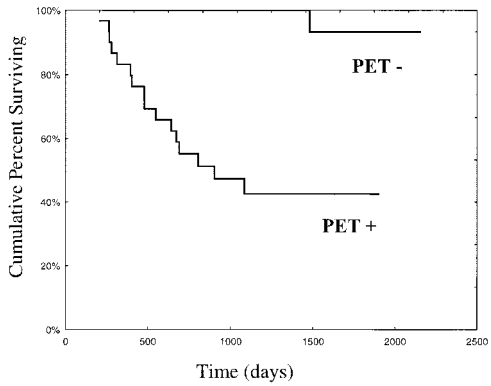

Figure 5. Kaplan-Meier OS curve. Kaplan-Meier estimate of OS in 30 patients with a positive pretransplantation [18F]FDG-PET scan compared with 30 patients with a negative pretransplantation [18F]FDG-PET scan.

During restaging after first- and second-line chemotherapy, the [18F]FDG-PET result became negative and each relapse was first suspected by [18F]FDG-PET. Also before and after HDT/SCT, the [18F]FDG-PET scan and CDM were negative for residual disease. However, the patients relapsed after 646 days and [18F]FDG-PET was the first examination that suspected the relapse. After additional allogeneic SCT, the patient is in CR.

Thus, from the 3 patients who had relapses after a negative pretransplantation [18F]FDG-PET scan, there were 2 relapses with a low-grade component that could explain the false negativity because low-grade lymphomas may express less FDG avidity. However, a negative pretransplantation scan cannot fully exclude minimal residual disease that causes a relapse after HDT/SCT as seen in the third patient. PFS and OS were also calculated by Kaplan-Meier survival analysis for the PET-negative group and are shown in Figures 4 and 5.

Statistical analysis

The detection of vital residual tumor by [18F]FDG-PET before HDT/SCT has a high predictive value for relapse in patients who were thought to be chemosensitive based on CDM. Positivity of [18F]FDG-PET (26 of 30 relapses) was associated with a shorter PFS (median, 432 days; range, 104-1902 days) compared with negativity of [18F]FDG-PET (3 of 30 relapses), which had a median PFS of 1466 days (range, 228-2155 days). Comparison between groups, using the log-rank test, indicated a statistically significant association between [18F]FDG-PET results and PFS ($P < .000001$) and OS ($P < .00002$). The 2-year actuarial PFS and OS rates for patients with negative [18F]FDG-PET scans were 96% and 100%, respectively, as compared with 23% and 55%, respectively, for those with positive [18F]FDG-PET results.

The data were also analyzed for NHL and HD patients separately, and for each subgroup multivariate analyses including the [18F]FDG-PET results and the corresponding prognostic score were performed. For the 41 NHL patients, the log-rank test indicated a statistically significant association between [18F]FDG-PET results and PFS and OS ($P < .000001$ and $P < .0004$, respectively), whereas for the 19 HD patients, the log-rank test was statistically significant for PFS but not OS ($P < .0025$ and $P = .13$, respectively). In the subgroup of NHL patients, the Cox regression analysis revealed a strong prognostic influence of the [18F]FDG-PET findings before transplantation on PFS and OS ($P < .0004$ and $P < .0018$, respectively), whereas the IPI was not a significant prognostic factor ($P = .78$ and $P = .65$, respectively). In the subgroup of HD patients, the Cox regression analyses revealed only a strong prognostic influence of the [18F]FDG-PET findings on PFS ($P < .008$) and not on OS ($P = .24$), whereas the prognostic score was not a significant prognostic factor for both PFS and OS ($P < .82$ and $P < .72$, respectively).

Discussion

Our study clearly demonstrates the important role of [18F]FDG-PET in the evaluation of relapsing lymphoma patients scheduled for HDT/SCT as well as its prognostic significance.

The improvement of outcome after induction treatment with the latest generation of chemotherapy implies that the cases of nonresponding or relapsing patients represent a cohort, which prognostically is becoming even more unfavorable as primary results get better. HDT/SCT has been shown to be the best available treatment for patients with NHL who have a relapse after conventional chemotherapy but who remain chemosensitive,[5] and 2 randomized studies showed that the event-free survival after 3 years for patients treated with HDT/SCT was well over 50%[4,21] for relapsing HD patients. Although these results indicate the superiority of HDT/SCT compared with conventional treatment in patients with relapsing lymphoma, a proportion of patients will develop recurrent disease after this toxic treatment modality. Several studies have investigated different prognostic factors for relapsed and progressive lymphoma patients, who may benefit from HDT/SCT.[22,23] The most important prognostic factors are the remission status before SCT and the chemosensitivity of the tumor.[24] Until now, morphologic imaging modalities (CT and MRI) using sequential determination of tumor size are used to assess tumor response induced by chemotherapy as well as to determine the chemosensitivity of the tumor. However, changes in anatomic structures can sometimes be only a late sign of chemosensitivity because initially enlarged tumor sites may remain enlarged due to the development of fibrosis or necrosis without tumor activity. On the other hand, normal-sized nodal structures may harbor small deposits of active chemoresistant tumor cells, which cause recurrent disease after HDT/SCT.

