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Assessment of Pediatric Thyroid Nodule Sonographic Features Applying the ACR TIRADS

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ABSTRACT

FNA is the recommended clinical approach in the conclusive diagnosis of thyroid nodules. ACR TIRADS assess the various criteria considered before performing the FNA/biopsy of any thyroid nodule. Even though these parameters are validated for adult patients, their use in pediatrics has not been well studied. This research looked in the accuracy of ACR TIRADS in pediatric cases. A retrospective study was done including children who presented with thyroid nodules. Participants were chosen if they were ≤ 14 years and had ultrasound imaging findings of thyroid nodules. Patients were excluded if they had an incidental thyroid nodule detected by other modalities with lack of baseline ultrasound scan, diffuse thyroid disease with no dominant nodule as seen in thyroiditis and Graves' disease, diffuse heterogeneity, thyroidectomy, and infection/abscess/ phlegmon. 50 thyroid nodules were studied and half were malignant. The ACR TIRADS sensitivity was calculated as 95.8%. Size was also studied to consider its effect on malignancy risk. The research's findings suggested that ACR TIRADS demonstrates good accuracy level for use in pediatric cases; however, size plays no significant role in the determination of malignancy risk of children's thyroid nodules.

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Keywords: ACR Tirads, Thyroid Nodule, Bethesda System for Reporting Thyroid Cytopathology, Predictivity Parameters, Fine Needle Aspiration FNA, Biopsy

Abbreviations
ACR – American College of Radiology, FNA – Fine needle aspiration, US – Ultrasound, TIRADS – Thyroid Imaging Reporting and Data Systems.

Introduction

The clinical approach to pediatric thyroid nodules is challenging compared to their adult counterparts. The challenges can be directly linked to the lack of specific pediatric guidelines. The assessment of pediatric nodules involves some unique characteristics, including pathophysiological differences, long-term outcomes, and clinical presentations [1]. For instance, nodular size may be unreliable as thyroid volume changes with age.

The ultrasound (US) is a crucial part of the clinical approach to thyroid nodule management in pediatric as well as in adult populations. Multiple guidelines have been proposed to expound on US imaging findings, the most popular of which are the Thyroid Imaging Reporting and Data Systems (TIRADSs), that provide universally accepted terminology to standardize US thyroid nodule descriptions among radiologists. Adtionally, (TIRADSs) establish the risk of malignancy in a given thyroid nodule and facilitate the communication between radiologists and clinicians. Furthermore, they aid in detecting malignant nodules for biopsy reducing incidences of unnecessary FNAs [2]. The American College of Radiology put forward parameters guiding the description of thyroid nodules known as ACR-TIRADS.

ACR-TIRADS was not designed for pediatric patients, but has been validated for adults [3]. Particular facets of the ACR-TIRADS make it advantageous for practical use with pediatric patients. ACR TIRADS' advantages include applicability, accessibility, and general acceptance in US medical practice. Additionally, this scheme is relatively straightforward [4]. ACR-TIRADS offers a promising solution in pediatrics to recognize nodules with high malignancy risk that warrant an FNA, yet there are few studies into this area.

Therefore, this research's objective was to look into the thyroid sonographic features applying the ACR-TIRADS and studying the decision to perform an FNA biopsy for pediatric population. The goal was to determine the efficiency of ACR-TIRADS in diagnosing pediatric thyroid nodules.

Objectives

- To assess the accuracy of ACR-TIRADS in diagnosing pediatric thyroid nodules.
- To determine the sensitivity of ACR-TIRADS in detecting malignant thyroid nodules in children.
- To evaluate the role of nodular size in determining the risk of malignancy in pediatric thyroid nodules.
- To validate the use of ACR-TIRADS in pediatric cases,

despite being originally designed for adults.

- To investigate the applicability and practicality of ACR-TIRADS in pediatric clinical practice.
- To contribute to the development of specific guidelines for the assessment of pediatric thyroid nodules.
- To provide evidence-based recommendations for the management of thyroid nodules in pediatric patients based on ACR-TIRADS.

