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Original Article



A Systematic Review and Meta-analysis on Ultrasound Detection of Thyroid Cancer in China

Jindong Niu¹, Hongyan Chen¹, Juan Peng¹, Hui Yuan^{1*}

¹Department of Ultrasound, First Affiliated Hospital of Kunming Medical University, No. 295, Xichang Road, Kunming City, Yunnan Province, 650032, China

* Corresponding author: Hui Yuan, Department of Ultrasound, First Affiliated Hospital of Kunming Medical University, No. 295, Xichang Road, Kunming City, Yunnan Province, 650032, China. Email: dryuanh@sina.com

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Abstract

Background: One major drawback of using ultrasound for diagnosing thyroid nodules is its limited ability to distinguish between benign and malignant nodules. In China, the common methods for risk stratification and guiding fine needle aspiration (FNA) in diagnosing thyroid nodules are the Chinese Thyroid Imaging Reports and Data Systems (C-TIRADS) and American College of Radiology-Thyroid Imaging Reporting and Data System (ACR-TIRADS).

Objectives: This review seeks to assess the effectiveness of C-TIRADS and ACR-TIRADS in accurately identifying the risk of malignancy in Chinese patients suspected of thyroid cancer.

Methods: A detailed search was conducted in PubMed, Google Scholar, Medline, Embase, Web of Science, Cochrane, and *China National Knowledge Infrastructure* (CNKI) databases from January 2018 to December 2022. The analysis only considered original articles from China reporting the use of C-TIRADS and ACR-TIRADS confirmed by histology and FNA.

Results: This review analyzed 26 studies with a total of 23,064 thyroid nodules from 19,114 patients to compare the diagnostic performance of C-TIRADS and ACR-TIRADS in predicting malignancy risk in thyroid nodules. Although the malignancy rates in each risk category were similar between the two systems, the TIRADS showed better diagnostic performance than C-TIRADS in terms of pooled specificity (95.0 % vs. 66.8 % of C-TIRADS). However, the pooled analysis showed that C-TIRADS had a better pooled sensitivity (94.6 % vs. 76.5% of ACR-TIRADS). The diagnostic odds ratio was 1.37 (95 % CI: 0.75-2.51) for ACR-TIRADS and 0.89 (95 % CI: 0.36-2.16) for C-TIRADS.

Conclusion: Based on the results, both C-TIRADS and ACR-TIRADS are effective in predicting the risk of malignancy in thyroid nodules with similar overall diagnostic accuracy. The combination of both systems can be beneficial in enhancing accuracy in suspicious or uncertain cases. The long-term experience of the trained radiologists can readily help in concluding the diagnosis. As no single system or combination of systems can provide a 100% accurate prediction of the malignancy of thyroid nodules, the ultimate diagnosis relies on the concluding assessment of experienced radiologists and the medical team.

Keywords: ACR-TIRADS, China, C-TIRADS, FNA (Fine Needle Aspiration), Malignant, Ultrasound, Thyroid nodules

1. Background

China is the leading figure in the demise rate from thyroid cancer globally. Current report inferences demonstrated that highest number of thyroid cancer frequencies globally belonged to United States and China, indicating the relation between thyroid cancer frequency and topographical issues (1). The occurrence of thyroid cancer in China is also meaningfully diverse based on sex and oldness. China is the nation with the highest population, and the number of cases of thyroid cancer in China will be massive (2). Assessing a nationwide epidemiological study on thyroid cancer has numerous implications for comprehensively understanding the national thyroid cancer epidemic and for promoting the development of relevant, health-focused strategies (3). Over the past three decades, global thyroid cancer rates have consistently increased. China has seen a continued rise in thyroid cancer cases, contributing to 15.6% of new reports and 13.8% of global deaths in 2012 (4). As per the intervention of the new technology, thyroid nodule's span, which can be detected by ultrasonography technique can be as

low as 0.2 cm. Earlier cancer cells, which were nondetectable subclinical thyroid carcinoma, have been detected through the advancement of ultrasound expertise and enhancement of medical facilities and skills of physicians, which is giving way to the accumulative frequency, combining together the thyroid microcarcinoma and thyroid (5). Enhanced ultrasound examinations primarily increased the number of thyroid cancer detection, revealing smaller tumors rather than an actual rise in overall incidence. The accuracy of ultrasound in thyroid cancer was fairly adjacent to the accuracy of fine needle aspiration (FNA) (6). Thyroid cancer is the fourth top cancer in China among urban citizens, with an annual rise of 14.5% since 2003-2007 (7). Thyroid cancer cases have been increasing globally since the 1990s, except in African countries due to limited diagnostic technology (2). Putting together men and women in the last thirty years, the cases of thyroid cancer occurrence in China has been commonly increasing. In addition, it is believed that this rate will keep upsurging in the forthcoming decades. On the other hand, there are certain procedures to ascertain the diagnosis of thyroid cancer. Physical examination of

