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Diagnostic value of American College of Radiology Thyroid Imaging Reporting and Data System combined with elastography in differentiating clinically atypical subacute thyroiditis from papillary thyroid carcinoma: a single retrospective research

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Abstract

Background Common ultrasound imaging is hard to distinguish thyroid nodules of clinically atypical subacute thyroiditis (CAST) with papillary thyroid carcinoma (PTC). The purpose of this study was to investigate the diagnostic value of real-time elastography combined with American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) in differentiating these two lesions.

Results Centripetal reduction echogenicity was only observed in the CAST nodules, with high specificity (100%) though low sensitivity (23.96%). Echogenic foci yielded good capability for differentiating PTC and CAST, with odds ratio (OR) of 36.572 and AUC of 0.788. Size and ES were independent factors to distinguish the two lesions with OR of 10.709 and 3.697, respectively. The combination of microcalcification, size < 10 mm and ES of 4 showed better AUC (0.885) than echogenic foci alone ($p < 0.001$). TI-RADS showed high sensitivity (91.23%) with specificity of 30.21% and AUC of 0.607 in predicting malignancy risk of PTC from CAST, while the AUC of ES and the combination of both methods were 0.508 and 0.585, respectively.

Conclusions Centripetal reduction echogenicity, echogenic foci, size and ES may assist in the differential diagnosis of CAST and PTC nodules. ACR TI-RADS is superior to ES and the combination of both methods for distinguishing these two lesions.

Keywords TI-RADS, Elasticity imaging technique, Ultrasonography, Thyroiditis, Subacute, Thyroid cancer, Papillary

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Background

Subacute thyroiditis (SAT) is a painful and self-limiting thyroid gland inflammation identified based on clinical and laboratory presentations [1]. In recent decades, clinically atypical SAT (CAST) has become increasingly of concern, of which patients are primarily presented with painless thyroid nodules found either by palpation or ultrasonography (US) accidentally [2]. In such cases, it is

difficult to fulfill the basic clinical diagnostic criterion of SAT, which might lead to misdiagnose.

Ultrasound is the primary imaging method for thyroid detection. The US of SAT patients can typically show focal or multifocal, ill-defined hypoechoic areas in one or both thyroid lobes with reduced vascularity [3, 4]. However, these ultrasonographic characteristics are easily confused with thyroid carcinoma, thus causing unnecessary imaging, fine-needle aspiration (FNA) and surgery, finally leading to increased anxiety and potential morbidity in patients [5, 6].

Some researchers have suggested using the Thyroid Imaging Reporting and Data System (TI-RADS) to stratify the risk of malignancy of thyroid nodules based on a constellation of suspicious US characteristics [7]. According to the 2017 TI-RADS of the American College of Radiology (ACR-TIRADS), thyroid nodules are classified from TR1 (benign) to TR5 (highly suspicious) based on total scores of five US features, while patients are recommended for FNA or US follow-up based on risk stratification and nodules' diameter [8]. Many studies proved that ACR-TIRADS could improve the accuracy of recommendations and reduce the rate of unnecessary FNA or biopsy for thyroid nodules effectively [9–12]. But one retrospective study spanning 5 years found that the correlation between ACR-TIRADS and Bethesda score was not significant, and both the number of patients and nodules per patient referred for FNAB continued to rise after using TI-RADS [13]. Moreover, the ACR TI-RADS committee admitted that certain features may warrant higher or lower point values to achieve optimal performance [14]. Therefore, whether TI-RADS merit is effective in all kinds of thyroid nodules and diseases should be further investigated.

As known, the stiffness of thyroid nodule is closely correlated with histopathology [15]. Malignancy nodules are harder than benign ones because of fibrous vascular interstitial components and sand-like calcified bodies. US elastography based on this principle has been shown to provide useful information for diagnosing malignant nodules and been more increasingly and widely used as a complementary tool of the common US in evaluating the properties of thyroid nodules [2, 16–20].

Recently, many scholars have investigated the diagnostic capability combined elastography with TI-RADS to diagnose thyroid nodules. However, the results were contradictory, some stated that combination of two methods performed better than one alone, while others did not [7, 21–25]. To our knowledge, relatively few studies have combined elastography with ACR-TIRADS to assess CAST nodules. Thus, the purpose of our study was to investigate the diagnostic performance combined elastography with ACR-TIRADS to distinguish CAST from

papillary thyroid carcinoma (PTC) nodules, thus contributing to a reduction in over-performed FNA or surgery in these patients, while performing more accurate recommendations for clinicians.

Methods

Study population

We searched the US database of our hospital from November 2017 to February 2021 and enrolled 157 CAST and 190 PTC patients. All CAST patients showed no clinical symptoms but had thyroid nodules that were found by palpation or US. All nodules were confirmed by cytopathology or histopathology. Patients with complete sonographic records and views of grayscale US (both cross and vertical views), color-Doppler US and elastography were recruited. The exclusion criteria were as following: patients under 18 years or with blur images of ultrasound. Finally, a total of 245 patients (89 CAST and 156 PTC patients) with 267 nodules participated in our study as shown in Fig. 1.

