A simplified version of TI-RADS exhibits comparable diagnostic performance in malignancy risk stratification of thyroid nodules

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Research Article

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Abstract

Evaluation of thyroid focal lesions using thyroid imaging reporting and data system (TIRADS) has been proceeding for a decade, but there is no consensus on any version of TIRADS. The purpose of this study was to validate a recently launched simplified Chinese version of TIRADS, with a compare to the American College of Radiology version of TIRADS. A total of 1306 patients with 1389 thyroid nodules were reviewed and assessed according the two TIRADSs, and the histopathological results were taken as golden standard. The results showed there were 973 benign nodules and 416 malignant nodules. The highest accuracies(AUCs)of C-TIRADS 4C and ACR-TIRADS 5 were taken as the optimized cut-off values for diagnosis. The sensitivity, specificity, PPV, NPV and AUC by C-TIRADS 4C and ACR-TIRADS 5 for thyroid nodule evaluation were 87.39%, 89.92%, 75.00%, 95.38% and 0.89, and 85.58%, 91.88%, 81.84%, 93.71% and 0.89, respectively, ($P > 0.05$ for all). We concluded that C-TIRADS and ACT-TIRADS have very good diagnostic performance in differentiating malignant from benign thyroid nodules by each optimized cut-off value, and the diagnostic performance of the fewer parameters based C-TIRADS 4C is comparable to the multiple parameters based ACR-TIRADS 5.

Introduction

Thyroid nodular lesions are common in adult population. The prevalence of thyroid nodules in adults is about 19–68% (Haugen et al.2016; Jiang et al.2016; Kitahara et al.2016; Morris et al.2016; Moon et al.2018), and that of malignant lesions is about 6.7–15% (Haugen et al.2016; Kitahara et al.2016; Morris et al.2016). Thyroid nodules comprise of benign, borderline and malignant lesions, and benign nodules are much more common than malignant nodules (Haugen et al.2016). Timely detection and accurate diagnosis of benign and malignant thyroid nodules are of significance for clinical management. However, malignant nodules before distal metastasis usually have no unique clinical manifestations and laboratory abnormalities, which makes it difficult to differentiate malignant nodule from benign nodule (Haugen et al.2016; Kwak et al.2011; Russ et al.2017; Shin et al.2016; Tessler et al.2017; Zhou et al.2020). High-resolution color Doppler ultrasound is the mostly used imaging modality for the evaluation of thyroid nodules and has some advantages, but the diagnostic performance is not satisfactory (Kwak et al.2011; Russ et al.2017; Shin et al.2016; Tessler et al.2017; Zhou et al.2020). In view of this disadvantage, clinical researchers have proposed a series of thyroid nodule risk stratification systems for thyroid nodules through research on the ultrasound features of thyroid nodules, in order to improve the diagnosis and treatment of thyroid nodules. Starting with the establishment of the Thyroid Imaging Reporting and Data System (TIRADS) in 2009 by Horvath et al, different versions of TI-RADS have been proposed (Horvath et al.2009). However, due to the similarities and discordance in terms and standards in the description and definitions of the ultrasound features of thyroid nodules adopted by different researchers when establishing the classification systems, and no system has been widely acknowledged and used so far (Fradin et al.2020; Grani et al.2019; Ha et al.2018, 2019; Horvath et al.2009; Kwak et al.2011; Russ et al.2017; Shin et al.2016; Tessler et al.2017; Xu et al.2019; Yoon et al.2019; Zhou et al.2020). There are some discordance in the number of evaluation parameters among different versions of TIRADS, such as ACR-TIRADS by the American College of Radiology, 23 parameters are used for scoring; and the recently launched Chinese version TIRADS (C-TIRADS) by The Superficial Organ and Vascular Ultrasound Group of the Society of Ultrasound in Medicine of Chinese Medical Association, 6 parameters are used for scoring (Zhou et al.2020). Multi-parameter scoring has the advantage of being systematic and comprehensive, but it is not convenient for application. If fewer parameters can work effectively, it will be better. Whether simplified fewer parameters can compromise or increase risk stratification level and diagnostic performance has not been investigated. The objective of this study was to compare the diagnostic performances of TIRADSs based on multiple and fewer parameters and validate the C-TIRADS.

