Original Article

Clinical significance of thyroid incidentalomas detected on fluorodeoxyglucose positron emission tomography scan (PETomas): An Indian experience

ABSTRACT

Thyroid incidentalomas (TIs) are being frequently detected on positron emission tomography (PET) scan. The risk of malignancy in these focal hot spots is substantially high as compared to incidentalomas detected on ultrasonography (USG)/magnetic resonance imaging/computed tomography (CT). Majority of the studies on the prevalence of TIs in PET and the risk of malignancy in them are retrospective and have had varied results. Very few prospective studies are available and very few Indian studies have been done on the subject. Hence, this study was undertaken to evaluate the clinical significance of TIs detected on fluorodeoxyglucose (FDG)-PET scan. The study included all patients undergoing FDG-PET scan for nonthyroid illness from October 2015 to October 2016. Twenty-three consecutive patients detected to have focal TI (FTI) were prospectively evaluated with detailed history and clinical examination, serum thyroid-stimulating hormone, total T4 and total T3 levels, USG neck, fine-needle aspiration cytology (FNAC), and surgery when indicated. The prevalence of FTI was 2.26%. Out of the 23 FTI cases, 19 patients agreed to undergo further evaluation and malignancy was detected in 5 patients (all papillary carcinomas) making a risk of malignancy of 26.3%. There was no significant correlation between CT attenuation characteristics and size of benign and malignant PETomas or between the maximum standardized uptake value (SUV_{max}) of benign and malignant PETomas. Hence, the risk of malignancy in thyroid PETomas is substantially high and warrants USG-guided FNAC and further work-up. Their SUV_{max} values, size, and CT attenuation characteristics do not contribute in differentiating benign from malignant lesions.

Keywords: Fluorodeoxyglucose, PEToma, thyroid incidentaloma

INTRODUCTION

Thyroid incidentaloma (TI) is defined as a newly identified focal thyroid lesion during an imaging study, such as ultrasonography (USG), computed tomography (CT) scan, positron emission tomography (PET) scan, and magnetic resonance imaging (MRI), performed to evaluate nonthyroid disease. The most important clinically pertinent question to be answered after detection of TI is whether it is malignant or benign. There is high prevalence of previously undetected thyroid nodules detected by current high-resolution ultrasound. The risk of cancer in these thyroid nodules is low, varying from 1.5% to 10%.[1] At present, none of the current diagnostic modalities (USG, CT, and MRI) are specific for thyroid malignancy.[2-4] ^{18}F fluorodeoxyglucose (FDG)-PET is a noninvasive whole-body imaging technique and is increasingly becoming the modality of choice for staging and planning treatment of various malignancies.[5,6] Numerous retrospective studies reveal that the percentage of TIs exhibiting increased ^{18}F-FDG uptake is 0.1%–4.3% on PET scan.[7-10] However, the TIs detected by ^{18}F-FDG-PET scan have a different connotation

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as the risk of malignancy detected as focal hot spots ranged from 14% to 47% in various studies.[5-10] Majority of the studies on the prevalence of TIs are retrospective and very few prospective studies are available. Furthermore, very few Indian studies (retrospective) have been done on the subject. Hence, this study was undertaken to study the clinical significance of TIs detected on FDG-PET scan.

METHODS

This is a cross-sectional study of consecutive patients detected to have TI on FDG-PET scans who were prospectively evaluated for thyroid malignancy in the incidentaloma. Clearance was obtained from the ethical committee of the institution. The study was done over a period of 1½ years in a newly opened PET-CT scan center at a tertiary care hospital of Armed Forces. It included all patients undergoing FDG-PET for nonthyroid illness from October 2015 to 2016. The study was carried out for total 18 months in view of the fact that last patient with indeterminate fine-needle aspiration cytology (FNAC) report had to be followed up for total 1 year which ended in April 2017. Patients with a history of previous thyroid cancer, thyroid surgery or thyroid lesion known before test, pregnancy, the scan being done for thyroid disease, or life expectancy <2 years were excluded from the study. All patients who were detected to have abnormal thyroid uptake of FDG in PET scan were further evaluated with detailed history and clinical examination, serum thyroid-stimulating hormone, total T4 and total T3 levels, USG neck, and FNAC if thyroid nodule was detected.

Serum total T4 and total T3 levels were measured using fully automated analyzer for Radioimmunoassay (Model SR 300, Make Stratec Germany) with reference values of 0.5–6.5 mIU/l, 4.6–13ug/dl, and 78–182 ng/dl, respectively.

^{18}F fluorodeoxyglucose positron emission tomography/computed tomography imaging protocol

All the patients were asked to be fasting for 6 h before study. The patients having blood glucose levels >60 mg/dl were excluded from the study. Dosing: 370 Mbq of fluorine-18-FDG was injected intravenously and whole-body imaging from head to mid-thigh was done after 60 min. GE Discovery 690 PET/CT was used for imaging. The PET/CT images were obtained with a 2-min bedtime as per the height of the patient. The CT component was used for attenuation correction. The CT scan settings were 60–160 mAs and 120 kVp. A slice thickness of 3.75 mm, a rotation time of 0.5 s, and a 256 × 256 matrix were used. Noncontrast CT was done. Normal attenuation of the thyroid gland is 104 ± 20. For this study, low attenuation was taken as below 80 Hounsfield units (HU) and high attenuation was taken above 125 HU. Focal uptake was defined as FDG uptake in <1 lobe of the thyroid gland. FDG uptake was considered abnormal at visual analysis when activity was considerably greater as compared to mediastinal blood on attenuation-corrected images. In addition, a pixel region of interest was outlined within the regions of increased FDG uptake, and the maximum standardized uptake value (SUV_{max}) was analyzed semi-quantitatively as per the following equation:

$$SUV = A/(ID/BW)$$

Where A: Decay-corrected activity in tissue (in millicuries per milliliter).
ID: Injected dose of FDG (in millicuries).
BW is the patient's body weight (in grams).

