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THE ROLE OF ULTRASOUND EXAMINATION AND FINE-NEEDLE ASPIRATION BIOPSY IN THE DIAGNOSIS OF FOLLICULAR THYROID CANCER (DATA FROM RSSPMC OF ENDOCRINOLOGY NAMED AFTER ACADEMICIAN Y.KH. TURAKULOV)

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Abstract

Follicular thyroid cancer is one of the malignant neoplasms that presents significant challenges for diagnosis at the preoperative stage. Ultrasound examination (US) is the primary non-invasive imaging method used for the initial assessment of thyroid nodules. It provides valuable information about nodule structure, size, vascularity, and potential signs of malignancy. However, despite its high diagnostic value, ultrasound alone is not always sufficient to reliably differentiate between follicular adenoma and follicular carcinoma. In this context, fine-needle aspiration biopsy (FNAB) plays a crucial complementary role. Nevertheless, even cytological analysis often fails to provide a definitive diagnosis, as the key criterion for malignancy—capsular and vascular invasion—can only be confirmed through histological examination. This study evaluates the diagnostic value of ultrasound and FNAB, their combined role in the comprehensive assessment of thyroid nodules, and specific approaches to suspected follicular carcinoma.

Justification

The necessity of a comprehensive analysis of the capabilities and limitations of US and FNAB in the diagnosis of follicular thyroid cancer is driven by the high clinical relevance of this pathology, the complexity of its diagnosis, and the importance of early tumor detection for selecting an appropriate treatment strategy. Investigating this topic contributes to the improvement of diagnostic algorithms for patients with thyroid nodules and enhances the effectiveness of preoperative diagnostics.

Objective

To analyze the role of US and FNAB in the diagnosis of follicular thyroid cancer based on clinical, instrumental, and morphological data collected at the Republican Specialized Scientific and Practical Medical Center of Endocrinology named after

Academician Y.Kh. Turakulov, with the aim of assessing their informativeness, diagnostic value, and determining an optimal diagnostic algorithm for the early detection of malignant follicular neoplasms.

Materials and Methods

The study included 109 patients who underwent examination and treatment for thyroid nodular formations at the clinic of the Republican Specialized Scientific and Practical Medical Center of Endocrinology named after Academician Y.Kh. Turakulov during the period from 2022 to 2023. The inclusion criterion was the presence of a thyroid nodule confirmed as follicular carcinoma based on postoperative histological examination.

Results

The study included 109 patients, the vast majority of whom were women—107 individuals (98.2%; 95% CI: 93.5–99.8). Only 2 men (1.8%; 95% CI: 0.2–6.5) were included, which may indicate a gender predisposition to thyroid pathologies or reflect specific sampling characteristics.

Analysis of the mean age of patients with different forms of thyroid cancer showed the following results: for the papillary type, the mean age was 52.5 years (SD = 16.0); for the follicular type, 55.0 years (SD = 13.9); and for the mixed type, 53.1 years (SD = 13.6). No statistically significant differences were found between the groups ($p = 0.704$), indicating that the sample was homogeneous in terms of age regardless of the tumor's pathomorphological variant.

Conclusion

The conducted study confirmed the high clinical relevance of a comprehensive approach to the diagnosis of thyroid nodules based on the combination of the EU-TIRADS ultrasound classification, the Bethesda cytological system, and histological verification.

Keywords: follicular thyroid cancer, ultrasound examination, fine-needle aspiration biopsy, cytological analysis.

Justification

Follicular thyroid carcinoma (FTC) is one of the most diagnostically challenging forms of differentiated thyroid cancer, accounting for approximately 10–15% of all malignant thyroid tumors [1]. Its morphological characteristics and clinical course

