Open Access

Original Article

Induction Response in Patients of Classical Hodgkin Lymphoma of Pediatric Age Group as Asseseed by CT Scan Post Chemotherapy Induction

Haider Ali Awan, Waqas Ahmed, Shakeel Ahmed, Sumbal Malik, Bilal Akhlaq, Rehan Mehmood

Department of Pediatric, Combined Military Hospital, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To assess the induction response to chemotherapy as adequate or inadequate using CT (computed tomography) scan texture analysis parameters in pediatric patients of classical Hodgkin lymphoma when compared with the gold standard PET findings.

Study Design: Prospective longitudinal study

Place and Duration of Study: Pediatrics department of Combined Military Hospital, Rawalpindi Pakistan, from Jan 2023 to Dec 2023.

Methodology: After the histopathological diagnosis was confirmed, Positron emission tomography and Computed tomography scans were done in all patients before the start and the end of two cycles of chemotherapy and response to treatment was compared using imaging changes before and after the procedure. Primary variables measured were early response assessment (ERA) by adequate and inadequate response to chemotherapy assessed by Computed tomography scan findings compared to those of Positron emission tomography scan results. Sensitivity and specificity was also calculated for Computed tomography findings versus Positron emission tomography scan results.

Results: Radiological lesion analysis by independent consultants for PET and CT scan for the tumors showed that patients showed adequate early response in 94(78.3%) cases in PET scan results versus 59(49.2%) cases on CT scan findings. Similarly inadequate response was labelled in 26(21.7%) cases when assessed by PET scan and 61(50.8%) when labeled after assessment of texture analysis of tumors on CT scan (p=0.034). The sensitivity of CT scan in detecting adequate and inadequate response when compared with the standard PET findings was 54.3% with a specificity of 69.2%.

Conclusion: We conclude that CT scan shows low sensitivity and specificity in detecting adequate and inadequate response to early stage chemotherapy in pediatric Hodgkin Lymphoma with PET being superior to check for response in these patients.

Keywords: Chemotherapy, CT scan, Hodgkin, Induction, PET scan, Response.

How to Cite This Article: *Awan HA, Ahmed W, Ahmed S, Malik S, Akhlaq B, Mehmood R. Induction Response in Patients of Classical Hodgkin Lymphoma of Pediatric Age Group as Asseseed by CT Scan Post Chemotherapy Induction. Pak Armed Forces Med J 2025; 75(Suppl-6): S940-S944. DOI: https://doi.org/10.51253/pafmj.v75iSUPPL-6.12117*

INTRODUCTION

Hodgkin lymphoma is one of the commonest malignancies seen in children and adolescents.[1] It is estimated that it constitutes more than 40% of all lymphomas diagnosed in the pediatric age group.[2] With the development of advanced diagnostic techniques, a considerable burden is being faced by medical setups for treatment and follow-up for the disease. With the current standard regimens for treatment, the overall prognosis for the disease is conducive if diagnosed and treated timely.[3] According to the disease progression at the time of diagnosis, the patients are divided into treatment groups (TGs) according to the intensity of the treatment required in the form of chemotherapy and/or radiotherapy.[4]

One of the major issues faced during treatment for the disease is the chemo and radiotherapy associated complications resulting in considerable morbidity and mortality in these patients.[5] Studies have shown that treatment associated sepsis and cardiac debility along with secondary primary cancers have a strong association with the intensity of chemotherapy and radiotherapy.[6] Long term studies have showed that mortality associated with the disease studied post-therapy was more due to complications than due to the disease itself.[7] This has resulted in protocols and follow-up standards to ensure intensity of chemotherapy and radiotherapy to be tailored to ensure adequate response (AR) to treatment, prevent inadequate response (IR) and prevention of complications.[8]

Texture analysis of tumor on PET (positron emission tomography) is considered the standard to evaluate response to chemotherapy in adults suffering from Hodgkin lymphoma.[9] There have been studies that have proposed that CT analysis for tumor texture

Correspondence: Dr Haider Ali Awan, Department of Pediatric, Combined Military Hospital, Rawalpindi Pakistan

Received: 22 Apr 2024; revision received: 15 Jul 2024; accepted: 07 Aug 2024

can provide satisfactory results to detect adequate or inadequate response to chemotherapy.[10] If significant, this would provide an excellent alternate in the pediatric age group considering the high cost and non-availability of PET scans in our country.

Our study aims to assess the induction response to chemotherapy as adequate or inadequate using CT (computed tomography) scan texture analysis parameters in pediatric patients of classical Hodgkin lymphoma.

