Role of Fluorine 18 Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)/Computed Tomography (CT) in Detection of Post-Thyroidectomy Recurrence in Differentiated Thyroid Cancer

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Abstract:

Aim: To demonstrate the role of 18F-FDG PET/CT for detection of post-thyroidectomy recurrence in differentiated cancer thyroid patients with negative radio-isotope iodine scan, yet showing elevated serum thyroglobulin level. **Procedure:** This is a prospective study which included 20 patients who had previous history of differentiated cancer thyroid. All patients after history taking and revising the medical sheet underwent Serum Thyroglobulin level Estimation & entire body scan I-131 (WBS) examination and then 18F-FDG PET/CT study. The findings of PET/CT imaging were compared with histopathology results or clinical follow-up results as a gold standard. **Results:** FDG PET/CT based analysis showed that 19 true positives and 1 was true negative as confirmed by the gold standard (Histopathology and clinical follow-up). 13 patients had either local recurrence or lymph node metastases without distant metastatic disease, 6 patients had different distant metastasis. 18F- FDG PET/CT based analysis showed that 19 true positives and 1 was true negative as confirmed by the gold standard (Histopathology and clinical follow-up). The sensitivity and accuracy of PET/CT (95%) were significantly better than those of the CT alone (84.2% and 80%, respectively) [P=0.03]. **Conclusion:** Combination between positron emission tomography (PET) and computed tomography (CT) allow anatomic, functional & molecular information. 18F-FDG PET/CT provided a critical role in assessment and management of patients with suspected differentiated thyroid recurrence, presenting with high serum thyroglobulin level and negative radio-isotope scan. The 18F-FDG PET/CT enhance diagnostic accuracy through giving exact anatomical localization of recurrent and/or metastatic tumor foci.

Key words: Cancer thyroid, Fluorodeoxyglucose, thyroglobulin.

Introduction

Cancer thyroid records for around 1% of all tumor cases & it is the 6th common cancer among females [(1)].

Differentiated thyroid cancer (DTC) is by and large portrayed by long haul survival, good prognosis and low aggressiveness. Its prognosis is identified with the age at analysis, tumor measurement, additional capsular expansion and nearness of far off metastases. Distant is moderately uncommon, with occurrence going from 4% - 27% [(2)].

Patients with differentiated cancer thyroid (DTC) have good prognosis, yet recurrence is noticed in up to 30% of such patients [(3)].
Most people diagnosed with cancer thyroid underwent total thyroidectomy taken after by radio-active iodine ablation. After treatment has completed patients will undergo regular checkups. Some visits, patients may do laboratory investigations, ultrasound, CT, MRI and isotope study [(4)].

In clinical practice, estimation of serum thyroglobulin (Tg) and the I-131 entire body scan (WBS) are the backbones of DTC quiet assessment after treatment and amid follow-up. In spite of the fact that the I-131 scan has high specificity, yet some of papillary and follicular thyroid carcinoma recurrences are not positive for I-131 uptake. However, an indicative situation is presented by patients with expanded levels of Tg, without identification of recurrent cancer utilizing conventional imaging devices, for example, the iodine-131 entire body scan [(3)].
It has been shown that F-18 FDG uptake represents less differentiated thyroid cancer cells or differentiated cells yet impervious to 131-Iodine treatment. The uptake of F-18 FDG is a poor prognosis [(5)].

Combination between positron emission tomography (PET) and computed tomography (CT) permit anatomic, functional and molecular data. The upsides of this combined system over PET alone have turned out to be self-evident. There is expanding confirmation to recommend that PET/CT includes corresponding data in in staging, re-staging and follow-up in post-thyroidectomy patients, prompting changes in management plans [(6)].

Patients and Methods

This prospective study included 20 patients distributed from patients under follow up at nuclear medicine and PET/CT units in

Nasser oncology center amid the period from June 2018 till June 2020.

