Original Article, PET/CT.

Prediction of Baseline Quantitative Indexes of F-18 FDG PET/CT to Outcome in Adult Non Hodgkin Lymphoma

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ABSTRACT:

Purpose: The aim of this study was to investigate the effectiveness of initial quantitative indexes of FDG PET 18F-FDG PET/CT in adult Non Hodgkin Lymphoma patients on therapy outcome. **Patients and Methods:** A total of 57 adult patients initially diagnosed with non-Hodgkin Lymphoma were retrospectively analyzed in this study within period of January 2018 till December 2019. Initial 18F-FDG PET/CT scan was done before chemotherapy, interim 18F-FDG PET/CT done after receiving two cycles of chemotherapy. SUV max, SUV mean SUV peak, MTV, and TLG was extracted from both initial and interim 18F-FDG PET /CT scans and recorded. Follow up period was 6 – 24 months.

Results: Regarding clinical outcome at end of chemotherapy, initial TMTV and TLG were found statistically significant (p 0.005) & (p 0.010) respectively. On multivariate analysis; ΔSUV max was found to be statistically significant (p <0.001). Regarding 2Y relapse free survival rate; initial 18F-FDG PET/CT TLG quantitative parameter was found statistically significant where 2Y-RFS rates for high- and low-TLG groups were 100% and 66.7% respectively (p 0.011).

Conclusion: ΔSUV max was found to successfully predict clinical outcome at end of chemotherapy cycles. Initial 18F-FDG PET/CT TLG quantitative parameter successfully predict 2 Y-RFS.

Keywords: Non Hodgkin lymphoma, FDG PET/CT, Metabolic Parameters.

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INTRODUCTION:

Malignant lymphoma is considered the most common hematological malignancy in adults and ranked as the four most common adult malignancy constituting about 8.4 % of all adult malignancies diagnosed annually [(1)].

18F-FDG PET/CT is a functional imaging modality utilized in diagnosis, initial staging, evaluation of early response to therapy, identification of metastatic lesions, and detection of relapse/recurrence. 18F-FDG PET/CT has an eminent role in the management of malignant lymphomas [(2)].

SUV max is the most frequently used relatively because of the suitability and great reproducibility of measurement. It reveals the metabolic activity of the most aggressive tumor cell. However, Metabolic Tumor Volume (MTV) and Total Lesion Glycolysis (TLG) can reveal more information than SUV max and rising evidences have specified their possible significance [(3)].

Quantitative analysis is able to detect small changes with high accuracy. Also, quantitative analysis is more observer independent than visual qualitative analysis. Numerous researches have explored that quantitative volumetric parameters extracted from baseline ^{18} F-FDG PET/CT such as total metabolic tumor volume (TMTV) or total lesion glycolysis (TLG) might have an important predictive role in diffuse large B-cell lymphoma, follicular lymphoma, peripheral T-cell lymphoma, extra-nodal natural killer/T-cell lymphoma, and Hodgkin lymphoma [(4)].

Liang et al. analyzed 18F-FDG PET/CT scans of 48 patients initially diagnosed with Follicular Lymphoma (FL). Upon performing a multivariable analysis, they found that TMTV and TLG were both independent prognosticators of progression free survival and overall survival. ROC curve analysis showed the optimal cut-off values for ΔTMTV and ΔTLG were 66.3% and 64.5 % respectively. They stated that baseline 18F-FDG PET/CT scans TMTV and TLG are significant predictors of PFS and OS in FL. Moreover, interim 18F-FDG PET/CT scan TMTV (ΔTMTV more than 66.3%) and TLG (ΔTLG more than 64.5%) reduction are appreciated parameter that may predict early therapy response evaluation in FL patients [(5)].

The aim of this study: to assess the prognostic and predictive value of in initial and interim 18F-FDG PET/CT metabolic and volumetric parameters value on therapy outcome.

