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Diffuse Thyroid Uptake in FDG PET/ CT Scan cCan Predict Subclinical Thyroid Disorders

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Abstract

Background: ^{18}F-FDG positron emission tomography (PET) has established itself in the field of oncology and it is useful in the initial staging and follow-up of a variety of malignancies. Significant thyroid uptake is often identified as an accidental finding on whole-body positron emission tomography for non-thyroid disease.

Aim of this study: to investigate the effect of ^{18}F-FDG on thyroid gland function after performing PET scan compared to thyroid function prior to scan.

Materials and Methods: 43 subjects who had an ^{18}F-FDG PET scan as part of a cancer screening program participated in this study. All cancers are diagnosed using ^{18}F-FDG, except for prostate cancer, brain cancer and neuro-endocrine tumors, which are diagnosed using Ga-68. Thyroid stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3) were measured.

Results: Clinical information and results of thyroid function tests were available for 43 patients. Twenty- three out of 43 patients (53.48%) had abnormally high TSH levels with incident hypothyroidism, while 20 out of 43 patients (46.51%) had abnormally low TSH levels with incident hyperthyroidism, and the association was significant ($p < 0.05$).

Conclusion: Thyroid hormone abnormality is strongly associated with the degree of diffuse thyroid uptake on ^{18}F-FDG PET. As a result, an autoimmune process could be the most likely pathological cause of diffuse thyroid uptake.

Keywords: Diffuse thyroid uptake, hyperthyroidism, positron emission tomography, 18F-Fluorodeoxyglucose

امتصاص الغدة الدرقية المنتشر لمادة FDG PET/ CT يتنبأ بوجود خلل وظيفي في الغدة الدرقية قبل حصول الاعراض

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الخلاصه

أثبت التصوير المقطعي بالإصدار البوزيتروني ^{18}F–FDG وجوده في مجال طب الأورام وهو مفيد في التدريج الأولي ومتابعة مجموعة متنوعة من الأورام الخبيثة. غالبًا ما يتم تحديد امتصاص الغدة الدرقية على أنه اكتشاف عرضي في التصوير المقطعي بالإصدار البوزيتروني لكامل الجسم لأمراض غير الغدة الدرقية.

تهدف هذه الدراسة إلى التحقيق من تأثير ^{18}F–FDG على وظيفة الغدة الدرقية بعد إجراء مسح PET مقارنة بوظيفة الغدة الدرقية قبل الفحص.

شملت الدراسة 43 شخصًا خضعوا لفحص ^{18}F–FDG PET كجزء من برنامج فحص السرطان. يتم تشخيص جميع أنواع السرطان باستخدام ^{18}F–FDG، باستثناء سرطان البروستات وسرطان المخ وأورام الغدد الصماء العصبية، والتي يتم تشخيصها باستخدام68–Ga. .تم قياس هرمون تحفيز الغدة الدرقية (TSH) ، هرمون الغدة الدرقية (T4) ، وثلاثي يودوثيرونين(T3) . بينت المعلومات السريرية ونتائج اختبارات وظائف الغدة الدرقية والتي كانت متاحة لـ 43 مريضا. ثلاثة وعشرون من أصل 43 مريضا (53.48٪) يعانون من ارتفاع غير طبيعي في مستويات هرمون TSH مع قصور الغدة الدرقية. بينما كان لدى عشرين من أصل 43 مريضًا (46.51٪) مستويات منخفضة غير طبيعية من TSH مع قصور الغدة الدرقية، مع وجود فروق معنوية احصائيا ($P < 0.05$)

تشير النتائج إلى أن هناك ارتباط بين اضطراب هرمون الغدة الدرقية وشدة درجة امتصاص الغدة الدرقية المنتشر في ^{18}F–FDG PET نتيجة لذلك، يمكن أن تكون عملية المناعة الذاتية هي السبب المرضي الأكثر احتمالاً لامتصاص الغدة الدرقية المنتشر

1. Introduction

Positron emission tomography (PET), using 2-[18F]-fluoro-2-deoxy-D-glucose (18F-FDG) as the radiopharmaceutical, has been used for diagnostic imaging of a variety of tumors as well as to monitor therapy response in many cancers [1]. Nowadays, the best choice modality for imaging in clinical oncology is the PET, which can detect malignant lesions by detecting regions where glucose transport and glycolysis are increased [2].

FDG uptake is increased not only in cancerous lesions, but also in inflammatory and contagious lesions. Precision in interpreting the FDG uptake can have an influence on the interpretation of the PET results and so effect the patient's clinical management and overall health [3].

FDG uptake can be found in a variety of lesions of head, lung, mediastinum, spine, joints, and vasculature using the FDG-PET whole-body screening protocol [4].

In a normal thyroid gland, FDG uptake is normally poor or absent, which is consistent with the hypothesis that the main substrates of bio-energetic metabolism are free fatty acids rather than glucose [5].

