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The Role of Metabolic Volumetric Parameters in Predicting Malignancy in Incidental Thyroid Nodules Detected in ^{18}F-FDG PET/CT Scans

^{18}F-FDG PET/BT Taramalarında Tespit Edilen Tesadüfi Tiroid Nodüllerinde Maligniteyi Öngörmede Metabolik Volumetrik Parametrelerin Rolü

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Abstract

Objectives: The metabolic activities of tumors can be calculated volumetrically during positron emission tomography/computed tomography (PET/CT) imaging using metabolic tumor volume (MTV) and total lesion glycolysis (TLG). This study aimed to evaluate the roles of MTV and TLG in predicting the malignancy risk of incidental thyroid nodules detected by PET/CT imaging.

Methods: Active metabolic areas of each section were manually drawn by region of interest to calculate the MTV of nodules, and all obtained values were then summed. TLG, the product of mean standardized uptake value and MTV, was calculated by multiplying two values. All participants underwent thyroid ultrasonography imaging. All nodules were divided into risk classes according to the European Thyroid Image Reporting and Data System (EU-TIRADS) that was developed by the European Thyroid Association. The American Thyroid Association Guidelines were used to determine which thyroid nodules would undergo thyroid fine-needle biopsy (FNAB). Results were classified according to the Bethesda scoring system.

Results: TLG levels were significantly higher in malignant or malignant-suspicious nodules than in benign nodules (p=0.013). Although MTV levels were high in malignant or malignant-suspicious nodules than in benign and non-diagnostic nodules, it was statistically insignificant at limit values (p=0.079). Areas under curve (AUC) were 0.726 (p=0.005) and AUC: 0.668 (p=0.039) for TLG and MTV, respectively. The 2.3 g cut-off value of TLG has a sensitivity of 85.7% and specificity of 59.0%. The 1.7 mL cut-off value of MTV has a sensitivity of 78.6% and specificity of 60.4%.

Conclusion: We believe that TLG evaluation will be useful in predicting high-risk malignancy or malignancy suspicion based on EU-TIRADS risk classification of incidental thyroid nodules detected in PET/CT images. We believe that unnecessary thyroid FNABs can be avoided for thyroid incidental nodules if such relation and cut-off values are determined and that it will be useful in hastening the operation of the necessary patients.

Keywords: Metabolic tumor volume, total lesion glycolysis, incidental thyroid nodules, ^{18}F-FDG PET/CT scans

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Öz

Amaç: Tümörlerin metabolik aktivitesi pozitron emisyon tomografi/bilgisayarlı tomografinin (PET/BT) görüntüleme sırasında hacimsel olarak hesaplanabilir. Bunlar metabolik tümör hacmi (MTV) ve toplam lezyon glikolizidir (TLG). Bu çalışmanın amacı, PET/BT görüntüleme ile saptanan tesadüfi tiroid nodüllerinde malignite riskini tahmin etmede hacimsel olarak metabolik aktivite gösteren MTV ve TLG'nin rollerini değerlendirmektir.

Yöntem: Nodülün MTV'sini hesaplamak için, her bölümün aktif metabolik aktif lezyonlara ilgi alanları ile manuel olarak çizildi; daha sonra elde edilen tüm değerler toplandı. Ortalama standardize uptake değeri ve MTV'nin ürünü olan TLG, iki değer çarpılarak hesaplandı. Tüm katılımcıların tiroid ultrasonografileri yapıldı. Tüm nodüller, Avrupa Tiroid Birliği (ETA) tarafından geliştirilen "EU-TIRAD"a göre risk sınıflarına ayrıldı. ATA Kılavuzu'na göre hangi tiroid nodüllerinin tiroid İİAB geçireceğine karar verildi. Sonuçlar Bethesda puanlama sistemine göre verildi

Bulgular: TLG düzeyleri, benign nodüllere göre malign veya malign-şüpheli nodüllerde anlamlı olarak yüksekti (p=0,013). MTV düzeyleri malign veya malign-şüpheli nodüllerde benign ve tanısal olmayan nodüllere göre yüksek olmasına rağmen sınır değerlerde istatistiksel olarak anlamlı değildi (p=0,079). Eğri altındaki alan (AUC) TLG için 0,726 (p=0,005) olarak hesaplandı. TLG için 2,3 g kesme değeri için duyarlılık %85,7 ve özgüllük %59,0 olarak bulundu. MTV için AUC 0,668 olarak hesaplandı (p=0,039). MTV için 1,7 mL cut-off için duyarlılık %78,6, özgüllük ise %60,4 idi.

