Original Paper, PET/CT.

Prognostic Value of Baseline and Interim Volume Based PET Parameters in Prediction of Early Therapy Response and Survival in Pediatric Patients with Bulky and Advanced HL.

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ABSTRACT:

Aim of work: Evaluate the prognostic value of baseline and interim volume-based ^{18} fluorine-labeled fluoro-2-deoxyglucose positron emission tomography (^{18}F-FDG PET) metabolic parameters in paediatric patients diagnosed with bulky and advanced Hodgkin lymphoma (HL), in respect to patients' progression-free survival, and their role in predicting early metabolic therapy response.

Patients and Methods: A retrospective study of a total of 59 paediatric patients with bulky and advanced stages HL who performed upfront and interim PET/CT scans. PET/CT parameters: maximum standardized uptake value (SUVmax), SUVmean, SUVpeak, metabolic tumour volume (MTV), and total lesion glycolysis (TLG) were extracted. Initial whole-body MTV and TLG were calculated. Early response assessment using Deauville scoring systems was used to evaluate interim ^{18}F-FDG PET/CT scan. Prediction of early therapy response and progression free survival of these parameters was evaluated. **Results**: Baseline albumin level predicted therapy response. Initial SUVmax and SUVpeak in bulky disease (P values=0.036 for both) were the only PET parameters that predicted therapy response and Progression-free survival. All the interim parameters with the changes between initial and interim quantitative PET/CT parameters are statistically significant and succeeded to predict 1.5 years- PFS in the advanced group. In the bulky group only the interim TMTV and TLG maintained their statistical significance.

Baseline whole body MTV and TLG ROC curves failed to predict therapy response and progression-free survival (PFS) for both groups.

Regarding clinical outcome, interim ^{18}F-FDG PET/CT Deauville scoring system was found to be statistically significant ($p < 0.001$). **Conclusion:** Interim PET/CT in paediatric Hodgkin lymphoma revealed that Deauville score remains the best indicator for prediction of therapy response.

All the interim parameters & the changes between initial and interim quantitative parameters succeeded to predict 1.5 years-PFS in the advanced group. Baseline PET/CT (SUVmax and SUVpeak) is suggested to predict response to therapy in paediatric patients with bulky disease.

Keywords: Volume based PET parameters, paediatric Hodgkin Lymphoma, prediction of early therapy response, progression free survival.

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Time of Submission: 17/06/2023. **Time of Acceptance:** 27/27/2023.

INTRODUCTION:

Hodgkin lymphoma (HL) is a malignancy usually derived from B-lymphocytes. In paediatric population, 40 % of lymphomas are considered Hodgkin's lymphoma (HL). In the last few years, many attempts are present to identify the most important prognostic factor that may be capable of early identification and stratification of high-risk patients who need to be subjected to more intensified treatment protocols [(1)]. Therapeutic options are different combinations of systemic chemotherapy and radiotherapy, which depend on the disease stage at time of initial diagnosis [(2)]. ^{18}F-FDG PET/CT is now a very important functional imaging modality used in initial staging and restaging of different types of lymphomas [(3)]. PET/CT is also considered a powerful tool for the differentiation between therapy responders and non-responders in adult and paediatric patients with Hodgkin lymphoma [(4)]. Patients with a positive interim PET/CT have shown a higher chance of relapse and poorer outcome [(5)]. Improvements and advances in PET/CT technology have led to increasing researchers' interest in the quantification of metabolic PET parameters and evaluation of their prognostic role. SUV max, total metabolic tumor volume (TMTV) and total lesion glycolysis (TLG) are the most frequently used quantitative parameters in the clinical research settings nowadays [(6)].

PATIENTS AND METHODS:

A retrospective study for paediatric patients with pathologically proven HL who performed upfront and interim PET/CT. Our study included patients younger than 18 years old, patients with bulky and advanced stages. Patients who are older than 18 years old, started chemotherapy prior to PET/CT and children with other pathological types of lymphoma were excluded from this study. Bulky disease is defined as a nodal mass more than one-third of the CXR intrathoracic diameter or a contiguous extra mediastinal nodal mass more than 6 cm in the longest transverse diameter or CC dimension. Advanced stages included stage III and stage IV according to Ann arbour staging. Clinical information was extracted from the medical records, including sex, age, pathological details, laboratory and imaging results, and treatment response and survival data. This study was approved by the Cairo university clinical research ethical committee.

