FDG PET/CT versus contrast enhanced CT in the management and post therapeutic follow up of lymphoma

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Abstract: Lymphoma comprises a histologically heterogeneous group of cancers derived from the cells of the immune system. The hallmark of the disease is the enlargement and proliferation of lymph nodes or secondary lymphoid tissues.

While CT and MR imaging rely on **anatomic changes** for diagnosis, staging and follow-up of lymphoma, PET-CT provides anatomic and metabolic information and has several advantages over other techniques. PET-CT has faster attenuation correction and lower location mismatches compared with the PET system alone.

In our study PET-CT provided its greatest benefit in the staging and restaging of lymphoma. PET-CT findings led to upstaging of 8 patients (27.6%) from stage I to stage II.

The sensitivity of CECT for detection of sites of involvement decreases as the number of sites of involvement increases in every case. PET-CT was much more sensitive than CECT in detecting extranodal site of involvement.

At mid treatment assessment the number of patients with discordant findings between PET-CT and CECT was only 2 cases while the number of patients with discordant findings at the Post-treatment assessment was 1 case.

Our study concluded that PET-CT may be better than contrast enhanced CT for routine baseline investigation of Stage I & II of Lymphoma. Also in our study there was no significant discordance between interim PET-CT and contrast-enhanced CT results therefore, either PET-CT or contrast-enhanced CT may be used for response assessment and predicting outcome in early stages of Lymphoma.

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1. Introduction

Integrated positron emission tomography (PET) and computed tomography (CT) performed with fluorine 18 (^{18}F) fluorodeoxyglucose (FDG) is one of the functional imaging modalities used to visualize glucose metabolism in living human tissues. Given its high sensitivity in detection of malignancy, FDG PET-CT is increasingly being used in evaluation of oncology patients **(Omami et al, 2014).**

Malignant lymphoma is the most common primary hematopoietic malignancy. Throughout its history, the management of lymphoma has been steadily improved by accurate imaging techniques, as accurate assessment of the initial extent of disease determines the optimal treatment plan and monitoring for treatment response, guides treatment duration and choice of therapeutic modality **(Swerdlow and Campo, 2016).**

Computed tomography (CT) has become the standard imaging technique to determine initial disease extent, to monitor disease regression during treatment, and to assess completeness of response at the end of planned therapy **(Connors, 2011).**

However, CT scanning has substantial limitations. It cannot detect small lesions, especially within or at the borders of solid organs and, even more importantly, it can only assess size and provides no information about cellular function. This latter limitation makes assessment of lymph nodes in the range of 0.5-1.5 cm problematic because CT scanning cannot reliably distinguish normal nodes from those involved with lymphoma, nor can CT scanning determine whether a residual mass is composed of fibro-necrotic scar tissue or persistent viable neoplastic cells **(Kanoun et al, 2014).**

Therefore PET assessment has been used for determining prognosis in adult patients to improve outcomes. However, FDG-PET has poor spatial resolution, and therefore localization of lesions can be inaccurate. The accuracy can be improved by combining FDG-PET and CT scanning (FDG PET-CT) **(Hochheggar et al, 2015).**

The CT portion of PET-CT provides the anatomic information useful for accurate interpretation of PET signal. It also provides a map used for attenuation correction of PET images **(Groheux et al., 2013).**

FDG PET-CT can help differentiate between residual tumour and fibrotic tissue during the course of chemotherapy, providing a more accurate diagnosis than does either CT or magnetic resonance (MR) imaging. PET-CT allows earlier detection of relapse than morphologic imaging with CT or MR imaging alone **(E.Abdelomonem, 2018).**

A basic knowledge of the mechanism of cancer imaging with FDG PET-CT is essential for accurate interpretation of PET-CT images **(Kobayashi et al., 2012).**

Physicians interpreting PET-CT scans should be familiar with the artefacts associated with the modalities, both individually and in combination as well as with the principles of PET-CT to ensure accurate scan interpretation and optimal patient care **(Sasikumar and Joy., 2017).**

Aim of the work

The aim of this study is to compare between the role of FDG PET-CT and the role of conventional CT in guiding the management and post therapeutic follow up of lymphoma.

