Poster # 74

# Clinical Staging of lymphomas using the Ann Arbor vs Lugano Classifications; Evaluating concordance of the two staging systems

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## Abstract

The Ann Arbor classification system for the staging of Lymphoma was originally established in 1971 using CT findings to evaluate and stage the disease in both the initial and post treatment stages. The utility of this modality was, however, limited to its anatomic evaluation with no functional information being offered. In 2014, the Lugano classification was established which incorporated 18F-Fluorodeoxyglucose-positron emission tomography as a means for objectively assessing the disease status with advantage of real time, functional information being incorporated which allowed for a true assessment of the disease status especially after treatment institution.

To evaluate the utility of the Lugano against the Ann Arbor classification, we prospectively followed patients with Lymphoma referred to our institution for initial staging, interim treatment, or end of treatment scanning.

103 patients were include in this prospective study with a total of 155 scans. The Ann Arbor staging matched the Lugano stage in 122 scans (78.7%). Non concordance was seen in 33 (21.3%) with an up-staged seen in 17 (10.9%) and a down-staged in 16 (10.3%) using the Lugano classification.

In conclusion it was seen that Lugano has a decided advantage over the Ann Arbor classification system, especially where patients were being scanned for treatment assessments and follow-up.

## Introduction

Lymphoma, (Hodgkin's {HL} and Non-Hodgkin's {NHL}), is a malignant cancer of the lymphatic system. With advancement towards understanding of the disease and availability of innovative treatment regimens, the disease has become amiable to treatment. However, for the optimal treatment strategy and initial and follow-up assessment, an accurate and reproducible system for staging is crucial, as the treatments offered are not without their toxic and adverse ill effects. Over the years staging has been done by the Ann Arbor with its modification to the Cotswold, which is primary morphological. Lugano which incorporates PET-CT, given in 2014 is functional / metabolic. The advantages offered by PET are

- stage before any treatment started, progressive restaging in response to therapy (interim scanning), and finally end of treatment. It can also help in the follow-up of differentiation of scar from residual tumor mass

However the availability and cost issues has a major limiting issue for PET-CT, especially in a economically compromised country as ours.

- In this study we strive to see the concordance of the two staging systems within our set-up and evaluate the advantages that may be offered by one over the other in terms of management.

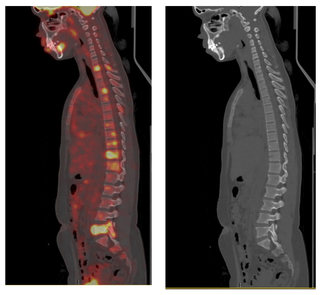

**Figure 1.** Metabolically active lesions identified in the marrow, not seen on CT, resulting in upgrade of initial stage

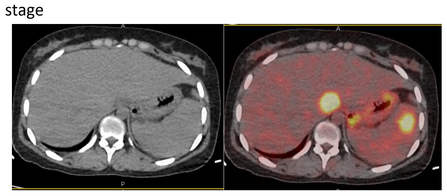

**Figure 2.** - Metabolically active lesions identified in the liver and spleen, not seen in CT, resulting in upgrade of stage

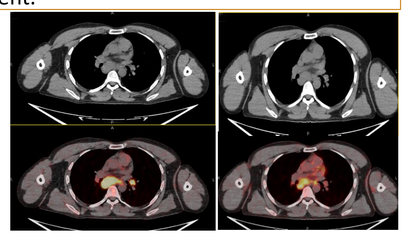

**Figure 3: -** Persistent functional activity identified in the sub-sternal lesion which appears to have decreased in size on CT; Partial Metabolic Response (PMR).

