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PET/CT Dual Time Point Scanning in Evaluation of Malignant Lymphoma

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ABSTRACT:

Purpose: The purpose of the present study is to evaluate the value of dual-time-point F-18 FDG PET/CT imaging in malignant lymphoma (ML) to differentiate between benign lesions and residual or relapsing malignant lesions. **Patients and methods:** This prospective study included 252 lymph nodes in 60 patients. F-18 FDG PET/CT scan was performed at 50 min (early scan) and at 100 min (delayed scan) after the injection. The maximum standardized uptake value (SUV max) of each lesion was calculated at early and delayed scans. We estimated the difference between early and delayed SUV max (D-SUV max) and the retention index (RI-SUV max) to evaluate the change of tracers handling in the lesions. Also, the early lesion/liver ratio and delayed lesion/liver ratio were calculated. Then their cut-off values were evaluated using receiver operating characteristic analysis. Correlations of these cutoff values with different clinico-pathological parameters were done. **Results:** The cut-off value in Early-SUV max was 4.05, Delayed-SUV max were 4.45, D-SUV max was 0.45, RI-SUV max was 0.155, Early lesion/liver ratio was 1.25 and in Delayed lesion/liver ratio was 1.35. The delayed-SUV max had the highest sensitivity and specificity of 85.3% and 92.6% respectively. The overall result of DTP PET/CT showed sensitivity of 95.3%, specificity of 76.4%, accuracy of 86.1%, and positive predictive value of 80.9% and negative predictive value of 94% respectively. Based on a total of true and false results in early and delayed PET/CT imaging, there was significant improvement in specificity in the delayed PET/CT imaging compared to the early PET/CT imaging. Correlation of DTP cut off value with the different clinico-pathological parameters showed that nodular sclerosis and lymphocytic predominance pathological subtypes had the highest sensitivity of 100%, while mixed cellularity showed the lowest sensitivity of 64.3%. In Hodgkin lymphoma lesions, cervical sites showed

the lowest sensitivity and specificity 90.2% & 61.4% respectively.

Conclusions: The dual time point FDG PET/CT scan is useful to differentiate between post-therapy changes as benign lesions and residual or relapsing malignant lesions in malignant lymphoma.

Key words: Dual-time-point scans - SUV max - retention index.

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INTRODUCTION:

Malignant lymphoma (ML) is one of the most common hematologic malignancy[1] .Fluorine-18-fluorodeoxyglucose (F-18 FDG) positron emission tomography/ computed tomography (PET/CT) is widely used for staging and treatment evaluation of ML[2,3]. PET/CT offers advantages over conventional imaging techniques, because it can demonstrate abnormal metabolic activity and extension of malignant diseases [4,5].

Dual time point imaging (DTPI) and delayed time point imaging have been used for the differentiation of inflammatory and malignant processes and to enhance the specificity of FDG PET imaging for diagnostic and prognostic purposes. The accumulation of FDG in cells, following its phosphorylation to FDG-6-phosphate by hexokinase, is facilitated by the glycolytic pathway. This biological pathway allows the characterization of tumor biology and also makes it possible to differentiate malignant cells from normal and inflammatory cells. However, it has now been demonstrated that both inflammatory and infectious disorders have increased glycolytic activity and therefore can mimic malignancy in many settings [6].

Dual time point PET/CT imaging may help in differentiation between benign and malignant lesions; however there is lack of agreement in some published data. Some reports indicated that F-18 FDG PET is sensitive and specific in the diagnosis and staging of patients with ML, with significant improvement in the diagnostic accuracy of FDG PET scan using dual-time-point scans[7,8].

Recently, Shinya et al.[2] evaluated the differences of FDG uptake in early and delayed scans, and compared the SUVmax and the retention index of SUVmax between the different grades of lymphoma as various cell types exhibit varying rates of F-18 FDG uptake.

The aim of this study: is to evaluate the value of dual time FDG PET/CT in assessment of patients with malignant lymphoma especially during follow up to differentiate between malignant viable tumor and inflammatory changes.

PATIENTS AND METHODS:

This prospective study was conducted at the National Cancer Institute, Cairo University in the period between March 2014 & December 2015. Sixty patients with histo-pathologically proven lymphoma were collected and followed up for therapy response assessment. Clinical information were extracted from the medical records, including age, sex, methods of diagnosis, detailed pathology, imaging findings.

Exclusion criteria: Patients with recent chemotherapy or radiotherapy and with corticosteroid therapy.

