

Original Article, PET/CT.

Role of FDG PET/CT in Diagnosing and Assessment of Therapy Response in Pediatric and Adult patients with Renal Lymphoma.

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ABSTRACT:

Background: The genitourinary system is not commonly affected by extra-nodal spread of lymphoma; primary renal lymphoma is very rare. The aim of this study is to evaluate the role of FDG PET/CT in assessment of the differences in distribution, pattern, therapy response and outcomes of renal lymphoma between the pediatric and adult age groups.

Materials & Methods: 62 patients (32 Adult and 30 Pediatric) with pathologically proven lymphoma with renal involvement in whom FDG PET/CT scan were retrospectively assessed with analysis of their clinical/radiological data, therapy response, prognosis and survivals. **Results:** Incidence of primary renal lymphoma in adult and pediatric age groups represent 15.6% and 3.3 % respectively. Focal pattern was the most common on both groups (93.8% and 76.7%

respectively). Bilateral renal involvement and the diffuse pattern of infiltration were more prevalent (78.6% & 23.6% respectively) among the pediatric group compared to (41.9 & 6.3%) in adult patients. Pediatric groups show better OS and EFS as well as good prognosis. Statistical significance was found between the two groups regarding the SUVmax of the renal lesion, Nodal SUVmax, EFS and OS, with P value 0.004, 0.024, 0.019 & 0.004 respectively.

Conclusions: Primary renal lymphoma incidence is less than the secondary type and more relevant in adult group. Pediatric group shows better OS and EFS as well as good prognosis.

Keywords: FDG PET/CT. Renal. Lymphoma. Survival.

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INTRODUCION:

The genitourinary system is not commonly affected by extra-nodal spread of lymphoma, of which the kidneys are the most commonly involved organ [1]. Primary renal lymphoma is rare, accounting for less than 1% of cases of extra-nodal lymphoma, and is defined as exclusive involvement of the kidneys without systemic disease [2]. Secondary lymphoma is much more common and frequently found at autopsy, in up to 38% of cases, from the direct spread of retroperitoneal adenopathy or hematogenous spread from systemic disease [3, 4]. Despite the relatively high prevalence of renal lymphoma, imaging studies detect renal abnormalities in only 3–8% of patients undergoing routine staging of disease. [5, 6]

Renal lymphoma has been described in both Hodgkin and non-Hodgkin lymphoma, with non-Hodgkin lymphoma, being far more common [7, 8]. In most cases, renal lymphoma is clinically silent, and radiologic detection seldom influences staging and treatment [4]. The imaging findings can be nonspecific, and there are overlapping features with other benign and malignant conditions which can create a diagnostic dilemma.

The aim of this study is to evaluate the role of PET/CT in assessment of the differences in distribution, pattern, therapy response and outcomes of renal lymphoma between the pediatric and adult age groups.

PATIENTS AND METHODS:

Study Design and Population

This exploratory retrospective study includes all patients with pathologically confirmed Hodgkin lymphoma (HL) or non-Hodgkin lymphoma (NHL) who were referred to the Nuclear Medicine Unit at the National Cancer Institute (NCI) for initial staging and post-therapy assessment using 18F-FDG PET/CT between January 2015 and June

2024. A total of 62 patients were included—32 adults and 30 pediatric cases. Relevant clinical data, including demographic information (age, sex), pathological findings, imaging results, treatment response, and survival outcomes, were collected from patient medical records.

Study Setting Inclusion Criteria: Patients with histologically confirmed malignant lymphoma.

Exclusion Criteria: Patients diagnosed with dual primary malignancies and pregnant females.

The study was approved by the NCI Institutional Review Board (IRB).

PET/CT Imaging Protocol:

Patient Preparation All patients fasted for 4–6 hours prior to imaging and avoided intense physical activity for at least 24 hours beforehand. Blood glucose levels were checked prior to 18F-FDG administration and required to be ≤ 180 mg/dL. Procedure details were explained to all patients before the scan. Patients received an intravenous injection of approximately 0.14 mCi/kg of 18F-FDG. Whole-body imaging from the skull to mid-thigh was performed about 60 minutes post-injection (range: 45–110 minutes).