PATEINT AND METHODS:

This Retrospective study included 57 adult patients presented at National Cancer Institute (NCI) within the period of January 2018 till December 2019. All patients, already had pathologically proven non Hodgkin Lymphoma, were referred to Nuclear Medicine department to perform their initial evaluation by 18F-FDG PET/CT in their pre-therapy stage.

Clinical information were obtained from the medical records, including age, sex, diagnostic methodologies, pathological details, other imaging modality findings, treatment response and survival data.

Inclusion criteria:

• Adult patients (older than 18 years old).

• Pathologically proven Non Hodgkin lymphoma.

• Patients who underwent baseline 18F-FDG PET/CT.

Exclusion criteria:

• Pediatrics (younger than 18 years old).

• Patients with relapsing Lymphoma.

• Patients having double primary tumors.

• Patients who received chemotherapy and/or radiotherapy prior to performing baseline 18F-FDG PET/CT.

• Patients who received radiotherapy as a sole treatment.

All patients were informed about details of the research. The ethical committee of NEMROCK and the radiation safety committee at NCI had given authorization for study design.

FDG PET-CT: Patients are instructed not only to fast for at least four to six hours prior to the scan (in order to keep adequate low glucose and insulin levels), but also to drink water to preserve good hydration.

Image Acquisition:

1. Positioning and field of view:

- Imaging from skull base to proximal thigh protocol is basically recommended.

- Arms should be elevated above the head in order to perform an optimum acquisition as arms along the side can result in beam-hardening artifacts.

- Urinary bladder emptying should be done prior to image acquisition in order to minimize radiation dose to kidneys and urinary bladder.

2. CT imaging Protocol:

- CT was performed for the purpose of anatomic localization and attenuation correction (AL/AC) or as an enhanced diagnostic CT scan.
- In case of AL/AC, a low milliampere-seconds setting is recommended in order to minimize radiation dose to the patient.
- In case of enhanced diagnostic CT scan, standard CT milliampere-seconds setting is recommended for optimization of spatial resolution of the CT scan.
- Intravenous iodinated contrast material is essential to achieve state of the art CT images, although high intravascular concentrations of intravenous contrast agents may result in an attenuation correction artifact on PET images, however the effect is modest. This effect is minimalized by the utilization of suitable correction factors.

3. PET Emission imaging Protocol:

- Emission images acquisition was acquired at least 45 up to 60 minutes post intravenous radiopharmaceutical administration.
- 18F-FDG uptake time should be standardized especially when two scans are being compared using SUV.
- Emission images acquisition time ranges from 1 - 2 minutes per bed position and generally based upon administered 18F-FDG activity, patient's body weight, and utilized PET scanner sensitivity. Classically for acquisition from skull base to mid-thigh, total acquisition time ranges from 15 up to 20 minutes.

Data Processing, Interpretation, and Analysis:

Images were transferred automatically to the processing workstation. They were displayed as multi-planar reconstructed images as PET images, CT images, and fused PET/CT images in the axial, sagittal, and coronal planes. 18F-FDG PET/CT scans were analyzed by two experienced Nuclear Medicine physicians. Accuracy of the scan was determined grounded on clinical and imaging follow up. A compatible PC was utilized to store data and yield graphic presentations of this study conducted results.

Imaging Interpretation:

• Qualitative (Visual) assessment:

For 18F-FDG PET/CT analysis, any focal, or patchy inhomogeneous 18F-FDG uptake, higher than mediastinal and hepatic reference in the same scan was interpreted as abnormal uptake of 18F-FDG, while CT images were reviewed for conforming CT changes.

