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Harnessing the prognostic potential of CT imaging in pediatric lymphoma: an in-depth analysis of disease evaluation and outcomes

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Abstract

Introduction: Pediatric lymphomas are a significant childhood malignancy primarily treated with chemotherapy. While CT imaging is crucial for disease evaluation, its prognostic value remains under-explored. This study investigates the potential of CT characteristics to predict treatment response and clinical outcomes in pediatric lymphoma patients. Investigate the prognostic value of CT characteristics in pediatric lymphoma treated with chemotherapy.

Materials and Methods: Retrospective analysis of 69 patients' medical records and CT scans. CT features (regression, size, nodal appearance, site involvement) were correlated with treatment response (regression, stable disease, progression, relapse, resolution) via univariate analysis.

Results: Most patients (76.8%) achieved good outcomes with tumor regression. However, a subset displayed stable disease (11.6%), progression (7.2%), relapse (1.4%), or resolution (2.9%). CT characteristics associated with poor outcomes ($p < 0.05$) included: multiple site involvement (neck, chest, abdomen), larger tumor size (>3 cm), discrete nodal appearance.

Conclusion: CT features hold promise for prognostication in pediatric lymphoma. Integrating these findings into clinical practice may improve risk stratification and guide personalized treatment strategies.

Keywords: Pediatric lymphoma, Computed tomography, Prognosis, Outcomes, Regression, Risk stratification

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Introduction

Pediatric lymphomas represent a significant portion of childhood malignancies, ranking as the third most common type. They can be broadly classified into Hodgkin's lymphoma (HL) and Non-Hodgkin's lymphoma (NHL). HL further encompasses the classical and nodular lymphocyte-predominant types, while NHL is categorized into B, T, and natural killer (NK) cell lymphomas based on the World Health Organization (WHO) classification. Non-Hodgkin lymphoma (NHL) accounts for approximately 50% of pediatric lymphomas, with the remainder being Hodgkin's lymphoma (HL) (1-3).

In the staging of high-grade lymphomas in children, contrast-enhanced CT studies of the chest, abdomen, and pelvis are the standard imaging modalities. However, it is important to note that extrapolating FDG-PET and PET/CT results from adult NHL to pediatric NHL is not appropriate due to the differences in disease biology, prognostic factors, staging systems, treatment approaches, and outcomes between these two groups (4-7).

Computed tomography (CT) is commonly utilized for evaluating lymphoma patients as it provides valuable information about both the nodal and extranodal components of the disease (8,9). Its accuracy in disease staging and monitoring therapeutic response makes it an indispensable tool in clinical practice (10-12).

While FDG PET/CT has gained worldwide acceptance as a baseline test for staging and prognostic prediction in lymphoma, it is not routinely used in the pediatric age group. Instead, CT remains the preferred modality for staging and predicting lymphoma survival in children (13-15).

To contribute to the understanding of CT's significance in predicting prognosis and outcomes in pediatric lymphoma, we conducted a retrospective study involving 69 known cases of lymphoma in pediatric patients who underwent CT scans at our hospital over a period of two years. The aim of our study was to assess the role of CT in predicting the prognosis and outcome of the disease in this specific population.

By analyzing the findings and outcomes of our study, we aim to provide valuable insights into the use of CT in pediatric lymphoma management, further improving our understanding of this important field and potentially impacting clinical decision-making for the benefit of young patients. The objectives of this study were to evaluate the prognostic value of computed tomography (CT) imaging in predicting outcomes and prognosis in pediatric lymphoma patients. Specifically, we aimed to assess the correlation between CT characteristics, such as tumor size, nodal involvement, extranodal disease, and clinical outcomes. Additionally, we sought to investigate the association between CT findings and treatment response, including regression, stability, progression, relapse, and resolution of lymphomatous deposits. Moreover, our objectives included identifying specific CT characteristics that are significantly associated with poor clinical outcomes in pediatric lymphoma patients.

