Article

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A Review about C-TIRADS, ACR-TIRADS, and K-TIRADS Combined with Real-Time Tissue Elastography to Diagnose Thyroid Nodules

Yan Ma[1], Xiaoguang Huo[1], Shanshan Kong[2], Wenzhe Xu[1], Wei Zhao[1], Min Zhu[3,*]

[1]Department of Ultrasound, Zibo Central Hospital, 255000 Zibo, Shandong, China
[2]Department of Radiology, Zibo Central Hospital, 255000 Zibo, Shandong, China
[3]Department of Neonatology, Zibo Maternal and Child Health Hospital, 255000 Zibo, Shandong, China
*Correspondence: zhumin@fybjsd.org.cn (Min Zhu)
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Purpose: This study aimed to evaluate the diagnostic efficiency of the Chinese version of thyroid imaging reporting and data system (C-TIRADS), American College of Radiology (ACR)-TIRADS, and Korean (K)-TIRADS combined with real-time tissue elastography to diagnose thyroid nodules.
Methods: A total of 574 thyroid nodule ultrasonographic images were retrospectively analyzed and classified based on the three TIRADS methods. The MedCale statistical software was used to construct the receiver operating characteristic (ROC) curve based on the pathological results of surgery. The diagnostic efficiency before and after assessing elastographies from the three TIRADS was compared between C-TIRADS, ACR-TIRADS, and K-TIRADS groups and within before and after TIRADS combined with elastic imaging. Furthermore, the unnecessary biopsy rates were also compared. Comparing area under ROC curve (AUC) with MEDCALC software (20.0.15, MedCalc Software Ltd., Ostend, Belgium), Delong test was used. The sensitivity and specificity were compared by STATA software (15.1, StataCorp LP, College Station, TX, USA) and Chi-square test. The rate of unnecessary biopsy was compared by SPSS software (23.0, IBM, Armonk, NY, USA) and Chi-square test.
Results: C-TIRADS, ACR-TIRADS, K-TIRADS cut-off values, and real-time tissue elastography (RTE) were 4b, 5, 5, and 3, respectively, and the areas under the ROC curve were 0.932, 0.914, 0.904, and 0.883, respectively. C-TIRADS had the highest AUC ($p < 0.05$) and sensitivity ($p < 0.001$), while ACR-TIRADS had the highest specificity ($p < 0.001$). After conducting a combined elastography with the three TIRADS, AUC showed increases of different degrees. Comparing TIRADS with TIRADS+RTE, the difference of C-TIRADS had statistical significance ($p < 0.001$), but the difference of ACR-TIRADS and K-TIRADS had no statistical significance ($p > 0.05$). The unnecessary biopsy rate showed decreases of different degrees. Differences between C-TIRADS and K-TIRADS were significant ($p < 0.05$), but in the case of ACR-TIRADS were not significant ($p > 0.05$).
Conclusions: C-TIRADS, ACR-TIRADS, K-TIRA and RTE showed high diagnostic efficiency, with C-TIRADS having the highest. Real-time tissue elastography can improve TIRADS diagnostic efficiency and reduce its unnecessary biopsy rate. In this case C-TIRADS showed again the highest efficiency.

Keywords: thyroid imaging reporting and data system; real-time tissue elastography; thyroid nodules; ultrasound; thyroid

Introduction

Thyroid nodule is a common and frequent disease in clinical practice. It can be diagnosed in 30–67% people worldwide by ultrasonography [1]. Ultrasonography has become the preferred method for thyroid examination due to its good its safety, efficiency, and economy profile. Thyroid carcinoma accounts for 7–15% of the cases of thyroid nodules, the majority of which are papillary carcinoma [2]. Thyroid carcinoma can be diagnosed with ultrasonographic features, including solidity, vertical positions, irregular margins, microcalcifications, and hypoechoic signs. In practice, thyroid nodules ultrasonographic assessment is complex and changeable, and different sonographers have different understandings and applications for malignant features. Thus, there is a lack of a unified standard method, which brings many problems for the diagnosis. In order to standardize thyroid nodules diagnosis and management, Horvath (a Chilean scholar) started developing the Thyroid Imaging Reporting and Data System (TIRADS) in 2009 [3]. This is the first guide for thyroid ultrasonographic malignant risk stratification in the world. Since then, many countries have released their own guidelines. In 2016, the Korean Thyroid Association (KTA)/Korea Society of Thyroid Radiology (KSThR) released the Korean (K)-TIRADS [4]. In 2017, the American College of Radiology (ACR) released the American College of Radiology (ACR)-TIRADS [5]. In 2020, the Superficial Organs and Angiology Group of the Ultrasound Medical Branch of Chinese Medical Association released the 2020 Chinese Guidelines for Ultrasound Malignant Risk Stratification of Thyroid Nodules (Chinese version of thyroid imaging reporting and data system [C-TIRADS]) [6]. C-TIRADS is specific to China's national conditions, which makes it more practical and convenient.