2. Patients and methods

- Twenty nine patients with stage I, II of different types of lymphoma were enrolled in this study from January 2017 to January 2019 at the Egyptian military hospitals.
- The research ethics committee (Faculty of medicine-Al Azhar University) approved the study protocol, and all patients were enrolled after written informed consent was obtained.
- The inclusion criteria show no age predilection and both sexes were included.
- Patients with history of atopic disorders and patients with renal function impairment (with serum creatinine>2 mg/dl) were excluded.
- Baseline staging work-up of all patients was done according to the standard protocol at our hospitals and the patients underwent PET-CT and contrast enhanced CT of the chest, abdomen, and pelvis; bone marrow aspiration and biopsy.
- The patients received standard treatment protocols at our hospital.
- Interim response assessment (with PET-CT and contrast-enhanced CT) was performed after two cycles of chemotherapy.
- Assessment with PET-CT and contrast enhanced CT was also performed after the completion of chemotherapy (within 4–6 weeks after the completion of chemotherapy).
- The revised response criteria by the international work group (2007) were used for response assessment.
- PET/CT is performed on an integrated scanner (G.E discovery vCT; tube 128 slices CT) that combines both CT and PET capabilities in two sequential gantries, avoiding the need for patient motion between the CT and PET components of the study and thereby leading to accurate co-registration of the CT and PET data.

Contrast-enhanced CT Protocol

- Contrast-enhanced CT of the chest, abdomen, and pelvis was performed by using a 64–detectors CT scanner. Patients were given 200–800 mL of 2% oral contrast material divided at 45 and 15 minutes before the examination.
- Intravenous bolus injection of a nonionic iodinated contrast material at a dose of 2-3mL/KG of body weight was performed just before initiation of scanning.
- Scans were acquired from the thoracic inlet to the pelvic floor by using 2.5-mm-thick sections, and contiguous 5-mm axial image reconstruction.
- Scanning protocols with 120 kVp and effective tube current that varied from 60 to 140 mAs were used.

PET-CT Protocol

- Patients fasted for at least 4 hours before the examination, and blood glucose levels were less than 140mg/dL. A dose of (0.18–0.21mCi/kg, minimum 3mCi) FDG was injected intravenously. The patients rested in a quiet room. After the 45–60-minute uptake period, the patients were taken for the PET-CT study.
- No oral or intravenous contrast agent was used for the CT part of the PET-CT examination.
- A section thickness of 4 mm and a pitch of 1 were used.
- After CT acquisition, PET acquisition of the same axial range begun with the patient in the same position on the table for 2–3 minutes per bed position.
- PET data were acquired by using a matrix of 128x128 pixels. CT-based attenuation correction of the emission images was used.
- After PET data acquisition was completed, the reconstructed attenuation corrected PET images, CT images, and fused images of matching pairs of PET and CT images were available for review in axial, coronal, and sagittal planes, as well as in maximum intensity projections and in three-dimensional cine mode.

Response Assessment:

- Any focus of elevated FDG metabolism (**in comparison with liver and mediastinum),** not located in areas of normal FDG uptake, was considered to be abnormal.
- The areas of FDG uptake were localized anatomically on non enhanced CT scans.

- Findings at PET-CT were defined as showing:

1. **Complete response (CR),**
2. **Partial response (PR),**
3. **Stable disease, or**
4. **Progressive disease** on the basis of the revised international workshop criteria.

- Response at contrast-enhanced CT was defined as CR, PR, stable disease, or progressive disease on the basis of standard criteria.
- Comparison between PET-CT findings and enhanced CT study findings was done.
- The results were tabulated and statistically analyzed.

3. **Results**

Statistical methods:

IBM SPSS statistics (V. 23.0, IBM Corp., USA, 2015) was used for data analysis. Data were expressed as Median and Percentiles for quantitative non-parametric measures in addition to both number and percentage for categorized data.

The following tests were done:

1. Wilcoxon signed rank test for comparison between two dependent groups for non-parametric data.
2. Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.

The probability of error at 0.05 was considered significant; while at 0.01 and 0.001 are highly significant.