Materials and Methods

Research Design and Patients

The research study was conducted per the principles of Standards for Reporting Diagnostic Accuracy (STARD) [5]. A retrospective study was conducted, including 50 pediatric patients of up to 14 years of age with ultrasound imaging findings of thyroid nodules. The patient database was obtained from King Faisal Specialist Hospital & Research Center (KFSH&RC). The selected participants had FNA and histopathological assessments done between January 2006 and June 2022. The study began after receiving the institutional review board's approval. Patient demographics, FNA and pathology reports were recorded, by reviewing the institutional clinical health information system (Powerchart). Subsequently, TIRADS were used to categorize imaging findings.

Research participants were chosen or rejected based on specific criteria. All pediatric patients with a thyroid nodule were chosen to participate in the study. The bases for the exclusion of patients were the following: (a) An incidental thyroid nodule detected by other modalities with lack of baseline ultrasound scan; (b) Diffuse thyroid disease with no dominant nodule as in Graves' disease or thyroiditis; (c) Diffuse heterogeneity and micro- or macro-calcification +/- enlargement; (d) Thyroidectomy; and (e) Infection/abscess/phlegmon.

Ethical Considerations

The Ethics Committee of KFSH&RC approved the study. Confidentiality was adhered to during the collection and analysis of data per KFSH&RC policies on subject privacy. Confidentiality was maintained for all data and records provided during the study. These data and records were not used for any purpose other than conducting the study. Personal patient information, including name, age, ultrasound examination type, and laboratory results, was collected and coded electronically using Microsoft Excel. The investigator used the radiology reporting station that can only be accessed by personal ID and password securely to store the data. A master list of codes and identities was maintained in a secure location and not recorded on the data collection sheet.

Ultrasonography

Thyroid ultrasonography was performed to examine ultrasonographic images and determine thyroid vascularity and volume. An in-depth review of the ultrasonographic images was systematically conducted according to the ACR TIRADS criteria for the categorization of US imaging findings. Radiologists classifying the various nodules were unaware of their histopathology, and various criteria were used to categorize them. The nodular size was measured and recorded. The nodule's shape was documented as wider than taller or taller than wider. The nodule's composition may be cystic, solid, or spongiform. Furthermore, the echogenicity is documented as isoechoic, hyperechoic, hypoechoic and anechoic. The margins of the nodules can be smooth, irregular, ill-defined, lobulated, or with extra-thyroidal extension. An analysis of the echogenic foci looks into its presence or absence. Additionally, the foci can be described as punctuate and differentiated as macro-calcifications, micro-calcifications, or artifacts. The concept behind ACR TIRADS that allows radiologists to determine malignancy is that individual US features cannot discriminate between benign and malignant thyroid nodules, therefore, a set of features is used to accurately distinguish them [6].

Thyroid Nodule Histopathology

FNAs were performed to collect samples to determine pathology. The clinician gave instructions to perform FNA procedures based on the ultrasonographic features, laboratory report, the probability of malignancy, and patient preference. The Bethesda System for Reporting Thyroid Cytopathology was used to classify the samples [7]. The various classes were as follows: papillary carcinoma, medullar carcinoma, follicular neoplasm, Hashimoto thyroiditis, benign, atypical, or non-diagnostic findings.

Statistical Considerations

Performing a retrospective chart review was essential in evaluating the sample size and influence. There was a sufficient number of cases for a single institution in the retrospective study. The keywords used in the chart review included pediatrics, thyroid nodule, thyroid cancer, and FNA. Data from 2006 to 2022 was retrieved.

Statistical analysis was done using R version 3.3.2. Numerical data were expressed as means and ranges, while categorical variables were described as numbers and percentages. Descriptive statistics included the tabulation of imaging information, patient age, demographic information, and laboratory reports. Predictivity parameters were used to determine diagnostic reliability including accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) [8]. These tests consider the true positives, true negatives, false positives, and false negatives.

Results

A total of 50 patients were chosen from the KFSH&RC database after applying the inclusion and exclusion criteria. All these patients had undergone US thyroid or US neck/soft tissue examinations from January 2006 to June 2022. Thyroid US are commonly used to examine thyroid nodules [9]. 43 (86%) patients had US thyroid examinations, and 7 (14%) patients had US neck/soft tissue examinations. The mean age was 11.50 years, with all patients being 14-year-old or younger. The youngest patient was four years old. Nodule size varied greatly. The largest thyroid nodule measured 4.9 x 3.1 cm.

