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Evaluating Postoperative Outcomes and Investigating the Usefulness of EU-TIRADS Scoring in Managing Pediatric Thyroid Nodules Bethesda 3 and 4

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What is already known on this topic?

The European-Thyroid Imaging Reporting and Data System (EU-TIRADS) is a risk stratification system used to evaluate the probability of malignancy in thyroid nodules, based on ultrasound characteristics. This scoring system assists clinicians in determining whether to suggest biopsy or further monitoring of thyroid nodules. The EU-TIRADS scoring system has undergone comprehensive investigation in adult populations, demonstrating acceptable accuracy in the prediction of malignancy. The EU-TIRADS scoring system has the potential to be a useful tool for evaluating thyroid nodules in children, but its accuracy and effectiveness still require confirmation.

What this study adds?

This study is the first comprehensive investigation that assesses the postoperative outcomes and explores the utility of EU-TIRADS scoring in the management of pediatric thyroid nodules categorized as Bethesda 3 and 4. Postoperative pathologies revealed varying EU-TIRADS scores. EU-TIRADS 5 produced a lower percentage of cases with malignancy in Bethesda 3, compared to the low risk and benign group, while in Bethesda 4 cases, EU-TIRADS scores increased as postoperative pathology worsened. These findings highlight the inconsistent results of EU-TIRADS in guiding clinical decision-making for pediatric thyroid nodules.

Abstract

Objective: The aim was to assess postoperative outcomes in pediatric thyroid nodules with atypia of undetermined significance (AUS/FLUS) or suspicious for a follicular neoplasm (SFN) and their respective the European-Thyroid Imaging Reporting and Data System (EU-TIRADS) scores.

Methods: Forty-four pediatric patients at a single center with thyroid nodules classified as AUS/FLUS or SFN from August 2019 to December 2022 were retrospectively reviewed. Data on demographics, thyroid function, nodule size, and ultrasonographic features were collected. Postoperative pathologies were categorized into benign, low-risk, and malignant neoplasms according to the World Health Organization 2022 criteria, and EU-TIRADS was used for retrospective radiological scoring.

Results: Among 21 (47.7%) of patients who had surgical intervention, 72% had Bethesda 3 and 28% had Bethesda 4 thyroid nodules. Post-surgical histopathological classifications were 43% benign, 19% low-risk, and 38% malignant. Of note, EU-TIRADS 3 and 5 scores were present in 44% and 56% of the benign cases, respectively. Malignant cases tended to produce higher EU-TIRADS

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scores, with 64% rated as EU-TIRADS 5. Bethesda category 4 nodules had a 66% malignancy rate, significantly higher than the 27% in category 3.

Conclusion: A substantial proportion of histologically benign cases were classified as EU-TIRADS 5, suggesting that EU-TIRADS may lead to unnecessary biopsies in benign cases. Malignant cases were more likely to have a higher EU-TIRADS score, indicating a positive correlation with malignancy risk, particularly in Bethesda 4 cases. However, the EU-TIRADS system's predictive value for malignancy in Bethesda 3 cases was poorer.

Keywords: Pediatric thyroid nodules, malignancy, AUS/FLUS, Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance, FN/SFN, Follicular Neoplasm or Suspicious for a Follicular Neoplasm, EU-TIRADS, European Thyroid Imaging Reporting and Data System, malignancy

Introduction

Fine-needle aspiration (FNA) is a valuable method for guiding the therapeutic management of patients with thyroid nodules by estimating the risk of malignancy (1,2). The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) includes six diagnostic categories: I) non-diagnostic or unsatisfactory; II) benign; III) atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS); IV) follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN); V) suspicious for malignancy; and VI) malignant (1,3).

