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# The Impact of $^{18}\text{F}$ -FDG-PET/CT Versus Conventional Imaging Modalities in Pediatric Nasopharyngeal Carcinoma.

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## ABSTRACT:

**Background:** Nasopharyngeal carcinoma (NPC) is one of the few epithelial-origin tumors observed in pediatric population accounting for around 1–5% of all pediatric cancers and characterized with higher incidence of advanced loco-regional compromise. **Aim of the work:** to explore the impact of  $^{18}\text{F}$ -FDG-PET/CT in pediatric nasopharyngeal carcinoma (PNPC) either during initial staging or re-staging after end of therapy versus conventional imaging (CI) modalities (MRI and Ce-CT). **Patients and methods:** 40 patients with biopsy proven PNPC (mean age 13, SD  $\pm$  2.3; range 9-17) mostly of non-keratinizing undifferentiated type III (95%) were included in the study. Whole body  $^{18}\text{F}$ -FDG-PET/CT, MRI and CE-CT of the head and neck were obtained in all patients, as well as MRI and CE-CT

of the chest and the abdomen (the interval between the different modalities ranged from 2-28 days). The findings of PET/CT were compared with those of CI modalities regarding the TNM staging either initially or after end of therapy. **Results:** the studied group of patients was divided into two categories for analysis; 21 patients were analyzed at initial staging (52.5%) and 19 patients (47.5%) were analyzed for restaging after end of 1st line of therapy. **In initial staging;** The **T stage** detectability revealed a higher sensitivity for MRI versus PET/CT with sensitivity of 100% vs. 95.2% for PET/CT and MRI respectively. Regarding the **N stage;** PET/CT shows higher sensitivity than CI modalities with sensitivity values of 95.2% and 88.8% and 77.7% for PET/CT, MRI, and CT respectively.

In respect of the **M stage**; the sensitivity values were 80%, 60% and 25% for PET/CT, MRI, and CT respectively.

**In re-staging**; PET/CT has higher sensitivity than CI modalities for local residual/recurrence (**T**), nodal (**N**) and distant metastases (**M**) with values of 100% vs. 86% in T stage, 100% vs. 91% in N stage and 100% vs. 66% in M stage

**Keywords:**  $^{18}\text{F}$ -FDG-PET/CT, PNPc, pediatric.

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for PET/CT and CI modalities respectively.

**Conclusion:**  $^{18}\text{F}$ -FDG-PET/CT is considered a potentially valuable imaging tool in PNPc either in initial staging or restaging which could effectively change the overall staging and hence the management.

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## **INTRODUCTION:**

Nasopharyngeal cancer (NPC) is an aggressive epithelial malignancy characterized with higher incidence of advanced loco-regional and distant compromise <sup>(1)</sup>. In Egypt, pharyngeal cancers account for 1.6% of all incident cancers yearly and NPC is considered the 2<sup>nd</sup> most common in this entity with 32.8% incidence rate <sup>(2)</sup>. Pediatric nasopharyngeal carcinoma (PNPC) is a rare epithelial-origin tumor accounting for around 1–5% of all pediatric cancers and 10% of all nasopharyngeal cancers, with better outcome for children than for adults <sup>(3,4)</sup>. The treatment of NPC is based on the use of combined radio- and chemotherapy <sup>(5)</sup>, with similar treatment strategies in PNPc <sup>(3)</sup> and though their known inherent chemo-

radio-sensitivity; around 13% of cases present with residual disease after the end of therapy <sup>(6)</sup>. The appropriate management strategy for NPC depends on proper staging using the TNM staging system <sup>(7)</sup>. Clinical examination and naso-pharyngoscopy are not sufficient for this purpose <sup>(8)</sup>. Imaging with Magnetic resonance imaging (MRI) and contrast enhanced computed tomography (CE-CT) scans are the commonly used anatomic conventional imaging (CI) techniques to assess tumor extent, and suspicious findings <sup>(9)</sup>. MRI is considered superior to CE-CT in staging NPC due to its high soft tissue resolution capabilities; however, it has its own limitations in the follow-up of these patients.

These limitations are mainly resulting from the effects of therapy and inability to differentiate tissue fibrosis from early residual or recurrent disease <sup>(10)</sup>.

Functional imaging using <sup>18</sup>F-FDG-PET/CT is considered a potential and promising imaging technique which can be used for accurate staging as well as follow-up of these patients with NPC <sup>(9)</sup>.