Evaluation of the fused images and CT images was done in cases where focal FDG activity was detected to ensure that uptake was from within the thyroid gland. Among the patients who were found to have focal FDG-avid thyroid lesions, CT findings of any thyroid focal lesion(s) and their size, presence of thyroid enlargement, thyroid heterogeneity, thyroid calcifications, and neck adenopathy were recorded.

Ultrasonography

All patients found to be having abnormal FDG uptake in the thyroid underwent USG of the neck which was carried out with LOGIQ P5 (GE, Milwaukee, USA) equipped with a 7–12 Mhz linear assay transducer. Thyroid parenchyma was studied (size and echogenicity), and the presence of nodules and lymph nodes and signs of thyroiditis were reported. Thyroid nodules were characterized according to the usual criteria (dimensions, echogenicity, margins, and presence or absence of macrocalcifications/microcalcifications).

Fine-needle aspiration biopsy

FNAC was recommended for the nodules with ^{18}F-FDG uptake when the nodule was suitable for biopsy (at least 5–8 mm in size and not posteriorly located). A repeat FNAC was recommended if the result was nondiagnostic or unsatisfactory. A thyroidectomy was recommended if FNAC showed malignancy or if there was suspicion of a malignancy. The specimens were obtained by a pathologist with a 21-G needle. Air-dried slides were stained with Giemsa stain, while those fixed in 96% alcohol were stained with hematoxylin and eosin and cytopathological evaluation was performed.

Analysis

The patients who were found to have incidental thyroid uptake were divided into two groups – diffuse uptake (dTI) and focal uptake (fTI). The patients having focal TIs (PETomas) underwent further evaluation by USG for size and echotexture

and histopathology by ultrasound-guided FNAC to detect any malignancy. Data analysis was done using the Statistical package for the Social Sciences (SPSS) version 20.0 (IBM Corp., Armonk, NY, USA). Qualitative data variables were expressed using frequency and percentage (%). Quantitative data variables were expressed using mean and standard deviation; two-independent sample *t*-test was used to find the significant difference between mean SUV of benign and malignant lesions. $P < 0.05$ was considered as significant.

RESULTS

A total number of 1016 patients met the inclusion criteria defined for the study. It included 558 male and 458 female patients. The most common malignancy showing increased thyroid uptake was cervical carcinoma, followed by breast cancer, lung cancer, colorectal carcinomas, ovarian cancer, and lymphomas in descending order of frequency.

Prevalence of thyroid incidentalomas

Out of the 1016 patients, incidental increased uptake of ^{18}F-FDG in the thyroid was seen in 55 patients (5.4%). Out of the 55 patients, focal uptake (PETomas or focal thyroid incidentaloma [FTI]) was seen in 23 patients and diffuse uptake (diffuse thyroid incidentaloma [DTI]) was seen in 32 patients [Figure 1]. Mixed pattern (focal + diffuse) was not seen in any of the cases. Fifteen cases (27.2%) were male whereas 40 cases (72.7%) were female. The prevalence of thyroid incidentalomas (FTI) was 2.26% (23/1016). Out of the 23 FTI cases, 19 patients were subjected to FNAC. Malignancy was detected in 5 patients and all were papillary carcinoma [Figure 2 shows the scan of the patient with FTI diagnosed to have papillary carcinoma and confirmed on biopsy specimen after total thyroidectomy], 11 were benign (benign nodule and colloid goiter), and 3 were indeterminate [Figure 1].

Thyroid function status

Majority of the patients were clinically euthyroid (92%). Three patients in the diffuse uptake group and one patient in the focal uptake group had features suggestive of thyrotoxicosis in the form of anxiety, heat intolerance, and resting tachycardia. Inpatients with diffuse uptake 2 had thyroiditis and one was diagnosed to have Graves' disease. Figure 3 shows diffuse uptake of FDG on PET scan diagnosed to have thyroiditis. Figure 4 shows the USG finding in the same patient. The one thyrotoxic patient with FTI had toxic adenoma.

Calcifications

Evaluation of the fused images and CT images done in patients who were found to have FTI revealed calcification in five patients. None of the patients with diffuse uptake showed calcification. However, none of the cases of PETomas with calcification on CT was associated with malignancy on histopathology.

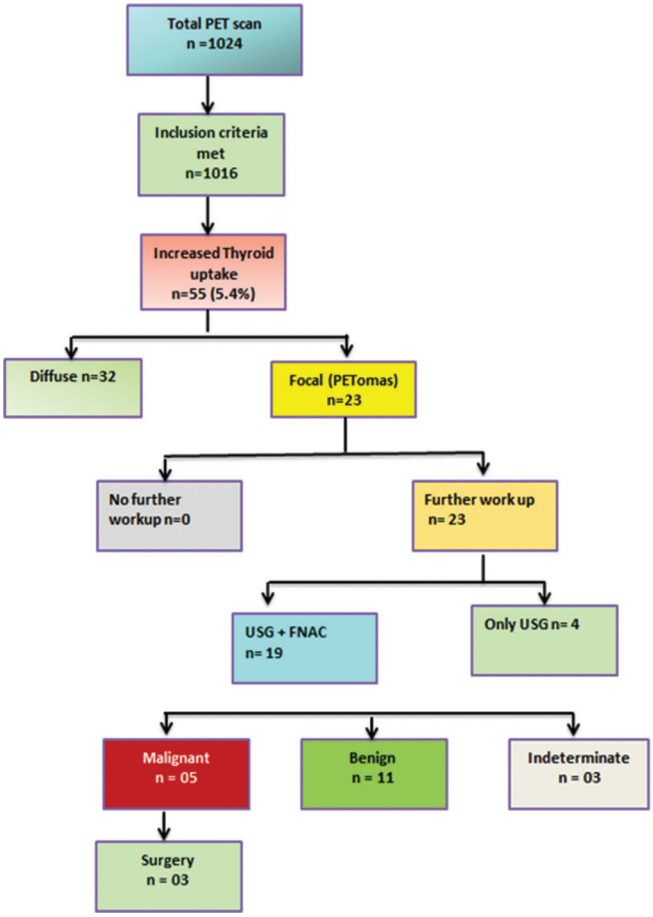

Figure 1: Flow of the study. Twenty-three cases had PETomas. Four patients refused to take part in the study after ultrasonography evaluation. Nineteen underwent further evaluation

Sonological finding

Among the 23 TIs, 13 (56.5%) were hypoechoic; 5 were hyperechoic (21.7%), and 5 were isoechoic (21.7%) nodules. The mean size of PETomas on USG was found to be 12.76 mm with a median size of 9 mm. Nearly 80% of the malignant and 36% of benign PETomas were hypoechoic on USG. About 20% of malignant and 27% of benign PETomas were hyperechoic and 27.7% of benign PETomas were isoechoic. There was no significant correlation in the echotexture of benign versus malignant PETomas.