Ultrasound examinations

Both conventional and real-time elastography (RTE) sonography were performed using APLIO 500 TUS-A500 (Toshiba Medical Systems, Tokyo, Japan) with a 4–17 MHz linear array transducer. All examinations were performed by ultrasound doctors with at least 10 years

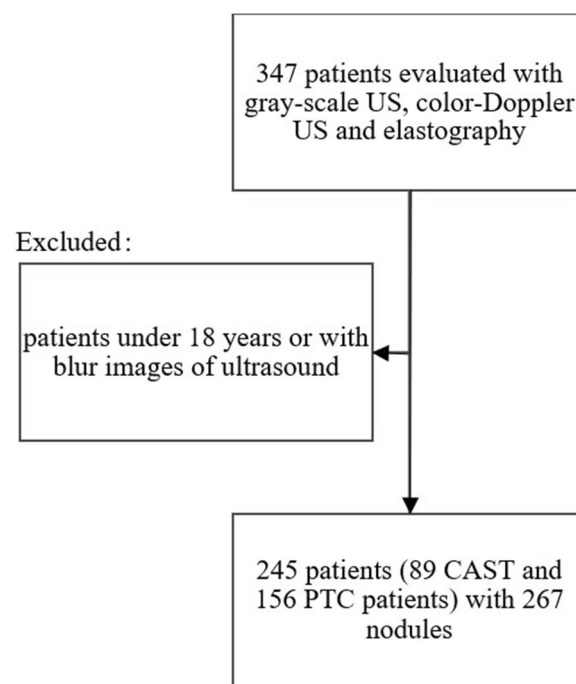


Fig. 1 Study population. CAST=clinically atypical subacute thyroiditis; PTC=papillary thyroid carcinoma; US=Ultrasonography

of experience in thyroid US. The US features in grayscale, color Doppler and RTE were evaluated. All selected thyroid nodules were assessed by the same doctors successively.

Image analysis

Two ultrasound doctors with more than 5 years of working experience were blinded to the pathological results and re-assessed the US features independently. Different opinions were discussed by them until a consensus was reached.

The grayscale US features of the nodules were assessed as follows: size (maximum diameter); composition (mixed cystic, solid or almost completely solid); echo (hyperechoic, isoechoic, hypoechoic or very hypoechoic); shape (taller than wide or wider than tall); margin (smooth, ill-defined, lobulated or irregular, extrathyroidal extension); echogenic foci (none, large comet-tail artifacts, macrocalcification, peripheral calcifications, microcalcification or calcifications mixed); centripetal reduction echogenicity (present or absent); posterior acoustic artifacts (none, enhancement, attenuation, enhancement or attenuation and enhancement mixed); nodule halo sign (present or absent); and echo of the gland (homogeneous or heterogeneous). Among these features, composition, echo, shape, margin and echogenic foci were graded using the 2017 ACR-TIRADS [8]. According to these five scoring characteristics, the thyroid nodules were classified from TR1 (benign) to TR5 (highly suspected to be malignant).

The color-Doppler US features were evaluated as follows: vascular distribution (none, internal, peripheral or

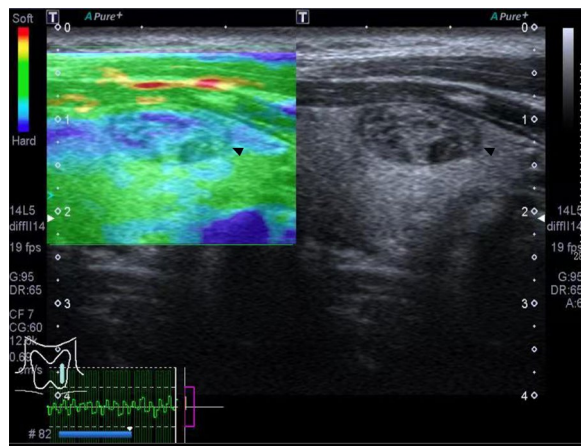


Fig. 2 Thyroid nodule showed ES of 2. A 37-year-old male came to hospital for a follow-up visit of thyroid. Ultrasound image showed thyroid nodule exhibited nearly entire green with little blue was scored as 2 (marked with a black triangle). ES=elasticity score

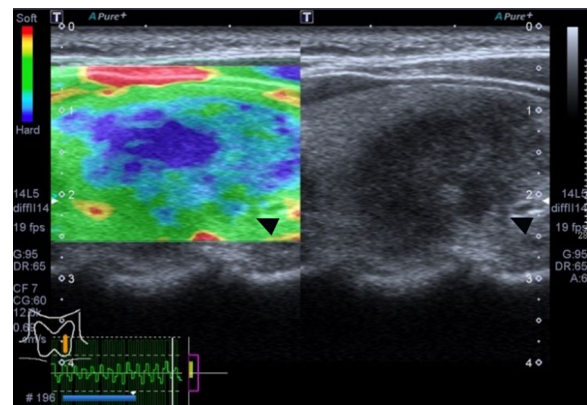


Fig. 3 Thyroid nodule showed ES of 3. A 50-years-old female came to hospital for a physical exam. Ultrasound image showed the nodule of subacute thyroiditis exhibited half in blue and half in green was scored as 3 (marked with a black triangle). ES=elasticity score

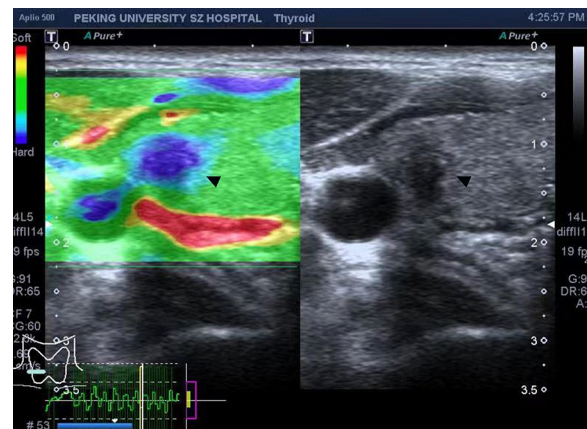


Fig. 4 Thyroid nodule showed ES of 4. A 39-year-old male came to hospital for preoperative examination. Ultrasound image showed the entire nodule of papillary thyroid carcinoma exhibited blue was consistent with ES of 4 (marked with a black triangle). ES=elasticity score

internal and peripheral mixed); flow grade (Adler) (0, 1, 2 or 3); and annular flow (present or absent).