complicate early detection, especially at the subclinical stage. A key diagnostic limitation lies in the inability to reliably distinguish follicular adenoma from carcinoma based solely on cytological material obtained through fine-needle aspiration biopsy (FNAB). Ultrasound examination (US) remains the first-line method in evaluating patients with thyroid nodules. While modern ultrasound criteria enable the identification of suspicious lesions with high sensitivity, their specificity for follicular carcinoma remains limited. Therefore, a comprehensive approach combining US with FNAB becomes increasingly important to improve the accuracy of preliminary diagnosis and to optimize patient management. Despite advancements in imaging and morphological techniques, the diagnostic accuracy for follicular thyroid cancer remains suboptimal. This necessitates local studies that account for regional clinical and demographic characteristics. The data collected at the clinic of the Republican Specialized Scientific and Practical Medical Center of Endocrinology named after Academician Y.Kh. Turakulov enable the evaluation of the effectiveness of current diagnostic algorithms and help identify potential directions for their optimization. Thus, investigating the role of US and FNAB in the diagnosis of follicular thyroid carcinoma is timely, scientifically justified, and of high practical relevance. It contributes to improving early oncological vigilance and reducing diagnostic errors. Xu et al., 2024 – Ultrasound features for differentiating follicular carcinoma: The authors identified that a combination of US findings—such as mixed vascularity, spiculated margins, capsule contact, and chronic thyroiditis—allows for high diagnostic accuracy in distinguishing follicular carcinoma from adenoma [2]. Borowczyk et al., 2021 – Meta-analysis of US features in follicular carcinoma: A systematic review revealed that capsular protrusion, calcifications, irregular contours, and marked hypoechogenicity were statistically associated with follicular carcinoma. Capsular or vascular invasion was the strongest predictor [3]. Gopalan et al., 2024 – Cureus: The review emphasized that only histology can reliably diagnose FTC. However, combining US, FNAB, and molecular testing significantly increases preoperative diagnostic accuracy and reduces the risk of unnecessary surgery [4].

Research objective

To analyze the role of ultrasound examination and fine-needle aspiration biopsy in the diagnosis of follicular thyroid carcinoma based on clinical, instrumental, and morphological data collected at the Republican Specialized Scientific and Practical Medical Center of Endocrinology named after Academician Y.Kh. Turakulov, with the aim of evaluating their informativeness, diagnostic value, and determining an optimal diagnostic algorithm for the early detection of malignant follicular neoplasms.

Materials and methods

Study setting and period

Study location

The study was conducted at the clinic of the Republican Specialized Scientific and Practical Medical Center of Endocrinology named after Academician Y.Kh. Turakulov.

Study period

The study included patients with nodular goiter who received inpatient treatment from 2022 to 2023.

Study population

A continuous (consecutive) sampling method was used to form the study population.

Inclusion criteria

Patients aged 17 to 64 years with nodular goiter, presenting with single or multiple nodules on ultrasound examination, were included. The EU-TIRADS classification was applied to each nodule, followed by FNAB under ultrasound guidance.

Exclusion criteria

Patients with diffuse goiter, diffuse toxic goiter, or toxic adenoma were excluded from the study.

Study design

The study included 109 patients with nodular goiter (107 women and 2 men) as part of a prospective, randomized, controlled study aimed at evaluating the effectiveness of ultrasound examination and ultrasound-guided fine-needle aspiration biopsy (FNAB) in the diagnosis of follicular thyroid carcinoma.

Description of Medical Intervention

All patients underwent an assessment of thyroid function, including the measurement of thyroid-stimulating hormone (TSH), free thyroxine (fT4), anti-thyroid peroxidase antibodies (anti-TPO), and anti-TSH receptor antibodies (anti-TSHR). Instrumental diagnostic methods included thyroid ultrasound and FNAB under ultrasound guidance. Surgical treatment involved total thyroidectomy, followed by a histopathological examination of the thyroid tissue.

Methods

The diagnosis of follicular thyroid carcinoma was confirmed by histopathological examination following thyroidectomy.

TSH reference range: 0.4–4.0 μIU/mL, fT4 reference range: 11.5–23.2 pmol/L, anti-TPO reference range: up to 34 pmol/L were measured using an immunochemiluminescent method with Mindray reagent kits (China).

Thyroid ultrasound was performed using the Chison 5 New Matrix ultrasound system (China).

FNAB was carried out using a disposable 5 mL syringe and microscope slides. Thyroidectomy was performed in the operating room by a surgical team from the surgical department.

Statistical Analysis

The normality of quantitative data distribution was assessed using the Shapiro–Wilk test, as well as by evaluating skewness and kurtosis values. Descriptive statistics for quantitative variables are presented as medians and interquartile ranges (Me [Q1; Q3]), while categorical variables are expressed as percentages. Statistical significance of differences between groups for quantitative data was assessed using the Mann–Whitney U test with Bonferroni correction. Analysis of nominal data was performed using Fisher's exact test. To evaluate changes in quantitative parameters within related samples, the Friedman test was used, followed by post hoc analysis with correction for multiple comparisons. Spearman's rank correlation coefficient was used to assess the relationship between variables, and linear and logistic regression analyses were performed to assess dependence. Confidence intervals for percentage values were calculated using the Clopper–Pearson method. The Kolmogorov–Smirnov test was also used to assess the conformity of quantitative indicators to a normal distribution. Differences were considered statistically significant at $p < 0.05$. Statistical analysis was carried out using StatTech v. 4.8.5 software (developed by Stattech LLC, Russia).