METHODOLOGY

This Prospective longitudinal study was carried out at the Department of Pediatrics, Combined Military Hospital Rawalpindi Pakistan from Jan 2023-Jun 2023 after approval form the ethical review board vide letter no 482. The sample size was calculated keeping the confidence interval at 95%, margin of error at 5% with the population proportion of Classical Hodgkin Lymphoma in the pediatric age group at 6%1. Minimum sample size came out to be 87 patients according to the WHO calculator. We included a total of 120 patients in our final study protocol for assessment.

Inclusion Criteria: Included all pediatric patients aged less than 18 years of age diagnosed with classical Hodgkin Lymphoma confirmed with histo-pathological evidence after tissue biopsy and placed on standard treatment institutional guidelines according to the EuroNet-PHL-C1 treatment stages keeping in line with the Ann Arbor classification, erythrocyte sedimentation rate and bulk of the tumor on presentation.[11]

Exclusion Criteria: Included children with major cardiac or respiratory disease, non-classical Hodgkin lymphoma, previous history of chemotherapy, non-consent of the parents or next of kin to be included in the study and poor image resolution or artifacts on PET and/or CT scan

The study method included all patients as per the inclusion criteria furnished. The parents of the children were thoroughly informed and counseled regarding the study procedure and possible outcomes and complications. After the histopathological diagnosis was confirmed, an initial CT scan and PET scan was done for reference before starting treatment. The patients were then allocated to their respective chemotherapy treatment groups according to the criteria furnished above. The patients in each allocated treatment group received 2 cycles of chemotherapy according to the defined intensity and schedule of treatment in line with disease severity. Both PET (18-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography) and CT scans were done in all patients before the start and the end of two cycles of chemotherapy and response to treatment was compared using imaging changes before and after the procedure. In all patients, contrast enhanced CT scan (CECT) was carried out of the cervical area, chest abdomen and pelvis. Images of the chest were taken in the arterial phase while those of the abdomen and pelvis were taken in the portal venous phase. The response seen on PET was assessed before and after therapy by independent nuclear medicine consultants in liaison with pediatric oncologist unaware of the study protocol and a Deauville score of 1-3 was considered adequate response and 4-5 as inadequate response to therapy.[12] CT scan assessment was done using texture analysis of the lesions before and after cycles of chemotherapy. The texture analysis was done by a consultant radiologist unaware of the study protocol and the results of the PET scan post-chemotherapy to make an unbiased analysis. Adequate response and inadequate response as determined by PET scan results were then compared with those of the CT scan findings by the assessing pediatric oncology consultant using the Lugano classification on the Deauville five-point scale.

Primary variables measured were early response assessment (ERA) by adequate and inadequate response to chemotherapy assessed by CT scan findings compared to those of PET scan results. Sensitivity and specificity was also calculated for CT findings versus PET scan results. Demographic data were statistically described in terms of mean and SD, frequencies, and percentages when appropriate. Independent samples t-test was used to compare statistically significant means. Frequency variables were used using the Chi-square test. A *p*-value of ≤0.05 was considered statistically significant. All statistical calculations were performed using Statistical Package for Social Sciences 26.0.

RESULTS

A total of 120 patients were assessed in the final study protocol. Mean age of patients was 12.98±1.47 years while the mean weight of the study group was 24.56±2.97 kg. Gender distribution showed 79(65.8%) males and 41(34.2%) females. The stage of Hodgkin Lymphoma according to guidelines showed that 13(10.8%) patients were Stage-I, 48(40%) were Stage-II,

36(30%) were Stage-III and 23(19.2%) were Stage-IV. Based on clinical workup and investigations, 16(13.3%) were assigned to treatment Group 1, 57(47.5%) were assigned to treatment Group 2 and 47(39.2%) were assigned to treatment Group 3. On investigative assessment of all patients, tumor lesions were present in the lymph nodes of 103(85.8%) patients, those involving the thymus were seen in 16(13.3%) patients and lesions detected in the lungs constituted 07(5.8%) patients (Table-I).

Table-I: Demographic and Clinical Characteristics (n=120)

Variable	Hodgkin Group (n=120)
Mean age (years)	12.98±1.47
Mean weight (kgs)	24.56±2.97
Gender distribution	
Male	79(65.8%)
Female	41(34.2%)
Hodgkin lymphoma stage	
Stage-I	13(10.8%)
Stage-II	48(40%)
Stage-III	36(30%)
Stage-IV	23(19.2%)
Treatment group assigned	
1	16(13.3%)
2	57(47.5%)
3	47(39.2%)
Lesions present	
Lymph node	103(85.8%)
Thymus	16(13.3%)
Lung	07(5.8%)

Radiological lesion analysis by independent consultants for PET and CT scan for the tumors showed that patients showed adequate early response in 94(78.3%) cases in PET scan results versus 59(49.2%) cases on CT scan findings. Similarly inadequate response was labelled in 26(21.7%) cases when assessed by PET scan and 61(50.8%) when labeled after assessment of texture analysis of tumors on CT scan (p=0.034) (Table-II).