Ophir *et al.* [7] in 1991 was the first proposing ultrasonic elastography. Lyshchik *et al.* [8] in 2005 was the first using it for a thyroidal examination. Over the course of long-term clinical practice, ultrasonic elastography has become an additional method to diagnose thyroid nodules in combination with conventional ultrasonography and fine-needle aspiration biopsy (FNA) [9]. Guidelines released by the World Federation for Ultrasound in Medicine and Biology (WFUMB) [10] and the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) [11] support the use of elastography to diagnose thyroid nodules. Real-time Tissue Elastography (RTE) assesses tissue elasticity via compression-induced tissue displacement. RTE elasticity score (ES) reflects tissue hardness. Increased thyroid nodules hardness is closely related to the risk of malignancy. There are few clinical reports about C-TIRADS combined with RTE to diagnose thyroid nodules. Therefore, this study aimed to analyze the diagnostic efficiency of C-TIRADS combined with RTE to evaluate whether RTE can improve the diagnostic efficiency of TIRADS. Additionally, the results were compared with ACR-TIRADS and K-TIRADS.

Methods

Study Population

A retrospective analysis was conducted with 550 patients with thyroid nodules, with a total of 574 nodules, who underwent ultrasound examination and received surgical treatment in the Zibo Central Hospital, from January to December 2021. Inclusion criteria: ① Nodules had complete ultrasound images and postoperative pathological results, ② patients underwent ultrasound examination within 1 month before the operation, ③ nodules maximum diameter ranged from 5 to 30 mm. Exclusion criteria: ① History of other tumors, ② poor image quality, ③ incomplete clinical data.

Conventional Ultrasound Examination and TIRADS Classification

Conventional ultrasonic examinations were performed by radiologists with over 5 years of experience in thyroid ultrasonography. During the examinations, the patients were placed in supine position, with the head tilted back and the neck completely exposed. The thyroid was comprehensively scanned in cross sections and longitudinal sections. If any thyroid nodule was found, its location, size, shape, margin, composition, internal echo, relationship with adjacent tissues, as well as the presence or absence of calcification, was recorded in detail. Nodule images were stored in the computer database system.

Ultrasound images were analyzed by two radiologists with over 10 years of experience in thyroid ultrasonography. Nodules were classified according to three ultrasound classification systems. During image analysis, radiologists were unaware of the pathological results of the nodules and the clinical data of the patients. In this study, the gold standard to identify benign and malignant tumor was postoperative pathology.

C-TIRADS identifies 5 positive indicators: Solidity, markedly hypoechoic signs, vertical positions, indistinct/irregular margins or extra-thyroidal invasion, and microcalcification. Each indicator adds 1 point to the total; 1 negative indicator: Calcification with a comet tail, minus one point for every negative indicator was found. C-TIRADS conducts classification according to scores: 1: No nodules, 2: –1 point, 3: 0 points, 4a: 1 point, 4b: 2 points, 4c: 3–4 points, and 5: 5 points. From 2 to 5, the nodules become more and more malignant.

ACR-TIRADS assesses nodule composition, echogenicity, shapes, margins, and calcification. It assigns different scores according to different ultrasonographic features. Scores for nodule composition: 0 points for cystic nodules, 0 points for spongiform nodules, 1 point for mixed cystic-solid nodules, and 2 points for completely solid nodules or almost solid nodules. Scores for nodule echogenicity: 0 points for anechoic signs, 1 point for isoechoic signs, 1 for hyperechoic signs, 1 point for mixed echoic signs, 2 points for hypoechoic signs, and 3 points for markedly hypoechoic signs. Scores for nodule shapes: 0 points for aspect ratio <1, and 3 points for aspect ratio >1. Scores for nodule margins: 0 points for smooth margins, 0 points for indistinct margins, 2 points for irregular margins, 2 points for lobulated margins, and 3 points for extra-thyroidal invasion. Scores for intranodular calcification: 0 points for no calcification, 0 points for calcification with a comet tail, 1 point for massive calcification, 2 points for peripheral or marginal calcification, and 3 points for microcalcification. ACR-TIRADS classification according to scores is as follows: 1: 0 points, 2: 2 points, 3: 3 points, 4: 4–6 points, and 5: $\geq$7 points. From 1 to 5, the nodules become more and more malignant.

