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Original Article

Role of PET/CT in T-cell Lymphoma

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ABSTRACT

Aim: This study aimed to investigate the impact of post-treatment positron emission tomography-computed tomography (PET/CT) findings on predicting disease prognosis in patients with T-cell lymphoma.

Methods: Patients diagnosed with T-cell lymphoma and admitted to the Medical Oncology Clinic of Gazi University Medical Faculty Hospital between 2004 and 2014 were retrospectively evaluated. The study included 24 patients who underwent PET/CT for staging. The correlation between post-treatment PET/CT findings and progression-free survival (PFS) and overall survival (OS) was analyzed.

Results: The 1- and 2-year PFS rates were 78.6% and 50% in the PET-negative group and 40% and 0% in the PET-positive group (p=0.007). No statistically significant difference was found between the two groups regarding 1- and 2-year OS rates (p=0.113). As a result of multivariate cox regression analyses, only age was found to be effective for OS and PFS, and the risk of progression and death increased with older age.

Conclusion: Post-treatment PET/CT findings were not independent predictors of PFS and OS in T-cell lymphomas. However, the small sample size and retrospective design of the study warrant further research with larger patient cohorts.

Keywords: Lymphoma, T-cell, positron emission tomography, prognosis

Introduction

Hodgkin's lymphoma (HL) and non-HL (NHL) are clonal lymphoproliferative diseases arising from immune system cells, each with distinct clinical presentations. Approximately 90% of all lymphomas are NHL and 10% are HL. According to the World Health Organization (WHO) 2008 classification, NHL is categorized into two main groups: B-cell lymphoma and T/NK cell lymphoma [1]. The prevalence of NHL increases with age and is more common in men than in women. Infections, environmental factors, and chronic inflammation have been shown to have an etiology [2]. Immunosuppression is the most clearly defined factor in the etiology of NHL and increases the risk of lymphoma by 50-100 times [3]. Lymphomas are classified based on their morphological appearance based on immune phenotype and genetic characteristics. In 2008, this classification was updated by the WHO. A tissue biopsy sufficient to reveal a large area of cells that exhibit the morphology is essential for a definitive lymphoma diagnosis [4]. Excisional diagnostic biopsy is recommended.

About 10-15% of all lymphomas in Western countries are T-cell NHLs, a diverse group of neoplasms with distinct morphological, immunophenotypic, and clinical characteristics. However, they are more prevalent in Asia [5]. Treatment usually consists of chemotherapy and radiotherapy, but high-dose therapy, autologous stem cell transplantation, and new agents are also used.

Positron emission tomography (PET) is a noninvasive nuclear imaging technique based on introducing a positron-emitting radiopharmaceutical into the body, followed by imaging the distribution and kinetics of the radioactive tracer. PET and computed tomography (CT) are combined in PET/CT and have been used to detect areas of involvement more effectively than CT, especially in aggressive lymphomas [6]. Although there is evidence that using PET in lymphoma staging is effective for progression-free survival (PFS), there is no evidence-based data showing that it increases overall survival (OS), but studies have shown that PET/CT is more sensitive than CT and other conventional methods for identifying lymphoma

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involvement [7-10]. PET also showed metabolic activity in the lesions. Fluorine-18-2-fluoro-2-deoxy-D-glucose PET (F18-FDG-PET) is a functional imaging modality used for initial and posttreatment staging. F18-FDG uptake before and after treatment is essential for determining treatment response and prognosis [11]. According to the PET result, it may be possible to direct the patient to more aggressive treatment modalities.

This study aimed to evaluate the relationship between post-treatment PET/CT findings and both PFS and OS in individuals diagnosed with T-cell lymphoma.

Methods

Patients diagnosed with T-cell lymphoma and admitted to the Medical Oncology Clinic of Gazi University Hospital between 2004 and 2014 were retrospectively evaluated. The study included 24 patients who underwent PET/CT for staging. Patients who had received chemotherapy or radiotherapy prior to F18-FDG PET/CT were excluded from the study. PET/CT was used to evaluate treatment responses in conjunction with conventional CT and magnetic resonance imaging methods. PET/CT performed following the completion of treatment was referred to as PET2. PET/CT was performed at least 3-4 weeks following the end of chemotherapy and at least 8 weeks following the end of radiotherapy. The Deauville criteria were used for the response evaluation. Complete response, partial response, stable disease, and progressive disease (PD) were the classifications used to describe treatment responses.