There are two categories of FDG uptake in the thyroid: focal and diffuse [6]. Diffuse uptake is associated with hypothyroidism and hyperthyroidism, while focal uptake has been related to malignancy [7]. Several studies have shown that FDG uptake in thyroid is related to the thyroid glands functionality and/or thyroid stimulating hormone (TSH) [8].

2. Patients and methods

The study was performed in the Nuclear Medicine department / Medical City / Baghdad, between November 2020 and March 2021. This study was performed in accordance with the Helsinki Declaration of 1975 and medical ethical standards; all patients were informed of the study's purpose and have consented to participate. A total of 43 patients (20 males and 23 females), their age ranges between 19 and 80 years, were included. Participants were those who had completed a whole-body PET scan as part of a cancer screening program. Those with a history of thyroid cancer were excluded, as well as those with hyperthyroidism and hypothyroidism based on thyroid function examination.

Thyroid function tests (TFTs), including thyroid stimulating hormone (TSH), thyroxine (T4) and triiodothyronine (T3), were performed before the PET scan and three months after the examination. The normal reference ranges of TSH, total T3 and total T4 are 0.38–4.31mIU/L, 1.22–2.43 nmol/L and 63.2-141.9 nmol/L, respectively .

3. Laboratory Evaluation

n vitro thyroid function tests, including TSH, T4 and T3 levels, were used to classify thyroid function. An automated, competitive chemiluminescent immunoassay AIA-2000 ST (Tosoh Bioscience, Inc. 6000 Shoreline Court, Suite 101, South San Francisco, U.S.A.) was used to test serum thyroxine. Serum TSH was measured using a 2-site immunoenzymatics sandwich assay (Shandong Chengwu Huabo Medical Equipment kit Sa. 191202 – China). A competitive-binding immunoenzymatic method was used to measure total thyroxine (Access Total T4 assay; Shandong Chengwu Huabo Medical Equipment kit Sa. 191202 – China). People with a high T4 or T3 levels in their blood and a low TSH level were diagnosed with hyperthyroidism. Hypothyroidism was diagnosed by a low serum T4 or T3 level and a high TSH level.

4. ^{18}F-FDG-PET/CT Imaging.

PET scans were performed on all subjects using an integrated 50-slice spiral CT (Discovery IQ; GE Medical Systems) that is designed for whole-body oncology examination. No intravenous or oral contrast material was used. Slice thickness was 5 mm for the CT scan, current was 430 mA, and energy was 120 kVp.

The ^{18}F-FDG was produced by an on-site cyclotron (GE Medical Systems, Inc, 3000 North Grandview Blvd Waukesha, Wisconsin, USA).

All patients were fasting and did not consume anything, except water, for at least 6-8 hours before the intravenous injection of 275 MBq of ^{18}F-FDG. Imaging started 45-90 minutes after the injection.Whole-body PET/CT images (from the base of the skull to the pelvis) were acquired in 3-dimensional mode with a 5-minute acquisition time per bed position.

Before the acquisition began, the PET/CT scanner was subjected to regular quality control checks. A default vendor-implemented iterative reconstruction algorithm was used to recreate the studies.

5. Statistical Analysis.

Mean and standard deviation (SD) were used to express all results. Microsoft Office Excel 2013 was used for all statistical analysis. Statistical significance was described as a p-value of less than 0.05.

6. Results

Table 1 shows the baseline characteristics of the study participants. The data revealed that six patients had diabetes mellitus (13.95%) and three patients had hypertension (6.97%). Besides, 10 patients were smokers (23.25%).

Table 1-Characteristics of the study group, Data are expressed as means ±SD and percentages.

Characteristics	Overall (n = 43)
Age (mean ± SD)	49.02± 15.56
Female	53.48% (23/43)
Male	46.51% (20/43)
Height (cm)	165.76 ± 10.67
Weight(Kg)	73.83 ± 16.54
BMI (Kg/m^2)	26.83 ± 5.18
Diabetes mellitus (%)	13.95% (6/43)
Hypertension (%)	6.97% (3/43)
Smoking (%)	23.25% (10/43)

The mean value of T3 (nmol/L) was 1.87 ± 0.34 and 1.76 ± 0.52 before and after ^{18}F-FDG uptake, respectively. The mean value for T4 was 112.78 ± 23.14 (nmol/L) before ^{18}F-FDG uptake and 116.30 ± 21.89 after uptake. For TSH (mlU/L), the mean values were 2.26 ± 1.73 and 2.05 ± 1.52, before and after ^{18}F-FDG uptake respectively. However, none of these differences were significant (p > 0.05) (Table 2).