Correlation with computed tomography attenuation

The PETomas were divided into three groups (low, iso, and high attenuation) on the basis of their attenuation value on CT measured in HU. These groups were compared using Chi-square test between malignant and benign PETomas and no correlation could be established [Table 1].

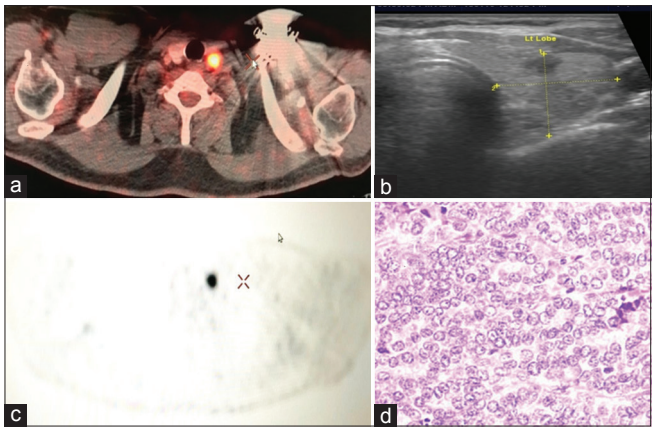

Figure 2: (a) Fluorodeoxyglucose positron emission tomography-computed tomography of a 49-year-old patient, axial section showing focal thyroid incidentaloma in the left lobe of the thyroid gland as an area of increased fluorodeoxyglucose uptake. (b) Ultrasonography image showing a 9 mm × 6 mm hypoechoic lesion in the left lobe of the thyroid gland. (c) Positron emission tomography image of the same patient showing PEToma. (d) Histopathology revealed papillary architecture with Orphan Annie eye nuclei suggestive of papillary carcinoma thyroid

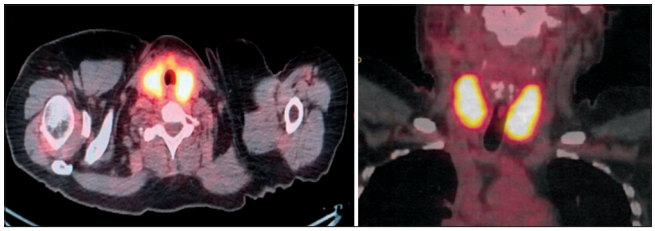

Figure 3: Diffuse increase in fluorodeoxyglucose uptake (dTI) in the patient of thyroiditis

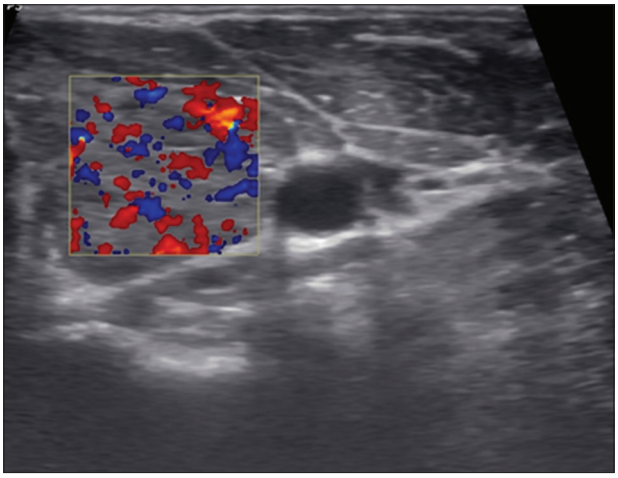

Figure 4: Ultrasonography of the patient with diffuse uptake in Figure 2 – showing enlargement and increased vascularity of both lobes – suggestive of thyroiditis

Correlation between mean computed tomography size, computed tomography attenuation, and mean maximum standardized uptake value of benign versus malignant PETomas

The mean CT size of benign and malignant PETomas was 10.82 and 15 mm, respectively, and the difference was insignificant ($P = 0.232$). The mean CT attenuation of benign and malignant PETomas was 63.8 and 38.8, respectively; however, the difference was not statistically significant ($P = 0.08$). The mean SUVmax of benign PETomas was 8.09 ± 5.96 and that of malignant PETomas was 14.2 ± 13.1 which is not significant with P = 0.368 using Mann–Whitney test [Figure 5].

Correlation between maximum computed tomography size with maximum standardized uptake value for malignant, benign, and indeterminate thyroid incidentalomas

Spearman r test was performed to find correlation between SUV_{max} and the maximal diameter of nodule in the malignant, benign, and indeterminate group. There was significant positive correlation between CT size and SUV for benign PETomas; however, no correlation was observed in the malignant and indeterminate group [Figure 6].

Receiver operating characteristic curve analysis to determine cutoff for SUV between benign and malignant PETomas

The area under the curve is 58%. When receiver operating characteristic (ROC) curve and mean SUV_{max} value for differentiating between benign and malignant lesions were used, the cutoff value for SUV_{max} was 7.84 from the ROC curve in our study with a sensitivity and specificity were 60% and 66.7%, respectively [Figure 7].

