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The Predictive Value of Abdominal Ultrasonography Compared to CT Scan for the Evaluation of Pediatric Lymphoma

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Abstract

Background: Given the children's susceptibility to the harmful radiation of computerized tomography (CT) scans, ultrasonography can be a good alternative in staging pediatric lymphoma. The present study aimed to assess the predictive value of abdominal ultrasonography compared to CT scan in children with lymphoma.

Materials and Methods: Fifty-two children with confirmed lymphoma were included in the present cross-sectional analytical study and underwent CT scan. The staging was performed based on the involvement pattern, lymph nodes, liver involvement, spleen involvement, and lymph node sizes. Then, the patients underwent ultrasonography followed by re-staging. The data were analyzed by SPSS 26. p-value less than 0.05 was considered statistically significant.

Results: The included patients consisted of 32 (61.5%) boys and 20 (38.5%) girls with the median age of 6.0 years (4.3-8.0). The number of the patients with positive paraaortic lymphadenopathy, iliac chain lymphadenopathy, mesenteric lymphadenopathy, increased liver size, changed liver parenchyma, increased spleen size, changed spleen parenchyma, increased kidney size, and changed kidney parenchyma evaluated by sonography and CT scan were 24 (46.2%) and 26 (50.0%), 3 (5.8%) and 3 (5.8%), 34 (65.4%) and 34 (65.4%), 49 (94.2%) and 48 (92.3%), 23 (44.2%) and 23 (44.2%), 45 (68.2%) and 21 (31.8%), 48 (92.3%) and 48 (92.3%), 50 (96.2%) and 50 (96.2%), and 49 (94.2%) and 48 (92.3%), respectively ($p \leq 0.001$). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of abdominal ultrasonography staging compared to CT scan were 100%, more than 90%, more than 75%, and 100%, respectively.

Conclusion: Due to the sufficient sensitivity and specificity, ultrasonography has the potential to be applied instead of CT scan for the abdominal staging of pediatric lymphoma.

Keywords: Computed Tomography, Lymphoma, Lymphadenopathy, Ultrasonography

Introduction

Lymphomas are the third most common malignancies in children and are divided into two general groups, Hodgkin and non-Hodgkin lymphomas. Hodgkin lymphoma alone accounts for 6-7% of childhood malignancies which originate from lymph nodes (1). These lymph nodes can be felt as a touchable mass in the abdomen, mediastinum, and neck. There are different types of lymphomas, but the four most common forms are Burkitt lymphoma, lymphoblastic lymphoma, anaplastic large cell lymphoma, and diffuse large B-cell lymphoma (2). This disease often occurs in males in the form of immunodeficiency and in conditions such as Ataxia-telangiectasia (AT). The common symptoms of Hodgkin lymphoma include high fever, weight loss, and night sweats. Lymphomas are diagnosed based on the location of a mass and the biopsy of the tissue involved. After diagnosis, staging is the next step for this type of malignancy

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based on which the treatment program and all the subsequent actions are planned (3). Epidemiological evaluations indicate that the global prevalence of lymphomas is increasing; particularly, the prevalence of Hodgkin lymphomas is very high in developing countries. The initial diagnosis of lymphomas is based on a thorough clinical examination, laboratory findings, and radiological findings (4). In the approach to lymphoma, the first step is a definitive diagnosis based on a biopsy, then evaluating the mass in terms of location, size and number, and finally evaluating the involvement of other organs such as the liver, spleen, and the site around the mesenteric vessels and abdominal aorta. Accordingly, radiology tools such as Computed Tomography (CT) scan and positron emission tomography (PET) scan play significant roles (5). Great imaging advances have been made in the past two decades. Nowadays, radiology is essential not only for diagnosis but also for staging and planning the treatment of lymphomas (6). After lymphoma is diagnosed, it is imperative to evaluate its involvement patterns. CT scan is classically used to examine the involvement patterns of lymph nodes and abdominal organs. It provides good cross-sectional images of the involvement of surrounding organs and solid organs. However, CT scans are not available in all regions, they are expensive, and it often takes a long time waiting for their implementation. CT scan is harmful, especially in children, and can lead to secondary complications (7). Most abdominal lymph nodes are easily accessible using ultrasonography; it can easily show the involvement of lymph nodes and help to stage the lymphoma. Ultrasonography is helpful in differentiating metastasis and lymphomatous mass by revealing the shape, size, echogenicity, internal tissue of lymph nodes, calcification, and vascular flow of lymph nodes using Doppler (4). Therefore, as an alternative to imaging tools such as CT scans, ultrasonography can be of benefit, especially in pediatric lymphoma. Unlike CT scans, ultrasonography is accessible and inexpensive, and its waves have no adverse effects on tissue. It is a direct, non-invasive and easy method to evaluate lymphadenopathies (8). The incidence of lymphoma has increased among children in recent years. Due to children's susceptibility to harmful CT scans, ultrasonography can be a good alternative in staging pediatric lymphoma. There have been few studies in this field, and the existing reports in the literature often belong to the far past. However, the issue is comprehensively examined in the present study. Conducted with the aim of assessing the predictive value of abdominal ultrasonography in children with lymphoma, the study provides a new approach to evaluating pediatric lymphoma.