Sonuç: PET/BT ile saptanan tesadüfi tiroid nodüllerinde, yüksek riskli malignite veya malignite şüphesine sahip olma açısından TLG değerlendirmesinin, EU-TIRADS'ye göre yüksek ve çok yüksek riskinin tahmin edilmesinde faydalı olacağına inanıyoruz. Böyle bir ilişki ve kesim değerlerinin kesin olarak tespit edilmesi durumunda, tiroid tesadüfi nodüller için gereksiz tiroid İİAB'lerinden kaçınılabileceğini ve gerekli hastaların ameliyatının geciktirilmemesi açısından faydalı olacağını düşünüyoruz.

Anahtar kelimeler: Metabolik tümör hacmi, toplam lezyon glikoliz, tesadüfi tiroid nodülleri, ^{18}F-FDG PET/BT taramaları

Introduction

Thyroid cancers account for 3.0% of all new cancer cases and 0.4% of all cancer deaths, and its prevalence is increasing worldwide (1). Positron emission tomography/computed tomography (PET/CT) imaging is recently being used for various diseases, especially in malignancies. Thyroid nodules, called thyroid incidentalomas, are detected by chance in approximately 1-4% of cases during these tomographies (2). ^{18}Flor-fluorodeoxyglucose (^{18}F-FDG) PET/CT is an examination that determines the metabolic activity of tumors. The highest metabolic activity point of tumors is referred as the maximum standardized uptake value (SUV_{max}) (3). There is no sufficient evidence in previous studies to support that SUV_{max} is beneficial in determining the malignancy risk in thyroid incidentalomas (4,5,6). The metabolic activity of tumors can be calculated volumetrically during PET/CT imaging using metabolic tumor volume (MTV) and total lesion glycolysis (TLG). MTV is a semi-quantitative parameter that has prognostic clinical value in many malignancies, whereas TLG is also a semi-quantitative parameter that corresponds to the cell mass of the target lesion associated with ^{18}F-FDG involvement (7). It is unknown whether MTV and TLG have roles in determining the malignancy risk in thyroid incidentalomas.

All thyroid incidentalomas detected with other imaging methods must be evaluated using thyroid ultrasonography imaging (USI) (8). This determines the localization, size, echo structure, nodule shape, and image characteristics (echogenicity, calcifications, edge layout, halo presence, blood flow, and extrathyroidal spread presence) of the nodule and the presence of lymphadenopathy (9). Malignancy risk is classified based on the USI findings, and it is decided whether or not to conduct thyroid fine-needle biopsy (FNAB) according to the European Thyroid Image Reporting and Data System (EU-TIRADS) developed by the European Thyroid Association (ETA) (10).

The contribution of PET/CT images to thyroid USI in determining the malignancy risk will enable more accurate decisions to be made in determining patients who will undergo thyroid FNAB or surgical intervention in cases with thyroid incidentaloma. This study aimed to evaluate the roles of MTV and TLG, which determine metabolic activity volumetrically, in predicting the malignancy risk of incidental thyroid nodules detected by PET/CT imaging.

Materials and Methods

The study was approved by Süleyman Demirel University Ethics Board (date: 13.02.2020, approval number: 37). After screening the archives, written and verbal information about the study was given to the participants. Consent was obtained from the patients before they were included in the study. Data of 6.480 patients who underwent ^{18}F-FDG PET/CT screening for non-thyroid malignancy or other reasons at our clinic between 2017 and 2020 were evaluated retrospectively. The hypometabolic and hypermetabolic thyroid nodules detected during this screening were described as thyroid incidentaloma. Thyroid incidentalomas were detected in 190 (2.93%) patients who underwent PET/CT scans. A total of 101 of these patients (63 women and 38 men) and 153 nodules were included in the study. The inclusion criteria were as follows: (a) No previous thyroid disease (no history of benign or malignant thyroid nodules), (b) no history of thyroidectomy, (c) no diffuse involvement in the thyroid during PET/CT, (d) thyroid FNAB and thyroid USIs performed in our hospital, and (e) consent to participate in the study. The design of the study is shown in Figure 1. The primary cancers and cancer rates of the patients included in the study are given in Table 1.

