

## BACKGROUND

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma (NHL). Disease involves the bone marrow in up to 27% of cases <sup>1</sup>

Positron emission tomography (PET), increasingly combined with computed tomography (PET-CT), is now a routine part of staging DLBCL to accurately evaluate nodal involvement.

Histologic evidence of DLBCL in staging marrow biopsy adversely affected overall survival (OS) and event-free survival, independent of the IPI<sup>2</sup> DLBCL with focal marrow deposits identified by PET-CT but not biopsy had progression-free survival (PFS) and overall survival similar to stage IV disease without involved marrow. Positive biopsy however may seem to confer inferior PFS in retrospective studies <sup>3</sup>

The role of FDG-PET/CT in staging of Diffuse Large B-Cell lymphoma (DLBCL) remains unclear. PET/CT provides a high level of accuracy for identifying focal skeletal marrow disease in Hodgkin's lymphoma (HL)<sup>4</sup>.

Bone marrow (BM) involvement by histology may have had a prognostic impact in older series of aggressive NHL with higher CNS involvement <sup>5</sup> more recent studies in patients treated with rituximab-containing chemotherapy regimens suggest that this may no longer be true in DLBCL<sup>4,6</sup>and HL <sup>7</sup>.

Whether the omission of staging Bone marrow biopsy (BMB) would change the risk assessment or treatment strategy of DLBCL is not known and whether difficulties in the correct interpretation of diffuse FDG uptake in bone marrow, leading to false-positives and poor specificity as has been previously reported in HL and NHL<sup>8</sup> can still be an issue is not clear.

## METHODS

This is a retrospective study of 114 patients with DLBCL from three community oncology practices in New Mexico, USA between January 1996- September 2016 Patients receiving BMB and PET/CT were included.

Imaging was acquired 90 minutes after administration of 370 MBq FDG. Focal or diffuse marrow involvement was identified by PET trained radiologist in all cases as previously described<sup>9</sup>.

Unilateral iliac crest biopsy and aspirate was used for staging is standard. Marrow biopsy specimens were obtained within 1 month of staging PET-CT. Descriptive statistics and a Chi-square methods were used to evaluate associations

## RESULTS

Mean age at diagnosis was 66 years (23-92), 54% were males, 82% received RCHOP therapy. Out of 114 patients, 27 (23%) patients did not have a staging BM biopsy. The sensitivity of PET/CT scan was 73% and Specificity 87%. Positive predictive value (PPV) 50% and Negative predictive value (NPV) 95%.

Patients with positive focal PET/CT were more likely (50% vs 5%),  $\chi^2$  (1, N=74) = 19.9, (p <0.001) to have a positive BMBX in comparison those with negative PET/CT scan. There was correlation of bone marrow involvement with clinical stage IV (31%), III (13%), II (5%), I (0%),  $\chi^2$  (1, N=74) = 10.14, (p=0.02) and IPI score: High (14%), Int-High (40%), Low-Int (10%), Low (3%) %,  $\chi^2$  (1, N=74) = 10.7, (p=0.019). Cytopenia was not associated with BM involvement  $\chi^2$  (1, N=74) = 1.37, (p=0.242).

The 5-year OS for PET/CT positive vs BM involved (38% vs 31% p=0.69), and PET/CT negative vs BM uninvolved patients (44% vs 50% p=0.46) were not statistically different.

Table 1: Demographics

Age	66 y (23-92)
Males	54%
Females	46%
RCHOP	82%

Table 2: PET/BM Concordance v Discordance outcomes

	5 year OS (95% CI)	p value
PET/CT +	38 (14-61)	0.69
BM+	31 (5-56)	
PET/CT-	44 (32-55)	0.46
BM-	50 (38-61)	

Table 3: Accuracy and predictability of PET/CT in DLBCL Staging

PET/CT	
Sensitivity	73%
Specificity	87%
PPV	50%
NPV	95%

Table 4: Correlation of DLBCL with PET and prognostic factors

	BM Involvement (%)	$\chi^2$	p value
PET/CT +	50	19.9	<0.001
PET/CT -	5		
Stage I	0	10.14	0.02
Stage II	5		
Stage III	13		
Stage IV	31		
IPI Low	3	10.7	0.019
IPI Int-low	10		
IPI Int-High	40		
IPI High	14		
Cytopeni present	21	1.36	0.242
Cytopeni absent	12		

## CONCLUSIONS

- PET/CT is a valuable diagnostic tool for detection of focal bone marrow involvement in DLBCL. The long-term prognostic value of PET/CT is similar to that obtained by a bone marrow biopsy.
- Our study confirms previous retrospective data suggesting high level of accuracy for detecting bone marrow involvement in patients with DLBCL<sup>3</sup>
- Patients with a Positive PET/CT had a Higher IPI, clinical Stage and Bone marrow involvement.
- The high negative predictive value may help to avoid bone marrow biopsies especially if clinically early stage disease.
- Cytopenia did not predict BM involvement.
- Unilateral iliac crest BMB, may miss a significant proportion of marrow disease compared with bilateral sampling<sup>10</sup> and an experienced PET reviewer may be able to adequately stage aggressive NHL patients sparing invasive staging biopsies

## REFERENCES

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