



Application of the ACR-TIRADS Classification in Managing Bethesda Class III Thyroid Nodules: An Experience from Baghdad Teaching Hospital

Salman WAH¹, Mohammed MS², Ghadhban BR³ and AlMashhadani M^{4*}

¹Lecturer of Surgery, College of Medicine, University of Baghdad, Iraq

²Specialist of General Surgery, Medical City, Iraq

³Professor of Surgery, College of Medicine, University of Baghdad, Iraq

⁴Consultant of Anesthesia and Intensive Care, Medical City, Iraq

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*Corresponding author: Marwan AlMashhadani, Consultant of Anesthesia and Intensive Care, Medical City, Baghdad, Iraq

Abstract

Background: The goal of the Bethesda system is to improve the preoperative diagnosis of thyroid nodules and facilitate effective communication between the provider performing the thyroid evaluation and the health care providers interpreting the results. The TIRADS (Thyroid Imaging Reporting and Data System) is a classification used in thyroid ultrasound imaging to assess the risk of malignancy in thyroid nodules. It is based on a set of characteristics such as the shape, edges, and calcifications of the nodule, helping doctors make accurate decisions regarding the need for biopsy or surgical intervention.

Aim of the Study: To study the role of sonographic diagnosis in managing Bethesda class III nodules.

Patients and Methods: A retrospective study was conducted from October 2024 to January 2026 at Baghdad Teaching Hospital. Seventy-five patients underwent ultrasonographic, FNA and surgery for their thyroid nodules. It was approved by the Iraqi Board ethical committee.

Results: The study found a significant difference in malignancy rates across TIRADS III, IV, and V, suggesting a possible trend where higher TIRADS categories may have more malignancy. All patients with TIRADS V nodules underwent total thyroidectomy, while 68% of TIRADS I V had total thyroidectomy. Re-aspiration was done to 2 cases with TIRADS V nodules, and 77% of cases underwent total thyroidectomy. TIRADS III has high specificity but poor detection, while TIRADS I V has low sensitivity and specificity.

Conclusion: In summary, the data reinforce the utility of TIRADS in guiding clinical decisions for thyroid nodules. While higher TIRADS categories correlate with increased malignancy risk, careful consideration of sensitivity and specificity is essential to balance the benefits of early malignancy detection against the risks of overtreatment.

Keywords: Bethesda; TIRADS; Ultrasonographic; Thyroid Nodules

Abbreviations

ACR TIRADS: American College of Radiology Thyroid Imaging Reporting and Data System; FNA: Fine Needle Aspiration; ATA: American Thyroid Association; SPSS: Statistical Package for Social Sciences; FNAB: Fine-needle Aspiration Biopsies; NPV: Negative Predictive Value; AME: Associazione Medici Endocrinologi.

Introduction

Thyroid nodules are common, often detected incidentally on imaging studies of the neck. They can be broadly classified as benign and malignant. The clinical significance of nodules largely depends on their size and the risk of malignancy. In general, nodules larger than 1 cm require further evaluation. Additional features such as the appearance on ultrasound and the presence of associated lymphadenopathy can help assess risk. Several systems have been proposed to classify thyroid nodules based on ultrasound appearance [1]. The most widely adopted system is the one proposed by the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TIRADS). With the Bethesda system for the classification of thyroid fine needle aspiration (FNA) cytology, nodules can be classified as benign, suspicious for nodular goiter, atypia/intra-follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm/suspicious for follicular neoplasm, carcinoma, or non-diagnostic (Bethesda II-VI) [2]. According to the original publication of the Bethesda system, Bethesda Class I and II nodules can be stratified as low-risk (negative for malignancy) and high-risk (positive for malignancy) nodules. Following an initial cytological assessment, nodules classified as Bethesda Class III (atypia/intra-follicular lesion of undetermined significance) have an intermediate risk of malignancy and require a repeat FNA to determine their management. Unfortunately, a repeat FNA is also non-diagnostic in 20% of Bethesda Class III nodules and subsequently falls into the “non-classifiable” category which has a low risk of malignancy (0-5%, 2.5% in) under the Bethesda system [3]. Thyroid nodules are classifiable under Bethesda system I-VI and ACR TIRADS 1-5. Understanding this classification is essential for diagnostic and management discussions. Moreover, classifiable risk implies management. For example, Bethesda class VI is treated with surgical resection, while class I is followed up with a repeat FNA. This critical nature of classification underscores its importance in clinical practice and for the subsequent discussion on sonographic evaluations.

