PET/CT versus contrast enhanced CT in the initial assessment and follow up of Thoracic Lymphoma

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Aims and objectives

Intrathoracic disease is observed in about 70-85% of Hodgkin's disease patients and in 25-50% of those with Non Hodgkin's lymphoma; it is characterized by enlargement of mediastinal lymph nodes, parenchymal abnormalities, pleural, pericardial and chest wall involvement [1].

CECT is limited due to its reliance on the size criteria to identify pathologic lymphadenopathy. The integration of PET with CT allowed a more reliable initial staging of Lymphoma because of its ability to detect metabolic activity in non enlarged lymph nodes as well as its high sensitivity to extra-nodal disease. FDG PET/CT is extremely useful for therapy response assessment due to its capacity to help distinguish between residual metabolically active tumor and areas of necrosis and fibrosis which can be seen a residual lesions in CECT [2].

There are substantial data on the use of FDG PET for assessment of treatment response in Hodgkin disease and aggressive NHL after the first-line or salvage chemotherapy [3]. The reported pooled sensitivity and specificity for the detection of residual disease after the first course of chemotherapy were 84% and 90%, respectively for HD and 72% and 100%, respectively, for aggressive NHL [4].

A bulky mediastinal nodal mass can be in patients with Hodgkin lymphoma. Size reduction after initial treatment is expected Hodgking disease yet complete disappearance of the mass is unusual. Detection of active neoplastic tissue in those residual masses is difficult with conventional imaging modalities [5].

Almost all cases of mediastinal Lymphoma are of the potentially curable types (HD,DLBCL), the use of PET-CT as a base line and post-chemotherapy imaging modality seems imperable because these lesions are expected to respond fully after the first course of chemotherapy despite the presence of residual yet non biologically active lesions in the CECT follow up studies.

The detection of early response to therapy can help to distinguish patients who can be cured with the standard treatment regimen or even less toxic treatment from other patients who must undergo an early switch to a more aggressive treatment, this will help to design a risk-adapted chemotherapy plan to a achieve a higher cure rate with a lower risk of chemotherapy related morbidity and mortality [6].
In this prospective study, we assessed 50 patients with pathologically proven intrathoracic Lymphoma disease. All patients performed contrast enhanced CT (CECT) and Positron emission tomography (PET-CT) for initial staging, CECT and PET-CT after the first course of chemotherapy (after 4-6 weeks) as well as CECT and PET-CT after the end of treatment (after 2-4 months). Biopsy and Histopathology results were the reference standard to which we compared the CECT and PET results.
Methods and materials

Fifty patients (25 male, 25 female; age range 2-82 y; average age 27.6 y) were included in this study. All patient had an intra-thoracic soft tissue lesion visible in initial contrast enhanced CT whether a pathologically enlarged lymph node or mass lesion. All patients underwent physical examination and laboratory testing for Lymphoma including LDH, ESR and CBC. Histopathological diagnosis of Lymphoma was established in all cases after biopsy whether surgical or image guided. Biopsy and histopathology were done for suspected extra-nodal sites of disease in the initial study and follow up to confirm the diagnosis as well as in cases with suspected disease relapse.

Patients who received previous chemo-or Radiotherapy or underwent previous surgery related to their Lymphoma disease. In women of childbearing age, inquiry about pregnancy was done for fear of risk of radioactive material upon the fetus and in cases of suspicion a pregnancy test was done.

All patients performed contrast enhanced CT (CECT) and PET/CT for initial staging, CECT and PET-CT after the first course of chemotherapy (after 4-6 weeks) as well as CECT and PET-CT after the end of treatment (after 2-4 months). In all cases PET-CT was done following CECT within less than one week.

All PET/CT examinations were analyzed by a consensus of two experienced observers of nuclear medicine physicians and radiologists. The PET images and the volume of CT scans were evaluated for the presence and extent of 18F-FDG-positive lymphoma in different lymph nodes groups and the presence of extra-nodal disease involvement in the initial studies as well as for residual/recurrent abnormalities during/after therapy.

