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Diagnostic Accuracy of PET/CT in Detecting Aggressiveness of Lymphoma Based on Sub Uptake

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ABSTRACT

Objective: To determine the diagnostic accuracy of PET/CT in detecting aggressiveness of lymphoma based on sub-uptake keeping bone marrow biopsy as the gold standard.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Armed Forces Institute of Radiology and Imaging, Rawalpindi Pakistan, from Sep 2020 to Mar 2021.

Methodology: One hundred thirty-eight patients of either gender, aged 20 to 80 years who were diagnosed with lymphoma (either Hodgkin's or non-Hodgkin's lymphoma) on initial PET/CT scan were enrolled in the study. All patients underwent PET/CT, and 18-FDG SUV was calculated. After obtaining values, all participants underwent bone marrow biopsy to determine the aggressiveness of lymphoma and findings were subjected to statistical analysis.

Results: The mean age of the patients was 54.92±16.86, and the mean SUV value was 17.04±8.03. There were 77(55.8%) males and 61(44.2%) females. Hodgkin's lymphoma was present in 28 (20.3%) patients and non-Hodgkin's lymphoma in 110(79.7%). The sensitivity, specificity, PPV, NPV and diagnostic accuracy of 18 FDG PET/CT SUV were 92%, 92.2%, 93.2%, 90.9% and 92.1%, respectively.

Conclusion: 18-FDG PET/CT SUV has high diagnostic accuracy and can detect aggressive lymphomas and further specify the areas for biopsy.

Keywords: Bone marrow biopsy, 18-FDG PET/CT SUV, Lymphomas.

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INTRODUCTION

The commonest haematological malignancy is lymphomas. According to a survey conducted in the United States, lymphomas account for about 5% of all cancers.[1] The approach currently used for staging lymphomas initially and evaluating treatment response over the past two decades is Computed tomography (CT) scan and bone marrow examination histopathologically.[2] Recently, many advances have been made in the imaging techniques used for cancer. Imaging cancer by positron emission tomography (PET) by utilizing 2-fluorine-18 fluoro-2-deoxy-D-glucose (FDG) is based on the finding that glucose uptake and its metabolism occurs at an abnormally elevated rate in the majority of cancers, including lymphomas.[3,4]

Differentiating indolent lymphomas from aggressive ones is clinically important because the histological subtype of lymphomas influences the choice of treatment.[5] In a few studies conducted in the past, the role of 18-FDG-PET was evaluated for differentiating different subtypes of lymphoma histologically.[6,7]

It is important to clinically distinguish indolent lymphomas from aggressive ones as the treatment is influenced by the lymphoma subtype as assessed histologically.[8,9] In few previous studies which evaluated 18-F-FDG-PET role in differentiating different histological subtypes of lymphoma revealed that the detection of lymphoma on 18F-FDG correlated well with the tumour's aggressiveness and there was a parallel increase in the standardized uptake value (SUV) with a more aggressive lesion.[10]

However, the previous studies mainly included individuals with diffuse large B-cell lymphoma (DLBCL), so it is still being determined whether these findings can be applied to other subtypes as detected histologically. Therefore, the current study aimed at evaluating the diagnostic accuracy of PET/CT in detecting the aggressiveness of lymphoma based on sub uptake keeping bone marrow biopsy as the gold standard. This study would guide a non-invasive technique that could predict the probability of aggressive lymphoma. In addition, it could be used to select areas for biopsies and thus can help guide future interventions.

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METHODOLOGY

The prospective longitudinal study was conducted at Armed Forces Institute of Radiology and Imaging, Rawalpindi, after taking approval from the Institutional Ethical Review Board (ERC/IERB). The sample size was calculated using the WHO sample size calculator, keeping expected sensitivity of PET/CT for detecting lymphoma aggressiveness as 79% and the prevalence of aggressive lymphoma as 24%.[11]

Inclusion Criteria: Patients of either gender, aged 20 to 80 years were diagnosed with lymphoma (either Hodgkin's or non-Hodgkin's lymphoma) on an initial PET/CT scan.

Exclusion Criteria: The patients diagnosed with more than one subtype of non-Hodgkin's or had a coexisting Hodgkin's and non-Hodgkin's lymphoma were excluded from the study.