Materials and Methods

The present research is a cross-sectional analytical study. The patients were selected among the individuals who had referred to Tabriz Children Hospital within 18 months from June 2017 to December 2018. The inclusion criteria were age less than 15 years, lymphoma diagnosis (by biopsy) in the last three months, and consent to participate in the study. The exclusion criteria were considered as unwillingness to participate in the study, any comorbidity other than lymphoma, and receiving chemotherapy. Fifty-two children suffering from lymphoma were included in the study after informed consent was received from their parents. They were referred for CT scan staging by a LightSpeed 16 CT scanner (GE Medical Systems, Milwaukee, Wisconsin, USA), and the data were recorded. Then, the children underwent abdominal ultrasonography staging by a WS80 Ultrasound System (Samsung Corp., Seoul, South Korea). This was done to check them for echogenicity,

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calcification and tissue homogeneity as well as the involvement and size of the lymph nodes, liver, spleen, and kidneys with no knowledge of the results reported after the CT scan. The involvements of abdominal viscera and paraaortic, mesenteric and iliac lymph nodes with a short-axis diameter (SAD) of more than 10 mm were considered as a positive ultrasonography result (9). Eventually, the ultrasonography staging data were compared with the CT scan results.

Statistical analysis

The data were analyzed by SPSS 26, and their normality was assessed by the Kolmogorov-Smirnov test. The qualitative data were described with frequencies reported as percentages, and the median (percentiles of 25 and 75) was used for abnormal quantitative data. Chi-square tests were also performed to analyze the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ultrasonography compared to the CT scan results.

Fisher's exact tests would serve the purpose if there were no basis for using Chi-square tests. Moreover, the Kappa test was used to assess the agreement between the ultrasonography and CT scan results. A p-value less than 0.05 was considered statistically significant.

Ethical consideration

The ethics committee of Tabriz University of Medical Sciences approved the study (IR.TBZMED.REC.1398.492).

Results

The patients included in this study were 32 (61.5%) boys and 20 (38.5%) girls with a median age of 6.0 (4.3-8.0) (Table I). As shown in Table II, the number of the patients with positive paraaortic lymphadenopathy, iliac chain lymphadenopathy, mesenteric lymphadenopathy, increased liver size, changed liver parenchyma, increased spleen size, changed spleen parenchyma, increased kidney size, and changed kidney parenchyma was determined by sonography and CT scans. These disorders were found in 24 (46.2%) and 26 (50.0%), 3 (5.8%) and 3 (5.8%), 34 (65.4%) and 34 (65.4%), 49 (94.2%) and 48 (92.3%), 23 (44.2%) and 23 (44.2%), 45 (68.2%) and 21 (31.8%), 48 (92.3%) and 48 (92.3%), 50 (96.2%) and 50 (96.2%), and 49 (94.2%) and 48 (92.3%), respectively. There was a statistically significant relationship between the results of ultrasonography and CT scan in children with lymphomas ($p \leq 0.001$). The diagnostic values of ultrasound to determine the status of lymphadenopathy, liver, spleen and kidney involvement are depicted in Table III. As it can be seen in the table, the sensitivity, specificity, PPV, NPV and accuracy of iliac chain lymphadenopathy, mesenteric lymphadenopathy, liver size, spleen size, spleen parenchyma, and kidney size were 100%. The sensitivity, specificity, PPV, NPV, and accuracy of the paraaortic lymphadenopathy variables evaluated by ultrasonography were 100%, 92.86%, 92.31%, 100%, and 96.15%, respectively, as compared to the CT scan findings. The liver parenchyma variable evaluated by ultrasonography had 100% sensitivity, 97.96% specificity, 75% PPV, 100% NPV, and 98.08% accuracy compared to the CT scan findings. In addition, regarding kidney parenchyma, the sensitivity, specificity, PPV, NPV, and accuracy of ultrasonography were 100%, 97.96%, 75%, 100%, and 98.08%, respectively, as compared to the CT scan findings.