All PET scans were performed according to the standard F18-FDG PET/CT imaging protocol at Gazi Faculty of Medicine, Department of Nuclear Medicine.

Ethical approval for this study was obtained from the Ethics Committee of University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital on November 11, 2015 (protocol number: E-15-596).

Statistical Analysis

The Statistical Package for the Social Sciences software for Windows 11.5 was used to analyze the data. We provided descriptive statistics for numerical variables as mean±standard deviation or median (minimum-maximum), while categorical variables were represented as number of cases and percentages (%). The Kaplan-Meier method was used to evaluate the survival data, and univariate survival analysis was performed via the log-rank test. Independent prognostic factors were identified by multivariate Cox regression analysis. PFS was defined as the duration from treatment initiation to the occurrence of disease progression, death, or most recent follow-up. OS was defined as the duration from treatment initiation until death or recent follow-up. All tests were conducted in a one-sided manner, and $p<0.05$ was considered statistically significant.

Results

The study included 24 patients diagnosed with T-cell lymphoma. Median age was 45 years (range 19-84 years). 75% of the patients were male (n=18). Splenic involvement was present in 20.8%, extranodal involvement in 45.8%, and B symptoms in 37.5%. 29.2% (n=7) of patients had stage 1, 25% (n=6) stage 2, 25% (n=6) had stage 3, and 20.8% (n=5) had stage 4 disease. Table 1 provides additional details about the patients' clinical and demographic characteristics.

Table 1. Demographic and clinical characteristics of patients

	n=24
Age, mean±SD	45.7±17.7
Sex, n (%)	
Male	18 (75.0)
Female	6 (25.0)
The type of lymphoma, n (%)	
NK/T HL	9 (37.5)
PTHL	6 (25.0)
AITL	5 (20.8)
T-cell lymphoblastic leukemia/lymphoma	2 (8.3)
Cutaneous anaplastic lymphoma	1 (4.2)
ALK + ALCL	1 (4.2)
IPI, n (%)	
0	4 (16.7)
1	8 (33.3)
2	5 (20.8)
3	7 (29.2)
Stage, n (%)	
1	7 (29.2)
2	6 (25.0)
3	6 (25.0)
4	5 (20.8)
Splenic involvement, n (%)	5 (20.8)
B symptoms, n (%)	9 (37.5)
Performance status, n (%)	
0	21 (87.5)
1	3 (12.5)
High LDH level, n (%)	11 (45.8)
Extranodal involvement, n (%)	11 (45.8)
Extranodal involvement site, n (%)	
Subcutaneous	4 (36.4)
Liver	1 (9.1)
Bone marrow	3 (27.3)
Meninx	1 (9.1)
Nazal cavity	2 (18.2)
Chemoteraphy type, n (%)	
CHOP	11 (45.8)
SMILE	4 (16.7)
R-CHOP	2 (8.3)
HCVAD	2 (8.3)
CHOEP	1 (4.2)
CVP	1 (4.2)

Table 1. Continued

	n=24
Other variables, n (%)	2 (8.3)
Number of chemotherapy applications, median (min-max)	5 (1-8)
Salvage regime, n (%)	9 (37.5)
Stem cell transplantation rate, n (%)	9 (37.5)
Radiotherapy, n (%)	9 (37.5)
Response, n (%)	
Complete response	16 (66.7)
Partial response	4 (16.7)
Progressive disease	4 (16.7)
PET1 positivity, n (%)	23 (95.8)
SUV 1, median (min-max)	9.2 (3.8-25.9)
PET3 positivity, n (%)	5 (25.0)
SUV 3, median (min-max)	5.1 (2.8-6.7)
Last response, n (%)	
Complete response	8 (33.3)
Partial response	2 (8.3)
Stable disease	2 (8.3)
Progressive disease	12 (50.0)
Relapse, n (%)	12 (50.0)
Exitus (n (%)	12 (50.0)