3. Diagnostic validity test: It includes agreement and disagreement between 2 studied techniques.

Table (1): Summary of the Findings

Staging	
Total No. of patients	**29**
Male patients	**17**
Female patients	**12**
Total No. of sites detected by PET-CT	**56**
Total No. of sites detected by CECT	**34**
Cases upstaged by PET-CT	**8**
Cases upstaged by CECT	**0**
Extranodal sites detected by PET-CT	**Liver 2cases**
	Bone marrow 4cases
	suprarnal 1case
Extranodal sites detected by CECT	**0**
Mid treatment	
Total No. of sites detected by PET-CT	**22**
Total No. of sites detected by CECT	**16**
No. of cases with difference in response criteria	**2**
Post treatment	
No. of cases with CR criteria at PET-CT	**16**
No. of cases with CR criteria at CECT	**15**
No. of cases with non CR criteria at PET-CT	**13**
No. of cases with non CR criteria at CECT	**14**
No. of Relapsed cases detected by PET-CT	**1**
No. of Relapsed cases detected by CECT	**1**

PET-CT versus CECT for Baseline Staging

- A total of **29** patients with stage I of different types of lymphoma were enrolled during the study period. There were **17** male cases and **12** female cases.
- All **29** patients underwent baseline contrast-enhanced CT (CECT) and PET-CT separately for staging.
- When we compared CECT against PET-CT for staging, PET-CT helped upstage disease in **8** of **29** patients (**27.6%**) as follows:

✓ Disease in **2** of them was upstaged on the basis of PET-CT findings of hepatic uptake in addition to the lymph nodes already seen at PET-CT and CECT.

✓ Disease in **4** of them was upstaged on the basis of bone marrow uptake at PET-CT in addition to the lymph nodes already seen at PET-CT and CECT.

The correlation of PET-CT findings with bone marrow biopsy at baseline was **100**% (4 of 4), and the improved detection of additional disease sites at PET-CT was statistically highly significant (**P=.000**).

✓ Disease in **1** of them was upstaged on the basis of PET-CT findings of suprarenal uptake in addition to the lymph nodes already seen at PET-CT and CECT.

✓ Lastly, disease in **1** of them was upstaged on the basis of PET-CT findings of additional uptake in lymph node groups other than those seen at CECT.

o A total of 56 disease sites were detected in **29** patients at PET-CT, while 34 sites were detected at CECT. **(Tables 2 & 3)**

o Among the patients with (**1**) site of involvement (n=**13**) detected by PET-CT: 92.3% of these cases were detected by CECT.

o Among the patients with **(2)** sites of involvement (n=**8**) detected by PET-CT: 75% of these cases were detected by CECT.

o Among the patients with **(3)** sites of involvement (n=**6**) detected by PET-CT: none of these cases (0%) was detected by CECT.

o Among the patients with **(4)** sites of involvement (n=**1**) detected by PET-CT: this case was not detected by CECT (0%).

o Among the patients with **(5)** sites of involvement (n=**1**) detected by PET-CT: this case was not detected by CECT (0%).

o The overall sensitivity for detection of diseased sites for PET-CT was **100**% while that for CECT was **62.1**%.

Table (2) No of sites involved at staging detected by PET-CT

			Total no of sites involved at staging					Total
			1.0	**2.0**	**3.0**	**4.0**	**5.0**	
Detected by PET-CT	1.0	Count	13	0	0	0	0	13
		%	100.0%	0.0%	0.0%	0.0%	0.0%	44.8%
	2.0	Count	0	8	0	0	0	8
		%	0.0%	100.0%	0.0%	0.0%	0.0%	27.6%
	3.0	Count	0	0	6	0	0	6
		%	0.0%	0.0%	100.0%	0.0%	0.0%	20.7%
	4.0	Count	0	0	0	1	0	1
		%	0.0%	0.0%	0.0%	100 %	0.0%	3.4%
	5.0	Count	0	0	0	0	1	1
		%	0.0%	0.0%	0.0%	0.0%	100.0%	3.4%
Total		Count	13	8	6	1	1	29
		%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	P
Pearson Chi-Square	116.000[a]	.000

Agreement (%) = (13+8+6+1+1)/29 = 29/29 = 100%Disagreement (%) = 0/0 = 0%Sensitivity for (1) = 100%Sensitivity for (2) = 100%Sensitivity for (3) = 100%Sensitivity for (4) = 100%Sensitivity for (5) = 100%
Sensitivity for (all) = 100%

