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Diagnostic Accuracy of Positron Emission Tomography-Computed Tomography (PET-CT Scan) in Detecting Bone Marrow Involvement in Patients with Diffuse Large B cell Lymphoma

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[1]Final approval of the version to be published, [2]Design, data collection and Analysis, [3]Collection and interpretation of data, [4]Design, drafting, analysis of the work, [5]Interpretation of data, [6]Final approval and critical review

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ABSTRACT

Objective: To evaluate the diagnostic accuracy of positron emission tomography combined with CT scan (PET-CT Scan) in detecting bone marrow involvement in patients with diffuse large B-cell lymphoma, keeping bone marrow biopsy as gold standard.

Methodology: From November 2017 to May 2018, a cross sectional validation study was carried out at the Aga Khan University in Karachi Department of Oncology's Section of Clinical Hematology. The study comprised a total of 112 patients who were identified as having diffuse large B cell lymphoma after a lymph node was implicated was histopathologically examined. All patients had a PET-CT scan and bone marrow biopsy technique as part of the staging workup. With bone marrow biopsy acting as the gold standard, the diagnostic efficacy of a PET-CT scan for identifying bone marrow involvement was evaluated.

Results: Of 112 patients, there were 71(63.39%) males and 41(36.61%) females. The mean age was 45.09±17.36 years. The mean duration of diagnosis was 17.19±6.02 days. Through biopsy, bone marrow involvement was identified in 40 (35.7%) cases. Through a PET-CT scan, bone marrow involvement was identified in 47 (41.9%) cases. The PET- CT scan in comparison with bone marrow biopsy for detecting bone marrow involvement in patients with DLBCL had a sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of 95%, 87.7%, 80.85%, 96.92% and 90.18% respectively.

Conclusion: PET-CT scan can accurately detect bone marrow involvement in patients with DLBCL so it can be used in most patients instead of invasive bone marrow biopsy procedure for staging of DLBCL patients.

Keywords: NHL, PET- CT scan, bone marrow biopsy, DLBCL, BMB, BMI.

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Introduction

Non-Hodgkin lymphomas (NHL) include a wide variety of neoplastic diseases. The most frequently occurring NHL is diffuse large B-cell lymphoma (DLBCL).[1]In up to 26% of cases, the disease involves the bone marrow.[2]Accurate staging is an important part of initial assessment of newly diagnosed DLBCL. The staging of DLBCL requires detection of degree of bone marrow involvement. This bone marrow invasion of malignant cells is regarded as an extra nodal site, and it adversely affects the prognosis, management, and outcome in DLBCL patients.[3,4]

A bone marrow biopsy (BMB) from the unilateral or bilateral posterior iliac crest has traditionally been used to assess bone marrow involvement (BMI) by the underlying lymphoma. The acquisition of histological material is the

major benefit of a bone marrow biopsy, which provides definitive proof of marrow involvement. However, the procedure is invasive and painful. It may be associated with significant anxiety, bleeding, and infections in some cases. [5] Study done by Y.Lidén et al in Sweden evaluated 235 patients undergoing bone marrow aspirate & marrow; the results showed that 70% patients reported pain during bone marrow procedure.[6]

The main disadvantage of staging BMB is that only a small piece of the entire bone marrow is assessed; because of this a proportion of cases can be missed, particularly if the marrow involvement is focal.[7-9] For assessment of staging and response evaluation in DLBCL, 18-F fluorodeoxyglucose (FDG) Positron Emission Tomography combined with CT scan (PET-CT) is emerging as a powerful tool. PET-CT scan can detect both nodal and extra nodal disease accurately and also visualizes the entire marrow instead of only a small portion. PET-CT scan is now integral part of routine staging of malignant lymphomas and the topic of debate is whether it can replace bone marrow examination or not.[2,3,10,11]

In Pakistan, the most common type of NHL is DLBCL, but there is no data comparing the accuracy of PET-CT scan with BMB for staging of Diffuse Large B-cell lymphoma. It is imperative to determine whether BMB should be part of the routine staging of DLBCL. Omitting iliac crest BMB will relieve distress and significant pain associated with the procedure. Therefore, the aim of this study was to evaluate and correlate the diagnostic accuracy of BMI by PET-CT scan with bone marrow biopsy.