A biopsy or FNA was performed in patients whose nodules showed high malignancy risk. The study looked into the incidence of malignancy to confirm the concept that an estimated 20% of pediatric thyroid nodules are malignant [10]. Twenty-five biopsies were done out of the 50 cases presented. Only cases that required FNA had histopathological assessments done. Of the 25 thyroid nodules biopsied, 6 (24%) were benign, 17 (68%) were malignant, and 2 (8%) were unsuccessful. Unsuccessful biopsies occurred when the nodular size was too small and did not fit the required FNA threshold. The most prevalent cancer among the patients was papillary thyroid carcinoma (7 of 9 cases ~ 77.78%), followed by follicular carcinoma (2 of 9 cases ~ 22.22%). There was one conventional variant case - the multifocal medullary thyroid carcinoma. There were individual cases of follicular adenomas, follicular neoplasm, and follicular hyperplasia. Furthermore, there were two patients with nodular hyperplasia and two cases of thyroiditis.

Table 1: Main Patient Characteristics. (n=50)

Characteristics	
• Age at exam, years (mean)	12
• Examination type	
• US thyroid, *n* (%)	43(86%)
• US neck/soft tissue, *n* (%)	7(14%)
• Nodule size	
• Maximal dimensions, cm	4.9 x 3.1
• Minimal dimensions, cm	0.16 x 0.1
• Benign/Malignant nodules, *n* (%)	6/18 (12/36)

US, ultrasound; cm, centimeter.

Table 2 breaks down the classification of the 50 thyroid nodules grouped into the different ACR TIRADS levels. Nodules that were not biopsied scored low points based on the ACR TIRADS. In such cases, FNA is not required as the nodule is considered to have a low malignancy risk. These thyroid nodules were considered benign. The TR4 category had a majority of the nodules. This class constitutes the nodules that present an intermediate malignancy risk. TR5, which indicates a high malignancy risk, had a 60% cancer prevalence rate. On the other hand, the TR1 category, which indicates low malignancy risk had the lowest cancer prevalence at 20%.

Table 2: Distribution of 50 Thyroid Nodules Grouped According to the ACR TIRADS Guidelines and Calculation of the Cancer Prevalence Rate of the Various TIRADS

TIRADS	Benign nodules	Malignant nodules	Total number	Cancer prevalence
TR1	4	1	5	20%
TR2	8	3	11	27.27%
TR3	6	2	8	25%
TR4	10	6	16	40%
TR5	4	6	10	60%

The primary clinical approach to pediatric thyroid nodules, according to 2015 ATA guidelines, is to conduct an FNA in cases of high malignancy risk. Table 3 shows the incidences in which biopsy occurred corresponding to the various ACR TIRADS. In the TR4 and TR5 categories, the choice to perform the biopsy was common. TR5 nodules present the highest malignancy risk. However, only one biopsy was carried out for the five thyroid nodules that fell into the TR1 category.

Table 4 summarizes the occurrence of malignancy with the decision to biopsy corresponding to the ACR TIRADS level to which a nodule belonged. Two unnecessary biopsies were done that provided inconclusive results. The main problem that hindered these biopsies was the small size of the nodules. The only collected FNA sample belonging to the TR1 category tested positive for malignancy. TR4 and TR5 categories had the highest number of malignancies. The probability of malignancy increased with increasing ACR TIRAD levels.