• Semi-Quantitative assessment:

The Total Metabolic Tumor Volume (TMTV), Total Lesion Glycolysis (TLG), Maximum Standardized Uptake Values (SUV max), Mean Metabolic Tumor Volume (Δ MTV), Mean Total Lesion Glycolysis (Δ TLG), Mean Standardized Uptake Value (Δ SUV max) were documented for the all active pathological lesions in every patient once manual application of the volumetric regions of interest on the trans-axial attenuation-corrected PET slices was applied; surrounding areas representing the maximum 18F-FDG accumulation as well as being away from any adjoining intersecting activity.

$$\textbf{SUV} = \frac{\text{Tracer activity in tissue (mCi/gm)} \times 100}{\text{Injected Radiotracer dose (mCi)/ Patient Weight (Kg)}}$$

Metabolic Tumor Volume (MTV) was calculated with 41 % of the max SUV uptake value threshold as stated by the European Association of Nuclear Medicine [(6)]. Total Metabolic Tumor Volume was obtained by gaining the sum of all metabolic volumes of all local or distant nodal and extra nodal lesions.

- **TLG** = Summation of all (mean SUV x MTV for every lesion) [(7)].
- **Δ SUV max** = (SUV max1 – SUV max2)/SUV max1) X 100 [(8)].
- **Δ MTV**= (MTV1 – MTV2)/ (MTV1) X 100 [(8)].
- **Δ TLG**= [(SUVmean1 X Vol1) – (SUVmean2 X Vol2)] / [SUVmean1 X Vol1] X 100 [(8)].

Additional sizable region of interest was drawn over the normal hepatic tissue whose max SUV was regarded as being the reference activity.

18F-FDG PET/CT Response Criteria:

Response evaluation based on 18F-FDG PET/CT founded on metabolic activity, specified by ^{18}F-FDG uptake. The SUV functions as a marker of metabolic activity, and response evaluation is now centered on visual assessment of 18F-FDG uptake and grouped according to the "five-point scale". The five-point scale integrates the Deauville criteria for evaluation on interim 18F-FDG PET/CT images [(9)].

Four groupings of response have been delineated as follows:

(a) Complete metabolic response—score of 1, 2, or 3.

(b) Partial and Stable metabolic response—score of 4 or 5 with reduced ^{18}F-FDG uptake.

(c) Progressive metabolic disease—score of 4 or 5 with increase uptake or with newly detected lesions.

Follow up Protocol:

Clinical and follow up data for patients were recovered from medical records at the hospital in order to assess patients' response to therapy up until the last visit of the patient. Interim, end of treatment and follow up 18F-FDG PET/CT were done regularly according to the following schedules: two to three weeks after the end of the second chemotherapy cycle, four to eight weeks after completion of therapy, about 6 months during follow up period for patients to confirm induction of complete remission.

Assessment of Survival:

• **Progression free survival:** time interval between maintenance of complete remission and manifestation of a relapsing event.

• **Overall survival:** time interval starting from beginning of therapy till death or last recorded follow up in the clinical sheet.

Statistical Analysis:

- Data management and analysis was performed using Statistical Package for Social Sciences (SPSS) vs. 25.
- Numerical data were checked for normality and were statistically described in terms of means and standard deviations or medians and ranges as appropriate. Comparison between numerical variables was done using Student t-test when normally distributed and ***Mann-Whitney U*** test if non- normally distributed for independent groups. For paired groups, Paired t- test was used to compare numerical variables when normally distributed and Wilcoxon signed rank test were used if non- normally distributed.
- Categorical data were described as numbers and percentages. When comparing categorical data, ***Chi*** square test or ***Fisher's*** exact test were performed as appropriate.
- Multiple Logistic regression analysis was used for determining independent variables associated with the clinical outcome.
- ***McNemar*** Test was used to compare Deauville Score and Q-PET and agreement between them was done using ***Kappa*** statistics.
- Survival analysis was done using Kaplan-Meier method and comparison between two or more survival curves using log rank test with Bonferroni adjustment when necessary.
- All numerical variables were categorized into binary groups for ***KaplanMeier*** analysis using the median value of each ($<$ or $\geq$ median). All statistically significant factors on Kaplan-Meier analysis entered the multivariate cox-regression analysis using forward likelihood-ratio (LR) method for variable selection.