Methodology

This cross-sectional validation study was carried out at the Aga Khan University in Karachi Department of Oncology's Clinical Haematology Section from November 2017 to May 2018. The institutional ethical review committee (ERC) of the Aga Khan University Hospital granted permission for this study to be conducted. Each patient gave their informed permission. All participants were informed of the study's goal, methodology, risks, and advantages prior to involvement.

Our study included 112 patients. Patients were selected using non-probability, consecutive sampling technique. Sample size was calculated by diagnostics accuracy with purchase departmental licensed version of PASS-11 NCSS, LLC. Hintze, J. (2011). PASS 11. By taking confidence interval=95%, prevalence rate of bone marrow involvement = (35/130=27%)[2] PET Sensitivity=92%[12], PET Specificity=100%.[12]

Patients of either gender aged b/w 15-75 years who have been newly diagnosed (within 30 days) Diffuse large B-cell lymphoma, on biopsy of an enlarged suspicious lymph node were included in the study. Patients with follicular lymphoma with diffuse large B-cell lymphoma transformation and patients with follicular lymphoma with diffuse large B-cell lymphoma transformation who received chemotherapy for lymphoma or any other malignancy were excluded from the study.

The data regarding age, gender, and duration of DLBCL diagnosis, was collected on pre-designed structured questionnaire. Patients were referred to radiology for a PET-CT scan and to the laboratory for a bone marrow biopsy. Whole-body PET-CT scans (from the base of the skull to mid-thigh) were performed after a 6 hour fast. Patients underwent blood glucose tests prior to administering FDG to ensure suitably low levels. They were adequately rehydrated, and were asked to remain seated or recumbent to ensure fewer artifacts and to minimize FDG uptake in muscles. Imaging was acquired using Celeste ion Scanner. Coronal, sagittal, and transversal PET-CT Scan projections were reconstructed and analysed using the software. The image interpretation was done by experienced a pair of radiologist and nuclear physicians. PET-CT scan was labelled as positive if value of (SUVmax) of FDG is increase in bone marrow when compared to liver.

For the staging of DLBCL Ann Arbor staging system l staging classification system for non-Hodgkin lymphoma was used. Stage I: involvement of a single lymph node region or of a single extra lymphatic organ or site, stage II: involvement of two or more lymph node regions on the same side of the diaphragm or localized involvement of an extra lymphatic organ or site, Stage III: involvement of lymph node regions or structures on both sides of the diaphragm, stage IV: diffuse or disseminated involvement of one or more extra lymphatic organs, or either: isolated extra lymphatic organ involvement with disease in distant sites involvement of the liver, bone marrow, pleura, or cerebrospinal fluid.[13]

A bone marrow trephine biopsy was done from the right or left posterior iliac crest to get an adequate (2 cm) length of bone trephine specimen. The obtained material was formalin-fixed, hematoxilin-eosin stained and subsequently evaluated morphologically by experienced haematologist and histopathologist. Pan-T (CD3), pan B

(CD20 or CD79a) stains were performed in all cases. BMI by lymphoma was considered if there was morphological evidence of lymphoma infiltration in the biopsy sections examined, supported by immunohistochemical stains.

True-positives (TP) Cases: Patients were labelled (TP) if BMI by both PET- CT Scan and bone marrow biopsy. True-negative (TN) Cases: Patients were labelled (TN) if patients with a negative BMI and PET/CT scan. False-positive (FP) Cases: Patients were labelled (FP) if their PET-CT scan was positive but their bone marrow examination was negative. False-negative (FN) Cases: Patients were labelled (FN) if patient is negative on PET-CT scan and positive on bone marrow examination.