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the neck helps to see if there are any changes in the lump or nodule in the thyroid (8). A clue about the condition of the thyroid can be given through testing the Thyroid Stimulating Hormone (TSH) in the blood level. Cancerous or non-cancerous nodules can be decided through an ultrasound imaging. Further test is required to confirm the cancerous state (9). Fine needle aspiration cytology Both fine needle aspiration cytology and FNA biopsy employ removing a sample from thyroid tissue, and then the sample is sent for pathological observation. In addition to ultrasound imaging, other imaging techniques such as Tomography (CT) scan, Computed Magnetic Resonance Imaging (MRI), and X-ray can be used to test the presence of cancerous cells (10). Thyroid cancer treatment response varies with cancer stage; despite advances in cancer science and targeted therapies, patient outcomes show limited improvement. The prevalence of thyroid nodules has been rising in recent years, making it crucial to detect high-frequency using ultrasound them **(6)**. Distinguishing benign from malignant nodules is challenging, given that benign nodules constitute around 80-90% of cases. While conventional ultrasound is still the most frequently used diagnostic tool for thyroid nodules, multiple ultrasound features are comprehensively analyzed to determine various risk-stratification systems (11). The American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) is a structured approach for evaluating thyroid nodules using ultrasound imaging. This system assigns a standardized score to each nodule, which guides healthcare professionals in determining whether further action, such as FNA or follow-up ultrasound, is needed. It helps in distinguishing suspicious nodules that may require additional testing from benign or non-suspicious nodules that can be safely monitored without immediate intervention. The ACR-TIRADS and Chinese Thyroid Imaging Reports and Data Systems (C-TIRADS) are common thyroid nodule risk systems. They assess malignancy risk but vary in aspects. One major difference is the number of categories used to classify the nodules (12). The ACR-TIRADS uses five categories (TR1-TR5), while the C-TIRADS has six categories (TIRADS 1-5 plus the "intermediate" category). The C-TIRADS is a novel approach designed to classify the potential malignancy risk associated with thyroid nodules, contributing to the diagnostic process. This system plays a pivotal role in assisting medical professionals in determining the necessity of a thyroid FNA procedure, aligning with the evaluated risk level of the nodule. The additional category in Chinese C-TIRADS allows for a more nuanced assessment of nodules that fall between benign and suspicious. Another difference is the specific ultrasound features used in each system to assess the nodules. The ACR-TIRADS emphasizes on the presence of microcalcifications and the shape of

the nodule, while C-TIRADS also considers the echogenicity and margins of the nodule. The ACR-TIRADS has been widely adopted by radiologists in many countries as a standard reporting system, whereas C-TIRADS has been used only in China in some studies to classify thyroid nodules, and its systematic performance has not been extensively explored. Therefore, this study aims to establish the effectiveness of C-TIRADS and ACR-TIRADS in accurately identifying the risk of malignancy in Chinese patients suspected of thyroid cancer and to disparate investigation of benign and malignant thyroid nodules and to analyze their sensitivity and specificity from the meta-analysis. The study hopes to provide effective accuracy between the C-TIRADS and ACR-TIRADS, which may aid in reducing the biopsies cases.

2. Objectives

Therefore, the present study aims to investigate the diagnostic performance and accuracy of C-TIRADS and ACR-TIRADS in detecting malignant and benign thyroid nodules.

3. Methods

3.1. Search strategy and keywords

The primary sources for the meta-analysis conducted in this study were PubMed, Google Scholar, and MEDLINE, while supplementary searches were carried out through EMBASE, Web of Science, Cochrane, and China National Knowledge Infrastructure (CNKI). The search spanned from January 2018 to December 2022. The search query utilized several keywords, such as "thyroid nodule", "thyroid cancer", "TIRADS", "C-TIRADS", "ACR-TIRADS", and "Chinese-TIRADS". Additionally, the researchers also conducted a manual search of the relevant literature and bibliographies of published articles to identify potential articles.