K-TIRADS identifies 3 sonographic features: Irregular margins, microcalcifications, and aspect ratio >1. Nodules are classified according to their sonographic features. K-TIRADS according to scores is as follows: 1: No nodules, 2: Spongiform nodules, simple cysts, or partially cystic nodules with comet tail artifacts, 3: Partially cystic or isoechoic/hyperechoic nodules without suspicious ultrasound signs, 4: Solid hypoechoic nodules without suspected ultrasound signs, or partially cystic or/and hyperechoic/isoechoic nodules with one or more suspicious ultrasound signs, 5: Solid and hypoechoic nodules with one or more suspected ultrasound signs.

Real-Time Tissue Elastography

During RTE assessment, the probe was perpendicular to the skin surface and slightly pressurized to keep away from the great cervical vessels as much as possible. At the same time, the probe was kept still for a few seconds to obtain a clear elastogram. During the examination, the patient was asked to breathe calmly and avoid swallowing. Images were shown on a split-screen. Nodule conventional ultrasound images were displayed at the left (including the nodule and enough surrounding normal thyroid tissue), and elastic images at the right. In elastic images red and green represented soft, and blue represents hard. The elasticity images were classified based on the Asteria standard [12]: Score 0 for cystic or mainly cystic lesions alternating blue, green and red with the "BGR" phenomenon. Score 1 for lesions in uniform green. Score 2 for lesions mainly in green with some blue areas. Score 3 for lesions mainly in blue with some green and red areas. Score 4 for lesions in uniform blue. The bluer areas, the higher the hardness and the higher the score.

New TIRADS Classification

All nodules were categorize combining the above-mentioned guidelines and RTE: C-TIRADS+RTE, ACR-TIRADS+RTE, K-TIRADS+RTE. When elastic score (ES) $\geq$3, the grade of TIRADS was increased by one leve. When ES $<$3, the grade of TIRADS was decreased by one level. When the grade of TIRADS was already at the lowest or highest grade, the grade of TIRADS remained unchanged even if ES $<$3 or ES $\geq$3.

Statistical Methods

SPSS (23.0, IBM, Armonk, NY, USA), MEDCALC (20.0.15, MedCalc Software Ltd., Ostend, Belgium), and STATA (15.1, StataCorp LP, College Station, TX, USA) were used for statistical analysis. Normally distributed quantitative data are presented as mean $\pm$ standard deviation. T-test was used to compare the age and size of benign and malignant nodules between two independent samples. Qualitative data are expressed as percentages (%). The χ^2 test was used to compare qualitative data between groups. Comparisons between groups of data not normally distributed were performed using the Mann-Whitney U test. A receiver operating characteristic (ROC) curve was performed using the pathological results as the gold standard. The area under ROC curve (AUC), sensitivity, specificity, and unnecessary biopsy rate were compared before and after TIRADS was combined with RTE. AUC comparison was performed with MEDCALC software using the Delong test. Sensitivity and specificity comparison was performed with STATA software using the Chi-square test. Spearman correlation analysis was used to assess the correlation between the different TIRADS grades and different ESs with nodule malignancy rates. $p < 0.05$ was considered statistically significant.

Results

Patient Characteristics and Pathological Results

A total of 550 patients (105 males and 445 females) aged 22–70 (48.32 $\pm$ 10.95) years old were included in the study. Among the 574 nodules analysed, 172 were benign and 402 were malignant, they had a maximum diameter of 5–30 (11.15 $\pm$ 5.35) mm. The age difference between patients with benign nodules (50.85 $\pm$ 11.17) and malignant nodules (47.24 $\pm$ 10.68) was statistically significant $p < 0.001$). The nodule size difference between benign nodules (16.20 $\pm$ 4.07) and malignant nodules (8.99 $\pm$ 3.41) was statistically significant ($p < 0.001$). Flowchart and pathological results of the 574 nodules are shown in Fig. 1 and Table 1.

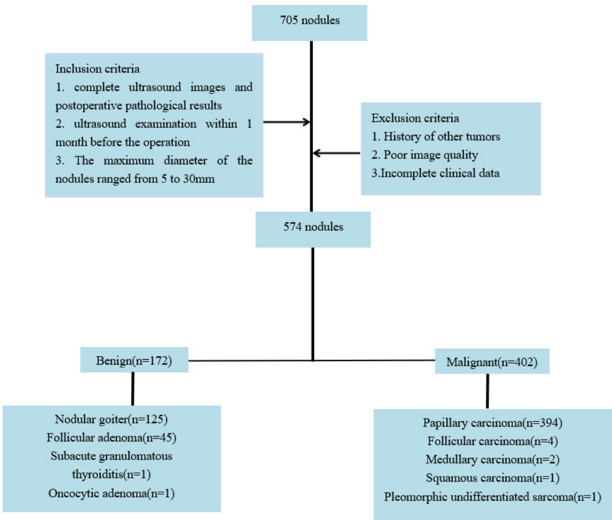

Fig. 1. Selection of study population flowchart.