Abnormal 18F-FDG uptake was defined as radiotracer accumulation outside the normal anatomic structures and of greater intensity than background activity, excluding normal areas of physiological uptake. For the analysis, lymph node chains were grouped into mediastinal, hilar, internal mammary and axillary lymph nodes. For each group, the number of sites affected was assessed as either single or multiple. The following extra-nodal sites were evaluated: lung, pleura, chest wall, bone and bone marrow. The findings for each of these sites were graded as positive or negative for lymphomatous infiltration.

In all cases estimation of 18- FDG uptake was done using SUVmax values for each group of enlarged nodes or mass lesion and comparison of values was done in the follow up studies respecting the ROI position as much as possible. Visual assessment was used as a secondary method for interpreting PET findings as positive or negative. According to the IHP definitions, residual masses of 2 cm or more in greatest transverse diameter
(GTD) with 18F-FDG activity visually exceeding that of mediastinal blood pool structures are considered PET positive, whereas residual masses 1.1 to 1.9 cm are considered PET positive only if their activity exceeds surrounding background activity. A smaller residual mass or a normal-sized lymph node (e.g., <1 × 1 cm) should be considered positive for disease if its activity is higher than that of the surrounding background.

Lung nodules ≤1.5 cm in patients should be considered as positive for lymphoma if FDG uptake is greater than the mediastinal blood pool. Lymphoma were not excluded in lung nodules >1.5 cm. New nodules in patients without established pulmonary lymphoma at baseline and who have evidence of a CR should be considered as negative for lymphoma, regardless of size and uptake, because they typically represent inflammatory lesions.

If there was a clearly multifocal increase in FDG uptake in the bone marrow, the patient was considered as PET positive excluding cases where there is diffuse pattern of uptake of reactive bone marrow hyperplasia after chemotherapy.

For CECT studies, size measurement was the parameter used for comparison of the pre and post treatment scans. The IWG (Cheson criteria) was used:

- In cases of sizable masses, measuring the sum of the products of the greatest dimensions (SPD) was done. Complete response (CR) was defined as disappearance of all detectable disease or Lymph nodes >1.5 cm must decrease to ≤1.5 cm.
- Partial response (PR) was defined as more than 50% in SPD.
- Stationary (SD) was defined as less than 50% decrease in SPD.
- Progressive disease (PD)/relapse was defined as new lesion or SPD increase >50% from nadir of any lymph node.

Data were statistically described in terms of range, mean standard deviation (SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Kruskal Wallis analysis of variance (ANOVA) test. For comparing categorical data, Chi square (2) test was performed. Exact test was used instead when the expected frequency is less than 5. P values less than 0.05 was considered statistically significant.
Results

Initial Staging

According to the Ann Arbor classification of Hodgkin's and Non Hodgkin's Lymphoma, the cases were staged as follows:

CT depicted 34 cases in stage I, 13 cases in stage II and 3 cases in stage IIE.

PET-CT depicted 31 cases in stage I, 2 cases in stage IE, 11 cases in stage II, 4 cases in stage IIE and 2 cases in stage IV.

PET-CT disagreed with CT in the initial staging of 5 cases (10%) where it upstaged 2 cases from stage I to IE, 1 case from stage II to IIE, 1 case from stage I to stage IV and 1 case from stage II to stage IV [Fig.1]

Follow up studies after the first course of chemotherapy [Table 1]

PET-CT and CECT were concurrent in results in 32% of cases and discordant in results in 68% of cases. PET-CT was true positive in 19 cases, true negative in 30 cases, false positive in 1 case and shows no false negative results (100% sensitivity, 96.7% specificity, 95% positive predictive value and 100% negative predictive value) [Fig.2]

Follow up studies after the end of chemotherapy

We divided the patients into two groups, group I represent patients which show no complete response in the first study (19 patients) with partial regression, stationary or progressive disease course and group II which represent patients with complete metabolic response after the first course of chemotherapy (31 patients)

Group I (19 cases) [Table 2]

PET-CT and CECT agreed in results in 52.5% of the cases and disagreed in 47.5 % of cases.

Group II (31 cases) [Table 3]
PET-CT and CECT agreed in results in 38.7% of the cases and disagreed in 61.3% of cases.

In the overall 50 cases in the study after the end of treatment, PET-CT and CECT were concordant in results in 20 cases (40%) and discordant in results of 30 cases (60%).