HL: Hodgkin lymphoma, PTHL: Peripheral T-cell lymphoma, AITL: Angioimmunoblastic T-cell lymphoma, ALK: Anaplastic lymphoma kinase, ALCL: Anaplastic large cell lymphoma, LDH: Lactate dehydrogenase, PET: Positron emission tomography, SUV: Standardized uptake value, CHOP: Cyclophosphamide, vincristine and doxorubicin, SMILE: Dexamethasone, methotrexate, ifosfamide, l-asparaginase and etoposide, R-CHOP: Rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone, HCVAD: Cyclophosphamide, vincristine, doxorubicin, dexamethasone, CHOEP: Cyclophosphamide, doxorubicin, vincristine, prednisolone, etoposide, CVP: Cyclophosphamide, prednisolone, vincristine, SD: Standard deviation, IPI: International Prognostic Index, min-max: Minimum-maximum

All patients underwent PET/CT before primary chemotherapy (PET1), and a positive result due to lymphoma was found in 23 patients. All chemotherapy completers (n=20) underwent PET/CT (PET2). Four patients did not undergo PET/CT because of the mortality of PD. PET2 was negative in 15 patients after the end of treatment. A total of 12 patients developed relapse/progression during follow-up. Among these patients only 4 of them had a positive PET result, while 8 of them had complete remission according to PET2.

Survival analyses were performed using the PET (PET2) result after the primary chemotherapy.

A statistically significant difference was observed in PFS between the PET2-negative and PET2-positive patient groups and between the groups divided according to the International Prognostic Index (IPI) score (p=0.007, p=0.045). No statistically significant discrepancy in OS was observed between patient groups classified as PET2-negative or PET2-positive, as well as among different IPI score categories (Figures 1-4).

Factors such as stage, high lactate dehydrogenase levels, and extranodal involvement did not significantly affect OS or PFS (Table 2).

As a result of univariate statistical analyses, the combined effects of all possible risk factors that are effective or thought to be effective on PFS and OS were investigated. IPI, PET2, and age variables were included in the baseline model. When the combined effects of all three factors were analyzed, none of these factors were found to be statistically significant predictors of PFS, whereas age was found to be predictive of OS independent of IPI and PET2, and the risk of death increased with increasing age [HR=1.106; 95% confidence interval (CI): 1.015-1.205 and p=0.022]. On the other hand, when retrospectively analyzed, only age was found to be effective for PFS and OS (HR=1.060; 95% CI: 1.012-1.110, p=0.013; HR=1.070; 95% CI: 1.014-1.129, p=0.013).