Materials And Methods

Study population

Patients who had undergone thyroid ultrasound examination and core needle biopsy or surgery in the First Affiliated Hospital of Hainan Medical University from January 2015 to December 2020 were selected as the potential research subjects, and the relevant data were retrospectively analyzed. Inclusion criteria: Patients with eligible quality sonographic images of thyroid nodule and had undergone histopathological study. Exclusion criteria: The ultrasound images of thyroid nodule were of poor quality or the image number was not enough, which could not fully display the nodular features; and an indeterminate histopathology. A single conglomerate of nodules was counted as one nodule. If a patient with several thyroid nodules, the highly suspicious malignant nodules and one of representative benign nodules were enrolled. A total of 1306 patients with 1389 thyroid nodules were included, and 42 patients with 58 thyroid nodules were excluded. Histopathological results of thyroid nodules were used as reference standard to determine the benign and malignant nature of nodules. The histopathological diagnosis was made according to the diagnostic criteria of the World Health Organization (Cameselle-Teijeiro et al.2018). Thyroid ultrasound imaging had been performed before surgery in all patients with thyroid nodular lesions. The C-TIRADS and the ACR-TIRADS were identified by retrospective analysis of ultrasound images by a physician with 16 years of experience in thyroid ultrasound evaluation.

This study was approved by the Institutional Review Board of the First Affiliated Hospital of Hainan Medical University, and informed consent was waived due to the retrospective design.

Ultrasound examination

Multi-parameter ultrasound systems (Siemens Acuson S2000; Mindray DC 8; Mindray Resona 7, Aloka Prosound α-7, Aloka Prosound α-10; Phillips EPIQ5 and GE Logiq E9) were used for thyroid examination. During the examination, the ultrasound systems were adjusted to small parts mode (thyroid gland), and a linear array transducer with a frequency of 5–14 MHz was used. During the examination, the patient took a supine position with head retroversion to fully expose the neck. The thyroid was scanned by cross and longitudinal sections to detect any lesions. If a thyroid nodule was found, its location, shape, orientation(ratio of anterior diameter to transverse diameter), margin(capsule), boundary, size, architecture(composition) and internal echogenicity, posterior acoustic effect, vascularity, and relation to abut tissue were identified and scrutinized. Absence or presence of abnormal lymph node in the neck was noted, with attention to the presence of punctuate hyperechoic foci and calcification. Representative images were saved in Picture Archiving and Communications Systems (PACS).

Assessment of thyroid nodules with reference to C-TIRADS (Zhou et al.2020).

Assessing a thyroid and thyroid nodule with C-TIRADS involves a comprehensive evaluation of its composition(architecture), echogenicity, shape (orientation), margin, and echogenic foci. Score points are assigned to optimized sonographic feature, with higher values indicating greater degrees of suspicion. The total score point of a nodule is calculated for classification to assign its TIRADS category, comprising seven categories from no nodule to benign, and highly suspicious malignancy and histology confirmed malignant nodule. Nodule-free thyroid was categorized as TIRADS 1, nodule with − 1 score point was categorized as TIRADS 2, nodule with 0 score point was categorized as TIRADS 3, nodule with 1 score point was categorized as TIRADS 4A, nodule with 2 score points was categorized as TIRADS 4B, nodule with 3 or 4 score points was categorized as TIRADS 4C, nodule with 5 score point was categorized as TIRADS 5, nodule with histopathology confirmed malignancy was categorized as TIRADS 6;and entirely simple cystic nodule or spongy nodule was categorized as TIRADS 2. Sonographic feature for score point: Solid composition = + 1, markedly hypoechoic = + 1, taller than wide ($A/W \geq 1$) = + 1, ill-defined or irregular or lobulated or extrathyroidal extension = + 1, hyperechogenicity with comet-tail artifact = -1,punctate hyperechogenicity (suspicious calcification) = + 1; if there are several hyperechoic patterns in a nodule, only the highest scored is included, and the others are excluded.

Assessment of thyroid nodules with reference to ACR TI-RADS (2017) (Tessler et al.2017).

Assessing a nodule with ACR-TIRADS involves a comprehensive evaluation of its composition, echogenicity, shape (orientation), margin, and echogenic foci. Score points were assigned to each sonographic feature, with higher values indicating greater degrees of suspicious malignancy. The total score of a nodule was calculated for classification to assign its TIRADS category, comprising five categories from benign to highly suspicious malignancy. The total score point of 0 was categorized as TIRADS 1, 2 as TIRADS 2, 3 as TIRADS 3, 4–6 as TIRADS 4, and 7 points or more as TIRADS 5. Nodular composition (architecture) for score: Cystic = 0, spongy = 0, mixed solid-cystic with dominant cystic = 1, solid = 2, dominant solid or indeterminate = 2. Internal echogenicity for score: Anechoic = 0, isoechoic = 1, hyperechoic = 1, indeterminate = 1, hypoechoic = 2, markedly hypoechoic = 3. Shape (orientation) for score: 0 point for wider than tall ($A/W < 1$), and 3 points for taller than wide ($A/W \geq 1$). Margin for score point: Smooth = 0, ill-defined = 0, irregular = 2, lobulated = 2, extrathyroidal extension = 3. Echogenic foci for score point: None = 0, hyperechoic with comet-tail artifact = 0, macrocalcifications = 1, peripheral or rim hyperechoic = 2, punctate hyperechoic = 3. Figures 1–3 illustrate some sonographic features of thyroid nodules and scoring of TIRADS.