Data was entered and analysis in to SPSS Version 21. Descriptive statistics was calculated in term of Mean±SD age of the patients. Whereas frequency and percentages were calculated for gender, bone marrow biopsy, PET-CT Scan as appropriated. A 2*2 table was constructed between BMB and PET-CT Scan for calculating sensitivity, specificity, true positive, true negative, positive predictive value, negative predictive value and accuracy. To determine the effect on the outcome variable, stratification was done according to age, gender, time since diagnosis, and radiological stage. The accuracy of the post-stratification diagnosis was calculated, and a value of <0.05 was considered significant.

Results

A total of 112 cases fulfilling the inclusion criteria were enrolled. The mean age of patients was 45.09±17.36 years (range: 15-74 years). Most of the patients 59(53%) were more than 42 years of age. There were 71(63.39%) males and 41(36.61%) females. Male patients predominated as compare to female patients as the ratio was 1.7. Mean duration of diagnosis was 17.19±6.02 days (range: 7-30 days). 63(56%) reported in less than 15 days of diagnosis, while 49(44%) patients were diagnosed more than 15 days ago.

A detailed workup of iliac crest BMB specimens showed, 40 (35.7%) patients had involvement while 72(64.3%) had no bone marrow involvement. On the other hand PET-CT showed BMI of DLBCL in 47(41.9%) cases. There were 25 cases with focal and 22 cases with diffuse involvement on PET-CT. Overall, the PET-CT scan with bone marrow biopsy had sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of 95%, 87.7%, 80.85%, 96.92%, and 90.18%, respectively, in detecting BMI in patients with DLBCL.

The results showed high true positive and true negative rates in both genders and both age groups (Table I).

Table I: Frequency of true positive, true negative, false positive and false negative results of PET-CT scan for bone marrow involvement in diffuse large B cell lymphoma according to age, gender and duration of diagnosis taking bone marrow biopsy as the golden standard.

Variables	PET/ CT-Scan	Bone Marrow Biopsy		Total
		Positive	Negative	
Overall	Positive	TP(a) 38(33.9%)	FP (b) 9(8%)	a + b 47(42%)
	Negative	FN(c) 2(1.8%)	TN (d) 63(56.3%)	c + d 65(58%)
	Total	a + c 40(35.7%)	b + d 72(64.3%)	112(100%)
Gender				
Male	Positive	True positive(a) 24(33.8%)	False positive (b) 5(7%)	a + b 29(40.8%)
	Negative	False negative(c) 2(1.8%)	True negative (d) 63(56.3%)	c + d 42(59.2%)
	Total	a + c 26(36.6%)	b + d 45(63.4%)	71(100%)
Female	Positive	TP(a) 14(34.1%)	FP (b) 4(9.8%)	a + b 18(43.9%)
	Negative	FN(c) 0(1.8%)	TN (d) 23(56.1%)	c + d 23(56.1%)
	Total	a + c 14(34.1%)	b + d 27(65.9%)	41(100%)
Age Groups				
≤42	Positive	TP(a) 14(34.1%)	FP (b) 4(9.8%)	a + b 18(43.9%)
	Negative	FN(c) 0(0%)	TN (d) 23(56.1%)	c + d 23(56.1%)
	Total	a + c 14(34.1%)	b + d 27(65.9%)	41(100%)
>42	Positive	TP(a) 21(35.6%)	FP (b) 4(6.8%)	a + b 25(42.4%)
	Negative	FN(c) 2(3.4%)	TN (d) 32(54.2%)	c + d 34(57.6%)
	Total	a + c 23(39%)	b + d 36(61%)	59(100%)
Duration of Diagnosis				
≤15 Days	Positive	TP(a) 20(40.8%)	FP (b) 3(6.1%)	a + b 23(46.9%)
	Negative	FN(c) 2(4.1%)	TN (d) 24(49%)	c + d 26(53.1%)
	Total	a + c 22(44.9%)	b + d 27(55.1%)	49(100%)
>15 Days	Positive	TP(a) 18(28.6%)	FP (b) 6(9.5%)	a + b 24(38.1%)
	Negative	FN(c) 0(3.4%)	TN (d) 39(61.9%)	c + d 39(61.9%)
	Total	a + c 18(28.6%)	b + d 45(71.4%)	63(100%)

True Positive (TP), True Negative (TN), False Positive (FP), False Negative (FN).