Relationship between TIRADS Grades, RTE, Ultrasonographic Features and Pathological Results

Nodule malignancy rates of TIRADS grades was compared against ES scores. TIRADS grades nodule malignancy rates were different to ES scores ($p < 0.001$). Spearman correlation analysis showed that there was a significant positive correlation between TIRADS grades, and different ES scores with nodule malignancy rates (all R $>$0.65, all $p < 0.01$) (Figs. 2,3, and Table 2).

Two-dimensional ultrasonographic features, such as hypoechoic or markedly hypoechoic signs, irregular margins, aspect ratio $>$1, microcalcifications, and solid nodules, were more present in malignant nodules compared to benign nodules (all $p < 0.001$). Please refer to Table 3.

Table 1. 574 Nodule cases pathological type.

	Pathological Type	Number (n)	Total (n)
Benign nodules	Nodular goiter	125 (72.7%)	172
	Follicular adenoma	45 (26.1%)	
	Subacute granulomatous thyroiditis	1 (0.6%)	
	Oncocytic adenoma	1 (0.6%)	
Malignant nodules	Papillary carcinoma	394 (98.0%)	402
	Follicular carcinoma	4 (1.0%)	
	Medullary carcinoma	2 (0.5%)	
	Squamous carcinoma	1 (0.25%)	
	Pleomorphic undifferentiated sarcoma	1 (0.25%)	

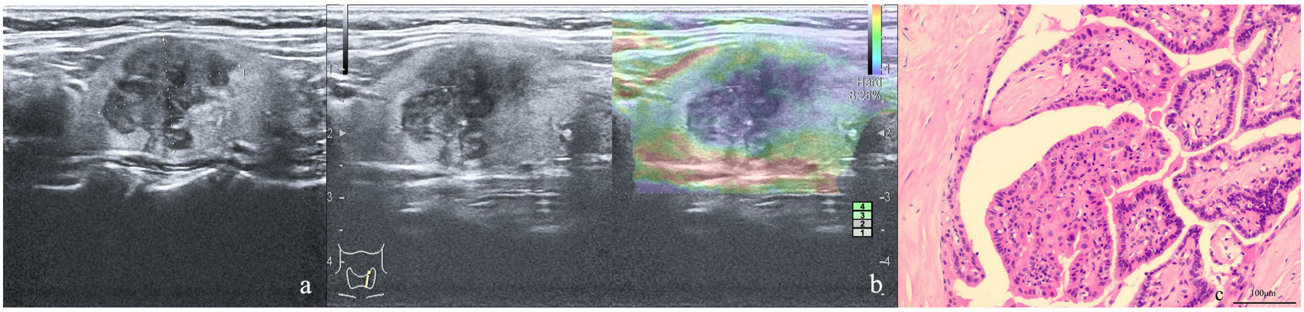

Fig. 2. A 49-year-old female with a maximum diameter 23 mm nodule. (a) Two-dimensional ultrasonographic features: Solid, hypoechoic, indistinct and irregular margins with microcalcifications. TIRADS classification: C-TIRADS 4c, ACR-TIRADS 5, K-TIRADS 5. (b) Elastography with an elasticity score of 3 (The nodule is predominantly blue and the normal tissue surrounding the nodules is green). Adjusted TIRADS, C-TIRADS 5, ACR-TIRADS 5, K-TIRADS 5. (c) Postoperative pathological results indicating papillary thyroid carcinoma (400×).