PET/CT image protocol: Patients were instructed to fast at least 4-6 hours prior to the scan to keep a glucose level below 150 mg/dl. Each patient was injected 5-10 MBq/Kg. The PET/CT acquisition was done from skull base to proximal thigh; sedation was needed in some cases to ensure proper image acquisition and to ensure the capability of lying stable. **Acquisition:** FDG PET/CT study was done using a dedicated PET/CT scanner (GE, PET/CT Discovery). This camera integrates a PET scanner with a dual-section helical CT scanner (40 slice Emotion; Siemens) and allows the acquisition of co-registered CT and PET images in one session.

Scanning started 60-90 min after tracer injection of 370-555 MBq of ^{18}F-FDG. Initially, patients were examined in the supine position with arms elevated, and CT scanning was started at the level of the Cervico-thoracic region with the following parameters: 400 mAs; 120 kV; slice thickness, 3 mm; pitch, 1.5. The CT scans were acquired during normal respiration reached caudally to the mid thighs. PET was performed immediately after acquisition of the CT images (5–7 bed positions; acquisition time, 2-3 min/bed position). The CT-data were used for attenuation correction, and images were reconstructed as 5-mm slices applying a standard iterative algorithm (ordered-subset expectation maximization).

Processing: Images were interpreted at a workstation equipped with fusion software (advantage Window AW version 5, GE) that provides multi-planar reformatted images and enables display of the PET images, CT images, and fused PET/CT images was interpreted by 2 experienced nuclear medicine physicians. The analysis was conducted on per patient and per lesion-based analysis. **Imaging interpretation:** Reconstructed images as PET, CT images, and fused PET/CT images in the axial, sagittal, and coronal planes were analysed by two experienced Nuclear Medicine physicians and assessed as follows;

- **Qualitative (Visual) initial assessment:** Any focal or inhomogeneous ^{18}F-FDG uptake, higher than the mediastinal and the hepatic references was interpreted as an abnormal ^{18}F-FDG uptake, after reviewing CT images to confirm a corresponding CT change.
- **Quantitative assessment:**

For quantitative assessment, we draw a semi-automated spherical volume of interest around the lesion then manually adjusted to exclude any areas of physiological FDG uptake continuous with the lesion as the bladder, and myocardium. The MTV, TLG, SUVmax, SUV mean, and SUV peak were documented. SUVmean corresponds to the mean value of all voxels within the ROI. SUVmax is defined as the single voxel within the entire tumor with the highest SUV value. SUVpeak is the mean value of radiotracer uptake within the ROI surrounding the pixel with the highest activity. MTV is defined as the number of voxels within the VOI, which had a greater uptake than a certain threshold. Metabolic Tumour Volume (MTV) was calculated with a threshold hepatic reference SUV mean is contour by drawing 3 cm spherical ROI in the normal right lobe of the liver. TLG is calculated as MTV multiplied by the mean SUV (TLG = MTV × mean SUV). As this parameter incorporates both the MTV and SUV, it represents both the size of the tumor and the degree of FDG uptake. TMTV and total TLG were calculated by gaining the sum of all the values of nodal and extra-nodal lesions.

Identification criteria for bone marrow and splenic involvement: Involvement of the bone marrow was measured when there is a focal or multifocal FDG uptake. Splenic infiltration was measured if there was a heterogeneous FDG uptake, or focal nodular lesions on PET/CT.**Differences in metabolic parameters between the baseline and interim PET/CT scan:** Mean MTV (Δ MTV), Mean Total Lesion Glycolysis (Δ TLG), Mean Standardized Uptake Value (Δ SUVmax) was also documented.

Interim ^{18}F-FDG PET/CT early response assessment criteria: Based on the five-point scale Deauville criteria, patients` response evaluation after two cycles of chemotherapy was divided into two groups of patients. Patients with a Deauville score of 1-3 were considered as complete metabolic responder patients. Patients with a score of 4-5 were considered as PET positive for residual disease after chemotherapy. In patients with no available end of treatment PET/CT, complete response was considered if the patient `s follow up for up to 3 years with no evidence of relapse.

Assessment of survival: Progression free survival is defined as the time interval between the maintenance of a complete disease remission and the manifestation of a progressive event.

