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# Analysis of Differential Value of Ultrasonography Assisted with C-TIRADS Classification and Autoantibody and TSH Detection in Benign and Malignant Thyroid Nodules

Zijie Yin [1], Xueqin Hou [2,*]

1. Department of General Internal Medicine, Shangcheng District People's Hospital, 310000 Hangzhou, Zhejiang, China

2. Hangzhou Dinglan Clinic of Traditional Chinese Medicine, 310000 Hangzhou, Zhejiang, China

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* **Correspondence**

Xueqin Hou

Hangzhou Dinglan Clinic of Traditional Chinese Medicine, 310000 Hangzhou, Zhejiang, China

E-mail: yzj78915@163.com

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**Abstract**

**Background:** This study analyzes the value of Chinese Thyroid Imaging Report and Data System (C-TIRADS) combined with autoantibodies and TSH-assisted ultrasonography in the differential diagnosis of benign and malignant thyroid nodules. **Methods:** The clinical data of 106 patients with thyroid nodules treated in our hospital from March 2022 to May 2023 were retrospectively analyzed. C-TIRADS classification, serum thyroglobulin antibody (TGAb), thyroid peroxidase antibody (TPOAb), and thyrotropin (TSH) level detection, and elastography examination were performed for all patients, and they were divided into malignant group (n = 44) and benign group (n = 62) according to the pathological diagnosis results of nodular lesions. The positive rate of thyroid nodules diagnosed by the three methods was compared, and the diagnostic efficiency of the three methods was analyzed. **Results:** According to C-TIRADS classification, the number of patients with category 3 was significantly higher while the number of patients with category 4B and 4C was obviously lower in the benign group compared with those in the malignant group ($p < 0.05$). The levels of TGAb, TPOAb, and TSH in malignant group were visibly higher than those in benign group ($p < 0.05$). The proportion of thyroid nodules with ultrasonic elastic score of 2 points in benign group was markedly higher than that in malignant group, while the proportion of thyroid nodules with ultrasonic elastic score of 4 points was significantly lower than that in malignant group ($p < 0.05$). The positive rates of C-TIRADS, serum TGAb, TPOAb, TSH, and ultrasound elastography in malignant group were strikingly higher than those in benign group ($p < 0.05$). Compared with the single detection of C-TIRADS classification, serum factors and ultrasound elastography for each individual test, the accuracy, sensitivity and specificity of the three combined detection were significantly higher, and the difference was statistically significant ($p < 0.05$). **Conclusion:** C-TIRADS combined with autoantibodies and TSH-assisted ultrasonography has a better effect in the detection of thyroid nodules, which can improve the differential diagnosis of benign and malignant nodules.

## 1 Introduction

Thyroid nodule is a common neck disease, with thyroid enlargement and pain as the main manifestation. In severe cases, patients will undergo cardiovascular and respiratory disorders, which can be a threat to the patient's life and health [1]. Clinically, thyroid nodules are generally categorized into benign and malignant nodules, and there are significant differences in the treatment and prognosis of these two nodules, so it is extremely important to accurately determine the nature of the nodule [2].

With the deepening of related research in recent years, elastography and Chinese Thyroid Imaging Reporting and Data System (C-TIRADS) have been applied to the differential diagnosis of benign and malignant thyroid nodules, with a remarkable effect. However, the results of the elastography assessment will be biased when there are calcifications and hemorrhages in the lesions, leading to a certain rate of misdiagnosis [3]. Identification of serum biomarker panel has been shown to aid the differentiation of malignant from benign thyroid nodules [4]. Serum thyroglobulin antibody (TGAb) is an autoantibody that marks thyroid autoimmunity and thyroid peroxidase antibody (TPOAb), another kind of autoantibody, inhibits thyroid hormones, T3 and T4 [5,6]. Thyrotropin (TSH) is a pituitary hormone that stimulates the production of thyroxine the from the thyroid gland [5]. They are all detected to exist in benign thyroid nodules at a lower level than those in the malignant group [7], and are proven as independent risk factors for patients with malignancy in thyroid nodules [8]. Currently, detection of their levels is conducted as a good adjunct in the evaluation of benign and malignant thyroid nodules, with a high degree of specificity [9].