The findings of PET, CT, and fused imaging were compared with histopathology or clinical follow-up results. All patients were informed about the study. The ethical committee of the NEMROCK Center and the radiation safety committee of NCI had given approval.

FDG PET-CT: Patients fasted for at least 4 h before the injection of 370-555 MBq 18F-FDG but drink water to maintain good hydration except if sedation is indicated. The fasting blood glucose is below 150 mg/dl. PET/CT study was done using (GE, PET/CT Discovery). All scans started 50 min as well as 100 min after tracer injection (5–7 bed positions; acquisition time, 2-3 min/bed position). Intravenous contrast agent was administered in most patients. 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 scan was acquired reached caudally to the mid thighs. PET over the same region was performed immediately after acquisition of the CT images. 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).

Interpretation:

Qualitative (Visual) assessment: Interpretation was accomplished by 2 experienced nuclear medicine physicians. The analysis was conducted on per patient basis and per lesion basis for 18F-FDG PET/CT interpretation, any focal uptake equal to or superior-to back ground was interpreted.

Quantitative assessment: The maximum standardized uptake value (SUV max) of lesion related F-18 FDG accumulation on 50 min (early SUVmax) and 100 min (delayed SUVmax) images for lesions in each patient, after manual application of the volumetric regions of interest on the trans-axial attenuation-corrected PET slices, around the areas demonstrating the greatest accumulation of 18F-FDG. Another sizable ROI was drawn over the liver where its max SUV was considered reference activity. A region of interest (ROI); which was manually drawn for SUVmax calculation on early PET and delayed PET scans, ROIs were placed in identical positions. We calculated RI-SUV max and delayed SUV max (D-SUVmax)

D-SUVmax = Delayed SUVmax-Early SUVmax.

RI-SUVmax = (Delayed SUV max-Early SUVmax)/ Early SUV max.

Response was assessed according to International Harmonization Project Criteria for Assessment of Response to Therapy for Lymphoma [(9)].

CR: complete resolution of FDG avid lesions.

PR: >50% decrease in sum or product of diameters of lesions with persistent residual FDG uptake in at least one site.

PD: any new FDG avid lesion; >50% increase in sum or product of diameters of previously involved sites with respect to nadir sum or product of diameters associated with abnormal FDG uptake; or new or recurrent bone marrow involvement.

SD: no complete remission; partial remission, or progressive disease.

Follow up: was performed after 6 months either by PET/CT or CT.

The lesion was considered as true-positive if its histopathology was positive or if it showed progression at follow-up session. The lesion is considered negative if histopathology was negative or if follow-up examinations did not show any pathologic progression. The lesion was considered as false-positive if histopathology was negative or if it showed no progression at follow-up sessions. The lesion is considered as false-negative if positive histopathology was elicited and/ or lesion growth was found in follow-up.

RESULTS:

This prospective study was conducted on 60 patients with pathologically proven malignant lymphoma referred for evaluation at the National Cancer Institute, Cairo University in the period between March 2014 and December 2015.

Per Patient analysis: The age of the patients ranged from 4 to 62 years with a

median and mean of 24.5 and 26.4 years respectively. There was a predominance of disease in males with male (56.7%) to female (43.3%) with ratio approximately 1.3:1. There was a high frequency of Hodgkin's disease found in 43 patients (72%); while 17 patients (28%) had Non-Hodgkin's disease. Regarding the Hodgkin lymphoma patients, nodular sclerosis and mixed cellularity are the most common types 36.3% and 26.7% respectively.

The Hodgkin lymphoma patients were initially staged according to Ann Arbor staging; there was a relatively high frequency of stage II (73.3%). The non-Hodgkin lymphoma patients were initially staged according to Cotswold's modification of the Ann Arbor system, a relatively high frequency of stage II (47.1%) was noted **(Table 1).**

Regarding B-symptoms, 72.1% of Hodgkin lymphoma patients didn't have B-symptoms at initial staging, while in non-Hodgkin lymphoma patients, 70.6% of patients showed B-symptoms at initial staging (Table 1). In non-Hodgkin lymphoma patients, 11 out of 17 patients (64.7%) had nodal lesions, 29.4% had extra-nodal lesions and only one patient had lung lesion, (Table 1).

Table (1): Initial Staging in HL & NHL Patients [n=60].