Statistical analysis: Management and analysis of data was performed using Statistical Package for Social Sciences (SPSS) vs. 25. Numerical data were checked for normality and were statistically described in terms of median (range) or mean (standard deviation) as appropriate. Categorical data were described as percentages and numbers. Separate analysis was done for patients with Bulky and advanced tumors. Comparing the numerical variables was performed using Student t-test when they are normally distributed and Mann-Whitney U test if non-normally distributed for the independent groups. When comparing the categorical data Chi-square or Fisher's exact test was performed as appropriate.

Survival analysis using Kaplan-Meier method and comparison between two or more survival curves using log rank test [(7)].

All numerical variables were categorized into binary groups for Kaplan-Meier analysis using the median value of each (≤ or > median).

Receiver operator characteristic (ROC) curve analysis was used to find the best cut-off values for the baseline whole body MTV and TLG for prediction of therapy response and disease-free survival. Progression-free survival (PFS) was calculated from the date of the maintenance of a complete disease remission to the date of the manifestation of a progressive event or last follows up. 95% confidence interval estimates were used. All tests were 2 tailed and P-value < 0.05 was considered statistically significant.

RESULTS:

This retrospective study was conducted at the National Cancer Institute (NCI) on 59 pediatric patients diagnosed with Pediatric Hodgkin lymphoma during the period between January 2020 till March 2023. Patients were divided into 2 groups: advanced group which included 53 patients and bulky group which included 21 patients; however, the 2 groups are overlapping as there are many patients with bulky disease are also classified as advanced stages. Median age was 12.5 years old. The sex ratio was similar in both groups with a higher predominance of male gender in both groups. A low frequency of B-symptoms was noted in both groups. Patients` clinico-laboratory characteristics are summarized in ***Table (1).*** Stage-III was predominant in both groups. The nodular sclerosis represented the majority of the HL subtypes in both groups; with 47.6% in bulky group and 43.4% in advanced group ***Table (2).*** In the advanced group, total number of patients were 53, 6 patients had missing response data (2 of them lost follow up, 4 of them did not perform interim PETCT scan).While in the bulky group, total number were 21 patients, 3 patients had missing response data.

A. Clinico laboratory characteristics in relation to therapy response in bulky and advanced groups:

Among all the clinico laboratory data, only the albumin level, measured before starting any kind of therapy that showed a statistical significance in predicting therapy response ***(Table 3).***

B. Initial qualitative PET/CT analysis of Bulky and advanced groups of paediatric patients with HD:

Regarding the splenic affection, it is divided into (focal and diffuse) and found to be of higher percentage in the advanced group of (n=31, 58.5 %) compared to (n=9, 42%) in the bulky group. Regarding the bone marrow affection, it's also divided into (focal and diffuse) with higher percentage in advanced group of (n=13, 24.5%) compared to (n=4, 19%) in the bulky group, also liver and lung affection were included and described in ***Table (4).***

Table (1): Clinico laboratory characteristics of both groups.

Clinical data	Advanced group (n= 53)	Bulky group (n= 21)
Age (years)	**Mean (SD)**	
	12.4 (5.1)	12.1(5.2)
Gender	**No. (%)**	
	Male	36 (67.9%)	15 (71.4%)
	Female	17 (32.1%)	6 (28.6%)
B-symptoms	**No. (%)**	
	Yes	27 (50.9)	8 (38.1)
	No	26 (49.1)	13 (61.9)
BMB	**No. (%)**	
	Positive	8 (15.1)	2 (9.5)
	Negative	45 (84.9)	19 (90.5)
Laboratory data	**Mean (SD)**	
	HB	9.9 (2.3)	10.1 (1.7)
	Albumin	3.4 (0.6)	3.4 (0.5)
	Median (range)	
	LDH	313.0 (163.0-1225.0)	259.0 (139.0-1225.0)

Table (2): Tumour characteristics and staging in both groups.

Tumor characteristics	Advanced group (n= 53)	Bulky group (n= 21)
HL subtypes	No. (%)	
Classic HL	17 (32.1%)	5 (23.8%)
Nodular sclerosis	23 (43.4%)	10 (47.6%)
Mixed cellularity	11 (20.8%)	4 (19%)
Lymphocyte-rich	2 (3.8%)	1 (4.8%)
Lymphocyte-depletion	0 (0)	1 (4.8%)
Stage	**No. (%)**	
I	-	2 (9.5)
II	-	4 (19)
III	38 (71.7)	11 (52.4)
IV	15 (28.3)	4 (19)

Table (3): Clinico-laboratory significance in relation to response in both groups.

