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Role of Pet CT in the Initial Assessment of Lymphoma

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Abstract
Precise radiologic assessment of response to therapy in lymphoma patients is crucial to determine the effectiveness of treatment and subsequently forecast the relapse. This study aims to demonstrate the predictive utility of PET-CT metabolic volumetric measures in the assessment of patients with lymphoma. A sample of 30 patients with lymphoma were selected between January 2023 to April 2024 and PET-CT was done before therapy and post therapy and the findings were assessed. In our study, we found that the ΔSUV max of the CMR (Complete Metabolic Response) group was significantly higher than that of all other groups. The ΔSUVmax of the PMR (Partial Metabolic Response) group was significantly higher than that of the SMD (Stable Metabolic Disease) group. The ΔSUVmax of the SMD group was also significantly higher than that of the PMD (Progressive Metabolic Disease) group. Additionally, the ΔSUVmax of the PMD group was significantly lower than that of all other groups. However, the ΔSUVmax, ΔMTV and ΔTLG% from the baseline to the end of therapy could be used in prediction of patient response to treatment and determine patient prognosis. This study suggests that pre-treatment PET/CT quantitative measures (apart from baseline SUVmax) are not conclusive in the prediction of patient response to treatment.

INTRODUCTION

Hodgkin disease (HD) and non-Hodgkin lymphoma (NHL), which are malignant lymphomas, make up the fifth most common type of cancer and account for 5% to 6% of all malignancies[1]. After a biopsy confirms the diagnosis of lymphoma, stagingis crucial for formulating a treatment plan that works and for estimating prognosis[2]. The Cotswold modification, which defines bulky disease, is added to the Ann Arbor classification, which serves as the basis for staging HD and NHL[3]. Despite significant advancements in the treatment of lymphoma patients, many continue to experience a lack of response and relapse[4,5]. The current pre-treatment prognostic measures, such as the FLIPI (prognostic score for follicular lymphoma), the IPI (international prognostic index) and CT-based response assessment, are not very good at identifying these individuals. New prognostic and predictive indicators that enable the early identification of patient categories at high risk are therefore desperately needed[6-9].

Positron Emission Tomography combined with Computed Tomography (PET/CT) plays a crucial role in the initial evaluation of lymphoma patients. It is highly accurate in staging lymphoma by detecting the extent and distribution of disease throughout the body. It helps differentiate between localized and disseminated disease, which is crucial for determining the appropriate treatment strategy and provides information on the metabolic activity of lymphoma lesions through the Standardized Uptake Value (SUV). This quantitative measurement helps assess the overall disease burden and guide treatment planning and is also a useful tool in identifying the most metabolically active sites for sampling.

It is sensitive in detecting involvement of extra lymphatic sites, such as bone marrow, liver, spleen, and other organs and helps to assess treatment response. Decrease in SUVmax (maximum Standardized Uptake Value) indicates response to treatment, while persistent or new lesions suggest residual or progressive disease. SUVmax and other PET/CT parameters such as MTV, TLG provide prognostic information. Higher SUV at diagnosis is associated with poorer outcomes, while favorable response on interim PET/CT scans predicts better overall survival and progression-free survival. PET/CT has advantages over conventional imaging (CT or MRI) due to its ability to detect functional changes in addition to anatomical findings. It enhances accuracy in staging and response assessment. In some lymphoma subtypes, PET/CT is used to monitor minimal residual disease after treatment completion. It helps to identify patients at risk of relapse and guide decisions for consolidation therapy.

Thus, PET/CT is integral in the initial evaluation of lymphoma patients for accurate staging, assessing disease burden, guiding treatment decisions, predicting outcomes, and monitoring response to therapy. Its role continues to evolve with advancements in imaging technology and understanding of lymphoma biology.

Aims and Objectives:

- To estimate the post treatment quantitative metabolic volumetric parameters
- To highlight the diagnostic and prognostic values of baseline and post-treatment PETCT quantitative metabolic volumetric parameters in the evaluation of lymphoma patients.

MATERIALS AND METHODS

This is a prospective study that was carried out from January 2023 to April 2024 at the Department of Radiology, Tirunelveli Medical College and Hospital.. PET/CT imaging was done on thirty patients with biopsy-proven lymphoma, including both HL and NHL, at baseline (before to treatment) and post-therapy (six to eight weeks following the conclusion of chemotherapy). The study was performed after approval of the Ethical Committee of Scientific Research. Patients were over the age of 13 and under the age of 75 and both sexes were involved. Any patient with renal impairment, atopic diseases, or poor general health was excluded. Additionally, excluded were those who got radiation therapy or underwent any kind of surgery.