DISCUSSION

TIs are being detected more frequently over the recent years due to the increasing number of FDG-PET scans being done for oncological and nononcological indications. TIs, especially those showing focal uptake of ^{18}F-FDG, are associated with a higher risk of malignancy as discussed earlier. There have been many retrospective studies and few prospective studies in the western literature; however, to our knowledge, no prospective Indian study on the prevalence of TIs has been done. The incidence of malignancy in them is varied in literature. Previous studies have reported prevalence rate of TIs detected by FDG-PET/CT ranging from 0.1% to 4.3%.[7-10] In the present study, 1016 patients underwent FDG-PET for nonthyroidal illnesses. Fifty-five patients were found to have incidental thyroid uptake (5.4%). Among these 55 patients, 32 patients showed diffuse uptake and 23 patients had focal uptake of FDG. The prevalence of TIs was found to be 2.26% (23/1016), which is similar to other studies that included a relatively large number of patients [Table 2].[9-23]

We considered diffuse uptake pattern to be having negligible chances of harboring malignancy and hence did not include them in further workup for ruling out malignancy. Kang

et al. showed that the ultrasound revealed a thyroid nodule in only 59.5% of patients with DTI while more than 99.0% of patients with FTI had confirmed thyroid nodule.[24] Moreover, several studies have shown that DTI is essentially related to an inflammatory disease of the thyroid, such as thyroiditis or more rarely Graves' disease.[25,26] A meta-analysis by Soelberg *et al*. also showed a low malignancy risk of 4.4% in DTI.[27] In fact in patients with incidentally detected diffuse uptake at FDG-PET/CT, the risk for thyroid cancer is comparable with the risk in the healthy population; in particular, US and US-fine needle aspiration biopsy (FNAB) features remain more reliable predictors of malignancy.[12] Kim *et al*.[10] and Chen *et al*.[28] also reported that diffuse pattern of incidental FDG uptake on PET scan is commonly associated with benign lesions; the most common being chronic thyroiditis. Out of the 32 patients with diffuse uptake in our study, three patients had biochemical evidence of thyrotoxicosis; all three were evaluated further and a Tc-99m scan was done – one was diagnosed as Graves and the other two as thyroiditis. Rest of the 29 patients had normal thyroid profile and were not evaluated further.

The FTI cases in our study showed malignancy in 5 cases out of the 19 cases who agreed for complete evaluation making a risk of malignancy of 26.3%. The study done in India in Mumbai by Vaish *et al*. where they evaluated retrospectively 37,000 consecutive patients found a very low prevalence of incidentaloma of 0.2%, but the risk of malignancy in them was 27%, similar to our study.[20] There have been many similar studies in the world. However, there is lot of variation found in the prevalence of malignancy in all the studies with risk ranging from 12% to 50%.[9-23] Why there is so much of variation in different studies? We think that most of the studies have been retrospective and there is lot of bias in such studies. The final result is obtained only from patients who have been evaluated completely and it is only the high-risk patients who are evaluated completely. This probably increases the prevalence of malignant lesions. Hence, we think that risk may not be in the 40%–50% range. However, the risk is high enough to support further investigation of TI with USG and FNAC. The study by Vaish *et al*. had 7.69% of metastatic involvement of the thyroid out of the total 27% of malignancies detected in the incidentalomas.[20] In a study done by Kim *et al*., the metastatic involvement of the thyroid was seen in 6.25% of cases.[10] Our study did not reveal any case of metastatic cancer to the thyroid.

Because of the high cost of PET/CT, it is not widely used in asymptomatic healthy participants for cancer screening. Our study population comprised patients who were known cases of a nonthyroid malignancy. Hence, the prevalence of incidentaloma may not be extrapolated to the general population. The existence of nonthyroid cancer itself is known to be a risk factor of thyroid cancer.[29] With regard to studies in healthy subjects, Kang *et al*. reviewed 331 subjects who underwent cancer screening and found focal PET incidentaloma in six participants.[8] Since one person showed malignancy, the incidence of thyroid cancer in PET incidentalomas was 16.7%. Chen *et al*. reported the cancer risk of focal PET incidentalomas as 14.0% (7/50 incidentalomas in

Table 1: Correlation between computed tomography attenuation - malignant versus benign thyroid incidentalomas

CT Attenuation group	FNAC findings		Total	*P*
	Benign	Malignant		
Low attenuation (<80HU)	16	5	21	0.594
ISO attenuation (81-124 HU)	1	0	1	
High attenuation (>125 HU)	1	0	1	
Total	18	5	23	

Table 2: Studies evaluating thyroid incidentalomas detected on FDG PET scan

Study	Year	Study type	Patients	Incidental thyroid uptake%	Histopathological confirmation	Risk of malignancy % (*n*)	SUV
Cohen *et al*	2001	Retrospective	4,525	102 (2.3%)	15	47% (*n*=7)	Useful
Kim *et al*	2005	Retrospective	4,136	90	39	13.8%(18/39)	NS
King *et al*	2007	Retrospective	15,711	22 (0.1%)	22	13.6%(2/22)	Not studied
Pagano *et al*	2011	Retrospective	10,881	191 (1.76%)	52	28.9%(15/52)	Useful
Nillson *et al*	2012	Retrospective	3,641	64 (1.8%)	27	25 (16/64)	Useful
Kao *et al*	2012	Retrospective	942	21 (2.2%)	6V	50%(3/6)	NS
Yang *et al*	2012	Retrospective	15,948	395 (2.5%)	53	29.5%(43/146)	NS
Chun *et al*	2015	Retrospective	2,584	52 (2%)	36	41%(15/36)	Useful
Jamsek *et al*	2015	Retrospective	5911	230 (3.89)	18	15.2	NS
Elzein *et al*	2015	Retrospective	1730	65 (3.76%)	16	12.5%(2/16)	NR
Barrio *et al*	2016	Retrospective	6,216	845 (13.6%)	98	16%(16/98)	Useful
Vaish *et al*	2016	Retrospective	37000	78 (0.2%)	33	21%(7/33)	NS
Eren *et al*	2016	Prospective	4,204	178 (4.2%)	56	*n*=(15/56)	NS
Thuillier *et al*	2017	Prospective	10,118	127 (1.3%)	90	10% (*n*=9)	NS
Bakhshayesh *et al*	2017	Prospective	1126	78 (7%)	18	16.6% (3/18)	NS