3.2. Selection criteria

The analysis considered only those studies that met the following criteria: (1) Clinical studies or research articles that focused on diagnostic analysis, (2) evaluation of thyroid nodules was done using ACR-TIRADS and C-TIRADS classification; (3) studies that used histopathological and cytological examination; (4) studies which provided sufficient and non-overlapping data; (5) studies published in English or Chinese.

Two reviewers independently reviewed the fulltext of the studies, and any that did not meet the criteria were excluded.

3.3. Exclusion criteria

The analysis excluded studies that fell into any of the following categories, including case reports, animal experiments, review articles, conference abstracts, in-vitro studies, studies that did not comply with ACR-TIRADS and C-TIRADS guidelines, studies lacking histological or pathological reference, and articles without informed consent.

3.4. Data collection and extraction

During the data extraction process, standard procedures were followed, and all information extracted was reviewed independently by two different researchers (13). Information pertaining to the study was recorded in a standardized format, which included general details such as the author, publication year, study type, number of patients, sex distribution, age range and average, as well as the number of nodules. The format also included information about the reference standard used for diagnosing malignancy. The Cochrane Critical Appraisal Checklist was used to assess the checklist for evaluating the risk of bias, and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool which utilized to assess various factors such as patient selection, index test, reference standard, flow, and timing. The level of bias and concerns about applicability were categorized as low, high, some concern, and no information. Any disagreements between the two reviewers were resolved through discussion, or a third reviewer was consulted for the final decision.

3.5. Data analysis and Statistical assessment

The RevMan 5.0 (Cochrane Rev Manager, Inc, USA) was utilized for data collection and statistical analysis. The study employed two main approaches: a

total meta-analysis of both benign and malignant cases across all included studies and a proportion meta-analysis for C-TIRADS and ACR-TIRADS. The statistical pooling of data was performed using a random-effects model, and Cochran's Q statistic and I0 test were applied to assess statistical heterogeneity. The cut-off point for heterogeneity assessment was 80% (P<0.005). If the *P*-value is less than 0.05, it is often interpreted as evidence of significant heterogeneity among the included studies. The pooled sensitivity, specificity, diagnostic odds ratio (DOR), risk ratio (RR), and risk difference (RD) with 95% CI were calculated using the bivariate model. To explore publication bias, the Beggar's funnel test was used. A P-value of less than 0.05 was considered statistically significant.

4. Results

4.1. Search results

The search yielded 984 articles from various databases such as PubMed, Google Scholar, Embase, Web of Science, and CNKI sources from January 2018 to December 2022. After removing duplicates and ineligible records, 89 full-text articles were screened based on their title and abstract, resulting in the exclusion of 55 irrelevant articles, of which 34 articles were excluded due to insufficient data, 17 articles due to lack of data interest, and four articles due to other TIRADS.) Therefore, leaving 26 studies for further analysis. The PRSISMA 2020 flowchart for the study protocol is presented in Figure. 1.



Figure 1. The PRSISMA 2020 flowchart for the study protocol

4.2. Study and patient characteristics

Twenty-six articles were included with 23,064

cases from 19,114 patients (Table 1). Table 1 provides information on the characteristics of both benign and malignant thyroid nodule cases in each study, as well as their classification based on C-TIRADS and ACR-TIRADS. The number of patients in each study ranged from 70 to 2,141 (Table 1). Out of the 23,064 thyroid nodules considered, 10,969 were determined to be benign, while 12,071 were malignant (Table 1). The number of nodules varied across studies, ranging from 92 to 2,544. The largest number of benign cases in a single study was 2,141, while the largest number of malignant cases was 1,681 cases. From the available reports, the total malignant male accounts for 2,535 (24.14%) cases, and the total malignant female accounts for 7,967 (75.86%). All studies used histopathological and/or cytological evidence as the gold standard for diagnosis, with histopathological results being prioritized when both were available.

4.3. Qualitative and meta-analysis study

The details of the investigated articles are presented in Table 1. The articles were published from January 2018 to December 2022 and had sample sizes ranging from 41 to 2,544 thyroid nodules. The overall prevalence of malignancy among the investigated 26 articles in the present metaanalysis were 47.56% (95% CI=1.09, 0.66-1.80) comprising 10,969 cases from a total of 23,064 cases (Figure. 2). The overall forest plot for RR which measures the relative risk between malignant and benign groups and the RD which measures the absolute difference in risk is presented in Figure. 3A and 3B, respectively.