In children with thyroid nodules the Bethesda categories 3 and 4 are the two cytopathological diagnoses that present clinicians with the greatest difficulty when making surgical decisions and assessing the risk of malignancy. It has been shown that the malignancy risk for Bethesda category 3 and 4 is higher in children compared to adults (4). For Bethesda category 4 nodules, the risk of malignancy is greater than for category 3 nodules (5). The 2015 American Thyroid Association (ATA) 2015 guidelines recommend surgery for thyroid nodules classified as AUS/FLUS or FN/SFN on the first FNA biopsy (FNAB) in order to definitively establish the diagnosis and provide appropriate treatment if the nodule is malignant (2). The 2022 European Thyroid Association (ETA) pediatric guidelines recommend repeating FNAB after six months for AUS/FLUS and FN/SFN nodules detected on the first FNAB. Surgical management is reserved for cases with significant growth, suspicious ultrasound (US) features, or persistent cytological abnormalities (6). The guidelines note that the risk of malignancy is higher in pediatric thyroid nodules compared to adult nodules, and that surgical management may carry greater risks and consequences in children due to their smaller size and less-developed anatomy. However, the guidelines do acknowledge that careful observation with repeat FNAB at 6 to 12 months may be an option in select cases, such as those with small nodules or those with significant comorbidities that increase the surgical risk (2).

Bethesda category 3 and category 4 are both considered indeterminate categories, meaning that the risk of malignancy is unclear based on cytology alone. Therefore, additional evaluation and clinical correlation are needed to determine the appropriate management. It is important for clinicians to consider the individual patient's clinical and imaging features, as well as the specific cytopathological diagnosis, when deciding on management for Bethesda category 3 and 4 nodules in children. The Thyroid Imaging Reporting and Data System (TIRADS), is a set of risk stratification systems to categorize thyroid nodules based on US features (7,8). The term TIRADS can refer to multiple guidelines, including ACR-TIRADS (American College of Radiology) (9), EU-TIRADS (ETA) (10), and K-TIRADS (Korean Society of Thyroid Radiology) (11,12). The EU-TIRADS is considered to have a more straightforward and potentially less time-consuming approach to nodule classification. The system allows assessment of high specificity US malignancy features, which include marked hypo-echogenicity, irregular shape, irregular margins, and microcalcifications (10). While the EU-TIRADS scoring system has been extensively studied in adult patients and has shown good accuracy in predicting malignancy (13), there needs to be more data on its usefulness in childhood thyroid nodules. Some studies have suggested that the EU-TIRADS scoring system may be helpful in childhood thyroid nodules (14), but further research is needed to confirm its accuracy and usefulness in this population.

In the present study, the aim was to evaluate the histopathologically confirmed postoperative outcomes of cases with AUS/FLUS and SFN detected in thyroid nodules and retrospectively investigate their EU-TIRADS scoring.

Methods

The study was conducted as a single-center, retrospective, cross-sectional analysis. It encompassed patients who presented with findings of AUS/FLUS or SFN on FNAB between August 2019 and December 2022. The follow-up principle for thyroid nodules used by our multidisciplinary team (pediatric endocrinologists, pediatric surgeons, pediatric radiologists, pediatric oncologists and pathologists) in patients with thyroid nodules who are diagnosed as

Bethesda category 3 in their initial biopsy and who do not show pathognomonic findings of malignancy, such as microcalcification, central vascularity or irregular borders on US, is to keep them under observation. These cases were re-evaluated with ultrasonography after 3-6 months, followed by a second FNAB. Our study included 21 of the 44 patients who underwent surgical intervention after being diagnosed with Bethesda categories 3 (AUS/FLUS) and 4 (FN/SFN) on FNAB of the thyroid. Of the remaining 23 patients, ten were lost to follow-up, the second biopsies of six patients were interpreted as benign, and the seven patients had not yet had post-biopsy follow-up. Demographic and clinical data, such as age, gender, serum free thyroxine (fT4), thyroid-stimulating hormone levels, dimensions of thyroid nodules, sonographic characteristics, and histopathological findings post-thyroidectomy were retrieved from the institutional electronic medical records. TBSRTC was employed to categorize the cytopathological findings of the thyroid FNABs. The inclusion criteria encompassed cases classified as AUS or FLUS under category 3, as well as those specified as SFN under category 4. It is noteworthy that our cohort did not consist of any patients classified as follicular neoplasm (FN). All participants underwent a complete thyroidectomy as part of their treatment protocol.

