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Role of Fluorine 18 Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)/Computed Tomography (CT) in Detection of Thyroid cancer Recurrence with positive thyroid tumor markers and negative thyroid scan.

Emam Abo Seif, Aliaa Elnagar, Yahia Mohammed Abdelaal

Department of Radiodiagnosis, Faculty of Medicine (for Girls) Al-Azhar University, Egypt dr_yahia.nayel@yahoo.com

Abstract: Background: Thyroid cancer is the 6th common cancer in women and accounts for approximately 1% of all cancer cases. Thyroid cancer is generally characterized by long term survival, good prognosis and low aggressiveness. Its prognosis is related to the age at diagnosis, tumor dimension, extra capsular extension and presence of distant metastases. Distant metastases is relatively rare with incidence ranging from 4- 27%. Combination between positron emission tomography (PET) and computed tomography (CT) allow anatomic, functional & molecular information. **Aim of the Study:** Role of Fluorine 18 fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) / Computed Tomography (CT) in detection of post-thyroidectomy recurrence in thyroid cancer patients with negative iodine radioisotope scan (I-131WBS) and elevated serum thyroglobulin (TG) level. **Patients and Methods:** this study will be performed on 30 patients presenting with pathologically proven recurrence differentiated thyroid carcinoma after total thyroidectomy with positive thyroid tumor markers and negative thyroid scan. **Results:** There was a high frequency of papillary carcinoma found in 22 patients (73.3%) while (16.6%) and (10%) patients had follicular carcinoma and Hurthle cell tumor respectively. **Conclusion:** The sensitivity & accuracy of PET & PET/CT (100%) were significantly better than those of the CT alone (85.7% and 44.5%, respectively), Co-registered 18F-FDG PET/CT provide precise anatomical localization of recurrent and/or metastatic thyroid carcinoma, leading to improved diagnostic accuracy.

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Keywords: Fluorodeoxyglucose, Post-Thyroidectomy, Thyroid Cancer, Radiodiagnsis

1. Introduction:

Thyroid cancer is the 6^{th} common cancer in women and accounts for approximately 1% of all cancer cases ⁽¹⁾.

Differentiated thyroid cancer is generally characterized by long term survival, good prognosis and low aggressiveness. Its prognosis is related to the age at diagnosis, tumor dimension, extra capsular extension and presence of distant metastases. Distant metastases is relatively rare with incidence ranging from $4-27\%^{(2)}$.

The role of F-18 FDG PET/CT in differentiated thyroid cancer (DTC) is well established, particularly in patients presenting with elevated thyroglobulin (Tg) levels and negative radioactive iodine whole body scan (WBS). It has been demonstrated that F-18 FDG uptake represents less differentiated thyroid cancer cells or dedifferentiated cells and PET positive lesions are more likely to be resistant to 131-Iodine treatment. The uptake of F-18 FDG is related to tumor size, thyroid capsule invasion and histological variants with a poor prognosis ⁽³⁾.

Combination between positron emission tomography (PET) and computed tomography (CT) allow anatomic, functional & molecular information. The advantages of this combined technique over PET alone have become obvious. There is increasing evidence to suggest that PET/CT adds complementary information in staging, re-staging and follow-up in post-thyroidectomy patients, leading to changes in management plans ⁽⁴⁾.

The sensitivity of using FDG PET/CT in the detection of cancer thyroid is very high and more accurate than the other imaging modalities as it is capable of differentiating among tumors, scars, fibrosis and necrosis ⁽⁵⁾.

Also PET/CT images from survey of the body could reveal abnormal areas of uptake indicating the spread of the thyroid cancer to lymph nodes, lungs, bones or central nervous system ⁽⁶⁾.

The fusion of the metabolic and morphologic information in PET/CT was able to increase the diagnostic accuracy, reduces pitfalls and changes

the rapeutic strategies in a considerable number of patients $^{(7)}\!.$

Aim of the Study

Detection of thyroid cancer recurrence in post thyroidectomy patients by using Fluorine 18 fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) / Computed Tomography (CT).

2. Material and Methods

This study will be performed on 30 patients presenting with pathologically proven recurrence differentiated thyroid carcinoma after total thyroidectomy. These patients were examined in the period between October 2017 and October 2019. The study was approved by the local ethical committee, and all patients agreed to participate in the study.

All patients included in this study were subjected to the following:

1- Patients met the following inclusion criteria:

• Histopathologically proved differentiated thyroid carcinoma.

• Total radio-surgical thyroid ablation.

• Elevated serum Tg levels (> 10ng/ml in patients with stimulated TSH level and >1ng/ml in patients with suppressed TSH level as determined by immune-chemiluminescence test).

Negative I-1131 WBS.

Exclusion criteria were as follows:

• Tg 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.
- Positive I-1131 WBS & another primary.

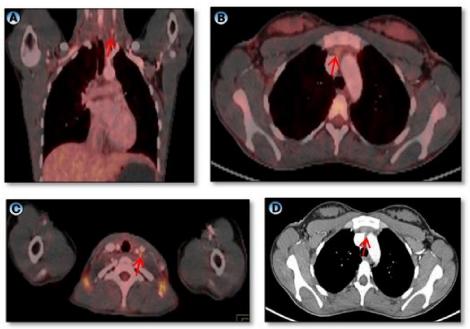
The finding of PET, CT, and fused imaging were compared with histopathology or clinical follow-up results as a gold standard. The evaluation of imaging was performed directly after imaging, and the results were used for further clinical decision making.

Images 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-byside 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.
- o Pulmonary deposits.
- Bone deposits.



Coronal and axial fused images (a, b, c), axial CT (d) with left supraclavicular and mediastinlal lymph nodes

This case was diagnosed according to PETCT features as metabolically active small left supraclavicular as well as small superior mediastinal lymph nodes. Pathological assessment revealed recurrent papillary thyroid carcinoma.

Statistical analysis

Data was collected, tabled and statistically analyzed using SPSS vs. 15.

3. Results:

Thirty patients with pathologically proven recurrence differentiated thyroid carcinoma after total thyroidectomy in this study. I- Different pathological types of the included patients (papillary carcinoma, follicular carcinoma and Hurthle cell tumor).

II- Distribution by site of different metastatic lesions in the included patients (Loco-regional recurrence and distant metastases)

III- Distribution of cervical nodal metastases at different levels.

IV- Comparison between final outcomes of CT, PET & PET/CT in Interpretation of cervical nodal lesions

V- Comparison between final outcomes of CT, PET & PET/CT Interpretation of distant bony metastases.

		Frequency	Percent
Loco-regional recurrence (N. 20)	Local recurrence.	6	21.4%
	CX LNs	12	42.8%
	Both	2	7.1%
Distant metastases (N.8)	Lung metastasis	4	14.2%
	Bone	0	0%
	Both	4	14.2%

4. Discussion:

Disease localization in thyroid cancer patients with isolated elevated TG level and no radioiodine concentration is a common and challenging clinical problem. Patients with radioiodine-negative tumor tissue have a less favorable prognosis, especially those with distant metastases. These tumors cannot be detected or treated with radio-iodine. Consequently, tumor cells will continue to grow undetected and the chance of cure decreases significantly⁽⁸⁾.

The search for residual sites of cancer is motivated by the possibility of curative surgical treatment in cases with localized disease and prevention of disease complications. It was shown that 18F-FDG PET is able to reveal iodine-negative tumor tissue with a diagnostic accuracy that is higher than that of other imaging modalities ⁽⁹⁾.

Conclusion

In 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-

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regional cervical nodal metastases as well as the distant metastases.

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