Table 2-Measurement of T3, T4, and TSH using PET/ CT in all participants (n=43)

Variable	Mean ± SD		p-value
	Before ^{18}F-FDG	After 3 months	
T3 (nmol/L)	1.87 ± 0.34	1.76 ± 0.52	> 0.05
T4 (nmol/L)	112.78 ± 23.14	116.30 ± 21.89	> 0.05
TSH (mlU/L)	2.26 ± 1.73	2.05 ± 1.52	> 0.05

Based on the serum level of T3, T4 and TSH, patients were classified as hyperthyroidism (increased serum levels) and hypothyroidism (decreased serum levels) to determine the functional status of the thyroid gland. It was found that hypothyroidism accounted for 53.48% and 37.20% with respect to T3 and T4 levels, respectively, but the differences were not significant compared to hyperthyroidism (46.51% and 62.79%, respectively; p-value > 0.05). In the case of TSH level, 53.48% were classified as hyperthyroidism and 46.51% as hypothyroidism, and the difference was significant (p-value < 0.05) (Table 3).

Table 3-Thyroid function as measured by thyroid uptake

Thyroid function tests	Diffuse Thyroid Uptake	p-value
T4 (nmol/L)		
Increased	62.79%	> 0.05
Decreased	37.20%	
T3 (nmol/L)		
Increased	46.51%	> 0.05
Decreased	53.48%	
TSH (mlU/L)		
Increased	53.48%	< 0.05
Decreased	46.51%	

7. Discussion

The clinical significance of diffuse thyroid uptake of 18F-FDG was investigated in subjects free of thyroid cancer or thyroid dysfunction. Diffuse thyroid uptake is linked to hypothyroidism or hyperthyroidism [9]. The degree of 18F-FDG uptake was related to risk of abnormal thyroid functional tests, as well as elevated TSH, T3, and T4 serum levels [10.[

Several studies have suggested that increased uptake of 18F-FDG in the thyroid gland could indicate autoimmune thyroid disorders such as Grave's disease or thyroiditis, or it could just be a physiological and normal phenomenon [11.[

Free fatty acids, plasma glucose, and thyroid-stimulating hormone concentrations in healthy subjects have also been linked to moderate hypermetabolism [12]. Increased FDG absorption in the thyroid is caused by blood flow increment, improved glucose metabolism, and autoimmune antibody-induced inflammation in Graves' disease [13]. As a result, it is possible to debate whether diffuse thyroid uptake of 18F-FDG PET indicates thyroid dysfunction that requires further clinical attention. Kurata et al. indicated that although diffused FDG uptake usually indicates Hashimoto's thyroiditis, the risk of thyroid cancer must be recognized in both diffused FDG uptake and diffused-plus-focal FDG uptake on PET scan [14]. In our results, the presence of diffuse thyroid uptake was found to be closely linked to low serum TSH levels in 46.51%, with the highest levels of T3 and T4 in 46.51% and 62.79%,

respectively (Table 3). This may indicate the presence of hypothyroidism in the in majority of the study subjects. It may also be explained by the fact that early stages of thyroiditis may have thyrotoxicosis symptoms, such as Hashitoxicosis.

These results suggest a close association between 18F-FDG uptake in the diffuse thyroid gland and hyperthyroidism. Our findings are consistent with those of Ankur et al. who found that 84% had abnormal TFTs with abnormal TSH levels associated with hypothyroidism which probably caused by autoimmune thyroiditis [15]. In 53.48% of the patients, TSH showed increased serum levels, with lower T4 and T3 levels (37.20% and 53.48%, respectively; Table 3), highest TSH, and the highest rate of hypothyroidism in the subclinical stage . Furthermore, the 18F-FDG visual uptake score's degree was linked to an increased risk of abnormal thyroid function tests (TFT) and TSH levels. These findings indicate that autoimmune thyroid disease is the most likely cause of diffuse thyroid uptake, which are consistent with Lee et al. who indicated that the degree of incidental diffuse thyroid uptake of 18F-FDG is closely correlated with increased serum anti-microsomal antibody and TSH levels. Therefore, the most plausible pathological cause of diffuse thyroid uptake may be cell damage by an autoimmune mechanism [16]. Subclinical hypothyroidism with autoimmune thyroiditis was found to be the most common cause of diffuse thyroid uptake. In our study and other previous studies, it was found that other autoimmune thyroid disorders, such as Graves' disease and chronic autoimmune thyroiditis, may also cause diffuse thyroid uptake. Furthermore, the presence and degree of diffuse thyroid uptake appears to indicate the severity of thyroid cell damage caused by an autoimmune mechanism [17.[

In conclusion, the presence of diffuse thyroid uptake in people who have never had cancer is linked to thyroid disorders and to elevated risk of overt hypothyroidism or hyperthyroidism. As a consequence, clinical testing at both the baseline and follow-up will aid in the identification of people who have thyroid dysfunction. The most likely pathological cause of diffuse thyroid uptake is thyroid cell damage caused by an autoimmune process. Our findings suggest that incidental diffuse thyroid uptake can warrant additional diagnostic testing, such as thyroid function tests combined with a thyroid autoantibody analysis, to rule out the possibility of benign thyroid disease.

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