Post-operative pathology results were divided into three categories, as classified by the World Health Organization (WHO) in 2022: benign neoplasms, low-risk neoplasms, and malignant neoplasms. Low-risk neoplasms are non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), thyroid tumors of uncertain malignant potential (UMP), and hyalinized trabecular tumor (HTT) (15,16). In this study, there were cases with NIFTP and UMP. Radiologic features of the nodule were scored according to the EU-TIRADS scoring system (2017) (10) The study was performed in accordance with the Helsinki Declaration of 1975. This study was approved by the Ethics Committee of Ankara City Hospital (approval number: E2-23-3317, date: 01.02.2023).

Statistical Analysis

All data analysis was performed with Statistical Package for Social Sciences, version 26.0 (IBM Inc., Armonk, NY, USA). Descriptive statistics were used to evaluate demographic and clinical characteristics. Data were defined as percent, mean ± standard deviation, and median (minimum-maximum). The chi-square test was used for comparing categorical variables. While investigating the associations between non-normally distributed and/ordinal variables, the correlation coefficients and their significance were calculated using the "Spearman test". Statistically, $p < 0.05$ was considered significant.

Results

In study population consisted of 21 patients who underwent surgical intervention following a diagnosis of Bethesda categories 3 (AUS-FLUS) and 4 (SFN) on FNAB. The median (minimum-maximum) age of the study population was 15.4 (11-17.5) years. Females constituted 86% (n = 18) of the patient population, while males represented 14% (n = 3). A family history of thyroid carcinoma was noted in one. In addition, one patient was under surveillance for an ovarian neoplasm. Thyroid function tests revealed hypothyroidism in 5% (n = 1), subclinical hypothyroidism in 10% (n = 2), and euthyroid status in the majority, 85% (n = 18). Notably, 42% (n = 9) of the patients presented with multiple thyroid nodules. Within this subgroup, 88% (n = 8) exhibited dual nodular formations, whereas 12% (n = 1) had three nodules.

The postoperative pathological analysis reported that 43% (n = 9) were classified as benign, 19% (n = 4) as low-risk neoplasms, and 38% (n = 8) as malignant. Within the low-risk neoplasm category, NIFTP constituted 75% (n = 3) of the cases, while UMP was observed in 25% (n = 1). FNAB cytopathological results and the WHO classification of postoperative pathology are depicted in Figure 1.

On evaluating the postoperative outcomes of thyroid nodules in relation to their EU-TIRADS scores, it was observed that in benign cases, 44% were rated as EU-TIRADS 3 and 56% as EU-TIRADS 5. Low-risk neoplasm cases were equally divided, with 50% being classified as EU-TIRADS 3 and the remaining 50% as EU-TIRADS 5. Among malignant cases, 13% were assessed as EU-TIRADS 3, 25% as EU-TIRADS 4, and 64% as EU-TIRADS 5. The classification

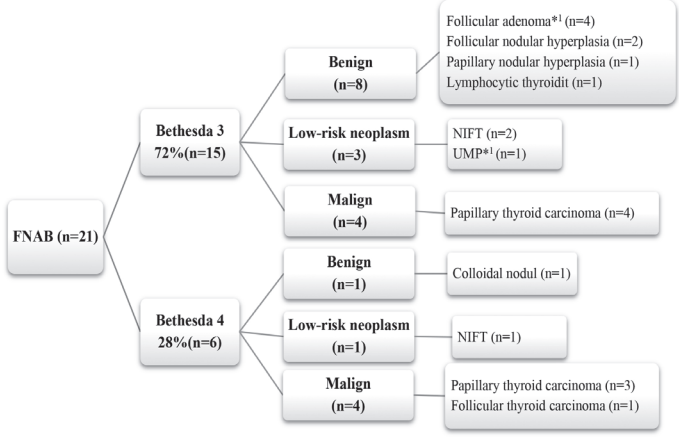

Figure 1. Postoperative pathology and FNAB results of the cases

*NIFT: non-invasive follicular thyroid neoplasm with papillary-like nuclear features, UMP: thyroid tumors of uncertain malignant potential*1 (1 = number of case), AUS: atypia of undetermined significance, FLUS: follicular lesion of undetermined significance, SFN: suspicious for follicular neoplasm, FNAB: fine-needle aspiration biopsy*

and distribution of EU-TIRADS scores with postoperative pathology outcomes are presented in Table 1.

