

Diagnostic utility of ultrasonography and fine needle aspiration cytology in the pre-operative assessment of suspicious thyroid nodules

B.S. Seneviratne¹, K.M.H. H. Kulatunga¹, S.S.N. Fernando¹, A.A. Pathirana¹, B.D. Gamage¹, A. Epa²,
M.K.A. Sampath¹, C. Sosai²

¹University of Sri Jayewardenepura, Sri Lanka

²Colombo South Teaching Hospital, Sri Lanka

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Abstract

Introduction and Background

The incidence of thyroid cancer in Sri Lanka has risen over the last two decades. According to current national cancer statistics, it has become the second commonest cancer in females. Ultrasonography and fine needle aspiration cytology (FNAC) are pre-operative investigations that are useful to assess the nature of thyroid nodules. Though, majority of thyroid nodules are benign, it is vital to identify the suspicious nodules pre-operatively, to decide the most appropriate treatment option.

Aim of the study was to determine the diagnostic utility of ultrasonography and FNAC in the pre-operative assessment of suspicious thyroid nodules in the local setting.

Methodology

A descriptive cross-sectional study conducted at the Colombo South Teaching hospital and Department of Pathology, University of Sri Jayewardenepura enrolling 135 patients with ultrasonically suspicious thyroid nodules. Ultrasound guided FNAC samples were collected from each patient for cytological assessment. TIRADS (Thyroid Imaging Reporting And Data System) classification was used for radiological assessment and the Bethesda system for cytological interpretation. Data was analyzed using the SPSS 23 software.

Results

The age of enrolled patients ranged from 15-76 years with a mean age of 49.8. Majority of the patients were females (81%) while 19% were males. Eleven FNAC specimens were excluded from the study due to insufficient cellularity.

Classification of the cases according to ultrasound findings

showed that the majority of the patients 51.61% (n=64) belonged to TI-RADS 3 (mildly suspicious). Thirty nine (31.45%) patients had moderately suspicious nodules (TI-RADS 4) and 21 cases (16.93%) were highly suspicious.

Conclusion

TI-RADS 5 category had the highest sensitivity and 100% concordance between the cytology and ultrasonography results.

Introduction

Over the past few decades, the incidence of thyroid malignancy has shown an upward trend across the world [1]. However, the thyroid cancer burden is largely heterogenous in different parts of the world, possibly due to variability of the genetic mutations, environmental risk factors, educational level and the availability of health care facilities [2]. In Sri Lanka thyroid malignancy is the second most common cancer in females [3].

As the incidence of thyroid cancer is rising it is necessary to have minimally invasive and reliable first line investigations to decide the management plan. Ultrasound imaging technique is the most frequently used pre-operative diagnostic test [4]. Sonographic findings in certain cases could be non-specific, and a definitive diagnosis is most often obtained from the fine needle aspiration cytology technique (FNAC), [5].

It is important to adhere to a standardized reporting system when interpreting sonographic findings. To address this issue several institutions have recently proposed a risk stratification system known as Thyroid Imaging Reporting And Data System (TI-RADS), following the principles of the widely accepted BI-RADS model for breast imaging [6]. Over the past few years the TIRADS recommended by the American college of radiology (ACR TI-RADS) gained popularity as this system was able to unify the language between the clinicians, radiologists and pathologists [7].

Ultrasonography is followed by Fine Needle Aspiration Cytology (FNAC) when necessary [8]. Interpretation of

Correspondence: B.S. Seneviratne

E-mail: bimalka@sjp.ac.lk

 <https://orcid.org/0000-0002-0451-0257>

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thyroid cytology findings is done according to the recommendations of the “Bethesda system of reporting thyroid cytology”,[9]. This system also helps to maintain uniformity when assessing FNAC smears and stratify patients according to the risk of malignancy [10].

The ultimate goal of these standardized diagnostic tests is to provide evidence based recommendations for the clinicians to decide the best management plan.

Objective

Aim of the study was to evaluate the diagnostic utility of ultrasound based TI-RADS findings and thyroid cytology results in the pre-operative assessment of suspicious thyroid nodules.

Methodology

A prospective study done over a period of 3 years (June 2018 to June 2021) at the department of radiology and department of pathology, Colombo South Teaching Hospital, Sri Lanka and the department of pathology, Faculty of Medical Sciences, University of Sri Jayewardenepura enrolling 135 patients with radiologically suspicious thyroid nodules.

Ethical clearance for the study was obtained from the Ethics Review Committee of the Faculty of Medical Sciences, University of Sri Jayewardenepura (65/19) and the informed written consent was obtained from all the participants prior to collecting the samples.

Ultrasonography of thyroid nodules was performed by a team of experienced radiologists and reported according to the ACR TI-RADS classification.

