

Efficacy of ultrasound findings in diagnosing thyroid nodules correlating with histopathology and surgical outcomes

Abstract:

Thyroid nodules are one of the most common clinical thyroid gland problems. Ultrasound and needle biopsy are preferred methods for distinguishing benign from malignant nodules. In this study, we investigated the correlation of pathological findings with ultrasound in operated thyroid nodules of patients referred to Razi Medical Training Center in Rasht, Iran.

Materials and methods:

This cross-sectional study assessed the correlation between ultrasound and pathological findings in surgically resected thyroid nodules. Data were retrospectively collected from patient records and analyzed by multiple experts. Statistical analysis was performed using SPSS software.

Result:

Out of 104 examined patients, their average age was 45.66 ± 13.34 years, of which 87.5% were women and 12.5% were men. Pathological results of operated thyroid nodules in 72.1% of patients were malignant, and 27.9% were benign. Ultrasound results of operated thyroid nodules in 76% of patients were malignant, and 24% were benign. In 88.5% of patients, the ultrasound findings were the same as pathological; in 11.5%, the diagnosis was different.

Conclusion:

The results of the present study showed that ultrasound is highly accurate in diagnosing thyroid nodule malignancy. A positive ultrasound result confirming the nodule's malignancy dramatically increases the probability of its malignancy.

Keywords: pathological findings, ultrasound, thyroid nodule

Introduction:

Hypothyroidism, characterized by elevated thyroid-stimulating hormone (TSH) levels and normal thyroxine (T4) levels, is often apparent before hypothyroidism develops [1]. This asymptomatic condition affects approximately 4-5.8% of the adult U.S. population, with women exhibiting a higher prevalence [2].

In primary thyroid failure, blood levels of thyroid hormone decrease, stimulating the pituitary gland to increase TSH output. Hypothyroidism can also result from pituitary failure. The prevalence of hypothyroidism in children aged 12 years and older is estimated to be 4.5%, with autoimmune thyroid disease being the most common cause in areas with regular iodine intake. Diagnosing the cause of the disease in women has little impact on their clinical treatment [3, 4].

Ultrasound and fine-needle aspiration biopsy are established modalities for differentiating benign and malignant thyroid nodules [5-7]. While international studies have demonstrated the prognostic value of ultrasonographic features such as hypoechogenicity, irregular margins, and the absence of a halo sign in predicting malignancy, limited data exists specifically for Iranian populations. Although the majority of benign thyroid nodules remain stable over time [8, 9], and size increase alone does not reliably indicate malignancy [9]; active surveillance strategies for larger nodules with low malignancy risk are emerging as a viable management option [10, 11]. However, regular monitoring is crucial as a small proportion of benign nodules may undergo malignant transformation [8, 9]. Notably, the presence of suspicious ultrasonographic features carries a more substantial predictive value for malignancy compared to nodule growth [8]. These findings suggest a personalized approach to managing thyroid nodules, potentially reducing routine annual ultrasound monitoring for benign cases [9, 11]. However, limited studies have examined the ultrasound appearance characteristics of thyroid nodules indicative of malignancy or benignity in Iranian patients, and current practice in Iran in this field is based on global studies [5, 6].

Methods:

This study explored the association between pathological findings and ultrasound in diagnosing surgically removed thyroid nodules in patients referred to the Razi Educational and Therapeutic Center in Rasht, Iran, in 2022 (Approval No. IR.GUMS.REC.1401.394). All ultrasounds were performed by a skilled radiologist specializing in thyroid. After obtaining ethical approval, baseline characteristics, such as age, sex, number of nodules, nodule location, pathology data, and ultrasound data, were extracted from patients' medical records. The study included patients with both pathology and ultrasound reports of thyroid nodules. Several experts in the field conducted the pathology reports.

Data Analysis:

The collected data were entered into the SPSS software for statistical analysis. Statistical tables and charts were used to describe the data. Mean and standard deviation were used to describe quantitative variables, and numbers and percentages were used to describe qualitative variables. Kappa agreement coefficient was used to assess agreement. The significance level was considered to be 5%.

Result:

Over one year, 104 patients were examined. The average age was 66.45 ± 13.34 years, with 91 (87.5%) female and 13 (12.5%) male. On average, the number of nodules per patient was 1.76 ± 0.64 , located as follows: 27 patients (26%) had nodules on the right, 17 patients (16.3%) had nodules on the left, 43 patients (41.3%) had nodules on both sides, six patients (5.8%) had nodules on the right and isthmus, one patient (1%) had nodules on the left and isthmus, and ten patients (9.6%) had nodules on the right, left, and isthmus.

The pathology results of the surgically removed thyroid nodules showed that 75 patients (72.1%) had malignant (PTC), and 29 patients (27.9%) had benign nodules. The ultrasound results of the surgically removed thyroid nodules indicated that 79 patients (76%) had a TIRADS score of 4 or higher, and 25 patients (24%) had a TIRADS score below 4 (Table 1).