Image Acquisition Parameters PET/CT scans were acquired using a Discovery PET/CT scanner (GE Medical Systems, USA). Patients were positioned supine with arms raised. CT parameters included 140 kV, 80 mA, pitch 1.375, and a slice thickness of 3.75 mm. PET data were acquired in 6–8 bed

positions at 2–3 minutes per position. Images were reconstructed using iterative reconstruction (3 iterations, 21 or 22 subsets) with time-of-flight and CT-based attenuation correction.

Image Analysis PET/CT images were reviewed on a dedicated workstation allowing evaluation of PET, CT, and fused PET/CT images. All scans were interpreted by 2 nuclear medicine experts in a blind manner of interpretation. Primary renal lymphoma is identified as a pathologically proven renal lymphomatous lesion with no other site of disease involvement, while the secondary type is referred to lymphomatous lesions include renal and extra-renal sites.

Qualitative Analysis: Visual assessment focused on detecting FDG uptake exceeding hepatic background activity in renal parenchyma (suggestive of lymphoma involvement) with exclusion of any focal activity related to the renal pelvis (physiological) as well as other nodal/ extra-nodal regions. **Semi-Quantitative Analysis:** Spherical volumes of interest (VOIs) were manually placed over suspicious regions, carefully avoiding physiological uptake. The maximum standardized uptake value (SUV_{max}) was recorded for each lesion.

Follow-up and Outcome Assessment:

Follow-up data, including clinical, laboratory, and imaging findings, were obtained from patient records to assess therapeutic response through the latest follow-up visit. Overall survival (OS) and disease-free survival (DFS) were evaluated specifically for patients with renal lymphoma.

Statistical analysis: Data were coded and analyzed using the Statistical Package for the Social Sciences (SPSS), version 28 (IBM Corp., Armonk, NY, USA). Quantitative variables were summarized using the mean, standard deviation, median, and range (minimum and maximum), while categorical variables were described using frequencies

and percentages. Comparisons of quantitative data were performed using the non-parametric Mann-Whitney U test [9]. For categorical variables, the Chi-square (χ^2) test was applied, and when expected frequencies were below 5, the Exact test was used as an alternative [10]. Survival analysis was conducted using the Kaplan-Meier method, with comparisons made using the log-rank test [11]. Overall survival (OS) was defined as the time from diagnosis to death or last follow-up. Hazard ratios with 95% confidence intervals were calculated for significant variables identified in the final step of Cox regression analysis. A p-value of less than 0.05 was considered statistically significant.

RESULTS:

Among the enrolled 62 patients presented with renal lymphoma. Thirty of them are below 18-year-old (pediatric group) and 32 are adults. Primary renal lymphoma are presented in 5 patients of the adult group and only on one child with percent of 15.6% and 3.3 % respectively. For the adult age group, Male to female ratio is ~3:1. The mean age 49.5 years (ranged from 21 to 75 years). Large B cell lymphoma is the most common

pathology presented in ~47% of the adult patients, 78% of patients have nodal involvement and 68.6% presented with extra-nodal site other than the kidneys. Regarding the pediatric patients, the mean age 8.1 years (ranged from 1 to 18 years). Non-Hodgkin lymphoma (NHL) present in ~43.3% of the pediatric patients followed by HL in 9 patients (30%), 8 children have Burkett's lymphoma (26.7%). Twenty out of 30

pediatric patients associated with nodal infiltrations (66.7%) while 73.3 % have extra-nodal site involvement. Demographic, pathologic data and clinical characteristics are illustrated in **Table (1)**. **Table (2)** summarize the detailed description of the lymphomas renal involvement as seen on the PET/CT studies. Bilateral renal involvement is more prevalent among the pediatric group presented in 22 patients (78.6%) compared to 30 (41.9%) adult patients. The percent of diffuse pattern of infiltration is also higher in

pediatric group (23.3%) compared to only 6.3% of the adults. Clearly the focal pattern is the most common on both groups representing 93.8% and 76.7% in adult and pediatric groups respectively.