RESULTS:

Patient characteristics: A total of 57 patients (40 men and 17 women; median age, 49 years) were included in the analysis. DLBCL subtype was the vast majority forming 78.9 % (45 patients). Regarding the presence of extra-nodal sites lymphomatous affection; only 5 patients (8.8%) had extra nodal sites ***(Table 1)***.

Table (1): Patients' clinical characteristics (no=57).

Characteristics	value
Number of patients	57
Age (years), Median (Range)	18 to 77 (49)
Gender:	
Male	40 (70.2%)
Female	17 (29.8%)
Pathologic subtype:	
DLBCL	45 (78.9%)
Follicular	5 (8.8%)
Burkitt	2 (3.5%)
T-cell	3 (5.3%)
MALT	1 (1.8%)
Small lymphocytic	1 (1.8%)
Ann-Arbour Staging:	
I-II	27 (47.4%)
III-IV	30 (52.6%)
Extra Nodal Sites:	
Present	5 (8.8%)
Absent	52 (91.2%)
B Symptoms:	
Present	31 (54.4%)
Absent	26 (45.6%)
LDH Level:	
Normal	37 (64.9)
Elevated	20 (35.1)

Quantitative PET parameters: SUV max, mean, Peak and TLG PET/CT initial and interim parameters ***(Table 2)***.

Table (2): PET parameters in Non-Hodgkin Lymphoma patients.

	Mean	(SD)	Median	(Range)
Initial 18F-FDG PET/CT Parameters (n=57)				
SUV max	22.6	(10.9)	21.7	(6.0 -57.0)
SUV mean	9.5	(5.1)	8.6	(2.8 - 28.0)
SUV peak	17.2	(9.2)	16.0	(4.2 -42.7)
TMTV (cm3)	348.0	(545.0)	110.9	(1.0 - 2443.0)
TLG (cm3)	3202.3	(5203.6)	1376.9	(10.2 - 26224.5)
Interim 18F-FDG PET/CT Parameters (n=49)*				
SUV max	6.8	(7.8)	5.4	(0.0 - 39.0)
SUV mean	3.2	(4.2)	2.9	(0.0 - 25.9)
SUV peak	4.8	(5.8)	4.0	(0.0 - 32.8)
TMTV (cm3)	82.4	(211.1)	7.0	(0.0 - 1019.8)
TLG (cm3)	414.5	(1062.2)	22.3	(0.0 - 5193.4)
Mean (Δ) 18F-FDG PET/CT Parameters (n=49)*				
Δ SUV max	62.5	(41.3)	76.0	(-74.8 - 100.0)
Δ MTV	32.5	(122.9)	91.9	(-414.2 - 100.0)
Δ TLG	41.9	(136.2)	97.8	(-469.8 - 100.0)

SUV: Standardized Uptake Value, TMTV: Total Metabolic Tumor Volumes, TLG: Total Lesion Glycolysis.

A comparison between the initial and interim 18F-FDG PET/CT parameters in patients diagnosed with NHL, there was statistically significant difference between initial and interim different metabolic parameters denoting good response to therapy ***(Table 3)***.

Table (3): Comparison between Initial and Interim quantitative PET parameters in Non-Hodgkin's Lymphoma patients.

	Initial PET-CT		Interim PET-CT		p-value
	Median	(range)	Median	(range)	
SUV mean	8.6	(2.8 -28.0)	2.9	(0.0 -25.9)	<0.001*
SUV max [Mean (SD)]	22.6	(10.9)	6.8	(7.8)	<0.001*
SUV peak [Mean (SD)]	17.2	(9.2)	4.8	(5.8)	<0.001*
TMTV (cm3)	110.9	(1.0 -2443.0)	7.0	(0.0 -1019.8)	<0.001*
TLG (cm3)	1376.9	(10.2 - 26224.5)	22.3	(0.0 -5193.4)	<0.001*

SUV: Standardized Uptake Value, TMTV: Total Metabolic Tumor Volume, TLG: Total Lesion Glycolysis.