	HL (43)	NHL (17)	P-value.
Initial staging.	**Ann Arbor staging.**	**Cotswold's modification.**	
Stage I.	**1 (2.3%)**	**0 (0.0%)**	**< 0.001***
Stage II.	**36 (83.7%)**	**8 (47.1%)**	
Stage III.	**5 (11.6%)**	**3 (17.6%)**	
Stage IV.	**1 (2.3%)**	**1 (5.9%)**	
Stage E.	**0 (0.0%)**	**5 (29.4%)**	
B-symptoms.			
B-symptoms.	**12 (27.9%)**	**12 (70.6%)**	**< 0.001***
No B-symptoms.	**31 (72.1%)**	**5 (29.4%)**	

Diagnostic Image analysis:

Using clinico-pathological & FU data as a reference standard, the results of early & delayed PET/CT images in both HD and NHL patients were assessed (table 2). The number of false positive results of the early PET/CT imaging was significantly higher than the number of false positive results in the delayed PET/CT imaging. Based on a total of true and false results in early and delayed PET/CT imagings, there was significant improvement in specificity in the delayed PET/CT imaging compared to the early PET/CT imaging **Table (2).**

Table (2): The difference between early and delayed PET/CT imaging in both HD and NHL.

Outcome.	HL		NHL	
	E.	D.	E.	D.
True positive.	53	84	39	39
True negative.	49	71	14	23
False positive.	69	28	10	1
False negative.	18	6	-	-
Sensitivity.	74.6%	84%	100%	100%
Specificity.	41.5%	71.7%	58.3%	95.1%

Deauville Criteria based lesion scoring in Hodgkin Lymphoma:

According to Deauville criteria in Hodgkin lymphoma lesions, the majority of lesions (155/189), were of grade 3(82%), 18 lesions (9.5%) were of grade 2, and 16 lesions (8.5%) were of grade 4. There were no patients with grade 0, 1 & 5 in the present study.

The outcome of Deauville criteria scoring system was evaluated to demonstrate the true & false positive results using a clinico-pathological & FU data as a reference standerd. False positive results were more frequent in grade 3. In contrast no false positive results were recorded in Grade 4 scoring. Accordingly; Grade 4 showed the highest sensitivity of 100% while grade 2 showed the lowest sensitivity of 44.4 %. **(Table 3).**

Table (3): Deauville Criteria based lesion scoring in Hodgkin Lymphoma [n=189].

	Deauville criteria.		
	2.	3.	4.
TP	4	63	16
TN	8	55	-
FP	1	35	-
FN	5	2	-
Sensitivity.	44.4%	96.9%	100%
Specificity.	88.9%	61.1%	-

Overall mean quantification difference between Early & Dual Time Point PET/CT values:

The mean values for SUVmax, lesion to liver ratio and retention index were used for lesion quantification based data analysis in early and dual time point FDG PET-CT. No significant difference detected. Therefore limited retention indeces reflect difference between early (conventional) and DTP PET-CT of 14.5% (Table 4).

Table (4): Overall lesion quantitative differences in early & DTP PET-CT in Lymphoma patients.

Items.	Early	Delayed
SUVmax.	**4.308**	**4.955**
Lesion/liver ratio.	**1.524**	**1.810**
RI-SUVmax.	**0.1452**	

Mean of DTP PET/CT values according to site and type of lesions:

Regarding the nodal lesions, the cervical region had the highest mean value in early-SUV, delayed SUV, D-SUV and RI-SUV 5.6, 6.9, 1.2 & 0.21 respectively **(Table 5).** In extra-nodal lesions, mean of early SUV, delayed SUV and early lesion/liver ratio were 3.9, 4.5 & 0.9 respectively. All these values were less than the mean values of nodal lesions.

For lung lesions, mean of early SUV, delayed SUV, D-SUV and RI-SUV were 3.6, 3.7, 0.1 & 0.03 respectively. All these values were less than the means of nodal and extra-nodal lesions as showed in **(Table 5).**

Table (5): Lesion site based quantitative analysis in early & delayed DT Point PET/CT Values at Different Sites.

