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RESEARCH ARTICLE

Evaluation of PET/CTRole in Diagnosis and Management of Pediatric Malignancy

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Abstract

Background: Successful management of solid tumors in children requires imaging tests for accurate disease detection, characterization, and treatment monitoring. 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) is a highly sensitive and specific imaging modality for whole-body evaluation of pediatric malignancies.The study aimed to retrospectively evaluate the efficacy of FDG PET/CT imaging system in the management of some pediatric malignancy and to determine if it provided additional diagnostic information on disease status; during the last 4 years (y). **Methodology:** 180 pediatric patients (118 male and 62 female) were included in the study. Their ages ranged from 6 month to 19 y at their first PET/CT examination. 78.3% of the patients were below 10 years old. 100 patients had lymphoma (82 Hodgkin and 18 Non-Hodgkin), 26 had soft tissue sarcoma (STS), and 54 had neuroblastoma. The indication, purpose, and findings of each PET/CT examination were reviewed, in addition to other imaging findings as well as clinical information including follow-up results for >1 y from their last PET/CT examination. 720 scan was performed for whole body in all patients for initial diagnosis & staging and restaging of recurrent malignancy. It is also, performed to assess cancer response to therapy and after therapy as a routine follow-up procedure or for further evaluation of suspected recurrence or for secondary malignancy. 1080 suspicious sites were evaluated in the studied patients, and those whose reports indicated areas of increased FDG uptake were selected. PET/CT findings were compared with the results of other diagnostic procedures (including CT and ultrasound), biopsy findings and follow-up data. **Results:** The current study represents that the, 18F-FDG PET/CT may influence the treatment decision if distant metastases or second primary tumors are detected with regard to staging of the primary tumor. Post Chemo-radiotherapy (CRT) PET/CT does aid subsequent management decisions. The overall sensitivities, specificities & positive and negative predictive values of the imaging system for all the suspicious sites were 98.1%, 97.2%, 97.6% and 97.8% respectively. It was 94.60%, 97.50%, 92.10%, and 98.30% respectively for detecting the

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local recurrence at the end of treatment; and 96.20%, 98.30%, 92.60%, and 99.10% after 1y of treatment. The sensitivities and specificities of 18F-FDG PET/CT for initial staging of malignant lymphomas are83.3%-100% and 93.75%-100% respectively. It ranged 66.70%-100% and 91.30%-100% respectively in sarcoma and 86.70%-100% and 95.80%-100% respectively in Neuroblastoma. **Conclusion:** The study concluded that the 18F-FDG PET/CT is the gold standard for noninvasive functional imaging in oncology. Technical developments in PET scanning in cancer management may increase the precision of radiotherapy planning and thus improve tumor control and reduce treatment-related morbidity. Recommendation regarding the use of PET/CT in the management of pediatric malignancy to facilitates the sparing of normal structures and the escalation of dose.

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Introduction:-

The presence of distant metastases is one of the most important prognostic factors in most cancer patients. Most tumors are classified according to the TNM staging system, and treatment is modified when distant metastases are present. Disease localized to primary sites and to regional lymph nodes is generally treated with curative strategies, including surgery, chemotherapy, and radiotherapy. In contrast, palliative treatment of patients with metastatic disease consists of less aggressive strategies. Moreover, distant metastases usually occur late during the course of cancer, whereas second primary cancers may be found even in early-stage patients. Early detection of distant metastases and second primary cancers is a fundamental precondition for guiding precise staging and optimal management**(Xu et al., 2012/2015)**.