Albumin level Mean (SD)	**Response**		
	Advanced group		**p-value**
	No (n=17)	*Yes (n=30)*	
	3.0 (0.6)	3.5 (0.5)	0.005*
	Bulky group		
	No (n=6)	*Yes (no=12)*	
	3.7 (0.5)	3.3 (0.4)	<0.038*

Table (4): Solid organ affection in both groups.

Solid organ affection	Advanced group (n= 53)		Bulky group (n= 21)
	No. (%)		
Spleen	Total 31 (58.5 %)		Total 9 (42.9%)
	Focal	20 (64.5)	5 (55.6)
	Diffuse	11 (35.5)	4 (44.4)
Bone marrow	13 (24.5%)		4 (19%)
	Focal	10 (76.9)	3 (75)
	Diffuse	3 (23.1)	1 (25)
Liver affection	4 (7.5%)		0 (0.0%)
Lung affection	4 (7.5%)		2 (9.5%)
Prescience of Pleural effusion	3 (5.7%)		1 (4.8%)

C. Initial quantitative PET/CT parameters in the bulky and advanced groups:

On performing univariate analysis of the quantitative PET/CT parameters in the bulky and advanced groups, none of the initial parameters in the advanced groups succeeded in predicting therapy response with P values for SUVmax, SUV peak, SUVmean, MTV and TLG are 0.365, 0.776, 0.335, 0.757 and 0.690 respectively. While in the bulky group only the initial SUVmax and SUVpeak (with p-value=0.036 for both) succeeded in predicting response assessment and were found to be statistically significant ***(Table 5)***.

While SUV mean, MTV and TLG failed to predict response to therapy with P-values 0.335, 0.385 and 0.067 respectively in the bulky group.

Table (5): Initial PET parameters in relation to response in the bulky group (n=18)

	Response		
	No (n=6)	Yes (n=12)	
Parameter	Mean (SD)		p-value
SUV $_{max}$	18.1 (9.0)	11.3 (3.9)	0.036*
SUV $_{Peak}$	14.2 (6.0)	9.1 (3.5)	0.036*

Prognostic value of baseline volume-Whole body MTV and TLG PET/CT metabolic parameters in the advanced group: Prediction of early therapy response using ROC curve analyses of the initial TMTV PET/CT parameter in the 47 patients , revealed AUC = 0.435 (95% CI: 0.245 – 0.625), p-value = 0.496 revealed non significance, with small discriminating ability (AUC, sensitivity, and specificity), ***(Figure 1)***. Prediction of response by performing ROC curve analyses of the initial total TLG revealed non significance, with small discriminating ability (AUC, sensitivity, and specificity), ***(Figure 1).***

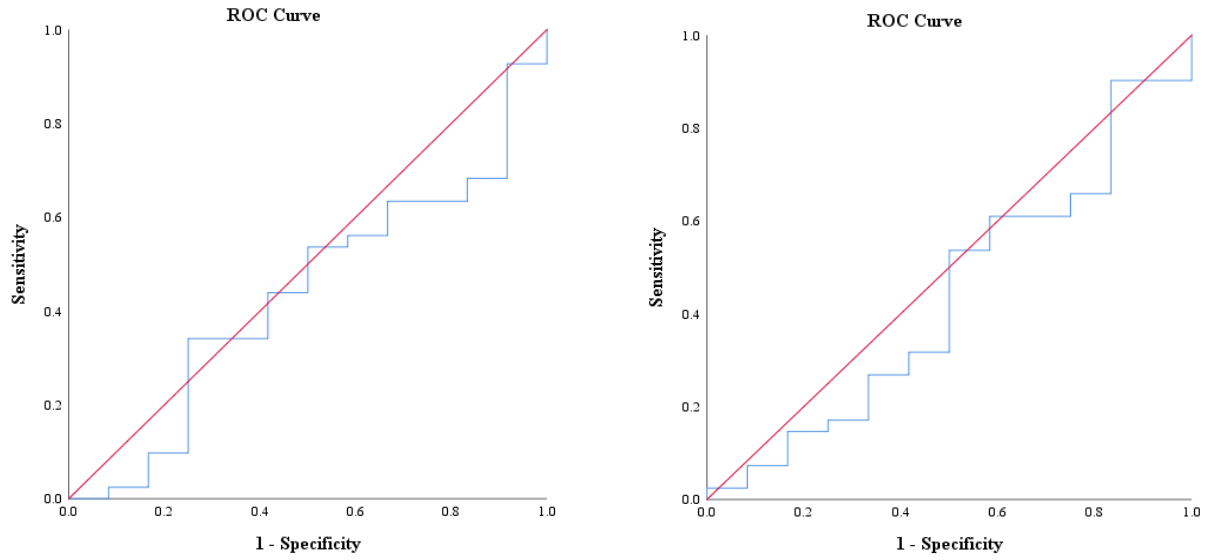

Figure (1): ROC curve for initial MTV and TLG of the whole-body measurement in the advanced group (TLG on the right side, TMTV on the left side).