**Aim of the study:** to explore the potential role of <sup>18</sup>F-FDG-PET/CT versus conventional imaging modalities (CE-CT and MRI) on the management of PNPC patients

#### **PATIENTS AND METHODS:**

40 patients with pathologically proven PNPC (29 males (72.5%) and 11 females (27.5%)), mean age 13, SD  $\pm 2.3$ ; range 9-17) were recruited in the current retrospective analysis; the studies were performed between January 2013 and September 2015 in Children Cancer Hospital, Egypt (CCHE). According to the WHO classification <sup>(11)</sup>; 38 patients (95%) had a pathology of non-keratinizing undifferentiated type2b, while only 2 patients (5%) were of squamous cell

carcinoma (SCC) type1. Patient's data were reviewed from the CCHE archiving system; whole body <sup>18</sup>F-FDG-PET/CT, MRI and CE-CT of the head and neck were obtained in all patients, as well as MRI and CE-CT of the chest and the abdomen (the interval between the different modalities ranged from 2-28 days).

#### **<sup>18</sup>F-FDG-PET/CT procedure**

Whole body <sup>18</sup>F-FDG-PET/CT studies were performed according to the EANM procedure guidelines for FDG PET/CT tumor imaging: version 2.0 <sup>(12)</sup>.

<sup>18</sup>F-FDG PET/CT study was done using a dedicated PET/CT scanner (Biograph, True Point; Siemens) ; scanning parameters are collimator width of 3.0 mm, pitch of 1.5, gantry rotation time of 0.8 s, and field of view of 50 cm integrated with a dual-section helical CT scanner (40 slice Emotion; Siemens)

The resulting images from CT reconstructed with a 512  $\times$  512 matrix and a 50-cm field of view, were converted using equivalent attenuation factors of 511 keV for attenuation correction.

PET, PET/CT, and CT images were reviewed using a dedicated workstation and software (E. soft; Siemens Medical Solutions), which allowed three-dimensional displays (transaxial, coronal, and sagittal) to be constructed using CT, PET, and PET/CT images and maximum intensity projection displays of the PET data.

Quantitative measurement with positron emission tomography were done using the maximum standardized uptake value (SUV max) The tumor SUV is a semi-quantitative parameter that represents the metabolic activity in a static image as measured by region-of-interest technique and corrected for both the injected activity per kilogram of body weight and the blood glucose level.

All PET/CT scans were reviewed and interpreted by at least two experienced nuclear medicine physicians.

### **MRI procedure**

Magnetic resonance imaging MRI sequences included a standard (spin-echo) T1-weighted sequence (repetition time [ms]/echo time [ms], 400–900/10–20), with or without gadolinium enhancement, and an intermediate weighted/T2-weighted sequence (1500–2500/70–100), without fat suppression. All MRI images

were reviewed and interpreted by two experienced radiology physicians.

### **Statistical analysis:**

The following criteria were accepted as our standard of reference: (a) histopathologic findings; (b) the combination of negative clinical findings, negative findings of other imaging studies or negative follow-up findings; (c) resolution of apparent abnormalities at subsequent PET/ CT studies without intervening therapy together with negative clinical follow-up findings; and (d) the combination of positive clinical findings at the time of PET/CT and resolution of the tumor after chemotherapy or radiation therapy. The PET/CT results were compared with the findings of CI on a per-patient basis. The same anatomical regions were compared (i.e. nasopharynx on CI compared with nasopharynx on PET/CT). The performance of both PET/CT and CI was evaluated through comparison with our reference standard. The PET/CT and CI findings were classified as true positive [(TP), positive imaging study confirmed by the presence of cancer], true negative [(TN), normal study with no further evidence of cancer], false positive [(FP), positive imaging study with no evidence of cancer] or false negative [(FN), normal study with further proven cancer].

The criteria that represent the reference standard for the presence or the absence of cancer included histopathologic sampling in eight patients and clinical and radiologic follow-up in 32 patients.

The sensitivity, the specificity, the negative and positive predictive values and the accuracy of PET/CT and CI were calculated from the performance tables.

Changes in the clinical decision-making resulting from PET/CT were reviewed and recorded for impact on patient management for each study.

## RESULTS:

The studied group of patients (40 patients) was divided into two categories for analysis according to the clinical indication of the performed whole body <sup>18</sup>F-FDG-PET/CT study. Twenty one patients were analyzed at initial staging (52.5%) and 19 patients (47.5%) were analyzed after end of 1<sup>st</sup> line of therapy for restaging.

### A. Analysis of 21 patients with PNPC presented for initial staging

The frequencies of TNM and overall staging in the three imaging modalities are summarized in *tables (1 and 2)*.