Analysis of Bethesda classifications revealed that 72% (n = 15) of cases fell into category 3, while the remaining 28% (n = 6) were classified under category 4. In our study, the incidence of malignancy among Bethesda 3 cases was lower at 27% (n = 4), with 53% (n = 8) benign and 20% (n = 3) classified as low-risk neoplasms. In contrast, Bethesda 4 cases tended to exhibit a higher malignancy rate of 66% (n = 4), with benign (n = 1) and low-risk neoplasms (n = 1) each constituting 17% of the cases. The data revealed a higher prevalence of malignancy in FNAB for Bethesda category 4 at 66% compared to 27% in Bethesda category 3 (p = 0.20), although not sigificant, as detailed in Table 2. This may be due to low number of cases.

In the Bethesda 3 category (n = 15), TIRADS scoring classified 37% of benign cases as EU-TIRADS 3, and 63% as EU-TIRADS 5. Among the malignant cases (n = 4), 25% were scored as EU-TIRADS 3, 25% as EU-TIRADS 4, and 50% as EU-TIRADS 5. For the low-risk neoplasm group, 33% were assigned EU-TIRADS 3, and 67% EU-TIRADS 5 (Table 3). In the Bethesda 4 category (n = 6), radiological scoring identified EU-TIRADS 3 in one benign case. In addition, one case with a low-risk neoplasm was also scored as EU-TIRADS 3. Among the malignant cases within this group, 25% (n = 1) were classified as EU-TIRADS 4, while the majority, 75%, (n = 3) were classified as EU-TIRADS 5 (Table 4). Notably, there was a significant correlation identified in the Bethesda 4 group, indicating an increase in EU-TIRADS scoring as the postoperative pathology results worsened (r = 0.87, p = 0.02).

The postoperative pathological analysis demonstrated a median (range) nodule size of 12 (5-35) mm in the malignant group, 25 (7-48) mm in the benign group, and 23 (8-32) mm in the low-risk neoplasm group; these sizes did not differ between the classifications (p = 0.33), as illustrated in Figure 2. Lymph node metastasis was found in 24% of the cases overall, affecting 13% of cases in Bethesda category 3 and 60% in Bethesda category 4. There was no correlation between lymph node metastasis and TIRADS.

Table 1. EU-TIRADS scoring of post-op pathology results

	EU-TIRADS 3	EU-TIRADS 4	EU-TIRADS 5	Total
Benign	44% (n = 4)	0% (n = 0)	56% (n = 5)	100% (n = 9)
Low-risk neoplasm	50% (n = 2)	0% (n = 0)	50% (n = 2)	100% (n = 4)
Malign	13% (n = 1)	25% (n = 2)	64% (n = 5)	100% (n = 8)
Total	33% (n = 7)	10% (n = 2)	57% (n = 12)	100% (n = 21)

EU-TIRADS: The European-Thyroid Imaging Reporting and Data System

Table 2. Pathology results of the cases according to post-operative WHO classification

	Post-operative pathology (WHO classification)		
	Benign (n = 9)	Low-risk neoplasm (n = 4)	Malign (n = 8)
Bethesda 3 (n = 15)	53% (n = 8)	20% (n = 3)	27% (n = 4)
Bethesda 4 (n = 6)	17% (n = 1)	17% (n = 1)	66% (n = 4)
Total (n = 21)	43%	19%	38%