Table 1. Characteristics of the included studies (January 2018-December 2022)								
Author & Vear	Total	Malignant cases N	Benign cases	Benign cases Total natients				
futifior a real	cases	(%)	N (%)	rotar patients	system			
Cheng 2022 (14)	125	67 (53.6)	58 (46.40)	109	C-TIRADS			
Fan 2021 (<mark>15</mark>)	2213	490 (22.14)	1723 (77.86)	759	C-TIRADS			
Gao 2018 (<mark>16</mark>)	342	239 (69.94)	103 (30.12)	372	ACR-TIRADS			
Gao 2019 (<mark>17</mark>)	2544	1681 (66.07)	863 (33.92)	1758	ACR-TIRADS			
Gao 2022 (<mark>18</mark>)	251	132 (52.59)	119 (47.41)	208	C-TIRADS			
Li 2021 (<mark>19</mark>)	237	132 (55.7)	105 (44.30)	237	C-TIRADS			
Li 2022 (<mark>20</mark>)	513	206 (40.1)	307 (59.84)	481	C-TIRADS			
Lin 2022 (<mark>21</mark>)	329	67 (20.4)	262 (79.64)	329	C-TIRADS			
Liu 2019 (22)	131	72 (55.0)	59 (45.04)	131	ACR-TIRADS			
Qi 2021 (23)	1096	414 (37.7)	682 (62.23)	884	ACR-TIRADS			
Qiao 2021 (<mark>24</mark>)	433	202 (46.7)	231 (53.35)	433	C-TIRADS			
Ruan 2019 (25)	1001	392 (39.1)	609 (60.84)	918	ACR-TIRADS			
Shen 2019 (<mark>26</mark>)	1612	773 (48.0)	839 (52.05)	1568	ACR-TIRADS			
Sui 2021 (<mark>27</mark>)	92	50 (54.3)	42 (45.65)	70	C-TIRADS			
Wang 2020 (28)	101	60 (59.4)	41 (40.59)	101	ACR-TIRADS			
Wang 2019 ^b (29)	351	242 (68.95)	109 (31.05)	176	ACR-TIRADS			
Wu 2021 (<mark>30</mark>)	104	66 (63.46)	38 (36.54)	104	C-TIRADS			
Xu 2018 (<mark>31</mark>)	2465	1005 (40.77)	1460 (59.23)	2031	ACR-TIRADS			
Zhang 2019 (32)	2064	750 (36.33)	1314 (63.66)	2032	ACR-TIRADS			
Zhang 2020 (33)	1271	736 (57.87)	535 (42.09)	1271	ACR-TIRADS			
Zhang 2021 (34)	434	187 (43.12)	247 (56.91)	408	C-TIRADS			
Zhang 2022 (35)	560	370 (66.07)	190 (33.93)	560	C-TIRADS			
Zhao 2019 (<mark>36</mark>)	117	57 (48.72)	60 (51.28)	108	ACR-TIRADS			
Zhou 2021 (37)	2141	1572 (73.43)	565 (26.39)	2141	C-TIRADS			
Zhu 2021 (<mark>38</mark>)	2309	891 (38.57)	1418 (61.41)	1697	C-TIRADS			
Zhu 2022 (39)	228	116 (50.88)	92 (40.35)	228	C-TIRADS			