With respect to stratification according to radiological staging of DLBCL, highest true positive cases were

21(51.2%), seen in stage IV. (Table II) The results showed diagnostic accuracy of more than 90% in both genders, diagnostic accuracy of PET-CT scan was slightly higher when duration of diagnosis of DLBCL was > 15 days. (Table III).Stratification according to radiological stages of DLBCL showed highest (100%) diagnostic accuracy in stage II, while stage III and stage IV had more than 90% diagnostic accuracy (Table IV)

Table II: Frequency of true positive, true negative, false positive and false negative results of PET-CT scan for bone marrow involvement in diffuse large B cell lymphoma according to various radiological stages taking bone marrow biopsy as the golden standard.

Radiological stage	PET/CT-Scan	Bone Marrow Biopsy		Total
		Positive	Negative	
Stage 1	Positive	TP(a) 5(20.8%)	FP (b) 4(16.7%)	a + b 9(37.5%)
	Negative	FN(c) 2(8.3%)	TN (d) 13(54.2%)	c + d 15(62.5%)
	Total	a + c 7(29.2%)	b + d 17(70.8%)	24 (100%)
Stage 2	Positive	TP(a) 6(28.6%)	FP (b) 0(0%)	a + b 6(28.6%)
	Negative	FN(c) 0(0%)	TN (d) 15(71.4%)	c + d 15(71.4%)
	Total	a + c 6(28.6%)	b + d 15(71.4%)	21 (100%)
Stage 3	Positive	TP(a) 6(23.1%)	FP (b) 2(7.7%)	a + b 8(30.8%)
	Negative	FN(c) 0(0%)	TN (d) 18(69.2%)	c + d 18(69.2%)
	Total	a + c 6(23.1%)	b + d 20(76.9%)	26(100%)
Stage 4	Positive	TP(a) 21(51.2%)	FP (b) 3(7.3%)	a + b 24(58.8%)
	Negative	FN(c) 0(0%)	TN (d) 17(41.5%)	c + d 17(41.5%)
	Total	a + c 21(51.2%)	b + d 20(48.8%)	41(100%)

Discussion

Diffuse large B-cell lymphoma is the most common type of non-Hodgkin lymphoma worldwide, accounting for 4% of new cancers annually and 30% of all non-Hodgkin lymphoma cases.[14] I t is the commonest NHL in Pakistan.[15] BMI in patients with DLBCL a has therapeutic and prognostic significance; hence its detection is paramount these patients. Up until now, bone marrow trephine biopsy is considered part of routine mandatory evaluation to document bone marrow involvement (BMI) as recommended by European Society of Medical Oncology.[16] This procedure is associated with pain and distress and may miss patchy bone marrow involvement.[17] 2-Deoxy-2-[18F] fluoro-D-glucose positron emission tomography/computed tomography (FDG PET/CT) is now increasingly being used for staging of initial patients with DLBCL and has shown in studies to be a highly sensitive method. Its role in detection of BMI as a non-invasive examination remains a topic of debate in oncology clinic.[16] A single BMB cannot exclude BMI with absolute certainty if infiltration is present at sites other than the one being examined.