Table (3) No of sites involved at staging detected by CECT

			Total sites involved at staging					**Total**
			1.0	**2.0**	**3.0**	**4.0**	**5.0**	
Detected by CECT	.0	Count	1	1	2	0	0	4
		%	7.7%	12.5%	33.3%	0.0%	0.0%	13.8%
	1.0	Count	12	1	4	1	0	18
		%	92.3%	12.5%	66.7%	100.0%	0.0%	62.1%
	2.0	Count	0	6	0	0	0	6
		%	0.0%	75.0%	0.0%	0.0%	0.0%	20.7%
	4.0	Count	0	0	0	0	1	1
		%	0.0%	0.0%	0.0%	0.0%	100.0%	3.4%
Total		Count	13	8	6	1	1	29
		%	100 %	100%	100%	100%	100%	100%

Chi-Square Tests

	Value	P
Pearson Chi-Square	52.002[a]	.000

Agreement (%) = (12+6)/29 = 18/29 = **62.1**%Disagreement (%) = (1+1+2+1+4+1+1)/0 = 11/29 = **37.9**%
Sensitivity for (1) = **92.3**%Sensitivity for (2) = **75.0**%Sensitivity for (3) = **0**%Sensitivity for (4) = **0**%

Sensitivity for (5) = **0**%Sensitivity for (all) = **62.1**%

PET-CT versus CECT for mid treatment evaluation.

- At mid treatment evaluation a total number of **22** disease sites were detected in **29** study patients at PET-CT, while **16** sites were detected at CECT (Table 4).
- **15** cases with no sites of involvement at mid treatment were detected by PET-CT, **14** cases of them were also detected by CECT, while **1** case was diagnosed as having **1** site of involvement by CECT.
- Among the patients with **(1)** site of involvement (n=**7**) detected by PET-CT, **7** cases were also detected by CECT.
- However among the patients with **(2)** sites of involvement (n=**6**) detected by PET-CT, only **1** case of them was detected by CECT, while **1** case was diagnosed as having no site of involvement and the other **4** cases were diagnosed as having only **1** site of involvement.
- Among the patients with **(3)** sites of involvement (n=**1**) by PET-CT, no cases were detected by CECT.
- The sensitivity of PET-CT for detection of improvement according to the number of sites involved was **highly significant** (P=0.000) (Table 15).
- The sensitivity of CECT for detection of improvement according to the number of sites involved was **significant** (P=0.014) (Table 16).
- The agreement between the two modalities in detecting sites of involvement in mid treatment evaluation was seen in **22** of **29** cases (**75.9**%), while the disagreement was seen in **7** of **29** cases (**24.1**%) (P<0.001) indicating highly significant agreement (Table 11).

Table (4) No of sites involved at mid treatment

			No of sites detected by CT at Mid treatment			Total
			.0	1.0	2.0	
No of sites detected by PET-CT at Mid treatment	.0	Count	14	1	0	15
		%	93.3%	8.3%	0.0%	51.7%
	1.0	Count	0	7	0	7
		%	0.0%	58.3%	0.0%	24.1%
	2.0	Count	1	4	1	6
		%	6.7%	33.3%	50.0%	20.7%
	3.0	Count	0	0	1	1
		%	0.0%	0.0%	50.0%	3.4%
Total		Count	15	12	2	29
		%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	P
Pearson Chi-Square	37.023[a]	.000

-Agreement (%) = (14+7+1)/29 = 22/29 = **75.9**%-Disagreement (%) = (1+1+4+1)/0 = 7/29 = **24.1**%

When the international work group response criteria (based on visual assessment) were used, **15** cases (**51.7**%) were diagnosed as having CR criteria according to the PET-CT findings, of which **14** cases were also diagnosed as having CR criteria by CECT and **1** case was diagnosed as having SD criteria by CECT.

- **3** cases (**10.3**%) were diagnosed as having PR criteria according to the PET-CT of which **3** cases were also diagnosed as having PR criteria by CECT.
- **11** cases (**37.9**%) were diagnosed as having SD criteria according to the PET-CT findings depending on the uptake, of which **10** cases were also diagnosed as having SD criteria by CECT while **1** case was diagnosed as having CR criteria by CECT.
- The agreement between the two modalities after applying the IWG response criteria in mid treatment evaluation was seen in **27** of **29** cases (**93.1**%), while the disagreement was seen in **2** of **29** cases (**6.9**%) (P<0.001) indicating highly significant agreement (Table 5).