Statistical analysis

Quantitative data with normal distribution was expressed as mean and standard deviation (M ± SD), quantitative data do not show normal distribution and qualitative data were expressed as median (interquartile range, IQR) and percentile. The consistency between C-TIRADS and ACR-TIRADS was studied, and the malignant risk stratification levels corresponding to each TIRADS were evaluated. Paired samples t-test and independent samples T test were used to test quantitative data with normal distribution. Qualitative data were analyzed by nonparametric test or Chi-square test. The receiver operating characteristic (ROC) curve area under curve (AUC) was used to evaluate the diagnostic performance of the two TIRADS, and the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated. The highest accuracy was taken as the best threshold for diagnosis. All statistical analyses were performed using SPSS statistical software version 23 (IBM Corp., Armonk, NY, USA) and Medcalc statistical software version 15.2.2 (Medcalc software BVBA, Ostend, Belgium), and a $P < 0.05$ was considered significant difference.

Results

Of the 1306 patients with 1389 thyroid nodules, there were 973 benign nodules and 416 malignant nodules, and demographic and ultrasound features of the patients with thyroid nodules are summarized in Table 1. Papillary carcinomas accounted for 96.88% of malignant nodules, nodular goiter accounted for 93.32% of benign nodules, and details of the distribution of pathologies of thyroid nodules are listed in Table 2. The highest accuracies(AUCs)of C-TIRADS 4C and ACR-TIRADS 5 were taken as the optimized cut-off values (thresholds) for diagnosis. Taking optimized category of C-TIRADS 4C as cut-off, 312 nodules were confirmed true positive (malignant lesion), 104 nodules were confirmed false positive (benign lesion), 928 nodules were confirmed true negative (benign lesion), and 45 nodules were confirmed false negative (malignant lesion). Taking optimized category of ACR-TIRADS 5 as cut-off, 356 nodules were confirmed true positive (malignant lesion), 79 nodules were confirmed false positive (benign lesion), 894 nodules were confirmed true negative (benign lesion), and 60 nodules were confirmed false negative (malignant lesion). The sensitivity, specificity, PPV, NPV and AUC by C-TIRADS 4C and ACR-TIRADS 5 for thyroid nodule evaluation were 87.39%, 89.92%, 75.00%, 95.38% and 0.89, and 85.58%, 91.88%, 81.84%, 93.71% and 0.89, respectively, and there was no significant difference between them ($P > 0.05$ for all), as summarized in Table 3. There were 112 benign nodules and 193 malignant nodules with maximal diameter < 10mm; comparison of diagnostic performance between two TI-RADSs for nodules with different sizes showed that there was no significant difference between nodules with maximal diameter < 10mm and ≥ 10mm by the cut-off of C-TIRADS 4C and ACR-TIRADS 5 for the sensitivity, specificity, PPV, NPV ($P > 0.05$ for all), and the AUC of C-TIRADS 4C was significantly lower than that of ACR-TIRADS 5 for thyroid nodules with maximal diameter < 10mm($P = 0.0015$), and the sensitivity and specificity had no significant difference, as summarized in Table 4. The AUC of C-TIRADS 4C for the nodules with maximal diameter < 10mm was significantly lower than the AUC of C-TIRADS 4C for all size nodules ($P < 0.001$).

Table 1
Demographic and ultrasound features of the patients with thyroid nodules

Characteristics	**Benign nodules(n = 973)**	**Malignant nodules(n = 416)**	***P***
Age(year)			
Mean	46.09 ± 12.66	44.69 ± 12.59	0.059
Range	7–82	7–84	
Gender			
Male(n,%)	222(22.82)	102(24.52)	0.489
Female(n,%)	751(77.18)	314(75.48)	
Size(mm)			
Mean	23.02 ± 10.93	12.58 ± 8.57	< 0.001
Range	(2–65)	(2–67)	
< 10mm(n,%)	112(11.51)	193(46.39)	< 0.001
≥ 10mm(n,%)	861(88.49)	223(53.61)	
Number			
Single(n,%)	61 (6.27)	58(13.94)	< 0.001
Multiple(n,%)	912(93.73)	358(86.06)	
Composition			
Cystic/spongiform(n,%)	55(5.65)	0(0.00)	< 0.001
Mixed cystic and solid(n,%)	457(46.97)	12(2.88)	< 0.001
Solid(n,%)	461(47.38)	404(97.12)	< 0.001
Echogenicity			
Anechoic(n,%)	33(3.40)	0(0.00)	< 0.001
Iso/hyperechoic(n,%)	540(55.49)	41(9.86)	< 0.001