Patients were enrolled in the study after written informed consent was taken from all participants. Demographical details, clinical history and physical examination of all patients were made, and findings were noted on a predesigned proforma. The blood sample was withdrawn from all patients, and CBC and serum LDH levels were evaluated. The presence/absence of extranodal disease was assessed clinically, and the lymphoma stage was determined using Ann Arbor staging criteria. Images of the PET/CT were obtained. Abnormal uptake of FDG was defined as an activity greater than the surrounding tissue in the background. It was not related to the areas where there is physiological uptake of the tracer (e.g. myocardium) or sites of excretion (e.g. ureters and urinary bladder). Areas were identified with abnormal uptake of FDG other than the liver and spleen based on standardised uptake value measurements (SUV). We defined SUV < 5 as "low-intensity lymphoma", 5 to 10 µCi/mL as "moderate intensity lymphoma", 10–15 µCi/mL as "intense intensity lymphoma", and >15 µCi/mL as "very intense/aggressive lymphoma.12 The highest SUV value for each patient was recorded. After recording the findings, all patients underwent histopathological evaluation of bone marrow. The findings of PET/CT regarding SUV uptake of 18-FDG were then compared with the findings of bone marrow biopsy. Hodgkin's lymphoma was defined by the presence of Reed-Sternberg cells (giant, multinucleated cells with abundant pale cytoplasm) on histopathological evaluation of bone marrow specimen and non-Hodgkin's lymphoma was defined by the presence of large lymphocytic cells with abundant cytoplasm and large round-ovoid nuclei with the thick nuclear membrane and multiple prominent nucleoli and absence of Reed-Sternberg cells on histopathological examination of a biopsy specimen obtained from bone marrow. On barrow marrow aspiration, lymphoma was labelled as aggressive by the presence of large immunoblastic and lymphoblastic cells. All findings were noted on a predesigned proforma and subjected to statistical analysis.

Statistical Package for the Social Sciences (SPSS) version 23.00 was used for analyzing the data. Mean and standard deviation were calculated for quantitative variables. Frequency and percentages were used. The 2 by 2 table was used for assessing the accuracy of PET/CT keeping findings of bone marrow biopsy as the gold standard. Sensitivity, specificity, positive predictive value and negative predictive value were calculated. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

The mean age of the patients was 54.92±16.86, and the mean SUV value was 17.04±8.03 µCi/mL. There were 17(12.3%) patients of young age (20 to 35 years), 39(28.2%) patients of early middle age (36 to 50 years), 27(19.6%) patients of late middle age (51 to 65 years) and 55(39.9%) patients of old age (66 to 85 years). There were 77(55.8%) males and 61(44.2%) females. Hodgkin's lymphoma was present in 28(20.3%) patients and non-Hodgkin's lymphoma in 110(79.7%). On PET/CT, aggressive lymphomas were found in 73 (52.9%), and on bone marrow biopsy, aggressive tumours were found in 74(53.6%) patients (Table-I).

Table-I: Frequency Distribution of Qualitative Variables (n=138)

Variables	Frequency/Percentage
Age Groups	
Young age (20-35 years)	17(12.3%)
Early middle age (36-50 years)	39(28.2%)
Late middle age (51-65 years)	27(19.6%)
Old age (66-80 years)	55(39.9%)
Gender	
Male	77(55.8%)
Female	61(44.2%)
Type of Lymphoma	
Hodgkin's lymphoma	28(20.3%)
Non-Hodgkin's lymphoma	110(79.7%)
PET/CT Findings	
Tumor aggressive	73(52.9%)
Tumor not aggressive	65(47.1%)
Bone Marrow Biopsy Findings	
Tumor aggressive	74(53.6%)
Tumor not aggressive	64(46.4%)

In patients with a positive finding on PET/CT for aggressive lymphoma, 68 (49.3%) were true positive, and 5(3.6%) were false positive, and in patients with a negative finding on PET/CT for aggressive lymphoma, 59(42.8%) were true negative and 6(4.3%) were false negative (Table-II). The sensitivity, specificity, PPV, NPV and diagnostic accuracy of 18 FDG PET/CT SUV were 92%, 92.2%, 93.2%, 90.9% and 92.1%, respectively (Table-III).

