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## Ultrasound Imaging Surpasses Fine-Needle Aspiration Cytological Evaluation in Categorizing Thyroid Nodules

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### ABSTRACT

The classification of thyroid lesions poses a considerable challenge, yet the utilization of ultrasonography has the potential to facilitate precise diagnosis, differentiation and management of such lesions, thereby minimizing the need for unnecessary biopsy procedures. The primary aim of this study was to assess the diagnostic accuracy of ultrasonography in the classification of thyroid nodules, in comparison with the conventional method of fine-needle aspiration. This retrospective study encompassed a cohort of 82 patients diagnosed with thyroid nodules. Two radiologists, unaware of each other's findings, conducted a comprehensive review of ultrasonographic features, including nodule margins, echotexture, vascularity and calcifications, as well as the results of fine-needle aspiration cytology (FNAC). The findings were subsequently validated by an experienced interventional radiologist. In order to assess the diagnostic performance of ultrasonography, the results were compared with those of FNAC. The findings obtained from ultrasonography were strongly correlated with the results of FNAC. Significant associations were observed between the criteria for Ultrasound and the findings of FNAC and ultrasonography, specifically in relation to nodule calcification and echogenicity. Ultrasonography can effectively classify thyroid nodules and aid in decision-making regarding the necessity of biopsy procedures. These findings reinforce the reliability of ultrasonography as a valuable tool in the accurate assessment of thyroid nodules.

## INTRODUCTION

Thyroid nodules (TNs) refer to the formation of solid or fluid-filled masses within the thyroid gland. The prevalence of TNs, as estimated through palpation, ranges from 3-7% in certain countries<sup>[1]</sup>. However, when high-resolution ultrasonography is employed to randomly select individuals, the prevalence of TNs can increase significantly, reaching up to 67% according to a specific study<sup>[2]</sup>. The detection and evaluation of thyroid nodules are imperative due to concerns regarding the possibility of thyroid malignancy. Thyroid cancer incidence has been steadily increasing and currently ranks as the fifth most commonly diagnosed cancer in adult women worldwide and the second most common in women over the age of 50<sup>[3,4]</sup>. The expanding prevalence of TNs may be attributed to advancements in diagnostic technologies.

Ultrasonography (USG) holds a prominent position as the primary method for evaluating TNs due to its widespread acceptance, cost-effectiveness and safety advantages<sup>[5-7]</sup>. However, it is important to note that USG is reliant on the technical expertise of the operator, making its utility somewhat constrained. In contrast, fine-needle aspiration cytology (FNAC) is widely regarded as the gold standard diagnostic test for assessing thyroid nodules<sup>[8,9]</sup>.

Various guidelines have been developed to assist radiologists and clinicians in efficiently identifying sonographic patterns and categorizing thyroid nodules. One notable example is the Thyroid Imaging Reporting and Data System (TI-RADS), which was introduced in 2009. TI-RADS utilizes specific patterns composed of two or more features, providing a standardized and simplified approach for radiologists to follow. This model has demonstrated favorable diagnostic performance, including high sensitivity (88%), negative predictive value (88%) and accuracy (94%)<sup>[10]</sup>. While radiologic findings play a significant role in the evaluation of thyroid nodules, they alone may not provide a conclusive diagnosis. Therefore, according to the guidelines outlined by TI-RADS, if a nodule is deemed suspicious based on USG findings, it should undergo FNAC. The results of FNAC serve as a valuable guide for determining the appropriate course of further management<sup>[10,11]</sup>. The primary objective of this study is to further expand on the existing literature by evaluating the accuracy of thyroid USG in comparison to FNAC for predicting thyroid cancer.

## MATERIAL AND METHODS

This retrospective study involved the analysis of reports and images pertaining to 82 patients who were diagnosed with thyroid nodules at a tertiary-level hospital in India. The case files and reports of these patients were obtained from the hospital's medical records department. The study included patients with

solid or partly solid nodules, while those with solely cystic nodules or nodules showing complete watery content without any complex components on sonography were excluded, as these nodules were considered benign. Patients with any missing USG or FNAC data were also not included in the study. The study was conducted in accordance with standard ethical guidelines<sup>[12]</sup>.