Ethical Approval. The study protocol was reviewed and approved by the Ethics Committee of the Republican Specialized Scientific and Practical Medical Center of Endocrinology named after Academician Y.Kh. Turakulov (Protocol No. 125/25 dated January 9, 2022). Informed consent to participate in the study was obtained from all 109 patients enrolled in the prospective study.

Results

Statistical analysis was performed using StatTech v. 4.8.5 software (developed by Stattech LLC, Russia). Quantitative variables were tested for normal distribution using the Kolmogorov–Smirnov test. In the absence of a normal distribution, data were described using the median (Me) and interquartile range (Q1–Q3). Categorical variables were described using absolute values and percentage proportions. The 95% confidence intervals for proportions were calculated using the Clopper–Pearson method. A total of 109 patients with thyroid nodular formations were included in the study. The age of the participants ranged from 17 to 64 years. The median age was 36.0 years, reflecting a predominance of patients in the young and middle-aged groups. The interquartile range (Q1–Q3) was from 28.0 to 48.0 years, indicating moderate variability in the distribution. Thus, the majority of patients were under the age of 50 (Table 1).

Table 1 – Descriptive statistics of quantitative variables

Indicator	Median (Me)	Interquartile Range (Q1–Q3)	n	Min	Max
Age (years)	36	28.0 – 48.0	109	17	64

Gender distribution demonstrated a significant predominance of female patients—107 individuals (98.2%; 95% CI: 93.5–99.8), whereas only 2 were male (1.8%; 95% CI: 0.2–6.5). This may reflect both the higher prevalence of thyroid pathology among women and the characteristics of the study sample. Analysis of regional distribution revealed that the largest number of patients came from Tashkent — 34 individuals (31.2%; 95% CI: 22.7–40.8), followed by Jizzakh — 26 patients (23.9%; 95% CI: 16.2–33.0), Khorezm — 9 (8.3%), and Andijan — 7 (6.4%). The remaining patients represented other regions, including Surkhandarya, Samarkand, Bukhara, Navoi, Namangan, and Fergana, with individual shares ranging from 0.9% to 4.6% of the total sample. Thus, most patients originated from large cities and administrative centers, which may be attributed to better access to healthcare services and diagnostic facilities in these areas (Table 2).

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Table 2. Descriptive Statistics of Categorical Variables

Indicator	Category	n	Percentage (%)	95% CI
Gender	Male	2	1,8	0.2 – 6.5
Gender	Female	107	98,2	93.5 – 99.8
Region	Tashkent	34	31,2	22.7 – 40.8
Region	Jizzakh	26	23,9	16.2 – 33.0
Region	Kashkadarya	1	0,9	0.0 – 5.0
Region	Surkhandarya	3	2,8	0.6 – 7.8
Region	Samarkand	3	2,8	0.6 – 7.8
Region	Bukhara	2	1,8	0.2 – 6.5
Region	Navoi	4	3,7	1.0 – 9.1
Region	Khorezm	9	8,3	3.8 – 15.1
Region	Karakalpakstan	2	1,8	0.2 – 6.5
Region	Tashkent Region	8	7,3	3.2 – 14.0
Region	Syrdarya	1	0,9	0.0 – 5.0
Region	Namangan	4	3,7	1.0 – 9.1
Region	Fergana	5	4,6	1.5 – 10.4
Region	Andijan	7	6,4	2.6 – 12.8

Analysis of clinical diagnoses by gender showed that most patients, regardless of gender, were diagnosed with autoimmune thyroiditis with a nodular component (AIT with a nodule). Among female patients, who made up 98.2% of the sample (n = 107), the most common diagnoses were: AIT with a nodule — 50 cases (46.7%), multinodular goiter — 33 cases (30.8%), and solitary nodular goiter — 21 cases (19.6%). Malignant neoplasms were detected in 2 women (1.9%). All male patients (n = 2) were diagnosed with AIT with a nodule. Differences in the distribution of clinical forms between genders were not statistically significant ($p = 0.524$).

When analyzing the association between place of residence and diagnosis, statistically significant differences were observed ($p < 0.001$). AIT with a nodule was most common among patients from Tashkent (14.0%), Jizzakh (10.3%), and Khorezm (7.0%). Multinodular goiter was more frequently seen among residents of Jizzakh (9.3%) and Khorezm (5.6%), whereas solitary nodular goiter was more prevalent in Tashkent (5.6%) and Surkhandarya (3.7%). Malignant neoplasms were recorded in patients from Jizzakh (1 case) and Khorezm (1 case), highlighting the presence of oncological forms of the disease in specific regions (Table 3).