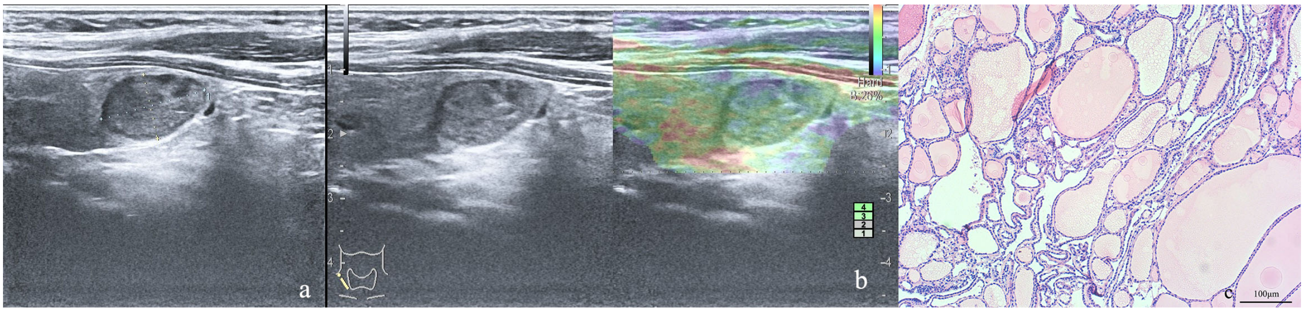

Fig. 3. A 50-year-old female patient with a 17 mm nodule. (a) Two-dimensional ultrasonographic features: Solid, hypoechoic, regular margins without calcifications. TIRADS classification: C-TIRADS 4a, ACR-TIRADS 4, K-TIRADS 4. (b) Elastography is mainly green with an elasticity score of 2. Adjusted TIRADS, C-TIRADS 3, ACR-TIRADS 3, K-TIRADS 3. (c) Postoperative pathological results indicating nodular goiter (100×).

TIRADS and RTE Diagnostic Efficiency

Cut-off values of C-TIRADS, ACR-TIRADS, K-TIRADS and RTE based on an independent diagnosis were 4b, 5, 5, and 3, respectively. C-TIRADS had the highest AUC, while K-TIRADS and RTE had the lowest AUC ($p < 0.05$). C-TIRADS had the highest sensitivity ($p < 0.001$), while ACR-TIRADS had the highest specificity ($p < 0.001$) (Fig. 4 and Table 4).

Diagnostic Efficiency after Combination of TIRADS with RTE

After combining TIRADS grades with RTE scores, C-TIRADS+RTE had the highest AUC ($p < 0.05$) and specificity ($p < 0.001$), while ACR-TIRADS+RTE and K-TIRADS+RTE had the highest sensitivity ($p < 0.001$). The AUC the three TIRADS grade after combining with RTE increased. The AUC of C-TIRADS+RTE was statistically higher than that of C-TIRADS ($p < 0.001$), but ACR-TIRADS+RTE and K-TIRADS+RTE were similar to ACR-TIRADS and K-TIRADS ($p > 0.05$). C-TIRADS+RTE

Table 2. Thyroid nodules malignancy rate based on different TIRADS classifications and ES.

Category	Benign (n)	Malignant (n)	Malignancy rate (%)	*p*	*R*
C-TIRADS				<0.001	0.745
2	3	0	0		
3	86	4	4.44		
4a	53	12	18.46		
4b	17	77	81.91		
4c	13	288	95.68		
5	0	21	100		
ACR-TIRADS				<0.001	0.789
1	9	0	0		
2	62	0	0		
3	34	5	12.82		
4	45	34	43.04		
5	22	363	94.29		
K-TIRADS				<0.001	0.794
2	11	0	0		
3	99	5	4.81		
4	35	23	39.66		
5	27	374	93.27		
ES				<0.001	0.659
0	18	0	0		
1	55	6	9.83		
2	45	24	34.78		
3	69	251	78.44		
4	7	99	93.4		

TIRADS, thyroid imaging reporting and data system; ES, elastic score. R: correlation coefficient.

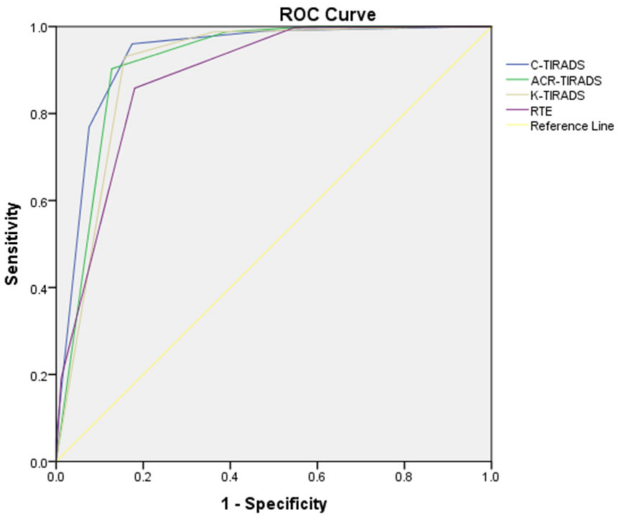

Fig. 4. C-TIRADS, ACR-TIRADS, K-TIRADS and RTE ROC curves.