	Malign	ant	Beni	gn	Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% CI
Cheng 2022	67	125	58	125	3.8%	1.33 [0.81, 2.19]	
Fan 2021	490	2213	1723	2213	3.9%	0.08 [0.07, 0.09]	-
Gao 2018	239	251	103	251	3.7%	28.62 [15.21, 53.84]	
Gao 2019	1681	2544	863	2544	3.9%	3.79 [3.38, 4.26]	-
Gao 2022	132	342	119	342	3.9%	1.18 [0.86, 1.61]	+
Li 2021	132	237	105	237	3.8%	1.58 [1.10, 2.27]	
Li 2022	206	513	307	513	3.9%	0.45 [0.35, 0.58]	-
Lin 2022	67	329	262	329	3.8%	0.07 [0.04, 0.10]	-
Liu 2019	72	131	59	131	3.8%	1.49 [0.92, 2.42]	
Qi 2021	414	1096	682	1096	3.9%	0.37 [0.31, 0.44]	+
Qiao 2021	202	433	231	433	3.9%	0.76 [0.59, 1.00]	
Ruan 2019	392	1001	609	1001	3.9%	0.41 [0.35, 0.50]	-
Shen 2019	773	1612	839	1612	3.9%	0.85 [0.74, 0.97]	~
Sui 2021	50	92	42	92	3.7%	1.42 [0.79, 2.53]	+
Wang 2020	60	101	41	101	3.7%	2.14 [1.22, 3.76]	
Wang 2019b	242	351	109	351	3.9%	4.93 [3.58, 6.79]	-
Wu 2021	66	104	38	104	3.7%	3.02 [1.72, 5.30]	
Xu 2018	1005	2465	1460	2465	3.9%	0.47 [0.42, 0.53]	-
Zhang 2019	750	2064	1314	2064	3.9%	0.33 [0.29, 0.37]	+
Zhang 2020	736	1271	535	1271	3.9%	1.89 [1.62, 2.22]	-
Zhang 2021	187	434	247	434	3.9%	0.57 [0.44, 0.75]	-
Zhang 2022	370	560	190	560	3.9%	3.79 [2.96, 4.86]	
Zhao 2019	57	117	60	117	3.8%	0.90 [0.54, 1.51]	-+
Zhou 2021	1572	2141	565	2141	3.9%	7.71 [6.73, 8.83]	
Zhu 2021	891	2309	1418	2309	3.9%	0.39 [0.35, 0.44]	+
Zhu 2022	116	228	92	228	3.8%	1.53 [1.06, 2.22]	
Total (95% CI)		23064		23064	100.0%	1.09 [0.66, 1.80]	+
Total events	10969		12071				
Heterogeneity: Tau ² =	1.70; Chi ²	= 4087	18, df = 3	25 (P < 0	.00001); I	² = 99%	
Test for overall effect:	Z = 0.33 (P = 0.74)				U.U1 U.1 I 10 100

Figure 2. Forest plot for diagnostic odds ratio of the 26 included studies



Figure 3. Forest plot for (A) risk ratio (RR), which measures the relative risk between malignant, and benign groups and (B) the risk difference (RD), which measures the absolute difference

4.4. Diagnostic performance analysis of C-TIRADS and ACR-TIRADS

The study analyzed the performance of C-TIRADS and ACR-TIRADS risk stratification categories in detecting malignant thyroid nodules. The diagnostic indicators were separately analyzed for C-TIRADS and ACR-TITRADS. The C-TIRADS had the higher pooled sensitivity (1.00) than ACR-TIRADS, while C-TIRADS had a higher pool sensitivity of 94.6% compared to 66.8% of ACR-TIRADS. Whereas the ACR-TIRADS had a higher pool specificity (95.0%) compared to C-TIRADS [76.5%; Table 2]. The DOR, RR, and RD plots were used to determine the optimal category between C-TIRADS and ACR-TIRADS. The prevalence of malignancy in C-TIRADS was 45.21% comprising 4,548 cases [95% CI=0.89, 0.36-2.16; Figure. 4]. The C-TIRADS forest plot for RR and RD is presented in Figure. 5A and 5B, respectively. Whereas the prevalence of malignancy in ACR-TIRADS was 49.38% comprising 6,421 cases- [95% CI=1.37, 0.75-2.51; Figure. 6]. The ACR-TIRADS forest plot for RR and RD is presented in Figure. 7A and 7B, respectively. Whereas the sensitivity and specificity plot is presented in Figure. 8A and 8B, respectively.

Diagnostics	C-TIRADS	ACR-TIRADS
Total Malignant cases	4548	6421
DOR	0.89 (0.36-2.16)	1.37 (0.75-2.51)
RD	-0.02 (-0.25-0.21)	0.06 (-01.0-0.21)
RR	0.95 (0.62-1.45)	1.10 (0.82-1.48)
Pooled Sensitivity	94.6	66.8
Pooled Specificity	76.5	95.0
DOR: Diagnostic Odds Ratio, RD: Risk Differ	ence, RR: Risk Ratio	