Prognostic value of baseline volume-based Whole body MTV and whole body TLG PET/CT metabolic parameters in the bulky group: Prediction of early therapy response by performing ROC curve analyses of the initial TMTV PET/CT parameter in the 18 patients, showed AUC = 0.256 (95% CI: 0.005 – 0.506). P-value = 0.087, and it revealed Non significance with low specificity, ***(Figure 2)***. Prediction of response by performing ROC curve analyses of the initial total TLG PET/CT parameter, showed AUC = 0.111 (95% CI: 0.0 – 0.267), p-value = 0.006, And it revealed despite significance, the point is useless because of the very small AUC, ***(Figure 2)***.

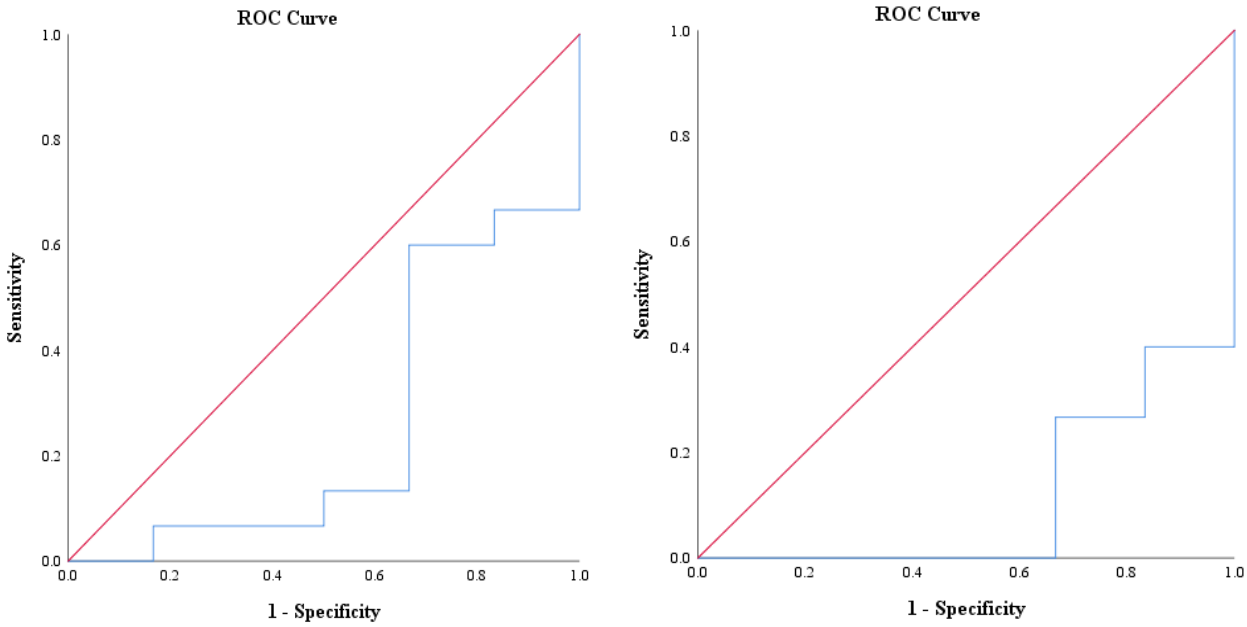

Figure (2): ROC curve for initial MTV and TLG of the whole-body measurement in the bulky group (TLG on the right side, TMTV on the left side).

Early assessment of response using Quantitative PET/CT parameters and Patient's outcome in both groups: In the advanced group, total number of patients were 53, 6 patients had missing response data (2 of them lost follow up, 4 of them did not perform interim PETCT scan), complete data were available for 47 patients. They are divided into: 30 responders (63.8%) and 17 non responder (36.2%), 4 patients developed progression, only 2 developed relapse after being responders in interim PETCT.