In RTE US, we could see a color-coded on the screen: Less elastic tissues (soft) appear in red, elastic tissues of intermediate degrees were shown in green, and highly elastic tissues (hard) appear in blue. Then, we visually scored the nodule from 1 to 5 based on the predominant color pattern within and around it according to the 5-point Rago criteria as shown in Fig. 2, 3, 4 and 5 [20]. The TR4 nodule was upgraded when the elasticity score (ES) was 5, while the TR5 nodule was downgraded when the ES was less than 5.

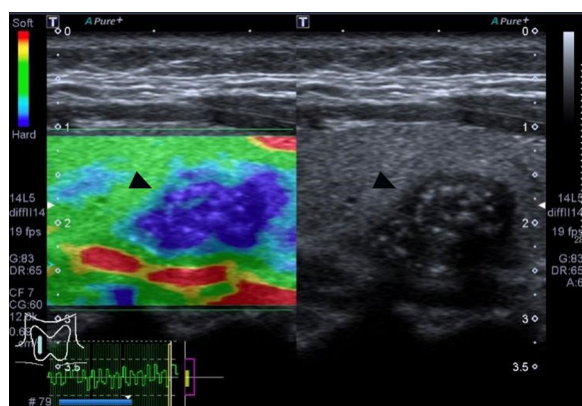


Fig. 5 Thyroid nodule showed ES of 5. A 43-year-old female came to hospital for a follow-up visit of thyroid. Ultrasound image showed the entire nodule of papillary thyroid carcinoma and its surrounding area were in blue was consistent with ES of 5 (marked with a black triangle). ES=elasticity score

Statistical analysis

For statistical descriptions, continuous variables were presented as the means with standard errors, and categorical variables are presented as *n*(%). For univariate analysis, the independent t test or Mann–Whitney U test was applied for continuous variables, while Fisher’s exact tests and chi-squared tests were conducted for categorical variables. Binary logistic regression was used, and the odds ratios (OR) were calculated to evaluate the valuable US features. The area under the curve (AUC) with 95% confidence intervals (CI), specificity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated according to the optimal cutoff point that maximized the Youden index for independent factors, and their combination in multiple regression analysis, TI-RADS grading, ES and modified TI-RADS was created. AUC was compared using the method described by DeLong et al [26], and receiver operating characteristic (ROC) curves were plotted. A *p* value less than 0.05 was considered statistically significant.

The degree of intra-observer and interobserver agreement between the two readers was measured using the *k* value, which was interpreted as follows: 0.80 < *k* < 1, perfect agreement; 0.60 < *k* < 0.80, substantial agreement; 0.40 < *k* < 0.60, moderate agreement; 0.20 < *k* < 0.40, fair agreement; 0 < *k* < 0.20, slight agreement; and *k* < 0, poor agreement. Statistical analysis was performed using SPSS software version 26 (IBM SPSS), GraphPad Prism 8 and MedCalc V20.104.

Results

The mean ages of the CAST and PTC patients were 42.08 ± 9.36 and 39.60 ± 11.39 years with 33.7% and 26.3% being male, respectively. There was no significant difference in age or sex between the CAST and PTC groups. Both inter- and intra-operator agreements of posterior acoustic artifacts, composition, echogenicity, shape, echogenic foci, nodule halo sign, TI-RADS grade, vascular distribution, vascular flow grade and echo of gland were 1.0. The inter-operator agreements for the ultrasonic features ranged from 0.896 to 0.948 (central reduction echogenicity: 0.908; margin: 0.976; annular flow: 0.896; TI-RADS scores: 0.991; ES: 0.948). And the intra-operator agreements for the ultrasonic features ranged from 0.952 to 0.986 (central reduction echogenicity: 0.952; margin: 0.953; annular flow: 0.945; TI-RADS: 0.986; ES: 0.965).

Sonographic characteristics

The sonographic characteristics of the nodules are summarized in Tables 1, 2 and 3. The nodule sizes, centripetal reduction echogenicity, echo of the gland, posterior acoustic artifacts, nodule halo sign, ES, margins and echogenic foci between the CAST and PTC groups showed significant differences (*p* < 0.05). The TI-RADS score, grading and modified TI-RADS grading of the CAST and PTC nodules also reached significant differences (*p* < 0.001). However, no significant differences were detected in composition, echogenicity, shape or all the color-Doppler US features between the two groups.

Table 1 Sonographic characteristics of CAST and PTC groups

Characteristic	CAST(n=96)	PTC(n=171)	<i>p</i> Value
Size(mm)	15.32 ± 8.39	12 ± 6.87	<0.001*
Centripetal reduction echogenicity			<0.001*
Present	23(23.96%)	0	
Absent	73(76.04%)	171(100%)	
Echo of gland			0.03*
Homogeneous	78(81.25%)	118(69.01%)	
Heterogeneous	18(18.75%)	53(30.99%)	

Table 1 (continued)