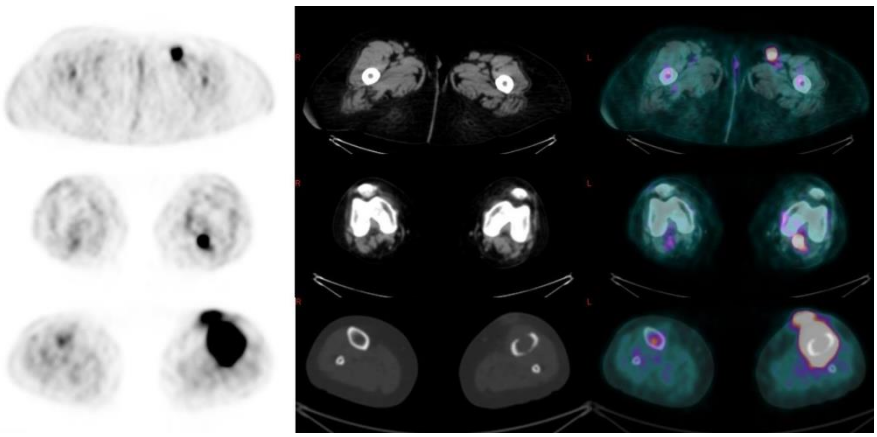
Analysis of initial ^{18}F-FDG PET/CT quantitative parameters in relation to Interim PET/CT after two chemotherapy cycles in NHL Patients: On analyzing different initial 18F-FDG PET/CT metabolic and volumetric parameters to detect if any variable can be used to predict results of interim 18F-FDG PET/CT; none of the initial 18F-FDG PET/CT parameters was found to be statistically significant ***(Table 4 and Figure 1 A, B)***.

Table (4): Correlation of Initial 18F-FDG PET/CT parameters in relation to Interim PET/CT results after 2 cycles of chemotherapy in NHL Patients.

Initial 18FFDG PET/CT	Interim PET/CT Results				p-value
	Diseased (PR/SD/PD) (n=34)		Free (CR) (n=15)		
	Median	Range	median	Range	
SUV max	21.0	(6.2 - 57.0)	24.8	(6.0 - 39.8)	0.241
SUV mean	8.3	(2.8 - 28.0)	9.7	(3.2 - 18.9)	0.696
SUV peak	14.4	(4.9 - 42.7)	19.8	(4.2 - 31.2)	0.368
TMTV (cm3)	122.1	(1.3 - 2443.0)	69.0	(2.7 - 1886.6)	0.544
TLG (cm3)	1381.1	(17.2 - 11445.7)	708.4	(10.2 - 21386.4)	0.529

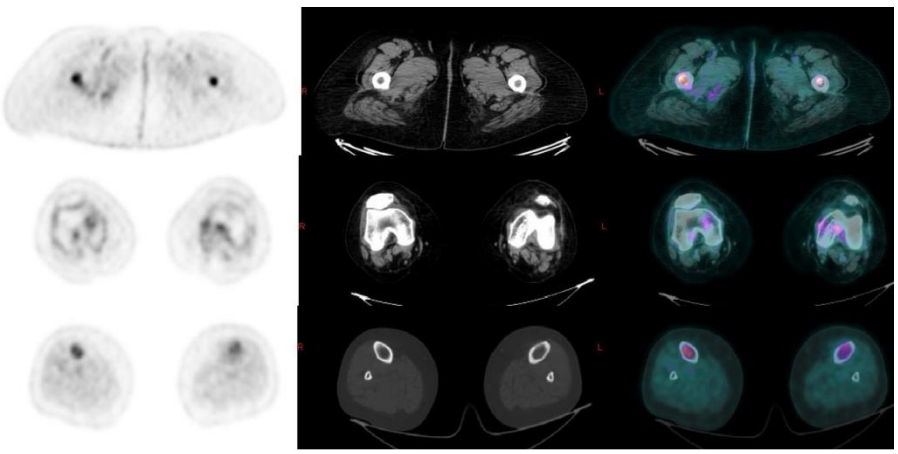
SUV: Standardized Uptake Value, TMTV: Total Metabolic Tumor Volume, TLG: Total Lesion Glycolysis, CR: Complete Remission, PR: Partial Remission, SD: Stable Disease, PD: Progressive Disease.