In our study, PET-CT detected 49(43.7%) cases with BMI however iliac crest BMB found BMI in only 40(35.7%) cases. The mismatch rate was around 8% in the current study which is lower than 17% mismatch rate found in a study done by Fadi El Karak et al.[12] All cases that showed no involvement on bone trephine showed patchy bone marrow involvement on PET- CT scan suggesting that patchy bone marrow involvement is an important factor for falsely negative bone marrow trephine biopsies. This shows that PET-CT scan is more sensitive than BMB for detection of BMI. PET-CT scan helps us to detect infiltration in any part of skeleton, whereas BMB is only confined to one site. However, we also found that 2 false negative cases .These cases were reported as no BMI on PET-CT scan whereas they showed involvement on BMB. Both these false negative cases belonged to radiological stage I. This may be due to the fact that PET-CT scan may miss early small infiltrations of bone marrow, whereas a BMB may be able to detect such changes. These findings are similar to another study done in Spain, which also noted as small number of false negative cases.[18] However

Table III: Diagnostic accuracy of PET-CT scan for bone marrow involvement in diffuse large B cell lymphoma according to age, gender and duration of diagnosis taking bone marrow biopsy as the golden standard.

Variables	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Overall	95%	87.5%	80.8%	96.9%	90.2%
Male	92.3%	88.9%	82.76%	95.2%	90.1%
Female	100%	85.1%	77.7%	100%	90.2%
<42 Years	100%	86.1%	77.2%	100%	90.5%
>42 Years	100%	86.1%	77.2%	100%	90.5%
Duration Of Diagnosis <=15 Days	90.9%	88.8%	86.9%	92.3%	89.8%
Duration Of Diagnosis >15 Days	100%	86.6%	75%	100%	90.4%

Sensitivity = TP/(TP+FN); Specificity = TN/(TN+FP); PPV=TP/(TP+FP); NPV = TN/(TN+FN);
Diagnostic accuracy = (TP+TN)/(TP+TN+FP+FN); PPV: positive predictive value; NPV: negative predictive value

Table IV: Diagnostic accuracy of PET-CT scan for bone marrow involvement in diffuse large B cell lymphoma according to various radiological stages taking bone marrow biopsy as the golden standard.

Radiological Stage	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
Stage I	71.4%	76.4%	55.5 %	86.6%	75%
Stage II	100%	100%	100%	100%	100%
Stage III	100%	90%	75%	100%	92.3%
Stage IV	100%	85%	87.5%	100%	92.6%

another researcher reported 80% false negative cases when he compared PET/CT and BMB of the posterior iliac crest in DLBCL.[19] The varying frequency of false negative cases raises the question if PET/CT scan should be used as a single tool for staging of DLBCL patients.

In our study the overall sensitivity and specificity of the PET-CT scan was 95% and 87.55 respectively. The diagnostic accuracy was found to be more than 90% across all both genders and all age groups (table III).A study done in of Pakistan in 2013 evaluated the role of PET-CT in staging and treatment of lymphoma. Out of 53 patients, 35 had Hodgkin's disease, while 18 had NHL. PET-CT reflected increased disease burden in 12 patients and 4 patients were upstaged from stage 3 to stage 4.[20] A review done by Kirby et al on importance of PET-CT reported similar findings.[21]

In a study done by Fadi El Karak et al[12] in Lebanon, included 54 patients with untreated diffuse large B-cell lymphoma. A correlation analysis of the detection of bone marrow involvement by PET-CT scan and bone marrow trephine biopsy was performed .PET-CT scan was more sensitive for the detection of bone marrow involvement than BMB (92.3% vs. 38.5%)

The sensitivity and specificity of the PET-CT scan in detecting bone marrow involvement were 75% and 92%, respectively, according to retrospective research by Ujjani CS et al[22] to support the usefulness of this imaging technique in diffuse large B-cell lymphoma. PET-CT scan was unable to detect two patients with diffuse marrow infiltration, as established by BMB, one with substantial involvement and one with focused involvement. Upon stratification of radiological stages, we found a diagnostic accuracy of 75% in stage I while for stages II and above the diagnostic accuracy was more than 92%. (table IV).This shows that patients at early stages of DLBCL may need to evaluated by BMB, in addition to PET-CT scan.

