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RETENTION INDEX (RI) OF Tc-99m MIBI THYROID SCINTIGRAPHY, ULTRASONOGRAPHY (USG), AND FINE-NEEDLE ASPIRATION CYTOLOGY (FNAC) IN THE ASSESSMENT OF THYROID NODULE

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Oral Presentation on
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Abstract

Background: Thyroid nodules are frequently encountered in clinical practice and most of which are benign in nature.However, it is still a challenge to effectively distinguish malignant nodules from benign since FNAC as the primarydiagnostic tool does not give a definitive diagnosis in 10 – 42% of case (indeterminate results). This prospective study wasdesigned to appraise the significance of Tc-99m MIBI scintigraphy using retention index parameter, USG, and FNAC in differentiating benign from malignant thyroid nodules.

Material and Method: Single injection, dual phase (15 and 120 minutes) thyroid scintigraphy using 370-555 MBq Tc-99mMIBI was performed in all participants. All participants also underwent ultrasonography, FNAC, and surgery.

Results: The mean of retention index for malignant thyroid nodule (1.04±0.50) was significantly higher than benign thyroidnodule (0.58±0.17; p=0.001). Using threshold

>0.58 as malignant thyroid nodule, the sensitivity, specificity, NPV, PPV, andaccuracy for Tc-99m MIBI were 87.5%, 70.6%, 92.3%, 58.3%, and 80% respectively. Sensitivity, specificity, NPV, PPV,and accuracy for USG were 87.5%, 52.9%, 90%, 46.7%, and 64%. FNAC showed 14 benign nodules, 6 indeterminate, and 5malignant nodules. Diagnostic performance of Tc-99m MIBI thyroid scintigraphy was not significant different from USG,but RI was capable to detect 5 out of 6 (83%) participants with indeterminate FNAC.

Conclusion: RI of Tc-99m MIBI scintigraphy may be useful in the assessment of thyroid nodule, especially those withindeterminate FNAC result.

Introduction

Thyroid nodules are frequently encountered in clinical practice and most of which are benign in nature. It could be simply distinguish from normal surrounding tissue by palpation or using ultrasound (USG). According to Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer 2009, the incidence of thyroid nodule is 5% in female and 1% male. Incidence was higher if (19-67%) if using USG to examine the thyroid nodule.[1-3] Thyroid cancer was found in 5-10% patients with thyroid nodule, while rest of them were benign. Gold standard for the diagnosis of thyroid nodule is tissue histopathologic examination taken from surgery or biopsy in non-operable nodule. There quite high number of patient was underwent unnecessary surgery. Surgery is a high cost procedure and non-free complication.[1-4]

USG, thyroid scan and fine needle aspiration cytology (FNAC) are diagnostic modalities could be use to help clinician to differentiate cancer from benign thyroid nodule.[2-4] There is no pathognomonic characteristic from USG test alone can be used to for the diagnosis of thyroid cancer.[2] Variation of diagnostic result of USG are operator dependent as well as specification of instrument and the criteria of diagnosis.[5-7]

^{99m}Tc pertechnetate thyroid scan is one of diagnostic modality to evaluate thyroid nodule. Thyroid scan has low specificity test, since only 5-15% of cold nodule observe from thyroid scan are malignant.[2-4]

FNAC is a specific test for the diagnosis of thyroid cancer. This modality has high negative predictive value.[2,3,8]However, it is still a challenge to effectively distinguish malignant nodules from benign since FNAC as primarydiagnostic tool does not give a definitive diagnosis in 10 – 42% of case (indeterminate results).

Technetium-99m hexakis-2-methoxyisobuthylisonitrile (^{99m}Tc-MIBI) can be used as radiopharmaceutical for thyroid scan. This radiopharmaceutical can be accumulated in cancer cells.[9-11]

The aim of this study was to evaluate the significance of ^{99m}Tc-MIBIscintigraphy using retention index parameter, USG, and FNAC in differentiating malignant from benign thyroid nodules.

Material and Method

This descriptive, comparative, and prospective study wasdesigned to evaluate the significance of ^{99m}Tc-MIBIscintigraphy using retention index parameter, USG, and FNAC in differentiating malignant from benign thyroid nodules. This study was conducted in Dr. HasanSadikin General Hospital from January to June 2012. The study

was approved by Health Research Ethics Committee, Faculty of Medicine UniversitasPadjadjaran. Subjects were patient with single thyroid cold nodule based on ^{99m}Tc pertechnetate thyroid scan, normal thyroid function and scheduled to be operated or biopsy. Pregnant and breast feeding patients, and patient with parathyroid adenoma were excluded. Histopathology test post surgery was used as gold standard.

Ultrasonography

Thyroid USG was done by using linear probe to produce gray scale images and read by radiologist. Kang score was used to evaluate thyroid nodule.

^{99m}Tc-MIBI thyroid scan

Static thyroid scan was done from anterior projection using gamma camera with energy setting 140 keV, window width 20%, 4 x zoom, 15 minute and 2 hour after injection of 370-555 MBq (10-15 mCi) ^{99m}Tc-MIBI. Region of interest (ROI) was manually draw over 2 images.

All subject also underwent FNAC, and surgery.

Statistic analysis

Statistic analysis was used to compare retention index of ^{99m}Tc-MIBI between subject with malignant and benign thyroid nodule. Diagnostic test using 2X2 table was applied to evaluate diagnostic performance of retention index of ^{99m}Tc-MIBI, USG and FNAC for the detection of malignant thyroid nodule. Statistic analysis was done using SPSS program for Windows 17.0 version.