Thus, despite the homogeneity of distribution by gender, significant regional differences in the structure of clinical diagnoses were identified, which may indicate

the influence of environmental factors, healthcare accessibility, and iodine status in different regions.

Table 3. Descriptive statistics of categorical variables by clinical diagnosis

Variable	Category	Malignant Neoplasm	Multinodular Goiter	Solitary Nodule	AIT with Nodule	p-value
Gender	Male	0 (0.0%)	1 (2.9%)	1 (4.8%)	0 (0.0%)	0.524
	Female	2 (100.0%)	33 (97.1%)	20 (95.2%)	52 (100.0%)	
Region	Tashkent	0 (0.0%)	13 (38.2%)	5 (23.8%)	16 (30.8%)	<0.001
	Jizzakh	0 (0.0%)	9 (26.5%)	3 (14.3%)	14 (26.9%)	
	Kashkadarya	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	
	Surkhandarya	0 (0.0%)	0 (0.0%)	2 (9.5%)	1 (1.9%)	
	Samarkand	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (5.8%)	
	Bukhara	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.8%)	
	Navoi	2 (100.0%)	1 (2.9%)	1 (4.8%)	0 (0.0%)	
	Khorezm	0 (0.0%)	1 (2.9%)	1 (4.8%)	7 (13.5%)	
	Karakalpakstan	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (3.8%)	
	Tashkent Region	0 (0.0%)	2 (5.9%)	3 (14.3%)	3 (5.8%)	
	Syrdarya	0 (0.0%)	1 (2.9%)	0 (0.0%)	0 (0.0%)	
	Namangan	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (7.7%)	
	Fergana	0 (0.0%)	3 (8.8%)	2 (9.5%)	0 (0.0%)	
	Andijan	0 (0.0%)	3 (8.8%)	4 (19.0%)	0 (0.0%)	

Analysis of hormonal and autoimmune parameters across clinical diagnostic groups revealed the following patterns. The level of TSH gradually increased from the group with malignant neoplasms (0.8 mIU/L) to the group with autoimmune thyroiditis with a nodular component (2.4 mIU/L). The level of fT4 remained relatively stable across all groups, ranging from 1.2 to 1.3 ng/dL. The most pronounced differences were observed in the levels of anti-TPO: in patients with autoimmune thyroiditis with a nodular component, the median value reached 210.3 IU/mL, whereas in other groups it did not exceed 28.1 IU/mL. These findings confirm the key role of the autoimmune component in the pathogenesis of autoimmune thyroiditis and highlight its distinctive laboratory features (Figure 1).

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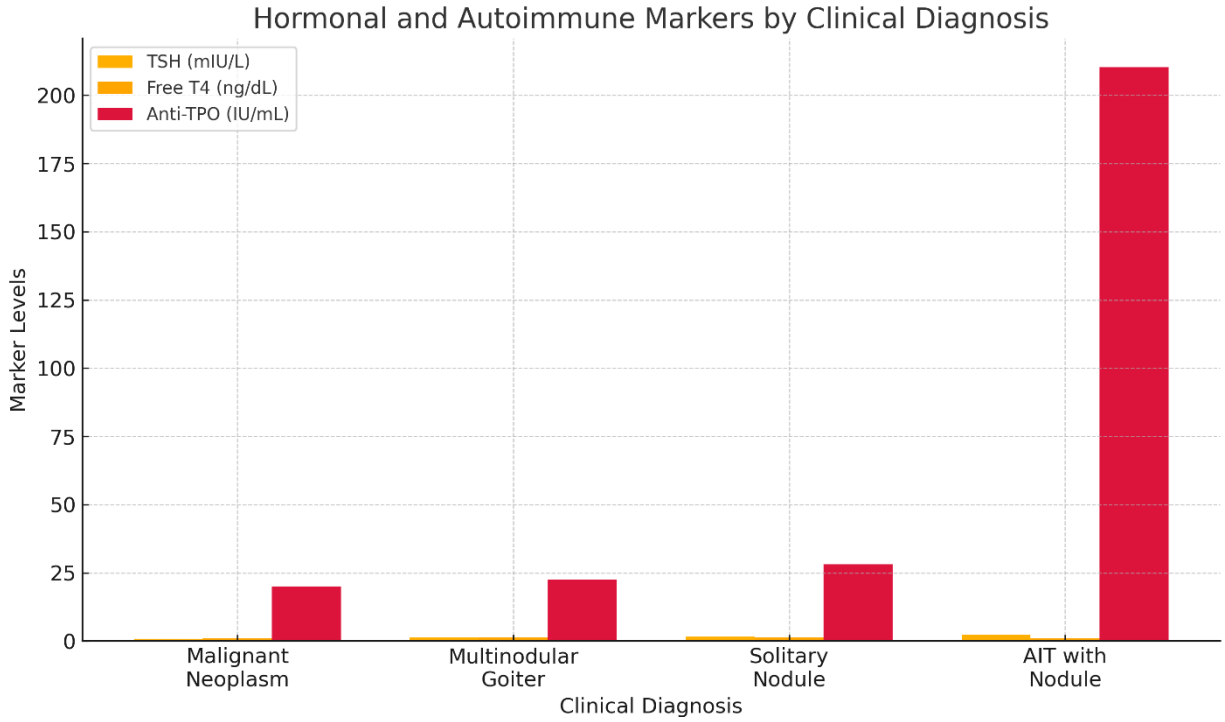