Characteristic	CAST(n= 96)	PTC(n= 171)	p Value
Posterior acoustic artifacts			< 0.001*
Absent	94(97.92%)	114(66.67%)	
Enhancement	1(1.04%)	15(8.77%)	
Attenuation	1(1.04%)	36(21.05%)	
Enhancement and attenuation mixed	0	6(3.51%)	
Nodule halo sign			< 0.001*
Present	6(6.25%)	46(26.90%)	
Absent	90(93.75%)	125(73.10%)	
Vascular distribution			0.07
None	15(15.63%)	25(14.62%)	
Internal	11(11.46%)	18(10.53%)	
Peripheral	27(28.13%)	27(15.79%)	
Internal and peripheral mixed	43(44.79%)	101(59.06%)	
Flow grade (Adler)			0.109
0	43(44.79%)	51(29.82%)	
1	28(29.17%)	64(37.43%)	
2	13(13.54%)	28(16.37%)	
3	12(12.50%)	28(16.37%)	
Annular flow			0.29
Present	5(5.21%)	4(2.34%)	
Absent	91(94.79%)	167(97.66%)	
ES			< 0.001*
2	7(7.29%)	1(0.58%)	
3	30(31.25%)	36(21.05%)	
4	27(28.13%)	104(60.82%)	
5	32(33.33%)	30(17.54%)	
Composition			0.555
Mixed cystic and solid	0	3(1.75%)	
Solid or almost completely solid	96(100%)	168(98.25%)	
Echogenicity			0.08
Hyperechoic or isoechoic	4(4.2%)	3(1.75%)	
Hypoechoic	92(95.8%)	162(94.74%)	
Very hypoechoic	0	6(3.51%)	
Shape			0.431
Wider than tall	33(34.4%)	68(39.77%)	
Taller than wide	63(65.6%)	103(60.23%)	
Margins			0.005*
Smooth or ill-defined	26(27.1%)	43(25.15%)	
Lobulated or irregular	70(72.9%)	111(64.91%)	
extrathyroidal extension	0	17(9.94%)	
Echogenic foci			< 0.001*
None or large comet-tail artifacts	84(87.5%)	47(27.49%)	
Macrocalcifications	5(5.21%)	12(7.02%)	
Peripheral calcifications	0	1(0.58%)	
Punctate echogenic foci	7(7.29%)	97(56.73%)	
Macrocalcifications and punctate echogenic foci	0	12(7.02%)	
Peripheral calcifications and punctate echogenic foci	0	2(1.17%)	

CAST = clinically atypical subacute thyroiditis; PTC = papillary thyroid carcinoma; ES = elastography score; $p < 0.05$ is defined as significant difference

Table 2 TI-RADS scores of CAST and PTC groups

TI-RADS	CAST(n=96)	PTC(n=171)	p Value
Score			< 0.001*
4	3(3.13%)	5(2.92%)	
5	0	3(1.75%)	
6	26(27.08%)	7(4.09%)	
7	20(20.83%)	23(13.45%)	
8	3(3.13%)	8(4.68%)	
9	39(40.63%)	42(24.56%)	
10	4(4.17%)	29(16.96%)	
11	0	4(2.34%)	
12	1(1.04%)	38(22.22%)	
13	0	9(5.26%)	
14	0	3(1.75%)	

CAST = clinically atypical subacute thyroiditis; PTC = papillary thyroid carcinoma; TI-RADS = Thyroid Imaging Reporting and Data System; *p value < 0.05 is defined as significant difference

Binary logistic regression analysis

As shown in Table 4, it was easy to see that only echogenic foci, size and ES had a statistical relation for predicting malignant nodules. Their OR were 36.572 (echogenic foci over score 3), 10.709 (size ≤ 10 mm) and 3.657 (ES of 4), respectively, with p values all less than 0.007.

Diagnostic value

The diagnostic value of echogenic foci, ES, size and their combination, centripetal reduction echogenicity, TI-RADS grade and modified TI-RADS grade for differentiating PTC and CAST were evaluated (Table 5, Additional file 1: Table S1). The combination of the three independent factors had larger AUC than echogenic foci alone (0.885 vs 0.788, p < 0.001), followed by centripetal reduction echogenicity, TI-RADS grade and modified TI-RADS (0.620, 0.607 and 0.585, respectively), while size and ES only showed AUCs of 0.395 and 0.508. The ROC curves of these features are plotted in Fig. 6a,6b.

Centripetal reduction echogenicity had 100% specificity and PPV to distinguish CAST from PTC with NPV of 70.08% and accuracy of 72.66%, though its sensitivity was 23.96%. TI-RADS grade showed a sensitivity of 91.23%

Table 4 Binary logistic regression analysis of the independent factors for predicting PTC

Characteristic	p Value	OR	95% CI
Size (referenced > 20 mm)	< 0.001*	–	–
≤ 10 mm	< 0.001*	10.709	3.371–34.020
10–20 mm	0.038	–	–
Echogenic foci	< 0.001*	36.572	14.018–95.418
ES (referenced score 5)	< 0.001*	–	–
3	0.337	–	–
4	0.001*	3.657	1.662–8.050

ES = elastography score; OR = odds ratio; CI = confidence intervals; *p < 0.05 is defined as a significant difference

but low specificity of 30.21% for diagnosing PTC. Echogenic foci had high specificity (92.71%), PPV (94.07) and accuracy (74.91%). The combination of echogenic foci, ES and size also showed a relatively high specificity (87.50%), PPV (91.72%) and accuracy (82.27%) with a sensitivity of 77.78%. ES and modified TI-RADS grade showed the same sensitivity, specificity, PPV, NPV and accuracy.

Discussion

Ultrasound is the main imaging way to detect thyroid. Typical ultrasonic characteristics of SAT show focal or multifocal, ill-defined hypoechoic areas in one or both thyroid lobes with reduced vascularity [3, 4]. However, such ultrasonographic features make it easy to overestimate the malignant risk of CAST patients and be confounded with thyroid carcinoma. Therefore, improving diagnostic performance of US in CAST patients is quite important.