Characteristics	Benign nodules(n = 973)	Malignant nodules(n = 416)	*P*
Hypoechoic(n,%)	382(39.26)	306(73.56)	< 0.001
Marked hypoechoic(n,%)	18(1.85)	69(16.58)	< 0.001
Shape			
Wider-than-tall(n,%)	938(96.40)	233(56.01)	< 0.001
Taller-than-wide(n,%)	35(3.60)	183(43.99)	
Margin			
Smooth/ill-defined(n,%)	917(94.24)	158(37.98)	< 0.001
Lobulated/irregular(n,%)	54(5.55)	219(52.64)	< 0.001
Extrathyroid extension(n,%)	2(0.21)	39(9.38)	< 0.001
Echogenic foci			
None or large comet-tail artifacts(n,%)	809(81.47)	88(21.15)	< 0.001
Macrocalcifications(n,%)	73(7.35)	28(6.73)	0.653
Peripheral calcifications(n,%)	18(1.81)	7(1.68)	1.000
Punctate echogenic foci(n,%)	93(9.37)	293(70.44)	< 0.001

Table 2
Distribution of pathologies of thyroid nodules

Pathology of benign nodule	Number (%)	Pathology of malignant nodule	Number (%)
Nodular goiter	908(93.32)	Papillary carcinoma	403(96.88)
Follicular adenoma	35(3.60)	Medullary carcinoma	8(1.92)
Eosinophilic adenoma	11(1.13)	Follicular carcinoma	4(0.96)
Chronic lymphocytic thyroiditis	16(1.64)	Anaplastic carcinoma	1(0.24)
Toxic nodular goiter	1(0.10)		
Granulomatous thyroiditis	2(0.21)		
Total	973(100.00%)		416(100.00%)

Table 3

Diagnostic performances by two TI-RADSs by different cut-off categories

Cut-off category	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)	AUC
C-TIRADS 4B,4C and 5	71.75(67.71–75.54)	95.92(94.37–97.14)	91.59(88.49–94.07)	84.58(82.16–86.80)	0.84(0.82–0.86)
*C-TIRADS 4C and 5	87.39(83.50-90.66)	89.92(87.92–91.69)	75.00(70.55–79.09)	95.38(93.86–96.61)	0.89 (0.87–0.90)
C-TIRADS 5	90.32(74.25–97.9)	71.43 (68.94–73.8)	6.73 (4.52–9.58)	99.69(99.10-99.94)	0.81(0.79–0.83)
ACR-TIRADS 4 and 5	55.57(51.87-59.)	98.19(96.86-99.0)	97.12(95.02–98.50)	66.80(63.75–66.76)	0.77(0.75–0.79)
#ACR-TIRADS 5	85.58(81.83–88.81)	91.88(89.98–93.52)	81.84(77.89–85.35)	93.71(91.98–95.17)	0.89(0.78–0.90)
*#P value	0.7863	0.6375	0.1421	0.8795	1.000

C-TIRADS: The Superficial Organ and Vascular Ultrasound Group of the Society of Ultrasound in Medicine of Chinese Medical Association version of thyroid imaging, reporting and data system; ACR-TIRADS: American College of Radiology version of thyroid imaging, reporting and data system;PPV: Positive predictive value; NPV: Negative predictive value; AUC: Area under the ROC curve; Variables in paratheses are 95% confidential intervals.

Table 4
Comparison of diagnostic performance between two TI-RADSs for nodules with different sizes

Characteristics	Sensitivity(%)	Specificity(%)	PPV(%)	NPV(%)	AUC(%)
Nodular diameter < 10mm					
C-TIRADS	86.22(81.02–90.44)	62.79(53.84–71.14)	80.17(74.58-85.00)	72.32(63.07–80.36)	0.75(0.70–0.79)
ACR-TIRADS	84.46(78.56–89.26)	83.04(74.78–89.47)	89.56(84.18–93.60)	75.61(67.05–82.90)	0.84(0.79–0.88)
P value	0.9424	0.1653	0.4697	0.8417	0.0015
Nodular diameter ≥ 10mm					
C-TIRADS	90.76(85.62–94.53)	93.94(92.19–95.40)	75.23(69.01–80.76)	98.05(96.89–98.86)	0.92(0.91–0.94)
ACR-TIRADS	86.55(81.36–90.74)	93.03(91.12–94.64)	76.28(70.55–81.39)	96.39(94.89–97.55)	0.90(0.88–0.92)
P value	0.8857	0.8912	0.9442	0.8090	0.1573

C-TIRADS: The Superficial Organ and Vascular Ultrasound Group of the Society of Ultrasound in Medicine of Chinese Medical Association version of thyroid imaging, reporting and data system; ACR-TIRADS: American College of Radiology version of thyroid imaging, reporting and data system;PPV: Positive predictive value; NPV: Negative predictive value; 95%CI: 95% confidential interval.