Table (5) Response criteria at mid treatment

			Response criteria by CECT at Mid treatment			Total
			CR	PR	SD	
Response criteria by PET-CT at Mid treatment	CR	Count	14	0	1	15
		%	93.3%	0.0%	9.1%	51.7%
	PR	Count	0	3	0	3
		%	0.0%	100.0%	0.0%	10.3%
	SD	Count	1	0	10	11
		%	6.7%	0.0%	90.9%	37.9%
Total		Count	15	3	11	29
		%	100%	100%	100%	100%

Chi-Square Tests

	Value	P
Pearson Chi-Square	49.581[a]	.000

Agreement (%) = (14+3+10)/29 = 27/29 = **93.1**% Disagreement (%) = (1+1)/0 = 2/29 = **6.9**%

Table (6) The sensitivity of PET-CT for detection of improvement

					Total
			Mid treatment	Staging	
PET-CT Sites Involved	.00	Count	15	0	15
		%	51.7%	0.0%	25.9%
	1.00	Count	7	13	20
		%	24.1%	44.8%	34.5%
	2.00	Count	6	8	14
		%	20.7%	27.6%	24.1%
	3.00	Count	1	6	7
		%	3.4%	20.7%	12.1%
	4.00	Count	0	1	1
		%	0.0%	3.4%	1.7%
	5.00	Count	0	1	1
		%	0.0%	3.4%	1.7%
Total		Count	29	29	58
		%	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	P
Pearson Chi-Square	22.657[a]	.000

Table (7) The sensitivity of CECT for detection of improvement

					Total
			Mid treatment	**Staging**	
CECT Sites Involved	.00	Count	15	4	19
		%	51.7%	13.8%	32.8%
	1.00	Count	12	18	30
		%	41.4%	62.1%	51.7%
	2.00	Count	2	6	8
		%	6.9%	20.7%	13.8%
	4.00	Count	0	1	1
		%	0.0%	3.4%	1.7%
Total		Count	29	29	58
		%	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	P
Pearson Chi-Square	10.568[a]	.014

PET-CT versus CECT for post-treatment evaluation

- By applying the international work group response criteria (based on visual assessment) for post treatment evaluation **16** cases (**55.2**%) were diagnosed as having CR criteria according to the PET-CT of which **15** cases were also diagnosed as having CR criteria by CECT while **1** case was diagnosed as having SD criteria by CECT.
- **3** cases (**10.3**%) were diagnosed as having PR criteria according to the PET-CT of which **3** cases were also diagnosed as having PR criteria by CECT.
- **9** cases (**31**%) were diagnosed as having SD criteria according to the PET-CT of which **9** cases were also diagnosed as having SD criteria by CECT.
- **1** case (**3.4**%) was diagnosed as having Progressive criteria according to the PET-CT of which **1** case was also diagnosed as having Progressive criteria by CECT.
- The agreement between the two modalities after applying the IWG response criteria in post treatment evaluation was seen in **28** of **29** cases (**96.6**%), while the disagreement was seen in **1** of **29** cases (**3.4**%) (P<0.001) indicating highly significant agreement (Table 8).

Table (8) Response criteria post treatment

			Response criteria by CECT post treatment				Total
			CR	PR	Progressive	SD	
Response criteria by PET-CT post treatment	CR	Count	15	0	0	1	16
		%	100%	0%	0%	10%	55.2%
	PR	Count	0	3	0	0	3
		%	0%	100%	0%	0%	10.3%
	Progressive	Count	0	0	1	0	1
		%	0%	0%	100%	0 %	3.4%
	SD	Count	0	0	0	9	9
		%	0%	0%	0%	90%	31%
Total		Count	15	3	1	10	29
		%	100%	100%	100%	100%	100%

Chi-Square Tests

	Value	P
Pearson Chi-Square	82.469[a]	.000

Agreement (%) = (15+3+1+9)/29 = 28/29 = 96.6%Disagreement (%) = 1/0 = 1/29 = 3.4%

Discussion

Many reports in published literature have evaluated the role of PET-CT for the staging and restaging of both NHL and Hodgkin disease.