WHO: World Health Organization

Table 3. EU-TIRADS scoring of Bethesda 3 and post-op pathology results

Bethesda 3	EU-TIRADS 3	EU-TIRADS 4	EU-TIRADS 5	Total (n = 15)
Benign	37% (n = 3)	0% (n = 0)	63% (n = 5)	100% (n = 8)
Low-risk neoplasm	33% (n = 1)	0% (n = 0)	67% (n = 2)	100% (n = 3)
Malign	25% (n = 1)	25% (n = 1)	50% (n = 2)	100% (n = 4)

EU-TIRADS: The European-Thyroid Imaging Reporting and Data System

Table 4. EU-TIRADS scoring of Bethesda 4 and post-op pathology results

Bethesda 4	EU-TIRADS 3	EU-TIRADS 4	EU-TIRADS 5	Total (n = 6)
Benign	**100% (n = 1)**	0% (n = 0)	0% (n = 0)	100% (n = 1)
Low-risk neoplasm	**100% (n = 1)**	0% (n = 0)	0% (n = 0)	100% (n = 1)
Malign	**0% (n = 0)**	25% (n = 1)	75% (n = 3)	100% (n = 4)

EU-TIRADS: The European-Thyroid Imaging Reporting and Data System

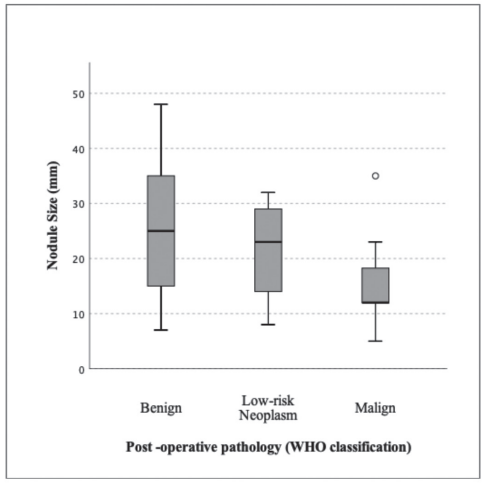

Figure 2. Nodule size (preoperative thyroid ultrasonography) compared to post-op pathology results

*p = 0.33

WHO: World Health Organization

Discussion

Thyroid FNA with US guidance is regarded as the most accurate test for diagnosing malignancy in thyroid nodules and reduces the need for surgery in benign nodules. It is important for clinicians to consider the individual patient's clinical and imaging features, as well as the specific histopathological diagnosis. The optimal management of thyroid nodules with a Bethesda 3 and 4 cytology in pediatric patients is debatable, due to the unpredictability but heightened cancer risk compared to adults. To the best of our knowledge, this study is the first to published study to evaluate postoperative histopathological results and assess the effectiveness of EU-TIRADS in managing pediatric thyroid nodules classified as Bethesda categories 3 and 4. The study evaluated twenty-one pediatric cases with Bethesda categories 3 and 4 and analyzed their EU-TIRADS scoring. The results suggest that EU-TIRADS cannot provide reliable guidance for clinical decisions in children with thyroid nodules. In addition, it was shown that the nodules postoperatively shown to be malignant may have smaller size, and thus, small nodules can also be malignant. In the Bethesda 4 category, there was a significant correlation between higher EU-TIRADS scores and the risk of malignancy development, in SFN cases.

In the context of paediatric EU-TIRADS use age, the evidence remains rather inconclusive. In the study by Yeste Fernández et al. (17), which analysed 31 cases with nodules, there were 5 cases with Bethesda 3 and 2 cases with Bethesda 4 and the results were collected in a very small cohort. Furthermore, a literature review, including the work of Tuli et al. (18) and Scappaticcio et al. (19), which used the SIAPC classification for FNAB pathologies, categorized cases into benign or malignant outcomes. Both studies demonstrated a suboptimal performance in the management of pediatric patients with thyroid nodules. The present study aimed to address the clinical challenges posed by Bethesda 3 and 4 thyroid nodules, with the goal of providing additional empirical evidence specifically targeting these ambiguous categories in the pediatric population.