Procedure was done at 6-8 weeks following the conclusion of treatment and at the time of diagnosis. Prior to the PET CT, patients fasted for. Intravenous cannula insertion and pre-scanning blood glucose level determination (below 200 mg/dl) were completed. An intravenous injection of radioactive tracer (18F-FDG) at a dosage of 0.06-0.08 mCi/kg was administered.
An hybrid PET/CT scanner scan was conducted 60 minutes post-injection.

The patient was lying on the table in a supine position. The first single-phase contrast-enhanced helical CT scan was carried out after 125 ml of a low osmolarity iodinated contrast medium were injected using a power injector at a rate of 4 ml/s. Immediately following CT scanning, a PET scan spanning the same field of view was acquired. In order to scan the complete patient, six to seven bed positions were scheduled in three-dimensional acquisition mode, with three to five minutes of acquisition time at each position. The images were moved to the workstation for sagittal, coronal and axial reconstruction and presentation. Images were fused together.

Target lesions were chosen by analyzing the images. The target lesions have the greatest SUVmax and can have up to five lesions per subject; the lean body mass was taken into account when calculating the quantitative FDG uptake. Initial and post-treatment

SUVmax, MTV and TLG were calculated, and the percentage changes in SUV, TLG and MTV per lesion were measured. Based upon how well they respond to treatment, patients are divided into four groups: PMR (partial metabolic response), which is defined as a decrease in SUL peak of greater than or equal to 30%; CMR (complete metabolic response), which is defined as no uptake; SMD (stable metabolic disease), which is defined as a decrease or increase in SUL peak of less than 30% and PMD (progressive metabolic disease), which is defined as an increase in SUL peak of greater than 30%. After statistical analysis, the findings were tabulated.

RESULTS AND DISCUSSIONS

The study included 30 patients (15 males and 15 females). Their ages ranged from 16-62 years. Histopathological analysis revealed that 18 (60%) patients had classical HL, while 12 (40%) patients had NHL.

Lesions with an outcome of progressive or stable disease were designated as non-responsive lesions, while those of partial complete response were grouped together as responsive lesions. In an effort to determine whether quantitative PET/ CT parameters can diferentiate between the individual groups, namely the CMR, PMR, SMD and PMD groups, comparisons of the various variables between the four groups were also performed (Table 2). All post-treatment quantitative PET/CT parameters were signifcantly lower than pre-treatment values in PMR, CMR and