Our study compared between the role of PET-CT and CECT in affecting the management of early stages of lymphoma.

The staging system of lymphoma depends on the sites of involvement, the relation to the diaphragm and the presence of extranodal involvement. Therefore at baseline staging, we compared the sensitivity for detection of diseased sites between PET-CT and CECT and their effect on staging.

PET-CT detected 22 additional disease sites in 11 patients (P<.0001). PET-CT detected 7 extranodal sites of involvement (2 sites of hepatic uptake, 4 sites of bone marrow uptake and 1 site of suprarenal uptake). The correlation of PET-CT findings with bone marrow biopsy at baseline staging was **100**% (4 of 4). This finding suggests that PET-CT may be useful as a non invasive modality for detecting bone marrow involvement. These results led to upstaging in 8 patients (27.6%) of 29 patients from stage I to stage II.

Our study also noticed that the sensitivity of CECT for detection of sites of involvement decreases as the number of sites of involvement increases in every case. In cases with 1 site of involvement the sensitivity was 92.3%, in cases with 2 sites of involvement the sensitivity was 75% while in cases with 3, 4 And 5 sites of involvement the sensitivity was 0%. This finding explains the accuracy of PET-CT in base line staging.

The overall sensitivity for detection of diseased sites for PET-CT was 100% while that for CECT was 62.1%.

Similar results were obtained in the study by **Bakhshi et al. (2012).** They prospectively evaluated the role of PET-CT and CECT for staging non lymphoblastic NHL treated by using standard protocols. They concluded that PET-CT may be better than CECT for routine baseline investigation, as it led

to upstaging of disease in 5 (14.7%) of 34 patients, depicted 18 additional disease sites in 15 patients (P =.0003), and showed 100% (4 of 4) concordance for bone marrow involvement.

Also in the study by **Schaefer et al. (2004)** non enhanced PET-CT was compared with CECT and found that PET-CT had a sensitivity and specificity of 94% and 100% respectively, compared with 88% and 50% for CECT.

Other studies compared between PET-CT and PET alone in the staging of Lymphoma. The study by **Auerbach et al. (2004)** showed PET-CT to be more accurate for staging of lymphoma (93%) than was PET alone (84%), with discordant image interpretation between PET and PET-CT in approximately 10% of patients.

Similar to our study, **Raanani et al. (2006)** concluded thatupstaging with PET-CT is evident mostly for stages I and II NHL. The addition of PET-CT to CT changes the treatment strategy in approximately one fourth of NHL patients and one third of Hodgkin disease patients and may obviate diagnostic CT in the majority of patients**.**

According to **Cheson (2011)** in staging of NHL or HD, PET-CT is associated with an extremely low false positive rate.

Many reports have shown that PET-CT may provide prognostic information allowing early in vivo evaluation of chemotherapy (interim PET), however many other reports have shown that there was no significant discordance between interim PET-CT and contrast-enhanced CT results.

Accoring to the IWG recommendations, mid treatment PET-CT (Interim PET) should be performed only as a part of clinical trials.

Our study compared between PET-CT and CECT findings after 2 cycles of chemotherapy.

PET-CT detected 22 sites of involvement in 14 cases out of the 29 cases while CECT detected 16 sites of involvement in 14 cases out of the 29 cases.

Fifteen cases were diagnosed as having no sites of involvement by PET-CT due to absence of FDG uptake while 1 case of these 15 cases was diagnosed as having residual enlarged lymph nodes at CECT according to the size criteria.

This is because CECT shows anatomic details, whereas PET-CT images, in addition to showing anatomic details, provide information about tissue metabolic activity. This additional ability of PET-CT helps in distinguishing viable tumor from residual scar tissue and necrosis.

The results of the other cases during mid-treatment assessment were as follows: 7 cases were diagnosed as having 1 site of involvement by PET-CT due to the presence of FDG uptake, and these 7 cases were also detected by CECT according to the standard size criteria.

While 6 other cases were diagnosed as having 2 sites of involvement by PET-CT due to the presence of FDG uptake, only 1case of them was detected by CECT, while 1 case of them showed no sites of involvement by CECT and the other 4 cases showed only 1 site of involvement by CECT depending on the standard criteria.