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Table I: The demographic characteristics of the subjects

characteristics	----
Age (year)	**6.0 (4.3-8.0)**
Gender (no. and %)	
Male	**32 (61.5%)**
Female	**20 (38.5%)**

Table II: Relationship of the abdominal ultrasound findings with the CT scan results in subjects with lymphoma

Characteristics	CT Scan	Sonography	P-value	P-value
Paraaortic lymphadenopathy, n (%)			< 0.001*	**< 0.001*** **
Positive	26 (50.0%)	24 (46.2%)		
Negative	26 (50.0%)	28 (53.8%)		
Iliac chain lymphadenopathy, n (%)			< 0.001**	**< 0.001*** **
Positive	3 (5.8%)	3 (5.8%)		
Negative	49 (94.2%)	49 (94.2%)		
Mesenteric lymphadenopathy, n (%)			< 0.001*	**< 0.001*** **
Positive	34 (65.4%)	34 (65.4%)		
Negative	18 (34.6%)	18 (34.6%)		
Assessment of liver size, n (%)			< 0.001**	**< 0.001*** **
Normal size	4 (7.7%)	3 (5.8%)		
Increased size	48 (92.3%)	49 (94.2%)		
Assessment of liver parenchyma, n (%)			< 0.001**	**< 0.001*** **
Normal	29 (55.8%)	29 (55.8%)		
Changed	23 (44.2%)	23 (44.2%)		
Assessment of spleen size, n (%)			< 0.001*	**< 0.001*** **
Normal size	7 (31.8%)	15 (68.2%)		
Increased size	21 (31.8%)	45 (68.2%)		
Assessment of spleen parenchyma, n (%)			< 0.001**	**< 0.001*** **
Normal	3 (5.8%)	3 (5.8%)		
Changed	48 (92.3%)	48 (92.3%)		
Assessment of kidney size, n (%)			0.001**	**0.001*** **
Normal size	2 (3.8%)	2 (3.8%)		
Increased size	50 (96.2%)	50 (96.2%)		
Assessment of kidney parenchyma, n (%)			< 0.001**	**< 0.001*** **
Normal	4 (7.7%)	3 (5.8%)		
Changed	48 (92.3%)	49 (94.2%)		

* P-value by chi-square test
** P-value by Fisher's exact test
*** P-value by Kappa agreement test

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Table III: Evaluation of the diagnostic value of ultrasound to determine the status of lymphadenopathy, liver, spleen and kidney involvement

Characteristics	Sensitivity	Specificity	PPV	NPV	Accuracy
Paraaortic lymphadenopathy	100.00%	92.86%	92.31%	100.00%	**96.15%**
Iliac chain lymphadenopathy	100.00%	100.00%	100.00%	100.00%	**100.00%**
Mesenteric lymphadenopathy	100.00%	100.00%	100.00%	100.00%	**100.00%**
Liver size	100.00%	100.00%	100.00%	100.00%	**100.00%**
Liver parenchyma	100.00%	97.96%	75.00%	100.00%	**98.08%**
Spleen size	100.00%	100.00%	100.00%	100.00%	**100.00%**
Spleen parenchyma	100.00%	100.00%	100.00%	100.00%	**100.00%**
Kidney size	100.00%	100.00%	100.00%	100.00%	**100.00%**
Kidney parenchyma	100.00%	97.96%	75.00%	100.00%	**98.08%**

NPV: negative predictive value, PPV: positive predictive value

Discussion

In the present study, the diagnostic value of abdominal ultrasonography was compared with that of CT scan in children with lymphoma. In this regard, the sensitivity of ultrasonography was 100% for lymphadenopathy and the evaluation of liver, spleen, and kidney masses. Its specificity and accuracy were > 90% and > 95%, respectively.

The incidence of various cancers has increased significantly in different countries over time. The use of CT scans has also led to the significant increased diagnosis of cancers over time (10), but it causes high doses of ionizing radiation in the body. As estimated, 2% of future cancers will be due to the increased use of CT scans (11, 12). Therefore, performing an abdominal CT scan at a high radiation dose increases the risk of cancer (13). Children are more susceptible to radiation than adults. Their young age may predispose them to the development of cancer in the coming years, considering that the prevalence of lymphoma is higher at the age of 10 to 19. The susceptibility of children to radiation risk is up to 10 times higher than that of adults (14). According to the annual rate of CT scans in the United States, it is estimated that a significant number of children will die from CT scan neoplasms (15). In a cross-sectional study (16), there was a direct relationship between CT scan and the risk of leukemia and brain tumors. Another study (17) indicated that increasing CT scans in children has enhanced the incidence of leukemia, myelodysplastic syndromes, and soft tissue neoplasms.