Regarding concordance between ultrasound and pathological findings, out of the 104 patients examined, the ultrasound and pathology findings agreed in 92 patients (88.5%) and disagreed in 12 patients (11.5%). The Cohen's kappa coefficient value is 0.7, indicating significant agreement ($P < 0.001$) at a 5% significance level.

For patients 44 years old or younger:

- Forty-seven patients (87%) had matching ultrasound and pathology findings, while seven (13%) had mismatched results.
- Cohen's kappa coefficient was 0.613, indicating a substantial agreement statistically significant at the 5% level ($p < 0.001$) (Table 2).

For patients older than 44 years:

- Forty-five patients (90%) had matching ultrasound and pathology findings, while five patients (10%) had mismatched results.
- The Cohen's kappa coefficient was 0.769, indicating an excellent agreement statistically significant at the 5% level ($p < 0.001$) (Table 2).

Among female patients, 80 (87.9%) had consistent findings between ultrasound and pathology, while 11 (12.1%) had discrepant results. Cohen's kappa coefficient was 0.685, indicating a substantial agreement at the 5% significance level ($p < 0.001$). For male patients, 12 (92.3%) had consistent findings, and 1 (7.7%) had discrepant results. Cohen's kappa coefficient was 0.806, indicating an almost perfect agreement at the 5% significance level ($p < 0.001$).

Among patients with more than two nodules, 38 (86.4%) had ultrasound findings that matched the pathology results, while 6 (13.6%) had discordant findings. Cohen's kappa coefficient was calculated to examine this agreement further, and it was found to be 0.586, indicating a significant agreement at the 5% significance level ($p < 0.001$).

Regarding the location of nodules in all 104 patients, 86 nodules (82.7%) were located on the right side, 71 nodules (68.3%) on the left side, and 17 nodules (16.3%) in the isthmus.

Among nodules in the right lobe, 76 (88.4%) had concordant findings between ultrasound and pathology, while 10 (11.6%) had discordant findings. Cohen's kappa coefficient was 0.675, indicating a substantial agreement statistically significant at the 5% level ($P < 0.001$). 62 (87.3%) had concordant findings for nodules in the left lobe, and 9 (12.7%) had discordant findings. Cohen's kappa coefficient was 0.683, indicating a substantial agreement statistically significant at the 5% level ($P < 0.001$). Among nodules in the isthmus, 14 (82.4%) had concordant findings, and 3 (17.6%) had discordant findings. Cohen's kappa coefficient was 0.611, indicating a substantial agreement statistically significant at the 5% level ($P < 0.001$).

This study evaluated the correlation between pathological findings and pre-operative ultrasound (US) features in thyroid nodules. Our findings demonstrated that ultrasound significantly predicts malignancy in thyroid nodules, with an overall concordance rate of 88.5% between US findings and pathological diagnoses.

Discussion

Thyroid nodules with indeterminate cytology present a diagnostic challenge, with malignancy rates ranging from 24.4% to 45.0% [12, 13]. While some guidelines recommend total thyroidectomy for nodules larger than 4 cm, recent studies suggest that nodule size does not significantly correlate with malignancy rates, tumour aggressiveness, or clinical outcomes [14]. Most malignant tumours found in indeterminate nodules are low-risk, well-differentiated carcinomas with excellent prognoses [14]. Factors associated with increased malignancy risk include cytological atypia, blurred nodule margins, and microcalcifications on ultrasound. A clinical risk score incorporating cytology and ultrasound features may help guide management decisions [12]. Given these findings, thyroid lobectomy may be a sufficient initial treatment for most solitary indeterminate nodules, regardless of size, potentially reducing unnecessary total thyroidectomies [15].

Gabriela Mintegui and colleagues conducted a study in 2022 to determine the correlation between sonographic, cytological, and pathological findings of thyroid nodules over the years. Materials and methods: Observational, descriptive and retrospective study of thyroidectomized patients between 2010 and 2014 at Clinical Hospital-Uruguay. Results demonstrated a significant association between EU-TIRADS 4-5 and the Bethesda classification. An adequate correlation was shown to differentiate benignity from malignancy when comparing ultrasound findings of thyroid nodules with FNA and PA[16].

Subhash C. Sylonia and colleagues conducted a study in 2020 on the accuracy of various imaging features in thyroid nodules associated with benignity and malignancy and the overall accuracy of ultrasound in determining malignant nodules. The study's objective are: (1) Ultrasonographic evaluation of the thyroid to characterize the thyroid disease and nodules (benign vs malignant) and their morphologic evaluation. (2) Sensitivity and Specificity based on radiological and cytopathological correlation for suspected thyroid lesions. The total number of cases was analyzed. They found that High-resolution sonography is recommended as the primary imaging modality in evaluating thyroid diseases. It has a high sensitivity and specificity in the diagnosis of thyroid diseases[17].

Carlos García-Moncó Fernández and colleagues conducted a study in 2018. The correlation between histological results and pre-operative ultrasound reports showed an initial sensitivity of 65%. After excluding 15 patients with occult microcarcinoma, the sensitivity increased to 81.6%. They concluded that although sensitivity was initially found to be relatively low in the TI-RADS scale study, it significantly improved when patients with occult microcarcinoma were excluded. Therefore, using the TI-RADS scale allows for the adequate selection of patients subjected to fine-needle aspiration of the nodule [7].