Figure 1. Hormonal and autoimmune profile of patients with different clinical forms of nodular thyroid disease

The analysis of gender distribution revealed that the vast majority of patients with confirmed histological changes were women. Among men (n = 2), only cases of papillary carcinoma were observed (6.7%), while no instances of follicular or benign nodular lesions were recorded. In contrast, among women (n = 107), follicular tumors predominated (66 cases, 100%) along with benign nodules (13 cases, 100%). Despite the evident predominance of pathology in women, the difference did not reach statistical significance ($p = 0.068$). The analysis of clinical goiter forms showed a statistically significant association with the histological diagnosis ($p < 0.05$). In patients with multinodular goiter, papillary carcinoma (40.0%) and benign lesions (69.2%) were more frequently identified, while follicular carcinoma was observed in 19.7% of cases. In cases of solitary nodules, papillary and follicular carcinoma occurred at comparable rates (26.7% and 18.2%, respectively), whereas benign nodules were rare (7.7%). Particular attention should be given to the group of patients with autoimmune thyroiditis (AIT), who showed a high frequency of follicular tumors (59.1%) and papillary carcinoma (33.3%). Benign lesions in this group were present in 23.1% of cases. The differences in the frequency of follicular tumors between clinical forms of goiter were statistically significant ($p = 0.008$). Similarly, the distribution of benign lesions also depended on the clinical form of goiter ($p = 0.012$) (Table 4).

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Table 4. Descriptive statistics of categorical variables by histopathological analysis

Indicator	Category	Papillary Carcinoma (%)	Follicular Carcinoma (%)	Benign (%)	p-value
Gender	Male	2 (6.7%)	0 (0.0%)	0 (0.0%)	0.068
	Female	28 (93.3%)	66 (100.0%)	13 (100.0%)	
Clinical Diagnosis	Malignant	0 (0.0%)	2 (3.0%)	0 (0.0%)	
	Multinodular Goiter	12 (40.0%)	13 (19.7%)	9 (69.2%)	0.008*
	Solitary Nodule	8 (26.7%)	12 (18.2%)	1 (7.7%)	
	AIT with Nodule	10 (33.3%)	39 (59.1%)	3 (23.1%)	0.012

A comparative analysis was conducted to evaluate the diagnostic effectiveness of the EU-TIRADS classification (ultrasound-based risk stratification system) and the Bethesda system (cytological classification of FNAB results) in relation to histologically verified thyroid nodules.
The reference standard was the result of histopathological examination following surgical intervention, with final diagnoses categorized as papillary carcinoma, follicular carcinoma, or benign lesions.

EU-TIRADS and histology

In EU-TIRADS categories 2–3, benign and follicular lesions were predominant:
— In EU-TIRADS 2, 2 cases of benign nodules were identified (15.4%), along with one case each of papillary and follicular carcinoma.
— In EU-TIRADS 3, follicular tumors were observed in 24.2% of cases, while benign nodules accounted for 53.8%.
The highest rate of follicular carcinoma was recorded in EU-TIRADS category 4, at 69.7%, whereas papillary carcinoma accounted for 16.7%.
In contrast, EU-TIRADS category 5 strongly correlated with papillary thyroid carcinoma, with 73.3% of patients in this category having histologically confirmed papillary cancer, and minimal presence of follicular carcinoma and complete absence of benign lesions (Table 5).