Mean of Site.	Early SUV.	Delayed SUV.	D- SUV.	RI-SUV.	Early lesion/liver ratio.	Delayed lesion/liver ratio.
Cervical	**5.6**	**6.9**	**1.2**	**0.21**	**1.6**	**1.9**
Axillary	**4.0**	**4.6**	**0.6**	**0.08**	**1.7**	**2.0**
Mediastinal	**4.5**	**4.9**	**0.3**	**0.07**	**1.3**	**1.5**
Abd-pelvic	**4.5**	**5.3**	**0.8**	**0.16**	**1.4**	**1.6**
Extra-nodal	**3.9**	**4.5**	**0.7**	**0.18**	**0.9**	**1.7**
Lung	**3.6**	**3.7**	**0.1**	**0.03**	**1.4**	**1.4**

Mean quantitative analysis in different pathological sub-types:

Table (6) shows the mean quantification values for variable quantitative indices in different pathological sub-types in both HD & NHL patients. A significantly higher mean values for Early, delayed as well as retention index in NHL compared to HD (P-value < 0.001, 0.008 and 0.013 respectively. Among different pathological sub-types of HD, nodular sclerosis exhibits the highest mean quantitative values in both early SUV and delayed SUV followed by mixed cellularity, while the lymphocytic predominance has the lowest quantitative values.

Table (6): Pathological sub-types related quantitative indices of DTP imaging:

Items.	Mean				P-value
	HL			NHL	
Early-SUV max.	**3.9**			**5.5**	**< 0.001***
	NS 4.4	**MC 3.8**	**LR 3.7**		
Delayed SUV max.	**4.6**			**6**	**0.008***
	NS 5.2	**MC 4.6**	**LR 4**		
D-SUV max.	**0.69**			**0.50**	**0.329**
	NS 0.8	**MC 0.8**	**LR 0.3**		
RI-SUV max.	**0.17**			**0.07**	**0.013***
	NS 0.18	**MC 0.21**	**LR 0.08**		
Early-lesion/liver ratio.	**1.5**			**1.7**	**0.075**
	NS 1.5	**MC 1.5**	**LR 1.6**		
Delayed-lesion/liver ratio.	**1.7**			**2**	**0.156**
	NS 1.8	**MC 1.7**	**LR 1.6**		

Quantitative-prognostic Image Analysis:

As a trial to assess the value of PET/CT, quantitative analysis, a Receiver Operator Characteristic (ROC) curve analysis was used in evaluation of different used quantitative indices to detect a cutoff point in that yield the best compromise between sensitivity and specificity. The cutoff point of 4.05 and 4.45 were marked for Early SUV & Delayed SUV respectively with no significant differences. Similarly in Early

and delayed lesion/liver ratios. Accordingly the significant difference in retention index was limited to 15.5% **(Table 7).**

Table (7): Quantitative Value of Different Parameters of DTP-PET/CT in Lymphoma Lesions [n=252].

	Cutoff.	Sensitivity.	Specificity.	AUC.
Early-SUV.	**4.05**	**71.3%.**	**82.8%.**	**0.816.**
Delayed-SUV.	**4.45.**	**85.3%**	**92.6%**	**0.932**
D-SUV.	**0.45.**	**73.6%**	**77.9%**	**0.887**
RI-SUV.	**0.155.**	**64%**	**80%**	**0.796**
Early-lesion/liver ratio.	**1.25.**	**80.6%**	**69%**	**0.79**
Delayed lesion/liver ratio.	**1.35.**	**86%**	**76.2%**	**0.881**

ROC curve for Delayed-SUV max:

The proper cut-off for SUV maxD to differentiate between the benign (inflammatory or post-therapy) and malignant (residual or relapsing) in 252 lesions of lymphoma was **4.45**, yielding a sensitivity of 85.3%, and specificity of 92.6%. The AUC in delayed SUV max was statistically significant with p-value < 0.001 **(Figure 1).**