Conventional imaging procedures (such as chest radiography, CT, abdominal ultrasonography, and bone scan) are commonly used to detect distant metastases and second primary cancers in patients with various cancers **(Ng et al., 2009;Fuster et al., 2008)**. However, conventional imaging procedures often do not reliably characterize the extent of disease because it is difficult to identify small distant lesions on the basis of morphologic criteria and to distinguish potential metastatic lesions from benign findings. ^{18}F-FDG PET is a functional imaging modality that is based on the increased glucose metabolism of malignant cells. However, anatomic information concerning distant lesions is limited on ^{18}F-FDG PET images, and the resolution is insufficient to detect small lesions**(Ng et al., 2009;Fuster et al., 2008;Antoch et al., 2005; Strobel et al., 2007;Veit-Haibach et al., 2009)**. Moreover, false-positive findings from inflammatory or granulomatous lesions in regions with a high prevalence of granulomatous disease are still problematic on ^{18}F-FDG PET images. These issues may restrict its use for assessing distant malignancies in cancer patients. The introduction of PET/CT scanners combined the functional data of PET with the detailed anatomic information of CT into a single examination**(Xu et al.,2012/2015)**.The poor spatial resolution of PET is substantially compensated for by integrated PET/CT, with co-registration of functional imaging with PET and anatomic imaging with CT. However, little is known about the validity of PET/CT relative to PET for detecting distant malignancies in cancer patients **(Xu et al.,2012/2015)**. In several previous studies, ^{18}F-FDG PET/CT was shown to be more sensitive and specific than conventional imaging procedures for the detection of distant malignancies in cancer patients at initial staging before treatment or restaging after treatment **(Ng et al.,2009;Fuster et al., 2008;Antoch et al., 2005; Strobel et al., 2007;Veit-Haibach et al., 2009)**. For this reason, combined PET and CT systems (PET/CT) have emerged as promising imaging modalities and are being more routinely used in clinical situations **(von Schulthess et al., 2006)**. Although many studies about whole-body PET/CT for various cancers were done, the results were still controversial and inconclusive. Despite growing numbers of reports on imaging adult malignancies with PET/CT, little data have been reported so far about the clinical relevance of this modality in pediatric patients**(Xu et al.,2012/2015)**.

The study aimed to retrospectively reviewed our initial clinical experience with FDG PET/CT in pediatric malignancies to evaluate the efficacy of this new imaging system and to determine if PET/CT provided additional

diagnostic information on disease status; the study also, evaluate the efficacy of this imaging technique in the management of some pediatric malignancies.

Materials and methods:-

One hundred and eighty pediatric patients (118(65.6%)male and 62(34.4%) female) with suspected or known malignancy, evaluated by ^{18}F-FDG imaging using a combined PET/CT system, between January 2011 and January 2015, included in the study. The male to female ratio was 2.27:1.The patient' stage was from 6 month to 19 years (y) old with a median age of 12 y at their first PET/CT examination. 141 (78.3%) of the patients were below 10 years old.One hundred patients had lymphoma (82 Hodgkin and 18 Non-Hodgkin), 26 had sarcoma, and 54 had neuroblastoma. The indication, purpose, and findings of each PET/CT examination were reviewed, in addition to other imaging findings as well as clinical information including follow-up results for >1 y from their last PET/CT examination.PET/CT examination was performed for whole body in all patients (720 scan) for initial diagnosis &staging and for restaging of recurrent malignancy. It is also, performed to assess cancer response to therapy and after therapy as a routine follow-up procedure or for further evaluation of suspected recurrence or for secondary malignancy.

One thousandand eighty suspicious sites were evaluated in the 180 included patients. Patients were selected according to their reports which indicate areas of increased FDG uptake. PET findings were considered positive when uptake occurred at sites of previous disease, in asymmetrical lymph nodes or in nodes unlikely to be affected by inflammation (mediastinal, except for hilar, and abdominal). PET findings were adjudged negative for neoplastic localizations in the following instances: physiological uptake (urinary, muscular, thymic or gastrointestinal), symmetrical nodal uptake, very low uptake and non-focal uptake. PET findings were compared with the results of other diagnostic procedures (including CT and ultrasound), biopsy findings and follow-up data.

After at least 4 h of fasting, a total body PET scan was done one hour after IV injection of 300 MBq of ^{18}F-FDG. 64 MSCT scan was performed using GE Discovery VCT simultaneously and used for attenuation correction, anatomical localization and diagnosis. Max. Variant of SUV; a semi-quantitative analysis would be done for selected ROI.s and the normal threshold is <2.5.