Thyroid USI Evaluation: An experienced endocrinologist (H.K.) performed the thyroid USIs for all participants using the Philips EPIQ 5 Device (Germany). The largest sizes of all thyroid nodules, their structures (cystic, solid, dominant cystic, or dominant solid), echogenicity (hypoechoic, isoechoic, or hyperechoic), halo (thin, thick, or irregular), border layout (regular or irregular), vascularity evaluation with Doppler (intranodular blood build-up, perinodular blood build-up, or no blood build-up), and calcifications (micro-macro or nucleus qualifications) were evaluated. All nodules were divided into risk classes according to EU-TIRADS that was developed by the ETA.

Implementation of Thyroid FNAB: The American Thyroid Association Guidelines were used to determine which thyroid nodules would undergo thyroid FNAB (2). The procedure was performed by a single endocrinologist (H.K.) using a 10 cc injector and 22 G needle tip as stated in the USI guide. At least two slides that were air dried were sent to the pathology laboratory on the same day in a closed container with liquid-based cytology solution and the remaining material.

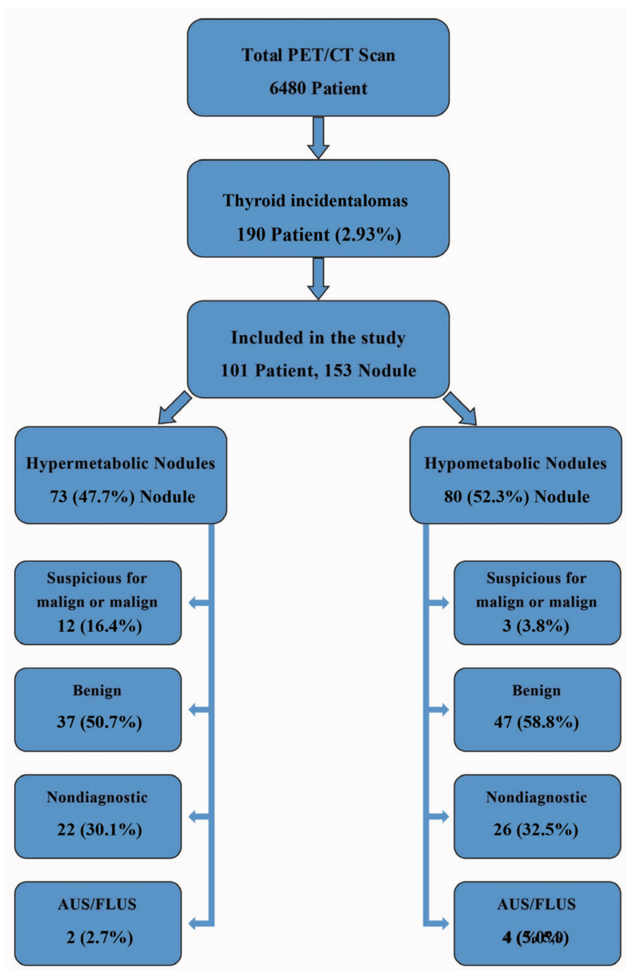

Figure 1. The design of the study

AUS/FLUS: Cytological atypia/follicular lesion of undetermined significance, PET/CT: Positron emission tomography/computed tomography

Table 1. Characteristics of patients included in the study

Variables	
Age (years)	63.72±12.22
Gender (male/female)	63/38
TSH (mIU/L)	1.04±1.7
Thyroid nodule diameter (mm)	19±12
Hypermetabolic/hypometabolic (n)	73/80
Bethesda scoring	
NDS Benign AUS/FLUS Suspicious for malign/malign	48 (31.4%) 84 (54.9%) 6 (3.9%) 15 (9.8%)
Primary cancer	
Breast cancer	19 (18.8%)
Laryngeal cancer	2 (2.0%)
Endometrial cancer	7 (6.9%)
Lung cancer	2 (2.0%)
Bladder cancer	1 (1.0%)
Lymphoma	8 (7.9%)
Rectal cancer	3 (3.0%)
Ovarian cancer	3 (3.0%)
Nasopharyngeal cancer	3 (3.0%)
Colon cancer	8 (7.9%)
Renal cell cancer	2 (2.0%)
Squamous cell carcinoma (skin)	1 (1.0%)
Malignant melanoma	2 (2.0%)
Gastric cancer	3 (3.0%)
Mediastinal mass	3 (3.0%)
Adrenal mass	1 (1.0%)
Breast mass	2 (2.0%)
Pancreatic mass	2 (2.0%)
Vertebral mass	1 (1.0%)
Small intestine mass	1 (1.0%)
Solitary pulmonary nodule	13 (12.9%)
Lung mass	14 (13.9%)
Fever of unknown cause	1 (1.0%)