Most of children experienced bilateral renal involvement (78.6 %) compared to 41.9 % in adult patients. There is no significant statistical difference in pattern between both groups, however, only laterality archived statistical difference ($P \sim 0.008$)

Table (1): Clinical characteristics in pediatric and adult patients with lymphomas renal involvement (n=62).

		Adult renal (n=32)		Pediatric renal (n=30)		P value
		Count	%	Count	%	
Sex	Male	20	62.5%	19	63.3%	0.946
	Female	12	37.5%	11	36.7%	
Pathology	NHL	12	37.5%	13	43.3%	< 0.001
	HL	2	6.3%	9	30.0%	
	T cell	1	3.1%	0	0.0%	
	Mantle cell	1	3.1%	0	0.0%	
	LBCL	15	46.9%	0	0.0%	
	Burkett's	1	3.1%	8	26.7%	
	Primary	5	15.6%	1	3.3%	
Type	Secondary	27	84.4%	29	96.7%	0.197
	P	25	78.1%	20	66.7%	
Nodal	N	7	21.9%	10	33.3%	0.312
	Supra	6	24.0%	9	40.9%	
	infra	3	12.0%	3	13.6%	
Site	Supra & Infra	16	64.0%	10	45.5%	0.422
	P	22	68.8%	22	73.3%	
	N	10	31.3%	8	26.7%	
Extra-nodal	P	22	68.8%	22	73.3%	0.691
	N	10	31.3%	8	26.7%	

Table 2: Description of pattern of renal lymphoma involvement on both pediatric and adult groups (n=62).

		Adult renal (n=32)		Pediatric renal (n=30)		P value
		Count	%	Count	%	
Renal Diffuse or focal	Diffuse	2	6.3%	7	23.3%	0.077
	Focal	30	93.8%	23	76.7%	
Solitary or Multiple	Solitary	11	36.7%	4	17.4%	0.123
	Multiple	19	63.3%	19	82.6%	
Side	Right	10	32.3%	5	17.9%	0.008
	Left	8	25.8%	1	3.6%	
	Bilateral	13	41.9%	22	78.6%	

Regarding the focal renal lesions, the mean longest respectively. Regarding SUVmax median was 12.8 dimension measured on CT was comparable (rang 7.6-14.68) for adult group and 8.9 (range 4.86- between both groups 4 cm in adult and 3.5 in 9.43) in pediatric patients. pediatrics with a range of (1.6-8.3 cm) and (1-8 cm)

Therapy Response Assessment & Survival Analysis:

Regarding follow up of the 62 patients with repeated 112 studies, regarding the adult group 16 patients (50 %) show disease progression compared to ~30 % (9 patients) of the pediatric age group. 46.7% of pediatric patients shows complete disease regression

compared only to 18.8% (6 patients) in adult group. Only two pediatric patients died during the follow up period, while seven (21.9%) of the adult group. as illustrated in **Table (3).**

Table 3: Assessment of therapy response in both adult and pediatric age groups.

		Adult renal		Pediatric renal		P value
		Count	%	Count	%	
Follow up	N	10	31.3%	8	26.7%	0.060
	Progression	16	50.0%	9	30.0%	
	Regression	10	31.3%	7	23.3%	
Event free Status	CR	6	18.8%	14	46.7%	0.034
	progression	17	53.1%	8	26.7%	
	no progression	15	46.9%	22	73.3%	
Overall Status	death	7	21.9%	2	6.7%	0.149
	survived	25	78.1%	28	93.3%	

Survival analysis:

Overall survival (OS) was calculated from the first visit date to death or last examination in both adult and pediatric groups with a range of 4–96 months for adult group. Seven out of the 32 adult patients representing (~21.9 %) and only 2 child died all through the observation period. Regarding the event

free survival (EFS) ~73% of pediatric group does not developed adverse event during the course of the disease and the follow up period compared to ~47% of the adult group which achieved significant statistical difference with Pvalue~0.034. (Figure 2).