Statistical Analysis:-

An important goal in diagnostic medicine research is to estimate and compare the accuracies of diagnostic tests which provide reliable information about a patient's condition and influence patient care. The purpose of a diagnostic test is to classify or predict the presence or absence of a condition or a disease. The clinical performance of a diagnostic test is based on its ability to correctly classify subjects into relevant subgroups**(Mandrekar and Mandrekar, 2005)**. The diagnostic test consist the following events: *D*: Person has a disease, *T+:* Positive test result, $\bar{D}$ *:* Person has no disease and *T- :* Negative test result **(Nyari, 2011)**.The accuracy of any test is measured by comparing the results from a diagnostic test (positive or negative) to the true disease or condition (presence or absence) of the patient.The two basic measures of quantifying the diagnostic accuracy of a test are the sensitivity and specificity **(Mandrekar and Mandrekar, 2005)**.

-***The sensitivity****P(T+| D)* of a diagnostic test is the probability of a positive test result once the person has the disease: P*(T+| D) = P(T+∩ D)/P(D)* = The number of ill persons with positive test results / The number of all persons who have the disease**(Nyari, 2011)**.

-***The specificity****P(T– |* $\bar{D}$ *)* of a diagnostic test is the probability of a negative test result once the person is healthy. *P(T –|* $\bar{D}$ *) = P(T –∩* $\bar{D}$ *)/P(* $\bar{D}$ *)* = The number of healthy persons with negative test results / The number of all healthy persons **(Nyari, 2011)**.

Sensitivity and specificity are characteristics of the test but they do not help a clinician to interpret the results of an individual test **(Peacock and Peacock, 2011)**. Therefore it is important to know how good the test is at predicting the true positives, i.e., the probability that the test will give the correct diagnosis. This is captured by the following predictive values **(Mandrekar and Mandrekar, 2005)**:

-Positive predictive value (PPV) (posterior probability)is a probability that someone does have the disease once the test has given a positive result [$P(D|T+)$]. PPV= the number of persons diagnosed as have that disease with positive test results / the number of all positive test results **(Nyari, 2011)**.

- Negative predictive value (NPV) is a probability that someone really does not have the disease once the test has given a negative result [$P(\bar{D}|T-)$]. NPV= the number of healthy persons with negative test results / the number of all negative test results **(Nyari, 2011)**.

-Prevalence (prior probability) is defined as the prior probability of the disease before the test is carried out **(Peacock and Peacock, 2011)**. It is a measure of disease that allows us to determine a person's likelihood of having a disease. Therefore, a prevalence rate is the total number of cases of a disease existing in a population divided by the total population **(Health.ny.gov, 2015)**. PPV and NPV are dependent on the prevalence of the disease in the patient population being studied **(Mandrekar and Mandrekar, 2005)**.Through Bayes Theorem of conditional probability, the prevalence, sensitivity and specificity lead to evaluation of the positive and negative predictive value **(Walker et al., 1990)**.

$$PPV = \frac{sensitivity \,.\, prevalence}{[sensitivity \,.\, prevalence] \;+\; [(1-specificity) \,.\, (1-prevalence)]}$$

$$NPV = \frac{specificity \,.\, (1-prevalence)}{[(1-sensitivity) \,.\, prevalence] \;+\; [specificity \,.\, (1-prevalence)]}$$

Results:-

The results of the present work are presented in tables (1-9).

Stage III was the most presenting stage in all malignant disease group (35%), followed by stage I (22.2%) then stages II (21.7%) and IV (21.1%) respectively. Tumor size was >5cm in 72.8% of patients. Chemotherapy (93.3%) and surgery (73.3%) was the most treatment modalities in all our patients but radiotherapy was used in 67.8% of them. However, 32.2% of patients didn't receive radiotherapy. On the other hands, 41.1% of patients presented with metastases, (table 1).