Table-II: Comparison of Lesion Analysis Post-Chemotherapy Between CT AND Pet Scan (n=120)

Variable	Pet Scan Findings	Ct Scan Findings	p-value
Patients Showing Adequate Early Response	94(78.3%)	59(49.2%)	0.034
Patients Showing Inadequate Early Response	26(21.7%)	61(50.8%)	

The sensitivity of CT scan in detecting adequate and inadequate response when compared with the standard PET findings was 54.3% with a specificity of 69.2% with a positive predictive value of 86.4% and a negative predictive value of 29.5% respectively (Table-III).

Table-III Sensitivity And Specificity Of Ct Scan Findings Compared With Pet Scan Results (n=120)

Variable	
Sensitivity	54.3%
Specificity	69.2%
Positive Predictive Value	86.4%
Negative Predictive Value	29.5%

DISCUSSION

The study was carried out in our center to find for alternative ways to assess early response to chemotherapy in pediatric patients with classical Hodgkin Lymphoma and whether we could use CT scan as a suitable alternative to PET scans for early assessment since the modality is not widely available in the country and is not cost effective especially in low socioeconomic medical setups.[13] There have been multiple studies that have proposed that early assessment and tailoring chemotherapy and/or omitting radiotherapy in early adequate response groups results in considerably less treatment associated morbidity and mortality which has become a major issue of debate when treating Hodgkin lymphoma.[14] With the available results on response to therapy, the prognosis for the disease is excellent with 5 year survival at more than 98%.[15] Hence tailored treatment by assessing early response through radiological modalities which are non-invasive and reliable would result in reducing treatment related complications and mortality.

18-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) is currently the gold standard radiological tool to detect responder and non-responders to Hodgkin lymphoma treatment.[16] The same was used to assess response in our study as well. While CT scan takes images of lesions with the contrast highlighting areas where tumors are located, the PET provides more information by selective uptake of the FDG trace material in areas of tumor activity and cellular proliferation. This makes it easy to detect highly proliferative areas when compared to those with normal proliferation.

The mean age of patients in our study group was between the range of 11-15 years which is in line with the median age HL diagnosis of 15-19 years. Since we included only pediatric patients less than 18 years of age, the slight decrease in mean age is expected. The

overall gender ratio showed a male predominance in line with studies done for the gender distribution of the disease. Hodgkin stages II and III remained the most common to be diagnosed in the pediatric age group.

When assessing for the detection of correctly identifying response post-chemotherapy, there was a considerable difference in the subjects labelled as early adequate and inadequate responders when compared between PET and CT scan image analysis by independent investigators. Both the groups had independent consultants unaware of the study protocol that gave their unbiased opinion based purely on the image analysis. The overall sensitivity and specificity in the pediatric age group for CT scan was 54.3% and 69.2% respectively. This is corroborated by studies done which show CT sensitivity in early response post-chemotherapy to be 61.1% and specificity to be 92.2%.[17] Our study showed similar findings for sensitivity but specificity for the pediatric age group was less than that when compared with adolescent and adult findings. Further studies are needed to assess reason for this difference. When compared with PET findings done for the same, the sensitivity and specificity of the test to detect similar responders is around 98-100% which shows PET to be superior to CT scan as the modality of choice for the time being.[18]

LIMITATIONS OF STUDY

The limitations are that the study is single center only. The inter-observer variability may need to be addressed even though we used independent, experienced consultants to assess the images.

RECOMMEDATIONS

The study recommends PET scan to be the gold standard for detecting early responders and inadequate responder to chemotherapy in pediatric age group and CT scan to be inferior in sensitivity as well as specificity.

CONCLUSION

We conclude that CT scan shows low sensitivity and specificity in detecting adequate and inadequate response to early stage chemotherapy in pediatric Hodgkin Lymphoma with PET being superior to check for response in these patients.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

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

HAA & WA: Data acquisition, data analysis, critical review, approval of the final version to be published.

SA & SM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

BA & RM: Conception, data acquisition, drafting the manuscript, 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.