Analysis of significance of Interim 18F-FDG PET/CT results to patients' clinical outcome at the end of chemotherapy cycles: On evaluating the significance of interim 18F-FDG PET/CT with clinical outcome, it was found to be highly significant in predicting clinical outcome of NHL patients at end of chemotherapy cycles; where 28.6% achieved CR in interim and maintained this clinical state at end of cycles, 16.3% had a positive interim PET/CT but achieved CR at end of cycles, 53.1% had positive interim PET/CT results and failed to achieve CR state at end of cycles, and 2% had a negative interim PET/CT but inferior clinical outcome indicating a relapsing disease ($p<0.039$).



Initial PET/CT parameters:
SUV max: 23.7,
SUV mean: 11.2,
SUV peak: 21,
MTV: 43.4,
TLG: 557.5.

Figure 1 (A): Initial PET, CT, Fused PET/CT images revealed metabolically active FDG avid left inguinal, left popliteal LNs, and proximal left tibial lymphomatous infiltrations.



Interim PET/CT parameters:
SUVmax: 0,
SUVmean: 0,
SUVpeak: 0,
MTV: 0,
TLG: 0.
Mean Δ PET/CT Parameters:
ΔSUV max: 100.
ΔMTV: 100.
ΔTLG: 100.

Figure 1 (B): Interim PET, CT, Fused PET/CT images revealed no evidence of any metabolically active FDG avid residual lymphomatous lesions.

Analysis of initial, interim & mean quantitative parameters in relation to clinical outcome of patients at the end of chemotherapy cycles: On performing univariante analysis relating initial 18F-FDG PET/CT quantitative parameters to patients' clinical outcome after receiving all chemotherapy cycles, initial TMTV and TLG were found statistically significant ***(Table 5)***. Moreover, on carrying out univariante analysis relating interim 18F-FDG PET/CT parameters and mean parameters to patients' clinical outcome, all of interim and mean 18F-FDG PET/CT quantitative parameters were found to be highly correlated with end of treatment clinical outcome ***(Table 6)***. On multivariate logistic regression (using the significant variables on the Univariante level), only Δ SUV max was found statistically significant and thus considered an independent predictor to the patient clinical outcome at the end of chemotherapy cycles.

Table (5): Initial 18F-FDG PET/CT parameters in relation to clinical outcome at the end of chemotherapy cycles in Non-Hodgkin's Lymphoma patients (n=52) **.

	Residual (n=28)		Free (n=24)		p-value
	Median	(range)	Median	(range)	
SUV mean	8.3	(2.8 -28.0)	23.0	(6.0-44.5)	0.666
SUV max [Mean (SD)]	21.6	(11.0)	22.2	(10.7)	0.831
SUV peak [Mean (SD)]	16.5	(9.0)	16.9	(9.2)	0.870
TMTV (cm3)	256.0	(3.4-2443.0)	66.3	(1.3-1886.6)	0.005 *
TLG (cm3)	2603.6	(28.8-26224.5)	633.0	(10.2-21386.4)	0.010 *

SUV: Standardized Uptake Value, TMTV: Total Metabolic Tumor Volume, TLG: Total Lesion Glycolysis. * Statistically significant p-value. ** 5/57 NHL patients lost follow up.

Table (6): Interim and Mean quantitative 18F-FDG PET/CT parameters in relation to clinical outcome at the end of chemotherapy cycles in Non-Hodgkin's Lymphoma patients (n=49) **.

