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Mortality Analysis by Means of F-18 FDG PET/CT in High Grade Extranodal Head and Neck Lymphoma

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Abstract

The aim of this study is to decide the diagnostic value of F-18 Fluorodeoxyglucose (FDG) Positron emission tomography/Computed tomography (PET/CT) in the predictive value of survival of the patients with diagnosis of extranodal lymphoma of the head and neck (ENL).

Materials and Methods: 18 patients (10 F, 8 M; mean: 54,3±21.1 years old) with the diagnosis of head and neck ENL were included in the study. The F-18 FDG PET/CT images of the patients were analyzed retrospectively and the maximum standardized uptake value (SUVmax) levels of the primary tumors at the initial evaluation were recorded and compared with mortality results of the patients in the follow up.

Results: The initial SUVmax levels of the patients with progressive and stable-responsive disease were not significantly different and the difference between the SUVmax levels of the patients who died was not statistically significant.

Discussion and Conclusion: F-18 FDG PET/CT is the gold standard imaging modality in the diagnosis and follow up of the lymphoma. Head and neck ENL is a special group of lymphoma with different prognosis. This analysis demonstrated that the mortality of the patients with high grade head and neck ENL might not be predicted by means of initial SUVmax levels.

Keywords**:** *lymphoma, extranodal, FDG, SUV, PET/CT.*

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Introduction

Head and neck ENL is a relatively rare disease and the study series are generally very small in the literature (1, 2). There are different primary sites of ENL including brain, orbital, sinus, tonsil and laryngeal lymphoma (2, 3). The most accurate analysis method for lymphoma is F-18 FDG PET/CT and considered routine method for staging, restaging, and treatment response evaluation in follow up of lymphoma. Previous studies also have shown prognostic efficiency of lymphoma (4). However there are conflicting results about the mortality prediction potential of F-18 FDG PET/CT for ENL patients (4, 5). The aim of this study is to analyze the relationship of the FDG uptake value (SUVmax) of the primary tumor and mortality of the patients with ENL of the head and neck region.

Materials and Methods

Patients

18 patients (10 F, 8 M; mean: 54,3±21.1 years old) were the subjects of this study. The patients included in the study were informed about the imaging study and informed consents of the patients or the guardians were obtained. The study was approved by the Mersin University Ethics Committee. The study was conducted according to the principles of Helsinki Declaration.

The included patients necessarily had mass lesion in the head and neck region diagnosed as high grade lymphoma by the pathology results. The patients with indolent lymphoma and/or generalized disease outside the head and neck were not included. The patients had single tumor site at the head and neck region and may be some additional lymph nodes outside the head and neck region were the neck (n=14), mediastinum (n=2), abdomen (n=5), axillary lymph nodes (n=2), liver (n=2) and interestingly two patients were present in this study group with ENL of the other organs (breast and uterus). The mean diameter of the primary lesions of the patients were 50,39±33,8 mm and SUVmax levels of these lesions were mean 20,7± 10,57. The metabolic and size characteristics as well as localization information is included in the Table 1. Two of the tumors were localized in the tongue, four in the brain, five in the sinuses, three in the tonsils and remaining four among the muscles and bone. The histopathological characteristics of the tumors are listed in the Table 1. Necessarily all the tumors were high grade lymphoma; twelve of them were B cell lymphoma, two were Hodgkin lymphoma, two were T cell and one was Burkitt lymphoma.

Table 1. Summary of the results of the patients in the study group

No	Primary	Other	Pathology	SUV	Mortality (Month)
1	Tongue	Cervical, abdomen	Diffuse large B cell	37	6
2	Tongue	Cervical	Diffuse large B cell	29,5	-
3	Occipital	Cervical, axillary	Anaplastic B cell	9	-
4	Occipital	Cervical	Diffuse large cell B lymphoma	13,3	-