Table 3: The Frequency of the Decision to Biopsy 50 Thyroid Nodules Grouped in ACR TIRADS

TIRADS	Frequency	Decision to biopsy	
		YES	NO
TR1	5	1	4
TR2	11	5	6
TR3	8	4	4
TR4	16	8	8
TR5	10	8	2

Table 4: The Occurrence of Malignancy in the 25 Thyroid Nodules that were Biopsied Grouped based on the ACR TIRADS

Pathological findings	TR1	TR2	TR3	TR4	TR5
Positive for malignancy	1	3	2	6	6
Negative result (benign)	0	1	2	1	2
Unnecessary biopsy	0	1	0	1	0

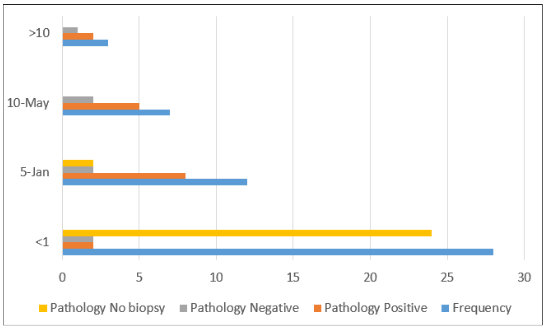
Table 5 offers insight into the possible correlation between nodular size and malignancy. The data was converted and presented as areas to simplify analysis using R version 3.3.2. Nodules that were not biopsied presented with low malignancy risk and thus did not warrant an FNA. The majority of nodules had areas lesser than 1 cm2. The nodules whose areas ranged from 1 to 5 cm2 had the highest number of malignancies. Additionally, out of the three nodules with areas greater than 10 cm2, two were malignant.

Table 5: The Correlation between the Size of 50 Thyroid Nodules and their Risk of Malignancy

Area (cm^2)	Frequency	Pathology		
		Positive	Negative	No biopsy
<1	28	2	2	24
1-5	12	8	2	2
5-10	7	5	2	0
>10	3	2	1	0

cm2, squared centimeters; Positive, malignant; Negative, benign; No biopsy, low points prohibiting the use of FNA.

Here is the Scatter Figure for Table 5 above:



The scattered figures below display the correlation of nodular size and occurrence of malignancy or benignity. Both figures have a widely dispersed pattern indicating weak or no association between size and malignancy.

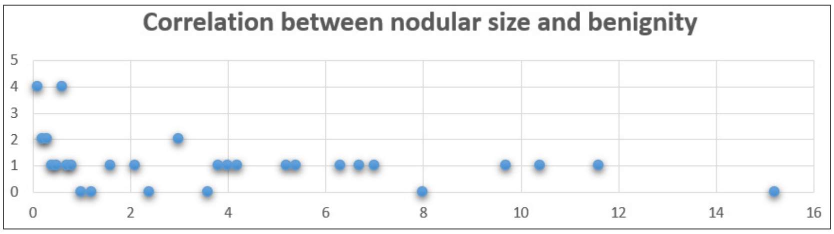


Figure 1: Correlation between Size of 50 Thyroid Nodules and Occurrence of Benignity

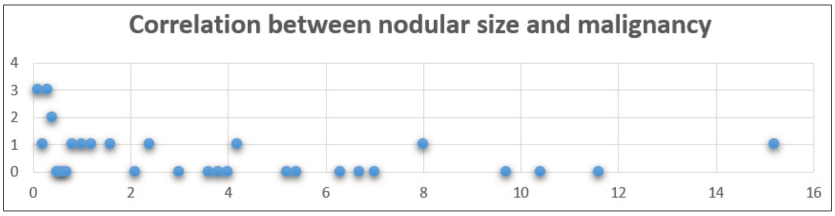


Figure 2: Correlation between Size of 50 Thyroid Nodules and Occurrence of Malignancy

Table 6 looks into whether a biopsy was done depending on two parameters – size and ACR TIRAD level. The nodules with areas greater than 10cm2 were all biopsied. These nodules fell in the TR3 and TR4 categories. For nodules with areas smaller than 1cm2, biopsies were carried out in some cases and ignored in others.

Table 6: The Decision to Biopsy 50 Nodules Depending on the Size and ACR TIRAD Level

Area (cm^2)	TR1		TR2		TR3		TR4		TR5	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
<1	0	4	1	6	0	4	3	8	1	1
1-5	0	0	2	1	2	0	1	0	5	1
5-10	0	0	2	0	1	0	2	0	2	0
>10	0	0	0	0	1	0	2	0	0	0

cm^2, squared centimeters.