**Table 1:** The frequencies and percentages of TNM in the three imaging modalities.

		PET/CT	MRI	CE-CT
<b>T</b>	<b>T0</b>	0	0	1 (4.7%)
	<b>T1</b>	0	0	0
	<b>T2</b>	19 (90.5%)	18 (85.7%)	17 (80.9%)
	<b>T3</b>	2(9.5%)	2(9.5%)	2(9.5%)
	<b>T4</b>	0	1 (4.7%)	1(4.7%)
<b>N</b>	<b>N0</b>	1 (4.7%)	2 (9.5%)	4(19%)
	<b>N1</b>	1(4.7%)	4 (19%)	4(19%)
	<b>N2</b>	19(90.5%)	15(71.4%)	13(61.9%)
	<b>N3</b>	0	0	0
<b>M</b>	<b>M0</b>	17(81%)	18 (85.7%)	18(85.7%)
	<b>M1</b>	4(19.1%)	3(14.2%)	3(14.2%)

**Table 2:** The frequencies and percentages of the overall stage in the three imaging modalities.

Stage	PET/CT	MRI	CE-CT
<b>0</b>	0	0	1 (4.7%)
<b>I</b>	0	0	0
<b>II</b>	2(9.5%)	4(19.1%)	5(23.8%)
<b>III</b>	15(71.4%)	13(61.9%)	11(52.4%)
<b>IVA</b>	0	1 (4.7%)	1 (4.7%)
<b>IVB</b>	0	0	0
<b>IVC</b>	4(19.1%)	3(14.2%)	3(14.2%)

The overall lesion detectability at initial staging revealed a sensitivity of 95.2 % (20/21 patients), 100% (21/21 patients) and 95.2% (20/21 patients) to detect the primary lesion by PET/CT, MRI and diagnostic CT respectively. Whereas, diagnostic results for nodal metastases detection showed a sensitivity of 95.2%, 88.8% and 77.7% for PET/CT, MRI and CT, respectively. The similarity and discrepancy in initial staging between PET/CT and both MRI and diagnostic CT results are summarized in *table (3)*. As compared with MRI; <sup>18</sup>F-FDG-PET/CT

was superior in staging 3 cases by upstaging 1 case and down staging two cases, while MRI was superior in 2 cases by upstaging from stage III to IVA and stage 4C (*table 3*). As compared with diagnostic CT; <sup>18</sup>F-FDG-PET/CT changed accurately overall staging in 6/21 patients (28.5%) by upstaging 5 cases and down staging 1 patient (*table 4*) while diagnostic CT was superior in 1 cases by its upstaging from stage III to stage IVA. *Fig 1*; showed patient with NPC referred for initial staging using PET/CT, MRI and CT.

**Table (3):** Comparison between <sup>18</sup>F-FDG-PET/CT and MRI in overall initial staging.

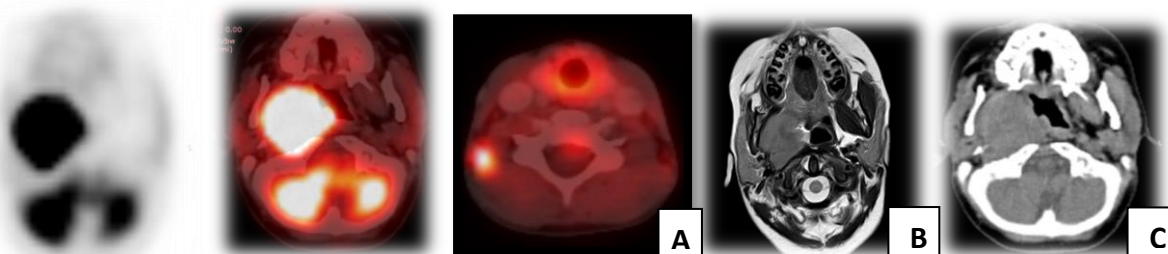
Agreement (N=16)	Number of patients	Stage of disease	
	14	III	
	2	IVC	
Disagreement (N=5)	Number of patients	MRI stage	PET/CT stage
	1	IVA*	III
	1	IVC*	III
	1	II	III*
	2	IVC	III*

\*The correct stage.

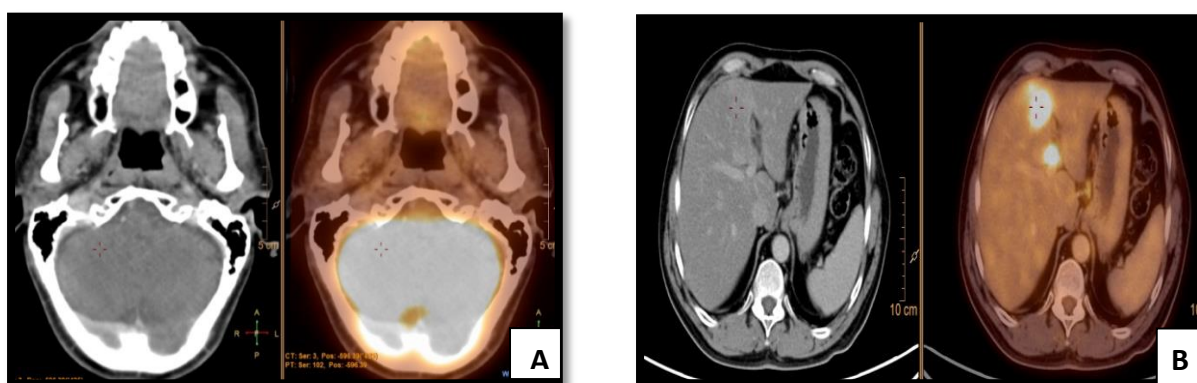
**Table (4):** Comparison between <sup>18</sup>F-FDG-PET/CT and diagnostic CT in overall initial staging.