The potential risk of over-diagnosis through ionizing radiation modalities has induced the International Image Gently and Euro-safe campaigns. In a study (18), it was indicated that some methods such as ultrasonography can help to diagnose appendicitis and reduce the use of CT scans. In another study (19), it was noted that ultrasonography could be used in suspected cases of nephrolithiasis instead of a CT scan. According to some recent studies (20-22), the results of lymphomas recurrences are generally obtained through clinical examination and laboratory findings. Therefore, patient survival is not affected by the type of diagnostic modality. According to a study by the American Academy of Pediatrics in 2014 (23), CT scans were excessively used in some diagnostic cases, which was advisable to be limited. Based on the available evidence, lymphoma often emerges in the mediastinum or as superficial lymphadenopathy (abdominal/pelvic). The present study has utilized this evidence to evaluate the possibility of reducing the number of CT scans for staging lymphomas in children.

In this study, the sensitivity and specificity as well as the positive and negative predictive values of abdominal ultrasonography were greater than 75% for the evaluation of lymphoma in children. Consistent with our study, Adedayo et al. (24) reported the diagnostic value of ultrasonography with the specificity and negative predictive values of 98.4 and 97.7%, respectively. On the other hand, the sensitivity and positive predictive values were 57.1 and 66.7, respectively; they were lower than the values obtained in the present study. Ultrasonography is a modality that somehow depends on the operator. This causes the difference of results in different studies to some extent. Given the positive predictive value of ultrasonography, which was greater than 75% in the present study, CT scans can be avoided for staging and diagnosis in three quarters of pediatric patients. It is a valuable step to reduce ionization radiation in patients.

The evaluation of abdominal masses in children is problematic. In this regard, specialists have always favored a modality with optimal diagnostic accuracy in a short time. According to recent studies, the accuracy of ultrasonography is generally high in diagnosing pathological abdominal masses. As an instance, in a study in Ethiopia (25), the total accuracy of ultrasonography was found to be 88.9%. The diagnostic accuracy of ultrasonography for the detection of hepatic and splenic lymphoma in dogs was examined by Crabtree et al. (26). As they calculated, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the ultrasound examination of hepatic and splenic abnormalities for the diagnosis of lymphoma were 72.7%, 80.6%, 77.4%, 76.3%, and 76.8% for the liver, respectively, and 100%, 23.3%, 64.6%, 100%, and 68.1% for the spleen, respectively. Rahmani et al. (27) performed a systematic review of ultrasonography in soft-tissue lipomas to better determine the true diagnostic value of this test. The sensitivity and specificity of ultrasonography in their study were 86.87% and 95.95%, respectively. Hashemi et al. (28) assessed the sensitivity and specificity of ultrasonography, compared to CT scan, to evaluate anterior mediastinum lymphadenopathies. They found that the sensitivity and specificity of ultrasonography were 84.6%, and 90.6%, and it could be used instead of CT scan. These values are almost consistent with the percentage obtained in the present study (i.e., 100%).

This study revealed the diagnostic value of ultrasonography in the evaluation of lymphoma. It is in agreement with the studies that have found ultrasonography very suitable for examining the spleen, liver, and kidneys in lymphoma patients. According to these studies, the diagnostic value of ultrasonography is equivalent to that of CT scan. There are several reasons for the inconsistency of some results, including different target populations, research environments, sample sizes, and inclusion and exclusion criteria such as the disease severity and underlying factors.

Conclusion

There are very few studies assessing the possibility of replacing CT scan with ultrasonography in the lymphoma staging of children. The present study comprehensively examined this issue and provided a new approach to evaluating pediatric lymphoma. It is concluded that using abdominal ultrasonography to examine pediatric lymphoma has high sensitivity, specificity, and positive predictive value. Therefore, frequent application of CT scans can be avoided, especially in high-risk patients with cancers. It can be replaced with ultrasonography to reduce the level of ionization radiation, complications, allergic reactions, and costs. Sonographic studies are commonly based on gray-scale imaging, but sonography results, as those in the present study, should be confirmed

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with new modalities such as Doppler ultrasound, contrast enhancement, and elastography. Also, further studies with different target populations and larger sample sizes are necessary to confirm the results gained here.

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Conflict of interest

The authors declare no conflict of interest.

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