Among thyroid nodules, Bethesda Class III nodules present the most challenging management dilemma. While many guidelines recommend follow-up indeterminate nodules after the initial Fine Needle Aspiration (FNA) diagnosis, repeat FNA or surgery is often suggested based

on the nodule size and the basic characteristics on cytology, such as atypia. Despite this approach, the clinical outcomes of repeatedly aspirated Bethesda Class III nodules tend to be benign in most cases. Thus, it becomes imperative to develop management strategies to limit unnecessary surgeries in benign Bethesda Class III nodules [1]. Sonography is a widely available imaging modality and is currently used as the first-line screening test for thyroid nodules. Moreover, sonographic evaluation is known to enhance the overall diagnostic accuracy of FNA cytology [4]. Although Bethesda Class III thyroid nodules on cytology are considered indeterminate, the preceding study confirms that sonography can better differentiate benign from malignant Bethesda Class III nodules compared to cytology alone, suggesting the pivotal role of sonographic evaluation in managing Bethesda Class III nodules. Thyroid nodules with atypia/follicular lesions of undetermined significance (Bethesda Class III) on the initial cytology have uncertain clinical significance and are often subject to repeat cytology or surgery. The effectiveness of sonographic features in predicting the clinical behavior of these nodules has been assessed in several studies, with conflicting results [5].

Aim of the Study

To study the role of sonographic diagnosis in managing Bethesda class III nodules.

Patients and Methods

This study is a retrospective analysis evaluating the role of sonographic diagnosis in the management of Bethesda Class III thyroid nodules. The study was conducted from October 2024 to January 2026 at Baghdad Teaching Hospital. It was approved by the Arab Board for Health Specializations in Iraq in 30th of December 2024 (2000106801). Seventy-five patients were included in this study. Thorough history and full examination were done to all of them.

Inclusion Criteria

Patients aged 18 years or older diagnosed with Bethesda Class III nodules based on fine-needle aspiration (FNA) cytology. All nodules had sonographic features of TIRADS III >15 mm, TIRADS IV, or TIRADS V.

Patients who underwent sonographic evaluation prior to repeat FNA, or surgical intervention.

Exclusion Criteria

Patients with an incomplete medical record or missing sonographic data.

Patients with prior thyroid surgery or known thyroid malignancy.

Nodules classified outside Bethesda Class III.

Data collected from Baghdad Teaching Hospital. All the included patients underwent thorough history about age, their complaints, family history, history of radiation and medications. Physical examination was done and blood test for thyroid function, then sonographic assessment followed by FNA from the largest nodule or the most suspected one. All the patients included in this study underwent surgery either lobectomy or total thyroidectomy.

High-resolution ultrasound was performed using a standardized protocol. The following sonographic features were recorded:

Echogenicity: Hypoechoic, isoechoic, or hyperechoic.

Margins: Well-defined, irregular, or micro-lobulated.

Calcifications: Presence of microcalcifications, macrocalcifications, or none.

Shape: Taller-than-wide or wider-than-tall.

Vascularity: Internal vascularity patterns assessed via Doppler imaging.

Size: Measured in three dimensions (length × width × depth). Larger nodules (≥1 cm) are typically assessed for malignancy risk, but smaller ones may be monitored if they have suspicious features.

The American Thyroid Association (ATA) recommends biopsy (FNA) for nodules ≥1 cm if they have suspicious features on US.

Composition (determines cystic or solid nature)

Solid: Higher risk of malignancy

Cystic (fluid-filled): Often benign

Mixed (solid + cystic): Variable risk.

