

Original Article

The relationship between positron emission tomography-computed tomography imaging and histopathological features of thyroid incidentalomas detected during follow-up for primary malignancy

ABSTRACT

Aim of the Study: While the rate of thyroid incidentaloma detected on positron emission tomography (PET) was reported as 4%, the malignancy rate was 14%–50%. We evaluated the thyroid nodules which were detected by PET-computerized tomography (CT) in cancer patients and analyzed the pathological results of those thyroid nodules diagnosed by fine needle aspiration biopsy (FNAB) and their correlation with the maximum standardized uptake (SUV_{max}) value and PET imaging features.

Materials and Methods: FNAB were performed for 40 thyroid incidentalomas. We analyzed the relationship between the histopathological findings and radiological features by Pearson's correlations and Chi-square-Fisher's exact tests to evaluate the factors associated with SUV_{max} .

Results: The median SUV_{max} values were 5.4 for thyroid nodules. Totally, 14 malignancies were detected by FNAB (35%). The sensitivity and specificity of SUV_{max} value for diagnosis of malignancy were 87.5% and 52%, respectively. Positive and negative predictive values were 36.8% and 92.8%. The most common malignant and benign pathologies were classic variant papillary carcinoma and benign colloid nodule. The median SUV_{max} was higher in colon cancer thyroid metastasis and oncocytic neoplasia (SUV_{max} 14.5 and 13.6, respectively). Histopathological type was not related with nodule size but positively associated with categorical SUV_{max} ($r = 0.318$, $P = 0.04$) and negatively correlated with both the density of the thyroid nodule in PET-CT ($r = -0.0042$, $P = 0.01$) and density of nodule in ultrasound (USG) ($r = -0.305$, $P = 0.05$). Margin of the thyroid nodule in USG ($P = 0.007$) and internal component of the nodule in PET ($P = 0.03$) were found to be important factors to differentiate benign or malignant lesion.

Conclusion: If the thyroid nodule is detected with flouro-2-deoxy-D-glucose uptake, to differentiate benign nodule from malignant, cytological examination is noteworthy to diagnose the more aggressive type of thyroid nodule and also thyroid metastasis from primary cancer.

KEY WORDS: Biopsy, malignancy, positron emission tomography-computerized tomography, thyroid incidentaloma

INTRODUCTION

Thyroid nodules have been reported in 5.3% of women and 0.8% of men.^[1] With improvements to radiological imaging modalities, incidental thyroid nodules are now found more frequently. Incidental thyroid nodules have been reported in 50%–60% of autopsy series without a palpable thyroid nodule clinically.^[2] Thyroid incidentaloma is an asymptomatic, unsuspected thyroid lesion that is diagnosed by an imaging study unrelated to the thyroid gland.^[3] These

lesions are detected by ultrasonography (USG), computerized tomography (CT) or flouro-2-deoxy-D-glucose (FDG) positron emission tomography (PET).^[3] The detection rates of thyroid incidentaloma by radiological modalities are 67% with USG, 16% with CT or MRI, and 2%–3% with

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PET.^[3] The risk of cancer in the thyroid nodules detected by USG is 1.5%–10%.^[4]

PET is a rapidly developing imaging modality which is used for diagnosis and tumor staging, to assess treatment response and to perform follow-up in oncology; it can also detect thyroid nodules incidentally.^[5] In contrast to USG or CT, PET provides not only the anatomical location of nodules, but it also provides information on metabolism and biological activity.^[6] FDG is trapped by metabolically active tissue so that tumor tissue may be seen as a hypermetabolic focus on PET imaging.^[3] Metabolic information, together with anatomical information detected by PET, means that detected thyroid incidentalomas are more likely to be malignant than thyroid incidentalomas detected by USG or CT.^[6] While the normal thyroid has no FDG activity on PET, abnormal FDG uptake in the thyroid gland may be benign or malignant. The risk of malignancy can be predicted by radiological features. Hypoechoogenicity, irregular margins, larger size, and punctate calcifications detected by USG increase the suspicion of malignancy.^[3,7] The sensitivity of these features to detect malignancy has been reported to be 94%.^[8] On the other hand, focal or unilateral FDG uptake on PET imaging is more likely to be associated with malignancies than diffuse uptake.^[3] Diffuse uptake is generally associated with benign diseases such as thyroiditis. It is difficult to differentiate benign from malignant thyroid incidentalomas based on maximum standardized uptake (SUV_{max}) values only.^[4]

The malignancy rate of thyroid incidentaloma detected by CT has been reported as 3.9%–11.3%.^[9] The prevalence of malignancy of thyroid incidentalomas detected by PET ranges from 14% to 47%.^[6] Metastatic involvement of the thyroid gland from a primary tumor was reported to be 1.2% in 162 patients with a known malignancy.^[10] The American Thyroid Association recommends fine needle aspiration biopsy (FNAB) for thyroid nodules >1 cm in diameter or nodules <1 cm in diameter with abnormal USG features.^[11]

The aim of our study was to evaluate thyroid nodules which were detected by PET-CT in patients with malignancy unrelated to thyroid cancer. We analyzed the pathological results of those thyroid nodules diagnosed by FNAB and their correlation with the SUV_{max} value and PET imaging features.