Data collection for this study was conducted by two qualified radiologists who examined the stored USG images and written reports. To ensure accuracy and validity, an experienced diagnostic radiology consultant reviewed the collected data and confirmed the findings. The agreement between the radiologists and the consultant was assessed by conducting a kappa test, which resulted in a kappa value exceeding 80%. This high value indicates substantial interrater reliability, indicating the adequacy of agreement between the reviewers.

The interpretation and reporting of the USG scans followed the guidelines provided by the American College of Radiology's TI-RADS criteria<sup>[13]</sup>. The interpretation and reporting of FNAC samples in this study were carried out by skilled histopathologists who adhered to the guidelines outlined in the Bethesda System for Reporting Thyroid Cytopathology<sup>[14]</sup>.

## RESULTS

Table 1 provides a comprehensive depiction of the demographic and clinical examination characteristics pertaining to the population of patients included in the study. The study encompassed a total of 82 participants, with females constituting 75.61% of the sample. The average age of the patients was 38.51±12.61 years.

Table 2 provides a comprehensive overview of the histopathological results, TI-RADS scoring, USG findings and FNAC findings pertaining to the TNs included in the study.

Table 1: Demographic and clinical examination data of study participants

| Variable  | Number | Percentage |
|---|--------|------------|
| <b>Age group</b>                                  |        |            |
| <20 years   | 1      | 1.22       |
| 20-60 years                                       | 71     | 86.59      |
| >60 years   | 10     | 12.20      |
| <b>Gender</b>                                     |        |            |
| Males   | 20     | 24.39      |
| Females   | 62     | 75.61      |
| <b>Positive family history for thyroid cancer</b> |        |            |
| Yes   | 1      | 1.22       |
| No  | 81     | 98.78      |
| <b>Nodule consistency</b>                         |        |            |
| Firm  | 1      | 1.22       |
| Soft  | 81     | 98.78      |
| <b>Lymphadenopathy</b>                            |        |            |
| Yes   | 4      | 4.88       |
| No  | 78     | 95.12      |
| <b>Rapid growth</b>                               |        |            |
| Present   | 1      | 1.22       |
| Absent  | 81     | 98.78      |
| <b>Fixity to surrounding structures</b>           |        |            |
| Mobile  | 82     | 100.00     |
| Fixed   | 0      | 0.00       |

Table 2: Histopathological results, TI-RADS, USG and FNAC findings of the TNs

| Parameters              | Category | Number | Percentage |
|-------------------------|----------|--------|------------|
| TI-RADS Scoring         | 2        | 18     | 21.95      |
|                         | 3        | 37     | 45.12      |
|                         | 4        | 27     | 32.93      |
|                         | 5        | 0      | 0.00       |
| USG Results             | Positive | 28     | 34.15      |
|                         | Negative | 54     | 65.85      |
| Bethesda classification | 2        | 73     | 89.02      |
|                         | 3        | 4      | 4.88       |
|                         | 4        | 0      | 0.00       |
|                         | 5        | 3      | 3.66       |
|                         | 6        | 2      | 2.44       |
| FNAC Findings           | Positive | 5      | 6.10       |
|                         | Negative | 77     | 93.90      |

Table 3: Validity of USG as a diagnostic tool for identification of thyroid carcinoma

| Statistic                 | Value | CI 95%       |
|---------------------------|-------|--------------|
| Sensitivity               | 75.00 | 19.41-99.37% |
| Specificity               | 68.83 | 57.26-78.91% |
| Positive predictive value | 11.11 | 2.35-29.16%  |
| Negative predictive value | 98.15 | 90.11-99.95% |

Out of the 82 cases included in the study, both USG and FNAC results were available. Among these cases, three yielded positive results for both tests, while 53 exhibited negative results for both tests. Additionally, 24 cases had a positive USG but negative FNAC, while only one case had a negative USG but positive FNAC. A statistically significant association was observed between the results of USG and FNAC ( $p < 0.05$ ), indicating a positive correlation with a phi coefficient of 0.22 ( $p < 0.05$ ). The diagnostic test validity statistics for USG in the identification of thyroid carcinoma are presented in Table 3.