Bethesda and histology

A similar analysis was conducted for the Bethesda system. In Bethesda category II (cytological benign nodules), 61.5% of cases were histologically benign; however, follicular carcinoma was found in 21.2% of cases, and papillary carcinoma in 3.3%, confirming the known limitations of this category in reliably excluding malignancy.

Bethesda category III (AUS/FLUS) was mainly associated with follicular tumors (18.2%) and benign lesions (30.8%). The strongest correlation with follicular carcinoma was observed in Bethesda category IV — 56.1%, while papillary carcinoma and benign lesions were less frequent (10.0% and 7.7%, respectively).

Bethesda categories V and VI demonstrated a clear association with papillary carcinoma — 23.3% and 56.7%, respectively. Benign and follicular tumors were rarely observed in these groups (Table 5).

Statistical significance

Statistical analysis confirmed a significant association between the category distributions of both classification systems and histological diagnoses.

For the EU-TIRADS system, significant differences were found between:

- papillary and follicular carcinoma ($p < 0.001$),
- papillary carcinoma and benign lesions ($p < 0.001$),
- follicular carcinoma and benign lesions ($p = 0.023$).

For the Bethesda system, similar differences were also statistically significant ($p < 0.001$), including:

- papillary vs. follicular carcinoma ($p < 0.001$),
- papillary carcinoma vs. benign lesions ($p < 0.001$),
- follicular carcinoma vs. benign lesions ($p = 0.011$).

Table 5. Descriptive statistics of categorical variables by histological diagnosis according to EU-TIRADS and Bethesda classification systems

System	Category	Papillary Carcinoma (%)	Follicular Carcinoma (%)	Benign Lesions (%)	p-value
EU-TIRADS	EU-TIRADS 2	1 (3.3%)	2 (3.0%)	2 (15.4%)	<0.001*
	EU-TIRADS 3	2 (6.7%)	16 (24.2%)	7 (53.8%)	
	EU-TIRADS 4	5 (16.7%)	46 (69.7%)	4 (30.8%)	
	EU-TIRADS 5	22 (73.3%)	2 (3.0%)	0 (0.0%)	
Bethesda	Bethesda II	1 (3.3%)	14 (21.2%)	8 (61.5%)	<0.001*
	Bethesda III	2 (6.7%)	12 (18.2%)	4 (30.8%)	
	Bethesda IV	3 (10.0%)	37 (56.1%)	1 (7.7%)	
	Bethesda V	7 (23.3%)	1 (1.5%)	0 (0.0%)	
	Bethesda VI	17 (56.7%)	2 (3.0%)	0 (0.0%)	

To assess the diagnostic value of the EU-TIRADS ultrasound classification system in detecting malignant thyroid nodules, a ROC analysis was conducted using histological diagnosis as the gold standard. The sample included 109 patients, of whom 96 had malignant and 13 had benign tumors according to histopathological examination.
A positive test result was defined as categorization into EU-TIRADS 4 or 5, indicating suspicious ultrasound features.
Based on the analysis, a ROC curve was constructed (Figure 2), reflecting the relationship between sensitivity and 1 – specificity across various classification thresholds.

- Sensitivity was 78.9%, indicating that the EU-TIRADS system correctly identified the majority of malignant thyroid nodules. However, some cancer cases classified as EU-TIRADS 2 and 3 were not flagged as suspicious, resulting in false-negative findings.
- Specificity was approximately 38.5%, reflecting a relatively high number of false-positive cases among patients with benign histological findings.
- The ROC analysis showed an AUC of 0.78, suggesting that EU-TIRADS demonstrates moderately high diagnostic accuracy and clinical usefulness in the preoperative identification of thyroid malignancies.