Agreement (N=14)	Number of patients	Stage of disease	
	10	III	
	1	IVC	
Disagreement (N=7)	Number of patients	CT stage	PET/CT stage
	1	IVA*	III
	1	IVC	III*
	1	0	III*
	2	III	IVC*
	2	II	III*

\*The correct stage.



**Figure (1):** 15 Yrs male child with NPC presented for initial staging. Axial PET/CT showed significant uptake in the RT nasopharynx and unilateral left lower cervical nodes (level III); T2N1M0. (B and C) MRI and CT detected the primary RT. NP mass with no pathological cervical nodes; CI staging: T2N0M0.



**Figure (2):** 13 Yrs male patient presented with treated NPC; for restaging after end of 1st line of ttt. (A): <sup>18</sup>F-FDG-PET/CT and Axial CT showed no abnormal lesion distinctive for local primary recurrence. (B): Axial CT and fused PET/CT images of the upper abdomen showing two FDG avid metastatic lesions in the PET component of the study with no corresponding CT changes. PET/CT upstage this case from stage 0 to stage IVC.

**Analysis of 19 patients with NPC presented for restaging after end of therapy**

The frequencies of TNM and overall staging in the three imaging modalities at restaging are summarized in tables (5 and 6).

(Tables 7 and 8) represent the detectability rates of the primary and

nodal lesions by the three imaging modalities.

<sup>18</sup>F-FDG-PET/ changed disease stage in 3/19 patients (16%) by upstaging one case and down staging the others (table 9).

Fig 2; showed a case of NPC referred for follow up with PET/CT upstage the case from 0 to stage IVC as compared to CT.

**Table 5:** The frequencies and percentages of TNM in the three imaging modalities

		PET/CT	MRI	CE-CT
<b>T</b>	<b>T0</b>	3	5(26.3%)	5(26.3%)
	<b>T1</b>	1(5.3%)	1(5.3%)	1(5.3%)
	<b>T2</b>	12(63.2%)	10(52.6%)	10(52.6%)
	<b>T3</b>	2(10.5%)	2(10.5%)	2(10.5%)
	<b>T4</b>	1(5.3%)	1(5.3%)	1(5.3%)
<b>N</b>	<b>N0</b>	6(31.6%)	6(31.6%)	6(31.6%)
	<b>N1</b>	0	0	0
	<b>N2</b>	12(63.1%)	13(68.4%)	13(68.4%)
	<b>N3</b>	1(5.3%)	0	0
<b>M</b>	<b>M0</b>	16(84.3%)	17(89.5%)	17(89.5%)
	<b>M1</b>	3(15.7%)	2(10.5%)	2(10.5%)

**Table 6:** The frequencies and percentages of the overall stage in the three imaging modalities.

Stage	PET/CT	MRI	CE-CT
<b>0</b>	3(15.7%)	3(15.7%)	3(15.7%)
<b>I</b>	1(5.3%)	0	0
<b>II</b>	2(10.5%)	2(10.5%)	2(10.5%)
<b>III</b>	9(47.9%)	10(52.6%)	10(52.6%)
<b>IVA</b>	1(5.3%)	2(10.5%)	2(10.5%)
<b>IVB</b>	0	0	0
<b>IVC</b>	3(15.7%)	2(10.5%)	2(10.5%)



**Table (7):** Comparative diagnostic results between different imaging modalities for local residual/recurrence detection.

	PET/CT	MRI	CT		PET/CT	MRI	CT
<b>True Positive</b>	15	13	13	<b>Sensitivity</b>	100%	86%	86%
<b>False Positive</b>	1	1	1	<b>Specificity</b>	75%	75%	75%
<b>True Negative</b>	3	3	3	<b>PPV</b>	93.8 %	92.8 %	92.8%
<b>False Negative</b>	0	2	2	<b>NPV</b>	100%	60%	60%

PPV: positive predictive value, NPV: negative predictive value

**Table (8):** Comparative diagnostic results between different imaging modalities for nodal detection on restaging.

	PET/CT	MRI	CT		PET/CT	MRI	CT
<b>True Positive</b>	12	10	10	<b>Sensitivity</b>	100%	90.9%	90.9%
<b>False Positive</b>	1	2	2	<b>Specificity</b>	85.7%	75%	75%
<b>True Negative</b>	6	6	6	<b>PPV</b>	83 %	83 %	83 %
<b>False Negative</b>	0	1	1	<b>NPV</b>	100%	85.7%	85.7%

PPV: positive predictive value, NPV: negative predictive value.