	Diseased (n=20)		Free (n=46)		p-value
	Median	(range)	Median	(range)	
Interim 18F-FDG PET/CT Parameters:					
SUV max	9	(3.0-39.0)	0.0	(0.0-7.0)	<0.001 *
SUV mean	3.6	(1.3-25.9)	0.0	(0.0-4.0)	<0.001 *
SUV peak	6.5	(1.7-32.8)	0.0	(0.0-5.1)	<0.001 *
TMTV (cm3)	37.1	(1.6-1019.8)	0.0	(0.0-29.4)	<0.001 *
TLG (cm3)	128.2	(2.5-5193.4)	0.0	(0.0-91.6)	<0.001 *
Mean (Δ) 18F-FDG PET/CT Parameters:					
Δ SUV max	48.4	(-74.8-86.7)	100.0	(36.4-100.0)	<0.001 *
Δ MTV	74.9	(-414.2-99.9)	100.0	(-138.4-100.0)	<0.001 *
Δ TLG	91.3	(-469.8-99.9)	100.0	(21.9-100.0)	<0.001 *

SUV: Standardized Uptake Value, TMTV: Total Metabolic Tumor Volume, TLG: Total Lesion Glycolysis. * ** 8 patients had no interim PET-CT.

Survival Analysis: On performing univariate analysis relating Initial, Interim, and Mean 18F-FDG PET/CT quantitative parameters to 2 years OS rate, nothing was found statistically significant. On carrying univariante analysis relating Initial, Interim, and Mean quantitative ^{18}F-FDG PET/CT parameters to 2 years RFS rate, initial TLG parameter was found statistically significant. On proceeding to multivariate cox regression analysis using the significant variables found on the univariante level, none of them was found to be statistically significant ***(Figure 2)***.

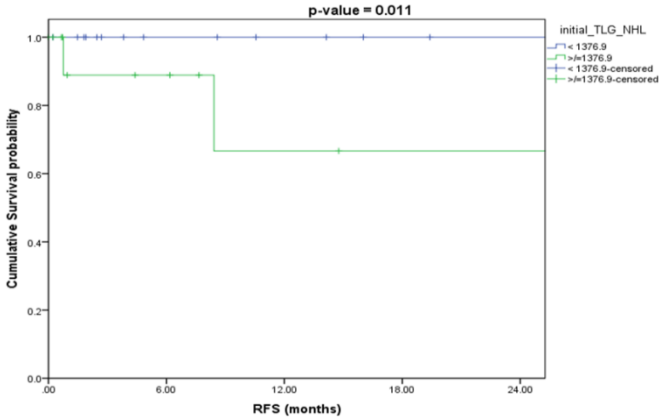


Figure (2): 2Y-RFS in NHL patients in relation to Initial TLG.

DISCUSSION:

^{18}F-FDG PET/CT has been accepted by the 2014 International Conference on Malignant Lymphoma imaging consensus guidelines as the standard imaging tool to assess FDG avid malignant lymphoma patients [(10)]. Its interim and end of treatment prognostic and predictive roles have recently gained interest and many have investigated their role in management of malignant lymphoma patients. Though many studies assessing the prognostic and predictive values of baseline 18F-FDG PET/CT volume based parameters in patients initially diagnosed with various malignant lymphoma subtypes demonstrated inconsistent and indecisive conclusions [(4)].

Consequently, the aim of our work was to evaluate the prognostic and predictive value of volume based 18F-FDG PET/CT initial and interim parameters; correlating them to early response evaluation after two to three cycles of chemotherapy, clinical outcome at end of chemotherapy cycles, overall survival rate, and progression free survival rate.