Each patient included in the study was subjected to:

- Full history taking.
- Reviewing medicinal sheet at whatever point accessible.
- Patients met the following **inclusion criteria**:
  - Histopathologically proved differentiated thyroid carcinoma.
  - Total radio-surgical thyroid ablation.
  - Elevated serum Thyroglobulin levels (> 10ng/ml in patients with stimulated TSH level and >1ng/ml in patients with suppressed TSH level).
  - Negative I-131 WBS.

  Exclusion criteria were as follow:
  - Thyroglobulin level (<10ng/ml in patients with stimulated TSH level and <1ng/ml in patients with suppressed TSH.
  - Positive I-131 whole body scanning.
  - Pathology other than DTC (e.g. undifferentiated or medullary thyroid carcinoma).
  - Incomplete radio-surgical thyroid ablation.
- FDG PET-CT study was performed using a Devoted PET-CT scanner (Biograph, True-Point; Siemens).
- All patients fasted for no less than 4 h before the infusion of 370-555 MBq 18F-FDG. Scanning began after 60-90 min of tracer injection. Blood glucose level is not above 150 mg/dL. Intravenous contrast agent was used in most patients. At first, patients were inspected in the recumbent position with arms lifted, and CT checking was begun at the level of the cervico-thoracic area. PET over a similar district was performed quickly after obtaining of the CT pictures (2-3min/bed position).
- The findings of PET/CT imaging were compared with histopathology results or clinical follow-up results as a gold standard.

Image Interpretation:

Images were interpreted at a workstation equipped with fusion software (Syngo; Siemens) that provides multi-planar reformatted images and enables display of the PET images, CT images, and fused PET/CT images in any percentage relation. Side-by-side image interpretation was accomplished by 3 experienced nuclear medicine physicians. The analysis was conducted on per patient basis and per lesion basis.

The following regions were used for anatomic assignment of tumor lesions:

- Locally recurrent masses at the operative bed.
- Cervical lymphadenopathy.
- Distant metastases.
- Mediastinal lymphadenopathy.
- Pulmonary deposits.
- Bone deposits.

Results:

FDG PET/CT based analysis showed that 19 true positives and 1 was true negative as confirmed by the gold standard (Histopathology and clinical follow-up).

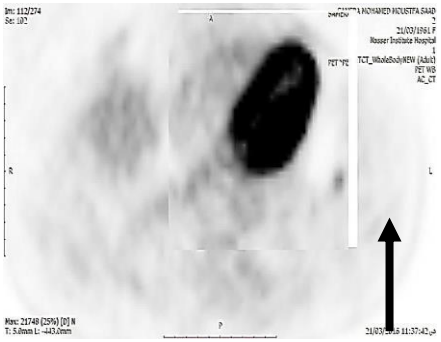
13 patients had either local recurrence or lymph node metastases without distant metastatic disease, 6 patients had different distant metastasis.

The sensitivity & accuracy of PET &PET/CT The sensitivity & accuracy of PET/CT (95%) were significantly better than those of the CT alone (84.2% and 80%, respectively) [P=0.03].

Illustrative Cases

Case 1

A 55 year old female patient, who underwent near-total thyroidectomy, followed by 120 mCi RAI-131 ablation for multi-centric papillary cancer thyroid. During follow up elevated thyroglobulin level 15mg/dl was detected, Diagnostic iodine whole body scan and neck ultrasound were negative, PET/CT was done and revealed solitary small sized left lower lung lobe pulmonary nodule SUVmax~11.8. Which insure the diagnosis of metastatic nature of this lesion.