Table (1): Patients Characteristics

Items	Lymphoma (100 Patients)		Soft Tissue Sarcoma (26 patients)		Neuroblastoma (54 patients)		Total (180 patients)	
	No.	%	No.	%	No.	%	No.	%
Age								
<10years	77	77	15	57.7	49	90.7	141	78.3
>10 years	23	23	11	42.3	5	9.3	39	21.7
Sex								
Male	71	71	17	65.4	30	55.6	118	65.6
Female	29	29	9	34.6	24	44.4	62	34.4
Stage								
I	34	34	6	23.1	0	0.0	40	22.2
II	30	30	3	11.5	6	11.1	39	21.7
III	32	32	16	61.5	15	27.8	63	35
IV	4	4	1	3.9	33	61.1	38	21.1
Tumor size								
>5cm	65	65	18	69.2	48	88.9	131	72.8
<5cm	35	35	8	30.8	6	11.1	49	27.2
Treatment Modalities:								
Chemotherapy	97	97	18	69.3	53	98.2	168	93.3
Radiotherapy	74	74	19	73.1	29	53.7	122	67.8
-Radiotherapy alone	2	2.7	7	36.8	0	0.0		
-CRT	72	97.3	12	63.2	29	100		
-No radiotherapy	26	26	7	26.9	25	46.3	58	32.2
Surgery	93	93	11	42.3	28	51.9	132	73.3
Metastases:								
Present	24	24	2	7.7	48	88.9	74	41.1
Absent	76	76	24	92.3	6	11.1	106	58.9

The true positive andnegative sites of the 1080 regions analyzed, was 562and 493respectively.The overall sensitivities, specificities & positive and negative predictive values of the imaging system for all the suspicious sites were 98.1%, 97.2%, 97.6% and 97.8% respectively (Tables 2-4).

Table (2): Evaluating Pediatric Malignancy by of PET/CT Scan

Items	Lymphoma (100 Patients)		Soft Tissue Sarcoma (26 patients)		Neuroblastoma (54 patients)		Total (180 patients)	
	Before PET/CT	After PET/CT	Before PET/CT	After PET/CT	Before PET/CT	After PET/CT	Before PET/CT	After PET/CT
Staging:								
I	36	34	4	6	1	0	41	40
II	25	30	5	3	8	6	38	39
III	29	32	14	16	13	15	56	63
IV	10	4	3	1	32	33	45	38
Response to therapy:(at the end of treatment)								
Complete remission(CR)	87	83	24	22	18	15	129	120
Progressive disease (PD)	8	12	1	3	19	22	28	37
Death	5	5	1	1	17	17	23	23
Follow up after therapy: (after 1y)								
Complete remission(CR)	85	88	19	17	16	13	120	118
Progressive disease (PD)	9	6	0	2	15	18	24	26
Death	6	6	7	7	23	23	36	36

Table (3): The Detection of the Site of Lesion in Pediatric Malignancy by PET/CT Scan

PET/CT Scan	True Positive	False Positive	True Negative	False Negative	Total No. of Scan
Head & Neck:	99	4	93	2	198
Chest:	42	2	140	3	187
Abdomen & Pelvis:	297	2	124	1	424
Extremities:	20	1	57	1	79
bony skeleton:	35	3	50	2	90
Body LN Chains:	69	2	29	2	102
Total	562	14	493	11	1080

Table (4):Efficacy of PET/CT Scan in Detecting the Site of Lesion in Pediatric Malignancy

PET/CT Scan	Prevalence	Sensitivity	Specificity	PPV	NPV
Head & Neck	51.00%	98.00%	95.90%	96.10%	97.90%
Chest	24.10%	93.30%	98.60%	95.50%	97.90%
Abdomen & Pelvis	70.30%	99.70%	98.40%	99.30%	99.20%
Extremities	26.60%	95.20%	98.30%	95.20%	98.30%
bony skeleton	41.10%	94.60%	94.30%	92.10%	96.20%
Body LN Chains	69.60%	97.20%	93.50%	97.20%	93.50%
Total	53.10%	98.10%	97.20%	97.60%	97.80%

PPV: Positive predictive value, NPV: Negativepredictive value

The sensitivities and specificities of 18F-FDG PET/CT for initial staging of malignant lymphomas were ranged 83.3%-100% and 93.75%-100% respectively. They ranged 66.70%-100% and 91.30%-100% respectively in STS and 86.70%-100% and 95.80%-100% respectively in Neuroblastoma.The negative and positive predictive valuesin evaluating the stage of lymphoma were 93.30%-100% and 40.00%-100% respectively. They ranged from 83.30%-100% and 33.30%-100% in STS and 95.10%-100% and 0.00%-100% in neuroblastoma respectively (Table 5).