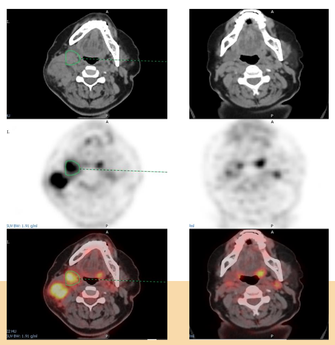

**Figure 4: -** Complete resolution of abnormal tissue with no remnant activity seen in the right sub-mandibular gland and level II lymph node; Complete Metabolic Response (CMR)

## Methods and Materials

### Research Questions

**○ Primary Research Question**

- To see for the ***concordance*** between the Ann Arbor and Lugano staging systems

**○ Secondary Research Question**

- To evaluate the ***utility*** of the Lugano against the Ann Arbor classification

**○ Research Methodology**

Patients with Lymphoma, referred to our institution, were prospectively followed for initial staging, interim treatment, or end of treatment scanning

### Setting

PET-CT Section, Dept Radiology, JPMC Karachi

### Duration

December 2020 to October 2022

### Study Design

Longitudinal, prospective, observational study

### Sample Size and Sampling

Purposive, criterion sampling

- 103 Patients, 155 Total scan

### Inclusion Criteria

All patients with Lymphoma that were referred for scanning for

- initial baseline staging (pre-treatment scan)
- interim, treatment response
- End of treatment evaluation
- Follow-up

### Exclusion Criteria

Not fulfilling the above

## Results

### Result Parameters

### Ann Arbor

The nodal lesion is defined as a lymph node that is 1.5cm or larger in its longest diameter.

### Lugano

Lugano defines a nodal lesion as any lymph node with FDG uptake even if it is smaller than 1.5cm

### Concordance

▪ Ann Arbor stage was matched to Lugano staging and Agreement/Concordance of the two staging systems was evaluated

▪ Utility of the Lugano against the Ann Arbor classification was seen

❖ SPSS software was used to calculate Kappa coefficient for standardized measure of agreement of the categorical scores

## Results (cont)

| Total Patients n = 103 | HL | NHL | T-Cell Lymphoma | Mantle Cell Lymphoma |
|---|---|---|---|---|
| **Males** n = 67 Age (Median) = **40** yrs | 36 | 29 | 1 | 1 |
| **Females** n = 36 Age (Median) = **37.5** yrs | 18 | 16 | 2 | --- |

## Results (cont)

Concordance/Grading

| Concordance | Yes | No | | |
|---|---|---|---|---|
| Total Scans n = 155 | 122 (78.7 %) | 33 (21.3 %) | | |
| **Grading** | **Baseline** | **No Change** | **Upgraded** | **Downgraded** |
| | | | Baseline | Post Rx | |
| Total Scans n = 155 | 83* (53.5%) | 39 (25.2%) | 4 (2.6 %) (Node, Spleen, Marrow) | 13 (8.4 %) | 16 (10.3 %) |

## Discussion

Concordance of the Ann Arbor and Lugano classifications are recorded in literature with similar results being reported (1-12). A good concordance for the baseline study was seen in our study which is also reported by Matika et al (2). However, these authors lay emphasis on the bone marrow studies to rule out marrow involvement which is an advantage offered by PET-CT, also corroborated by our study as two patients were upgraded at their baseline scanning to have marrow involvement (Figure 1). The study also showed advantage in identifying other organ involvement (e.g. spleen and liver) (Figure 2), which were not recognized on the CT. Definitive advantage in the change of stage was seen for the post treatment and follow-up studies (figures 3 and 4), with an upgrade seen in 13 scans (8.4% of scans.) and a downgrade reported in 16 scans (10.3 % of scans) . Similar study statistics have also been reported by others in literature.

The advantage of PET over the CT is seen in relation to the ability of the modality to employ metabolic imaging which is real time whereas CT is only morphological and cannot attribute towards the functioning status of any lesion / area. However, this advantage is overrided by the ***costs*** and ***availability*** of PET, especially in economically struggling situations, as ours, where even basic health needs are compromised. The importance of proper evaluation of cancer patients need to be understood and the advantage offered by PET imaging system realized with efforts being made in facilitation by the Health Policy makers of the system.