These studies show that PET-CT scan is highly accurate and sensitive in DLBCL and can be used as an alternative, non-invasive method for the assessment of BMI. The diagnostic accuracy and sensitivity of PET scan in detecting bone marrow involvement reported in our study is comparable to the results of other studies in literature. In our study, we found that the PET-CT scan was able to identify bone marrow involvement in most cases. Further large scale prospective studies are needed in future to determine whether routine staging with bone marrow trephine biopsy can be omitted from the evaluation protocol of patients with DLBCL.

Limitation: Our study had a few limitations. Firstly the sample size, while not very small, was not large enough to enable us to properly control the confounding factors. In addition to this our study involved a single center study so results should be treated with caution. Further elaborate research on this subject is warranted.

Conclusion

These findings support the high degree of accuracy of PET-CT for detecting marrow illness in DLBCL in the hands of skilled practitioners and provide new insight on the type and clinical importance of marrow involvement. To spare the sick patient pain and anxiety, a PET-CT scan should be performed before to the BMB for the staging of DLBCL.

References

1. Susanibar-Adaniya S, Barta SK. Update on Diffuse large B cell lymphoma: A review of current data and potential applications on risk stratification and management. Am J Hematol. 2021;96(5):617-629. https://doi.org/10.1002/ajh.26151
2. Saiki Y, Tomita N, Uchida A, et al. Biopsy remains indispensable for evaluating bone marrow involvement in DLBCL patients despite the use of positron emission tomography. Int J Hematol. 2021;113(5):675-681. https://doi.org/10.1007/s12185-021-03080-3
3. Chen-Liang TH, Martin-Santos T, Jerez A, Senent L, Orero MT, Remigia MJ, et al. The role of bone marrow biopsy and FDG-PET/CT in identifying bone marrow infiltration in the initial diagnosis of high grade non-Hodgkin B-cell lymphoma and Hodgkin lymphoma. accuracy in a multicenter series of 372 patients. Am J Hematol. 2015;90(8):686-90. https://doi.org/10.1002/ajh.24044
4. Cheson BD. Staging and response assessment in lymphomas: the new Lugano classification. Chin Clin Oncol. 2015;4(1):5.
5. Brunetti GA, Tendas A, Meloni E, Mancini D, Maggiore P, Scaramucci L, et al. Pain and anxiety associated with