Fine Needle Aspiration cytology specimens were collected from the radiologically malignancy suspected thyroid nodules using 23/24 gauge needles. Thereafter, thin smears were prepared from the aspirate and immediately fixed in 95% alcohol for 20 minutes and stained with hematoxylin and eosin. Cytopathological assessment was done by two independent consultant pathologists following the guidelines of the “Bethesda system of reporting thyroid cytology”. The data was analyzed using SPSS version 23 to determine the accuracy of radiological and cytological results and the concordance between the two methods.

Results

Study included patients with radiologically suspicious thyroids that were reported as TI-RADS 3 (mildly suspicious), TI-RADS 4 (moderately suspicious), or TI-RADS 5 (highly suspicious). Initial sample size was 135,

however 11 cases had to be excluded from the study following guided FNAC, due to poor cellularity of the cytology smears precluding accurate assessment. Final sample size was 124. Age range of the patients was 15-76 years with a mean age of 49 years. Majority of the patients were females (81%) while 19% were males.

In the current study, radiologically suspicious thyroid nodules were more frequently found in the 3rd to 6th decade of life. The patients in this age group were approximately 80% of the study sample. Distribution of the patients with suspicious nodules according to ultrasound findings showed that the majority of the patients 51.61% (n=64) belonged to TI-RADS 3 (mildly suspicious). Thirty nine (31.45%) patients had moderately suspicious nodules (TI-RADS 4) and 21 cases (16.93%) were highly suspicious.

US guided FNAC results of the patients with suspicious nodules were categorized according to the Bethesda system of reporting (figure 2). Fifty five (44.35%) out of 124 suspicious nodules were reported as Bethesda 2 (benign). Twenty six cases (20.96 %) were reported as Bethesda 3 and 15 cases (12.09 %) as Bethesda 4.

Seventeen cases had (13.7 %) cytological features suspicious of malignancy and eleven (8.87%) were reported as malignant (Bethesda 6).

Further to the analysis of thyroid cytology results, TI-RADS findings of the 124 patients were correlated with the FNAC results (table 1).

Out of 64 in TI-RADS 3 only one case (1.56%) was reported as Bethesda 5 (suspicious of malignancy). The remaining cases (n=40) were in Bethesda 2 (benign), Bethesda 3 (n=15) and eight in Bethesda 4 categories.

Thirty nine out of 124 had moderately suspicious nodules (TI-RADS 4), out of which 04 were in Bethesda 5 and 02 in

Table 1: TI-RADS and thyroid cytology results

TIRADS system for Reporting	Bethesda System of Reporting					Total
	2	3	4	5	6	
TR 3	40	15	08	01	0	64
TR 4	15	11	07	04	02	39
TR 5	00	00	00	12	09	21
Total	55	26	15	17	11	124

Bethesda 6 categories. A significant number was in Bethesda 2 /benign category. The percentage of cases in Bethesda 5 and were 06 was 15.38%.

TI-RADS 5 had 21 cases, and 12 were reported as suspicious of malignancy (Bethesda 5) and 09 as malignant (Bethesda 6). None of the cases in TI-RADS 5 were cytologically reported below the level of Bethesda 5.

Risk of malignancy (Bethesda 5 & 6 cases) in TI-RADS categories are given below (figure1).

Discussion

A wide spectrum of diseases give rise to enlargement of the thyroid gland which results in the development of a diffuse or nodular goiter [11]. However, in the majority of cases the cause of thyroid enlargement is due to a benign pathological entity [12]. Ultrasonography of thyroid is a popular, first line investigation to identify the suspicious nodules that need further investigations. Several important criteria have been suggested by different institutions and organizations to maintain uniformity in the interpretation of ultrasound findings of thyroid. The current study followed the ultrasonographic features recommended by the American college of radiology (ACR TI-RADS), and the key imaging features that were taken into consideration included composition of the nodule, echogenicity, shape, and margin of the nodule. Based on the ultrasound features American college of radiology classify the nodules in to TI-RADS 1 (benign), TI-RADS 2 (not suspicious), TI-RADS 3(mildly suspicious), TI-RADS 4 (moderately suspicious) and TI-RADS 5 (highly suspicious) categories. Higher the total score greater the TI-RADS group and the possibility of malignancy [13]. Above classification helps to standardize the ultrasound results.

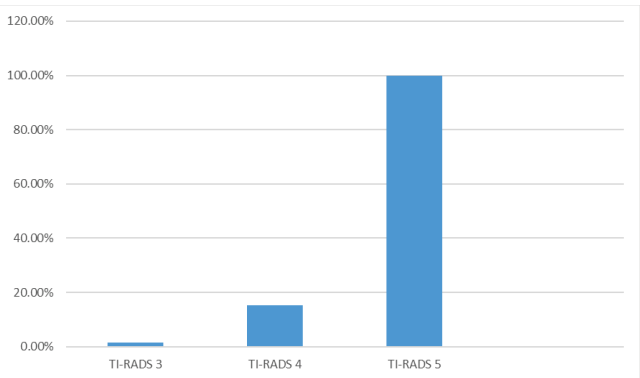


Figure 1: TI-RADS 3- 1.56%, TI-RADS 4 - 15.38%, TIRADS 5- 100%

The current study was based on radiologically suspicious nodules belonging to TI-RADS 3, 4 and 5 categories. TI-RADS 1 and 2 categories include “benign” and “not suspicious” lesions and according to ACR recommendations FNAC is not recommended.TI-RADS 6 includes proven malignant nodules and was not considered in this study [14].