Results

Total subjects included in this study was 25, consist of 24 female and 1 male, aged 16-17 years old. Diameter of thyroid nodule based on USG was 9-130 mm. Malignant thyroid nodule (papillary and follicular) was observed in 8 subjects, and benign (adenomatous, colloid goiter and thyroiditis) in 17 subjects. Using t-test analysis, there is no significant different ($p>0.05$) between characteristic subject with malignant and benign nodule.

Table 1. Comparation of diagnostic value of retention index of ^{99m}Tc-MIBI, USG and FNAC in subject with malignant and benign thyroid nodule

Diagnostic Test	Nodule Characteristic Malignant	Benign	Sensitivity (%)	Specificity (%)	accuracy (%)
RI* ^{99m}Tc-MIBI			87.5	70.6	76
> 0.58	7	5			
< 0.58	1	12			
USG			87.5	52.9	64
malignant	7	8			
benign	1	9			
FNAC			62.5	76.5	72
malignant	5	0			
Indeterminate	2	4			
benign	1	13			

*Retention index

The mean and standard deviation of retention index for malignant thyroid nodule was 1.04±0.50 with ranged 0.39-2.04. That was significantly higher ($p=0.001$) than benign thyroidnodule (0.58±0.17). Using cut-off > 0.58 of retention index for malignant thyroid nodule, the sensitivity, specificity, NPV, PPV, andaccuracy for ^{99m}Tc-MIBI were 87.5%, 70.6%, 92.3%, 58.3%, and 80% respectively. Sensitivity, specificity, NPV, PPV,and accuracy for USG were 87.5%, 52.9%, 90%, 46.7%, and 64%. Sensitivity, specificity, NPV, PPV,and accuracy for FNAC were 62.5%, 76.5%, 81.3% and 55.5% respectively.(table 1) Diagnostic performance of ^{99m}Tc-MIBI thyroid scan was not

significant different from USG, but retention index was capable to detect 5 out of 6 (83%) participants with indeterminate FNAC. Diagnostic performance of combination between retention index of ^{99m}Tc-MIBI and FNAC showed sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 100%, 93.3%, 85.7%, 100% and 94.7% respectively.

Tabel 2. Kappa score of retention index of ^{99m}Tc-MIBI, USG and FNAC in subject with malignant and benign thyroid nodule

	Histopathologic test		
Diagnostic test	**Malignant**	**Benign**	**Kappa value**
RI* ^{99m}Tc-MIBI			0.51
> 0.58	7	5	
< 0.58	1	12	
USG			0.38
Kang score > 2	7	8	
Kang score < 2	1	9	
FNAC			0.33
malignant	5	4	
benign	3	13	

Kappa analysis was done to evaluate concordance between retention index of ^{99m}Tc-MIBI (k=0.51), USG (k=0.38 and FNAC (k=0.33) with histopathologic test. K value of for retention ^{99m}Tc-MIBI was higher compared to USG and FNAC. (table 2)

Discussion

Proportional test of characteristic using t-test between subject with malignant and benign thyroid nodule showed no significant different with p >0.05, so those 2 groups could be compared.

Camarthy and Coakly showed that ^{99m}Tc-MIBI was normally distributed in thyroid gland, clearance rate was different based on number of mitochondria. Since this study

using retention index as parameter, ^{99m}Tc-MIBI scan was done as early and late images. Retention index was calculated by comparing number of ^{99m}Tc-MIBI uptake from 2 images.[12,13]

Retention index 0.39 was found in 1 subject with malignant thyroid nodule. This discrepancy between low retention index and malignancy may be due to the diameter of nodule was relatively small (26 mm). This study showed 5 subjects with retention index 0.68-0.93 were benign. This discrepancy could be due to several factors such as, diameter of tumor relatively bigger, with high vascularity and proliferation.[14] All those 5 subjects underwent Doppler USG to evaluate vascularity. The results showed no significant different compared to subject with benign thyroid nodule. Proliferation index could not be determined, since Ki-67, PCNA and MIB-1 were not done.

Diagnostic performance of retention index of ^{99m}Tc-MIBI, USG and FNAC in thyroid cold nodule based on sensitivity, specificity, positive predictive value, negative predictive value and accuracy were not significantly different. Kappa analysis showed that kappa value of retention index of ^{99m}Tc-MIBI, USG and FNAC were 0.51, 0.38 and 0.33 respectively. Retention index of ^{99m}Tc-MIBI has moderate degree of agreement with histopathologic test, while USG and FNAC had poor degree of agreement.

Retention index of ^{99m}Tc-MIBI has higher sensitivity compared to 2 other modalities and FNAC has higher specificity, by combining retention index of ^{99m}Tc-MIBI with FNAC can increase diagnostic value. Cold nodule with indeterminate or positive malignant based on FNCA and retention index of ^{99m}Tc-MIBI > 0.58 are malignant nodule. Cold nodule with indeterminate or benign based on FNCA and retention index of ^{99m}Tc-MIBI ≤ 0.58 are benign nodule. Combine these 2 modalities showed sensitivity,

specificity, positive predictive value, negative predictive value and accuracy were 100%, 93.3%, 85.7%, 100% and 94.7% respectively.

Conclusion

Retention index of ^{99m}Tc-MIBIscan was a useful test to differentiate malignant from benign thyroid nodule, particularly to patient withindeterminate FNAC result.

Diagnostic performance of retention index of ^{99m}Tc-MIBI was better compared to USG and FNAC in differentiating malignant from benign thyroid nodule.

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