**Table (9):** Comparison between <sup>18</sup>F-FDG-PET/CT and MRI/Ce-CT in overall initial staging

<b>Agreement</b>	<b>Number of patients</b>	<b>Stage of disease</b>	
	<b>(N=16)</b>	3	0 (No evidence of disease)
	2	II	
	8	III	
	1	IVA	
	2	IVC	
<b>Disagreement</b>	<b>Number of patients</b>	<b>MRI/Ce-CT stage</b>	<b>PET/CT stage</b>
<b>(N=3)</b>	1	0	II*
	1	III	I*
	1	IVA	IVC*

\*The correct stage

## DISCUSSION:

We reviewed 40 consecutive patients presented in the PET/CT unit in children cancer hospital, Egypt (CCHE) with biopsy-proven PNPC. We aimed to explore the impact of the  $^{18}\text{F}$ -FDG-PET/CT on the management of these patients either in initial staging or follow-up and compare it with other anatomic CI modalities.

We grouped the studied patients (40 patients) into two categories according to the clinical indication of the study. Category (1) initial staging: (21 patients) and Category (2) follow-up: (19 patients).

### Category (1) initial staging:

We compared  $^{18}\text{F}$ -FDG-PET/CT, MRI, and CT in the detection of primary site of PNPC (T status), the loco-regional node (N status), the distant metastatic disease (M status) and consequently the impact on the overall staging, of the 21 patients enrolled we found that;

The **T stage** detectability in initial staging revealed a sensitivity of 95.2%, 100% and 95.2% for  $^{18}\text{F}$ -FDG PET/CT, MRI and diagnostic CT respectively. It was accurately determined in all cases using

MRI, while it was underestimated in  $^{18}\text{F}$ -FDG PET/CT and diagnostic CT.  $^{18}\text{F}$ -FDG PET/CT could not truly detect a T4 primary NPC which is defined as a tumor with intra-cranial extension. This underestimation of the tumor extent may be because of obscuring of the tumor extension by the high physiological FDG uptake by the brain <sup>(12)</sup>. Similarly; *Ng et al.*, in a series of 111 untreated NPC patients that the 2nd most common cause of discrepancies between MRI and  $^{18}\text{F}$ -FDG PET/CT findings in T status delineation was in the intracranial region (14% patients), while CT showed false negative evidence of the primary disease in the nasopharynx in one case which was recorded as T0, this was explained that there were no appreciable local anatomical changes <sup>(14)</sup>. Also, *Nordin et al.*, re-evaluated the two patients falsely detected in their study as T0 depending on CT alone and reach an agreement that there were no significant regional anatomical disruption noted in the nasopharyngeal region, however, these patients  $^{18}\text{F}$ -FDG PET/CT showed the lesions had high metabolic activity <sup>(15)</sup>.

Regarding the **N stage**;  $^{18}\text{F}$ -FDG PET/CT shows higher sensitivity than CI modalities with sensitivity of 95.2%, %, 88.8% and 77.7% for  $^{18}\text{F}$ -FDG PET/CT, MRI, and CT respectively.  $^{18}\text{F}$ -FDG PET/CT understaged the nodal status in one patient among the 21 enrolled patients in our study. It was falsely reported negative as N0 which was proven later in follow-up studies to be N1 with small retropharyngeal nodes. This finding corresponds with one of the reported limitations of  $^{18}\text{F}$ -FDG PET/CT in nodal staging where the retropharyngeal LNs involvement is not detected as accurately as seen in MRI. This limitation is likely related to the blooming artifact in  $^{18}\text{F}$ -FDG PET/CT that may result in difficulties in differentiating a primary nasopharyngeal mass from an adjacent retropharyngeal LN. Hence, to improve the detectability of these nodes, the addition of a contrast-enhanced CT to the fused  $^{18}\text{F}$ -FDG- PET/CT is recommended (14, 16).

Similar result was reported by *Yen et al.*, compared the accuracy of MRI and  $^{18}\text{F}$ - $^{18}\text{F}$ -FDG-PET/CT in detecting metastatic involvement of various nodal groups in 84 patients with primary NPC (18); they found

that the accuracy of  $^{18}\text{F}$ -FDG PET/CT varies depending on the site of nodal spread, and it was particularly useful in assessing the lower cervical node metastases. Interestingly they found also that dual-phase  $^{18}\text{F}$ -FDG PET/CT may increase the sensitivity, specificity, and accuracy for the detection of cervical node involvement, to 100% in the delayed phase as compared to 84%, 98%, and 90%, respectively, for MRI ( $p = 0.046$ ).