US guided FNAC samples of the suspicious nodules were reported according to the Bethesda guidelines. This system includes six different categories as Bethesda 1 (non diagnostic or unsatisfactory), 2 (benign), 3 (atypia of undetermined significance or follicular lesion of undetermined significance), 4 (follicular neoplasm or suspicious of follicular neoplasm), 5 (suspicious for malignancy) and 6 (malignant). [12]

Results of the current study on gender distribution and peak incidence matched the studies done in other parts of the world. A review done by Reina Yao et al has suggested a possible association between oestrogen receptors and thyroid cancer [15]. Jonklaas J et al have collected and analyzed data from a prospective registry (USA) and shown a similar age distribution along with female preponderance in thyroid cancer [16].

In the current study there were 64 cases in TI-RADS 3, and only 01 case (1.56%) was reported cytologically as suspicious of malignancy (Bethesda 5). From the remaining 63, forty were (62.5%) in Bethesda 2 category and reported as colloid goiter, chronic thyroiditis or hyperplastic nodule. Remaining cases were in Bethesda 3 (n=15) and Bethesda 4 (n=8).

Prospective study done in a tertiary care center in India by Periakaruppan et al [17] included a total of 184 patients. TIRADS 3 had 45 patients, and none were classified as

Table 2: TIRADS & Bethesda correlation (Periakaruppan et al)

	Bethesda 1	Bethesda 2	Bethesda 3	Bethesda 4	Bethesda 5	Bethesda 6	Total
TIRADS 2	10	106	01	-	-	-	117
TIRADS 3	01	42	01	01	-	-	45
TIRADS 4	04	04	-	02	02	01	13
TIRADS 5	01	01	-	02	04	01	09
Total	16	153	02	05	06	02	184

Bethesda 5 or 6. There were 42 in Bethesda 2, and 01 case in each of Bethesda 1, 3, and 4 [table 2].

There were 39 cases out of 124 in the present study reported as TI-RADS 4. As the TI-RADS score increases the risk of malignancy rises, in keeping with this a higher number (n=6) was reported as Bethesda 5 and 6 (6/39, 15.38%).

According to the current results the malignancy risk of TI-RADS 5 was 100% as all the cases were cytologically reported as Bethesda 5 or 6.

A cross-sectional study conducted by Moifo et al, in Marne La Vallee, France [18] included 430 cases out of which 23 (5.3%) were malignant. The malignancy risks in this study were 0% for TIRADS 2, 2.2% for TIRADS 3, 5.9% - 57.9% for TIRADS 4 and 100% for TIRADS 5.

A prospective study conducted by Srinivasan MNS & Amoghl VN et al [19] including 364 patients with suspicious thyroid nodules revealed a risk of malignancy of 0.64%, 4.76% - 83.33%, 100% for TIRADS categories 3, 4 and 5 respectively. Out of the important sonographic features, irregular margins had the highest positive predictive value (95.45%).

A retrospective cross-sectional study by Grace Dy J et al [20], including 149 patients has documented that the solid nature of the suspicious nodule was the most reliable sonographic finding to predict malignancy (95% CI 1.3257 to 18.2011, p=0.017). The risk of malignancy for TIRADS categories 3, 4, and 5 were 12.5%, 12.82% - 53.70% and 66.67%.

Conclusion

Diseases of thyroid gland are becoming more prevalent in Sri Lanka, signifying a larger burden on the national health care system. Ultrasonography and guided FNAC are effective and practical, pre-operative diagnostic tests to determine the cause of thyroid enlargement. Nodules categorized as TI-RADS 5 (highly suspicious) had a complete concordance as it is 100% between radiological and cytological results (p value < 0.05). It can be mentioned with a high level of confidence that TI-RADS 5 along with cytology results are sensitive in identifying malignant nodules.

Majority of the cases (62.5%) in TIRADS 3 were cytologically benign (Bethesda 2). Close collaboration between the clinician, radiologist and cytopathologist can minimize costly interventions for many of the cases which would finally follow a benign clinical course.

At the same time it is vital to have a clear understanding of the limitations and pitfalls of the pre-operative diagnostic techniques, to overcome inaccuracies that would be misleading. In such instances the pre-operative diagnostic tests can be repeated to ensure more accurate assessment.

In conclusion there is a remarkable correlation between TI-RADS 5 and thyroid cytology but less so with TI-RADS 3 and 4. In a resource poor setting, the role and reliability of the pre-operative diagnostic tests in the assessment of suspicious thyroid nodules must be understood in order to minimize overdiagnosis of malignancy leading to inappropriate surgery.

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