Mihiri Chami Wettasinghe and colleagues conducted a study in 2019. Using multivariate analysis, they identified ultrasound features statistically significantly associated with thyroid malignancies. Internal vascularity, hypoechogenicity, and microcalcifications showed a statistically significant positive association with thyroid malignancy. After statistical reviews, were identified as the most helpful criterion in predicting thyroid malignancy [18].

Danielle M and colleagues conducted a study on patients under 19 years old in 2018. Patients underwent fine-needle aspiration biopsy under ultrasound (US) guidance. Demographic and ultrasound features were examined to determine which were associated with malignancy. They concluded that in children with thyroid nodules, single nodules, larger nodule size, solid parenchyma, taller-than-wide shape, punctate calcifications, irregular margins, and abnormal lymph nodes raise concerns for malignancy [19].

Their aim was to investigate the natural history of benign thyroid nodules on initial fine needle aspiration (FNAB) to increase the percentage of nodules that increase by more than 50% as an indicator of malignancy.

Soo-Yeon Kim, Kyunghwa Han and colleagues conducted a study in 2014. The study included 854 benign thyroid nodules confirmed by FNAB. Suspicious ultrasonographic (US) features included marked hypoechogenicity, irregular or microlobulated margins, microcalcifications, and

a longer than wide shape. Univariate and multivariate generalized linear mixed models assessed the association with more than 50% nodule growth in volume. They found that repeat FNAB for nodules that showed more than 50% growth was unlikely to lead to a diagnosis of malignancy. A positive FNAB result for malignancy was significantly more likely in the presence of suspicious US features[8].

Jin Chung and colleagues conducted a study in 2012. This study examined the incidence of thyroid cancer in cases with nondiagnostic results from fine needle aspiration cytology (FNAC) and explored management strategies based on ultrasound (US) findings. A significant association was found between nodule size and malignancy ($P < 0.05$). Most benign nodules were classified as sonographically benign (97.6%); however, suspicious nodules were diagnosed as cancerous in 43.2% of cases. Notable ultrasound features linked to malignancy included marked hypoechogenicity, microlobulated or irregular margins, microcalcifications, and a longer-than-wide shape ($P < 0.05$). The diagnostic performance of ultrasound revealed a sensitivity of 90.0%, specificity of 65.0%, positive predictive value of 29.5%, and negative predictive value of 97.6%. Overall, ultrasound evaluation proved to be an effective tool for predicting malignancy in thyroid nodules with nondiagnostic FNAC results[20].

The findings shown that the combination of accurate ultrasound evaluations, mainly using the TIRADS classification, can significantly contribute to the early diagnosis and management of thyroid tumours. This could potentially reduce the need for unnecessary fine needle biopsies (FNA) and simplify the clinical management of thyroid nodules.

The study showed a higher concordance rate in patients over 44 (90%) than those 44 years and younger (87%). Furthermore, two or fewer nodules had a higher concordance rate (90%) than patients with more than two nodules (86%). These findings underscore the reliability of the US, especially when combined with demographic and clinical factors.

Conclusion

This study reaffirms the critical role of ultrasound in the diagnostic evaluation of thyroid nodules. The high concordance between ultrasound and pathological findings supports using ultrasound as a primary screening tool in clinical practice.

Future studies should focus on multicenter and prospective analyses to confirm these results further. In addition, integrating advanced imaging techniques and molecular markers with ultrasound can increase diagnostic accuracy and provide a more comprehensive evaluation of thyroid nodules.

- **Availability of data and materials:**

All data and materials are provided in the manuscript. Data sets used and/or analyzed during the current study are available to the corresponding author upon reasonable request.

Declarations

- **Ethics approval and consent to participate**

The study was conducted by the Declaration of Helsinki and received approval from the Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran. (Approval No. IR.GUMS.REC.1401.394)

- **Consent for publication**

Written informed consent was obtained from the patient to publish this study.

Disclaimer (Artificial intelligence)

Author(s) at this moment declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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Table 1- The frequency distribution of pathological and ultrasound findings of surgically removed thyroid nodules in the studied patients

Pathology	Ultrasound		
	Malignant	Benign	Total
Malignant	71 (94.7%)	4 (5.3%)	75 (72.1%)
Benign	8 (27.6%)	21 (72.4%)	29 (27.9%)
Total	79 (76%)	25 (24%)	104

Table 2- The frequency distribution of pathological and ultrasound findings of surgically removed thyroid nodules based on the age of patients

Age	Pathology	Ultrasound		
		Malignant	Benign	Total
44 years and below	Malignant	39 (90.7%)	4 (9.3%)	43 (79.6%)
	Benign	3 (27.3%)	8 (72.7%)	11 (20.4%)
Above 44 years	Malignant	32 (100%)	0 (0.0%)	32 (64%)
	Benign	5 (27.8%)	13 (72.2%)	18 (36%)
Total		79 (76%)	25 (24%)	104