While in the bulky group, total number were 21 patients, 3 patients had missing response data (did not perform interim PETCT scan), complete data were available for 18 patients. The bulky group is divided into 12 responders (66.7%) and 6 non-responder (33.3%), 2 patients developed progression and only 1 patient developed relapse. No death had been recorded in both groups. All interim PET/CT parameters were measured, and all showed statistical significance denoting good response to therapy with p-value =<0.001 in both groups. Regarding univariate analysis of the changes between the initial and interim quantitative PET/CT parameters in the advanced group, % Δ SUV max, % Δ TMTV and % Δ TLG found to be statistically significant (with p-value=0.001 for the change of these three parameters) to predict response assessment as described in ***Table (6).***

Table (6): Changes between initial and interim parameters in relation to response in the advanced group (n=47).

	Response		
Parameter	No (n=17)	Yes (n=30)	p-value
SUVmax	Median (range)		
% Δ SUV $_{max}$	71.0% (-354.0-92.2)	100.0% (61.3-100.0)	<0.001*
MTV (Total)			
% Δ MTV	95.1% (44.6-100.0)	100.0% (96.8-100.0)	<0.001*
TLG (Total)			
% Δ TLG	97.0% (18.6 -100.0)	100.0% (97.6-100.0)	<0.001*

While in the bulky group only % Δ SUV max and% Δ TMTV were found to be statistically significant to predict response assessment with P values of 0.041 and 0.032 respectively. While % Δ Total TLG was not statistically significant to predict response assessment with P values of 0.102 ***(Table 7).***

Table (7): Changes between initial and interim parameters in relation to response in the bulky group (n=18).

	Response		
Parameter	No (n=6)	Yes (n=12)	
SUV_{max}	Median (range)		p-value
% Δ SUV_{max}	62.8 (28.4-92.2)	93.9 (61.3-100.0)	0.041*
TMTV	Median (range)		p-value
% Δ MTV	95.9 (81.7-100.0)	100.0 (90.9-100.0)	0.032*

Survival analysis: In the bulky group, on performing the univariate analysis relating patients' characteristics, initial and interim qualitative PET/CT parameters to PFS, none of the studied parameters succeeded to be statistically significant predicting the survival in the bulky group. While in the advanced group with follow up duration ranged from (3-29.6 months) with median follow up duration = 7.2 months and 1.5 years PFS rate with a percentage of (87.6%) in the advanced group. Only the interim parameters including TMTV, TLG with P-value = (0.019 for both). Also, the SUVmax, % Δ SUV max, % ΔTMTV, and % ΔTLG (with P-values 0.049, 0.028, 0.05 and 0.008 respectively), were found to be statistically significant to independently predict 1.5 years PFS rate ***(Table 8).***

Table (8): Kaplan-Meier univariate PFS analysis for the change in PET parameters between initial and interim in the advanced group (n=47).

Interim parameters	Median	N	1.5 Y- PFS (%)	p-value
SUV_{max} ***(Initial-interim)***	≤ 10.4	24	76.5	0.049*
	>10.4	23	100.0	
% Δ SUV max	≤ 87.9	24	73.6	0.028*
	>87.9	23	100.0	
% Δ TMTV	≤ 99.9	20	64.1	0.005*
	>99.9	27	100.0	
% Δ TLG (Total)	≤ 99.9	21	67.3	0.008*
	>99.9	26	100.0	

DISCUSSION:

Classic Hodgkin lymphoma has evolved over the past century from a consistently deadly illness to one of the most treatable diseases. The added metabolic information supplied by FDG-PET/CT resulted in superior staging performance as well as therapeutic response evaluation based on variations in ^{18}F-FDG PET/CT parameters between initial and interim or end of treatment scans. Several studies have also assessed the prognostic and predictive usefulness of quantifying volume-based measures derived from the baseline PET/CT, such as MTV and TLG, rather than the mass single largest diameter will probably give a more relevant estimate of the tumour burden for prognostic purposes, especially in the advanced disease. A tumour volume more than 200 mL was found to be related to a higher risk of disease relapse. Consequently, the aim of our work was to evaluate the prognostic value of baseline volume-based ^{18}F-FDG PET metabolic parameters in paediatric patients with bulky and advanced stages Hodgkin lymphoma, in respect to patients' progression-free survival, and evaluating their role in predicting early metabolic therapy response. In our study, we found that regarding the demographic and laboratory data of the advanced group; of all the studied risk factors, only the age (with the mean age of 13 years in the responder group and 9 years in the non-responder group with p-value=0.011) and albumin level (with the mean value of 3.5 for the responder and 3.0 for the non-responder group with p-value=0.005) were found to be statistically significant in predicting therapy response. Similarly, ***Lopci et al.*** 2011, found in a retrospective study of 98 paediatric patients with HL, that age at the time of diagnosis was a good predictor of progression free survival; an earlier onset of HD seemed to predict a significantly worse prognosis (age≤13.3 years) and a higher risk of disease progression or relapse (p=0.03) **(8)**. As regards the prognostic value of initial PET/CT parameters including SUVmax, SUVmean, SUVpeak, TMTV and TLG in the advanced group nothing was found to be statistically significant in predicting therapy response and patients` outcome. Similarly, ***Furth et al.*** 2009, found in a study that included 40 paediatric patients that initial SUVmax with a median value of 11.1 (comparable to our median value of 12.7) is of no significant difference in early and advanced-stage HL patients **(9)**.