5	Sphenoid sinus	Uterus	Diffuse large cell B lymphoma	35	12
6	Ethmoid sinus	-	Hodgkin	41,3	6
7	Maxillary sinus	Cervical, lung, spleen	Burkitt	18,6	2
8	Brain	Breast	Diffuse large B cell	41,3	6
9	Tonsil	Nazopharengs, cervical	Diffuse large B cell	9,1	
10	Maxilla	Supraclavicular,cervical	NK cell nonhodgkin lymphoma	12	2
11	Maxilla	Cervical	Diffuse large B cell	8	
12	Brain	-	Diffuse B cell	25,3	
13	Tonsil	Mediastinum	Diffuse B cell	18,2	
14	Tonsil	Mediastinum	T cell	9,81	
15	Cervical	Mediastinum, abdominal, spleen	Hodgkin	25,3	
16	Nasal septum	Cervical	Diffuse B cell	11,2	
17	SCM	Cervical	Burkitt	29,2	
18	Right mandibule	Cervical, axillary, pleural, abdominal	Diffuse B cell	20,5	

SUV: Standardized uptake value, SCM: Sternocleidomastoid muscle

Imaging

The patients were prepared for the examination with at least 4 hours fasting and limiting physical effort at least 24 hours before the study. The radiopharmaceutical injection was performed (mean 370 MBq (10 mCi), according to the body weight) to each patient via venous line 60 minutes before the imaging. The imaging was performed by PET/CT scanner (GE, Discovery PET/CT 610, US) with additional low dose CT scan (130 kV, 50 mAs, a pitch of 1.5, a thickness of 5 mm, in 70 cm field of view) for attenuation correction without intravenous contrast administration but oral contrast administration, from the skull base to the upper thigh with the acquisition time of 3 min per bed position.

Interpretation of the images was performed by two experienced Nuclear Medicine physicians. The SUVmax levels corresponding to the region of interest drawn as elliptic shape were calculated by the computer software.

Statistics

The descriptive settings of continuous parameters were given as mean and standard deviation, and for categorical variables as number and percentage. Kaplan Meier analysis was used to compare survival time and LogRank test was used for comparison of groups. Statistical analysis was performed in MedCalc package program.

Results

During the follow up of 18 patients of mean 18.33±24.68 months 11 patients had disease progression and 6 patients died in mean 11±12.87 months and one patient responded to the treatment (Fig. 1).

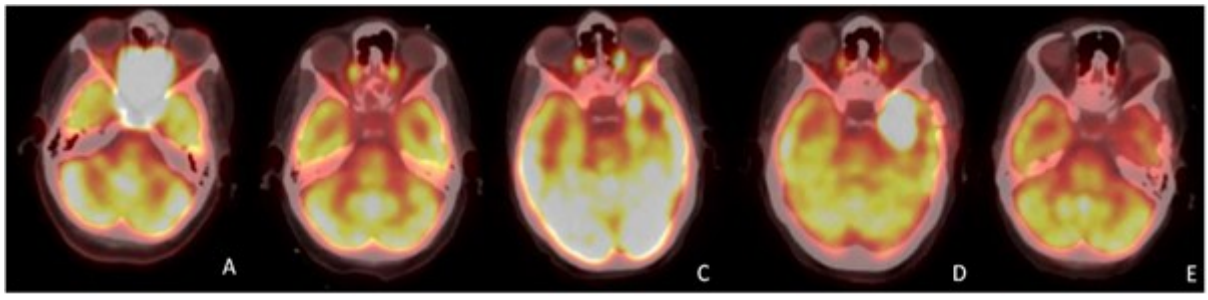

Figure 1. B cell lymphoma of the sphenoid sinus at the first staging (A), at the first treatment response evaluation at 3rd month follow up (B), at first recurrent lesion in the follow up at medial temporal lobe (C), progressive FDG accumulation in the previously determined lesion in medial temporal lobe (D), after performance of the biopsy (E) F-18 FDG PET/CT fusion images; the patient died in the first year follow up.

The SUVmax levels of the patients at the initial diagnosis were compared in the disease progressive and non progressive patients as well as the patients who died and survived. The analysis showed no statistical difference between the levels (Table 2).

Table 2. The SUVmax levels of the patients with and without disease progression and survived and died.

	SUVmax	P value
Progression-Non-progression	23±12,45 vs 18±8,39	0,3
Death-Survivors	27,6±11,7 vs 17,2±8,4	0,05

Kaplan-Meier analysis curves also showed no significant difference between the patient groups' survival analysis when the cut-off level was accepted as '20.7' (Fig. 2).