MATERIALS AND METHODS

The data of 1840 patients with primary malignancy were evaluated retrospectively. A total of 40 cancer patients with thyroid incidentaloma who had been followed up at two Medical Oncology Centers in Turkey between 2009 and 2014 were included in this study. All patients underwent FNAB to histopathological confirmation. Thyroid incidentalomas were detected by PET-CT, which were performed for diagnosis, staging, and treatment response assessments for a primary malignancy unrelated to the thyroid. Eligibility was limited to patients with a primary malignancy and patients who

had incidental thyroid nodules detected by FDG activity on PET-CT during diagnosis or treatment of a primary malignancy. Thyroid USG was performed; then, all patients underwent FNAB guided by thyroid USG. Patients with a known history of thyroid malignancy, patients who had insufficient primary disease information or thyroid nodule biopsy results, and patients who did not agree to undergo thyroid biopsy were excluded from the data analysis. All pathological slides of primary malignancies and thyroid nodules were re-evaluated to confirm the histopathological subtypes and the diagnosis of metastasis from known malignancies by an experienced cytopathologist at both centers.

Thyroid USG imagings were reported according to internal echogenicity, density, margins, and presence of calcifications. The presence of solidity, hypoechoogenicity, irregular margins, microlobulation, and microcalcification was accepted as USG abnormalities.^[7] PET-CT imagings were also evaluated according to thyroid nodule density, internal component, and SUV_{max} values. The age of the patients at diagnosis, primary tumor, histopathological type, tumor stage, thyroid nodule size, thyroid nodule size, and USG and PET-CT findings of thyroid nodules including data on the margins, internal components, density, presence of calcification, cervical lymphadenopathy, and history of cervical radiotherapy were retrospectively obtained from patient charts after written informed consent was obtained from patients or their relatives.

Statistical analysis

After SUV_{max} was obtained from the PET-CT images, it was categorized as 0, 2.2–2.9, 3–4.9, 5–6.9, 7–9.9, or >10. Histopathological diagnosis was also divided into benign or malignant. The clinicopathological factors of the patients were compared using the Chi-square and Fisher's exact tests according to the categorical data of the histopathological diagnosis. We also evaluated any factors associated with the SUV_{max} categories using the Chi-square and Fisher's exact tests. We analyzed the relationship between the histopathological findings and radiological features by Pearson's correlations. All *P* values are two-sided, and *P* < 0.05 was considered statistically significant. All data were analyzed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA) software.

RESULTS

In total, 40 cancer patients with a median age of 58 years (range: 36–84 years) were retrospectively analyzed. Most of the patients were female (*n* = 26, 65%). The primary malignancies were breast (37.5%), lung (20%), colon (17.5%), pancreatic (7.5%), renal cell carcinoma (5%), ovarian (5%), gastric cancer (2.5%), melanoma (2.5%), and sarcoma (2.5%) in order of frequency. Sixteen (40%) thyroid nodules were right sided and 18 nodules (45%) were left sided, whereas five presented with bilateral (12.5%) and one (2.5%) with an isthmus location. Only four patients had a history of previous

cervical radiotherapy, and seven patients had a history of thyroid disease such as goiter or hyper- or hypo-thyroidism.

Median thyroid nodule diameter was 18 mm (range: 8–59 mm). Thyroid USG revealed solid nodules in 50% of patients; in addition, 18 nodules were hypoechoic (45%), 11 nodules (27.5%) were microlobular, 15 (37.5%) had irregular margins, and three nodules (7.5%) had microcalcifications. Cervical lymphadenopathies were detected in four patients (10%) by USG or PET-CT. PET-CT detected 31 (77.5%) focal areas of thyroid uptake; 25 (62.5%) nodules detected by PET were hypoechoic, 27 (67.5%) were solid, and 30% had irregular margins. The results of the frequency of clinical and radiological features are shown in Table 1. The median SUV_{max} values were 5.4 (range: 0–17.8) and 8.5 (range: 0–23.9) for thyroid nodules and primary cancer, respectively [Figure 1].