To investigate discrepancy of ultrasound characteristic between nodules of CAST and PTC, we compared some grayscale US and color-Doppler US features, ACR-TIRADS, ES and combination of ACR-TIRADS and ES grading between these two diseases.

Unfortunately, our results showed that combining ES and ACR-TIRADS could not improve the diagnosis efficiency of PTC and CAST, which was not exactly the same but was similar to the previous study. Wang et al. found that though RTE increased the sensitivity of ACR-TIRADS (93.6% vs. 87.6%), but decreased its AUC and

Table 3 TI-RADS and modified TI-RADS grades of CAST and PTC groups

	TI-RADS			Modified TI-RADS		
	CAST (n=96)	PTC (n=171)	p Value	CAST (n=96)	PTC (n=171)	p Value
4	29 (30.21%)	15 (8.77%)	< 0.001*	37 (38.54%)	37 (21.64%)	< 0.001*
5	67 (69.79%)	156 (91.23%)		59 (61.46%)	134 (78.36%)	

TI-RADS = Thyroid Imaging Reporting and Data System; *p < 0.05 is defined as significant difference

Table 5 Comparison of AUC between different ultrasound characteristics for differentiating PTC and CAST nodules

P value	Echogenic foci	Size	ES	Model	TI-RADS	Modified TI-RADS
Echogenic foci	–	–	–	–	–	–
Size	<0.001*	–	–	–	–	–
ES	<0.001*	0.051	–	–	–	–
Model	<0.001*	<0.001*	<0.001*	–	–	–
TI-RADS	<0.001*	0.959	0.026*	<0.001*	–	–
Modified TI-RADS	<0.001*	0.651	<0.001*	<0.001*	0.560	–
Centripetal reduction echogenicity	<0.001*	0.709	0.010*	<0.001*	0.696	0.336

AUC = area under the curve; PTC = papillary thyroid carcinoma; CAST = clinically atypical subacute thyroiditis; ES = elastography score; TI-RADS = Thyroid Imaging Reporting and Data System; Model = combination of echogenic foci, size and ES. * $p < 0.05$ is defined as significant difference

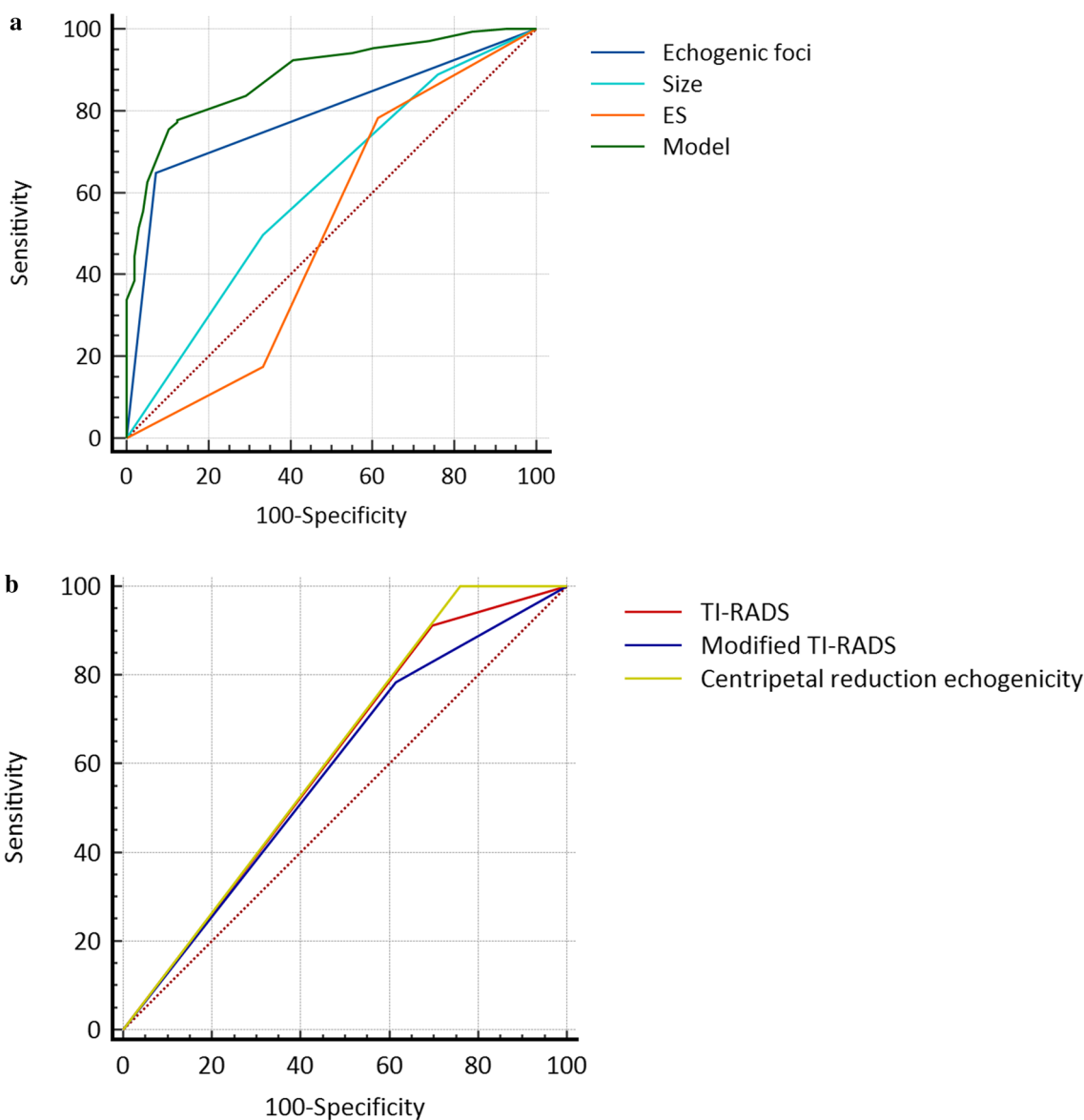


Fig. 6 **a.** ROC curves of echogenic foci, size, ES and model (combination of echogenic foci, size and ES). **b.** Roc curves of TI-RADS, modified TI-RADS and centripetal reduction echogenicity. ES=elasticity score; ROC=Receiver operating characteristic. ROC=Receiver operating characteristic; TI-RADS=Thyroid Imaging Reporting and Data System