On the other hand, in our study, the relatively lower values of sensitivity and accuracy of CI modalities as compared with fused  $^{18}\text{F}$ -FDG-PET/CT nodule staging. Also, *Ng, et al and Yen et al.*, Reported that  $^{18}\text{F}$ -FDG PET/CT has a sensitivity of 97–100% and specificity of 73–97% in assessing cervical nodes in patients with NPC, and MRI has a sensitivity of 84–92% and specificity of 73–97% (14, 17). This is likely due to the inherent ability of MRI and CT in assessment of lymph nodes relies on parameters such as nodal size and enhancement that may lead to the failure to detect small nodes while  $^{18}\text{F}$ -FDG PET/CT is better suited for assessing metastasis in lymph nodes that appear morphologically normal according to size criteria (18).

In respect of **M stage**; our study showed that  $^{18}\text{F}$ -FDG PET/CT interpretation reveals 4 patients (19%) with true positive distant metastases at initial presentation (M1), they were located in bone, liver and lung (2 patients) with 80% and 100% sensitivity and specificity respectively. MRI detected an additional lesion in the bone marrow and falsely missed the lung lesions. While CT already missed the liver and the bone lesions, and it falsely detected an additional lung lesion which was proven later by the follow-up to be inflammatory in nature. So as seen in our study  $^{18}\text{F}$ -FDG PET/CT may help in proper detecting distant metastasis, and this will lead to adjustment of the patient's stage and management plan. However, in view of small sample size, we could not compare it with CI.

Similarly, *Ng et al.*, also found that  $^{18}\text{F}$ -FDG PET/CT correctly modified the M staging in eight patients (7.2%) and disclosed a second primary lung malignancy in one patient (0.9%) among the 111 studied NPC patients<sup>(14)</sup>.

*Chang et al.*, applied a meta-analysis study to evaluate the accuracy of  $^{18}\text{F}$ -FDG PET/CT in distant metastases of NPC, and

they concluded good diagnostic performance of the whole-body  $^{18}\text{F}$ -FDG PET/CT in M staging of NPC<sup>(19)</sup>.

**The overall staging**; our study analysis showed that  $^{18}\text{F}$ -FDG-PET/CT altered the overall initial staging and hence the initial management in 14% of patients (3 patients) and 28.5 % (6 patients) as compared with diagnostic CT and MRI respectively. This is consistent with other studies that show that  $^{18}\text{F}$ -FDG PET/CT have the potential to change management in patients with NPC when compared with conventional imaging because of their superior ability to detect nodal and distant metastases<sup>(20, 21)</sup>.

*Gordin et al.*, conducted a study to assess the impact of  $^{18}\text{F}$ -FDG-PET/CT in the management of NPC; of the 33 patients with NPC with change of management in 57%<sup>(20)</sup>. It eliminated the need for previously planned diagnostic procedures in 33% of the patients, induced a change in the planned therapeutic approach in 15% which proved by PET/CT. Also, *Law et al.*, evaluated 48 patients with NPC who underwent PET/CT imaging before starting treatment, the management strategy was changed in 33% of them<sup>(21)</sup>.

**Category (2) Follow-up:**

Change in management strategy in the present study is related to development of metastases (8%) or nodal spread (25%). We compared  $^{18}\text{F}$ -FDG-PET/CT, MRI, and CT in the detection of the site of residual/recurrent disease NPC (T status), the loco-regional node (N status), the distant metastatic disease (M status) and consequently the impact on the overall re-staging in the 19 patients.

**Residual / recurrent disease;**

$^{18}\text{F}$ -FDG- PET/CT provided a higher sensitivity in detecting the local residual recurrence disease as compared to the CI modalities with values of 100% for  $^{18}\text{F}$ -FDG- PET/CT versus 86 % for both MRI and CT. There were two patients reported in both CI modalities as no evidence of disease (T0) no significant anatomical changes that could be attributed to local residual/recurrence in the primary site of disease.

However, they were demonstrated in  $^{18}\text{F}$ -FDG- PET/CT evaluation revealed with intense FDG accumulation in these two lesions were proven later during clinical follow-up to be local recurrent disease. This particular clinical example has been

described previously where CI modalities like CT or MRI have resulted in understaging or missed tumor lesions since they rely only on anatomical alterations to be readily identified at imaging <sup>(15)</sup>.

Although we followed the EANM procedure guidelines for FDG-PET/CT tumor imaging version 2.0. With at least 10 days interval after chemotherapy and 3 months interval following radiotherapy <sup>(12)</sup>, however, still there are no conclusive data on the optimum interval between chemo-radiotherapy and FDG-PET/CT, with variable body response towards injury <sup>(23)</sup>. In addition, the possibility of local inflammation/infection could be another possibility <sup>(15)</sup>.