bone marrow aspiration and biopsy: a prospective study on 152 Italian patients with hematological malignancies. Ann Hematol. 2011;90(10):1233-5. https://doi.org/10.1007/s00277-011-1166-7
6. Lidén Y, Landgren O, Arnér S, SJÖLUND KF, Johansson E. Procedure-related pain among adult patients with hematologic malignancies. Acta Anaesthesiol Scand. 2009;53(3):354-63. https://doi.org/10.1111/j.1399-6576.2008.01874.x
7. Avigdor A. Staging DLBCL: bone marrow biopsy or PET-CT? Blood. 2013;122(1):4-5. https://doi.org/10.1182/blood-2013-05-502575
8. Adams HJ, Nievelstein RA, Kwee TC. Opportunities and limitations of bone marrow biopsy and bone marrow FDG-PET in lymphoma. Blood rev. 2015;29(6):417-25. https://doi.org/10.1016/j.blre.2015.06.003
9. El-Galaly TC, d'Amore F, Mylam KJ, de Nully Brown P, Bøgsted M, Bukh A, et al. Routine bone marrow biopsy has little or no therapeutic consequence for positron emission tomography/computed tomography-staged treatment-naive patients with Hodgkin lymphoma. J Clin Oncol. 2012;30(36):4508-14. https://doi.org/10.1200/JCO.2012.42.4036
10. Barrington SF, Mikhaeel NG, Kostakoglu L, Meignan M, Hutchings M, Müeller SP, et al. Role of imaging in the staging and response assessment of lymphoma: consensus of the International Conference on Malignant Lymphomas Imaging Working Group. J Clin Oncol. 2014;32(27):3048-58. https://doi.org/10.1200/JCO.2013.53.5229
11. Pelosi E, Penna D, Douroukas A, Bello M, Amati A, Arena V, et al. Bone marrow disease detection with FDG-PET/CT and bone marrow biopsy during the staging of malignant lymphoma: results from a large multicentre study. Q J Nucl Med Mol Imaging. 2011;55(4):469-75.
12. El Karak F, Bou-Orm IR, Ghosn M, Kattan J, Farhat F, Ibrahim T, et al. PET/CT Scanner and Bone Marrow Biopsy in Detection of Bone Marrow Involvement in Diffuse Large B-Cell Lymphoma. PloS one. 2017;12(1):e0170299. https://doi.org/10.1371/journal.pone.0170299
13. Cheng, J., Bell, D. Ann Arbor staging system. Reference article, Radiopaedia.org. (accessed on 17 Mar 2022) https://doi.org/10.53347/rID-63815
14. Thandra KC, Barsouk A, Saginala K, Padala SA, Barsouk A, Rawla P. Epidemiology of Non-Hodgkin's Lymphoma. Med Sci (Basel). 2021;9(1):5. https://doi.org/10.3390/medsci9010005
15. Iftikhar R, Mir MA, Moosajee M, Rashid K, Bokhari SW, Abbasi AN et al. Diagnosis and Management of Diffuse Large B-Cell Lymphoma: Society of Medical Oncology, Pakistan Society of Hematology, and Pakistan Society of Clinical Oncology Joint Clinical Practice Guideline. JCO Glob Oncol. 2021;7:1647-1658. https://doi.org/10.1200/GO.21.00320
16. Teagle AR1, Barton H1, Charles-Edwards E2, Dizdarevic S1,3,4, Chevassut T2,4. Use of FDG PET/CT in identification of bone marrow involvement in diffuse large B cell lymphomaand follicular lymphoma: comparison with iliac crest bone marrow biopsy Acta Radiol. 2017 Dec;58(12):1476-1484 https://doi.org/10.1177/0284185117701305
17. Cheng G, Chen W, Chamroonrat W, Torigian DA, Zhuang H, Alavi A. Biopsy versus FDG PET/CT in the initial evaluation of bone marrow involvement in pediatric lymphoma patients. Eu J Nuclear Med Molecular Imaging.2011; 38(8):1469-1476. https://doi.org/10.1007/s00259-011-1815-z
18. Cortés-Romera M, Sabaté-Llobera A, Mercadal-Vilchez S, et al. Bone marrow evaluation in initial staging of lymphoma: 18F-FDG PET/CT versus bone marrow biopsy. Clin Nucl Med. 2014;39(1):e46-e52. https://doi.org/10.1097/RLU.0b013e31828e9504
19. Adams HJ, Kwee TC. Do not abandon the bone marrow biopsy yet in diffuse large B-cell lymphoma. J Clin Oncol. 2015;33(10):1217. https://doi.org/10.1200/JCO.2014.58.7360
20. Awan U, Siddiqui N, SaadUllah M, Bashir H, Farooqui ZS, Muzaffar N, et al. FDG-PET scan in assessing lymphomas and the application of Deauville Criteria. J Pak Med Assoc. 2013;63(6):725-30.
21. Kirby AM, Mikhaeel NG. The role of FDG PET in the management of lymphoma: what is the evidence base? Nucl Med Commun. 2007;28(5):335-54. https://doi.org/10.1097/MNM.0b013e3280895e23
22. Ujjani CS, Hill EM, Wang H, Nassif S, Esposito G, Ozdemirli M, et al.F-FDG PET-CT and trephine biopsy assessment of bone marrow involvement in lymphoma. Br J Haematol. 2016;174(3):410-416. https://doi.org/10.1111/bjh.14071