Similarly 1 another case was diagnosed as having 3 sites of involvement by PET-CT due to the presence of FDG uptake, this case showed only 2 sites of involvement by CECT depending on the standard criteria.

PET-CT was more accurate than CECT in this setting related to its superiority in distinguishing between viable tumor and necrosis or fibrosis in residual lymph node.

Therefore, in our study the agreement between PET-CT and CECT at mid treatment in detecting sites of involvement was seen in **22** of **29** cases (**75.9**%) and the disagreement was seen in **7** of **29** cases (**24.1**%) (P<0.001) indicating highly significant agreement.

However, after applying the IWG criteria 15 cases were diagnosed as having CR criteria by PET-CT due to absence of metabolic activity in the residual nodes. Only 14 cases of these 15 cases were diagnosed as having CR criteria by CECT while 1 case was diagnosed as having SD criteria due to the stationary size of the lymph nodes.

Three other cases were diagnosed as having PR criteria by both PET-CT and CECT. Also 11 other cases were diagnosed as having SD criteria by PET-CT depending on the metabolic activity while CECT detected only 10 of these cases and the other case showed CR criteria depending on the standard size criteria.

The number of patients with discordant findings between PET-CT and CECT at the interim assessment was 2 cases.

The agreement between the two modalities after applying the IWG response criteria in mid treatment evaluation was seen in 27 of 29 cases (93.1%), while the disagreement was only seen in 2 of 29 cases (6.9%) (P<0.001) indicating highly significant agreement.

Similar results were seen at the study by **Bakhshi et al. (2012)** which concluded that there was no significant discordance between interim PET-CT and contrast-enhanced CT results (P =.47). The number of patients with discordant findings at the interim and assessment was 8.

Cashen et al. (2008) reported 50 patients with DLBCL who received six cycles of R-CHOP who underwent PET-CT after two or three cycles and after

completion of therapy. They found an NPV of 87% and a PPV of 27% after two to three cycles compared with 92% and 80%, respectively, after six cycles, and they concluded that interim PET-CT was a poor predictor of outcome.

Other studies, **Micallef et al. (2009)** and **Pregno et al. (2009)** have also failed to show an advantage to a mid treatment PET-CT scan.

Barnes et al. (2010) suggested that an interim PET-CT was no more predictive than an end of treatment study in HD.

Moskowitz et al. (2010) treated 98 patients with DLBCL using a dose dense R-CHOP–like regimen, with FDG PET-CT after four cycles. Those with a negative scan were treated with two cycles of ICE. Those with a positive scan underwent a biopsy, which, if negative, led to three cycles of ICE. If positive, patients underwent ICE and ASCT. They noted an 87% false positive rate. Importantly, the interim PET-CT did not predict PFS.

The study by **Gallamini et al. (2014)** of 260 advanced stage HD patients imaged after 2 of 6 intended cycles (ie, PET-2) of ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine), Showed no treatment change based on PET-2 results. The sensitivity, specificity, NPV, and PPV for PET-2 were 73%, 94%, 94%, and 73%, respectively. After a mean follow-up of 27 months, the 3-year failure free survival was 28% for PET-2+ve patients and 95% for PET-2-ve patients (P<.0001).

However, many reports support the importance of Interim PET-CT. **Kostakoglu et al. (2003)** and **Mikhaeel et al. (2005)** concluded that PET may help predict response as early as after one cycle of treatment.

Similarly**, Haioun et al. (2005)** treated 90 patients with aggressive NHL and prospectively assessed PET before chemotherapy, after two cycles and after completion of treatment. Early PET results predicted CR rate, event free survival, and overall survival, irrespective of international prognostic index (IPI) risk group or rituximab therapy.

However, the number of patients in this study with a positive scan ranged from 40% to 53%. Although the long term outcome (PFS) of PET negative patients was fairly consistent among this study at 82% to 93%, there was considerable variability in those with a positive scan, 0% to 43%.

The study by **Raanani et al. (2006)** found that PET-CT resulted in a change in treatment in 45% of patients with HL compared with CECT.

Hutchings et al. (2006) reported that 61 of 77 newly diagnosed patients with HL had a negative PET scan after two cycles of chemotherapy; three patients experienced progression but were still alive. In contrast, 11 of 16 patients with a positive scan experienced relapse, and two died. Early PET results were superior to CT scanning.