In our cohort 53% of the nodules were classified as Bethesda 3 and were determined to have benign pathologies postoperatively. This finding is corroborated by the study of Canberk et al. (20) with a substantial cohort (n = 405), which identified 67% of AUS instances as benign. These concurrent findings raise questions about the ATA stance in favor of prompt surgical involvement for AUS/FLUS nodules (2). Since FNAB alone is insufficient for definitive surgical decision-making, supplemental radiological evidence is necessary for guidance.

In the present study, the postoperative results of AUS/FLUS cases showed 27% malignancy rate while SFN cases showed 66% malignancy rate. In 2019, Cherella et al. (4) reported malignancy rates of 44% and 71% for AUS and SFN nodules, respectively. Published pediatric studies show that the malignancy rates for Bethesda 3 nodules range from 8.3% to 44% (4,21,22,23) and for Bethesda 4 nodules range from 35% to 100% (23,24,25). These studies suggest that the rates of malignancy in both groups are different but the risk of malignancy in pediatric patients with Bethesda 4 nodules is relatively high compared to Bethesda 3.

Multiple US scoring systems are available to categorize nodules for fine-needle biopsy (FNB) indications, including fine-needle cytology (10,26). In the study by Borysewicz-Sańczyk et al. (27) conducted in Poland, a 29% malignancy rate was found among 17 pediatric cases with Bethesda categories 3-4-5-6. While all cases classified as Bethesda 5 and 6 were confirmed malignant postoperatively, two cases categorized as Bethesda 4 and labeled as high suspicion according to ATA classification were reported as benign histopathologically. In addition, none of the six Bethesda 3 cases, deemed low suspicion, were found to have malignancy. Conversely, the study of Richman et al. (28) evaluated the ACR TI-RADS against ATA guidelines in pediatric thyroid nodule management. Their findings indicated that while ACR TI-RADS may decrease the biopsy rate in benign nodules, it might also result in a significant number of pediatric cancers not being biopsied (22.1%), suggesting potential inadequacy of ACR TI-RADS in pediatric cases. The high frequency of benign cases classified as EU-TIRADS

5 in the present study may have led to unnecessary FNAB procedures. While most of the malignant cases in our cohort align with EU-TIRADS 4-5, 13% of cases were classified as low-risk, a lower proportion than the 22% reported by Richman et al. (28) using ACR-TIRADS. This suggests that while EU-TIRADS corresponds with the recognized literature in identifying higher-risk cases, there may be a discrepancy in the classification of lower-risk malignancies, indicating a potential area for review or adjustment in classification criteria. Moreover, in the study conducted by Creo et al. (29), malignant nodules were primarily identified within the ATA's high or intermediate suspicion groups. These authors concluded that pediatric radiologists' overall impressions were similarly sensitive but more specific than the ATA risk stratification. They also concluded that no US-based method perfectly separated benign from malignant nodules, affirming the ongoing necessity for FNAB in cases of suspicious nodules.

In the study of Yeste Fernández et al. (17), an evaluation of 31 pediatric thyroid nodules, Bethesda classification was applied, with categories ranging from 1 to 5, and 14 nodules underwent surgery, six of which were malignant. While 16% (n = 5) of the cases were Bethesda 3 without postoperative malignancy, 6.52% (n = 2) were Bethesda 4 with malignancy found. All malignant nodules were categorized as EU-TIRADS 4 or 5. The study highlighted the limitations of the case numbers but found EU-TIRADS classification had a sensitivity of 100%, specificity of 25%, PPV of 44%, and NPV of 100%, making it a reliable diagnostic tool for FNAB decision-making. In our analysis, which exclusively evaluated cases classified as Bethesda 3 and 4, we included a notably larger sample size compared to prior research. In our study, 25% of the 15 cases classified as Bethesda 3 were malignant and exhibited radiological assessments consistent with EU-TIRADS 3-4-5. In the Bethesda 4 group, which comprised six cases, the malignancy rate was 66%, with all cases radiologically assessed as EU-TIRADS 4-5. When evaluating both studies, it appears that EU-TIRADS scoring provides a more dependable guide for FNAB in cases classified as Bethesda 4. However, this level of reliability does not extend to the Bethesda 3 category, where EU-TIRADS scoring does not exhibit the same predictive strength for FNAB decision-making.