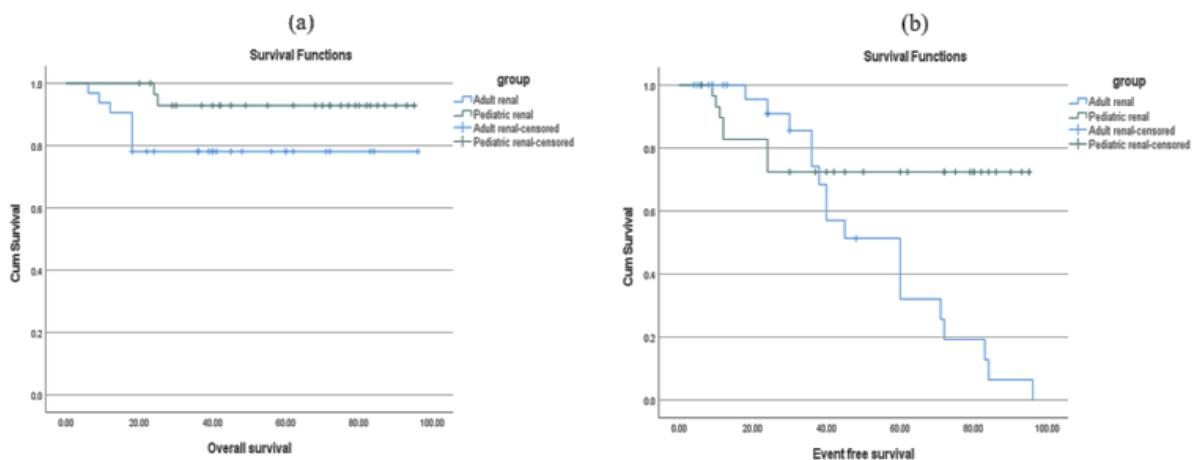


Figure (2) Kaplan-Meier estimate of overall survival (a) and event-free survival (b) in both adult and pediatric age groups.

Mann-Whitney test is used to compare between the adult and pediatric groups regarding the SUVmax of the renal lesion, Nodal SUVmax, EFS and OS, there was significant statistical

difference in these four aspects with P value 0.004, 0.024, 0.019 & 0.004 respectively. (Table 4)

Table 4: Comparison in event free survival and overall survival between pediatric and adult patients with lymphomas renal involvement (n=62).

	Adult renal					Pediatric renal					P value
	Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	
Age	49.25	12.74	49.50	21.00	75.00	8.20	4.41	8.00	1.00	18.00	<0.001
Size	4.05	1.55	3.80	1.60	8.30	3.65	1.55	3.50	1.00	8.00	0.288
SUVmax	14.68	7.60	12.85	4.90	37.00	9.43	4.86	8.90	2.70	22.00	0.004
nodal SUVMax	16.18	10.08	12.50	4.90	40.20	9.38	5.55	9.40	1.40	19.40	0.024
Event free survival	35.03	26.39	30.00	4.00	96.00	52.70	30.88	55.00	6.00	95.00	0.019
Overall survival	42.50	23.50	39.50	6.00	96.00	60.87	24.78	69.00	20.00	95.00	0.004

DISCUSSION:

Extra-nodal lymphoma spread to the genitourinary system is not common, of which the kidneys are the most commonly involved organ [1]. Primary renal lymphoma is rare, accounting for less than 1% of cases of extra-nodal lymphoma, and is defined as exclusive involvement of the kidneys without systemic disease [2]. Secondary lymphoma is much more common, via the direct spread of retroperitoneal adenopathy or hematogenous spread from systemic disease [3, 4]. Despite the relatively high prevalence of renal

lymphoma, imaging studies detect renal abnormalities in only 3–8% of patients undergoing routine staging of disease. [5, 6]. In most cases, renal lymphoma is clinically silent, and radiologic detection seldom influences staging and treatment [4]. The imaging findings can be nonspecific, and there are overlapping features with other benign and malignant conditions which can create a diagnostic dilemma. The aim of this study was to evaluate the role of PET/CT in assessment of the differences in distribution,