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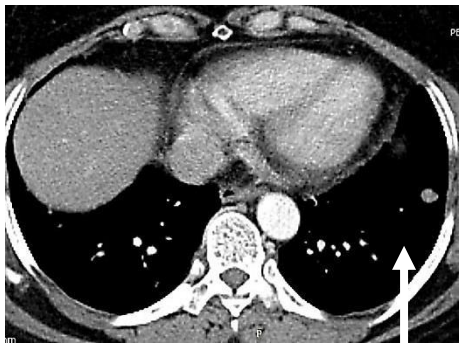

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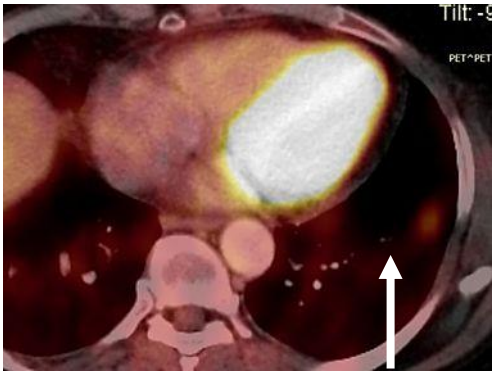

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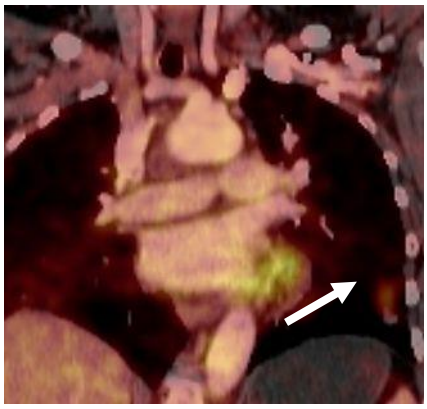
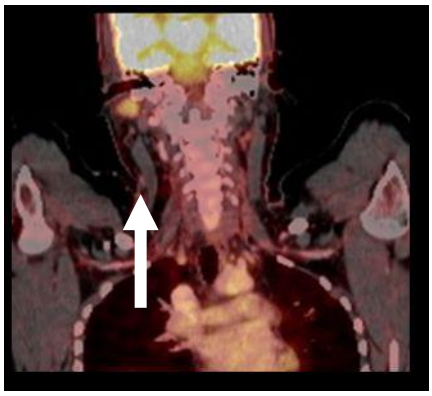


(D)

Axial PET only (A), CT (B) Axial & Coronal fused PETCT images (C & D) showed pulmonary nodule (Arrows).

Case 2

A 27 year old male patient, who underwent total thyroidectomy, followed by 120 mCi RAI-131 ablation for papillary cancer thyroid. Follow up iodine whole body scan was done 1 year later and was negative inspite of elevated thyroglobulin level (=12 mg/dl).PET/CT was done and revealed right retro-mandibular /pre-auricular soft tissue nodule likely nodal with SUVmax~7.2.



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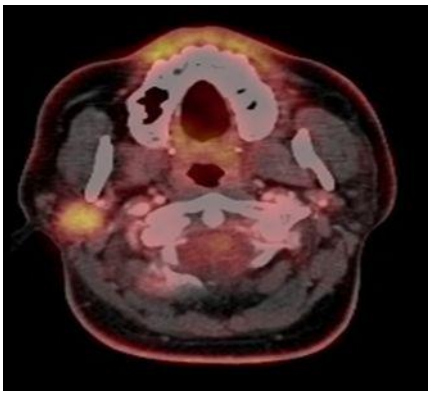

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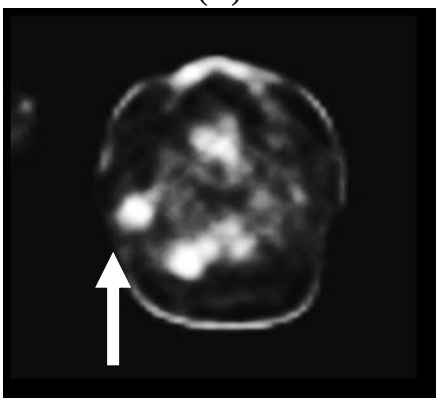