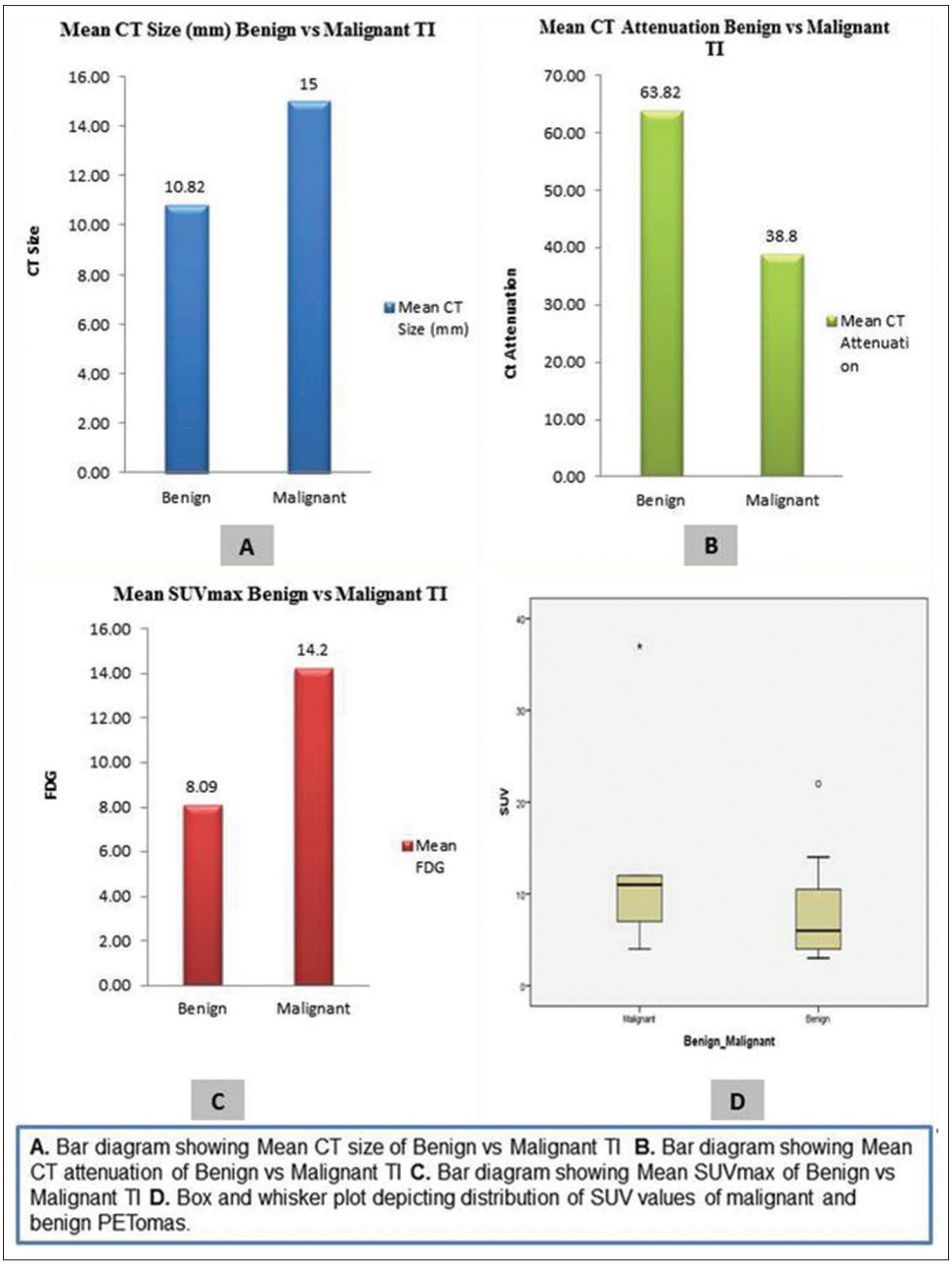

Figure 5: Correlation between mean computed tomography size, computed tomography attenuation, and maximum standardized uptake value of benign versus malignant PETomas

4803 participants).[7] Similarly, Minamimoto *et al*. reported the cancer risk of 32.9% (94/286 incidentalomas) in their study of 43,996 participants.[30] A study by Ohba *et al*. showed that focal TI identified by FDG-PET has a high probability of malignancy even in healthy, relatively young participants. In their study, thyroid cancer was proven in 11 of 20 focal PET incidentalomas in 1501 healthy participants.[29] The cancer risk was 55%, markedly higher than in previous reports. This may be due to their meticulous close examination and follow-up of all focal PET incidentalomas using US and FNAB and the long-term follow-up. They had done 3-year follow-up for the 1529 incidentalomas scanned over 1-year period. We have done a follow-up of 1 year for the patients whose FNAC result was indeterminate, and there was no increase in size and USG characteristics of these incidentalomas.

Out of the 19 FTI cases, 5 were found to have papillary carcinoma, 3 were indeterminate (Bethesda Grade 3–4), and 11 were benign. The patients with indeterminate lesions were followed up by USG and clinical examination for 1 year and no change in size and USG features developed, and at the end of 1-year repeat, FNAC continued to be indeterminate