The data were analyzed using Statistical Package for Social Sciences (SPSS) version 26.0 and Microsoft office 2023. The data was explained using descriptive statistics, which include measures of frequency, range, mean, and standard deviation. A chi-square test (for comparing percentages or other non-continuous variables). Statistical significance was determined when the p-value was 0.05 or lower.

Results

The mean age of the patients was 41.08 ± 11.144 , the percentage of females was more than males: females 86.7% vs. males 13.3%, all of them are multinodular goiter, as shown in Figure 1. The most common complaint of the patients was complaining of neck swelling 52%, then pressure symptoms 37.1%. Hyperthyroidism was the third presentation 9.3%. Hoarseness of voice was the least presentation 1.3% (Table 1). There was highly significant difference between the histopathology results p-Value = 0.000 (Table 2).

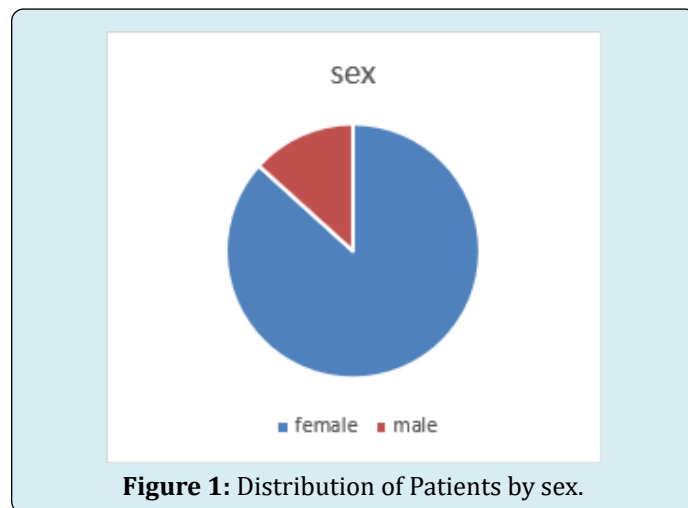


Figure 1: Distribution of Patients by sex.

Presentation	Frequency	Percent
Hoarseness	1	1.30%
Hyperthyroidism	7	9.30%
Neck Swelling	39	52%
Pressure symptoms	28	37.40%
Total	75	100%

Table 1: Patient's presentation in the study.

Histopathology	Benign	Follicular Ca	Papillary Ca	p- Value
Frequency (percent)	58 (77.3%)	4 (5.3%)	13 (17%)	0

Table 2: Comparison of Histopathology Results among the Patients.

The difference in malignancy rates across the TIRADS III, I V and V is statically significant p-Value= 0.004. This suggesting a possible trend where higher TIRADS categories may have more malignancy (Table 3). All patients had TIRADS V nodule underwent total thyroidectomy, while 68% of TIRADS IV had total thyroidectomy. Fifteen patients out of

48 who had TIRADS I V underwent lobectomy, three of them went through another surgery for total resection because of malignancy (Table 4). Table 5 shows that re-aspiration had been done t2 cases with TIRADS V nodules. While 29% of class IV had re-aspiration been done 37% of TIRADS III had re-aspiration.

TIRADA	Total Cases	Malignant	Benign	p-Value
III	8	1	7	0.004
IV	48	7	41	
V	19	9	10	

Table 3: Comparison between Sonographic Classification and their Histopathology Results.

		Surgery			Total	p-Value
		Lobectomy	Lobectomy then Completion	Total Thyroidectomy		
TIRADS	III	3	0	5	8	0.065
	IV	12	3	33	48	
	V	0	0	19	19	
Total		15	3	57	75	

Table 4: TIRADS Classification and Surgical Procedures.

		Re-aspiration		Total
		No	Yes	
TIRADS	III	5	3	8
	IV	34	12	48
	V	19	2	19
Total		56	19	75

Table 5: TIRADS Classification and Re-aspiration.

Table 6 shows that 18 patients underwent lobectomy but three of them had total thyroidectomy later on because the histopathological report showed malignancy. Forty-four

cases out of 57 (77%) who underwent total thyroidectomy were benign.