In our retrospective study, we evaluated 57 adult patients initially diagnosed with Non-Hodgkin lymphoma referred to Nuclear Medicine unit at National Cancer Institute. 24 patients (46.2 %) achieved CR, while 28 patients (53.8 %) had residual disease at end of chemotherapy. We found that baseline 18F-FDG PET/CT TMTV and TLG, all interim 18F-FDG PET/CT metabolic and volumetric parameters; including SUV max, SUV mean, SUV peak, MTV, TLG, Δ SUV max, ΔMTV, and ΔTLG, all were highly independently correlated with clinical outcome. On multivariate analysis level, only ΔSUV max maintained its significance and thus was considered as an independent predictor of clinical outcome.

Correspondingly, ***Sasanelli et al***, through analyzing 114 patients initially diagnosed with DLBCL, stated that baseline 18F-FDG PET/CT TMTV is highly significantly correlated with clinical outcome at end of chemotherapy cycles [(11)].

Similarly ***Oñate-ocaña et al***, analyzed 50 patients diagnosed with DLBCL aiming to evaluate the prognostic value of interim 18F‑FDG PET/CT scans in association with some clinical characteristics in a way to obtain early prognostic indicator of clinical outcome at end of chemotherapy cycles and OS rate.

On performing interim 18F‑FDG PET/CT scans, 30 patients achieved CR while 10 showed PR. Though, at the end of chemotherapy cycles, 38 patients reached a CR state while 5 patients maintained the PR state and progressive disease was exhibited in 7 patients on performing interim 18F‑FDG PET/CT scan. In addition, they concluded that a reduction of ≥ 94 % in TMTV in the interim 18F‑FDG PET/CT accomplished sensitivity of 86% and specificity of 50% for the precise prognosis of a CR state at end of chemotherapy cycles [(12)].

Moreover, ***Casasnovas et al***, prospectively analyzed 85 patients initially diagnosed with NHL and performed ΔSUV max reduction after two cycles and four cycles of chemotherapy with a cut off value of 66 % and 70 % respectively. They concluded that generally ΔSUV max reduction better predicts clinical outcome at end of chemotherapy cycles better than visual analysis and that ΔSUV max reduction post four cycles ($p < 0.0001$) had better predictive significance than ΔSUV max post two chemotherapy cycles ($p < 0.0164$) [(13)].

In our study, we also analyzed initial, interim, and mean 18F-FDG PET/CT parameters in order to detect the prime predictor of OS and PFS rates in patients initially diagnosed with NHL. The best predictors of PFS was initial 18F-FDG PET/CT TLG parameter ($p < 0.011$) with 2 years RFS of 66.7 % in patients having interim TLG ≥ 1376.9.

Zhou et al, in analyzing 91 patients newly diagnosed with DLBCL, reported that upon examining the prognostic value of MTV, TLG, IPI index, and Ann Arbour stage, only initial TLG maintained its statistical significance and was independently associated with 5 years progression free survival rate ($p < 0.001$) [(5)].

Moreover, ***Esfahani et al***, retrospectively analyzed 20 patients initially diagnosed with DLBCL. All 20 patients underwent initial and interim 18F-FDG PET/CT scans. Each initial and interim scan was analyzed and SUV max, SUV mean, TMTV, and TLG were extracted. They stated that among the baseline 18F-FDG PET/CT parameters, baseline TLG was only predictor of PFS ($P < 0.05$). They also reported that neither initial nor interim TMTV could predict PFS rate [(7)].

On the contrary, ***Narkhede et al,*** reported poor significance of baseline 18FFDG PET/CT MTV and TLG in relation to clinical outcome, PFS, and RFS of patients initially diagnosed with DLBCL.

This discrepancy with our results might be due to the fact that the included patients were only diagnosed with DLBCL with other histopathological NHL subtypes being excluded while in our study all NHL histopathological subtypes were included and analyzed including low, intermediate, and high grade subtypes [(14)].

CONCLUSIONS:

^{18}F-FDG PET/CT as total metabolic tumor volume (TMTV) or total lesion glycolysis (TLG) as volume based parameters are prognostic parameters at interim PET and have predictive value to predict clinical outcome and survival in Non-Hodgkin Lymphoma.

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