Table (5): Efficiency of PET/CT Scan in Evaluating the Stage of Pediatric Malignancy

PET/CT Scan	Prevalence	Sensitivity	Specificity	PPV	NPV
Lymphoma					
Stage I	34.00%	100.00%	97.00%	94.40%	100.00%
Stage II	30.00%	83.30%	100.00%	100.00%	93.30%
stage III	32.00%	90.60%	100.00%	100.00%	95.80%
stage IV	4.00%	100.00%	93.75%	40.00%	100.00%
Soft Tissue Sarcoma					
Stage I	23.10%	66.70%	100.00%	100.00%	91.00%
stage II	11.50%	100.00%	91.30%	60.00%	100.00%
stage III	61.50%	87.50%	100.00%	100.00%	83.30%
stage IV	3.90%	100.00%	92.00%	33.30%	100.00%
Neuroblastoma					
Stage I	0.00%	100.00%	98.10%	0.00%	100.00%
stage II	11.10%	100.00%	95.80%	75.00%	100.00%
stage III	27.80%	86.70%	100.00%	100.00%	95.10%
stage IV	61.10%	97.00%	100.00%	100.00%	95.50%

PPV: Positive predictive value, NPV: Negativepredictive value

The sensitivities, specificities, PPV and NPV of PET/CT scan forpatients reaching complete remission (CR) at the end of treatment of pediatric Malignancy were 100%, 76.50%,95.40%, and 100% in lymphoma, it were100%,50.00%, 91.70%, and 100% in STS and100%,92.30%,83.30%, and 100% in neuroblastoma. After one year of follow up, the percentage becomes 96.60%, 100%, 100% and 80.0% in lymphoma, 100%, 77.80%, 89.50% and 100% in STS, and100%, 92.70%, 81.30% and 100% in neuroblastoma(Tables 6&7).

Table (6): Efficiency of PET/CT Scan in Evaluating the Response to Therapy at theEnd of Treatment of Pediatric Malignancy

PET/CT Scan	Prevalence	Sensitivity	Specificity	PPV	NPV
Lymphoma					
CR	83.00%	100.00%	76.50%	95.40%	100.00%
PD	12.00%	66.70%	100.00%	100.00%	95.70%
Death	5.00%	100.00%	100.00%	100.00%	100.00%
Soft Tissue Sarcoma					
CR	84.61%	100.00%	50.00%	91.70%	100.00%
PD	11.54%	33.30%	100.00%	100.00%	92.00%
Death	3.85%	100.00%	100.00%	100.00%	100.00%
Neuroblastoma					
CR	27.80%	100.00%	92.30%	83.30%	100.00%
PD	40.70%	86.40%	100.00%	100.00%	91.40%
Death	31.50%	100.00%	100.00%	100.00%	100.00%

Table (7): Efficiency of PET/CT Scan in the Follow up of Patients after 1 Year of Therapy in Pediatric Malignancy

PET/CT Scan	Prevalence	Sensitivity	Specificity	PPV	NPV
Lymphoma					
CR	88.00%	96.60%	100.00%	100.00%	80.00%
PD	6.00%	100.00%	96.80%	66.70%	100.00%
Death	6.00%	100.00%	100.00%	100.00%	100.00%
Soft Tissue Sarcoma					
CR	65.40%	100.00%	77.80%	89.50%	100.00%
PD	7.70%	0.00%	100.00%	0.00%	92.30%
Death	26.90%	100.00%	100.00%	100.00%	100.00%
Neuroblastoma					
CR	24.10%	100.00%	92.70%	81.30%	100.00%
PD	33.30%	83.30%	100.00%	100.00%	92.30%
Death	42.60%	100.00%	100.00%	100.00%	100.00%

The overall sensitivities, specificities & positive and negative predictive values of the imaging system was 94.60%, 97.50%, 92.10%, and 98.30% respectively for detecting the local recurrence at the end of treatment and were 96.20%, 98.30%, 92.60%, and 99.10% after 1y of treatment(Tables 8-9).