CT was true positive in 6 cases, true negative in 17 cases, false positive in 26 cases and false negative in 1 case (85.7% sensitivity, 39.5% specificity, 18.6% positive predictive value and 94.5% negative predictive value), in comparison PET-CT shows 7 true positive cases and 43 true negative cases with no false positive or negative cases, proving 100% sensitivity and specificity as well as 100% positive and negative predictive values.

**Mediastinal Lymphoma cases**

44 cases with pathologically proven mediastinal lymphoma were presented in our study. 31 HD cases and 13 NHL cases.

CECT depicted 30 cases in stage I, 12 cases in stage II and 2 cases in stage IIE. PET-CT depicted 27 cases in stage I, 2 cases in stage IE, 10 cases in stage II, 3 cases in stage IIE and 2 cases in stage IV.

In the first follow up study after chemotherapy, PET-CT detected complete regression in 29 cases (65.9%) CT agreed with this in only 6 cases (13.6%), shows partial regression in 18 cases (40.9%) and stationary course in 5 cases (11.4%). PET-CT shows partial regression in 10 cases (22.7%), CT agrees in 8 cases (18.2%) and shows stationary disease course in 2 cases (4.5%). PET-CT detected progressive disease in 5 cases (11.4%), 2 of them show partial regression by CT (4.5%) while 3 of them were stationary (6.8%). Both modalities were in agreement in 31.8% and in disagreement 68.2% of case results.

In the second follow up study 37 cases (84%) were in complete remission according to PET-CT, CT agrees with this result in 14 cases (31%), shows further partial regression in 13 cases of them (29.5%) and 10 cases were stationary (22.7%). 2 cases show partial regression in PET-CT that were stationary in size in CT (4.5%). 4 stationary cases in both CT and PET were reported (9%) and 1 case (2.3%) show disease relapse in extra-nodal pleural site by PET-CT despite complete remission in CECT.

**Extra-nodal Thoracic Lymphoma cases**
8 cases presented with extra-nodal sites of thoracic Lymphoma disease were detected in the study. 4 cases were pathologically proven as parenchymal lung infiltration whether nodules or area of consolidation. 2 cases had pleural lymphomatous lesions and 2 other cases with chest wall lesions, 1 of them had associated bony Lymphoma in the sternum. PET-CT was 100% sensitive and specific in detection of extra-odal thoracic disease as compared to 62.5% sensitivity and 97.6% specificity for CECT.

In the first follow up study of the extra-nodal disease sites, both imaging modalities were concordant in results in 4 cases (50%) and discordant in 4 cases (50%). CECT shows 80% sensitivity and 93% specificity compared to 100% sensitivity and specificity with PET-CT.

In the second follow up study, PET-CT ad CECT were concurrent in results in 37.5% ad discordant in 62.5% of cases. CECT shows 75% sensitivity and 93.5% specificity compared to 100% sensitivity and specificity with PET-CT.
Fig. 1: Bar chart showing the CT and PET-CT staging of Lymphoma cases in the study.

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Fig. 2: Agreement percentages between both modalities in treatment response after first course of chemotherapy.

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Fig. 3: 27 years old male with pathologically proven Hodgkin's Lymphoma presented in CT with enlarged anterior mediastinal left paratracheal lymph node (measures about 2 x 1.8 cm) that shows an SUVmax of 3 in PET-CT which - in addition - shows two other sites of hypermetabolic activity in the chest that were not demonstrated in CT, a soft tissue lesion within the left pectoral muscles with SUVmax of 11.1 and the sternum with an SUVmax of 11.7. The case was upstaged from stage I to stage IV.

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### Table 1: Comparison between PET-CT and CT results in treatment response after the first course of chemotherapy

<table>
<thead>
<tr>
<th>Disease response in PET-CT</th>
<th>Disease response in CECT</th>
<th>CR</th>
<th>PR</th>
<th>ST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete regression</td>
<td></td>
<td>6</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>60%</td>
<td>12%</td>
<td>38%</td>
<td>10%</td>
</tr>
<tr>
<td>Mixed response</td>
<td></td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2%</td>
<td>0%</td>
<td>2%</td>
<td>0%</td>
</tr>
<tr>
<td>Partial regression</td>
<td></td>
<td>0</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>22%</td>
<td>0%</td>
<td>18%</td>
<td>4%</td>
</tr>
<tr>
<td>Progressive</td>
<td></td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>14%</td>
<td>2%</td>
<td>4%</td>
<td>8%</td>
</tr>
<tr>
<td>Stationary</td>
<td></td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2%</td>
<td>0%</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>7</td>
<td>31</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>14%</td>
<td>62%</td>
<td>24%</td>
</tr>
</tbody>
</table>