In order to improve the diagnostic accuracy of benign and malignant thyroid nodules, 106 patients with thyroid nodules were recruited in this study. The diagnostic value of ultrasound elasticity score, C-TIRADS score, and the combined detection of serum TGAb, TPOAb, and TSH was compared to assess the diagnostic efficiency of above methods in determining the benign and malignant thyroid nodules.

## 2 Materials and methods

### 2.1 Clinical data

The clinical data of 106 patients with thyroid nodules treated in our hospital from March 2022 to May 2023 were retrospectively analyzed. Patients were divided into malignant group (n = 44) and benign group (n = 62) according to the pathological diagnosis results of nodular lesions. The difference in general data between the two groups was not statistically significant ($p > 0.05$), but comparable, as seen in Table 1.

**Table 1** Comparison of general data between the two groups.

| Groups | Cases | Gender (cases) | | Average age | Average duration of | Thyroid nodule (cases) | |
|---|---|---|---|---|---|---|---|
| | | Male | Female | (years old) | disease (years) | Solitary | Multiple |
| Benign group | 62 | 32 | 30 | 46.78 ± 4.58 | 4.08 ± 1.23 | 26 | 36 |
| Malignant group | 44 | 22 | 22 | 47.62 ± 4.89 | 4.34 ± 1.34 | 19 | 25 |
| $x^2$/t | | 0.027 | | 0.905 | 1.033 | 0.016 | |
| *p* | | 0.870 | | 0.368 | 0.304 | 0.898 | |

### 2.2 Inclusion criteria

(1) Patients met the diagnostic criteria in *New guidelines for the management of thyroid nodules and differentiated thyroid cancer* [10]. (2) Patients who were determined to have thyroid nodules by thyroid

ultrasonography and X-ray. (3) Patients underwent the testing of serum TGAb, TPOAb, and TSH levels. (4) Patients who were determined to have malignant or benign thyroid nodules by pathology. (5) Patients' clinical data were complete.

### 2.3 Exclusion criteria

(1) Patients with other malignant tumors. (2) Patients with unclear ultrasound images. (3) Patients with neck injuries.

### 2.4 Detection methods

#### 2.4.1 Ultrasonic examination method

Following diagnostic ultrasound machine line array probes were used, including RS80A (manufacturer: Samsung, frequency: 3-12 MHz, Korea) and Preirus (manufacturer: Hi-Tachi; frequency: 5-12 MHz, Japan). Two attending physicians were responsible for the independent scanning. Patients were asked to take supine position, and straightened the neck as much as possible to fully expose the anterior neck area, with head slightly tilted back. Firstly, routine ultrasound scanning of the thyroid gland was performed to observe the size, morphology, parenchymal echogenicity, blood flow of thyroid gland, the internal echogenicity of the nodule, the growth site, the aspect ratio, the edge, the border, the presence or absence of calcification, as well as the relationship of the nodule with thyroid capsule, trachea, esophagus, and cervical vessels. Color Doppler flow imaging was then used to detect blood flow within and around the nodes, and finally the cervical lymph nodes were observed for any abnormalities. Longitudinal, transverse, and maximal sections of the nodule were retained. At the end of the conventional scanning, elastography sampling frame was switched. Patient were instructed to breathe calmly. Then the operator fit the probe to the skin, and held the probe at the lesion to make 2 times/s of tiny vibration, applying pressure to the skin as perpendicular as possible and maintaining it for 2 s, to cover the whole range of the lesion. For the larger lesion, the most part of the lesion and part of the normal thyroid tissue were taken to perform elastographic assessment once in both longitudinal and transversal section. The freeze button on Samsung ultrasound instrument was pressed when the pressure indicator on the instrument display was completely green, and Hi-Tachi ultrasound instrument was frozen when the pressure-strain curve appeared to be sinusoidal with periodic changes. Then the images were played back, and after selecting the satisfactory images, two-dimensional and elastographic images were observed in comparison with each other, and the stiffness of the focal area was compared with that of the surrounding tissues.