Table-II: Table comparing findings of 18-FDG PET/CT SUV with findings of Bone Marrow Biopsy (n=138)

Findings on Pet/CT	Findings On Bone Marrow Biopsy	
	Positive for Aggressive tumor	Negative for Aggressive tumor
Positive for Aggressive Tumor	True positive 68(49.3%)	False positive 5(3.6%)
Negative for Aggressive Tumor	False negative 6(4.3%)	True negative 59(42.8%)

Table-III: Diagnostic Parameters Table (n=138)

Diagnostic Parameters	Values
Sensitivity=True Positive/(True Positive +False Negative)	92%
Specificity=True Negative/(True Negative +False Positive)	92.2%
Positive Predictive Value=True Positive/(True Positive + False Positive)	93.2%
Negative Predictive Value= True Negative/(True Negative+False Negative)	90.9%
Diagnostic Accuracy=(True Positive +True Negative)/All Patients	92.1%

DISCUSSION

Positron emission tomography (PET) with fluorodeoxyglucose (FDG), the analogue of glucose, is now accepted clinically and is used widely as a tool of imaging for evaluating lymphoma's stage and the treatment given.[12] It has also been effective in detecting the recurrence of lymphoma.[13] In addition, it has been shown to have higher sensitivity for determining the extent of lymphoma compared to anatomical imaging techniques such as CT or MRI 14,.[15]

Imaging of the whole body by using PET/CT has been found to have high sensitivity and specificity in both Hodgkin's and non-Hodgkin's lymphoma16. The current study revealed that the sensitivity, specificity, PPV and NPV of 18-FDG SUV on PET/CT were 92%, 92.2%, 93.2%, 90.9% and 92.1%, respectively, and the diagnostic accuracy was 92.1%. Thus, the results denote that a high SUV value of 18-FDG on PET/CT was associated with aggressive lymphoma.

Studies have determined the predictive value of 18-FDG SUV for detecting aggressive lymphomas and differentiating aggressive from indolent lymphomas.[17,18] Few studies also determined the diagnostic accuracy of 18-FDG for various subtypes of lymphoma histologically19. In a meta-analysis by Chen *et al*. the accuracy of 18-FDG SUV was assessed in diagnosing bone marrow involvement in patients with lymphoma.[12] Bone marrow involvement in the studies included in this meta-analysis revealed tumour aggressiveness. This meta-analysis revealed that the median sensitivity and specificity of 18-FDG PET/CT for aggressive NHL were 79% and 94%, respectively. The diagnostic accuracy was revealed to be around 81.3%. For indolent NH lymphomas, the sensitivity and specificity were 24.5% and 100%, respectively, which was quite less in terms of sensitivity as com-pared to aggressive NHL.[12] The current study findings regarding diagnostic accuracy for the aggressive tumour were high compared to this meta-analysis. This may be because Hodgkin's and non-Hodgkin's were evaluated in the current study, and diagnostic accuracy regarding the type of lymphoma was not assessed. However, it was assessed as a whole for lymphomas.

The current study has highlighted the importance of PET/CT as a non-invasive technique for revealing the probability of aggressive lymphoma and thus providing accurate information in order to guide further management of such patients, thus helping in reducing overall morbidity and mortality associated with the condition and decreasing burden of the cost of extra investigations that might have to be carried out in the absence of such imaging modality.

LIMITATIONS OF STUDY

The diagnostic accuracy of 18-FDG SUV was not assessed according to the different subtypes histologically. Lastly, the accuracy was not assessed for recurrent lymphomas.

CONCLUSION

The current study concluded that 18 FDG SUV on PET/CT showed high diagnostic accuracy, i.e., 92.1% for detecting aggressive lymphomas and is a non-invasive technique compared to bone marrow biopsy. Therefore, it can further guide specific areas from which biopsy can be attained to confirm the diagnosis and decide on appropriate management. Future studies should be conducted on large sample sizes to confirm these findings. They thus can guide establishing guidelines for using this non-invasive technique that can help determine further intervention.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SW: Conception, interpretation of data, drafting the manuscript, approval of the final version to be published.

TSS: Study design, data analysis, drafting the manuscript, cri-tical review, approval of the final version to be published.

HS: Critical review, approval of the final version to be published.

MHS: Data acquisition, interpretation of data, approval of the final version to be published.

KS: & MM: Study design, Drafting the manuscript, interpretation of data, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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