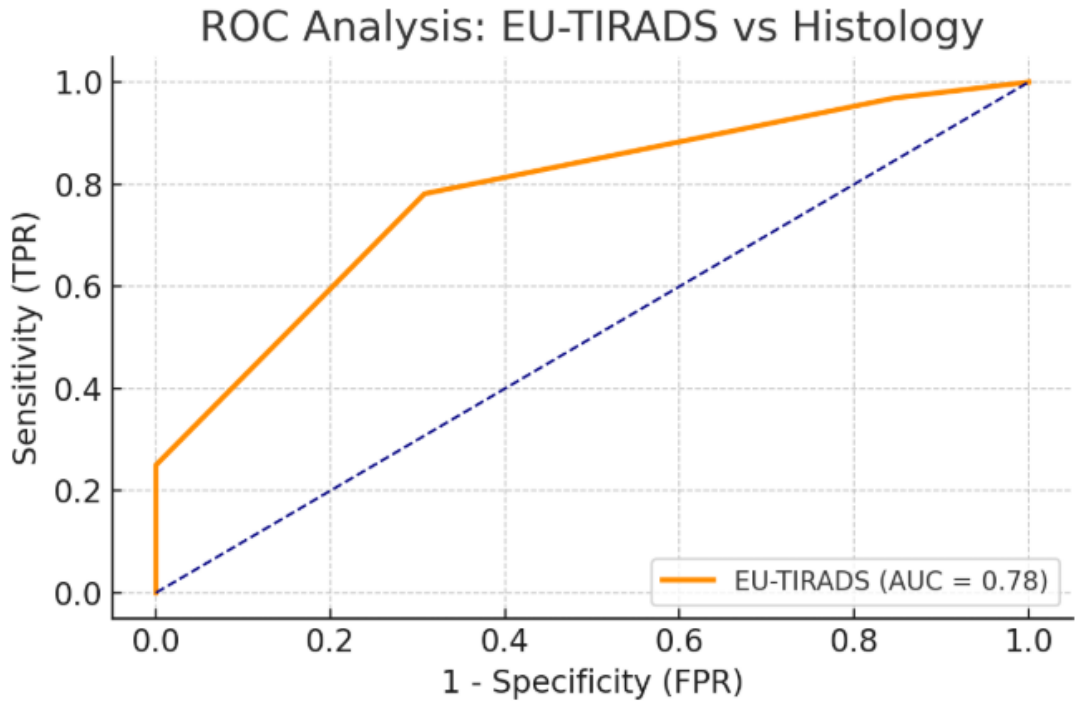

Figure 2. ROC analysis of the diagnostic performance of the EU-TIRADS ultrasound classification system compared to histological findings

To assess the diagnostic performance of the Bethesda cytological classification system in detecting malignant thyroid tumors, a ROC analysis was performed using histological diagnosis as the reference standard. The study included data from 109 patients, of whom 96 had histologically confirmed malignant tumors and 13 had benign lesions. Bethesda categories V and VI were considered a positive test result (suspicious for malignancy or malignant cytology), while categories II–IV were treated as negative. Based on the results, a ROC curve was generated to illustrate the relationship between sensitivity and 1 – specificity for the Bethesda system (Figure 3). Sensitivity was 83.3%, reflecting a strong ability of cytological classification to detect malignancies, although some malignant cases were categorized as indeterminate or benign. Specificity was 76.9%, indicating that a portion of benign lesions were misclassified as suspicious or malignant, leading to false positives. The area under the ROC curve (AUC) was 0.87, which demonstrates good overall diagnostic accuracy of the Bethesda system in differentiating malignant from benign thyroid nodules.

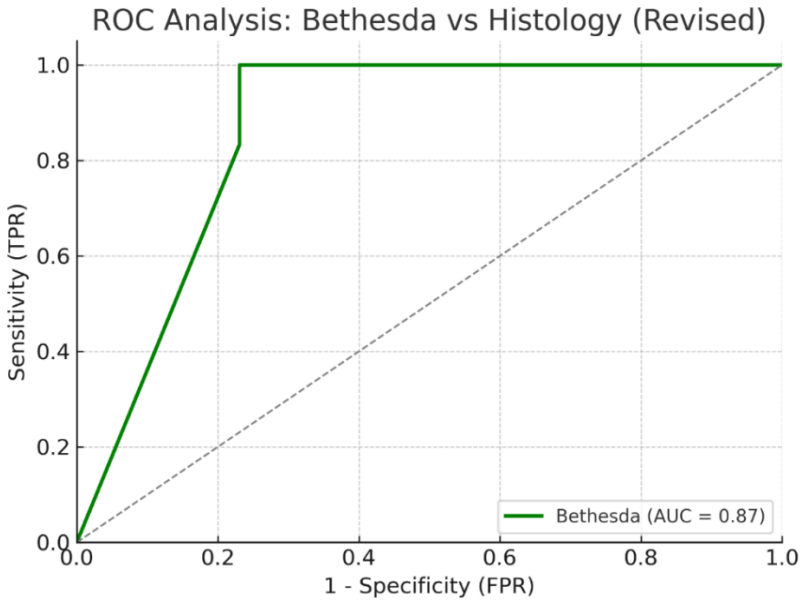

Figure 3: ROC analysis of the diagnostic performance of the Bethesda system compared with histological diagnosis.