#### 2.4.2 Serum testing method

3 mL of venous blood was drawn from the elbow of all patients in the morning in fasting state, put still, and centrifuged at 3500 rpm for 5 min to collect the serum in the upper layer. Serum TGAb, TPOAb, and TSH levels were detected using a fully automatic chemiluminescence analyzer (Siemens ADVIAcentaurXP, Germany).

### 2.5 Judgment criteria

(1) C-TIRADS classification criteria [11]: category 1: no nodule; category 2: benign; category 3: probably benign, with a malignancy rate of <2%; category 4A: low suspicion for malignancy, with a malignancy rate of 2%-10%; category 4B: moderate suspicion for malignancy, with a malignancy rate of 10%-50%; category 4C: high suspicion for malignancy, with a malignancy rate of 50%-90%; category 5: highly suggestive of malignancy, with a malignancy rate of >90%; category 6: biopsy proved malignancy. Categories 2 to 4A were recorded as benign nodules and categories 4B to 5 as malignant nodules.

(2) Ultrasound elasticity score criteria [12]: 1 point for all green color within the lesion; 2 points for most of

the lesion being green and a little blue; 3 points for the lesion showing green and blue within the lesion and both in roughly equal proportions; 4 points for most of the lesion being blue or accompanied by a little green within the lesion; 5 points for the lesion and the surrounding tissues being blue (which may be accompanied by a little green). 1-3 points were recorded as benign nodules and 4-5 as malignant nodules.

(3) According to the laboratory diagnostic criteria [13]: the normal reference ranges of thyroid serologic indexes TGAb, TPOAb, and TSH: TGAb: 0-60 U/mL; TPOAb: 0-60 U/mL; TSH: 0.38-5.57 μU/mL. TGAb, TPOAb and TSH are judged to be positive if their levels exceed the normal range.

### 2.6 Statistical methods

Statistical analysis was performed using SPSS 20.0. Count data were expressed as cases (%). Comparisons between the two groups were carried out using $x^2$ test, and measurement data were expressed as mean ± standard deviation. Independent samples t-test was used for comparison between the two groups. Differences were considered statistically significant at $p < 0.05$

## 3 Results

### 3.1 Comparison of C-TIRADS classification of thyroid nodules between the two groups

According to C-TIRADS classification, the number of patients with category 3 was higher while the number of patients with category 4B and 4C was lower in the benign group compared with those in the malignant group ($p < 0.05$). The results were displayed in Table 2.

### 3.2 Comparison of serum factor levels between the two groups

The levels of TGAb, TPOAb, and TSH in malignant group were visibly higher than those in benign group ($p < 0.05$). The results were displayed in Table 3.

**Table 2** Comparison of C-TIRADS classification of thyroid nodules between the two groups [cases (%)].

| Groups | Cases | 3 | 4A | 4B | 4C | 5 |
|---|---|---|---|---|---|---|
| Benign group | 62 | 46 (74.20) | 11 (17.74) | 5 (8.06) | 0 (0.00) | 0 (0.00) |
| Malignant group | 44 | 1 (2.27) | 9 (20.46) | 23 (52.27) | 10 (22.73) | 1 (2.27) |
| $x^2$ | | 53.940 | 0.124 | 25.876 | 15.559 | 1.423 |
| $p$ | | <0.001 | 0.725 | <0.001 | <0.001 | 0.233 |

**Table 3** Comparison of serum factor levels between the two groups (mean ± standard deviation).

| Groups | Cases | TGAb (U/mL) | TPOAb (U/mL) | TSH (μU/mL) |
|---|---|---|---|---|
| Benign group | 62 | 76.47 ± 42.38 | 260.37 ± 87.69 | 1.64 ± 1.02 |
| Malignant group | 44 | 155.28 ± 50.62 | 421.63 ± 100.23 | 4.87 ± 1.24 |
| t | | 8.698 | 8.789 | 14.680 |
| $p$ | | <0.001 | <0.001 | <0.001 |

### 3.3 Comparison of ultrasound elastography scores of thyroid nodules in two groups

There was no statistically significant difference in the comparison of the percentage of people with ultrasound elasticity scores of 3 and 5 points for thyroid nodules in the two groups ($p > 0.05$). The proportion of thyroid nodules with ultrasonic elastic score of 2 points in benign group was markedly higher than that in malignant group, while the proportion of thyroid nodules with ultrasonic elastic score of 4 points was significantly lower than that in malignant group ($p$ < 0.05). The results were displayed in Table 4.