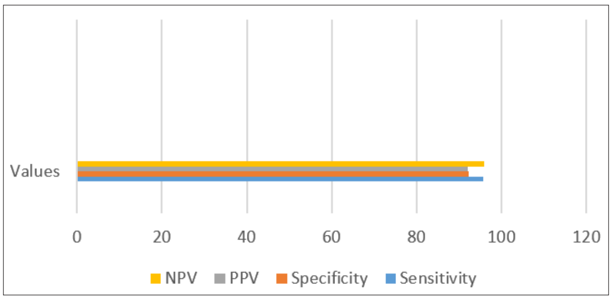
The diagnostic reliability of ACR TIRADS in providing sufficient evidence for an FNA was considered in this study. These predictivity tests are examined according to 95% confidence intervals (CI) [7]. Sensitivity entails a test's ability to correctly determine cases while specificity looks into a test's ability to calculate healthy cases [10]. In this study, ACR TIRADS had a sensitivity of 95.8% and specificity of 92.3%. Table 7 shows the various predictivity parameters obtained in this study.

Table 7: Values Obtained in ACR TIRADS Predictivity Tests

	Sensitivity (CI) (%)	Specificity (CI) (%)	PPV (CI) (%)	NPV (CI) (%)	Accuracy (%)
Values	95.8	92.3	92	96	94

CI, 95% confidence interval; PPV, positive predictive value; NPV, negative predictive value

Th Figure Below Summarizes Table 7:



Discussion

Principal Findings

An in-depth review of the results obtained in the study reveals that ACR TIRADS is useful in the essential discrimination of benign and malignant thyroid nodules in children [11]. The system's implementation of various tiers to determine a nodule's malignancy risk proved efficient for pediatric cases. According to the results, the risk of malignancy progressively increased with rising TIRADS levels. These findings corroborate the results obtained in ACR TIRADS analysis of adult thyroid nodules [12].

The sensitivity values greater than 50% indicate that the test can adequately identify malignancies in pediatric patients. ACR TIRADS accuracy is essential as thyroid nodules are likely to be detected in 50% to 60% of healthy patients [4]. Although thyroid nodularity stands at 0.5% in pediatric populations, these nodules present with a greater risk of malignancy making accurate clinical detection essential in their management [13]. Specificity values above 50% are crucial because 75% of thyroid nodules in pediatrics are benign [14].

The clinical diagnostic and treatment strategies for thyroid nodules in children and adolescents is detailed in the Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer, a 2015 American Thyroid Association publication [1]. ATA recommends carrying out a FNA or US finding following the identification of a child presenting with a concerning history [15]. Elements of a concerning pediatric patient history include previous exposure to radiation, genetic disposition, and a young age at the time of examination.

Previously, the 2009 ATA guidelines for managing adult thyroid nodules were also used for children and adults [16]. A revised version of the 2015 guidelines was created providing more recommendations a better clinical approach to thyroid nodules [17].

The study's results are in line with the ATA pediatric guidelines, as a biopsy was carried out for patients whose nodules scored high points [4]. ACR TIRADS examines certain features of the thyroid nodule as seen in ultrasound. Each feature is graded and earns points depending on the extent of suspicion, which is collected. The total sum is used to classify the nodules into the various levels of the ACR TIRADS. The higher the points, the higher the TIRAD level. It is also crucial to remember that a higher TIRAD level is associated with a higher malignancy risk. For instance, TR5 is considered a high malignancy risk class. Therefore, the decision to biopsy the nodule was based on the TIRAD level, with higher levels receiving additional scrutiny.

The decision to biopsy was not relaying on the nodule's ACR TIRAD level alone. Other factors were considered, such as size. ACR TIRADS for adult nodules does not implement size to designate TIRAD level [4]. Instead, size is considered when deciding to perform a biopsy. Pediatric management is different in that size has a minor implication on the choice of carrying out a FNA. Ultrasonographic images indicating suspicious nodules will be biopsied regardless of size. In pediatrics, malignancy risk is determined by ultrasound features and patient history with a minor consideration of size [18].