Furthermore, as regards the bulky group; initial PET/CT parameters SUVmax, SUVpeak (p-value= 0.036 for both) were found statistically significant, while TMTV (p-value= 0.385) and TLG (p-value= 0.067) failed to validate their prognostic values which is mainly related to small number of patients in such group.

Also, ***Reed et al.*** 2021, found in a retrospective study that included paediatric patients with Hodgkin lymphoma that only baseline TMTV predicted treatment response of all the investigated parameters with p-value= 0.017 [(10)]. In the present study we also performed ROC curves analyses for baseline whole body MTV and whole body TLG in order to predict therapy response and progression-free survival in both bulky and advanced groups, unfortunately the results revealed non significance, with small discriminating ability.

On the contrary, ***Zhou et al.*** 2020; found that in 47 patients with paediatric lymphoma that the baseline TLG is an independent prognostic factor for PFS [(11)]. Also, ***Sharma*** 2012, found that Whole body metabolic tumour burden (MTB) appeared to be beneficial quantitative PET/CT parameter for the early treatment response assessment [(12)].

We confirmed the prognostic role of interim PET/CT scan parameters in evaluating early response to therapy in patients initially diagnosed with advanced stages with HL as well as the bulky group; all interim PET/CT parameters (including TMTV and total TLG) revealed significance in predicting therapy response. Similar results reported by ***Lopci et al.*** 2019, that included 703 pediatric Hodgkin lymphoma patients with bulky masses in a cohort study for assessment of therapy response and found that the PET/CT results obtained after 2-4 cycles of CTH is a good predictor of PFS and patients' outcome as well.

We authenticated the predictive value of qualitative analysis of interim PET/CT scans using the Deauville Scoring system which proved its statistical significance in predicting clinical outcome in both groups; with median value of 4 and p-value of p-value <0.001, in both the bulky and the advanced groups [(13)].

Similarly, ***Isik et al.*** 2017, retrospectively included 72 paediatric patients whom were analysed for prediction of therapy response, concluded that the interim PET Deauville score is superior to other interpretative methods in the prediction of the outcome.

We also found that the changes between initial and interim quantitative PET/CT parameters, % Δ SUV max, % Δ TMTV and % Δ TLG, are statistically significant (with p-value=0.001), and succeeded to predict response assessment in the advanced group, while in the bulky group only the % Δ SUV max (p-value= 0.041), % Δ TMTV (p-value= 0.032) maintained their statistically significant. However, ***Ibrahim et al.*** 2023. Found that Deauville score is an easier method with better performance than ΔSUVmax% in predicting the chemotherapy response in the enrolled 52 patients [(14)]. Also, ***Hussein et al.*** 2015, found in a prospective study that included 195 pediatric Hodgkin lymphoma patients; that the quantitative assessment of the interim PET/CT parameters has powerful potential value in prediction of OS and PFS [(15)]. Our study limitations included the small sample size, diffuse bone marrow infiltration TMTV and TLG were not measured due to difficult ROI drawing and variation in follow up durations. Finally, the results of the present study were authenticated by means of clinico- radiological follow up rather than tissue biopsy. We concluded that interim PET/CT Deauville score, metabolic parameters found to be indicators for prediction of early response to therapy. All the interim parameters with the changes between initial and interim quantitative PET/CT parameters succeeded to predict 1.5 year-PFS in the advanced group. While in the bulky group only the interim TMTV and TLG maintained their statistically significant as well as, % Δ TMTV, Δ TLG. Baseline SUVmax and SUVpeak are suggested to predict response to therapy in pediatric patients with bulky disease.