Materials and Methods

Study Population and Clinical Data

This retrospective study was conducted with the approval of the Institutional Ethical Review Board Committee at the National Institute of Child Health. Written informed consent was obtained from the legal guardians of all participants.

Inclusion and Exclusion Criteria

Patients diagnosed with lymphoma according to the World Health Organization classification by our hospital pathologists were eligible for inclusion. We included patients who had undergone contrast-enhanced CT scans of the head and neck, chest, abdomen, and pelvis (both unenhanced and contrast-enhanced sequences) within the study period and had visible tumors identified on the CT scans.

Exclusion criteria were:

- Incomplete CT data (missing scans or sequences).
- Underlying medical conditions that could significantly affect CT interpretation (e.g., recent surgery, metal implants).

- Known contraindications to contrast agents used in CT scans.

A computerized search of the hospital database identified 69 patients who met the inclusion criteria during the two-year period from January 2021 to December 2022. Their clinical data, including age, gender, tumor location, stage, treatment received, and clinical outcome, were collected and documented for analysis.

Image Analysis

CT examinations of all patients were conducted using a PQ5000 spiral CT scanner (Picker, New York, NY, USA). The imaging protocol included a series of unenhanced sections followed by intravenous bolus injection of contrast medium (Ultravist 300; Bayer Schering Pharma, Berlin-Wedding, Germany) at a rate of 2.5–3 mL/sec, with a total volume of 75–90 mL. The section thickness for all single spiral CT images was set at 10 mm. For multidetector CT, contiguous axial images and multiplanar reconstructions (MPR) were routinely performed, with a section thickness of 5 mm and a reconstruction interval of 1.25 mm.

To ensure accurate interpretation of the CT findings, a consensus review was conducted by two experienced radiologists (M.H with 8 years of experience in diagnostic imaging, and S.M with 12 years of experience in diagnostic imaging). They were aware that the study population consisted of lymphoma patients; however, they were blinded to the specific pathological type, tumor stage, and survival outcomes. The radiologists assessed various qualitative CT parameters, including tumor location, tumor size, presence of intratumoral necrosis, and lymph node enlargements. In cases where multiple tumors were present, the largest tumor was selected as the representative tumor for each patient. Tumor size was measured in the maximal dimension on the transverse plane. Areas showing reduced or absent contrast enhancement were considered indicative of intratumoral necrosis. Lymph node enlargements were defined as short axis measurements exceeding 1 cm, abnormal round morphology, or the presence of central necrosis.

The rigorous evaluation of the CT findings by experienced radiologists using standardized criteria ensures the reliability and consistency of the image analysis in this study. The blinded assessment prevents bias and enhances the objectivity of the results obtained from the CT scans.

Statistical Analysis

This section details the statistical methods used to assess the prognostic value of CT findings in predicting patient outcomes following chemotherapy for lymphoma. Patient outcomes were categorized into good or poor based on disease status after a 24-month follow-up (no recurrence/stable disease vs. progression during treatment or recurrence within 24 months). Recurrence was further classified as local, distant, or both. To evaluate the relationship between CT characteristics and prognosis, several radiologic variables were chosen based on their established role in lymphoma staging and their potential to influence treatment response and survival. These variables included involvement site (single vs. multiple), tumor size (greater than or equal to 3.0 cm vs. less than 3.0 cm), presence of intratumoral necrosis, lymph node involvement (site and appearance), and involvement of extranodal and extra-intestinal sites. The Chi-square (χ^2) test was used to compare the frequency of these findings between the good and poor outcome groups. A statistically significant difference (p-value < 0.05) would indicate a potential association between the variable and patient outcome. Following the initial analysis, variables with a significant association with outcome (p-value < 0.05) were incorporated into a multivariate logistic regression model. This model allows us to assess the independent contribution of each significant radiologic variable to predicting poor outcomes while accounting for the potential influence of other variables. By employing both univariate and multivariate analyses, this comprehensive statistical approach strengthens our understanding of the relationship between specific CT findings and prognosis in childhood lymphoma.