Gallamini et al. (2007) performed PET-CT scans before treatment and after two cycles of ABVD in 260 previously untreated patients with HL. The 2-year PFS for patients with PET-2–positive results was 12.8% compared with 95% for those with a negative result (P≥.001). PET-CT results were the most important prognostic factor, more powerful than the International Prognostic Score. These impressive results have since been confirmed by **Cerci et al. (2010).**

Other studies by **Barnes et al. (2011, Kostakoglu et al. (2012) anf Filippi et al. (2013)** evaluated interim PET-CT after 2 cycles of chemotherapy and have been shown to be prognostic of survival.

Our study also compared between PET-CT and CECT findings after treatment course.

The agreement between PET-CT and CECT after applying the IWG response criteria in post treatment evaluation was seen in 28 of 29 cases (96.6%), while the disagreement was seen in 1 of 29 cases (3.4%) (P<0.001) indicating highly significant agreement.

The number of patients with discordant findings at the Post-treatment assessment was 1case. This case was diagnosed as having CR criteria by PET-CT due to the absence of FDG uptake while according to standard size criteria CECT diagnosed this case as having SD criteria. This observation suggests that either CECT or PET-CT may be used for post-treatment analysis.

Similar results were seen in the study by **Bakhshi et al. (2012)** which concluded that there was no significant discordance between post-treatment PET-CT and contrast enhanced CT results (P >.99).

PET-CT for surveillance is performed after treatment with the goal of early detection of recurrence. However, several studies have shown that it is the patient or the physician who first suspects relapse. According to **Jerusalem et al. (2003)** PET has failed to show clear benefit in surveillance.

Petrausch et al. (2010) reported a retrospective analysis of 75 patients with DLBCL undergoing PET during follow up. From 35 who were asymptomatic, only 4 had a positive scan, 3 of which were associated with recurrence. More than half of patients had a scan because of suspicion of relapse, and half were confirmed as recurrence by biopsy. Although 36% had a positive scan during follow-up, only 23% experienced a recurrence. The PPV was 0.85, but usefulness was limited to high-risk patients with symptoms suggestive of relapse and those older than age 60 years.

Mocikova et al. (2010) reported that scans identified recurrence in the absence of symptoms in

3.9% of patients with HD. Thus, scans can be avoided, particularly in patients at low risk for recurrence.

Lee et al. (2010) performed a retrospective analysis of 192 patients with HD in first remission. Half had early-stage disease. They detected 16 events by surveillance scans (including 12 relapses and four secondary malignancies) at a median follow-up of 31 months.

The PPV was only 22.9%, resulting in a cost of $100,000 for each event, leading to the recommendation that the test had limited clinical impact.

Kostakoglu et al. (2014) concluded that it is crucial to recognize that the PPV of PET is less reliable than its NPV because of infection, inflammation, and reactive changes after treatment.

According to **(Kostakoglu et al., 2014)** once lymphoma patients enter remission, continued FDG-PET-CT scanning is not recommended during post-remission surveillance, owing mainly to low specificity and poor PPV**.**

However **(Smith el., 2015)** concluded that PET-CT allows accurate identification of patients at highest risk of early relapse and mortality and may inform the need for additional therapy.

Similarly the studies by **Trotman et al. (2011)** and **Dupuis et al. (2012)** have shown that PET at the end of induction chemotherapy improves the accuracy of response assessment compared with conventional CT alone and that PET assessed response is better in predicting progression free survival and possibly overall survival.

In conclusion, our study evaluated the role of PET-CT and contrast enhanced CT for staging, interim, and posttreatment analysis in early stages NHL and HL treated by using standard protocols.

PET-CT may be better than contrast enhanced CT for routine baseline investigation, as in our study, PET-CT findings led to upstaging of disease in 8 (27.6%) of 29 patients, depicted 22 additional disease sites in 11 patients, and showed 100% (4 of 4) concordance for bone marrow involvement.

There was no significant discordance between interim PET-CT and contrast-enhanced CT results (93.1% agreement) or between post treatment PET-CT and contrast-enhanced CT results (96.6% agreement).

Therefore, either PET-CT or contrast-enhanced CT may be used for response assessment and predicting outcome in stage I and II HL and NHL.

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