Table (8): The Detection of Local Recurrence byPET/CT

Uptake on PET/CT	Local Recurrence		No Local Recurrence		Total No. of Patients	
	At the end	After 1y	At the end	After 1y	At the end	After 1y
Positive	35	25	3	2	38	27
Negative	2	1	117	116	119	117
Total	37	26	120	118	157	144

Table (9): The Efficacy of PET/CT in Detecting the Local Recurrence or Disease Relapse

PET/CT Scan	Prevalence	Sensitivity	Specificity	PPV	NPV	Accuracy
At the end	23.60%	94.60%	97.50%	92.10%	98.30%	96.80%
After 1 year	18.10%	96.20%	98.30%	92.60%	99.10%	97.90%

PPV: Positive predictive value, NPV: Negativepredictive value

Discussion:-

Successful management of solid tumors in children requires imaging tests for accurate disease detection, characterization, and treatment monitoring. Technologic developments aim toward the creation of integrated imaging approaches that provide a comprehensive diagnosis with a single visit. These integrated diagnostic tests are not only convenient for young patients but also save direct and indirect health-care costs by streamlining procedures, minimizing hospitalizations, and minimizing school or work time lost for children and their parents**(Uslu et al., 2015)**. Pediatric malignancies are regarded as distinct from adult malignancies in view of their low frequency, treatment strategy, and expected prognosis. Special attention should be required in interpreting images of pediatric patients, taking these conditions into consideration**(Tatsumi et al., 2007)**. However, modern radiotherapy techniques heavily rely on high-quality medical imaging. PET provides biologic information about the tumor, complementary to anatomic imaging. Integrated PET/CT has found its way into the practice of radiation oncology, and ^{18}F-FDG PET is being introduced for radiotherapy planning. The functional information possibly augments accurate delineation and treatment of the tumor and its extensions while reducing the dose to surrounding healthy tissues. In addition to ^{18}F-FDG, other PET tracers are available for imaging specific biologic tumor characteristics determining radiation resistance**(Troost et al., 2015)**.

PET is used for many cancers for diagnosis, initial staging, assessment of treatment response **(Meta et al., 2001)**, restaging, detection of clinically suspected recurrence, and surveillance **(la Fougère et al., 2006; Freudenberg et al., 2007;Cohade et al., 2003)**. Compared with conventional PET, PET/CT provides greater accuracy in localizing ^{18}F-FDG uptake, with resultant improvement in observer performance **(von Schulthess et al., 2006;Podoloffet al.,2009;Patel et al., 2013)**.In the current study, The overall sensitivities, specificities & positive and negative predictive values of the PET/CT imaging system for all the suspicious sites were 98.1%, 97.2%, 97.6% and 97.8% respectively. It was 94.60%, 97.50%, 92.10%, and 98.30% respectively for detecting the local recurrence at the end of treatment and were 96.20%, 98.30%, 92.60%, and 99.10% after 1y of treatment. ***Tatsumi et al., 2007***also,demonstrated that PET/CT exhibited significantly high sensitivity, specificity, and accuracy than conventional imaging (CI) and showed accurate findings in 90% (72/80) of lesions with discordant findings between them. Additional information of PET/CT relative to CI was observed in more than one third of examinations compared.Accordingly,***Xu et al.,2012/2015*** documented in his meta-analysis that whole-body PET/CT has excellent diagnostic performance for the overall evaluation of distant metastases with or without second primary cancers in cancer patients. On the other hands,***Patel et al., 2013/2015***founded a lack of evidence supporting using the PET/CT in post-treatment surveillance and is reflected in practice guidelines **(Special Report, Podoloff et al., 2007)**. He evaluates patients with lymphoma, colorectal cancer, and head and neck cancer. Current National Comprehensive Cancer Network guidelines also, do not recommend surveillance. Nevertheless, PET/CT is commonly used for surveillance (**Wagner-Johnston et al., 2011)**. Possible risks of using PET/CT for surveillance include overtreatment based on false-positives and unnecessary radiation exposure **(Huang et al., 2009; Patel et al.,2013/2015)**. Therefore, a negative follow-up 18F-FDG PET scan is a strong indicator of absence of disease relapse, whereas a positive scan should be validated with other imaging modalities or biopsy **(Rhodes et al., 2006)**. Several recent studies have demonstrated that routine follow-up by 18F-FDG PET/CT and other imaging techniques may be

overused for routine surveillance of patients with HL, contributing to increased cost and radiation exposure without a clear survival benefit (**Nievelsteinet al., 2012; Levineet al., 2006;Rathore et al., 2012)**. More data are needed to determine which patient group will benefit from which surveillance test for how long and at which frequency**(Uslu et al., 2015)**.