## Conclusions, Limitations, Future Directions

### Conclusion

▪Good concordance Baseline

▪ Concordance suffers with follow-up after treatment
PET-CT to be mandated wherever/ wherever possible

▪ Efforts made of education of patients/attendants towards importance of scanning and its subsequent follow-up, especially with treatment

### Limitations

▪ Single Center Study

▪ Several variables / confounding variables which need to be taken into consideration

▪ On-going study (follow-up will improve study statistics)

### Future Directions

Add Metabolic Tumor Volume (MTV), Tumor lesion Glycolysis (TLG) or Artificial Intelligence / Deep Learning

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## References

1. Cheson BD. PET/CT in Lymphoma: Current Overview and Future Directions. Vol. 48, Seminars in Nuclear Medicine. 2018.
2. Makita S, Maruyama D, Maeshima AM, Taniguchi H, Yuda S, Toyoda K, et al. A comparison of clinical staging using the Lugano versus Ann Arbor classifications in Japanese patients with Hodgkin lymphoma. Asia Pac J Clin Oncol. 2020 Jun 1;16(3):108–14.
3. Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, et al. Recommendations for initial evaluation, staging, and response assessment of hodgkin and non-hodgkin lymphoma: The lugano classification. Vol. 32, Journal of Clinical Oncology. American Society of Clinical Oncology; 2014. p. 3059–67
4. Cheson BD. Staging and response assessment in lymphomas: The new Lugano classification. Chin Clin Oncol. 2015;4(1):1–9.
5. Fueger BJ, Yeom K, Czernin J, Sayre JW, Phelps ME, Allen-Auerbach MS. Comparison of CT, PET, and PET/CT for staging of patients with indolent non-hodgkin's lymphoma. Mol Imaging Biol. 009;11(4):269–74.
6. Hutchings M, Loft A, Hansen M, et al: Position emission tomography with or without computed tomography in the primary staging of Hodgkin's lymphoma. Haematologica 91: 482-489, 2006. [Internet]. [cited 2023 Feb 3]. Available from: http://www.sciepub.com/reference/177747
7. Munakata W, Terauchi T, Maruyama D, Nagai H. Revised staging system for malignant lymphoma based on the Lugano classification. Jpn J Clin Oncol [Internet]. 2019 Oct 1 [cited 2023 Jan 18];49(10):895–900. Available from: https://academic.oup.com/jjco/article/49/10/895/5555767
8. Yoo KH. Staging and response assessment of lymphoma: a brief review of the Lugano classification and the role of FDG-PET/CT. Blood Res [Internet]. 2022 Apr 30 [cited 2023 Jan 18];57(0):S75–8. Available from: https://www.bloodresearch.or.kr/journal/view.html?doi=10.5045/br.2022.2022055
9. Hutchings M, Barrington SF. PET/CT for Therapy Response Assessment in Lymphoma. J Nucl Med [Internet]. 2009 [cited 2023 Jan 3];50:21–30. Available from: www.clinicaltrials.gov
10. Moghbel MC, Mittra E, Gallamini A, Niederkohr R, Chen DL, Zukotynski K, et al. Response Assessment Criteria and Their Applications in Lymphoma: Part 2. Journal of Nuclear Medicine. 2017;58(1).
11. 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. Journal of Clinical Oncology. 2014;32(27):3048–58.
12. Barrington SF, Kluge R. FDG PET for therapy monitoring in Hodgkin and non-Hodgkin lymphomas. Eur J Nucl Med Mol Imaging. 2017;44:97–110.
13. Kostakoglu L, Nowakowski GS. End-of-Treatment PET/Computed Tomography Response in Diffuse Large B-Cell Lymphoma. Vol. 14, PET Clinics. 2019.
14. El-Galaly TC, Gormsen LC, Hutchings M. PET/CT for Staging; Past, Present, and Future. Semin Nucl Med [Internet]. 2018;48(1):4–16. Available from: https://doi.org/10.1053/j.semnuclmed.2017.09.001
15. McCarten KM, Nadel HR, Shulkin BL, Cho SY. Imaging for diagnosis, staging and response assessment of Hodgkin lymphoma and non-Hodgkin lymphoma. Pediatr Radiol. 2019;49(11):1545–64.