In total, 14 malignancies (35%) were detected by FNAB in thyroid nodules. The sensitivity and specificity of the PET-CT SUV_{max} value for the diagnosis of malignancy were 87.5% and 52%, respectively. On the other hand, the positive and negative predictive values were 36.8% and 92.8%, respectively. While the most common malignant pathology was classic variant papillary carcinoma (25%), others included papillary carcinoma oncocytic variants (2.5%), papillary microcarcinoma (2.5%), and thyroid metastasis from colon carcinoma (2.5%). Benign colloidal nodules were the most frequent benign pathology (*n* = 18, 45%). The remaining benign pathologies were lymphocytic thyroiditis (10%), atypia with unknown significance (7.5%), and oncocytic neoplasia (2.5%). The median SUV_{max} was higher in thyroid metastasis from colon cancer and oncocytic neoplasia (median SUV_{max} 14.5 and 13.6, respectively) and lower in benign colloid nodules (median SUV_{max} 4) [Table 2]. Figure 2 shows the benign and malignant thyroid nodules detected by PET/CT.

Thyroid nodule USG margins (*P* = 0.007) and thyroid nodule PET internal components (*P* = 0.03) were found to be important factors to differentiate thyroid nodules as benign or malignant. Nodules with irregular margins on USG and hypoechoic nodules on PET-CT were more malignant histopathologically than hyperechoic nodules with regular margins. Although all malignant nodules had one of the USG abnormalities, this was not statistically significant (*P* = 0.07). Table 3 shows the relationship between the pathological, clinical, and radiological features of the detected thyroid nodules.

We could not find any correlation between nodule size and histopathological findings or SUV_{max} categorical values by the Pearson's correlation analysis. However, histopathologically benign or malignant nodules were positively associated with the SUV_{max} categories (*r* = 0.318, *P* = 0.04) and negatively correlated with the density of the thyroid nodule by PET-CT (*r* = -0.394, *P* = 0.01), the density of nodule by USG (*r* = -0.305, *P* = 0.05), and the stage of the primary tumor (*r* = -0.326, *P* = 0.04). Furthermore, SUV_{max} categorical values were negatively associated with primary malignancy

Table 1: The characteristics of the study group

Characteristics	<i>n</i> (%)
Gender	
Female	26 (65)
Male	14 (35)
Primary	
Malignancy	15 (37.5)
Breast	7 (17.5)
Colon	1 (2.5)
Gastric	2 (5)
RCC pancreas	3 (7.5)
Ovary	2 (5)
Lung	8 (20)
Sarcoma	1 (2.5)
Melanoma	1 (2.5)
Cervical RT	
Present	4 (10)
Absent	36 (90)
Thyroid disease	
Hypothyroid	4 (10)
Hyperthyroid	1 (2.5)
Goiter	2 (5)
Absent	33 (82.5)
Nodule location	
Right	16 (40)
Left	18 (45)
Bilateral	5 (2.5)
Isthmus	1
USG internal echogenicity	
Solid	20 (50)
Cystic	5 (12.5)
Mix	7 (17.5)
Unknown	8 (20)
USG echogenicity	
Hyper	7 (17.5)
Iso	10 (25)
Hypo	18 (45)
Unknown	5 (12.5)
Margin	
Microlobular	11 (27.5)
Circumscribed	7 (17.5)
Irregular	15 (37.5)
Unknown	7 (17.5)
Calcification	
Absent	32 (80)
Micro	3 (7.5)
Macro	1 (2.5)
Mix	1 (2.5)
Eggshell	2 (5)
Unknown	1 (2.5)
Cervical LAP	
Present	4 (10)
Absent	36 (90)
PET activity	
Focal	31 (77.5)
Unilateral	3 (7.5)
Bilateral	4 (10)
Diffuse	2 (5)
PET density	
Hyper	15 (37.5)
Hypo	25 (62.5)
PET internal component	
Solid	27 (67.5)
Cystic	8 (20)
Unknown	5 (12.5)
PET nodule margin	
Regular	12 (30)
Irregular	12 (30)

Contd...

Table 1: Contd...