REFERENCES

1. Lo AC, Dieckmann K, Pelz T, Gallop-Evans E, Engenhart-Cabillic R, Vordermark D, et al. Pediatric classical Hodgkin lymphoma. Pediatric Blood & Cancer 2021; 68: e28562. https://doi.org/10.1002/pbc.28562
2. Flerlage JE, Hiniker SM, Armenian S, Benya EC, Bobbey AJ, Chang V, et al. Pediatric Hodgkin lymphoma, version 3.2021. Journal of the National Comprehensive Cancer Network 2021; 19(6): 733-754. https://doi.org/10.6004/jnccn.2021.0027
3. Ghafoor T. Prognostic factors in pediatric Hodgkin lymphoma: experience from a developing country. Leukemia & Lymphoma 2020; 61(2): 344-350. https://doi.org/10.1080/10428194.2019.1665666
4. Lundgaard AY, Hjalgrim LL, Rechner LA, Lundemann M, Brodin NP, Joergensen M, et al. The risk of late effects following pediatric and adult radiotherapy regimens in Hodgkin lymphoma. Strahlentherapie und Onkologie 2021; 197: 711-721. https://doi.org/10.1007/s00066-020-01721-w
5. Kendel NE, Stanek JR, Willen FK, Audino AN. Characterizing age-related differences in Hodgkin lymphoma in children, adolescents and young adults. Pediatric Hematology and Oncology. 2024: 1-10. https://doi.org/10.1080/08880018.2024.2337627
6. Marks LJ. Improving risk stratification to guide treatment decisions for children, adolescents, and young adults with Hodgkin Lymphoma. Journal of the National Comprehensive Cancer Network 2021; 19(6): 666-668. https://doi.org/10.6004/jnccn.2021.7041
7. Lee JM, Choi JY, Hong KT, Kang HJ, Shin HY, Baek HJ, et al. Clinical characteristics and treatment outcomes in children, adolescents, and young-adults with Hodgkin's lymphoma: A KPHOG lymphoma working-party, multicenter, retrospective study. Journal of Korean Medical Science 2020; 35(46). https://doi.org/10.3346%2Fjkms.2020.35.e393
8. Ansell SM. Hodgkin lymphoma: A 2020 update on diagnosis, risk-stratification, and management. American journal of hematology 2020; 95(8): 978-789. https://doi.org/10.1002/ajh.25856
9. Spijkers S, Littooij AS, Kwee TC, Tolboom N, Beishuizen A, Bruin MC, et al. Whole-body MRI versus an [18 F] FDG-PET/CT-based reference standard for early response assessment and restaging of paediatric Hodgkin's lymphoma: a prospective multicentre study. European Radiology 2021; 31: 8925-8936. https://doi.org/10.1007/s00330-021-08026-1

10. Abenavoli EM, Linguanti F, Anichini M, Miele V, Mungai F, Palazzo M, et al. Texture analysis of 18F-FDG PET/CT and CECT: Prediction of refractoriness of Hodgkin lymphoma with mediastinal bulk involvement. Hematological Oncology 2024; 42(2): e3261. https://doi.org/10.1002/hon.3261
11. Mauz-Körholz C, Landman-Parker J, Balwierz W, Ammann RA, Anderson RA, Attarbaschi A, et al. Response-adapted omission of radiotherapy and comparison of consolidation chemotherapy in children and adolescents with intermediate-stage and advanced-stage classical Hodgkin lymphoma (EuroNet-PHL-C1): a titration study with an open-label, embedded, multinational, non-inferiority, randomised controlled trial. The Lancet Oncology 2022; 23(1): 125-137. https://doi.org/10.1016/S1470-2045(21)00470-8
12. Taroco MGR, Cuña EG, Pages C, Schelotto M, González-Sprinberg GA, Castillo LA et al. Prognostic value of imaging markers from 18FDG-PET/CT in paediatric patients with Hodgkin lymphoma. Nuclear Medicine Communications 2021; 42(3): 306-614. https://doi.org/10.1097/MNM.0000000000001337
13. Al-Sharify ZT, Al-Sharify TA, Al-Sharify NT, editors. A critical review on medical imaging techniques (CT and PET scans) in the medical field. IOP Conference Series: Materials Science and Engineering; 2020: IOP Publishing. https://doi.org/10.1088/1757-899X/870/1/012043
14. Lewis WD, Lilly S, Jones KL. Lymphoma: diagnosis and treatment. American family physician 2020; 101(1): 34-41.
15. De Vries S, Schaapveld M, Janus CP, Daniëls LA, Petersen EJ, van der Maazen RW, et al. Long-term cause-specific mortality in Hodgkin lymphoma patients. JNCI: Journal of the National Cancer Institute 2021; 113(6): 760-769. https://doi.org/10.1093/jnci/djaa194
16. Al Tabaa Y, Bailly C, Kanoun S. FDG-PET/CT in lymphoma: where do we go now? Cancers 2021; 13(20): 5222. https://doi.org/10.3390/cancers13205222
17. Yassin A, El Sheikh RH, Ali MM. PET/CT vs CECT in assessment of therapeutic response in lymphoma. Egyptian Journal of Radiology and Nuclear Medicine 2020; 51: 1-11. https://doi.org/10.1186/s43055-020-00353-5
18. Trotman J, Barrington SF. The role of PET in first-line treatment of Hodgkin lymphoma. The Lancet Haematology 2021; 8(1): e67-e79. https://doi.org/10.1016/S2352-3026(20)30357-4