specificity (0.825 vs. 0.866 and 69.6% vs. 82.1%, respectively), so could not improve its diagnostic efficiency [27]. But there were several studies showed that combining RTE and ACR-TIRADS is beneficial. Ma et al. found that RTE increased the AUC and sensitivity of ACR-TIRADS ($p > 0.05$ and $p < 0.001$, respectively), in spite of decreasing specificity ($p < 0.001$) [28]. A study containing 1525 nodules showed that RTE could improve the sensitivity and specificity of ACR-TIRADS to differentiate benign and malignant nodules in different sizes with ROC all over 0.70 [22]. However, it was worth noting that none of them are comparing RTE and ACR-TIRADS in CAST and PTC nodules like ours. Various component and pathology types of nodules may be the key to cause discrepancies among different studies. The diagnosis efficiency combined RTE with ACR-TIRADS in CAST patients requires more research and prospective study.

Fortunately, we found some valuable indicators. We found that six of grayscale US features had been showed significant differences even if only two of them were independent factors to differentiate CAST and PTC nodules. Although centripetal reduction echogenicity showed no statistical significance in multiple logistic regression analysis, it was only seen in CAST. Our study showed that this sign could reach 100% specificity and PPV with a relatively high accuracy of 72.66%, though with a low 23.96% sensitivity, consisting with previous research [29]. This feature might correlate with the histological progression of SAT [29]. On the one hand, from early to late stage, the histological progress starts with colloid extravasation and microabscesses induced by destruction of follicular epithelial cells and the colonization of follicles mainly caused by neutrophils, gradually turns to the assembly of histiocytes, lymphocytes and multinucleated giant cells engulfing colloid, and finally increase amounts of interfollicular fibrosis [30]. One the other hand, sonographic representation of SAT often begins with marked hypoechoic, turns to echo elevation and reduction of the lesion and eventually recovers with isoechoic US founds, which matches its pathologic features [29]. Centripetal reduction echogenicity might be a manifestation of this gradual recovery process.

Most microcalcifications in thyroid nodule refer to psammoma bodies, which represent the active biological process of tumor cells, and are more common in PTC than other type of thyroid cancer [31, 32]. Therefore, we were not surprised to find that microcalcification showed high value for predicting PTC, with an OR of 36.572 (95% CI 14.018–95.418). This result was consistent with Zhang et al [2]. They observed that microcalcification was uncommon in CAST and showed an OR of 35.864 (95% CI 3.909–329.002, $p = 0.002$) to distinguish PTC from CAST. Moreover, we observed that punctate

echogenic foci had a high specificity and PPV (92.71% and 94.07%, respectively) with a relatively low sensitivity and NPV (64.91% and 59.73%, respectively) to predict PTC. And these results showed some overlap and contradiction with previous literature. In Wang et al. and Nabahati et al. researches, microcalcification had similar high specificity (96.77% and 95.6%, respectively), but a much low sensitivity (24.3% and 18.2%, respectively) to predict PTC [33, 34]. But compared with ours, the presence of PTC nodules was low in the cited previous studies, thus may explain why our results were different.

In addition, the lesions that were ≤ 10 mm showed a relatively high malignancy risk of PTC compared with those greater than 10 mm (OR: 10.709, 95% CI 3.371–34.020). This might be related to the widespread use of US in thyroid examination, thus increase the detection rate for papillary thyroid microcarcinoma (PTMC), of which the largest dimension is 10 mm or less [35]. However, this sign showed low sensitivity and specificity with an AUC of 0.395. Similarly, ES of 4 was valuable to differentiate these two lesions with an OR of 3.657 (95% CI 1.662–8.050) but with low AUC of 0.508. Some researchers have pointed out that ES performs well in predicting thyroid carcinoma [22, 36]. However, most benign nodules in these studies showed ES of 1 or 2 and did not enroll SAT nodules, whereas most malignant nodules showed ES of 3 or 4, which was contrary to our study. We found that 92.71% of CAST showed ES of more than 3 points, which was similar to the previous study [37]. It was worth noting that ES of 5 was even harder to differentiate these two diseases than ES of 4. This was probably because that the thyroid stiffness of SAT patients was variable, of which could increase significantly in the early phase and gradually return to normal in the recovery phase [38]. Therefore, ES of RTE could not provide conclusive information to distinguish CAST and PTC nodules due to variable elastography of CAST nodules.

Although size or ES alone showed unsatisfactory diagnostic value, the model combining echogenic foci, size and ES even showed greater performance than echogenic foci alone in predicting malignant nodules (AUC: 0.885 vs. 0.788). We should remain on high alert for nodules that are less than 10 mm with microcalcification and ES of 4 in the daily work.