Results

Patient Characteristics

Our study included 69 patients diagnosed with lymphoma, with a mean age of 7.8 years (range: 4.8-14.2 years). The majority (52, 75.4%) were male with a mean age of 8.1 years (range: 6.7-9.1 years), while the remainder (17, 24.6%) were female with a mean age of 7.6 years (range: 4.8-13.5 years). According to the Ann Arbor Staging system, most patients (63, 91.3%) presented with advanced-stage lymphoma. All patients received cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)-based chemotherapy as part of their treatment regimen (Table 1). The follow-up period ranged from 12 to 36 months, with a mean of 26 months. Treatment outcomes were categorized as follows:

- **Good Outcome (n=63, 91.3%):** No evidence of relapse and stable disease after at least 24 months of therapy.
- **Poor Outcome (n=6, 8.7%):** Progression of lesions during treatment (n=5) or relapse within 24 months after therapy (n=1).

Table 1. Clinical characteristics of included patient sample.

Characteristics	Number of cases	Percentage (%)
Gender		
Male	52	75.3
Female	17	24.6
Age (years)	8.1 (6.7-9.1)	
Ann Arbor Stage		
1-2	6	8.6
3-4	63	91.3
4. Clinical Outcome		
Progression or relapse within 24 months	6	8.6
No evidence of relapse within 24 months	63	91.3

CT Characteristics

Table 2 summarizes the distribution of CT findings in our patient cohort.

- **Site Involvement:** Multiple site involvement (neck, chest, abdomen) was observed in 45 patients (65.2%), while 24 patients (34.8%) had single-site involvement.
- **Tumor Size:** Most patients (63, 91.3%) had tumors less than 3 cm in diameter. Only six cases had tumors larger than 3 cm.
- **Organomegaly:** Hepatosplenomegaly was present in 17 patients (24.6%), splenomegaly in two (2.9%), and hepatomegaly in 17 (24.6%). However, 33 patients (47.8%) did not exhibit organomegaly.
- **Nodal Involvement:** All patients (100%) had nodal involvement, with sites including the neck, chest, and abdomen (anterior/posterior triangles, supraclavicular, axilla, mediastinum, hila).
- **Extranodal Involvement:** Extranodal involvement was identified in 31 cases (44.1%), with sites including the nasal cavity, paranasal sinuses, lungs, liver, spleen, gastrointestinal tract, and musculoskeletal tissues.
- **Intratumoral Necrosis:** Necrosis was present in 13 cases (18.8%).

Table 2. CT findings of included patients.

Characteristics	Number of cases	Percentage (%)
1. Involvement site		
Single	24	34.7
Multiple	45	65.2
2.Tumor size		
<3cm	63	91.3
>3cm	6	8.6
3.Lymph node involvement		
Discrete	58	84.0
Confluent	2	2.8
Both	9	13.0
4.Visceromegaly		
Hepatosplenomegaly	17	24.6
Splenomegaly	2	2.9
Hepatomegaly	17	24.6

Absent	33	47.8
5.Intratumoral necrosis		
Present	13	18.8
Absent	56	81.1
6.Extranodal involvement		
Present	31	44.9
Absent	38	55.0
7.Extraintestinal findings		
Present	9	13.0
Absent	60	86.9

Analysis of Clinical Outcomes

Univariate analysis using the Chi-square test identified statistically significant associations between certain CT features and clinical outcomes (Table 3). These features included:

- **Multiple Site Involvement:** Patients with involvement of multiple sites were more likely to experience poor outcomes ($p < 0.05$).
- **Tumor Size:** Larger tumors (>3 cm) were associated with a higher risk of poor outcomes ($p < 0.05$).
- **Nodal Appearance:** Discrete nodal involvement on CT scans was linked to worse prognosis ($p < 0.05$).

These findings suggest that multiple site involvement, larger tumor size, and discrete nodal characteristics on CT may be potential prognostic indicators for lymphoma patients. Further investigation using multivariate models is warranted to assess the independent predictive value of these features while accounting for other factors.

Table 3. Summary of univariate analysis.