Characteristics	n (%)
Diffuse	2 (5)
Unknown	14 (35)
Pathology	
Benign	26 (65)
Malignant	14 (35)
SUV _{max} nodule	
0	5 (10)
2.2-2.9	9 (12.5)
3-4.9	10 (22.5)
5-6.9	4 (25)
7-9.9	8 (10)
>10	4 (20)
Thyroid surgery	
Present	13 (32.5)
Absent	27 (67.5)

RT=Radiotherapy, LAP=Lymphadenopathy, FNAB=Fine needle aspiration biopsy, Ca=Cancer, RCC=Renal cell carcinoma, SUV_{max}=Maximum standardized uptake value, PET=Positron emission tomography, USG=Ultrasonography

($r = -0.399, P = 0.01$). Table 4 shows the results of the Pearson’s correlation analysis.

DISCUSSION

The frequency of thyroid nodules detected incidentally in PET-CT, which was performed for primary malignancy unrelated to thyroid cancer, has increased with widespread use of PET imaging in cancer patients. In the literature, the incidence of thyroid incidentaloma detected by PET is reported to be 2%–3%.^[6,12] In addition, the rate of malignancy has been reported as 14%–50% by histopathology in thyroid incidentaloma, which was determined by PET imaging.^[13] In a Korean study, 3% of thyroid incidentalomas were detected by PET imaging, which was performed for cancer screening in healthy subjects, but only two nodules (20%) were malignant.^[14] All patients in our study population had a primary malignancy. The retrospective evaluation of PET scans from 1330 patients detected thyroid incidentalomas in 2.2% of them. Fifteen patients underwent surgery, and a malignancy rate of 26.7% was reported.^[14] Another large series included PET imaging data on 4,252 patients and revealed 102 (2.3%) thyroid incidentalomas; malignancy was detected in seven nodules.^[15] We retrospectively analyzed the PET-CT data of 1,840 patients with malignancy and revealed 40 thyroid nodules with focal or diffuse FDG uptake (2.1%). FNAB is the main diagnostic modality to evaluate incidental thyroid nodules.^[3] The rate of tissue biopsy for thyroid incidentalomas detected by PET has been reported to occur in 1%–83% of patients in the literature.^[6] The most common malignancy detected by FNAB was papillary thyroid carcinoma, in the range of 81.3%–83%.^[16] All of our patients underwent FNAB to identify primary thyroid malignancy or metastasis from the primary tumor. Our results show that 14 malignant (35%) and 26 benign nodules were diagnosed, similar to rates in the literature. The most common malignant and benign lesions were classic papillary carcinoma (71.4%) and benign colloid nodule (69.2%), respectively. Two (14.2%)

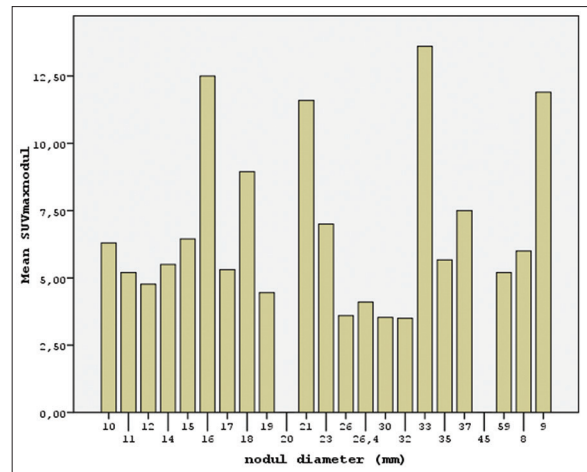


Figure 1: The histogram of standardized uptake value maximum and thyroid nodule size

thyroid nodules were diagnosed as papillary carcinoma oncocytic variants.

Clinically detectable thyroid nodules have a 5% of malignancy risk.^[17] A higher SUV_{max} of thyroid nodule on PET has been associated with a greater risk of malignancy.^[3] However, there is no definite SUV_{max} value that differentiates benign from malignant.^[18] If PET associated thyroid incidentaloma is diagnosed as malignant, it is usually a more aggressive histological type and has a worse prognosis.^[14] Increased FDG uptake may be associated with a more aggressive histological type,^[6] but there is controversy about the positive correlation between SUV_{max} values and malignancy potential.^[6] The FDG uptake pattern of thyroid nodules can predict the malignant potential of thyroid nodules. Unilateral and focal FDG uptake is more likely to be associated with malignancy.^[6] Focal uptake of FDG has been associated with a 34.8% risk of malignancy.^[19] Choi *et al.* showed that 17 out of 44 thyroid nodules with focal FDG uptake on PET were diagnosed histologically as malignant.^[4] Although we detected 31 nodules with focal FDG uptake, this was not related to malignancy. The prevalence of thyroid focal lesions on PET was 4% (70/1763) in the Choi *et al.*’s study.^[4] Diagnostic FNAB was performed on 29 of 70 patients, and 17 nodules were found to be malignant by histopathology. In the present study, the SUV_{max} of malignant lesions was higher than that of benign lesions (6.7 vs. 10.7, $P < 0.05$). Diffuse FDG uptake could indicate normal variation, chronic thyroiditis, or Graves’ disease.^[19] In the literature, 47.4% of 133 cases of thyroid diffuse uptake were diagnosed as autoimmune thyroiditis or hypothyroidism.^[20] Although 22.5% of our nodules showed diffuse FDG uptake, 65% of the FNAB results were benign, and this was not found to be an important factor to differentiate benign from malignant lesions.