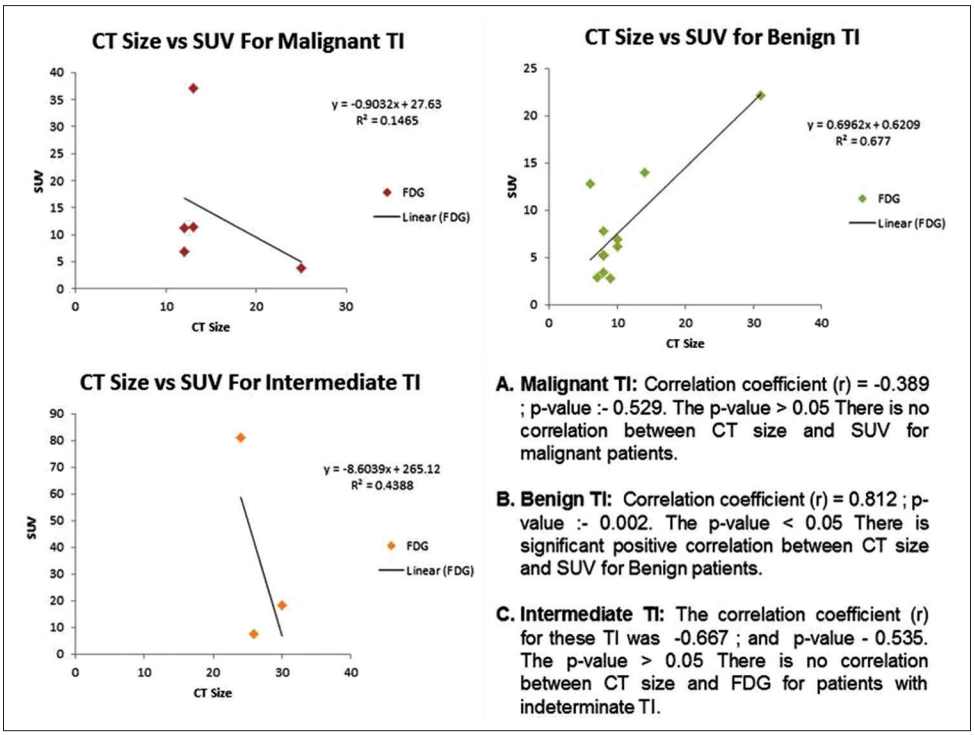

Figure 6: Correlation between nodule size and metabolic activity (maximum standardized uptake value)

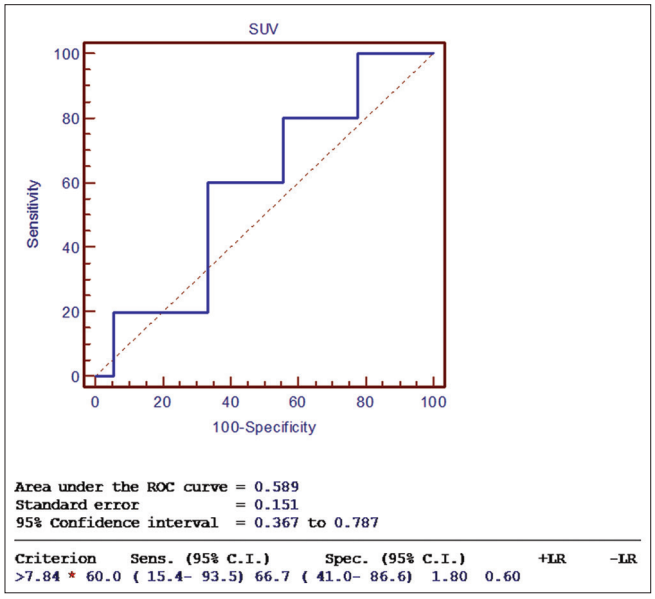

Figure 7: Receiver operating characteristic curve to differentiate between benign and malignant lesions on positron emission tomography/computed tomography

and hence we considered them benign. All the malignancies detected were of papillary type. A study by Yi *et al*. where they evaluated 140 consecutive cases of nonsmall cell lung cancer detected six patients (4.3%) having seven foci of increased FDG uptake in the thyroid. Four of the lesions were found to be papillary thyroid cancers at FNAB.[31] Shie *et al*.[32] also reported that the most prevalent thyroid malignancy in these nodules to be papillary carcinoma. This is not surprising as papillary thyroid cancer is the most common malignancy involving the thyroid gland.

Many studies have compared mean SUV_{max} between benign and malignant focal hypermetabolic uptake on FDG-PET/CT scan; however, there is discordance in the findings. Studies by Kang *et al*., Cohen *et al*., Pagano *et al*., Chun *et al*., and Barrio *et al*.[8,9,12,16,19] showed a statistically significant difference between mean SUV_{max} of benign and malignant lesions. However, studies by Kao *et al*.,[14] Elzein *et al*.,[18] Vaish *et al*.,[20] and Thuillier *et al*.[22] did not show any significant difference in the mean SUV_{max} [Table 2]. Our study did not show any significant difference between the mean SUV_{max} of benign and malignant TIs ($P = 0.386$), and there was a considerable overlap between mean SUV_{max} of benign and malignant lesions. ROC curve analysis done in our study revealed cutoff mean SUV_{max} value for differentiating between benign and malignant lesions to be 7.84 (sensitivity and specificity of 60% and 66.7%, respectively). The probable reason for the lack of significant difference and variation in cutoffs in various ROC curve analyses could be that the SUV_{max} apart from size would also depend on the glucose transporter 1 (GLUT1) expression in the lesion which is an important aspect that influences isotope uptake. The expression of GLUT1 is variable in thyroid cancer and varies with the differentiation.[33] The majority of thyroid cancers are known to be well differentiated which, therefore, accounts for this phenomenon. Moreover, papillary carcinomas may have lower SUV, probably because of partial

volume effects.[6] Therefore, SUV_{max} levels may not be a reliable indicator of malignancy in a focal TI. There is no definite SUV_{max} cutoff value established which can differentiate malignant and benign PETomas and therefore further studies are needed. Furthermore, using a high SUV_{max} as the sole indicator of cancer may be misleading since both benign Hurthle cell adenomas and follicular adenomas have higher SUV_{max} compared with other benign conditions.[34,35] However, there are also few studies which demonstrated significance of SUV_{max}. In the study by Pagano et al. A retrospective study of 11,040 FDG-PET/CT scans performed for all causes from 2005 to 2009, 159 cases showed incidental thyroid uptake. However, finally only 52 cases were retrospectively analyzed as they fitted into the inclusion criteria of complete evaluation having been done. They found that SUV_{max} value >5 was the strongest independent predictive factor of malignancy together with euthyroidism. Mitchell *et al*. examined 48 various types of surgically resected thyroid nodules and reported that SUV_{max} could distinguish benign and malignant nodules.[36] They evaluated preoperatively 48 nodules in 31 patients with FNAC and PET scan before surgical resection. Final pathologic diagnoses were compared with PET/CT findings. Fifteen of 48 lesions were malignant and 33 were benign. Nine of 15 malignant lesions were FDG-avid (sensitivity 60%). Thirty of 33 benign lesions were FDG-cold (specificity 91%). Positive and negative predictive values were 75% and 83%, respectively. They concluded that SUV_{max} has high negative predictive value for malignancy, making this a potentially useful tool in the evaluation of thyroid nodules with indeterminate fine-needle aspiration.