TSH: Thyroid-stimulating hormone, NDS: Non-diagnostic, AUS/FLUS: Cytological atypia/follicular lesion of undetermined significance

Histopathological Evaluation: An experienced pathologist (M.Ç.) evaluated all the test samples. Samples sent on air-dried glasses were stained with Giemsa stain, whereas those sent in liquid were stained with hematoxylin-eosin, Giemsa, and Papanicolaou stains. At least four slides were prepared, and cytopathological evaluation was performed. Results were classified as non-diagnostic, benign, cytological atypia/follicular lesion of undetermined significance (AUS/FLUS), follicle neoplasia suspicion, malignancy-suspicious, and malignant according to the Bethesda scoring system (11). Nodules that were suspected to be malignant were considered malignant. The malignant and benign nodules were statistically evaluated.

PET/CT Protocol and Image Analysis: All PET/CT examinations were conducted using the Philips GEMINI TF PET/CT scanner (Philips Medical Systems, Cleveland, Ohio, USA) with time-of-flight imaging and a 64-slice CT scanner. Patients were prohibited from consuming caffeine, alcohol, and nicotine 24 h before the procedure. The blood sugar concentrations of all patients after 6 h of fasting were measured using a glucometer device (120 and 200 mg/dL for non-diabetic and diabetic patients, respectively). Then, intravenous 3.7 MBq/kg (0.1 mCi/kg) ^{18}F-FDG injection was given. All patients were orally hydrated with 1.5 L contrast during the 60-min waiting period. CT scan was performed first, followed by a PET scan (Figure 2). Three experienced nuclear medicine specialists (S.S.Ş., M.Y., and M.E.) evaluated the PET and CT images (non-corrected and attenuation-corrected) in rotating maximum intensity projection and cross-sectional view (transverse-sagittal-coronal). The highest ^{18}F-FDG involvement value in the thyroid nodules was determined using the semi-quantitative SUV_{max} value, is the highest activity involvement area in the nodules. The SUV_{max} value was calculated using the following formula: SUV_{max}: maximum activity in the range of interest (MBq/mL)/[injected dose (MBq)/body weight (g)] To calculate the MTV of nodules, active metabolic areas of each section were manually drawn by region of interest, and all obtained values were then summed. Meanwhile, TLG is the product of SUV_{mean} and MTV values.

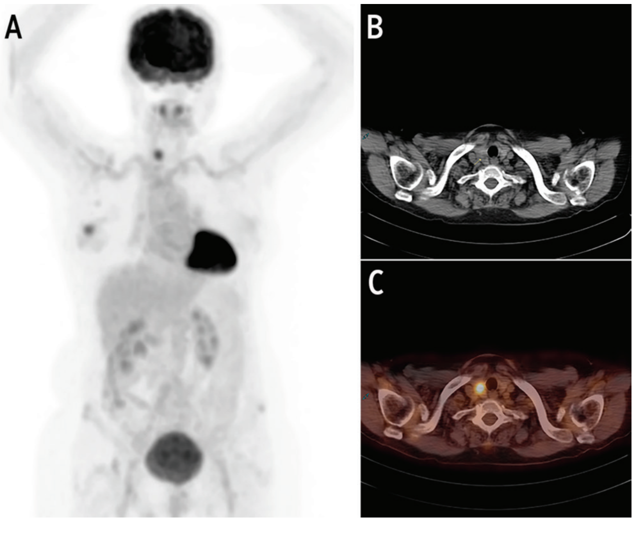

Figure 2. PET/CT findings of a breast cancer-diagnosed patient. Primary tumor in the right breast and hypermetabolic thyroid nodule in the right lobe of the thyroid gland were seen in the (A) total body PET maximum intensity projection image, (B) axial CT image, and (C) axial PET/CT fusion image

PET/CT: Positron emission tomography/computed tomography

Statistical Analysis

The Shapiro-Wilk test was used to evaluate the fitness of continuous variables to the normal distribution. The Kruskal-Wallis test was used to compare groups for variables that were not normally distributed. The Bonferroni-corrected Mann-Whitney U test was used to determine differences in variables between the groups. The comparison of categorical data was performed using the chi-square test. The diagnostic power of the possibility of malignant or premalignant results in incidental thyroid nodules using PET/CT imaging was evaluated with the receiver operating characteristic (ROC) curve analysis. The highest cutoff value for the sensitivity and specificity of these parameters in determining the malignancy risk was also calculated. Statistical Package for Social Sciences for Windows version 22.0 was used for statistical analyses, and $p<0.05$ was considered statistically significant.