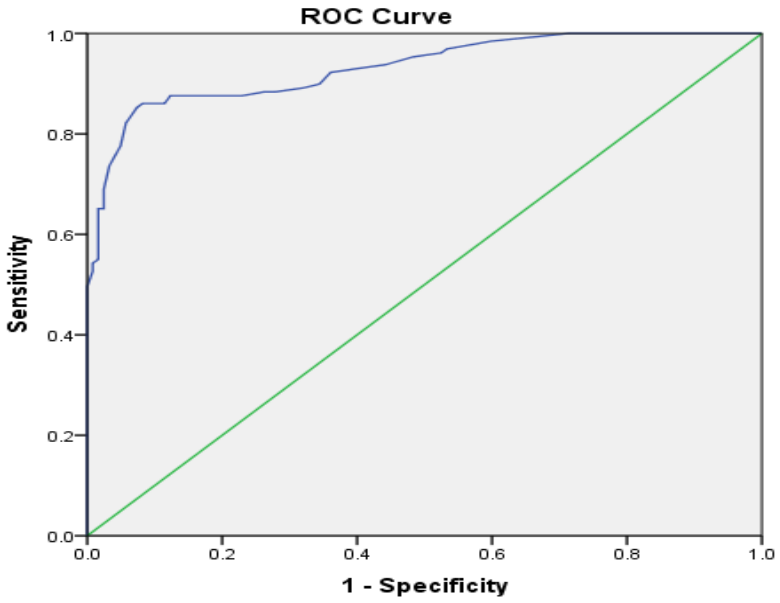

Figure (1): ROC Curve for Delayed-SUV in 252 Lesions of Lymphoma.

ROC curve for D-SUV max:

The D-SUV_{max} cut-off value for proper differentiation between the benign (inflammatory or post-therapy) and malignant (residual or relapsing) lesions were **0.45**, yielding a sensitivity of 73.6%, and specificity of 77.9%. The AUC in D-SUVmax was statistically significant with p-value < 0.001.

ROC curve for RI-SUV max:

The RI-SUV_{max} cut-off value for proper differentiation between the benign (inflammatory or post-therapy) and malignant (residual or relapsing) lesions was **0.155**, yielding a sensitivity of 64%, and specificity of 80%. The AUC in RI-SUVmax was statistically significant with p-value < 0.001. **(Figure 2).**

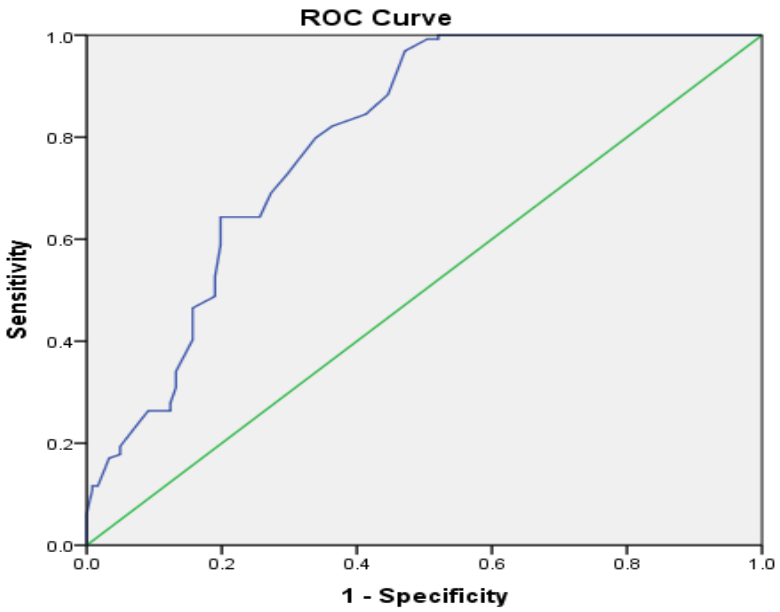

Figure (2): ROC Curve for RI-SUV in 252 Lesions of Lymphoma.

DTP PET/CT cutoff value in relation to pathological subtypes:

The correlation of DTP PET/CT cutoff value with pathological subtypes was done. In Hodgkin lymphoma, nodular sclerosis and lymphocytic predominance showed the highest sensitivity of 100%, while mixed cellularity showed lowest sensitivity of 64.3% (five of these lesions were located at cervical regions). Amongst the three Hodgkin lymphoma subtypes, lymphocytic predominance showed the highest specificity of 100%.

Non-Hodgkin lymphoma lesions showed sensitivity of 100% and specificity of 95.8% (Table 8).

Table (8): DTP PET/CT cutoff Value in relation to pathological subtypes in HD and NHL patients.

	HL			NHL
	NS	MC	LR	
TP	43	38	3	39
TN	31	27	13	23
FP	21	7	-	1
FN	-	6	-	-
Sensitivity	100%	64.3%	100%	100%
Specificity	59.6%	75%	100%	95.8%

DTP PET/CT cutoff value in relation to type of lesions:

In Hodgkin lymphoma lesions, the nodal lesions showed the lowest specificity of 69.2% with high number of false positive 28 lesions, while the lung lesions showed highest sensitivity & specificity of 100% with no false positive lesions

In non-Hodgkin lymphoma lesions, the nodal and lung lesions showed the highest specificity of 100% while the extra-nodal lesions showed the lowest specificity of 66.7%. (Table 9).