Discussion

The treatment of focal thyroid nodules mainly depends on the benign and malignant pathology. If benign thyroid nodules do not cause compression symptoms and do not impair the cosmetic appearance, the usual management is follow-up. Surgical treatment has been a necessary approach for malignant nodules (Haugen et al.2016). Color Doppler ultrasound has high value in identifying thyroid nodules. However, due to the complex and diverse sonographic features of benign and malignant thyroid nodules, there is partial overlap between them, which makes it difficult to determine the pathology of thyroid nodules without typical features (Haugen et al.2016; Tessler et al.2017). Using scores of different sonographic features of thyroid nodule for risk stratification is an evaluation strategy proposed in recent decades. The results of this study showed that the recently launched simplified version C-TIRADS has high clinical significance for malignancy risk stratification of thyroid nodules, and the AUC with cut-off of C-TIRADS 4C is 0.89, which is equal to that of ACR-TIRADS 5 and higher than that 0.84 for C-TIRADS 4B, 4C and 5, and 0.81 for C-TIRADS 5. With C-TIRADS 4C as the diagnostic threshold, the sensitivity and specificity in the diagnosis of thyroid malignant nodules were 87.39% and 89.92%, respectively, which are similar to that of ACR-TIRADS 5. AUC of C-TIRADS 5 in our study is lower than the AUCs of C-TIRADS 5 and ACR-TIRADS 5 in the study by Zhou et al, and the AUC of our C-TIRADS 4C is higher than the AUC of ACR-TIRADS 5 in the study by Zhou et al (2020). AUC of ACR-TIRADS 5 in this study is 0.89, which is higher than those in the previous studies of accuracy of 0.52 and AUC of 0.835 and 0.864 (Hoang et al.2018; Magri et al.2020; Peng et al.2020).

There were 112 benign nodules and 193 malignant nodules with maximal diameter < 10mm in this study; the AUC of C-TIRADS 4C for the small size nodules was significantly lower than the average AUC of C-TIRADS 4C for all size nodules; the AUC of C-TIRADS 4C was significantly lower than that of ACR-TIRADS 5 for them, and the sensitivity and specificity had no significant difference, indicating that C-TIRADS does not exhibit significant diagnostic efficiency for thyroid nodules with maximal diameter < 10mm. The AUC of C-TIRADS 4C for thyroid nodules with maximal diameter ≥ 10mm was slightly higher than that of ACR-TIRADS 5, but there is no significant difference. The AUC of 0.90 of ACR-TIRADS 5 for thyroid nodules with maximal diameter ≥ 10mm is higher than the accuracy of 0.69 reported by Ha et al (2018).

Similar to ACR-TIRADS, C-TIRADS also evaluates thyroid nodules from five aspects: structural composition, internal echogenicity, shape, margin and boundary, and hyperechoic foci, but the C-TIRADS has more advantages. Firstly, a category for normal thyroid without nodule and a category for histopathology confirmed nodule have been added to C-TIRADS, enabling appropriateness and completeness for the thyroid evaluation. Secondly, the sonographic features for malignant risk stratification adopted by C-TIRADS are more rational, for these chosen features have been optimized and selected through a multiple logistic model with forward stepwise selection and logistic regression analysis, instead of assigning scores to every sonographic feature (Zhou et al.2020). Thirdly, both TIRADS have elaborated, defined and classified the sonographic features of thyroid nodules in detail, and scored according to the sonographic features, but the scoring methods and assigning methods are different (Tessler et al.2017; Zhou et al.2020). For example, the score of fine punctate calcification is 3 points in ACR-TIRADS and 1 point in C-TIRADS; the score of hyperechoic foci with comet tail artifact is 0 point in ACR-TIRADS, and − 1 point in C-TIRADS. The score of ACR-TIRADS involves 23 sonographic features, while C-TIRADS involves only 6 sonographic features, the latter is simplified and clearer. Fourthly, C-TIRADS can reduce radiologist's time for accumulative scoring, and has better clinical practicability. Simplified scoring parameters C-TIRADS can reduce or avoid inaccurate scoring deviation caused by the difference of the scorers' understanding of images, such as treating hypoechoic as markedly hypoechoic, and spongy nodules as cystic-solid mixed nodules. Punctate echogenic foci are easily confused with small comet-tail artifact, and the scoring difference between the two systems is great, which may cause bias and error (Tessler et al.2017; Zhou et al.2020a, 2020b). Fifthly, the risk stratification of C-TIRADS targets directly to the degree of malignancy, and it's convenient for understanding by other physicians.