The possible explanation of relative low specificity (75%) versus higher sensitivity (100%) of FDG-PET in our study is similar to data reported by *Mohandas et al.* with FDG-PET sensitivity in head and neck cancers is ranging from 67% to 100% and specificity ranging from 77% to 100% <sup>(13)</sup>.

Moreover, the negative predictive value of  $^{18}\text{F}$ -FDG- PET/CT was interestingly high (100%) in our small study population as compared to those of MRI and CT (60%).

Similar results was stated by *Nordin et al.*, with higher negative predictive value of PET/CT versus CI modalities and they concluded that this indicates more reliable negative PET/CT result when there is no clinical evidence of disease meanwhile the conventional imaging modality may have 29% incidence of false negative result<sup>(15)</sup>.

However, false-negative results with <sup>18</sup>F-FDG- PET/CT may occur under the following conditions: (a) improper scan timing e.g. too early after completion of chemo- or radio-therapy; (b) tumors in sites with high physiological FDG uptake; (c) microscopic or small tumor volume disease beyond the resolution of the scanner<sup>(17)</sup>.

**The overall re-staging** this study has resulted in down-staging 3 patients who were incorrectly over-staged with CI modalities alone. This was in line with *Nordin et al.*, as they reported that the use of PET/CT in the post therapy management of NPC patients, as it demonstrated the ability of PET/CT in correcting tumor over staging in few

patients found to be falsely positive using the conventional imaging modalities alone which could be attributed to the effect of therapy and regional anatomical changes as explained above<sup>(15)</sup>. On the other hand, <sup>18</sup>F-FDG- PET/CT has up-staged one case by discovering single metastatic pulmonary nodule which could not be detected by MRI. This is consistent with known inferior ability of current MRI sequences as compared to low-dose FDG PET/CT for the assessment of the pulmonary status<sup>(25, 26)</sup>. Our findings also agreed with *Cheuck et al.*, who evaluated PNPC patients and they concluded that PET/CT might be potentially beneficial in overall staging than CI modalities and it provides simple and reliable tool for follow-up of pediatric patients<sup>(4)</sup>.

## CONCLUSION:

<sup>18</sup>F-FDG-PET/CT is considered a potentially valuable imaging tool in PNPC either in initial staging or restaging which could effectively change the overall staging and hence the management of these patients.

## REFERENCES:

- 1- **Chin SC, Fatterpekar G, Chen CY, Som PM.:** MR imaging of diverse manifestations of nasopharyngeal carcinomas. *AJR. Am. J. Roentgenol.* 180(6):1715–1722; 2003.
- 2- **Ibrahim AS, Seifeldin IA, Ismail K, Hablas A, Hussein H, and Elhamzawy H. :** Cancer in Egypt, Gharbiah: Triennial Report of 2000–2002, Gharbiah Population-based Cancer Registry. Cairo: Middle East Cancer Consortium; 2007.
- 3- **Sultan I, Casanova M, Ferrari A, Rihani R, Rodriguez-Galindo C.:** Differential features of nasopharyngeal carcinoma in children and adults: a SEER study. *Pediatr Blood Cancer.*55(2):279-84; 2010.
- 4- **Cheuk Daniel KL, Sabin Noah D, Hossain Moinul, Wozniak Amy, Naik Mihir, Rodriguez-Galindo Carlos, Krasin Matthew J, and Shulkin Barry L:** Positron emission tomography-computed tomography for staging and follow-up of pediatric nasopharyngeal carcinoma . *Eur. J. Nucl. Med. Mol. Imaging.* 39(7): 1097–1106; 2012.
- 5- **Taheri-Kadkhoda Z, Bjo`rk-Eriksson T, Johansson KA, Mercke C.:** Long-term treatment results for nasopharyngeal carcinoma: the Sahlgrenska University Hospital experience. *Acta. Oncol.* 46(6):817–827; 2007.
- 6- **Zheng XK, Chen LH, Wang QS, Wu FB.:** Influence of [18F] fluorodeoxyglucose positron emission tomography on salvage treatment decision making for locally persistent nasopharyngeal carcinoma. *Int. J. Radiat. Oncol. Biol. Phys.* 65(4):1020– 1025; 2006.
- 7- **Edge SB, Byrd DR, Compton CC, Fritz GA, Greene LF. Trotti A. eds.:** *AJCC Cancer Staging Manual.* 7th ed. New York, NY: Springer; 2010.
- 8- **Manavis J, Sivridis L, Koukourakis MI:** Nasopharyngeal carcinoma: the impact of CT-scan and of MRI on staging, radiotherapy treatment planning, and outcome of disease. *Clin. Imaging.* 29 (2): 128–133; 2005.
- 9- **Lin Xiao-Ping, Zhao Chong, Chen Ming-Yuan, Fan Wei, Zhang Xu, Fang Sheng and Liang Pei Yan:** Role of <sup>18</sup>F-FDG PET/CT in diagnosis and staging of nasopharyngeal carcinoma. *Chinese Journal of Cancer.* 27(9): 259-262; 2008.
- 10- **Sun Y, Ma J, and Huang Y.:** The study of the comparison of CT and MRI in nasopharyngeal carcinoma. *Chinese Journal of Clinical Oncology.* 14: 788-791; 2005.