Benign Malignant Odds Ratio Odds Ratio Study or Subgroup Events Total Events Total Weight IV, Random, 95% CI IV, Random, 95% CI Cheng 2022 125 125 7.1% 1.33 [0.81, 2.19] 67 58 Fan 2021 490 2213 1723 2213 7.2% 0.08 [0.07, 0.09] Gao 2022 132 342 342 7.2% 1.18 [0.86, 1.61] 119 Li 2021 237 237 7.1% 1.58 [1.10, 2.27] 132 105 0.45 [0.35, 0.58] Li 2022 206 513 307 513 7.2% Lin 2022 67 329 7.1% 0.07 [0.04, 0.10] 329 262 Qiao 2021 202 433 231 433 7.2% 0.76 [0.59, 1.00] Sui 2021 50 92 42 92 7.0% 1.42 [0.79, 2.53] 3.02 [1.72, 5.30] Wu 2021 66 104 38 104 7.0% Zhang 2021 187 434 247 434 7.2% 0.57 [0.44, 0.75] Zhang 2022 370 560 190 560 7.2% 3.79 [2.96, 4.86] Zhou 2021 1572 2141 565 2141 7.2% 7.71 [6.73, 8.83] Zhu 2021 891 2309 1418 2309 7.2% 0.39 [0.35, 0.44] Zhu 2022 116 228 92 228 7.1% 1.53 [1.06, 2.22] Total (95% CI) 10060 10060 100.0% 0.89 [0.36, 2.16] 4548 5397 Total events Heterogeneity: Tau² = 2.86; Chi² = 2604.42, df = 13 (P < 0.00001); I² = 100% 0.01 0.1 10 100 Test for overall effect: Z = 0.26 (P = 0.79) Favours [Malignant] Favours [Benign]

Figure 4. Forest plot for diagnostic odds ratio of C-TIRADS



Figure 5. Forest plot for (A) risk ratio (RR) and (B) the risk difference (RD) for C-TIRADS



Figure 6. Forest plot for diagnostic odds ratio of ACR-TIRADs



Figure 7. Forest plot for (A) risk ratio (RR) and (B) the risk difference (RD) for ACR-TIRADS

Study or Subgroup	S	ensitivity, 95% Cl	Study or Subgroup		Specificity, 95%
Cheng 2022		0.91 [0.85, 0.97]	Cheng 2022		0.82 [0.74, 0.90
Fan 2021	•	1.00 [0.98, 1.02]	Fan 2021		0.21 [0.13, 0.29
Gao 2018	->	0.97 [0.93, 1.01]	Gao 2018	·	0.49 [0.39, 0.59
Gao 2019		0.93 [0.88, 0.98]	Gao 2019		0.78 [0.70, 0.86
Gao 2022	•	1.00 [0.98, 1.02]	Gao 2022		0.16 [0.09, 0.23
Li 2021	•	1.00 [0.98, 1.02]	Li 2021		0.53 [0.43, 0.63
Li 2022	→	0.97 [0.93, 1.01]	Li 2022		0.19 [0.11, 0.27
Lin 2022	•	1.00 [0.98, 1.02]	Lin 2022		0.18 [0.10, 0.26
Liu 2019		Not estimable	Liu 2019	-	0.93 [0.88, 0.98
Qi 2021		0.74 [0.65, 0.83]	Qi 2021		0.70 [0.61, 0.79
Qiao 2021	•	1.00 [0.98, 1.02]	Qiao 2021	-	0.12 [0.05, 0.19
Ruan 2019		0.81 [0.73, 0.89]	Ruan 2019		0.77 [0.69, 0.85
Shen 2019	→	0.97 [0.93, 1.01]	Shen 2019	-	0.87 [0.80, 0.94
Sui 2021	•	0.99 [0.96, 1.02]	Sui 2021	-	0.92 [0.86, 0.98
Wang 2020		0.80 [0.72, 0.88]	Wang 2020		0.82 [0.74, 0.90
Wang 2019b		0.90 [0.84, 0.96]	Wang 2019b	-	0.90 [0.84, 0.96
Wu 2021		0.93 [0.88, 0.98]	Wu 2021		0.27 [0.18, 0.36
Xu 2018	->	0.96 [0.92, 1.00]	Xu 2018		0.53 [0.43, 0.63
Zhang 2019		0.88 [0.81, 0.95]	Zhang 2019	-	0.84 [0.77, 0.91
Zhang 2020		0.84 [0.77, 0.91]	Zhang 2020	-	0.90 [0.84, 0.96
Zhang 2021	•	1.00 [0.98, 1.02]	Zhang 2021		0.28 [0.19, 0.37
Zhang 2022	•	1.00 [0.98, 1.02]	Zhang 2022		0.19 [0.11, 0.27
Zhao 2019		0.89 [0.83, 0.95]	Zhao 2019	-	0.88 [0.81, 0.95
Zhou 2021	•	1.00 [0.98, 1.02]	Zhou 2021		0.42 [0.32, 0.52
Zhu 2021	→	0.97 [0.93, 1.01]	Zhu 2021		0.41 [0.31, 0.51
Zhu 2022	-	0.93 [0.88, 0.98]	Zhu 2022		0.55 [0.45, 0.65
	•	0.94 [0.92, 0.97]		•	0.56 [0.44, 0.69
-1 -0.5 0	0.5 1				
0	Sonsitivity		-1 -0.5	Specificit-	