The threshold interval of C-TIRADS for malignant risk range is appropriate, and the malignant risk of five categories is not less than 90%, and our study results of AUC of 0.89 of C-TIRADS 4C and AUC of 0.81 of C-TIRADS 5 showed high consistency and limited deviation (Zhou et al.2020). The main objective of ACR-TIRADS category was to determine recommendations for FNA and follow-up, with a low threshold of malignant risk range from the estimated at 2% or less for ACR-TIRADS 1 to the greater than 20% for ACR-TIRADS 5, but in this study, the AUC of 0.89 was high, which indicate that many thyroid nodules with ACR-

TIRADS 5 has much higher malignant risk, other than 20% or plus, as reported by other studies (Ha et al.2018; Hoang et al.2018; Magri et al.2020; Peng et al.2020; Zhou et al.2020).

In our study, the best threshold for ACR-TIRADS to diagnose thyroid malignant nodules is TIRADS 5, while the best threshold for C-TIRADS to diagnose thyroid malignant nodules is C-TIRADS 4C, other than C-TIRADS 5, and the assessment results of C-TIRADS are different from guidelines, indicating that the threshold for malignant risk of C-TIRADS can occur deviation or variation, and the reason may be that some malignant nodules do not present sufficient sonographic features in very small size, and these led to inappropriate scoring and lower diagnostic performance. Similar condition has also occurred in other study, e.g., Basha et al found that in their multicenter prospective study on validity of ACR-TIRADS based 948 thyroid nodules, the best cut-off value for predicting malignant thyroid nodules was > ACR-TIRADS 3, other than ACR-TIRADS 5 (Basha et al. 2018).

In this study, both C-TIRADS 4C and ACR-TIRADS 5 showed similar excellent specificity and NPV, indicating that they are better in differentiating malignant from benign thyroid nodules. This suggests that simplified scoring and categorization for thyroid nodule is benefit to patients and radiologists, and fine needle aspiration biopsy for lower malignant risk nodules may spare, for the thyroid cancer is indolent, it’s not so urgent to practice biopsy, and follow-up may be an alternative.

The C-TIRADS and ACR-TIRADS presented comparable diagnostic performance in this study, however, unlike ACR-TIRADS has been validated by many studies, the C-TIRADS is a relatively recently launched system, and further validation is required in future (Basha et al. 2018; Ha et al.2018; Hoang et al.2018; Magri et al.2020; Middleton et al.2019; Peng et al.2020; Zhou et al.2020).

This study has some limitations: (1) This study is a retrospective design, although standardized examination and standardized image acquisition are used in the previous ultrasound examination, static image storage may affect the evaluation of various ultrasonic features, especially the determine of very hypoechoic, nodular margin and tiny liquid around the solid composition, and real-time dynamic display can evaluate each ultrasonic feature more accurately. (2) The number of nodules included in this study is not large enough, and surgery and pathology are regarded as the "gold standard", instead of the combination of surgery and FNA cytology, which cannot fully include benign lesions, which may inevitably induce selection bias. (3) In this study, the malignant nodules are mainly papillary carcinoma (96.88%), while the benign nodules are nodular goiter (93.32%), and the pathological types are relatively narrow. Therefore, in the future, a large sample should be studied to evaluate the diagnostic efficiency of medullary carcinoma, follicular carcinoma and Anaplastic carcinoma.

Conclusions

C-TIRADS and ACT-TIRADS have very good diagnostic performance in differentiating malignant from benign thyroid nodules by each optimized cut-off value, and the diagnostic performance of the fewer parameters based C-TIRADS 4C is comparable to the multiple parameters based ACR-TIRADS 5. The AUC of C-TIRADS 4C for the thyroid nodules with maximal diameter < 10mm is significantly lower than the

AUC of C-TIRADS 4C for thyroid nodules of all size, and is significantly lower than that of ACR-TIRADS 5 for the thyroid nodules with maximal diameter < 10mm. The diagnostic efficiency of C-TIRADS 4C for thyroid nodule with maximal diameter < 10mm is poorer than that for larger size nodule.

Declarations

Conflict of Interest Statement

The authors declare they have no conflict of interests relating to this article.