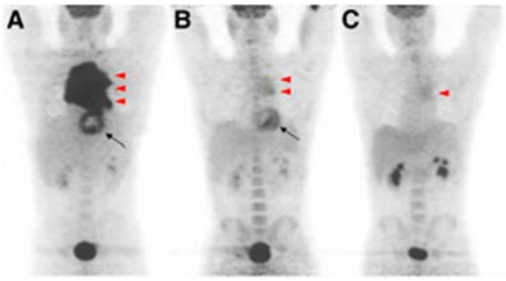

Fig 1:PET-CT OF 40 years old patient showing mediastinal mass

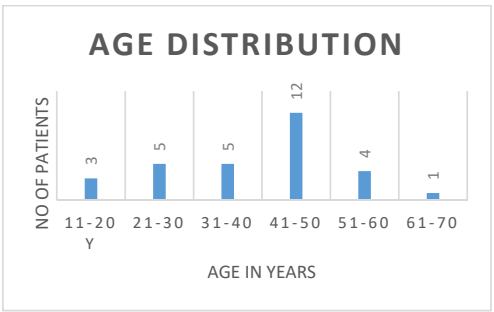

Fig. 2: AGE Distribution

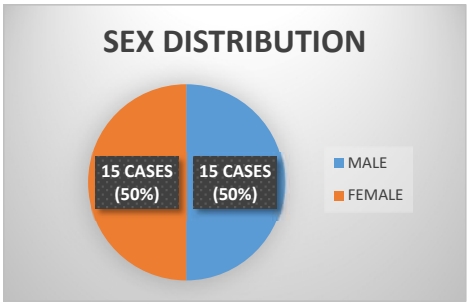

Fig. 3: SEX Distribution

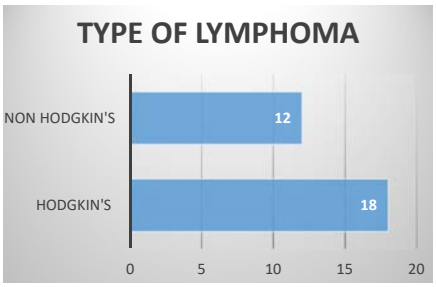

Fig. 4: Type of lymphoma

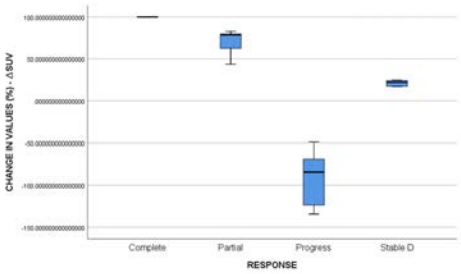

Fig 5: Box-and-whisker plots of SUV in PMR, CMR, SMD and PMD groups

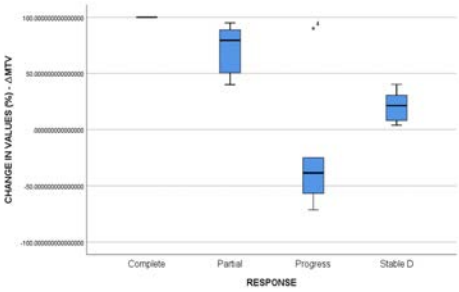

Fig 6: Box-and-whisker plots of MTV in PMR, CMR, SMD and PMD groups

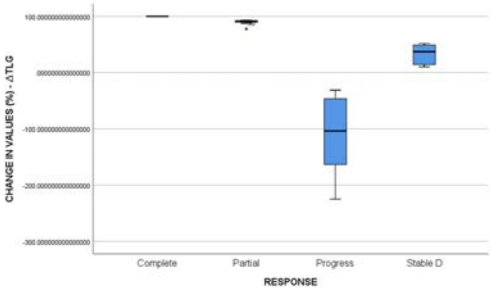

Fig 7: Box-and-whisker plots of TLG in PMR, CMR, SMD and PMD groups

Table 1: The sensitivities, specificities, PPV, NPV, accuracies, AUC, and P values of the optimum threshold values of the quantitative PET/CT parameters for differentiation of responsive from the non-responsive group

Parameter	Optimum threshold value	Sensitivity	Specificity	PPV	NPV	AUC	p-value
Baseline SUV	> 4.55	100.00%	41.67%	72.00%	100.00%	76.67%	0.0055
Post-treatment SUV	≤1.4	55.56%	100.00%	100.00%	60.00%	73.33%	0.0015
ΔSUV	> 28	100.00%	100.00%	100.00%	100.00%	100.00%	0.00000001
Post-treatment MTV	≤1	55.56%	100.00%	100.00%	60.00%	73.33%	0.0015
ΔMTV	> 42.9	94.44%	91.67%	94.44%	91.67%	93.33%	0.00000251
Post-treatment TLG	≤15.3	61.11%	100.00%	100.00%	63.16%	76.67%	0.00060453
ΔTLG	> 55	100.00%	100.00%	100.00%	100.00%	100.00%	0.00000001

Table 2 : Comparison of quantitative PET/CT parameters between all groups

		Partial response	Complete response	Stable disease	Progressive disease	P-value
Baseline SUV	Median	9.250	10.900	3.400	9.900	0.000152
	Range	12.0	4.4	2.6	10.6	
	IQR	6.5	1.7	2.1	4.5	
Post-treatment SUV	Median	1.950	0.000	2.700	19.150	<0.00001
	Range	5.9	0.0	1.8	12.8	
	IQR	4.6	0.0	1.6	6.4	
ΔSUV (%)	Median	78.57	100.00	21.98	-84.30	<0.00001
	Range	39.12	0.00	7.35	85.35	
	IQR	17.80	0.00	6.98	62.43	
Baseline MTV	Median	104.000	155.000	190.000	25.500	0.00089
	Range	176.0	80.0	273.1	112.0	
	IQR	84.5	22.5	141.8	41.5	
Post-treatment MTV	Median	14.000	0.000	144.750	26.000	<0.00001
	Range	56.0	0.0	195.7	37.0	
	IQR	39.5	0.0	150.2	34.8	
ΔMTV (%)	Median	79.42	100.00	21.38	-38.54	<0.00001
	Range	55.02	0.00	36.45	161.43	
	IQR	42.15	0.00	25.97	64.11	
Baseline TLG	Median	300.00	410.00	435.00	93.50	0.110543
	Range	1371	210	982	269	
	IQR	500	45	531	265	
Post-treatment TLG	Median	25.00	0.00	305.00	241.00	0.001396
	Range	104	0	920	461	
	IQR	70	0	410	401	
ΔTLG (%)	Median	91.67	100.00	37.17	-103.65	<0.00001
	Range	15.31	0.00	41.48	193.75	
	IQR	3.88	0.00	36.39	136.34	

SMD groups and signifcantly higher than pre-treatment values in the PMD group. There were statistically signifcant diferences in SUV, MTV and TLG between all four groups.

The term "lymphoma-proliferative disorders" refers to a group of lymphoid neoplasms that present with various histologic and clinical characteristics. These cancerous illnesses are related by their genesis in the lymphatic system and its different cellular constituents. Their response to treatment is evaluated by PET CT in this study.