pattern, therapy response and outcomes of renal lymphoma between the pediatric and adult age groups. Few studies have been published on the use of PET/CT to evaluate renal involvement by lymphoma, yet, the comparison between the adult and pediatric age group in the distribution, pattern, therapy response and outcomes is not well recognized. In current study, primary renal lymphoma are presented in 5 patients of the adult group and only on one child with percent of 15.6% and 3.3 % respectively. In agreement with **Sharkawy et al.** study stated that primary renal lymphoma is rare and represent only 1% of all lymphomas. ⁽¹²⁾ Large B cell lymphoma was the most common pathology presented in ~47% of the adult patients, while in pediatric group NHL, HL & Burkett's lymphoma presented in ~43.3%, 30 % & 26.7% respectively. Associated nodal involvement was comparable between the two groups 78% of adult and 66.7% in pediatric patients. **Nicolau et al.** in their study illustrated that thirteen of the 14 lymphomas were B-cell lymphomas, and one was a Hodgkin lymphoma ⁽¹³⁾.

In agreement with our study, renal lymphoma may be unilateral or bilateral. It may present as a solitary mass or as multiple renal masses,

and it may develop as infiltrative renal disease or as direct invasion from contiguous retroperitoneal adenopathy ^(12, 14 & 15). Focal pattern was the most common on both groups representing 93.8% and 76.7% in adult and pediatric groups respectively. Bilateral renal involvement and the diffuse pattern of infiltration were more prevalent (78.6% & 23.6% respectively) among the pediatric group compared to (41.9 & 6.3%) in adult patients. Regarding the focal renal lesions, the mean longest dimension measured on CT was comparable between both groups 4 cm in adult and 3.5 in pediatrics with a range of (1.6-8.3 cm) and (1-8 cm) respectively. Regarding SUVmax median was 12.8 (rang 7.6-14.68) for adult group and 8.9 (range 4.86-9.43) in pediatric patients. **Nicolau et al.** stated that all 14 adult renal lymphomas patients enrolled in his study had a SUVmax median~ 10.99 ⁽¹³⁾. Follow up of the 62 patients with repeated 112 studies were evaluated, only two pediatric patients died during the follow up period, while seven (21.9%) of the adult group. 16 adult patients (50 %) show disease progression compared to ~30 % (9 patients) of the pediatric age group. 46.7% of pediatric patients shows complete disease regression compared only to 18.8% (6 patients) in adult group. Overall

survival (OS) was calculated from the first visit date to death or last examination in both adult and pediatric groups with a range of 4–96 months for adult group. Seven out of the 32 adult patients representing (~21.9 %) and only 2 child died all through the observation period. Regarding the event free survival (EFS) ~73% of pediatric group does not developed adverse event during the course of the disease and the follow up period compared to ~47% of the adult group which achieved significant statistical difference with Pvalue~0.034. **Chen et al.** stated that, the prognosis of primary renal lymphoma is largely unknown. The 5-year survival rate is ~45%. , in contrary to our results, his study shows that younger patients and bilateral primary renal lymphomas are associated with a poorer prognosis (shorter survival time and more rapid progression) ⁽¹⁶⁾.

The limitation of the current study include: first, relatively small number of the studied cohort with inadequate representation of all pathological subtypes. Second, small number of patients which limited the statistical confidence for positive and negative predictive values. Third, variation in therapy protocols and duration of disease as well as follow up period. Fourth, there is inherent difficulty in using PET/CT to evaluate renal masses because of the presence of radiotracer within the excretory tract. However, evaluation of CT and fused PET/CT images was used to differentiate physiologic and tumoral sites of FDG uptake. Finally, we did not evaluate enhancement behavior of the masses on CT images because iodinated IV contrast agent was not administered for all patient performed the PET/CT examinations. However, we can consider our data to contribute significant information that might aid in the development of renal lymphoma descriptive and prognostic information.

CONCULIONS:

Incidence of primary renal lymphoma in adult and pediatric age groups represent 15.6% and 3.3 % respectively. Focal pattern was the most common on both groups (93.8% and 76.7% respectively). Bilateral renal involvement and the diffuse pattern of infiltration were more prevalent (78.6% & 23.6% respectively) among the pediatric

group compared to (41.9 & 6.3%) in adult patients. Pediatric groups shows better OS and EFS as well as good prognosis. Statistical significance was found between the two groups regarding the SUVmax of the renal lesion, Nodal SUVmax, EFS and OS, with P value 0.004, 0.024, 0.019 & 0.004 respectively.

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