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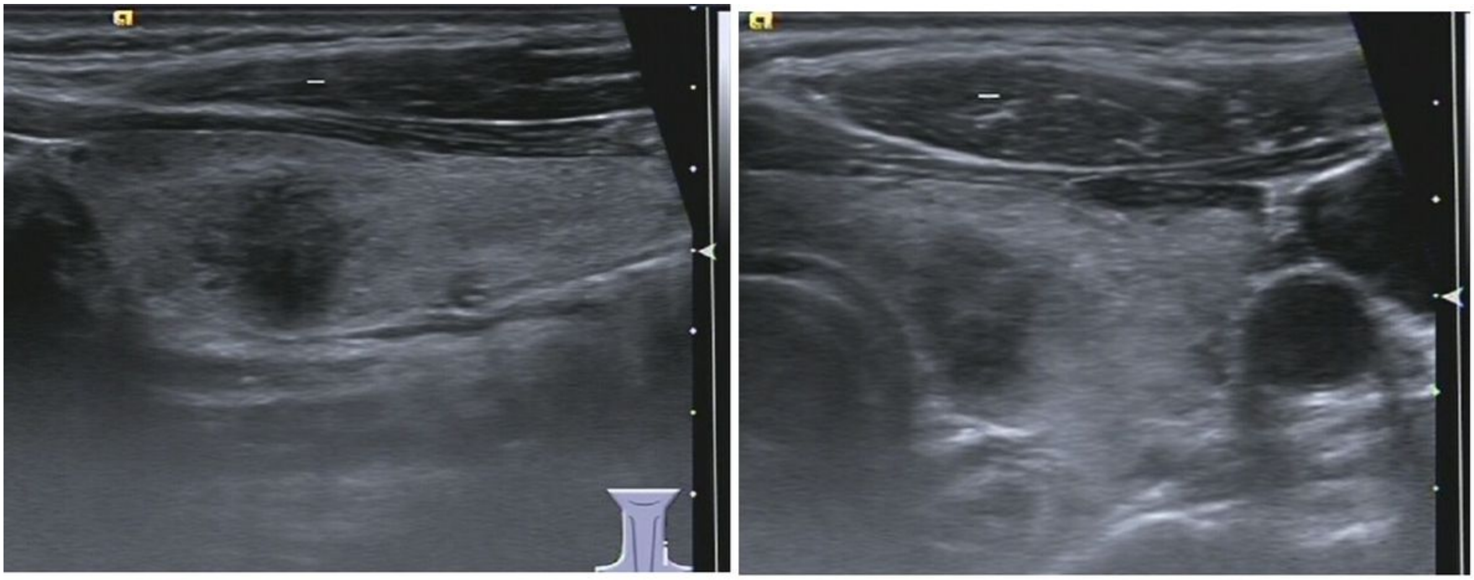
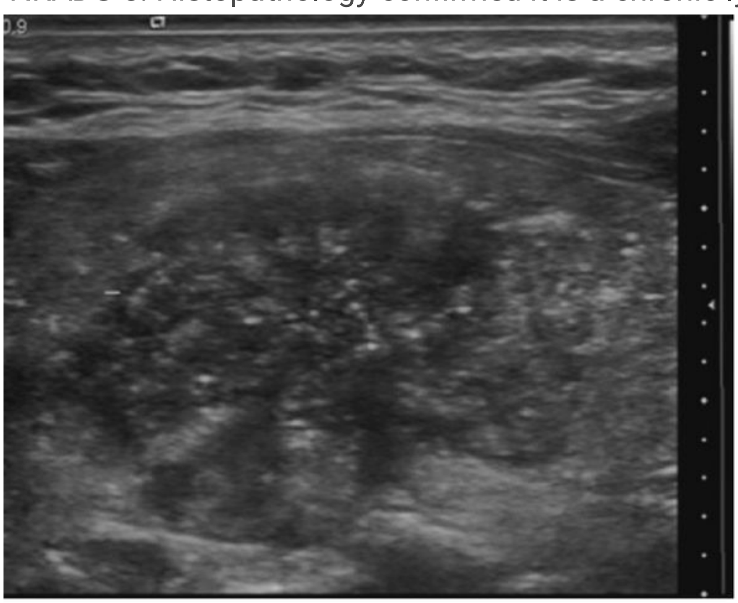
Figures



A B

Figure 1

Figure 1a Longitudinal scanning sonography of a 37-year-old woman with thyroid nodule. Figure 1b Cross scanning sonography of a 37-year-old woman with thyroid nodule. The nodule locates at left lobe of the thyroid, characterized by 9.8mm×9.2mm×9.4mm in size, solid composition, irregular shape, A>T orientation, hypoechoic, ill-defined margin, and absence of posterior acoustic effect. C-TIRADS 4C, ACR-TIRADS 5. Histopathology confirmed it is a chronic lymphocytic thyroiditis.