Table (9): DTP PET/CT Cutoff Value in relation to type of lesions in HD and NHL patients.

	HL			NHL		
	Nodal.	Extra-nodal.	Lung.	Nodal.	Extra-nodal.	Lung.
TP	82	-	2	36	3	-
TN	63	2	6	20	2	1
FP	28	-	-	-	1	-
FN	6	-	-	-	-	-
Sensitivity.	93.2%	-	100%	100%	100%	-
Specificity.	69.2%	100%	100%	100%	66.7%	100%

DTP PET/CT in different sites:

Regarding to the sensitivity and specificity according to different sites of lesions using the cutoff value of DTP, the cervical region in Hodgkin lymphoma patients showed the lowest specificity of 61.4 % with false positive 27 lesions.

Figure 3 (A&B) showed delayed imaging in patient with NHL with residual viable tumor that showed more progressive course during follow up .

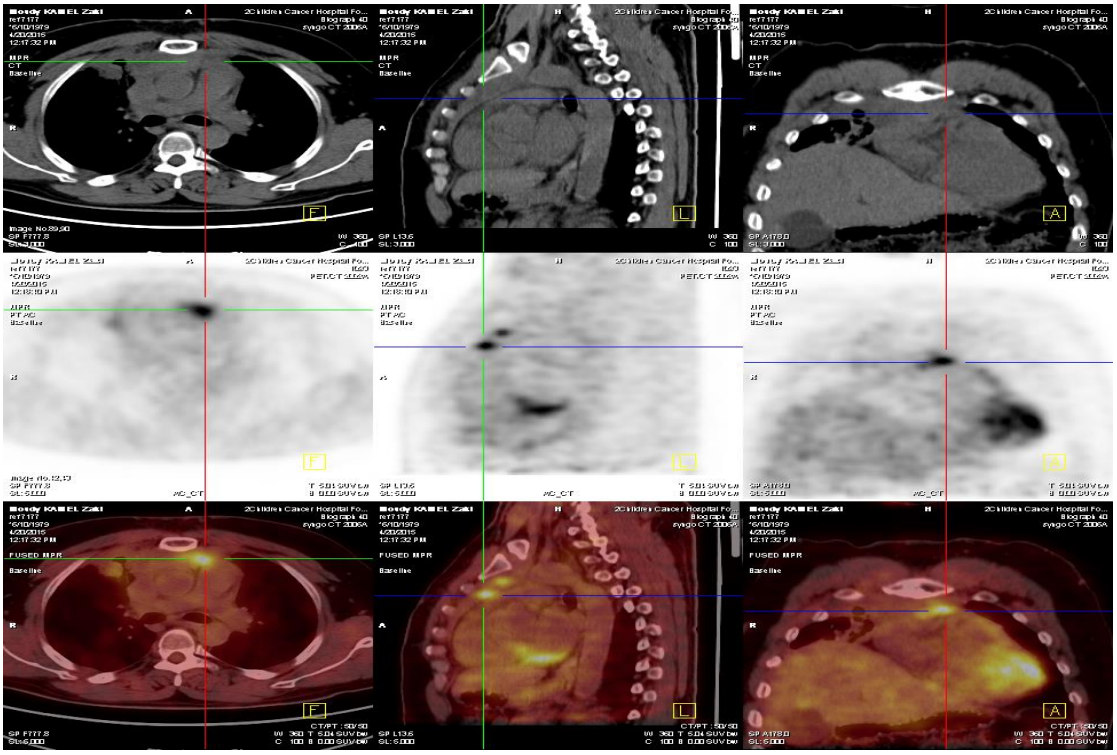

Figure (3 A): 35 yrs old male patient with NHL (large B cell), with large anterior mediastinal mass following treatment with residual viable FDG uptake in delayed scan with SUV of 5.