### 3.4 Comparison of diagnostic positivity of thyroid nodules by three methods

The positive rates of C-TIRADS, serum TGAb, TPOAb, TSH, and ultrasound elastography in malignant group were strikingly higher than those in benign group ($p$ < 0.05). The results were displayed in Table 5.

### 3.5 Analysis of diagnostic efficacy of three methods for thyroid nodules

Compared with the accuracy, sensitivity, and specificity of the use of C-TIRADS classification, (TGAb, TPOAb, and TSH) level detection, or ultrasound elastography alone, those of the use of the detection method that combines the three methods were significantly higher, and the difference was statistically significant ($p$ < 0.05). The results were depicted in Table 6.

**Table 4** Comparison of ultrasound elastography scores of thyroid nodules in two groups [cases (%)].

| Groups | Cases | 2 points | 3 points | 4 points | 5 points |
|---|---|---|---|---|---|
| Benign group | 62 | 10 (16.13) | 47 (75.81) | 5 (8.06) | 0 (0.00) |
| Malignant group | 44 | 1 (2.27) | 26 (59.10) | 16 (36.36) | 1 (2.27) |
| $x^2$ | | 5.313 | 3.354 | 12.974 | 1.423 |
| $p$ | | 0.021 | 0.067 | <0.001 | 0.233 |

**Table 5** Comparison of diagnostic positivity of thyroid nodules by three methods [cases (%)].

| Groups | Cases | C-TIRADS classification positive | TGAb positive | TPOAb positive | TSH positive | Ultrasound elastography positive |
|---|---|---|---|---|---|---|
| Benign group | 62 | 5 (8.06) | 10 (16.13) | 14 (22.58) | 11 (17.74) | 5 (8.06) |
| Malignant group | 44 | 34 (77.27) | 17 (38.64) | 19 (43.18) | 19 (43.18) | 17 (38.64) |
| $x^2$ | | 53.006 | 6.868 | 5.094 | 8.208 | 14.625 |
| $p$ | | <0.001 | 0.009 | 0.024 | 0.004 | <0.001 |

**Table 6** Analysis of diagnostic efficacy of three methods for thyroid nodules.

| Groups | Accuracy (%) | Sensitivity (%) | Specificity (%) |
|---|---|---|---|
| C-TIRADS classification | 85.85 (91/106) | 77.27 (34/44) | 91.94 (57/62) |
| TGAb | 65.09 (69/106) | 38.64 (17/44) | 83.87 (52/62) |
| TPOAb | 63.21 (67/106) | 43.18 (19/44) | 77.42 (48/62) |
| TSH | 66.04 (70/106) | 34.09 (19/44) | 83.87 (51/62) |
| Ultrasound elastography | 69.81 (74/106) | 38.64 (17/44) | 91.94 (57/62) |
| Combined detection | 89.62 (95/106) | 84.09 (37/44) | 93.54 (58/62) |
| $x^2$ | 35.613 | 38.159 | 11.682 |
| $p$ | <0.001 | <0.001 | 0.039 |

## 4 Discussion

Relevant report has depicted that the incidence of thyroid nodules has become increasingly younger and the incidence rate is also rising [14]. It is especially important to identify benign and malignant thyroid nodules because of the wide variation in treatment regimens and medications.