Due to its high measurement repeatability and applicability, SUVmax is the most often used index in FDG PET analysis for a variety of purposes. It provides information on the metabolic activity of the most aggressive tumor cell. Recently, total lesion glycolysis (TLG), which is the product of mean SUV and MTV and metabolic tumor volume (MTV), a measurement of tumor volume with a high metabolism, have drawn the attention of researchers. Tumor burden is represented by volume-based indices called MTV and TLG, which are anticipated to be useful in response assessment and prognosis prediction.

We compare all baseline and posttherapy PET/CT parameters among the four groups: responsive lesions, which are defined as PMR (partial metabolic response) and CMR (complete metabolic response); non-responsive lesions are defined as SMD (stable metabolic disease) and PMD (progressive metabolic disease). We discovered that the CMR group's baseline SUV was significantly higher than the SMD group's, but it was lower than the PMR group's. Compared to the SMD and PMD groups, the pre-treatment SUV of the PMR group was significantly higher. Compared to the other groups, the CMR group's posttreatment SUV was much lower. The PMD group's post-treatment SUV was much higher than that of any other group.

The findings of our investigation were consistent with the study conducted by Huang[10], which evaluated patients' responses to treatment following the completion of six to eight treatment cycles. The low SUVmax group (pre-treatment SUVmax=9.0) had a significantly greater complete remission rate

There are multiple subtypes of lymphoma that is aggressive. These include peripheral T-cell lymphoma, difuse large B-cell lymphoma (DLBCL), mantle cell lymphoma, CNS lymphoma, Burkitt lymphoma, and AID-associated lymphoma. Baseline SUVmax also has a significant impact on the identification of foci of aggressive transformation and the prediction of the existence of more aggressive histological components, which may have therapeutic and diagnostic implications.

According to Ngeow[11], areas with SUV of >10 in an indolent lymphoma patient indicate the potential for transformation or the potential existence of an

aggressive component over and beyond what the histology suggests.

These results imply that MTV and TLG are helpful in prognosis prediction and treatment response expectation. But when it came to evaluating the first (baseline) reaction, baseline MTV and TLG in our trial did not outperform baseline SUVmax.

In both the responsive and nonresponsive groups, there was no discernible difference between the baseline MTV and TLG in our investigation. The increase in baseline MTV and TLG is primarily seen in non-responder groups; however, it is statistically not accurate predicting of treatment response. We note that the range of baseline MTV and TLG is lower in responsive than nonresponsive groups, but it is clinically insignificant and their statistical.

123 elderly patients who were first diagnosed with HL were included in a prospective research by Albano[12], which contradicts our findings. According to Akhtari[13], patients may be more accurately risk-stratified if three-dimensional tumor burden measurements, such as MTV and TLG, were obtained from baseline PET/CT scans.

In a study by Zhou *et al.* involving 43 patients, where 28 patients underwent both baseline and end-of-treatment PET/CT scans, the ΔSUVmax% (percentage change in maximum standardized uptake value) between these scans was found to be significantly different between patients who progressed (n=14) and those who remained progression-free (n=14) (41.70% vs. 82.34%). They also noted that using ΔSUVmax% as a predictor of progression, patients with ΔSUVmax% < 66.95% had lower progression-free survival (PFS) compared to those with ΔSUVmax% > 66.95%.

In our study, we found that the ΔSUVmax of the CMR (Complete Metabolic Response) group was significantly higher than that of all other groups. The ?SUVmax of the PMR (Partial Metabolic Response) group was significantly higher than that of the SMD (Stable Metabolic Disease) group. The ΔSUVmax of the SMD group was also significantly higher than that of the PMD (Progressive Metabolic Disease) group. Additionally, the ΔSUVmax of the PMD group was significantly lower than that of all other groups.

With respect to the quantitative measures following treatment, we observed that the CMR group's post-treatment SUV and post-treatment MTV were much lower than those of any other group. The PMD group had significantly higher post-treatment SUV and post-treatment MTV than any other group. The CMR group's post-treatment TLG was significantly lower than that of the other groups, while the PMR group's post-treatment TLG was much lower than that of the SMD and PMD groups.

These findings indicate that, when evaluating treatment response, only baseline SUVmax had a significant predictive value among baseline PET/CT measures. It appears that ΔSUVmax, ΔMTV and ΔTLG% from pre-treatment to post-therapy PET/CT can be used to predict the prognosis of patients.

CONCLUSION

However, the ΔSUVmax, ΔMTV and ΔTLG% from the baseline to the end of therapy could be used in prediction of patient response to treatment and determine patient prognosis. This study suggests that pre-treatment PET/CT quantitative measures (apart from baseline SUVmax) are not conclusive in the prediction of patient response to treatment. The specificity was found to be low future clinical trials are required in light of these findings to determine the usage of these indicators in other prognostic models (particularly if connected with PFS and OS), in an effort to improve risk assessment, patient prognosis and treatment decision.

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