Furthermore, our study exhibited that TR5 showed high sensitivity (91.23%) and low specificity and AUC (30.21% and 0.607) to distinguish PTC and CAST, indicating that ACR-TRADS had both high performance and misdiagnosis rates to differentiate these two diseases. In fact, previous studies have proven that SAT nodules can present ultrasound features like taller-than-wide shape or microcalcification that mimic malignant nodules [39, 40]. More than half of the CAST

nodules (69.79%) in our showed a lobulated or irregular margin and taller-than-wide shape, of which awarded more points and were divided into TR5, thus overestimating their malignancy risk.

There were some limitations in our study. First, this was a retrospective study, and some patients with both CAST and PTC might not have been recruited due to the absence of FNA or surgery results. Thus, an inevitable selection bias may have existed. Second, this was a single-center study, and the sample size of CAST was still small. Therefore, our results need to be verified with multicenter studies and large sample sizes.

Conclusions

In this study, we found that ACR-TIRADS classification was superior to ES of RTE and their combination in differentiating CAST and PTC nodules. It is vital for physicians to recognize that the ACR-TIRADS are both sensitive but not specific to distinguish these two lesions. Centripetal reduction echogenicity, echogenic foci, size and ES of US features are useful to some extent. Importantly, we should pay closer attention to nodules less than 10 mm with microcalcification and ES of 4.

Abbreviations

ACR-TIRADS	American College of Radiology Thyroid Imaging Reporting and Data System
AUC	Area under the curve
CAST	Clinically atypical subacute thyroiditis
CI	Confidence intervals
ES	Elasticity score
FNA	Fine needle aspiration
NPV	Negative predictive value
OR	Odds ratios
PTC	Papillary thyroid carcinoma
PPV	Positive predictive value
PTMC	Papillary thyroid microcarcinoma
ROC	Receiver operating characteristic
RTE	Real-time elastography
SAT	Subacute thyroiditis
TI-RADS	Thyroid Imaging Reporting and Data System
US	Ultrasonography

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s43055-023-01159-x>.

Additional file 1. Table S1: Diagnostic value of the ultrasound characteristics for distinguishing PTC from CAST

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Author contributions

All authors contributed to the study conception and design. Chen XX, Hu ZM and Sun DS conceived and designed the study. Chen XX, Hu ZM and Luo HY collected the clinical and image data. Chen XX and Luo HY analyzed the image data and performed the statistical analysis. Chen XX, Luo HY and Zhao CY wrote the manuscript. Liao MY provided suggestion for data collecting. All authors read and approved the final manuscript.

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Availability of data and material

Not applicable.

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the ethics committee of Perking University Shenzhen Hospital (No.2022-128). And the Perking University Shenzhen Hospital Research Ethics Committee has confirmed that the informed consent was waived.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

- Ray I, D'Souza B, Sarker P et al (2022) Management of subacute thyroiditis: a systematic review of current treatment protocols. *Int J Gen Med* 15:6425–6439
- Zhang Q, Liao L, Peng Q et al (2021) Value of contrast-enhanced ultrasound in differentiating clinically atypical subacute thyroiditis from papillary thyroid carcinomas. *Ultrasound Med Biol* 47:3384–3392
- Lee MYW, Lam WWC, Wong WY (2016) Subacute thyroiditis-an often overlooked sonographic diagnosis. *J Ultrasound Med J* 35:1095–1100
- Park HK, Kim DW, Lee YJ et al (2015) Suspicious sonographic and cytological findings in patients with subacute thyroiditis: two case reports. *Diagn Cytopathol J* 43:399–402
- Hoang JK, Langer JE, Middleton WD et al (2015) Managing incidental thyroid nodules detected on imaging: white paper of the ACR Incidental Thyroid Findings Committee. *J Am Coll Radiol J* 12:143–150
- Zeng W, Tan S, King TFJ (2022) Subacute thyroiditis presenting as a painful suspicious thyroid nodule. *Endocrinol Diabetes Metab Case Rep J*. <https://doi.org/10.1530/EDM-21-0135>
- Schenke S, Zimny M (2018) Combination of sonoelastography and TIRADS for the Diagnostic Assessment of Thyroid Nodules. *Ultrasound Med Biol J* 44:575–583
- Tesslern FN, Middleton WD, Grant EG et al (2017) ACR Thyroid Imaging, Reporting and Data System (TI-RADS): white paper of the ACR TI-RADS committee. *J Am Coll Radiol J* 14:587–595
- Lee YB, Oh YL, Shin JH et al (2021) Comparison of four ultrasonography-based risk stratification systems in thyroid nodules with nondiagnostic/unsatisfactory cytology: a real-world study. *Cancers Basel J* 13:1948
- Hoang JK, Middleton WD, Farjat AE et al (2018) Reduction in thyroid nodule biopsies and improved accuracy with American College of Radiology Thyroid Imaging Reporting and Data System. *Radiol J* 287:185–193
- Kim PH, Suh CH, Baek JH et al (2021) Unnecessary thyroid nodule biopsy rates under four ultrasound risk stratification systems: a systematic review and meta-analysis. *Eur Radiol J* 31:2877–2885
- Grani G, Lamartina L, Ascoli V et al (2019) Reducing the number of unnecessary thyroid biopsies while improving diagnostic accuracy: toward the "Right" TIRADS. *J Clin Endocrinol Metab J* 104:95–102
- Hawkins SP, Jamieson SG, Coomarasamy CN et al (2021) The global epidemic of thyroid cancer overdiagnosis illustrated using 18 months of consecutive nodule biopsy correlating clinical priority, ACR-TIRADS and Bethesda scoring. *J Med Imaging Radiat Oncol J* 65:309–316