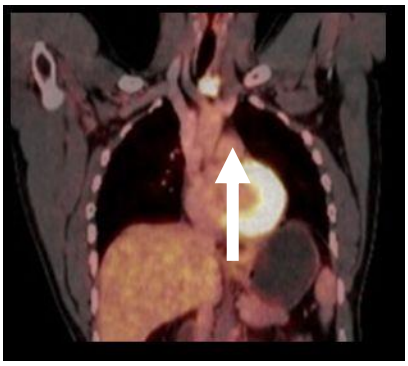
(C)

(D)

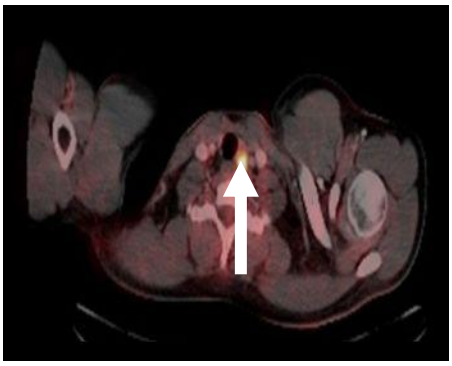
Coronal and axial fused PET/CT images (A & B), PET only (C) & axial CT (D) with right retromandibular/ retro-auricular soft tissue lesion / Lymph node (Arrows).

Case 3

A 70 year old female patient, who underwent total thyroidectomy, followed by 100 mCi RAI-131 ablation for follicular cancer thyroid. Follow up iodine whole body scan was negative with elevated thyroglobulin level (=15.5 mg/dl). Neck ultrasound revealed operative bed ill-defined soft structure, PET/CT demonstrates operative bed soft tissue lesion and with increased activity (SUV 4) denoting operative bed recurrence.



(A)



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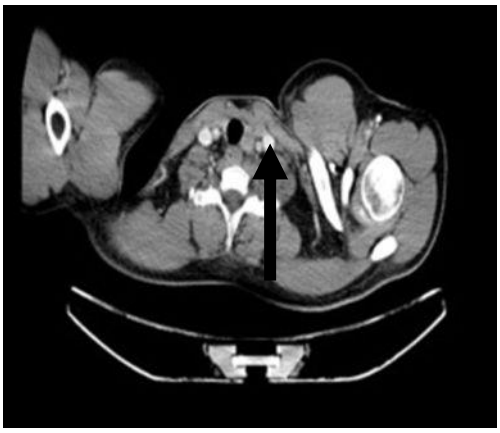

C)

Coronal and axial fused PET/CT images (A & B), axial CT (C) showed operative bed soft tissue lesion.

Discussion

Thyroid cancer is the sixth common malignancy in female and records for around 1% of all malignant cases [(1)].

Differentiated cancer thyroid (DTC) is characterized by long time survival, good outcome and low aggressiveness. Its prognosis is related to the patient's age at time of diagnosis, tumor measurement, additional capsular expansion & distant metastatic lesions. Distant metastases is moderately uncommon with rate running from 4-27% [(2)].

The vast majority determined to have thyroid malignancy underwent total thyroidectomy followed ablation by radio-

active iodine. Following treatment has been completed patients will have regular check-ups. Some visits, patients may do laboratory investigations, ultrasound, CT, MRI and isotope study [(4)].

The thyroglobulin is fundamentally utilized as a tumor marker to assess the outcome of treatment for cancer thyroid & to screen for recurrence. Not all thyroid malignancies will produce thyroglobulin, but most widely recognized types are papillary and follicular thyroid cancer, frequently do, bringing about expanded levels of serum (TG) level. The level of thyroglobulin might be identified with tumor mass, degree of differentiation and area of metastasis. Low level of Tg (1ng/ml or less); gives us a sensitive test, whereas higher cut-off levels result in a greater specificity at the expense of decreasing sensitivity in detection of recurrent cancer. Thyroid suppression & withdrawal of suppression enhances the serum thyroglobulin levels. Thyroglobulin observation is the only screening test for recurrent cancer thyroid in patients who have low risk & no evidence of recurrence before I-131 scan [(7)].