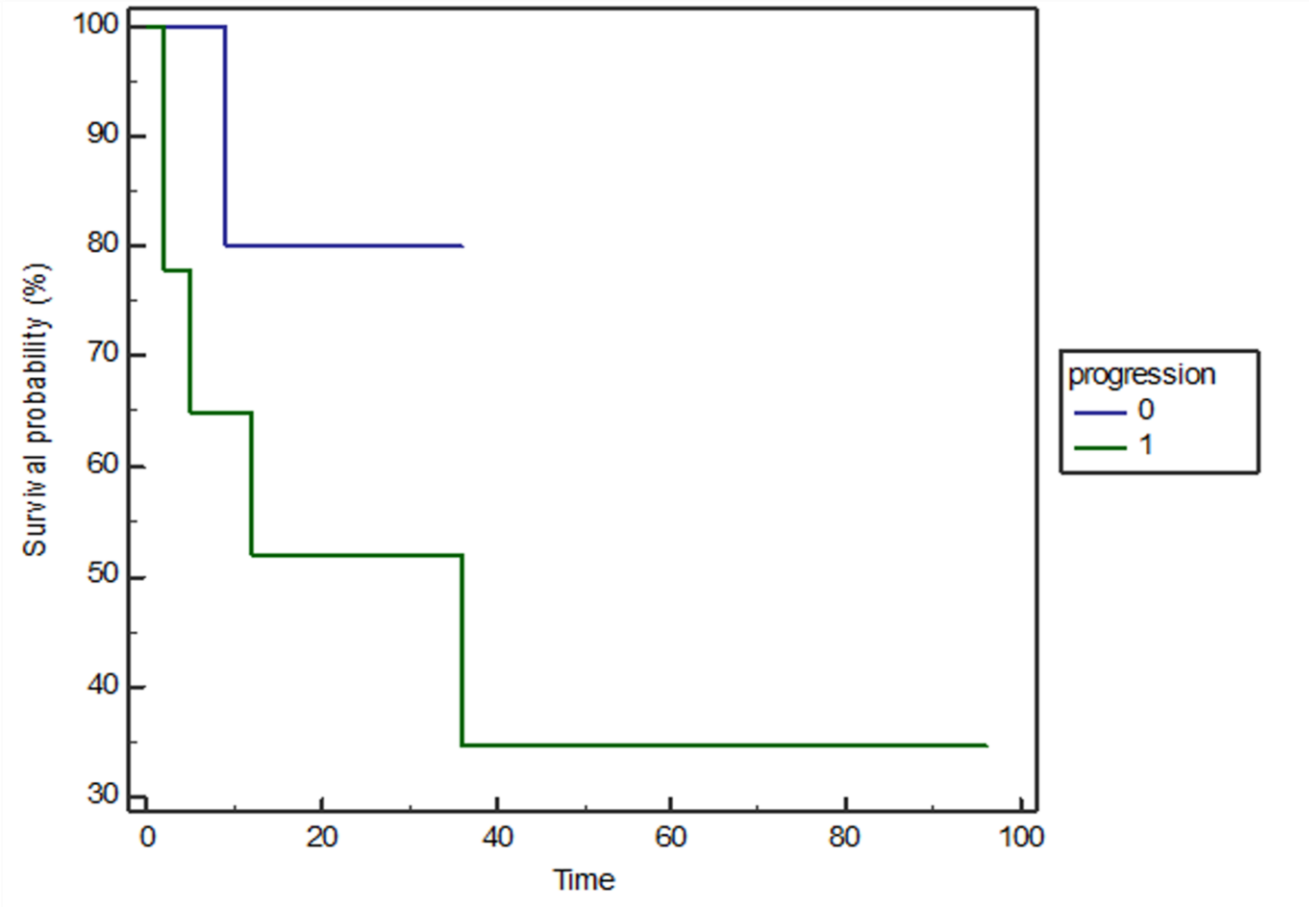

Figure 2. Kaplan Meier curves.

Discussion

The most common site for the presentation of ENL is the gastrointestinal tract and head and neck is the second common site with diffuse B cell type (6). The disease presentation as well as prognostic parameters are completely different compared to the other type of lymphoma patients in this special subgroup. These group of patients are generally worse prognostic patients especially the high grade group. This study included the patients with high grade lymphoma and analysis of these patients' mortality results. In this study group most of the patients were B cell and rarely T cell lymphoma as previous studies identified series of NHL of head and neck which were also B cell NHL and fewer T cell lymphomas with worse outcome (7). In this study group there were no laryngeal lymphomas however there are several samples of laryngeal lymphoma in the largest series involving only four cases (8, 9). Relatively rare subgroup is tonsil lymphoma with less than <1% of the head and neck tumors which was presented with three cases in this study group (10). Brain lymphoma includes the 2-4% of ENL's and this study group had four patients presented as brain lymphoma (11). Since the brain has physiological FDG uptake it might be difficult to differentiate brain lymphoma but it might be useful in showing

the recurrence as well as other sites of involvement and exclude the diagnosis (11). In this study we could show the recurrent brain lesion in high contrast despite the physiological uptake. This may be related to the high grade nature of the included tumors.