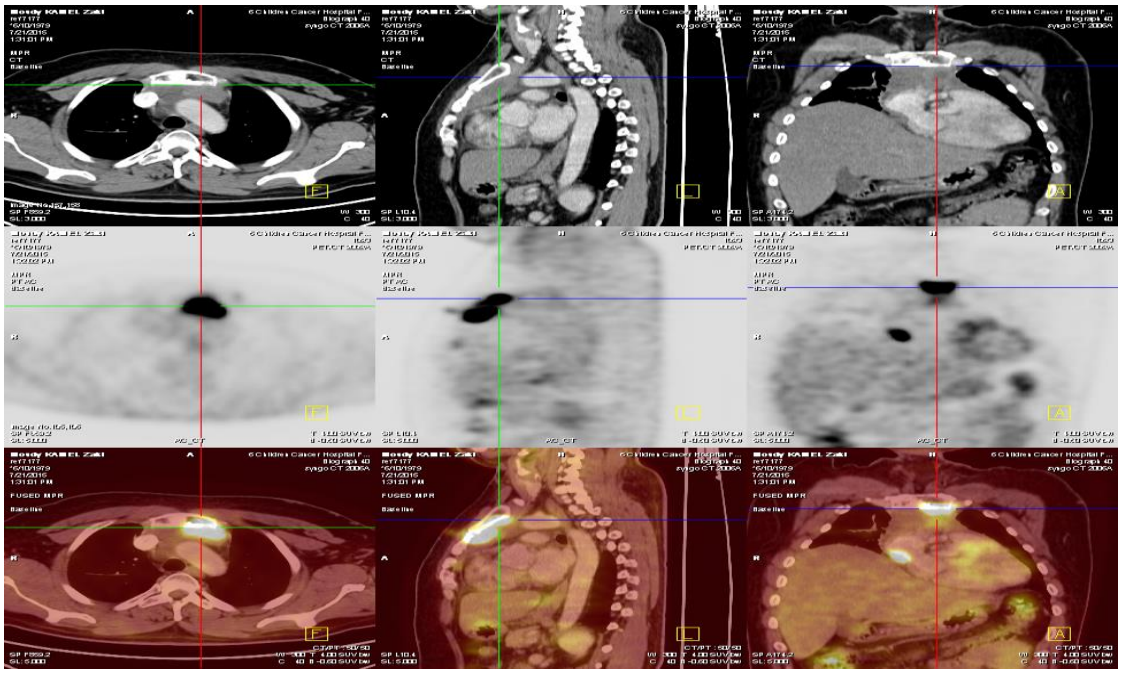

Figure (3 B): Follow up after 3 months without treatment, there was disease progression in the size of the mass with high FDG uptake in delayed scan SUV max~15.5 with appearance of other new lesions that indicated disease progression.

DISCUSSION:

FDG is not tumor specific with increased accumulation in a variety of benign entities, including infections, drug toxicity, radiation therapy, postoperative, degenerative changes, or injection leakage[10]. So, there is a considerable overlap between the SUV max of malignant and benign lesions, causing false positive results of F-18-FDG PET/CT. [11, 12, and 13].

Dual–time-point FDG PET/ CT exploits the unique differences in the kinetics of FDG uptake between benign and malignant entities to differentiate between the two pathologic entities [14,15]. Indeed, the uptake of FDG in malignant tissues does not reach a maximum until 2–4 hours after FDG injection, whereas most inflammatory lesions or normal tissues typically achieve maximum uptake of the tracer within 1 hour. It has therefore been hypothesized that this difference in the kinetics of FDG uptake could be used to improve the ability of PET to distinguish benign from malignant processes by acquiring FDG PET images at two different time points after FDG injection. Malignant lesions tend to increase in intensity between the two scans, whereas benign lesions tend to remain stable or decrease slightly in intensity[14,15]. The present study is prospective study from March 2014 to December 2015 with follow-up 6 months for 60 lymphoma patients. The aim of the study is to evaluate the usefulness of dual time point PET/CT.

Dual time point PET/CT has been used for the differentiation of inflammatory and malignant processes and found to enhance the specificity of FDG PET imaging for diagnostic and prognostic purposes [16].

Kumar et al. reported that F-18 FDG uptake in malignant cells was related to low glucose-6phosphatase activity, and increased glucose uptake through glucose transporter proteins in these cells. In contrast, such a prolonged period of F-18 FDG uptake is not seen in benign lesions. They reported the delayed average SUVs showed a minimal increase in sensitivity from 38% to 41%. They found that changes in dual-time-point SUVs would be a more valuable diagnostic tool than imaging at a delayed single time point alone [17].

In lymphoma, the F-18 FDG uptake is probably associated with Glut1 expression[18] and Ki-67 values[19,20]. In many malignant tumors, scan start times of 45–60 min have been reported to cause significant underestimation of the true SUVs, because SUVs do not reach maximum levels until several hours after F-18 FDG injection [21, ***22***] .