There is no consensus on the role of SUV_{max} to differentiate benign from malignant thyroid nodules.^[19] A SUV_{max} cutoff value 9.1 has been reported as being sensitive (81.6%) and specific (100%) to diagnose malignant nodules^[21] Hales

Table 2: The pathological findings and maximum standardized uptake value of the thyroid nodules

Benign pathology	Malignant pathology	n	Median SUV _{max}
Oncocytic neoplasia		1 (2.5)	13.6
Lymphocytic thyroiditis		4 (10)	7.1
Atypia with unknown significance		3 (7.5)	3.1
Benign colloid nodule		18 (45)	4
	Classical papillary carcinoma	10 (25)	5.9
	Papillary microcarcinoma	1 (2.5)	6
	Papillary carcinoma oncocytic variant	2 (5)	5.9
	Colon carcinoma metastasis	1 (2.5)	14.5

SUV_{max}=Maximum standardized uptake value

Table 3: The comparison of characteristic in respect to pathological features

Characteristics	Benign (%)	Malignant (%)	P
Gender			
Female	16 (61.5)	10 (71.4)	0.5
Male	10 (38.5)	4 (29.6)	
Cervical RT			
Present	1 (3.8)	3 (21.4)	0.07
Absent	25 (95.2)	11 (78.6)	
USG internal			
Echogenicity			0.2
Solid cystic	10 (38.4)	10 (71.4)	
Mix	4 (15.3)	1 (7.2)	
Unknown	5 (19.2)	2 (14.2)	
USG echogenicity	7 (27.1)	1 (7.2)	
Hyper	4 (15.3)	3 (21.6)	0.1
Iso	8 (30.6)	2 (14.2)	
Hypo	9 (23.4)	9 (64.2)	
Unknown	5 (30.7)	0	
Margin			
Microlobular	8 (31)	3 (21.6)	0.007
Circumscribed	7 (27)	0	
Irregular	5 (19.5)	10 (71.4)	
Unknown	6 (22.5)	1 (7.1)	
Calcification			
Absent	23 (88.6)	9 (64.2)	0.2
Micro	1 (3.8)	2 (14.2)	
Macro	0	1 (7.2)	
Mix	0	1 (7.2)	
Eggshell	1 (3.8)	1 (7.2)	
Unknown	1 (3.8)	0	
Cervical LAP			
Present	3 (11.4)	1 (7.2)	0.6
Absent	23 (88.6)	13 (92.8)	
USG anomaly			
Present	21 (80.7)	14 (100)	0.07
Absent	5 (19.3)	0	
PET density			
Hyper	10 (50)	5 (45.7)	0.8
Hypo	10 (50)	9 (64.3)	
PET internal component			
Solid	14 (53.8)	13 (92.8)	0.03
Cystic	7 (26.9)	1 (7.2)	
Unknown	5 (19.3)	0	
SUV _{max} categorical			
2.2-2.9	5 (19.2)	0	0.09
3-4.9	7 (26.9)	2 (14.3)	
5-6.9	5 (19.2)	5 (35.7)	
7-9.9	4 (15.3)	0	
>10	3 (11.5)	5 (35.7)	
0	2 (7.9)	2 (14.3)	

RT=Radiotherapy, LAP=Lymphadenopathy, SUV_{max}=Maximum standardized uptake value, PET=Positron emission tomography, USG=Ultrasonography

et al. reported that the sensitivity and specificity of PET to predict malignancy of thyroid nodule are 57% and 50%, with