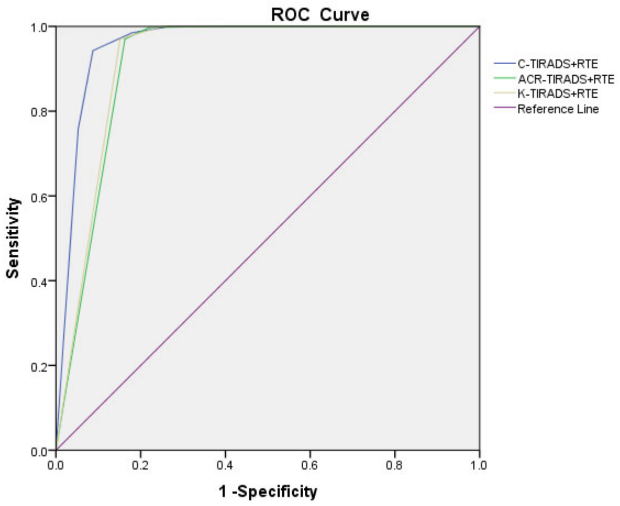

Fig. 5. C-TIRADS+RTE, ACR-TIRADS+RTE, K-TIRADS+RTE ROC curve. C-TIRADS+RTE, ACR-TIRADS+RTE, K-TIRADS+RTE AUC were 0.958, 0.915, 0.921, respectively. ROC, receiver operating characteristic; TIRADS, thyroid imaging reporting and data system; RTE, real-time tissue elastography; AUC, area under ROC curve.

sensitivity decreased and its specificity increased, ACR-TIRADS+RTE sensitivity increased and its specificity decreased, K-TIRADS+RTE sensitivity and specificity increased ($p < 0.001$) (Fig. 5, Tables 4,5).

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Table 3. Benign nodules and malignant nodules ultrasonographic features.

Features	Benign (n)	Malignant (n)	χ^2	p
Composition			167.6	<0.001
Cystic	8 (100%)	0		
Cystic and solid	70 (86.4%)	11 (13.6%)		
Solid or almost solid	94 (19.4%)	391 (80.6%)		
Margin			245.74	<0.001
Regular	151 (67.4%)	73 (32.6%)		
Indistinct/Irregular	21 (6.3%)	313 (93.7%)		
Extra-thyroidal invasion	0	16 (100%)		
Aspect ratio			111.81	<0.001
<1	163 (45.8%)	193 (54.2%)		
>1	9 (4.1%)	209 (95.9%)		
Calcification			103.65	<0.001
None or comet tail sign	133 (45.1%)	162 (54.9%)		
Massive calcification	16 (64.0%)	9 (36.0%)		
Peripheral calcification	2 (66.7%)	1 (33.3%)		
Microcalcification	21 (8.4%)	230 (91.6%)		
Echogenicity			254.72	<0.001
Anechoic	8 (100%)	0		
Isoechoic/Hyperechoic	106 (83.5%)	21 (16.5%)		
Hypoechoic	57 (14.9%)	325 (85.1%)		
Markedly hypoechoic	1 (1.8%)	56 (98.2%)		

Table 4. C-TIRADS, ACR-TIRADS, K-TIRADS and RTE ROC curves. C-TIRADS, ACR-TIRADS, K-TIRADS and RTE ROC curves.

Method	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
C	0.932 (0.908–0.951)	96.02	82.56	92.76	89.93	91.98
ACR	0.914 (0.888–0.936)	90.3	87.21	94.33	79.38	89.37
K	0.904 (0.877–0.927)	93.03	84.3	93.28	83.79	90.41
RTE	0.883 (0.810–0.871)	85.82	81.98	91.8	71.17	84.67
C+RTE	0.958 (0.901–0.946)	94.28	91.28	96.23	87.19	93.38
ACR+RTE	0.915 (0.856–0.910)	97.01	83.72	93.26	92.29	93.02
K+RTE	0.921 (0.859–0.912)	97.01	84.88	93.74	92.38	93.37

RTE, real-time tissue elastography; C, C-TIRADS; ACR, ACR-TIRADS; K, K-TIRADS; AUC, area under ROC curve; PPV, positive prediction value; NPV, negative prediction value; Note: AUC data is presented as mean (95% confidence interval). ROC, receiver operating characteristic; TIRADS, thyroid imaging reporting and data system.

Unnecessary Biopsy Rates before and after Combining TIRADS with RTE

The unnecessary biopsy rate was defined as the proportion of nodules with benign postoperative pathology results, among nodules for which FNA was used. If FNA was performed on all nodules as recommended by guidelines, the corresponding unnecessary biopsy rate was obtained. Unnecessary biopsy rates for C-TIRADS and ACR-TIRADS was low ($p < 0.001$) before its combination with RTE. After it was combined with RTE, the unnecessary biopsy rates of the three TIRADS showed a decrease of different degrees. C-TIRADS and K-TIRADS were significantly different ($p < 0.05$), ACR-TIRADS was not significant ($p > 0.05$) (Table 6).