During the last years, several reports showed that [18F]FDG-PET is the most helpful noninvasive metabolic imaging technique allowing differentiation between active tumor and fibrosis[25,26] and demonstrated the important prognostic value after completion of first-line therapy in patients with both HD[27] and aggressive HL.[10] Moreover [18F]FDG-PET has become a potential tool to differentiate between responders and nonresponders at an earlier time point during chemotherapy than conventional diagnostic methods.[12,28] [18F]FDG-PET seems to be the ideal tool for therapy monitoring of aggressive lymphoma patients and in particular to evaluate the tumor response before HDT/SCT. However, reports about the prognostic role of [18F]FDG-PET in patients scheduled for HDT/SCT is limited. A recent study of Cremerius et al[14] investigated the predictive value of sequential [18F]FDG-PET before and after front-line HDT/SCT in 22 patients with NHL. Six of the 7 patients who did not achieve a partial metabolic response after complete induction therapy developed lymphoma progression, whereas 10 of the 15 patients with complete response or at least partial metabolic response remained in CR. The median PFS and OS of patients with less than partial metabolic response after HDT/SCT were 9 and 29 months, respectively. Direct comparison between these data and our own is not possible because the concept and patient population are totally different. The study was based on the use of HDT/SCT

as a front-line therapy in patients with high-intermediate or high-risk disease according to the IPI and underlined the biologic importance of a sustained response to induction chemotherapy before transplantation. The use of HDT/SCT for this patient population is still controversial and the criteria used to describe the response[29] (< 25% decrease of standard uptake value) is used mainly for solid tumors in a neoadjuvant setting rather than for lymphoma patients. Another study, published by Becherer et al[13] retrospectively looked at 16 HD/NHL patients at first relapse who all received a [18F]FDG-PET scan prior to HDT/SCT. The 1-year PFS and OS were 100% for the PET-negative group and only 18% and 55% for the PET-positive group, respectively. They concluded that [18F]FDG-PET is accurate in the prediction of relapse prior to HDT/SCT. The main disadvantage of this study was the rather small number of patients, the short follow-up, and the inclusion of patients who had chemorefractory disease.

The prognostic role of [18F]FDG-PET in patients scheduled for HDT/SCT has never been tested in a large population of chemosensitive patients in induction failure or first/subsequent relapse. Our data indicate that whole-body [18F]FDG-PET has a high prognostic value for pretransplantation evaluation in patient with aggressive lymphoma still chemosensitive to salvage chemotherapy. Although a negative scan cannot exclude minimal residual disease leading to a late relapse after HDT/SCT, patients with a negative pretransplantation scan have a favorable outcome because only 3 patients with a negative pretransplantation scan had relapse. CDM had no additional value; the relapses occurred late and in 2 of these patients, the biopsy at the site of relapse showed a low-grade lymphoma. It seems reasonable to assume in NHL containing high-grade and low-grade components, [18F]FDG-PET will preferably assess the therapy response of the high-grade component, whereas the low-grade components may escape detection. On the other hand, patients with a residual [18F]FDG uptake before transplantation have a high risk for relapse and a poor prognosis because 26 of 30 patients in this group had a relapse after HDT/SCT and 16 patients died. A possible explanation for the 4 false-positive results were infectious lesions outside the residual mass in 2 patients with infectious parameters at the time of scanning and inflammation in the involved site in 2 patients with residual disease on CT, who received irradiation prior to the [18F]FDG-PET scan.

Although the data clearly indicate the important role of [18F]FDG-PET in relapsing patients still sensitive to chemotherapy, this study has possible limitations. First, patient selection bias is inherent in retrospective analysis. By using strict inclusion criteria on all patients present in our PET database leading to a well-subscribed and homogenous group and by using a strict blinding procedure on the scoring of the [18F]FDG-PET scans, we tried to minimize this problem. Secondly, HD and NHL patients were mainly studied together. An attempt was made to analyze the data for NHL and HD separately, including the influence of the prognostic factors. For the large NHL group, the same results as for the overall group were noticed and the multivariate analyses indicate that [18F]FDG-PET before transplantation is a stronger prognostic factor than the IPI. For the 19 HD patients, the log-rank test was statistically significant for PFS but not for OS. PET-positive HD patients, who had a relapse after HDT/SCT, seem to have a better chance of cure after additional chemotherapy and allogeneic transplantation. Comparison of the [18F]FDG-PET results and the prognostic score showed that [18F]FDG-PET had a stronger prognostic influence on PFS. However, due to the small number of patients, especially in the HD subgroup, the conclusions remain preliminary. Third, we did not use attenuation correction. However, a study of Kozerke et al[30] showed that the use of attenuation correction did not improve the accuracy of [18F]FDG-PET in the detection of lymph node or organ involvement in lymphoma patients. Of more importance seemed to be the experience of the reader regarding the anatomic assignment, knowledge of physiologic uptake, and artifacts and systematic and skillful examination of all regions scanned.

In conclusion, the current data indicate that [18F]FDG-PET after salvage chemotherapy in patients scheduled for HDT/SCT could become part of routine assessment. Patients with a negative pretransplantation scan are unlikely to relapse after HDT/SCT and have a favorable outcome. On the other hand, if abnormal [18F]FDG uptake is seen, further investigation is mandatory to exclude inflammatory or infectious lesions. But most likely, this patient will have residual disease and HDT/SCT will not be the treatment of choice at that point. These patients may benefit from more experimental treatment options in an ultimate attempt to overcome the poor clinical outcome. [18F]FDG-PET enlarges the concept of chemosensitivity used to select patients who may benefit from HDT/SCT, but further large prospective studies are warranted before it is at the point of becoming an absolute requirement for disease assessment in patients scheduled for HDT/SCT.

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