Our findings indicate that in Bethesda 3 cases, the presence of EU-TIRADS 5 scores is lower in malignant cases, whereas it is higher in the low-risk and benign groups. In Bethesda 4 cases, a positive correlation was observed between EU-TIRADS scores and the deterioration of postoperative pathology findings. This result emphasizes the intricate relationship between EU-TIRADS scoring, Bethesda categories, and definitive postoperative pathology diagnoses.

Our results suggest that the size of nodules in the malignant group tended to be smaller compared to the benign and low-risk neoplasm groups but this was not significiant. The range of sizes within each group was wide and overlapped. Nodules classified as TBSRTC category IV and V are recommended for surgical resection due to their high risk of malignancy. It has been suggested that for nodules with TI-RADS scores less than or equal to 3, US surveillance instead of FNA can be performed (30). One study retrospectively assessed the effectiveness of three US risk stratification systems (ACR-TIRADS, ATA, and EU-TIRADS) in pediatric patients with thyroid nodules and a history of radiation exposure. With 52 patients, 27% had papillary thyroid cancer (PTC) upon final histology. The systems showed high specificity (95-97%) and negative predictive value (88-93%), but they failed to recommend biopsies in a significant number of PTC cases, often due to nodules being smaller than 1 cm. This study suggested that while these systems are reliable, they could be improved by adjusting the size criteria for biopsy recommendations (31). It's important to note that nodule size alone is not a definitive indicator of malignancy, and other factors such as imaging characteristics and biopsy results must be considered.

Study Limitations

Limitations of this study include the small sample size, data collection from a single center, and the need for postoperative follow-up results. So, there is a need for more in-depth studies with larger sample sizes and results from long-term follow-ups.

Conclusion

The optimal management of AUS/FLUS and FN/SFN thyroid nodules in children is still an area of active research, and it should be individualized based on factors such as the patient's age, the size and characteristics of the nodule, and the results of diagnostic FNAB. The postoperative pathology assessment showed a discernible variability in EU-TIRADS scores. Specifically, within the Bethesda 3 category, instances of malignancy exhibited a comparatively diminished percentage of EU-TIRADS 5, in contrast to its more pronounced occurrence within the low-risk and benign cohorts. Conversely, among Bethesda 4 cases, there emerged a conspicuous ascending trajectory in EU-TIRADS scores concomitant with a worsening trend in postoperative pathology diagnoses. These findings accentuate the nuanced and debatable nature of the EU-TIRADS scoring system's utility in effectively guiding the intricate clinical

decision-making process concerning pediatric thyroid nodules. The EU-TIRADS scoring system has the potential to be a useful tool for evaluating thyroid nodules in children, but its accuracy and effectiveness still require confirmation through well-designed large studies.

Acknowledgement

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Ethics

Ethics Committee Approval: This study was approved by the Ethics Committee of Ankara City Hospital (approval number: E2-23-3317, date: 01.02.2023). The study was performed in accordance with the Helsinki Declaration of 1975.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: Aylin Kılınç Uğurlu, Abdurrahman Bitkay, Fatih Gürbüz, Esra Karakuş, Gülşah Bayram Ilıkan, Çağrı Damar, Seda Şahin, Merve Meryem Kıran, Nedim Gülaldı, Müjdem Nur Azılı, Emrah Şenel, İnci Ergürhan İlhan, Mehmet Boyraz, Concept: Aylin Kılınç Uğurlu, Esra Karakuş, Müjdem Nur Azılı, Design: Aylin Kılınç Uğurlu, Data Collection or Processing: Aylin Kılınç Uğurlu, Abdurrahman Bitkay, Esra Karakuş, Müjdem Nur Azılı, Analysis or Interpretation: Aylin Kılınç Uğurlu, Esra Karakuş, Literature Search: Aylin Kılınç Uğurlu, Writing: Aylin Kılınç Uğurlu.

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