A case presentation has shown single site MALT lymphoma involvement of the parotid gland which is the rarest lymphoma presentation (12). Since this study was designed as high grade lymphoma analysis the case in this group with MALT lymphoma was excluded from the group. Orbital lymphoma subgroup constitutes 8% of the ELN's which might show high FDG uptake (13). However the orbital type lymphoma patients in this study group was also excluded because the tumor was low grade.

Most of the patients included in this study group were B cell type; either diffuse large B cell or anaplastic type in one patient. B cell lymphoblastic lymphoma might also present as head and neck tumor and might involve skin or bone (14). Three of the B cell lymphoma patients in this study group were also skin or mandible lesions. Prognostic information obtained from the F-18 FDG PET/CT has been investigated by previous research. In a previous analysis including NK-T cell head and neck ENL patients' high tumor FDG uptake has found to be associated with local invasion and aggressive tumor and unfavorable outcome (15). Among the two patients with NK cell and T cell head and neck tumors in this study group the one with NK cell type died in two months after the diagnosis. However that patients' SUVmax level 12 was not significantly higher than the mean of the study group. F-18 FDG PET/CT has high prognostic value in most of the malignant tumors which has been previously well documented.

The F-18 FDG PET/CT is the most relevant imaging modality in staging of the lymphoma patients. According to a previous study compared CT alone and PET/CT; metabolic imaging has changed the stage of disease in 16% of patients with ENL (16). In an analysis including 139 patients with ENL PET/CT imaging has shown higher diagnostic accuracy in especially head and neck tumors (17). In another study including 26 patients with the head and neck ENL's have shown favorable disease outcome in the patients with lower FDG uptake (15). The researchers additionally found that SUVmax might improve the prognostic value of the F-18 FDG PET/CT study (15). Similarly, Byun et al. have found significant correlation between SUVmax and the outcome of the patients in their patient population including NHL patients (18). Contrary to these results Schrepfer et al. have demonstrated that high SUVmax levels was correlated with better survival in patients with primary ENL of head and neck region (15). These findings were also supported by the results of this study. According to the results of the study of Suh et al. pretreatment F-18 FDG PET/CT can predict the survival outcome in patients with ENKTL of the head and neck and high SUVmax is associated with worse survival (19). These results are in correlation with the results of the generalized lymphoma patient groups according to the previous studies (20), as well as other malignancies (21). Furthermore the histological aggressiveness of the type of the lymphoma has found to be in association with SUVmax levels (22). The mean SUVmax levels of the tumors of patients in previous series of Suh et al. was lower than the patients in this study group '5.5'.5 The group of the patients in this analysis represents high grade lymphoma thus the mean SUVmax levels of the primary tumors were higher. A recent review analyzed the role of F-18 FDG PET/CT imaging in head and neck tumors however there are limited information about the ENL of the head and neck (23).

The limitation of this study were retrospective nature of the study but the study has the strength of including special subgroup of the patients with the same region and being high grade tumors. The length of the follow

up period was sufficient enough to draw a conclusion of the mortality analysis. Although the outcome of this study was not predicted in the beginning of the study there is no such data in this kind of homogeneous patient population previously.

Conclusion

This study results showed that mortality assessment by means of the uptake of the primary tumor of the patients with head and neck ENL is not possible. Further studies with larger patients groups and longer term follow up results might verify this observation.

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Authorship Contributions

Concept: Z.P.K. **Design:** Z.P.K. **Supervision:** Z.P.K., P.P.O., E.S., A.A., G.O., **Data Collection and/or Processing:** Z.P.K., P.P.O., E.S., A.A., G.O., **Analysis and/or Interpretation:** Z.P.K., P.P.O., E.S., A.A., G.O., **Literature Review:** Z.P.K., **Writer:** Z.P.K.

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

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