In the present study, the sensitivity and specificity of early DTP PECT/CT imaging were 100% & 58.3% as compared to 100% and 95.1 % of delayed images in NHL, while in HD; it showed sensitivity and specificity of 74.6% & 41.5% in HD as compared to 84 % & 71.7 % in delayed images respectively.

Farghaly et al., [23] Used DTP PET/CT in differentiation between malignant and benign lesions in cancer patients. They reported a specificity of 57% and PPV of 59% in differentiating malignant from benign lesions. They suggested that the low specificity and PPV of DTP likely result from the overlap between benign and malignant lesions and could be explained by F-18-FDG uptake in benign tumors was correlated with glucose transporter-1 expression, However, the retention index of F-18-FDG showed a positive correlation with the expression of hexokinase Type II.[24]. They found that, the specificity of DTP F-18-FDG PET/CT scanning in differentiating malignant from benign lesions was 57%, the accuracy was 73%, PPV was 59%, and NPV was 100%.

In the present study, we also found that the mean SUV value for nodal lesions was the highest compared to extra nodal and lung lesions, the cervical nodal lesions showed the highest mean value in all nodal lesions. Such preferential FDG uptake to lymphomatous nodal lesions rather than extra nodal one can be explained by their native biological nature, cellular density, their higher ability to contain lymphomatous cells as well as residency & migration of inflammatory cells therein.

Significantly higher mean values were detected for early, delayed as well as retention index in NHL compared to HD (P-value<0.001, 0.008 and 0.013 respectively). This was attributed to the higher proliferation index & relatively lower glucose 6-phosphatase activity, as well as, higher expression of hexo-kinase II in NHL especially B-cell subtype compared to HD.[24].

Similarly Nakayama et al., reported the mean values of early SUV max, delayed SUV max, D-SUV max, and RI-SUV max were 6.70 ± 5.43, 8.62 ± 6.27, 1.91 ± 1.33 and 0.38 ± 0.23 in ML, and 3.37 ± 2.43, 4.16 ± 2.44, 0.80 ± 1.04 and 0.25 ± 0.25 in benign lesions, respectively. That reported significant differences between ML and benign lesions in those indices (P<0.01)[25].

Costantini et al., [26] found a considerable overlap in the early or delayed SUV max among most benign and malignant lesions. The degree of overlap became less evident with delayed imaging, likely because the uptake of FDG continues to increase in malignant tissues for several hours after FDG injection, whereas benign lesions

show a decrease or remain stable over time.

In our study, the delayed-SUV max of cutoff 4.45 showed sensitivity and specificity of 85.3% and 92.6% respectively; which is higher than early SUVmax (sensitivity: 71.3% and specificity: 82.8%). The AUC of Delayed-SUVmax was the greatest among these six indices.

Also, ***Nakayama et al.,***[26,25] reported that delayed SUVmax and D-SUV max were significantly better predictors of ML than early SUVmax. The delayed-SUV max cutoff was 4 with sensitivity, specificity, PPV and NPV of 75.4, 60, 76.2 and 61% respectively with P-value <0.005. They also, showed that the cutoff of D-SUV max was 1 and showed sensitivity of 82.6%, specificity of 65.2%, PPV of 80.1% and NPV of 68.8% with P-value <0.005. The D-SUV max was significantly better predictor of ML than early SUVmax. The AUC of D-SUV max was the greatest among these four indices.

In principle, RI-SUV max must have a merit of not being dependent on scale and is a useful index[2,27]. Some authors reported RI is a good predictor for diagnosis and prognosis, and is superior to only early imaging [28, 29]. The reason is unknown why RI-SUV max was not the best predictor [30].

In our study, the cutoff of RI-SUV max was 0.155; it showed sensitivity of 64% and specificity of 80%. Also, ***Nakayama et al.,***[25] reported Cutoff of RI-SUV max was 0.22 and showed sensitivity, specificity, PPV and NPV of 72.8, 55. 7, 73.6 and 58.6% respectively with no statistical significance. Furthermore ***Costantini et al.***[26,27] reported the use of retention index cutoff of 10% or higher to increase specificity to 80%, whereas the sensitivity decreased moderately to 77%.

CONCLUSIONS:

The dual time point FDG PET/CT is additional useful imaging method to differentiate between post-therapy changes and residual or relapsing malignant lesions in lymphoma as DTP has a high NPV denoting its high reliability to rule out malignancy. PET/CT dual time scanning may help to consider proper site to proceed to more invasive tests, such as biopsy.

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