I-131 whole body scan had been at the focal point of detection of recurrent cancer thyroid; it distinguishes iodine-avid cancers & is insufficient in undifferentiated lesions. Another advantage of I-131 WBS over other imaging modalities is its capacity to detect distant metastasis. Similar to Thyroglobulin, I-131 turns out to be more sensitive after thyroid suppression withdrawal & thyrotropin stimulation [(7)].

The differentiated thyroid cancer cells after total thyroidectomy & radioiodine ablation may develop a process of transformation thus losing all their capacity to take up and hold 131-iodine, yet regardless they hold the capacity to retain FDG [(7)].

As of late announced that the loss of I-131 take-up in recurrences depends not just on an abatement in vitality subordinate transport interceded by the Na+/I-symporter (NIS) gene but potentially on a decrease in the particles managing its intracellular metabolism. In addition, high glucose transporter type1 (GLUT-1) gene expression underpins the utilization of PET with particular tracers in clinical administration of such cancers [(2)].

The role of F-18 FDG PET/CT in differentiated thyroid cancer is entrenched, especially in patients presented with high thyroglobulin measures and negative (WBS). It has been shown that F-18 FDG

uptake shows less differentiated thyroid cancer cells or dedifferentiated cells and PET positive lesions are more likely to be resistant to 131-Iodine treatment. The take-up of F-18 FDG is identified with tumor estimate, invasion of the capsule and histological variations with a poor prognosis [(5)].

Combination between (PET) (CT) permit anatomic, functional & molecular date. The upsides of this combination over PET alone have turned out-obvious. There is expanding proof to recommend that PET/CT includes corresponding data in staging, re-staging and follow-up in post-thyroidectomy patients, prompting changes in treatment plans [(6)].

The sensitivity of utilizing FDG PET/CT in the recognition of cancer thyroid is very high and more precise than the other imaging modalities as it is fit for of differentiating among tumors, scars, fibrosis and necrosis [(9)].

Additionally PET/CT pictures from survey of the body could show abnormal areas of uptake indicating the spread of the thyroid malignancy to lymph nodes, lungs, bones or CNS [(9)].

The combination of the metabolic and morphologic data in PET/CT could expand the indicative diagnostic accuracy, lessens pitfalls and changes therapeutic strategies in an impressive of patients [(10)].

Studies on the value of 18F-FDG PET for DTC have focused on patients in whom radioiodine scintigraphy is negative related with an expansion of TG level. It has been demonstrated that 18F-FDG PET is the most exact strategy in this circumstance, and sensitivities and specificities go somewhere in the range of 85% and 94%. For the treatment of iodine-negative tumor tissue, surgery is the only curative therapy healing treatment alternative; subsequently correct limitation of 18F-FDG tumor foci is obligatory for effective resection of disease in these cases [(9 & 10)].In our study, FDG PET/CT demonstrated to have a critical part in patients with suspected differentiated thyroid recurrence, presenting with high serum thyroglobulin level and negative radi-isotope scan. The co-enlisted 18F-FDG PET/CT enhances diagnostic accuracy through giving exact anatomical localization of recurrent and/or metastatic tumor foci [(8)].

The overall sensitivity and specificity in our study for the detection of tumor tissue by 18F-FDG PET/CT per individual patient were 100%, and so with a diagnostic accuracy of 100% also. Comparison

between CT alone & PET/CT in our study clearly demonstrated that both sensitivity & accuracy of PET/CT (100%) were significantly higher than those of CT alone (85.7% and 44.5%, respectively) with a significant difference of (P=0.03) [(9)].

Conclusion:

18F-FDG PET/CT has a role in patient with differentiated thyroid cancer, specifically those presented by elevated serum thyroglobulin level and negative iodine 131 scan. Co-registered 18F-FDG PET/CT provide precise anatomical localization of recurrent and/or metastatic thyroid carcinoma, leading to improved diagnostic accuracy. Co-registered 18F-FDG PET/CT has a higher sensitivity and accuracy than those of CT or PET alone, regarding the loco-regional cervical nodal metastases as well as the distant metastases.

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