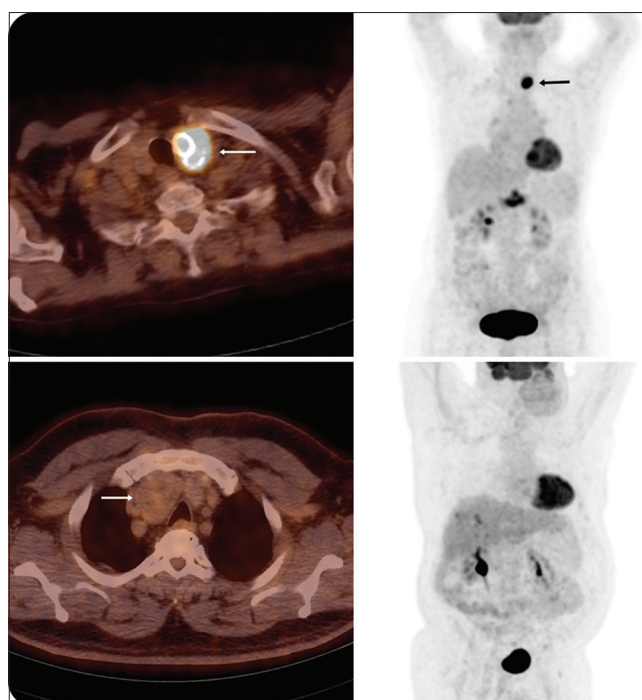


Figure 2: The positron emission tomography-computerized tomography imaging of patients with thyroid metastasis of colon cancer

positive and negative predictive values of 50% and 57%, respectively.^[14] However, these authors evaluated only eight FDG-positive patients. In one meta-analysis, it was shown that the sensitivity and specificity of PET for the detection of cancer in thyroid nodules were 89% and 55%, respectively.^[22] The best cutoff SUV_{max} value for differentiation was 2.05. In another study, it was reported that every unit increase in SUV_{max} is associated with poor survival.^[23] While we found that the sensitivity and specificity of PET-CT to identify malignancy were 87.5% and 52%, the positive and negative predictive values were 36.8% and 92.8%, respectively. The low positive predictive value of our results indicates that FDG uptake alone is not enough to predict malignancy. Therefore, the features of imaging combined with USG findings and FNAB may be more valuable.

Kim *et al.* reported that greater tumor and cervical lymph node metastasis detected by PET were associated with positive FDG uptake in thyroid cancer patients compared to FDG-negative patients. They reported 71.6% FDG uptake of thyroid cancer.^[24]

Table 4: The Pearson’s correlation analysis for the results of ultrasonography and positron emission tomography

	Nodule diameter (mm)	Age	Primary malignancy	Pathology categorical	Stage	USG internal component	PET integral component	SUV _{max} categorical
SUV _{max} categorical								
<i>r</i>	0.03	0.125	-0.399	0.318	-0.012	-0.159	-0.042	
<i>P</i>	0.8	0.4	0.01	0.04	0.9	0.3	0.7	
Pathology categorical								
<i>r</i>	-0.189	0.279	-0.260		-0.326	-0.305	-0.394	0.318
<i>P</i>	0.2	0.08	0.1		0.04	0.05	0.01	0.04

SUV_{max} =Maximum standardized uptake value, PET=Positron emission tomography, USG=Ultrasonography

Only 10% of our patients had FDG-positive cervical lymph nodes by imaging. Neither cervical lymph nodes nor a previous history of cervical radiotherapy was found to be related to malignancy.

Kao *et al.* analyzed 942 PET scans retrospectively and reported a 7% incidence of thyroid incidentaloma;^[25] 21 of the nodules were FDG-avid incidentalomas, while 45 were not FDG avid. Only six patients underwent FNAB, and malignancies were identified in three of them (two papillary, one medullary thyroid cancer). The positive predictive value of FDG-avid thyroid incidentaloma for underlying malignancy was 50%. These authors did not find a statistically significant relationship between the SUV_{max} value and malignancy potential. However, not all of their patients had malignancy. Mitchell *et al.*^[26] reported that 9 of 15 thyroid carcinomas were FDG positive (sensitivity of 60%). We found only four thyroid incidentalomas without FDG uptake on PET-CT, and 90% of thyroid incidentalomas had FDG uptake with a median SUV_{max} of 5.4. According to our histopathological findings, the median SUV_{max} was 4.5 and 6.1 for benign and malignant lesions, respectively (*P* = 0.09). In another study, Brindle *et al.* reported that 30 thyroid incidentalomas were further investigated by biopsy (37%), and seven malignant nodules (23%) were diagnosed.^[27] The median SUV_{max} were 5.4 and 9.9 for benign and malignant lesions, respectively. The most frequent primary malignancies associated with PET imaging were lung, colorectal, lymphoma, and esophageal cancer in order of frequency. These authors did not provide a convincing SUV_{max} to differentiate between benign and malignant lesions. The primary malignancies in our study were breast, lung, colon, and other cancers in order of frequency. PET-CT is mostly used in our oncology center for the staging of breast and lung cancer.