	Regression	Stable	Progression	Relapse	Resolution	p-value
Patient n (%)	53 (76.8)	8 (11.6)	5 (7.2)	1 (1.4)	2 (2.9)	
Age (years)	7.41 ± 3.68	7.87 ± 3.18	10.2 ± 3.83	9	5.5 ± 0.70	0.719
Male: Female	2.53	All male	1.5	All male	All male	0.329
Multiple involvement site, n (%)	31 (58.5)	8 (100)	5 (100)	1 (100)	2 (100)	0.033
Tumor size, n (%) <3 cm >3 cm	51 (96.2) 3 (5.7)	7 (87.5) 1 (12.5)	1 (20) 4 (80)	1 (100) 0	1 (50) 1 (50)	0.036
Nodal appearance, n (%) Discrete Confluent Both	44 (83) 1 (1.9) 8 (15.1)	7 (87.5) 0 1 (12.5)	5 (100) 0 0	1 (100) 0 0	1 (50) 1 (50) 0	0.024
Extra nodal involvement, n (%)	26 (49.1)	1 (12.5)	3 (60)	0	1 (50)	0.202
Intratumoral necrosis, n (%)	10 (18.9)	3 (37.5)	5 (100)	0	0	0.01
Tumor type, n (%) Hodgkin's lymphoma Non-Hodgkin's lymphoma	30 (56.6) 23 (43.4)	7 (87.5) 1 (12.5)	2 (40) 3 (60)	0 1 (100)	1 (100) 0	0.096
Advanced disease, n (%).	48 (90.6)	7 (87.5)	5 (100)	1 (100)	2 (100)	0.061

Detailed Outcomes Analysis by Category

We further analyzed the data by categorizing patients based on treatment outcome (regression, stable disease, progression, relapse, resolution).

- **Regression:** The majority of patients (76.8%) demonstrated regression of lymphoma. Analysis of CT characteristics within this group revealed:
- Multiple site involvement: 58.5%
- Tumor size < 3 cm: Majority
- Discrete nodal appearance: Majority

Stable Disease: Eleven patients (11.6%) exhibited stable disease. Here, the findings were:

- Multiple site involvement: 100% ($p = 0.033$)
- Tumor size > 3 cm: Majority ($p = 0.036$)
- Discrete nodal appearance: Majority ($p = 0.024$)

Progression/Relapse: A small number of patients experienced progression (7.2%) or relapse (1.4%). The distribution of CT features did not show significant trends within these categories.

Resolution: Two patients (2.9%) achieved complete resolution.

Discussion

Lymphoma represents a significant global health burden, accounting for a substantial portion of childhood malignancies (16, 17). This study aimed to investigate the potential role of computed tomography (CT) in predicting prognosis and outcomes for pediatric lymphoma patients. By analyzing various CT characteristics and their association with clinical outcomes, we sought to gain insights into the utility of CT for assessing disease progression and treatment response.

Treatment Response and Heterogeneity

Our findings revealed a positive treatment response, with the majority of patients (76.8%) experiencing lymphoma regression following chemotherapy. This aligns with established knowledge regarding the effectiveness of chemotherapy in reducing lymphoma tumor burden (18). Our study further emphasizes the importance of chemotherapy as a cornerstone treatment for pediatric lymphoma, corroborating its efficacy demonstrated in prior research (19, 20).

However, a subset of patients exhibited stable disease (11.6%), progression (7.2%), relapse (1.4%), or resolution (2.9%). These observations highlight the heterogeneity of lymphoma and the variable treatment responses observed in clinical practice. Identifying factors associated with poor clinical outcomes remains crucial for refining treatment strategies and optimizing patient management (21).

CT Characteristics and Prognostic Value

Our study identified several CT characteristics with significant associations to clinical outcomes. Multiple site involvement, tumor size, and discrete nodal appearance emerged as factors linked to poorer prognosis. Patients with involvement of multiple sites displayed a higher likelihood of unfavorable outcomes. Similarly, larger tumor size was associated with a greater risk of poor outcomes. Discrete nodal appearance on CT scans, potentially indicative of a more aggressive disease process, was another factor associated with a worse prognosis.