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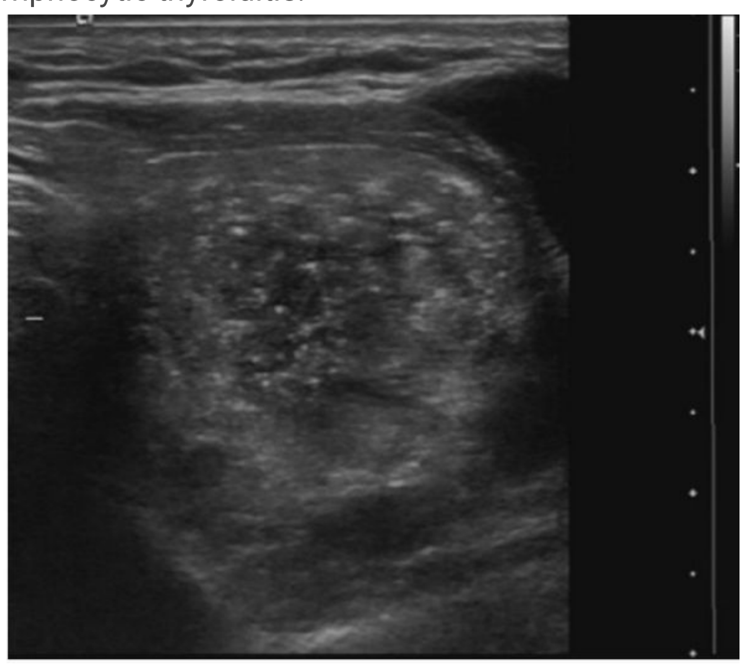
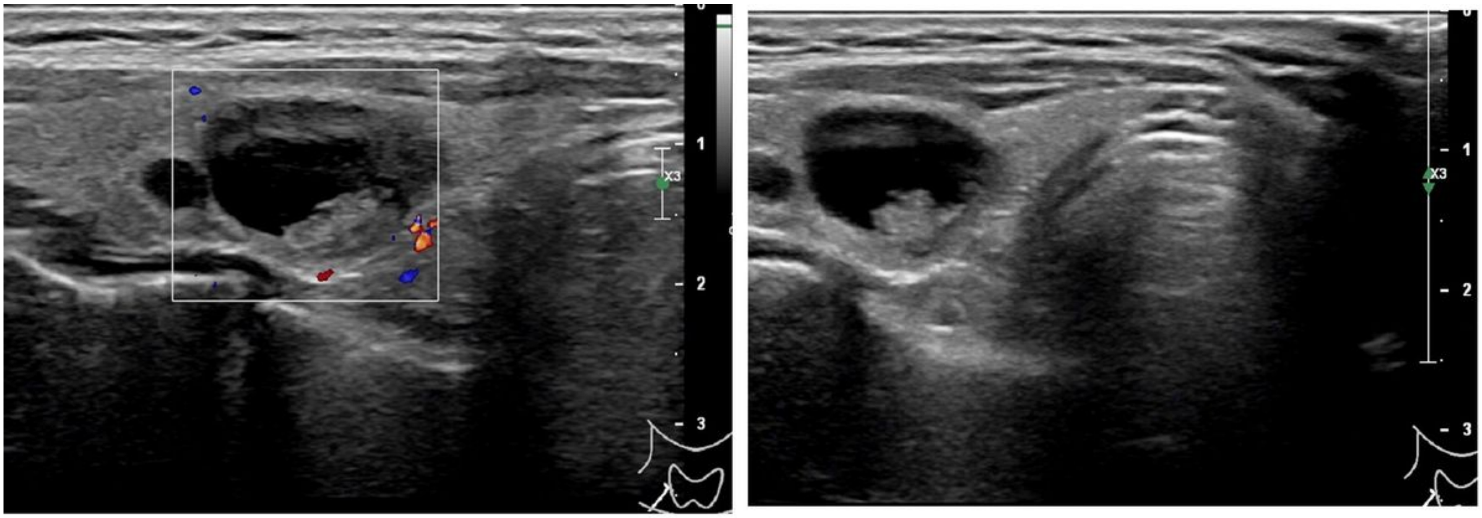


B

Figure 2

Figure 2a Longitudinal scanning sonography of a 45-year-old woman with thyroid nodule. Figure 2b Cross scanning sonography of a 45-year-old woman with thyroid nodule. The nodule locates at left lobe of the thyroid, characterized by 21.2mm×15mm×13mm in size, solid composition, irregular shape, A<T orientation, heterogeneous iso/hypoechoic, numerous tiny punctate hyperechoic foci, ill-defined margin, and absence of posterior acoustic effect. C-TIRADS 4C, ACR-TIRADS 5. Histopathology confirmed it is a papillary carcinoma.



A B

Figure 3

Figure 3a Longitudinal scanning sonography of a 53-year-old man with thyroid nodule. Figure 3b Cross scanning sonography of a 53-year-old man with thyroid nodule. The nodule locates at right lobe of the thyroid, characterized by 20mm×11.8mm×10.7mm in size, liquid and solid composition, irregular shape, A<T orientation, dominantly anechoic and heterogeneous iso/hypoechoic, well-defined and discernable margin, and presence of posterior acoustic enhancement effect. C-TIRADS 3, ACR-TIRADS 3. Histopathology confirmed it is a papillary carcinoma.