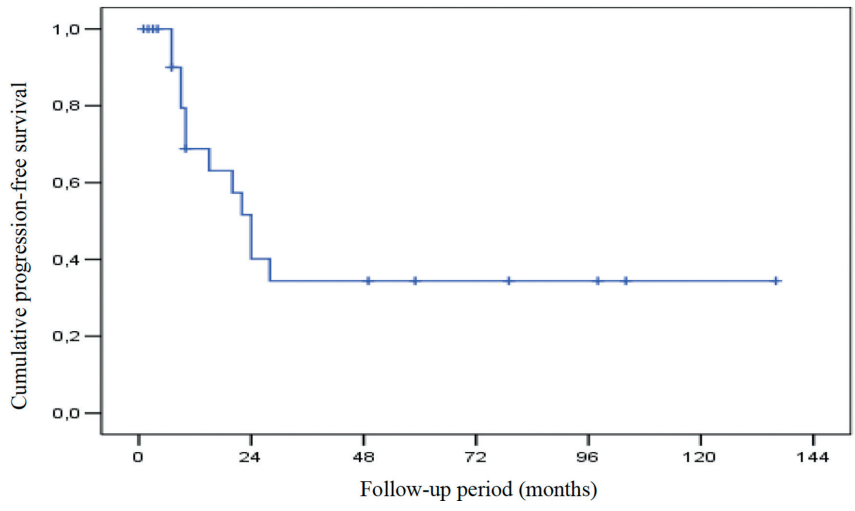

Figure 1. Progression-free survival

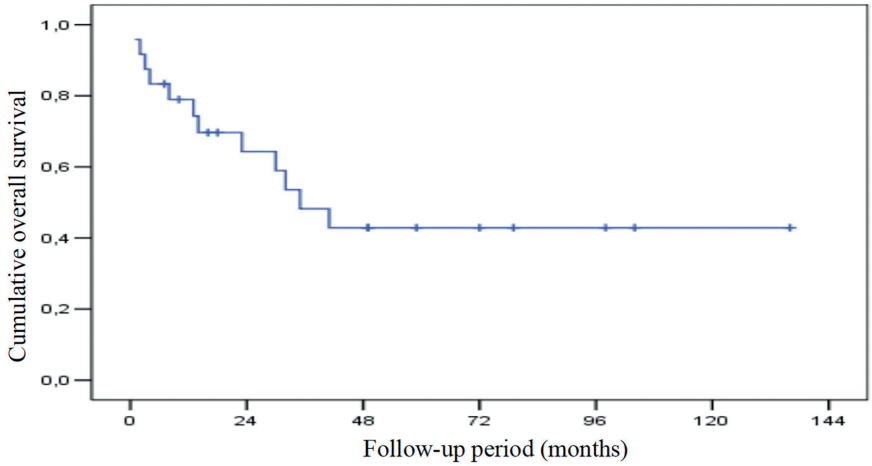

Figure 2. Overall survival in all patients

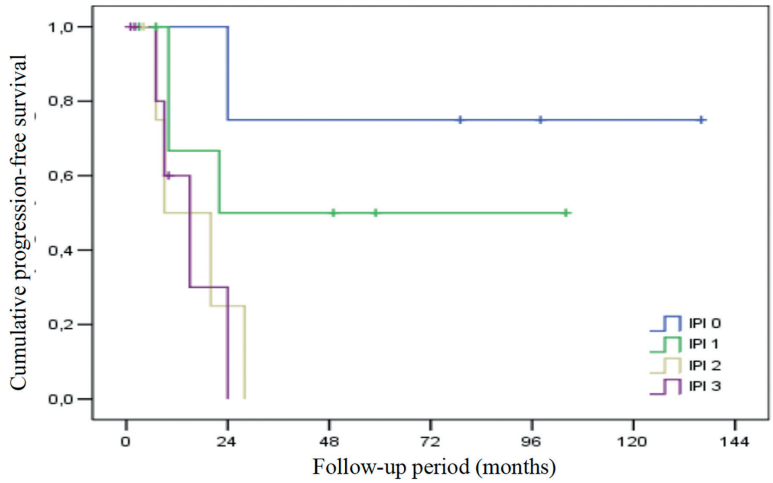

Figure 3. Relationship between IPIs and progression-free survival
IPI: International prognostic Index

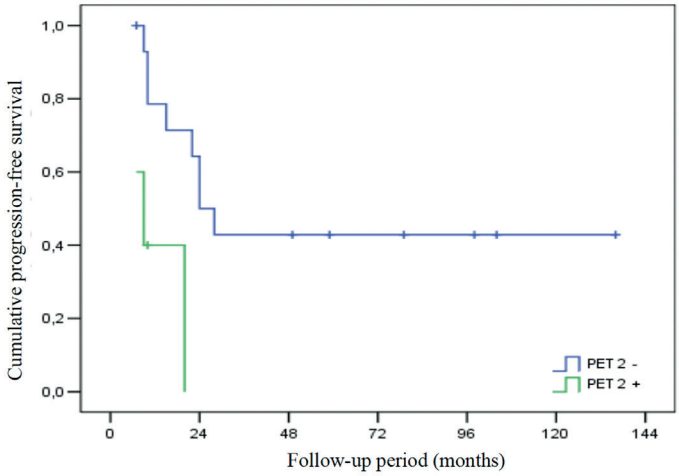

Figure 4. Relationship between PET2 and progression-free survival
PET: Positron emission tomography

Discussion

In this study, 24 patients with T-cell lymphoma were assessed with post-treatment F18-FDG-PET/CT. After a median follow-up period of 26.5 months (range 1-136 months), PET/CT was performed in 83.3% of patients at the end of treatment. PET scans were negative in 15 patients post-treatment, with progression/relapse occuring in 4 patients who remained PET2-positive. Relapse/progression was observed in 8 of the 15 patients with negative PET results post-treatment. PET positivity predicted relapse/progression in 80% of the patients, which is consistent with the literature, whereas 46% of PET-negative patients remained in remission.