Figure 8. (A) Sensitivity plot and (B) specificity plot of the included 22 full-texts

4.5. Risk of bias

Figures 9A, 9B, and 9C display the funnel plot results for the overall analysis, C-TIRADS, and ACR-TIRADS, respectively. The funnel plots revealed high heterogeneity and indications of publication bias. The assessment of risk of bias and funnel plots was conducted independently, and the result of the QUADAS-2 considering of patient selection, index flow, and timing as important characteristics is presented in Figure. 10. Reporting bias could have contributed to the observed asymmetry in the funnel plots, resulting from discrepancies in the direction of the results. The potential consequences of publication bias in our meta-analysis include selective reporting of outcomes and analyses, as well as funnel plot asymmetry.



0

0R 101



0.3

a

0.5

D1 D2 D3 D4 Overall Cheng 2022 • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • • •			Risk of bias domains						
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Figure 10. QUADAS-2 plot of the included 22 full-texts

5. Discussion

The present systematic review considers the meta-analytic approach of the thyroid nodules representing the review of the comparative analysis of C-TIRADS and ACR-TIRADS in China reported from January 2013 to December 2022. We collected and analyzed 26 articles involving 10,969 malignant cases and 12,071 benign cases from a total of 23,064 nodules to assess the diagnostic performance of C-TIRADS and ACR-TIRADS. The C-TIRADS was developed by the Chinese Medical Association in 2020 as a standardized system for categorizing thyroid nodules based on their sonographic

appearance (40). Whereas the ACR-TIRADS is a similar system developed by the American College of Radiology in 2018 (41). It also assigns a score to thyroid nodules based on their sonographic appearance, but it includes a more detailed set of features, including vascularity, size, and lymph node involvement. The total number of full-texts for C-TIRADS and ACR-TIRAD was 14 and 12, respectively. The study utilized diagnostic indicators such as OR, RR, and RD to assess the overall efficacy of C-TIRADS and ACR-TIRADS. This approach offered more compelling evidence and contributed towards enhancing the comprehension and widespread adoption of both C-TIRADS and ACR-TIRADS. In this

study, the total percentage of male patients detected for malignant was (24.14%). Although thyroid cancer is more prevalent in women than in men, which is about one-third of as many women, in the last thirty years, the rate of death has been increasing among men. The percentage of male patients in C-TIRADS ACR-TIRADS was 22.64% and 26.08%, and respectively. This upward trend is expected to be short-lived, while the ratio of elderly individuals with thyroid cancer and mortality rates is predicted to steadily rise (11). However, the rising unit menaces of the death rate of thyroid cancer in the male population gives a valuable hint in the prevention of thyroid cancer and control in China. It reminds us that additional courtesy requirements need to be paid in handling the burden of thyroid cancer in men. Fascinatingly, the augmented unit consequence on the demise of thyroid cancer in males did not disturb men's death rate in the upcoming year, which can be related to a favourable time (period effect) disturbing superior layers of thyroid cancer mortality when compared to undesirable ones (42). Our study compared the diagnostic performance of the C-TIRADS and ACR-TIRADS from samples from China and observed that both the TIRADS have good diagnostic performance. In this study, the DOR for C-TIRADS is 0.89 (0.36-2.16), while the DOR for TIRADS is 1.37 (0.75-2.51). However, the confidence intervals for both DORs overlap, indicating that the difference between the two DORs is not statistically significant. Therefore, we cannot conclude that either CIRADS or TIRADS is statistically more significant based solely on the DOR values provided. However, the sensitivity of the C-TIRADS and ACR-TIRADS was 94.6% and 66.8%, respectively, and specificity was 76.5% and 95.0%, respectively. Therefore, indicating that both of them have a good diagnostic performance overall. The C-TIRADS having the highest sensitivity and the ACR-TIRADS having the highest specificity is inconsistent with other reports (12, 31). It is important to note that the DOR alone may not be the only factor to consider when evaluating the diagnostic accuracy of a test. Other factors, such as sensitivity, specificity, and positive and negative predictive values, should also be considered when assessing the performance of a diagnostic test. The accuracy of ACR-TIRADS and C-TIRADS in classifying thyroid nodules may vary depending on the specific population being studied, the imaging techniques used, and the experience level of the radiologist interpreting the images (43). Therefore, it is difficult to make a definitive statement regarding which system is more accurate. In terms of diagnostic accuracy, studies have shown that both C-TIRADS and ACR-TIRADS are effective in predicting the malignancy risk of thyroid nodules. Another study found that both C-TIRADS and ACR-TIRADS had diagnostic performance in identifying similar malignant nodules, with overall sensitivity and