Early detection of distant malignancies in cancer patients is crucial for guiding subsequent staging procedures and treatment **(Xu et al.,2012/2015)**.Accordingly to the results of the study of ***Tatsumi et al., 2007***, PET/CT is expected to serve as a powerful imaging modality, especially in staging or in evaluating suspected recurrence, in pediatric malignancies.The sensitivities and specificities of 18F-FDG PET/CT or 18F-FDG PET for initial staging of malignant lymphomas are 96%–99% and 95%–100%, respectively**(Kabickova et al., 2006; Furth et al., 2006; Cheng et al., 2013; Miller et al., 2006;Paulino et al., 2012;Punwani et al., 2010;Uslu et al., 2015)**.In the present study, the sensitivities and specificities of 18F-FDG PET/CT for initial staging of malignant lymphomas were ranged 83.3%-100% and 93.75%-100% respectively. They ranged 66.70%-100% and 91.30%-100% respectively in STS and 86.70%-100% and 95.80%-100% respectively in Neuroblastoma. Nevertheless, ***Uslu et al., 2015*** reported that, some investigators found that the use of 18F-FDG PET/CT has shown high negative predictive value, and therefore an early negative scan is a reliable indicator for therapy response (negative predictive value, 85.7%–100%; positive predictive value, 41.2%– 85.7%)**(Riad et al., 2010;Bakhshi et al., 2012;Ilivitzki et al., 2013)**.In the present study, negative and positive predictive valuesin evaluating the stage of pediatric lymphoma were 93.30%-100% and 40.00%-100% respectively.***Furth et al., 2009,*** reported that a negative 18F-FDG PET/CT scan after 2 cycles of chemotherapy is a strong indicator of relapse-free survival, with a negative predictive value of 100% in HL patients. Therefore, an 18F-FDG PET/CT scan has been advocated by many investigators and has led to early intensification of chemotherapy in apparent non-responders **(Furth et al., 2009; Levine et al., 2006; Meany et al., 2007;Uslu et al., 2015)**.Additionally, PET or PET/CT has clear advantage in evaluating soft-tissue masses and, thus, has been reported to be useful in patients with lymphoma or other malignancies after treatment **(Rohren et al., 2004;Kostakoglu and Goldsmith, 2003; Weber, 2005)**. ***Schaefer et al., 2004*** reported that PET/CT was particularly useful in demonstrating absence of residual active disease in adult lymphoma after treatment **(Uslu et al., 2015)**. As absence of FDG uptake on the residual soft tissue is known to be a strong indicator for better prognosis in adults, accurate interpretation with confidence is valuable in managing patients in a post-treatment status. PET/CT has an advantage over CI or PET alone in this regard as well**(Tatsumi et al., 2007)**.Furthermore, ***Choi et al., 2014,*** in a study of 30 neuroblastoma patients, found that 18F-FDG PET is more sensitive than CT in the evaluation of distant lymph node involvement and can help in detecting recurrent lymph node metastases. Therefore, 18F-FDG PET/CT might be particularly helpful in older patients who present with small, resectable primary tumors and chronic lymph node metastases **(Uslu et al., 2015)**. However false-positives were noted because of thymic rebound, inflamed lymph nodes, physiologic cardiac uptake **(Depas et al., 2005)**, infections or inflammation **(Rhodeset al., 2006)**, and reconverted marrow. This is a typical false-positive paradox, that is, false-positive results are more probable than true-positive when the overall population has a low incidence of a condition**(Uslu et al., 2015)**.