There is no exact factor predicting malignancy for thyroid incidentalomas. Thyroid nodule size has not been shown to predict malignancy,^[3] but the FDG uptake pattern is related to malignancy potential.^[6] We analyzed radiological factors to differentiate benign and malignant lesions and found that thyroid USG irregular margins and PET-CT solid components were associated with malignancy, but not the FDG uptake pattern. Although malignant lesions had a tendency toward a higher SUV_{max} than benign lesions, this was not statistically

significant (*P* = 0.09). SUV_{max} categorical values were positively related with pathological findings in the correlation analysis. Furthermore, benign or malignant lesions were negatively correlated with the stage of the primary disease, USG and PET lesion solidity. There was no relationship between tumor nodule diameter and radiological features.

The risk of malignancy among thyroid incidentalomas detected by PET is 47%,^[6] so tissue diagnosis is required, especially to differentiate aggressive forms of thyroid carcinoma or primary cancer thyroid metastases. All of our patients had a known malignancy, so decisions regarding thyroid nodules depended on the stage of the primary malignancy. Although thyroid cancer has an indolent nature, thyroid metastases and oncocytic type papillary carcinoma have aggressive features. Although the thyroid is a rare site for tumor metastasis,^[19] the rate of metastasis has been reported to be 3.9%–24.2%.^[19] Renal cell, breast, and lung cancer are the most common primary tumors which can metastasize to the thyroid, whereas colorectal cancer metastases are rarely seen and are rather associated with lung and liver metastases.^[28] Choi *et al.* reported that one metastasis from esophageal carcinoma and 16 papillary carcinomas were detected by biopsy of incidental thyroid nodules.^[4] Similarly, only one of our 14 (7.1%) malignant thyroid nodules was metastatic from colon cancer. Because of this solitary thyroid metastasis without extra-thyroid metastases, this patient underwent total thyroidectomy with curative intent and was followed without disease for 12 months.