- 11- Barnes L, Eveson JW, Reichart P, Sidransky D.:** Pathology and Genetics of Head and Neck Tumours. In: World Health Organization Classification of Tumors, IARC Press, Lyon; 2005.
- 12- Boellaard R., Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, et al.,:** FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. *EJNMMI*. 42 (2): p. 328-354; 2015.
- 13- Mohandas A, Marcus C, Kang H, Truong MT, Subramaniam RM.:** FDG PET/CT in the management of nasopharyngeal carcinoma. *AJR. Am. J. Roentgenol*. 203(2):W146-57; 2014.
- 14- Ng SH, Chan SC, Yen TC, et al.:** Staging of untreated nasopharyngeal carcinoma with PET/CT: comparison with conventional imaging work-up. *Eur. J. Nucl. Med. Mol. Imaging*. 36:12–22; 2009.
- 15- Nordin Abdul Jalil Secondino, Simona Abdul Rahim, Noraini, Pedrazzoli Paolo, Siena Salvatore, Rossetti Claudio, Aris Tahir:** Imaging in nasopharyngeal carcinoma: the value of 18-Fluorine Fluorodeoxyglucose PET/CT in comparison to conventional imaging modalities CT and MRI. *Radiol. Oncol*. 43(4): 247-257; 2009.
- 16- King AD, Ma BB, Yau YY, et al.:** The impact of 18F-FDG PET/CT on assessment of nasopharyngeal carcinoma at diagnosis. *Br. J. Radiol*. 81:291–298; 2008.
- 17- Yen TC, Chang YC, Chan SC, et al.:** Are dual phase 18F-FDG PET scans necessary in nasopharyngeal carcinoma to assess the primary tumour and loco-regional nodes? *Eur. J. Nucl. Med. Mol. Imaging*. 32:541–548; 2005.
- 18- Nishioka T, Shiga T, Shirato H, Tsukamoto E, Tsuchiya K, Kato T, Ohmori K, Yamazaki A, Aoyama H, Hashimoto S, Chang TC and Miyasaka K.:** Image fusion between 18FDG-PET and MRI/CT for radiotherapy planning of oropharyngeal and nasopharyngeal carcinomas. *Int. J. Radiat. Oncol. Biol. Phys*. 53: 1052-1057; 2002.
- 19- Chang MC1, Chen JH, Liang JA, Yang KT, Cheng KY, Kao CH.:** Accuracy of whole-body FDG PET and FDG-PET/CT in M staging of nasopharyngeal carcinoma: a systematic review and meta-analysis. *Eur. J. Radiol*. 82(2): p. 366-373; 2013.



- 20- Gordin A, Golz A, Daitzchman M, et al.:** Fluorine- 18 fluorodeoxyglucose positron emission tomography/ computed tomography imaging in patients with carcinoma of the nasopharynx: diagnostic accuracy and impact on clinical management. *Int. J. Radiat. Oncol. Biol. Phys.* 68:370–376; 2007.
- 21- Law A, Peters LJ, Dutu G, et al.:** The utility of PET/CT in staging and assessment of treatment response of nasopharyngeal cancer. *J. Med. Imaging Radiat. Oncol.* 55:199–205; 2011.
- 22- Ng SH, Joseph CT, Chan SC, Ko SF, Wang HM, Liao CT, Chang YC, Lin WJ, Fu YK and Yen TC:** Clinical usefulness of 18F-FDG PET in nasopharyngeal carcinoma patients with questionable MRI findings for recurrence. *J. Nucl. Med.* 45: 1669-1676, 2004; 2006.
- 23- Schwenger NF, Schraml C, Muller M, Brendle C, Sauter A, Spengler W, et al.:** Pulmonary lesion assessment: comparison of whole-body hybrid MR/PET and PET/CT imaging – pilot study. *Radiology.* 264(2):551–8; 2012.
- 24- Lee KH, Park CM, Lee SM, Lee JM, Cho JY, Paeng JC, et al.:** Pulmonary nodule detection in patients with a primary malignancy using hybrid PET/MRI: is there value in adding contrast-enhanced MR imaging? *PLoS One.* 11;10 (6) :e0129660; 2015.