Discussion

1. Diagnostic Performance of EU-TIRADS and Bethesda

A comparative analysis showed that both classification systems — EU-TIRADS and Bethesda — have diagnostic value in stratifying the risk of malignancy in thyroid nodules. However, based on ROC analysis, the Bethesda system demonstrated better diagnostic accuracy (AUC = 0.87) compared to EU-TIRADS (AUC = 0.78).

These findings are consistent with several international studies that highlight the prognostic value of cytological evaluation in fine-needle aspiration interpretation [1–3]. Bethesda categories V and VI showed the highest diagnostic precision for papillary thyroid carcinoma, while EU-TIRADS 5 also correlated significantly with histologically confirmed malignancy. Nevertheless, the relatively low specificity of EU-TIRADS (38.5%) suggests a tendency toward overdiagnosis, particularly in patients with benign nodules — a limitation also emphasized in the works of Magri et al. and Trimboli et al. [4,5].

2. Diagnostic Uncertainty in Intermediate Categories

Particular attention should be given to intermediate-risk categories: EU-TIRADS 3–4 and Bethesda III–IV. These groups are characterized by a high proportion of follicular tumors, which are challenging to verify using FNA due to the inability to assess capsular or vascular invasion cytologically. This observation aligns with publications by Cibas et al. and Faquin et al., which emphasize that Bethesda categories III and IV require either careful clinical follow-up or diagnostic lobectomy [6,7]. These findings support the need for further stratification of patients in these categories using molecular markers, repeat biopsies, or close monitoring based on clearly defined clinical criteria.

3. Clinicopathological Correlations

The results of the analysis also revealed associations between histological tumor types and clinical characteristics of the patients. Follicular tumors were more frequently observed in women and in patients with autoimmune thyroiditis, suggesting a possible link between chronic inflammation and tumor development. These findings are supported by previous literature, including a study by Lee et al. (2022), which described an association between autoimmune thyroiditis and both follicular and papillary thyroid tumors [8].

4. Clinical Significance and Practical Recommendations

The combined analysis of the EU-TIRADS and Bethesda systems demonstrates the high diagnostic value of an integrated approach. In clinical practice, the most appropriate strategy appears to be the use of the EU-TIRADS system for initial ultrasound screening, followed by fine-needle aspiration (FNA) and Bethesda classification in patients with suspicious nodules. This approach allows clinicians to capitalize on the strengths of both systems—namely, the high sensitivity of ultrasound and the high specificity of cytological evaluation. These findings are in agreement with

current clinical guidelines from the American Thyroid Association (ATA, 2015) and the updated European Thyroid Association recommendations (ETA, 2023) [9,10].

Clinical Relevance of the Findings

The results of this study help inform diagnostic decision-making and guide the development of improved clinical protocols for managing patients with thyroid nodules.

Study Limitations

The main limitations include the relatively small sample size and the presence of a retrospective component, which limited the completeness of some data.

Future Research Directions

Further research should focus on improving diagnostic accuracy within the intermediate-risk categories of EU-TIRADS 3–4 and Bethesda III–IV, where a high proportion of indeterminate results persists. Promising directions include the incorporation of molecular testing and the integration of clinical, hormonal, and autoimmune markers into a unified diagnostic model.

Conclusion

This study confirmed the high clinical relevance of a comprehensive approach to the diagnosis of thyroid nodules based on the integration of EU-TIRADS ultrasound classification, the Bethesda cytological system, and histological verification. The Bethesda system demonstrated the highest diagnostic accuracy (AUC = 0.87), particularly in detecting papillary thyroid carcinoma, due to its high specificity and predictive value. At the same time, EU-TIRADS showed excellent sensitivity (78,9%), making it an essential tool for the initial risk assessment of malignancy. Intermediate-risk categories remain the most diagnostically challenging, highlighting the need for additional stratification tools such as molecular markers, clinical-laboratory indicators, and longitudinal observation. These findings underscore the necessity of a multidisciplinary diagnostic approach that combines ultrasound data, cytological results, clinical history, and hormonal-autoimmune profiles. Such an approach improves the accuracy of preoperative diagnostics and helps to optimize patient management strategies in cases of thyroid nodular disease.

Additional Information

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Author Contributions. D.B. Nurmukhamedov — data collection and processing, creation of the electronic database, statistical analysis, interpretation of the results, and drafting of the main text of the article. F.A. Khaidarova — scientific supervision of the study, manuscript editing, and final approval.
The authors declare that their authorship complies with the ICMJE authorship criteria. All authors equally contributed to the preparation of the manuscript, including the concept development, data acquisition and analysis, drafting and revision of the article, and final review and approval of the text.

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