A significant association ($P = 0.041$) was seen with respect to size on USG and the nature of malignancy on FNAC. Benign lesions were larger in size whereas malignant lesions were smaller in size. A possible explanation could be that malignant PETomas are picked up earlier on PET scan. No similar finding was found during review of available literature. No significant ($P = 0.361$) association was seen between echotexture and benign versus malignant PETomas.

There are studies on the usefulness of CT characteristics of the thyroid lesions which can further help in assessing the risk of the nodule being malignant. Yoon *et al*.[37] have reported that nodular calcification or a rim of calcification, and a mean attenuation value >130 HU on contrast-enhanced CT are associated with a greater risk of malignancy. In our study, although there was significant association between calcifications on CT scan and focal uptake of FDG ($P < 0.01$); all of them were benign on histopathology. We had carried out only noncontrast CT. The attenuation characteristics of the nodule on CT have been also suggested to improve the accuracy of diagnosis of malignancy. Choi *et al*.[38] reported improved accuracy using CT attenuation. Yi *et al*.[31] also reported in their study that malignant nodules had low attenuation on CT images. However, attenuation value on CT could not definitively discriminate a benign from a malignant nodule. In our study of the 23 TIs with focal uptake, 21 (91.3%) had low attenuation on CT and one each had intermediate and high attenuation. Both benign and malignant lesions had low attenuation. The mean attenuation value of malignant PETomas (38.8) was lower than that of benign PETomas (63.8). However, the difference in mean attenuation between benign and malignant TIs was not significant ($P = 0.082$).

Despite the varied results of various studies, one aspect is clear that chances of an incidentaloma detected on PET scan being malignant are much more than when detected incidentally by other modalities. Not only because of advanced molecular imaging technology of PET whereby otherwise unrecognized microcarcinomas are discovered, but also may be because of the fact that most participants submitted to ^{18}F-FDG PET studies are patients referred for staging, restaging, or assessment of treatment responses of various malignancies, in which the pretest probability for secondary tumors may be higher.[39]

This is probably one of the very few prospective studies on TIs detected on FDG-PET study in the Indian setting. However, the study has limitations. Seventeen percent of patients who had PETomas did not undergo further evaluation. The sample size was small in view of the study being duration based and center being newly established wherein the initial workload was less which subsequently picked up over 6 months. The cases with indeterminate cytology were followed up for a period of 1 year only; probably, it is too short a time to declare them benign.

All the positive cases who gave informed consent could be followed up to conclusion with histopathological diagnosis. The study gives an opportunity to further follow-up cases on USG/FDG-PET alone in rest of the cases who did not give consent for histological evaluation as most of the patients would undergo a repeat PET for their primary illness.