Discussion

This study shows that malignant nodules mainly grade as 4 and 5 in the different TIRADS classifications, and as 3 and 4 based on RTE scores. Similarly, ultrasonographic features, such as solid nodules, indistinct/irregular/extrathyroidal invasion, aspect ratio >1, microcalcifications, and hypoechoic/markedly hypoechoic signs, were more common in malignant nodules as well. This confirms the rationale behind the guideline's classification rules, and it can also illustrate the representativeness of the included samples. These findings are in line with previous studies [13–15].

Zhu *et al*. [16] in 2021 reported ACR-TIRADS had the highest sensitivity, while C-TIRADS had the highest specificity. Qi *et al*. [17] in 2021 reported K-TIRADS

Table 5. Diagnostic efficiency differences between before and after combining TIRADS with RTE.

Method	AUC		Sensitivity (%)		Specificity (%)	
	Z	p	χ^2	p	χ^2	p
C vs. C+RTE	3.56	<0.001	274.58	<0.001	77.78	<0.001
ACR vs. ACR+RTE	0.05	0.961	22.93	<0.001	33.93	<0.001
K vs. K+RTE	1.11	0.266	22.99	<0.001	33.68	<0.001

RTE, real-time tissue elastography; C, C-TIRADS; ACR, ACR-TIRADS; K, K-TIRADS; AUC, area under ROC curve.

Table 6. Unnecessary biopsy rates before and after combining TIRADS with RTE.

Method	Nodules Recommended for FNA (n)	Benign Nodules (n)	Unnecessary Biopsy Rate (%)
C	130	27	20.77
C+RTE	127	10	7.87
χ^2			6.52
p			0.003
ACR	125	25	20
ACR+RTE	128	18	14.06
χ^2			1.12
p			0.209
K	180	70	38.89
K+RTE	133	22	16.54
χ^2			10.39
p			<0.001

RTE, real-time tissue elastography; C, C-TIRADS; ACR, ACR-TIRADS; K, K-TIRADS; FNA, fine-needle aspiration biopsy.

had the highest sensitivity, while C-TIRADS had the highest specificity. In this study, C-TIRADS, ACR-TIRADS, K-TIRADS cut-off values were 4b, 5, and 5, respectively based on an independent prediction. C-TIRADS, ACR-TIRADS, K-TIRADS showed a high diagnostic efficiency, in line with previous studies [6–22]. Among them, C-TIRADS had the highest AUC making it the most suitable guidelines for the cohort of samples included in this study.

Real-time tissue elastography is widely used to diagnose thyroid nodules because is a non-invasive technique, is efficient, simple and convenient. In this study, the AUC, sensitivity, and specificity were lower than those of the TIRADS, but they still had high diagnostic efficiency. Some previous studies confirmed the high diagnostic efficiency ES as well [13,23,24]. A study including 1525 nodules divided the nodules in four groups according to their sizes: $\leq$5 mm, 5–10 mm, 10–20 mm, and 20–25 mm. In all four groups, ES showed a high diagnostic efficiency, with AUCs ranging 0.832–0.954, sensitivity ranging 74.1–94.1%, and specificity ranging 81.2–96.4% [13]. Gör gülü *et al.* [23] in 2021 reported an ES AUC, sensitivity, and specificity of 0.960, 100%, and 86.2%, respectively. In another study including 236 nodules, ES AUC, sensitivity, and specificity of ES were 0.831, 80.6%, and 85.6%, respectively [24]. The meta-analysis conducted by Razavi *et al.* [25] in 2013 reported that ES AUC, sensitivity, and specificity were 0.89, 82%, and 82%, respectively. Sun *et al.* [26], reported that ES AUC, sensitivity, and specificity 0.89, 79%, and 77%. On the other hand, there are other studies showing a poor efficiency for ES. Three studies showed that ES sensitivity was 67.8%, 15.7%, and 47%, respectively [27–29]. This could be explained due to a reduced size of malignant nodules and thus the tissue was not hard enough, resulting in low scores, and subjective factors related to the operator and study samples that were not representative. Other reports showed that, due to biological heterogeneity, the internal fibrotic proliferation of nodules smaller than 5 mm was not obvious, and its hardness was similar to that of the surrounding normal thyroid tissue [30]. In addition, in order to evaluate lesions tissue hardness, RTE requires enough normal tissue to conduct the contrast, therefore, nodules should not be too large. Some scholars have proposed that RTE should not be used to diagnose nodules of >30 mm [31]. In view of the above reports, the nodule size range selected for our study was 5–30 mm.