Tomita et al. [12] retrospectively evaluated the predictive value of F18-FDG-PET (post-PET) after first-line treatment for peripheral T-cell lymphomas (PTHL). Thirty-six patients were included. Sixteen patients presented with PTHL-not otherwise specified (PTHL-NOS) and 20 with angioimmunoblastic T-cell lymphoma (AITL). Post-PET results were positive in 31% (11/36) and negative in 69% (25/36) of the patients. In the groups with positive and negative PET results, the 3-year PFS rates were 18% and 62%, respectively ($p<0.001$). Patients with positive post-PET results developed PD in 9 of 11 patients (positive predictive value 82%). In comparison, 16 of 25 patients in the negative post-PET group did not develop PD (negative predictive value 64%). The 3-year OS rates were 44% for PET-positive patients and 84% for PET-negative patients ($p=0.03$). These findings suggest that post-PET can predict prognosis in patients with PTHL. In the study by Cahu et al. [13], a total of 54 T/NK cell lymphoma patients (15 PTHL-NOS and 11 AITL patients) were evaluated using PET/CT before (n=44) and after (n=31) treatment. Interim evaluation by PET/CT was negative in 25 of 44 patients, whereas 19 of 31 patients achieved complete remission on PET/CT after treatment. In patients with anaplastic lymphoma kinase (ALK)-positive anaplastic large cell lymphoma, a 4-year PFS rate of 80% was observed, with post-treatment PET/CT showing a negative predictive value of 83% (n=9). In ALK T/NK lymphomas, patients with a negative interim PET/CT evaluation exhibited a 4-year PFS rate of 59%, whereas those with a positive interim PET/CT evaluation showed a PFS rate of 46% ($p=0.28$, n=35). Similarly, no statistically significant disparity was observed in 4-year PFS between patients with negative and positive PET/CT after treatment (51% and 67%, respectively, $p=0.96$). The 4-year cumulative relapse incidence in ALK-T/NK lymphomas was 53% among patients who had negative post-treatment PET/CT. Despite F18-FDG uptake upon diagnosis, negative interim or posttreatment PET/CT scans do not exhibit a significant association with improved PFS in ALK-positive T/NK lymphomas.

In this study, patients with negative PET2 results had 1- and 2-year PFS rates of 78.6% and 50%, respectively, and a mean PFS of 68.4 months. In contrast, the 1- and 2-year PFS rates for PET2-positive patients were 40% and 0%, respectively, with a mean PFS of 12.6 months. A statistically significant disparity in PFS was observed between the groups ($p=0.007$). There were no statistically significant differences in 1- and 2-year OS between PET2-negative and PET2-positive patients.

Unlike the studies by Tomita et al. [12] and Cahu et al. [13], Li et al. [14] examined interim PET scans and post-PET outcomes in a cohort of 88 patients with T/NK cell lymphomas (23 PTHL-NOS and 3 AITL), who underwent treatment with CHOP and various anthracycline-free chemotherapy protocols. The study found that both interim and posttreatment PET results were independently associated with PFS and OS in patients with T/NK cell lymphoma. However, it is important to note that in this study, only 13 patients with PTHL (all PTHL-NOS) underwent post-PET evaluation. The contradictory results of these investigations might be attributable to variations in treatment protocols and histological types.

Study Limitations

This study has some limitations, including the retrospective nature of our investigation, the limited number of patients included in the study, the inhomogeneity of histological tumor distribution, differences in first-line chemotherapy regimens, and differences between the completion of chemotherapies (1-8 cycles).

Conclusion

In this study, post-treatment PET/CT findings were not found to be independent predictors of PFS and OS in T-cell lymphomas. Although numerous studies have demonstrated the role of PET/CT in diagnosing and staging T-cell NHL, further prospective randomized clinical trials are needed to confirm the value of interim evaluation and post-treatment PET/CT in predicting disease prognosis.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Ethics Committee of University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital on November 11, 2015 (protocol number: E-15-596).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: E.Ç., M.B., Surgical and Medical Practice: E.Ç., M.B., Concept: E.Ç., M.B., Design: E.Ç., M.B., Data Collection or Processing: E.Ç., Analysis or Interpretation: E.Ç., M.B., Literature Search: E.Ç., M.B., Writing: E.Ç., M.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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