The ideal timing for a PET/CT after CRT has yet to be established, although, most commonly, within the literature, scans 3 months post CRT are used with the hope of minimizing post-treatment inflammation, maximizing potential tumor cell kill after CRT and without delaying the scan for too long to allow progression of residual disease**(Sherriff et al., 2015)**.On the other hand,post-CRT PET/CT does aid subsequent management decisions. Patients with a negative PET/CT scan after radical CRT have a 91.8% chance of remaining free of local recurrence 19 months post treatment. A higher SUV_{max} on the post-CRT PET/CT may predict local recurrence and warrants further investigation **(Sherriff et al., 2015)**.A substantial fraction (≤65%) of patients with positive PET results will still be cured, and patients with negative or positive results seem to do well if their PETresults are negative at the completion of chemotherapy (typically 6 cycles) **(Sher et al., 2009)**. Therefore, other investigators suggest performing follow-up 18F-FDG PET/CT scans at later time points **(Longo, 2013)**. In NHL patients, ***Yang et al., 2009*** reported that a persistent tumor 18F-FDG uptake on 18F-FDG PET/CT scans predicted worse overall survival and event-free survival. However, this principle may not hold for all types of NHL**(Bakhshi et al., 2012;Depas et al., 2005)**. A recent study on non-lymphoblastic lymphoma patients showed that 18F-FDG PET/CT and CT scans could not predict survival **(Bakhshi et al., 2012)**. Reported sensitivities and specificities of 18F-FDG PET/CT for therapy response assessment of HL and NHL at 2 wk to 3 mo after completion of therapy showed wide ranges of 75%–100% and 75%–90.9%, respectively**(Riad et al., 2010;Bakhshi et al., 2012; Furth et al., 2009;Levineet al., 2006; Meany et al., 2007)**. In the present study, the sensitivities and specificities of PET/CT scan for patients reaching complete remission (CR) at the end of treatment of pediatric malignancy were 100% and 76.50% in

lymphoma. It was 100% and 50.00% in STS and 100% and 92.30% in neuroblastoma. After one year of follow up, it becomes 96.60% and 100% in lymphoma, 100% and 77.80% in STS, and 100% and 92.70% in neuroblastoma.More systematic data evaluations are needed to determine the best time point for interim scans for response assessment of pediatric lymphomas. Information about the value of 18F-FDG PET or 18F-FDG PET/CT follow-up studies of pediatric HL and NHL after therapy is based on few non-responders per evaluated study population **(Miller et al., 2007;Amthauer et al., 2005;Depas et al., 2005; Furth et al., 2009;Levineet al., 2006;Hernandez-Pampaloni et al., 2006; Rhodes et al., 2006;Wickmann et al., 2003)**. 18F-FDG PET/CT has shown high sensitivity and specificity for the diagnosis of disease relapse in HL and NHL (95%–100% and 90%–100%, respectively) **(Riad et al., 2010;Depas et al., 2005; Rhodes et al., 2006)**. In the current study, the overall sensitivities and specificities of the imaging system for detecting the local recurrence were 94.60% and 97.50% respectively at the end of treatment and were 96.20% and 98.30% after 1y of treatment. More evidence is needed on diagnostic algorithms for the detection of tumor recurrence**(Uslu et al., 2015)**.

Conclusion:-

PET with the glucose analog, ^{18}F-FDG PET, is increasingly recognized as a powerful tool in evaluating patients with various malignant tumors***(Rohren et al 2004)***. Recently, combined PET and CT systems (PET/CT) have emerged as promising imaging modalities and are being more routinely used in clinical situations***(von Schulthess et al 2006)***. Despite growing numbers of reports on imaging adult malignancies with PET/CT, little data have been reported so far about the clinical relevance of this modality in pediatric patients. This study aimed to retrospectively evaluate the efficacy of FDG PET/CT imaging system in the management of some pediatric malignancy and to determine if it provided additional diagnostic information on disease status; during the last 4 years (y). The study concluded that the ^{18}F-FDG PET/CT is the gold standard for noninvasive functional imaging in oncology. It is a useful technique for the staging and follow-up of pediatric malignancy. Technical developments in PET scanning in cancer management may increase the precision of radiotherapy planning and thus improve tumor control and reduce treatment-related morbidity. It has a very high but not absolute specificity for pediatric malignancy. Thus, combined PET/CT imaging had an impact on patient management affecting both the diagnostic and therapeutic approach. ***Recommendation*** regarding the use of PET/CT in the management of pediatric malignancy to facilitates the sparing of normal structures and the escalation of dose.

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