Ultrasound elastography is mainly based on the differences in elasticity coefficients among tissues, and can visually detect the hardness of lesions through images in gray scale or color coding, in which the internal components of benign thyroid nodules are often dominated by colloid, with a softer texture and higher elasticity, and the cells of malignant thyroid nodules are often dominated by grits, with a higher hardness and lower elasticity [15,16]. Ultrasound elastography has been shown to have high sensitivity and specificity for differential diagnosis of thyroid nodules [17]. This study obtained similar results by retrospectively analyzing 106 patients with thyroid nodules diagnosed using ultrasound elastography. However, this diagnostic technique has its limitations. Calcified and fibrotic lesions are difficult to diagnose, and improper force application by the operator can affect the assessment of lesion stiffness by strain elastography and lead to false-negative or false-positive results [18]. Sun's study has demonstrated that the overall mean sensitivity and specificity of ultrasound elastography for differentiation of thyroid nodules are 0.79 and 0.77 for elasticity score assessment and 0.85 and 0.80 for strain ratio assessment, indicating that ultrasound elastography has a certain diagnostic value for the nature of thyroid nodules, but it needs to be used clinically in conjunction with other diagnostic methods [17].

C-TIRADS, which is established to resolve the inconsistencies in terms of reporting terminology or management recommendations due to subjective interpretation of medical images of thyroid nodules, has been used in different hospitals in China, with a good performance in the identification of thyroid nodules [11]. The higher C-TIRADS classification category represents the higher likelihood of malignant thyroid nodules [19]. C-TIRADS classification is mainly used to score nodules comprehensively by incorporating suspected microcalcifications into suspected malignant features as indications of malignancy, which can further provide a reference basis for clinical treatment [19]. However, since some benign and malignant nodules have overlapping ultrasonographic signs, the use of C-TIRADS classification alone for the diagnosis of benign and malignant thyroid nodules is limited [19]. Our results proved that ultrasound elastography had some clinical value in correcting the classification of C-TIRADS nodules of category 4 in the thyroid gland, which is in line with the findings of Ding [20]. Previous study has demonstrated that the combination of shear wave elastography (SWE), one technique of ultrasound elastography, with C-TIRADS exhibits an better ability of differentiating malignant thyroid nodules from benign tumors than SWE or C-TIRADS alone [21].

Thyroid hormones are sensitive indicators of thyroid function, of which TGAb, TPOAb, and TSH levels are all strikingly elevated in the patients with hypothyroidism [22-24]. Serum TGAb destroys thyroxine through antibody-dependent cell-mediated cytotoxicity, leading to the destruction of target cells and the spillover of antibodies into the bloodstream [22]. TPOAb destroys target cells through a moderately strong antibody-dependent cell-mediated cytotoxicity, prompting the spillover of cytoplasmic "peroxidase" into the bloodstream to stimulate the organism [23]. Notably, the levels of TGAb and TPOAb in malignant thyroid nodules were significantly higher than those of the benign group [25]. Serum TSH is a hormone secreted by the pituitary gland, which regulates the proliferation and differentiation of thyroid cells, the blood supply to the thyroid gland, as well as the synthesis and secretion of thyroid hormones [24]. There is a certain relationship between its level and patient's pituitary gland secretion [24]. Baser's study has demonstrated that serum TSH level was higher in patients with malignant thyroid nodules than in those with benign nodules [26]. Moreover, detection of TSH level has been conducted to exclude hot nodules during the prediction of malignancy in thyroid nodules by ultrasound elastography [27].

The correlation analysis of this study revealed that the sensitivity, specificity, and accuracy of ultrasonography assisted with C-TIRADS classification combined with autoantibody and TSH detection in the diagnosis of malignant thyroid nodules were better than those of the individual tests, suggesting that C-TIRADS combined with autoantibodies and TSH-assisted ultrasonography improved the differential diagnosis of benign and malignant nodules.

## 5 Conclusion

Ultrasonography assisted with C-TIRADS classification combined with autoantibody and TSH detection has a better effect in the detection of thyroid nodules, which can improve the differential diagnosis of benign and malignant nodules. Therefore, it is worth to further popularize the application in the clinic.

## Acknowledgements

Not applicable.

## Conflicts of Interest

The authors declare no conflicts of interest.

## Author Contributions

Z.Y. and X.H.: Conceptualization, Data curation, Formal analysis, Methodology, Writing-Original draft, Writing-review and editing. All authors have read and agreed to the published version of the manuscript.

## Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee, and the patients were informed and consented.

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## Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

## Supplementary Materials

Not applicable.

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