These findings align with existing literature that emphasizes the role of CT imaging in lymphoma prognosis and outcome prediction. The Lugano Classification, a pivotal contribution to the field, established recommendations for initial lymphoma evaluation, staging, and response assessment (23). This influential work underscores the importance of CT imaging in accurate lymphoma staging and treatment response evaluation. By providing standardized guidelines, the Lugano Classification facilitates consistent interpretation and reporting of CT findings, recognizing CT as a vital tool for assessing disease extent, nodal involvement, and extranodal disease.

Imaging in Lymphoma Management: A Broader Perspective

The study by Cao et al. (2022) further emphasizes the consensus within the International Conference on Malignant Lymphomas Imaging Working Group regarding the significance of imaging techniques like CT for lymphoma staging and treatment response assessment (25). This international effort highlights the need for standardized imaging protocols and interpretation criteria to ensure reliable and reproducible results, ultimately serving as a guide for clinicians and radiologists to optimize CT use in lymphoma management.

While CT offers valuable information for prognosis and treatment planning, advancements in imaging modalities like 18F-FDG PET/CT have revolutionized lymphoma management (24). The expert consensus from the LYSA/LYSARC/ILSG International Expert Meeting, as outlined by Xie et al. (2019), underscores the value of PET/CT in providing metabolic information that complements anatomical details provided by CT. PET/CT helps evaluate the metabolic activity of lymphoma lesions, offering insights into treatment response and guiding crucial treatment decisions, particularly for DLBCL patients.

Limitations and Future Directions

This study has limitations inherent to its retrospective design, including potential selection bias and incomplete data collection. The relatively small sample size of 69 patients restricts the generalizability of findings and increases statistical variability. Additionally, conducting the study at a single center limits the external validity and generalizability of results. Our focus on CT imaging potentially overlooks contributions from other modalities like PET/CT. Furthermore, the lack of long-term follow-up and survival data limits our understanding of the prognostic value of CT over time. Finally, the study did not account for potential confounding factors that may influence treatment response and outcomes.

Future research should address these limitations by employing larger, multicenter, prospective studies to enhance generalizability and reduce selection bias. Additionally, incorporating PET/CT data alongside CT findings could provide a more comprehensive picture of lymphoma characteristics and improve prognostic accuracy. Long-term follow-up data on patient survival would further strengthen the understanding of the prognostic value of CT in pediatric lymphoma. Moreover, future studies should account for potential confounding factors such as patient demographics, treatment variations, and underlying genetic mutations to provide a more holistic view of factors influencing treatment response and prognosis..

Conclusion

This study explored CT features for prognosis in pediatric lymphoma treated with chemotherapy. While most patients responded well, CT characteristics like multiple site involvement, larger tumor size, and discrete nodal features linked to poorer outcomes. These findings suggest CT's potential role in prognosis, but future research with larger, prospective designs and long-term follow-up is needed for further validation.

Conflict of interests

The authors declare that they have no competing interests.

IRB approval

The study was approved for publication by the National Institute of Child Health’s Institutional Review Board. The IRB number is NICH/23/0110.

Ethics Statement

The manuscript complies with the ethical recommendations of the Declaration of Helsinki of the World Medical Association (WMA).

Authors contributions

MH, **FS**, **SK**, **LAA**, **SM**, and **NF** contributed to the conception and design of the manuscript. **MH**, **LAA**, **SK**, **SM**, and **NF** supervised the project. **MH**, **MKK**, **NF**, **SM**, and **LAA** provided the materials and contributed to data collection and processing. **FS**, **MKK**, **KK**, and **SK** contributed to the interpretation and analysis of the project. **FS**, **MKK**, **KK**, **SM**, and **SK** contributed to the literature review and writing of the manuscript respectively. **MH**, **FS**, **MKK**, **KK**, and **LAA** critically revised the manuscript.

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