Overall, the diagnostic efficiency of the three TIRADS improved when they were combined with RTE scores, C-TIRADS increasing more its efficiency. Previously, only one study conducted this type of analysis with C-TIRADS. A total of 788 thyroid nodules were divided into $\leq$10 mm and >10 mm groups to explore the diagnostic value of C-TIRADS combined with elastography for nodules of different sizes. In the $\leq$10 mm group, elastography improved the AUC, sensitivity, and specificity. However, in the >10 mm group, changes in AUC, sensitivity, and specificity did not improve. Therefore, C-TIRADS combined with elastography can improve diagnostic efficiency, in nodules nodules ≤10 mm [32]. As for the combined diagnosis of K-TIRADS and elastography, the study conducted by Celletti *et al*. [33] in 2021 showed that RTE improved the AUC (0.847 vs. 0.769) and sensitivity (92.9% vs. 71.4%) and decreased its specificity (76.5% vs. 82.4%). Another study reported that after combining with elastography, K-TIRADS AUC (0.885 vs. 0.888) and specificity decreased (79.6% vs. 83.6%), and sensitivity increased (96.2% vs. 89.1%) [34]. These results show how beneficial is combining RTE and K-TIRADS. A study including 1525 nodules, showed that RTE improved the AUC, sensitivity, and specificity of ACR-TIRADS in four groups of nodules with different sizes [13]. In another study, elastography decreased the AUC (0.906 vs. 0.907) and specificity (83.6% vs. 88.4%) and improved sensitivity (96.2% vs. 86.5%) of ACR-TIRADS [34]. These results show how beneficial is combining RTE and K-TIRADS Wang *et al*. [14] in 2020 showed that the addition of RTE improved the sensitivity of ACR-TIRADS (93.6% vs. 87.6%), but decreased its AUC and specificity (0.825 vs. 0.866, 69.6% vs. 82.1%, respectively), so ACR-TIRADS combined with RTE did not improve its diagnostic efficiency.

TIRADS can recommend FNA to diagnose nodules, but many nodules that underwent FNA were pathologically confirmed to be benign. Therefore, TIRADS needs continuous improvement to reduce unnecessary biopsies. In this study, C-TIRADS, ACR-TIRADS, and K-TIRADS showed low unnecessary biopsy rates. C-TIRADS and ACR-TIRADS had the lowest unnecessary rates. After combining with RTE, the number of nodules requiring biopsy for C-TIRADS and K-TIRADS decreased. There are few related reports. Wang *et al*. [14], found that after combining with elastography, ACR-TIRADS unnecessary biopsy rate was reduced (40.5% vs. 48.5%).

This study has some limitations. First, this is a retrospective study and static images are not accurate enough to display some ultrasonographic features, such as margins. Second, all nodules in this study underwent surgical treatment, with rare benign nodules, and papillary carcinoma accounting for the vast majority of malignant nodules, but there are few other types of malignant nodules. Finally, this study is a single-center study without a multi-center comparison, and there is no inter-observer consistency analysis.

Conclusions

C-TIRADS, ACR-TIRADS, K-TIRADS, and RTE have a high diagnostic efficiency. Real-time tissue elastography can improve the diagnostic efficiency of the three TIRADS and reduce the unnecessary biopsy rate. Among them, C-TIRADS shows the highest efficiency.

Abbreviations

C-TIRADS, Chinese version of thyroid imaging reporting and data system; ACR-TIRAD, American College of Radiology-TIRADS; K-TIRADS, Korean-TIRADS; ROC, receiver operating characteristic; RTE, real-time tissue elastography; AUC, area under ROC curve; FNA, fine-needle aspiration biopsy; WFUMB, World Federation for Ultrasound in Medicine and Biology; EFSUMB, European Federation of Societies for Ultrasound in Medicine and Biology; ES, elasticity score.

Availability of Data and Materials

Data to support the findings of this study is available on reasonable request from the corresponding author.

Author Contributions

YM and MZ—designed the study; YM, XH, and MZ—prepared the manuscript; YM, XH, SK, and WX—collected and assembled the data; YM, MZ, WX, and WZ—participated in data analyses. All authors had read and submitted final approval of the manuscript.

Ethics Approval and Consent to Participate

This study has been approved by the Ethics Committee of Zibo Central Hospital (202203006).

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Conflict of Interest

The authors declare no conflict of interest.

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