Results

Of the 153 thyroid incidentalomas (9.8%) included in the study, 15 had malignant or malignant-suspicious histopathology. Of the thyroid nodules examined, 73 (47.7%) were hypermetabolic and 80 (52.3%) hypometabolic. Results of the thyroid FNABs for hypermetabolic nodules found that 12 (16.4%) were malignant or malignant-suspicious, 37 (50.7%) benign, 22 (30.1%) non-diagnostic, and 2 (2.7%) AUS/FLUS. Of the hypometabolic nodules, 3 (3.8%) were malignant or malignant-suspicious, 47 (58.8%) benign, 26 (32.5%) non-diagnostic, and 4 (5.0%) AUS/FLUS. The median level of thyroid-stimulating hormone was 1.04±1.7, and all of the cases included in the study were euthyroid.

The largest dimensions of the nodules were between 8 and 80 mm, and the median size was 19±12 mm in the thyroid USI evaluations.

No significant differences were detected in nodule size in PET/CT incidental thyroid nodules between the groups as a result of thyroid FNAB according to the Bethesda classification (p=0.063).

According to USI risk scoring, 6 (3.9%) of the nodules were EU-TIRADS 3, 44 (28.8%) EU-TIRADS 4, and 103 (67.3%) EU-TIRADS 5. No significant differences were detected in EU-TIRADS scores among the groups as a result of thyroid FNAB according to the Bethesda scoring system (p=0.488).

The PET/CT and USI findings of the PET/CT incidental thyroid nodules according to the Bethesda score are given in Table 2. SUV_{max} levels were significantly higher in malignant or malignant-suspicious nodules than in benign and non-diagnostic nodules (p<0.001 and p=0.002, respectively). SUV_{mean} levels were significantly higher in malignant or malignant-suspicious nodules than in benign and non-diagnostic nodules (p<0.001 and p=0.001, respectively). TLG levels were significantly higher in malignant or malignant-suspicious nodules than in benign nodules (p=0.013). Although MTV levels were high in malignant or malignant-suspicious nodules than in benign and non-diagnostic nodules, it was statistically insignificant at limit values (p=0.079).

The diagnostic power of the variables in predicting the risk of being malignant or malignant-suspicious in the incidental thyroid nodules detected in PET/CT scan were evaluated using ROC analysis. As shown in the ROC, the area under curve (AUC) was 0.827 (p<0.001) for SUV_{max}. The 2.4 cut-off value of SUV_{max} has a sensitivity of 85.7% and specificity of 71.2. AUC was 0.812 (p<0.001) for SUV_{mean}. The 1.8 cut-off value of SUV_{mean} has a sensitivity of 78.6% and specificity of 69.1%. AUC was 0.726 (p=0.005) for TLG. For the 2.3 g cut-off value of TLG, the sensitivity and specificity were 85.7% and 59.0%, respectively. AUC for MTV was 0.668 (p=0.039). For the 1.7 mL cut-off value of MTV, the sensitivity was 78.6% and specificity 60.4% (Figure 3).

Discussion

In this study, SUV_{max} and TLG were found useful in determining the risk of malignant and malignant-suspicious nodules with TFNB indication based on EU-TIRADS risk classification in thyroid nodules detected in PET/CT images. To the best of our knowledge, this study is the first to show a TLG increase in thyroid incidentalomas detected with PET/CT in malignant and malignant-suspicious lesions in thyroid FNAB than in benign ones.