		Histology		Total
		Benign	CA	
Surgery	Lobectomy	15	0	15
	Lobectomy then completion	0	3	3
	Total Thyroidectomy	44	14	57
Total		59	17	75

Table 6: Surgical Procedures and Histological Outcomes.

Table 7 shows that TIRADS III has high specificity (86.4%) and high NPV (76.1%), meaning it correctly rules out malignancy but is poor at detecting it. TIRADS IV has low sensitivity (41.2%) and low specificity (30.5%), making it unreliable. TIRADS V has higher sensitivity (52.9%) and

high specificity (83.1%), making it the best classifier for malignancy. Overall (IV + V as positive): Very high sensitivity (94.1%) (detects almost all malignancies) but low specificity (13.6%) (many false positives).

TIRADS	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
III	5.90%	86.40%	11.10%	76.10%
IV	41.20%	30.50%	14.60%	64.30%
V	52.90%	83.10%	47.40%	86%
All (IV+V Vs III)	94.10%	13.60%	23.90%	88.90%

Table 7: Sensitivity and Specificity for Sonographic Method.

Discussion

This study provides valuable insights into the demographic characteristics, clinical presentations, and histopathological outcomes of patients presenting with thyroid-related conditions. Due to its ease of use, safety, accuracy, and affordability, US-FNA is the first-line technique for the diagnostic assessment of nodular thyroid disease. The frequency of benign thyroid surgeries performed has decreased, thyroid cancer diagnosis rates have increased, and thyroid nodule evaluation with US-FNA has improved thyroid cancer detection rates [6]. The mean age of the study population was 41.08 - 11.144 years. Notably, females comprised the majority of the sample (86.7%), while males accounted for only 13.3%. This finding aligns with previous studies indicating a higher prevalence of thyroid disorders in females, which may be attributed to hormonal influences, including estrogen's role in modulating immune responses and thyroid function [7].

The most common symptom reported by patients was neck swelling (52%), followed by pressure symptoms (37.4%). Hoarseness of voice was the least frequently reported complaint. Neck swelling as a primary symptom is also a well-documented presentation of both benign and malignant thyroid conditions [8]. The predominance of pressure-related symptoms is consistent with the natural progression of thyroid enlargement, which can cause mechanical compression of adjacent structures such as the trachea and esophagus [9].

Histopathological examination revealed that benign lesions were the most common (78.7%), followed by papillary carcinoma (16%) and follicular carcinoma (5.3%). The predominance of benign pathology aligns with existing literature, which suggests that most thyroid nodules are non-malignant [10]. The significant difference in histopathological outcomes ($p = 0.000$) underscores the importance of cytological and histopathological evaluation differentiating benign from malignant thyroid lesions.

The significant difference in malignancy rates across TIRADS III, IV, and V ($p = 0.004$) suggests that the TIRADS system effectively stratifies thyroid nodules based on malignancy risk. The validity of TIRADS in clinical practice is supported by this pattern, which is consistent with findings from earlier studies that showed a progressive increase in malignancy risk with higher TIRADS categories. According to Periakaruppan, et al.'s study [11], TIRADS 5 nodules were 35.4 times more likely to be malignant than TIRADS 3 nodules. While TIRADS 5 nodules in the study by George NA, et al. [12] exhibited a 5.23-fold increased risk of cancer in comparison to TIRADS 3 nodules. The ability of TIRADS to differentiate risk underscores its potential in guiding

diagnostic and therapeutic decisions [13].

Surgical interventions varied notably across TIRADS categories. All patients with TIRADS V nodules underwent total thyroidectomy, whereas 68% of those with TIRADS IV nodules received the same treatment. Notably, 15 patients with TIRADS I V nodules initially underwent lobectomy; among them, three required subsequent total thyroidectomies due to malignancy findings. This progression underscores the challenges in preoperative risk assessment and the potential need for more aggressive initial surgical approaches in certain cases.