REFERENCES:

1. ***Hu J, Zhang X, Tao H, et al.*** The prognostic value of Epstein−Barr virus infection in Hodgkin lymphoma: A systematic review and meta-analysis. Front Oncol. 27; 12; 2022.

2. ***Agrawal K, Mittal BR, Bansal D, et al***. Role of ^{18}F- FDG PET/CT in assessing bone marrow involvement in pediatric Hodgkin's lymphoma. Ann Nucl Med. Feb; 27 (2):146–51; 2013.

3. ***Isik EG, Kuyumcu S, Kebudi R, et al***. Prediction of outcome in pediatric Hodgkin lymphoma based on interpretation of 18FDG-PET/CT according to ΔSUV max, Deauville 5-point scale and IHP criteria. Ann. Nucl. Med. Nov 1; 31 (9):660–8.; 2017,

4. ***Hussien AEM, Furth C, Schönberger S, et al***. FDG-PET response prediction in pediatric Hodgkin's lymphoma: Impact of metabolically defined tumor volumes and individualized SUV measurements on the positive predictive value. Cancers (Basel). 28; 7 (1):287–304; 2015.

5. ***Frood R, Burton C, Tsoumpas C, et al.*** Baseline PET/CT imaging parameters for prediction of treatment outcome in Hodgkin and diffuse large B cell lymphoma: a systematic review; 2021.

6. ***Bakhshi S, Bhethanabhotla S, Kumar R, et al***. Posttreatment PET/CT rather than interim PET/CT using Deauville criteria predicts outcome in pediatric Hodgkin lymphoma: A prospective study comparing PET/CT with conventional imaging. Journal of Nuclear Medicine. Apr 1; 58 (4):577–83; 2017.

7. ***Karl Pearson F.R.S.*** X. On the criterion that a given system of deviations from the probable in the case of a correlated system of variables issue that it can be reasonably supposed to have arisen from random sampling, Philosophical Magazine Series 5, 50:302, 157-175; 1900.

8. ***Lopci E, Burnelli R, Guerra L, et al***. Post-chemotherapy PET evaluation correlates with patient outcome in paediatric Hodgkin's disease. Eur. J. Nucl. Med. Mol. Imaging. Sep; 38 (9):1620–7; 2011.

9. ***Furth C, Steffen IG, Amthauer H, et al.*** Early and late therapy response assessment with [^{18}F] fluorodeoxyglucose positron emission tomography in pediatric Hodgkin's lymphoma: Analysis of a prospective multi-centre trial. Journal of Clinical Oncology. 10; 27 (26):4385-91; 2009.

10. ***Reed JD, Masenge A, Buchner A, et al.*** The utility of metabolic parameters on baseline ^{18}F-FDG PET/CT in predicting treatment response and survival in paediatric and adolescent Hodgkin lymphoma. J. Clin. Med. 1; 10 (24); 2021.

11. ***Zhou Y, Hong Z, Zhou M, et al***. Prognostic value of baseline 18F-FDG PET/CT metabolic parameters in paediatric lymphoma. J. Med. Imaging Radiat. Oncol. 1; 64 (1):87-95; 2020.

12. ***Sharma P, Gupta A, Patel C, et al***. Pediatric lymphoma: Metabolic tumor burden as a quantitative index for treatment response evaluation. Ann. Nucl. Med. 26 (1):58-66; 2012.

13. ***Lopci E, Mascarin M, Piccardo A, et al***. FDG PET in response evaluation of bulky masses in paediatric Hodgkin's lymphoma (HL) patients enrolled in the Italian AIEOP-LH2004 trial. Eur. J. Nucl. Med. Mol. Imaging. 1; 46 (1):97–106; 2019.

14. ***Ibrahim F, Gabelloni M, Faggioni L, et al***. Is Semi-quantitative Methods Superior to Deauville Scoring in the Monitoring Therapy Response for Pediatric Hodgkin Lymphoma? J. Pers. Med. 28; 13 (3):445; 2023.

15. ***Hussien, S, Moustafa, H, Omar, W et al.*** The value of Quantitative Analysis in evaluation of the prognostic role of interim FDG-PET/CT in pediatric Hodgkin's lymphoma in Egypt. The Egyptian Journal Nuclear Medicine, 11 (11), 12–27; 2015.