The results obtained in the research support this approach. The evidence is presented when analyzing the nodules of a 1 cm2 area. Even though the TR4 class is considered an intermediate risk, not all nodules were biopsied. ATA does insist on a nodule size cutoff before performing an FNA [19]. However, other factors were considered in making this decision, including a clear observation of ultrasound features. Nodules of various sizes also fell into the same class, nullifying the hypothesis that a larger nodule carries more risk. Additionally, a multivariable analysis involving size and TIRADS level established that higher ACR TIRADS are linked to an increased probability of malignancy.

Ultrasound has an essential role in determining thyroid malignancy [20]. There are several US-based risk stratification systems (RSSs) aside from the ACR. ACR was the fundamental point of this study because it is advantageous compared to the other guidelines. Several aspects of the system enhance its suitability for practical use in pediatric thyroid nodules. Firstly, ACR is relatively straightforward and can be well-understood by various practitioners with different qualification levels. The scheme's point-based perspective determines the malignancy risk by investigating the number of abnormal thyroid ultrasound features. This allows radiologists to account for all suspicious US features observed in the nodule's appearance compared to other pattern-based models [4]. Furthermore, the system offers medical professionals a universally accepted lexicon boosting standardization.

ACR TIRADS limitations should also be considered. This system exhibits high reproducibility in various experiments. However, its reliability is a variable parameter, with disagreements occurring between adjacent TIRADS categories. Scientific research is yet to determine whether reliability is affected by the patient's age.

Results on the frequency of malignant nodules support a key point held by the medical society about pediatric thyroid nodules. Thyroid nodules occur less frequently in children than adults [21]. The incidence of pediatric thyroid nodules is 0.1% to 5%, while that of adult nodules stands at 68% [1]. Despite their low incidence, pediatric thyroid nodules require significant clinical expertise as they have a greater risk of malignancy compared to adult ones [22]. To verify, thyroid nodules in children have a 25% malignancy risk [23]. Furthermore, pediatric thyroid cancers have more risk of cervical lymph node metastases, pulmonary metastases, extra-thyroidal extension, and recurrence.

The analysis of these results is of crucial importance as they provide evidence augmenting the idea that thyroid cancer is more prevalent compared to other forms of pediatric endocrine cancer [24].

Strengths and Weaknesses

The strengths of this research include: (1) the study highlights the suitability of ACR TIRADS for practical use as a clinical diagnostic approach to thyroid nodules in children and adolescents; (2) the study demonstrates that thyroid nodular size has no effect on implementation of FNA/biopsy as a diagnostic solution.

The weakness of the study should also be investigated. First, the retrospective study design is a limitation. The use of previous hospital records and static US images could create a selection bias. Moreover, the sample population size was small and was obtained from a single institution. The use of a small cohort is limiting as it leads to the recording of a small number of malignant nodules. There needs to be more data on malignancies to stifle the research's ability to anticipate the true population effect. Another limitation exists in the exclusion criteria involving patients who presented with thyroiditis, Graves' disease, incidental thyroid nodules, diffuse heterogeneity with micro- and macro-calcification, and infection. There was no follow-up, meaning that patients who underwent surgical resection in future were accounted for, resulting in possible alterations to the current results. Finally, there are chances of false positives or false negatives during the evaluation of US images. This weakness occurs because there is really no clear definition of what radiologists with varied experience constitute as the overall impression of the thyroid nodule.

Conclusion

The research shows that the application of ACR TIRADS in the study of thyroid sonographic features is beneficial in the differentiation of benign and malignant thyroid nodules and facilitates a reliable basis for the decision to perform an FNA/ biopsy in pediatric population (≤ 14 years old) [4]. Moreover, thyroid nodule size does not significantly affect malignancy risk and is not considered when deciding whether or not to carry out an FNA/biopsy. FNA is an accurate and reliable diagnostic approach regardless of nodular size, as the cytological features is unaffected by the nodule's diameter as long as the specimen is sufficient [25,26].

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Institutional Review Board Statement

The research study was carried out in accordance with the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of KFSH&RC (ethic cade: _ /approved date:¬_)

Data Availability Statement

The author can make all data present in this research available on request.

Conflict of Interest Statement

The author maintains no conflict of interest in regard to this research.

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