Thyroid incidentaloma is detected in approximately 1.6-2.46% of patients during PET/CT imaging (12,13). Similar to the literature, in this study, thyroid incidentaloma was

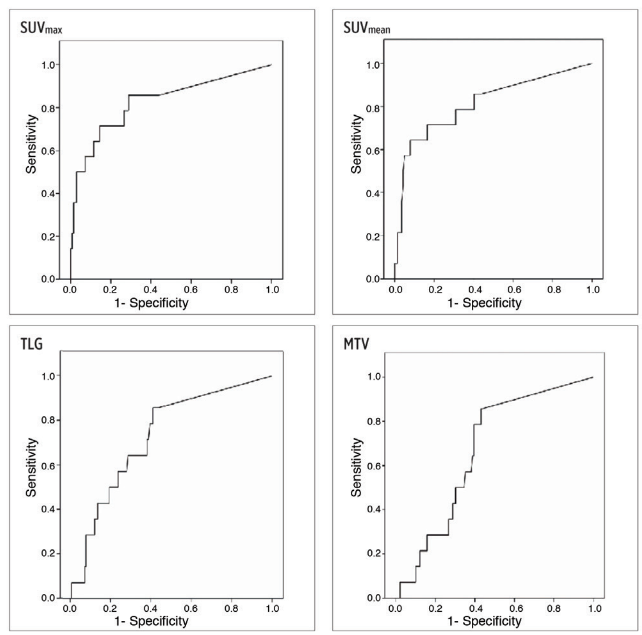

Figure 3. ROC analysis of PET parameters in predicting the risk of malignancy of thyroid incidentalomas

ROC: Receiver operating characteristic, PET: Positron emission tomography, SUV: Standardized uptake value, TLG: Total lesion glycolysis, MTV: Metabolic tumor volume

Table 2. PET/CT and USG findings according to Bathesda scoring of thyroid FNAB results

	Benign	Suspicious for malign/malign	AUS/FLUS	NDS	p
SUV_{mean}	1.01±1.32	2.80±1.79[a, b]	0.97±1.52	1.06±1.28	**0.002**
SUV_{max}	1.60±2.18	5.33±2.93[a, b]	1.59±2.53	1.64±2.07	**0.001**
MTV (mL)	3.80±7.52	5.76±9.78	1.05±1.66	3.89±7.55	0.166
TLG (g)	10.46±24.34	21.14±37.51[a]	3.12±5.13	8.33±16.41	**0.042**
EU-TIRADS	5±1	5±0.0	5±1	5±1	0.488
Nodule diameter (mm)	22±15	18±14	15.5±5	17±9	0.063

[a]Significantly different from benign (p<0.013), [b]Significantly different from NDS (p<0.013), PET/CT: Positron emission tomography/computed tomography, FNAB: Fine-needle biopsy, SUV: Standardized uptake value, MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, EU-TIRADS: European Thyroid Imaging and Reporting Data System, AUS/FLUS: Cytological atypia/follicular lesion of undetermined significance, NDS: Non-diagnostic

detected in 2.93% of cases. The malignancy rates of these thyroid incidentalomas detected with PET/CT vary between 10% and 64% (12). In this study, on the other hand, malignancy was detected in 9.8% of incidental thyroid nodules. Of the 153 nodules included in the study, 47.7% were hypermetabolic, and 16.4% of the thyroid FNAB results of hypermetabolic nodules were malignant. In the meta-analyses of Soelberg et al. (12) and Bertagna et al. (13), the malignancy rates of hypermetabolic nodules were 34.8% and 34.6%, respectively. It is possible that the low malignancy rate in all thyroid incidentalomas and hypermetabolic thyroid incidentalomas was due to the high proportion of patients with biopsy compared with the literature. In addition, the high rate (31.3%) of non-diagnostic cytology in the study may contribute to the low malignity rate. In our study, thyroid FNAB was performed in 101 (53.15%) of 190 patients with thyroid incidentaloma. In the meta-analyses of Soelberg et al. (12) and Bertagna et al. (13), this rate was 46% and 35%, respectively. The similar rates in both meta-analyses can be explained with the inclusion of the same articles in the study.

No consensus has yet been reached on using SUV_{max} to predict malignancy. In the thyroid incidentalomas detected using PET/CT scan, only half of the studies in the literature found that the relation of SUV_{max} with malignancy is at a statistically significant level. A significant cut-off SUV_{max} value for malignancy was given in very few studies (12,13). In this study, higher ^{18}F-FDG intake was detected in patients who had suspected malignancy or malignancy as a result of thyroid FNAB from among thyroid incidentalomas. The mean SUV_{max} values in benign and malignant/malignant-suspicious lesions were 1.60±2.18 and 5.33±2.93 (p=0.001), respectively. The coincidence rate in terms of SUV_{max} was low between the benign, malignant, and malignant-suspicious groups. The cutoff value of SUV_{max} was 2.4 for predicting malignant or malignant-suspicious lesions. In a meta-analysis that included 22 studies, Soelberg et al. (12) found a significant relation between SUV_{max} and malignancy in eight studies. They found that the SUV_{max} values of benign and malignant lesions were 4.8±3.1 and 6.9±4.7, respectively (p<0.001) (11). The median SUV_{max} was higher in the benign and malignant groups than in our study.