CONCLUSION

The risk of malignancy in thyroid PETomas is substantially high and warrants USG-guided FNAC and further workup. Their SUV_{max} values, size, and CT attenuation characteristics do not contribute in differentiating benign from malignant lesions.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Burguera B, Gharib H. Thyroid incidentalomas. Prevalence, diagnosis, significance, and management. Endocrinol Metab Clin North Am 2000;29:187-203.
2. Brander A, Viikinkoski P, Nickels J, Kivisaari L. Thyroid gland: US screening in a random adult population. Radiology 1991;181:683-7.
3. Ezzat S, Sarti DA, Cain DR, Braunstein GD. Thyroid incidentalomas. Prevalence by palpation and ultrasonography. Arch Intern Med 1994;154:1838-40.
4. Mazzaferri EL. Thyroid cancer in thyroid nodules: Finding a needle in the haystack. Am J Med 1992;93:359-62.
5. Sasaki M, Ichiya Y, Kuwabara Y, Akashi Y, Yoshida T, Fukumura T, *et al.* An evaluation of FDG-PET in the detection and differentiation of thyroid tumours. Nucl Med Commun 1997;18:957-63.
6. Kresnik E, Gallowitsch HJ, Mikosch P, Stettner H, Igerc I, Gomez I, *et al.* Fluorine-18-fluorodeoxyglucose positron emission tomography in the preoperative assessment of thyroid nodules in an endemic goiter area. Surgery 2003;133:294-9.
7. Chen YK, Ding HJ, Chen KT, Chen YL, Liao AC, Shen YY, *et al.* Prevalence and risk of cancer of focal thyroid incidentaloma identified by 18F-fluorodeoxyglucose positron emission tomography for cancer screening in healthy subjects. Anticancer Res 2005;25:1421-6.
8. 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.
9. 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.
10. Kim TY, Kim WB, Ryu JS, Gong G, Hong SJ, Shong YK, *et al.* 18F-fluorodeoxyglucose uptake in thyroid from positron emission tomogram (PET) for evaluation in cancer patients: High prevalence of malignancy in thyroid PET incidentaloma. Laryngoscope 2005;115:1074-8.
11. King DL, Stack BC Jr., Spring PM, Walker R, Bodenner DL. Incidence of thyroid carcinoma in fluorodeoxyglucose positron emission tomography-positive thyroid incidentalomas. Otolaryngol Head Neck Surg 2007;137:400-4.
12. Pagano L, Samà MT, Morani F, Prodam F, Rudoni M, Boldorini R, *et al.* Thyroid incidentaloma identified by ^{18}F-fluorodeoxyglucose positron emission tomography with CT (FDG-PET/CT): Clinical and pathological relevance. Clin Endocrinol (Oxf) 2011;75:528-34.
13. Nilsson IL, Arnberg F, Zedenius J, Sundin A. Thyroid incidentaloma detected by fluorodeoxyglucose positron emission tomography/computed tomography: Practical management algorithm. World J Surg 2011;35:2691-7.
14. 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.
15. Yang Z, Shi W, Zhu B, Hu S, Zhang Y, Wang M, *et al.* Prevalence and risk of cancer of thyroid incidentaloma identified by fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography. J Otolaryngol Head Neck Surg 2012;41:327-33.
16. Chun AR, Jo HM, Lee SH, Chun HW, Park JM, Kim KJ, *et al.* Risk of malignancy in thyroid incidentalomas identified by fluorodeoxyglucose-positron emission tomography. Endocrinol Metab (Seoul) 2015;30:71-7.
17. Jamsek J, Zagar I, Gaberscek S, Grmek M. Thyroid lesions incidentally detected by (18)F-FDG PET-CT – A two centre retrospective study. Radiol Oncol 2015;49:121-7.
18. Elzein S, Ahmed A, Lorenz E, Balasubramanian SP. Thyroid incidentalomas on PET imaging – Evaluation of management and clinical outcomes. Surgeon 2015;13:116-20.
19. Barrio M, Czernin J, Yeh MW, Palma Diaz MF, Gupta P, Allen-Auerbach M, *et al.* The incidence of thyroid cancer in focal hypermetabolic thyroid lesions: An 18F-FDG PET/CT study in more than 6000 patients. Nucl Med Commun 2016;37:1290-6.
20. Vaish R, Venkatesh R, Chaukar DA, Deshmukh AD, Purandare NC, D'cruz AK, *et al.* Positron emission tomography thyroid incidentaloma: Is it different in Indian subcontinent? Indian J Cancer 2016;53:186-9.
21. Şencan Eren M, Özdoğan Ö, Gedik A, Ceylan M, Güray Durak M, Seçil M, *et al.* The incidence of 18F-FDG PET/CT thyroid incidentalomas and the prevalence of malignancy: A prospective study. Turk J Med Sci 2016;46:840-7.
22. Thuillier P, Roudaut N, Crouzeix G, Cavarec M, Robin P, Abgral R, *et al.* Malignancy rate of focal thyroid incidentaloma detected by FDG PET-CT: Results of a prospective cohort study. Endocr Connect 2017;6:413-21.
23. Bakhshayesh Karam M, Doroudinia A, Joukar F, Nadi K, Dorudinia A, Mehrian P, *et al.* Hypermetabolic thyroid incidentaloma on positron emission tomography: Review of laboratory, radiologic, and pathologic characteristics. J Thyroid Res 2017;2017:7176934.
24. Kang BJ, O JH, Baik JH, Jung SL, Park YH, Chung SK. Incidental thyroid uptake on F-18 FDG PET/CT: Correlation with ultrasonography and pathology. Ann Nucl Med 2009;23:729-37.
25. Kurata S, Ishibashi M, Hiromatsu Y, Kaida H, Miyake I, Uchida M, *et al.* Diffuse and diffuse-plus-focal uptake in the thyroid gland identified by using FDG-PET: Prevalence of thyroid cancer and Hashimoto's thyroiditis. Ann Nucl Med 2007;21:325-30.
26. Lee JY, Choi JY, Choi YH, Hyun SH, Moon SH, Jang SJ, *et al.* Diffuse thyroid uptake incidentally found on 18F-fluorodeoxyglucose positron emission tomography in subjects without cancer history. Korean J Radiol 2013;14:501-9.
27. 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.
28. Chen W, Parsons M, Torigian DA, Zhuang H, Alavi A. Evaluation of thyroid FDG uptake incidentally identified on FDG-PET/CT imaging. Nucl Med Commun 2009;30:240-4.
29. Ohba K, Nishizawa S, Matsushita A, Inubushi M, Nagayama K, Iwaki H, *et al.* High incidence of thyroid cancer in focal thyroid incidentaloma detected by 18F-fluorodeoxyglucose [corrected] positron emission tomography in relatively young healthy subjects: Results of 3-year follow-up. Endocr J 2010;57:395-401.
30. Minamimoto R, Senda M, Uno K, Jinnouchi S, Iinuma T, Ito K, *et al.* Performance profile of FDG-PET and PET/CT for cancer screening on the basis of a Japanese nationwide survey. Ann Nucl Med 2007;21:481-98.
31. Yi JG, Marom EM, Munden RF, Truong MT, Macapinlac HA, Gladish GW, *et al.* Focal uptake of fluorodeoxyglucose by the thyroid in patients undergoing initial disease staging with combined PET/CT for non-small cell lung cancer. Radiology 2005;236:271-5.
32. Shie P, Cardarelli R, Sprawls K, Fulda KG, Taur A. Systematic review: Prevalence of malignant incidental thyroid nodules identified on fluorine-18 fluorodeoxyglucose positron emission tomography. Nucl Med Commun 2009;30:742-8.
33. Schönberger J, Rüschoff J, Grimm D, Marienhagen J, Rümmele P, Meyringer R, *et al.* Glucose transporter 1 gene expression is related to thyroid neoplasms with an unfavorable prognosis: An immunohistochemical study. Thyroid 2002;12:747-54.

34. 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.
35. Bogsrud TV, Karantanis D, Nathan MA, Mullan BP, Wiseman GA, Collins DA, *et al.* The value of quantifying 18F-FDG uptake in thyroid nodules found incidentally on whole-body PET-CT. Nucl Med Commun 2007;28:373-81.
36. 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.
37. Yoon DY, Chang SK, Choi CS, Yun EJ, Seo YL, Nam ES, *et al.* The prevalence and significance of incidental thyroid nodules identified on computed tomography. J Comput Assist Tomogr 2008;32:810-5.
38. 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.
39. 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.