CONCLUSION

PET is a rapidly developing imaging modality. Although incidental thyroid uptake on PET is commonly related to benign histopathology, malignancy is detected one-third of these lesions by biopsy. FDG-avid malignant thyroid nodules such as oncocytic variants or metastases from the primary tumor tend to be a more undifferentiated and more aggressive histopathological type. Recognition of the pattern of FDG uptake and SUV_{max} combined with USG findings can guide appropriate treatment.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, *et al.* The spectrum of thyroid disease in a community: The Whickham survey. *Clin Endocrinol (Oxf)* 1977;7:481-93.
2. Furmanchuk AW, Roussak N, Ruchti C. Occult thyroid carcinomas in the region of Minsk, Belarus. An autopsy study of 215 patients. *Histopathology* 1993;23:319-25.
3. Jin J, McHenry CR. Thyroid incidentaloma. *Best Pract Res Clin Endocrinol Metab* 2012;26:83-96.
4. Choi JY, Lee KS, Kim HJ, Shim YM, Kwon OJ, Park K, *et al.* Focal thyroid lesions incidentally identified by integrated 18F-FDG PET/CT: Clinical significance and improved characterization. *J Nucl Med* 2006;47:609-15.
5. Hall NC, Kloos RT. PET imaging in differentiated thyroid cancer: Where does it fit and how do we use it? *Arq Bras Endocrinol Metabol* 2007;51:793-805.
6. Katz SC, Shaha A. PET-associated incidental neoplasms of the thyroid. *J Am Coll Surg* 2008;207:259-64.
7. Yoon JH, Cho A, Lee HS, Kim EK, Moon HJ, Kwak JY, *et al.* Thyroid incidentalomas detected on 18F-fluorodeoxyglucose-positron emission tomography/computed tomography: Thyroid imaging reporting and data system (TIRADS) in the diagnosis and management of patients. *Surgery* 2015;158:1314-22.
8. Kim EK, Park CS, Chung WY, Oh KK, Kim DI, Lee JT, *et al.* New sonographic criteria for recommending fine-needle aspiration biopsy of nonpalpable solid nodules of the thyroid. *AJR Am J Roentgenol* 2002;178:687-91.
9. Shetty SK, Maher MM, Hahn PF, Halpern EF, Aquino SL. Significance of incidental thyroid lesions detected on CT: Correlation among CT, sonography, and pathology. *AJR Am J Roentgenol* 2006;187:1349-56.
10. Are C, Hsu JF, Schoder H, Shah JP, Larson SM, Shaha AR, *et al.* FDG-PET detected thyroid incidentalomas: Need for further investigation? *Ann Surg Oncol* 2007;14:239-47.
11. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, *et al.* Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2009;19:1167-214.
12. Are C, Hsu JF, Ghossein RA, Schoder H, Shah JP, Shaha AR, *et al.* Histological aggressiveness of fluorodeoxyglucose positron-emission tomogram (FDG-PET)-detected incidental thyroid carcinomas. *Ann Surg Oncol* 2007;14:3210-5.
13. Van den Bruel A, Maes A, De Potter T, Mortelmans L, Drijkoningen M, Van Damme B, *et al.* Clinical relevance of thyroid fluorodeoxyglucose-whole body positron emission tomography incidentaloma. *J Clin Endocrinol Metab* 2002;87:1517-20.
14. Kang KW, Kim SK, Kang HS, Lee ES, Sim JS, Lee IG, *et al.* Prevalence and risk of cancer of focal thyroid incidentaloma identified by 18F-fluorodeoxyglucose positron emission tomography for metastasis evaluation and cancer screening in healthy subjects. *J Clin Endocrinol Metab* 2003;88:4100-4.
15. Cohen MS, Arslan N, Dehdashti F, Doherty GM, Lairmore TC, Brunt LM, *et al.* Risk of malignancy in thyroid incidentalomas identified by fluorodeoxyglucose-positron emission tomography. *Surgery* 2001;130:941-6.
16. Soelberg KK, Bonnema SJ, Brix TH, Hegedüs L. Risk of malignancy in thyroid incidentalomas detected by 18F-fluorodeoxyglucose positron emission tomography: A systematic review. *Thyroid* 2012;22:918-25.
17. Hegedüs L. Clinical practice. The thyroid nodule. *N Engl J Med* 2004;351:1764-71.
18. Bertagna F, Giubbini R. F18-FDG-PET/CT thyroid incidentalomas and their benign or malignant nature: A critical and debated issue. *Ann Nucl Med* 2011;25:151-2.
19. Agrawal K, Weaver J, Ngu R, Krishnamurthy Mohan H. Clinical significance of patterns of incidental thyroid uptake at (18)F-FDG PET/CT. *Clin Radiol* 2015;70:536-43.
20. Karantanis D, Bogsrud TV, Wiseman GA, Mullan BP, Subramaniam RM, Nathan MA, *et al.* Clinical significance of diffusely increased 18F-FDG uptake in the thyroid gland. *J Nucl Med* 2007;48:896-901.
21. Agrawal K, Weaver J, Ul-Hassan F, Jeannon JP, Simo R, Carroll P, *et al.* Incidental Focal Thyroid Uptake on 18F-FDG PET Study d Large Retrospective Single Centre Experience in the United Kingdom. In: 27th Annual Congress of the European Association of Nuclear Medicine, 18e22 October, Gothenburg, Sweden; 2014. Abstract No. OP 693; 2014.
22. Wang N, Zhai H, Lu Y. Is fluorine-18 fluorodeoxyglucose positron emission tomography useful for the thyroid nodules with indeterminate fine needle aspiration biopsy? A meta-analysis of the literature. *J Otolaryngol Head Neck Surg* 2013;42:38.
23. Pryma DA, Schöder H, Gönen M, Robbins RJ, Larson SM, Yeung HW, *et al.* Diagnostic accuracy and prognostic value of 18F-FDG PET in hürthle cell thyroid cancer patients. *J Nucl Med* 2006;47:1260-6.
24. Kim BS, Kim SJ, Kim IJ, Pak K, Kim K. Factors associated with positive F-18 flurodeoxyglucose positron emission tomography before thyroidectomy in patients with papillary thyroid carcinoma. *Thyroid* 2012;22:725-9.
25. Kao YH, Lim SS, Ong SC, Padhy AK. Thyroid incidentalomas on fluorine-18-fluorodeoxyglucose positron emission tomography-computed tomography: Incidence, malignancy risk, and comparison of standardized uptake values. *Can Assoc Radiol J* 2012;63:289-93.
26. Mitchell JC, Grant F, Evenson AR, Parker JA, Hasselgren PO, Parangi S, *et al.* Preoperative evaluation of thyroid nodules with 18FDG-PET/CT. *Surgery* 2005;138:1166-74.
27. Brindle R, Mullan D, Yap BK, Gandhi A. Thyroid incidentalomas discovered on positron emission tomography CT scanning – Malignancy rate and significance of standardised uptake values. *Eur J Surg Oncol* 2014;40:1528-32.
28. Wychulis AR, Beahrs OH, Woolner LB. Metastasis of carcinoma to the thyroid gland. *Ann Surg* 1964;160:169-77.