Makis and Ciarallo (14) found a statistically significant difference in SUV_{max} between benign (mean SUV_{max} 4.8) and malignant thyroid incidentalomas (mean SUV_{max} 6.3); however, since there was a wide overlap of SUV_{max} values between the two, a significant SUV_{max} cut-off value was not determined. Kumar et al. (15) detected increased ^{18}F-FDG involvement in 55 of 1.016 patients for non-thyroid reasons (prevalence 2.26%). No significant difference was detected in their study between the mean SUV_{max} of benign and malignant thyroid incidentalomas (p=0.386). Although the incidence of thyroid incidentaloma is similar to that in our study, no significant differences were detected in SUV_{max} values between benign and malignant and malignant-suspicious lesions in our study. The reason for this might be that glucose transporter 1 expression, which plays an important role in the cell intake of ^{18}F-FDG, varies according to the differentiation in thyroid cancers (16). Barrio et al. (17) detected malignancies in 21 (21.4%) of 98 thyroid incidentalomas, which had focal ^{18}F-FDG involvement in 6.216 PET/CT scans. Similar to our study, they detected a statistically significant difference between benign and malignant thyroid incidentalomas in terms of SUV_{max}. To predict malignancy, the cut-off value of SUV_{max} was >2.

The number of studies conducted on volume-based metabolic parameters is quite limited in thyroid incidentalomas detected with ^{18}F-FDG PET/CT. Kim et al. (18) evaluated the predictive value of volume-based metabolic parameters (MTV and TLG) for pathological lateral lymph node metastasis (LNM) and its aggressiveness in differentiated thyroid cancers detected by chance with ^{18}F-FDG PET/CT and found that high MTV and TLG values were associated with LNM (18). In the present study, the TLG values were significantly higher in malignant or malignant-suspicious nodules than in benign and non-diagnostic nodules. Although the MTV values of malignant or malignant-suspicious nodules were high than in benign and non-diagnostic nodules, it was statistically insignificant at limit values. In this study, 96.1% of the thyroid incidentalomas that underwent thyroid FNAB were in the high or very high-risk group than using the EU-TIRADS risk scoring. Furthermore, 67.3% of the nodules were in the very high-risk group. The significance of TLG results in this study may be related to this.

Kim and Chang (19) compared intratumoral heterogeneity with thyroid FNAB results in thyroid nodules that were evaluated with PET/CT, and unlike this study, they reported a statistically significant difference between SUV_{max}, TLG, and MTV values between the malignant and malignant-suspicious groups according to the Bethesda classification. However, they detected no significant differences between the malignant and benign groups (19). In our study, 96.1% of the thyroid incidentalomas that underwent thyroid FNAB might be associated with being in a high or very high-risk group based on EU-TIRADS risk scoring.

Study Limitations

This study had several limitations. First, the study had a retrospective design. Second, pathologies after thyroidectomy were excluded because a limited number of patients underwent thyroidectomy. In addition, the number of incidental thyroid nodules detected to be malignant after thyroid FNAB was relatively small.

Conclusion

As a result, we believe that evaluating SUV_{max} and TLG will be useful in predicting the high and very high risk of EU-TIRADS for having high-risk malignancy or malignancy suspicion from the incidental thyroid nodules detected by PET/CT. However, this must be supported with prospective studies, and more patients should be included. We believe that unnecessary thyroid FNABs for thyroid incidental nodules can be avoided if such relation and cutoff values are determined and that it will be useful in hastening the operation of the necessary patients.

Ethics

Ethics Committee Approval: The study was approved by Süleyman Demirel University Ethics Board (date: 13.02.2020, approval number: 37).

Informed Consent: Retrospective cross sectional study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.E., H.K., S.S.Ş. Concept: M.E., H.K., S.S.Ş. Design: M.A., M.Y. Data Collection or Processing: B.T., H.K. Analysis or Interpretation: M.E., B.T., H.K., Literature Search: Ş.M.B., M.A. Writing: M.E., H.K., M.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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