14. Wildman-Tobriner B, Buda M, Hoang JK et al (2019) Using artificial intelligence to revise ACR TI-RADS risk stratification of thyroid nodules: diagnostic accuracy and utility. *Radiol J* 292:112–119
15. Bhatia KS, Tong CS, Cho CC et al (2012) Shear wave elastography of thyroid nodules in routine clinical practice: preliminary observations and utility for detecting malignancy. *Eur Radiol J* 22:2397–2406
16. Moraes PHM, Takahashi MS, Vanderlei FAB et al (2021) Multiparametric ultrasound evaluation of the thyroid: elastography as a key tool in the risk prediction of undetermined nodules (Bethesda III and IV)-histopathological correlation. *Ultrasound Med Biol J* 47:1219–1226
17. Gorgulu O, Gorgulu FF, Koc AS (2021) Can the unnecessary operations for suspected thyroid nodules be avoided by the combined use of the strain ratio and elastography score? *Braz J Otorhinolaryngol J* 87:338–345
18. Okasha HH, Mansor M, Sheriba N et al (2021) Role of elastography strain ratio and TIRADS score in predicting malignant thyroid nodule. *Arch Endocrinol Metab J* 64:735–742
19. Zhang YX, Xue JP, Li HZ et al (2021) Clinical value of shear wave elastography color scores in classifying thyroid nodules. *Int J Gen Med J* 14:8007–8018
20. Zhao CK, Xu HX (2019) Ultrasound elastography of the thyroid: principles and current status. *Ultrasonogr J* 38:106–124
21. Petersen M, Schenke SA, Firla J et al (2022) Shear wave elastography and Thyroid Imaging Reporting and Data System (TIRADS) for the risk stratification of thyroid nodules-results of a prospective study. *Diagn Basel J* 12:109
22. Pei SF, Zhang B, Cong SZ et al (2020) Ultrasound real-time tissue elastography improves the diagnostic performance of the ACR thyroid imaging reporting and data system in differentiating malignant from benign thyroid nodules: a summary of 1525 thyroid nodules. *Int J Endocrinol J* 2020:1749351
23. Jie X, Xiao LC, Lei S et al (2016) The diagnostic value of combination of TI-RADS and ultrasound elastography in the differentiation of benign and malignant thyroid nodules. *Clin Imaging J* 40:913–916
24. Yang JR, Song Y, Xue SS et al (2020) Suggested amendment of TI-RADS classification of thyroid nodules by shear wave elastography. *Acta Radiol J* 61:1026–1033
25. Yang BR, Kim EK, Moon HJ et al (2018) Qualitative and semiquantitative elastography for the diagnosis of intermediate suspicious thyroid nodules based on the 2015 American Thyroid Association Guidelines. *J Ultrasound Med J* 37:1007–1014
26. DeLong ER, DeLong DM, Clarke-Pearson DL (1998) Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biom J* 44:837–845
27. Wang HX, Lu F, Xu XH et al (2020) Diagnostic performance evaluation of practice guidelines, elastography and their combined results for thyroid nodules: a multicenter study. *Ultrasound Med Biol J* 46:1916–1927
28. Ma Y, Huo X, Kong S et al (2023) A review about C-TIRADS, ACR-TIRADS, and K-TIRADS combined with real-time tissue elastography to diagnose thyroid nodules. *Discov Med J* 35:1–10
29. Pan FS, Wang W, Wang Y et al (2015) Sonographic features of thyroid nodules that may help distinguish clinically atypical subacute thyroiditis from thyroid malignancy. *J Ultrasound Med J* 34:689–696
30. Prajapati S, Hernandez-Prera JC (2019) Putting all the pieces together: clinical, macroscopic and microscopic characteristics of subacute thyroiditis. *Head Neck Pathol J* 13:231–234
31. Kwak JY, Kim EK, Son EJ et al (2007) Papillary thyroid carcinoma manifested solely as microcalcifications on sonography. *AJR Am J Roentgenol J* 189:227–231
32. Xue T, Liun C, Liu JJ et al (2021) Analysis of the relevance of the ultrasonographic features of papillary thyroid carcinoma and cervical lymph node metastasis on conventional and contrast-enhanced ultrasonography. *Front Oncol J* 11:794399
33. Wang N, Xu Y, Ge C et al (2006) Association of sonographically detected calcification with thyroid carcinoma. *Head Neck J* 28:1077–1083
34. Nabahati M, Moazezi Z, Fartookzadeh S et al (2019) The comparison of accuracy of ultrasonographic features versus ultrasound-guided fine-needle aspiration cytology in diagnosis of malignant thyroid nodules. *J Ultrasound J* 22:315–321
35. Dideban S, Abdollahi A, Maysamie A et al (2016) Thyroid papillary microcarcinoma: etiology, clinical manifestations, diagnosis, follow-up, histopathology and prognosis. *Iran J Pathol J* 11:1–19
36. Liu BX, Xie XY, Liang JY et al (2014) Shear wave elastography versus real-time elastography on evaluation thyroid nodules: a preliminary study. *Eur J Radiol J* 83:1135–1143
37. Xie P, Xiao Y, Liu F (2011) Real-time ultrasound elastography in the diagnosis and differential diagnosis of subacute thyroiditis. *J Clin Ultrasound J* 39:435–440
38. Ruchala M, Szczepanek-Parulska E, Zybek A et al (2012) The role of sonoelastography in acute, subacute and chronic thyroiditis: a novel application of the method. *Eur J Endocrinol J* 166:425–432
39. Park SY, Kim EK, Kim MJ et al (2006) Ultrasonographic characteristics of subacute granulomatous thyroiditis. *Korean J Radiol J* 7:229–234
40. Lee YJ, Kim DW (2016) Sonographic characteristics and interval changes of subacute thyroiditis. *J Ultrasound Med J* 35:1653–1659

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