## DISCUSSION

The prevailing global consensus is that USG alone is not sufficient for the definitive diagnosis of thyroid cancer. However, it is important to note that the field of radiology is continually evolving and advancing. As a result, new studies are emerging that aim to challenge the notion that USG alone is inadequate for thyroid cancer diagnosis<sup>[15-17]</sup>.

The existing literature reveals significant discrepancies among various studies concerning the diagnostic performance of USG in the detection of thyroid cancer. For instance, Shweel et al. conducted a study that reported a sensitivity of 76.2%, specificity of 83%, negative predictive value (NPV) of 88.8% and positive predictive value (PPV) of 66.4%<sup>[18]</sup>. Similarly, Trimboli et al. found a sensitivity of 61%, specificity of 83% and NPV of 83%<sup>[19]</sup>. On the other hand, Wang et al.<sup>[6]</sup> and Xing et al.<sup>[21]</sup> demonstrated higher sensitivities with values of 95.7 and 92%, respectively<sup>[20,21]</sup>.

The latest gold standard for diagnosis of thyroid cancer remains FNAC. A meta-analysis that examined the Bethesda reporting system reported a sensitivity of 97%, specificity of 50.7%, negative predictive value (NPV) of 96.3% and positive predictive value (PPV) of 55.9%<sup>[22]</sup>. In a separate study comparing the

effectiveness of the TI-RADS criteria in ultrasound USG to the Bethesda reporting system for FNAC, the Bethesda system demonstrated a sensitivity of 90%, specificity of 94.3% and accuracy of 91.1%<sup>[23]</sup>. Notably, these values were not significantly superior to the diagnostic performance measures demonstrated by ultrasound alone in some of the previously mentioned studies. Furthermore, a study conducted at a single center found a false negative rate of 15% for FNAC, suggesting that the Bethesda risk stratification system may sometimes underestimate the rates of malignancy<sup>[24]</sup>.

**Limitations and directions for future research:** It is important to consider several limitations when interpreting the results of our study. First and foremost, our study is constrained by a small sample size, which may impact the generalizability and statistical power of the findings. Conducting a larger study, especially in a specialized center, would likely yield more reliable and robust data.

Another limitation stems from the nature of the study itself. Patients were only referred for Fine-Needle Aspiration Cytology (FNAC) if they exhibited suspicious findings on ultrasound (US). Consequently, it becomes challenging to determine the proportion of false negative cases, wherein patients may have negative US scans but eventually receive positive FNAC results. A larger sample size could help address this issue and provide more comprehensive insights into the diagnostic accuracy of US and FNAC.

Additionally, the nature of healthcare in the region where our study was conducted poses another limitation. Many patients opt for private healthcare, often seeking medical services outside the country. As a result, a substantial amount of patient data was missing within the hospital system, leading to a significant exclusion of patients from our study, as previously mentioned.

Considering these limitations, it is essential to interpret our study findings cautiously and recognize the potential impact that these limitations may have on the generalizability and reliability of the results. Future research endeavors should aim to address these limitations by conducting larger-scale studies with comprehensive patient data collection and considering the referral patterns for diagnostic procedures.

## CONCLUSION

The reliability of USG as a diagnostic tool for TNs remains debated. Some studies and consensus suggest that USG alone is insufficient and requires FNAC. However, other research indicates that advancements in USG quality and techniques may bring its accuracy on par with FNAC. Future large-scale studies in specialized centers are recommended to assess and

compare the diagnostic reliability of modern USG scans for TNs, potentially leading to a shift in the current diagnostic approach and improved patient care.

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