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Fig. 4: 12 years old male with HD presented with a large anterior mediastinal soft tissue mass lesion measuring about 17 x 12.5 cm. It shows FDG uptake in PET-CT with SUVmax 14.2. 6 weeks after chemotherapy, the mass lesion shows partial regression in size in CT yet with no detectable FDG uptake denoting full metabolic response to therapy.

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### Table 2: Comparison between PET-CT and CT results in Group I after the end of treatment

<table>
<thead>
<tr>
<th>Disease response in PET-CT</th>
<th>Disease response in CECT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CR</td>
</tr>
<tr>
<td>Complete regression</td>
<td>13</td>
</tr>
<tr>
<td>68.5%</td>
<td>26.3%</td>
</tr>
<tr>
<td>Partial regression</td>
<td>2</td>
</tr>
<tr>
<td>10.5%</td>
<td>0%</td>
</tr>
<tr>
<td>Stationary</td>
<td>4</td>
</tr>
<tr>
<td>21%</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
</tr>
<tr>
<td>100%</td>
<td>26.3%</td>
</tr>
</tbody>
</table>

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Fig. 5: 26 years old female with NHL. The initial CECT revealed an anterior mediastinal soft tissue lesion measuring about 5 x 3 cm. The PET-CT shows an SUVmax of 11.7 (First raw). Six weeks after chemotherapy, the anterior mediastinal mass lesion has reduced in size measuring about 2 x 2 cm with complete resolution of hyperactivity denoting full metabolic response in PET-CT (Second raw). After 3 months, the PET-CT study shows a 4 x 3 cm soft tissue lesion resting on the mediastinal pleura of the right upper lobe with estimated SUVmax = 18.4, it was confirmed pathologically to represent extra-nodal pleural recurrence and disease relapse.

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Table 3: Comparison between PET-CT and CT results in Group II after the end of treatment

<table>
<thead>
<tr>
<th>Disease response in PET-CT</th>
<th>Disease response in CECT</th>
<th>CR</th>
<th>PR</th>
<th>ST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete regression</td>
<td></td>
<td>12</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>30</td>
<td>96.7%</td>
<td>38.7%</td>
<td>29%</td>
<td>29%</td>
</tr>
<tr>
<td>Disease relapse</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>3.2%</td>
<td>3.2%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>31</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>100%</td>
<td></td>
<td>42%</td>
<td>29%</td>
<td>29%</td>
</tr>
</tbody>
</table>

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Fig. 6: 26 years old female with HD presented in CECT by enlarged anterior mediastinal prevascular lymph node measuring 3 x 2 cm with an SUVmax of 6.9 in PET-CT together with a left upper lobe soft tissue nodule measuring about 3 x 3 cm with an SUVmax of 10.5 (First raw). 6 weeks after chemotherapy, the CT shows partial regression in the size
of the mediastinal lymph node, measuring about 2 x 1 cm as well as in the size of the left lung nodule measuring about 2 x 1 cm, both show resolution of hypermetabolic activity in the PET-CT denoting full response to treatment (Second raw).

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Conclusion

In potentially curable cases of Lymphoma (HD, DLBCL) which was the histopathology for all the cases of mediastinal Lymphoma in our study, the use of PET-CT was essential as a base line study because these cases are expected to respond fully after the first course of chemotherapy despite the presence of a residual mass that can be non biologically active in the follow up studies regardless of its size. PET-CT will also be useful in these cases to exclude unexpected extra-nodal sites of the disease at the initial staging which will upstage the case leading to a change in treatment strategy from the start.

PET-CT proved higher sensitivity and specificity over CECT in our study. The major strengths of PET-CT over CECT were in its higher ability for detection of extra-nodal sites of Lymphoma at initial staging and in its much higher capability to exclude active disease in residual nodal/mass lesions in the follow up studies in addition to its ability for early detection of relapse sites (nodal or extra-nodal) which also can help in directing biopsy procedure in indeterminate cases where histopathology is mandatory.
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References