Re-aspiration procedures were performed in 2 cases with TIRADS V nodules, 29% of TIRADS IV cases, and 37% of TIRADS III cases. This trend suggests a higher degree of diagnostic uncertainty in lower TIRADS categories, leading to repeated fine-needle aspiration biopsies (FNAB). The necessity for re-aspiration in TIRADS III and IV categories may reflect the inherent limitations in accurately distinguishing benign from malignant nodules based solely on initial cytological evaluation.

When using TIRADS as positive indicators for malignancy, the sensitivity increased to 94.1%, effectively identifying almost all malignant cases. However, this approach resulted in a low specificity of 13.6%, leading to a higher rate of false-positive results. In comparison with other studies, a study by Singaporewalla, et al. [14], the sensitivity and specificity of US TIRADS were 70.6% and 90.4% respectively, while a study by Suresh, et al. found the sensitivity of US TIRADS was 72.3%, however the specificity was lower at 66.7% [12]. This is similar to the study by Kim, et al. [15] who had studied the role of ultrasound classification in managing Bethesda III, the sensitivity, specificity, positive and negative predictive values of US diagnoses were 63.6%, 95.2%, 93.3%, 71.4%, and 79.1%, respectively. Chandramohan, et al. [16] discovered that the PPV for malignancy for TIRADS 4 and TIRADS 5 nodules was 36% 64% and 91%, respectively. According to Srinivas, et al. 39, the probability of cancer for those classified as TIRADS 4 and 5 was 83.3% and 100%, respectively.

In contrast to previous research that cite their findings, such as the Mendes, et al. [17] report the concordance rates of US TIRADS and FNAC with final histology in predicting malignancy were 75.4% and 95%. The total concordance percentage of US TIRADS and FNAC with post-operative HP was 75.4% and 81.8%, respectively, according to Abdelkader, et al. [18], whereas these values were 75% and 83.3%, respectively, in the study by Suresh, et al. [12]. As a result, this study results found that PPV and NPV of the TIRADS were 23.9% and 88.9%, respectively which are slightly similar to those of earlier research.

The specificity and negative predictive value (NPV) of TIRADS III were high, at 86.4% and 76.1% respectively, indicating its reliability in correctly identifying benign nodules. However, its low sensitivity suggests limited effectiveness in detecting malignancies. Conversely, TIRADS IV demonstrated low sensitivity (41.2%) and specificity (30.5%), rendering it less reliable for accurate risk stratification as the 2016 guidelines by the American Association of Clinical Endocrinologists (AACE), American College of Endocrinology (ACE), and Associazione Medici Endocrinologi (AME) highlight the role of molecular testing in cases with indeterminate cytology, aiding in the decision-making process for surgical intervention [19]. TIRADS V exhibited higher sensitivity (52.9%) and specificity (83.1%), making it the most effective category for malignancy detection among the three. These findings are consistent with previous studies that have evaluated the diagnostic performance of various TIRADS classifications [20].

Due to constraints such as a small sample size and the use of a different radiologist for each case, in conclusions of this study differ from those of earlier investigations. The observation that 77% of patients who underwent total thyroidectomy had benign histopathological results raises concerns about potential overtreatment. This highlights the critical need for precise risk stratification to avoid unnecessary surgical interventions, aligning with the goals of various TIRADS guidelines to optimize patient management [21].

Conclusion

In summary, the data reinforce the utility of TIRADS in guiding clinical decisions for thyroid nodules. While higher TIRADS categories correlate with increased malignancy risk, careful consideration of sensitivity and specificity is essential to balance the benefits of early malignancy detection against the risks of overtreatment.

The findings suggest that while the TIRADS system effectively stratifies malignancy risk, significant challenges remain, particularly with TIRADS IV due to its low specificity and sensitivity. Integrating molecular testing and adjunctive diagnostic methods could improve specificity and reduce overtreatment, ultimately enhancing patient outcomes.

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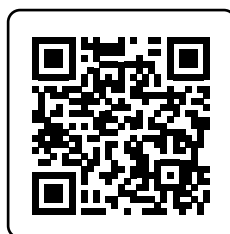
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