specificity ranging from 70-90% (38). In fact, both ACR-TIRADS and C-TIRADS are widely used and have shown promising results in detecting thyroid However, in another nodules. meta-analysis conducted by Dong et al. in 2023, which compared the diagnostic performance of ACR-TIRADS and C-TIRADS, it was found that both systems had similar overall accuracy in detecting malignant thyroid nodules based on surgical histological evidence (44). However, C-TIRADS demonstrated higher sensitivity in some studies, and several studies have reported that ACR-TIRADS may be slightly more accurate than C-TIRADS in predicting malignancy, particularly for smaller nodules. Another study reported that ACR-TIRADS had a higher diagnostic accuracy than C-TIRADS in a sample of 214 thyroid nodules, with an area under the curve (AUC) of 0.899 compared to 0.828 for C-TIRADS. Because of these reasons, it is required to consider two or more assessment systems for nodules that were deemed suspicious or indeterminate and exhibited a limited number of highly malignant features in a clinical setting (23). It is important to note that no single system can accurately predict the malignancy of thyroid nodules with 100% accuracy and that ultimately the final diagnosis should be made by a trained medical professional based on a comprehensive analysis of all clinical and imaging features. When there is doubt about the accuracy of the diagnosis result of the ultrasound instrument, the long-term experience of the trained radiologists can readily help in concluding the diagnosis. In conclusion, both C-TIRADS and ACR-TIRADS are useful diagnostic tools for predicting the risk of malignancy in thyroid nodules, with similar overall diagnostic accuracy. In terms of diagnostic performance, studies have reported mixed results on which system is more accurate in identifying malignancy. Some studies have found ACR-TIRADS to have higher sensitivity and specificity, while others have found Chinese C-TIRADS to be more accurate. It is worth noting that the diagnostic performance of both systems can vary depending on the population being studied and the experience of the radiologist using the system. Some studies suggest that ACR-TIRADS may be slightly more accurate, particularly for smaller nodules. Some other studies reported the opposite stating that C-TIRADS is more accurate (12, 45). Overall, both ACR-TIRADS and C-TIRADS are useful tools for risk stratification of thyroid nodules, and the choice of which system to use may depend on factors such as local practice patterns and the preferences of individual radiologists. It is important to note that these systems are not intended to replace biopsy as the definitive diagnostic tool for thyroid nodules but rather to guide the decision-making process regarding the necessity of biopsy. The findings of this study also suggest that when a nodule's diagnosis is suspicious or uncertain, using a combination of two TIRADS can be beneficial in enhancing accuracy. Additionally, it is advisable to evaluate the diagnostic consistency of the two TIRADS at the optimal cut-off point. The ACR-TIRADS is a frequently utilized TIRADS that exhibits high specificity and is successful in decreasing unnecessary FNA rates (46). Our study has some limitations. First, the study setting was China and all malignant thyroid tumors were from Chinese patients. Second, the study compared only ACR-TIRADS and C-TIRADS and did not consider other systems, such as EU-TIRADS and K-TIRADS.

6. Conclusion

The results of the analysis suggest that both C-TIRADS and ACR-TIRADS are effective diagnostic tools for predicting the risk of malignancy in thyroid nodules, with similar overall diagnostic accuracy. The findings of the present study also suggest that when a nodule's diagnosis is suspicious or uncertain, using a combination of two TIRADS can be beneficial in enhancing accuracy. In this context, the long-term experience of the on-the-field radiologists can readily help in concluding the diagnosis. Since a single system or a combination of the systems cannot accurately predict the malignancy of thyroid nodules with 100% accuracy, ultimately, the final decision of the diagnosis is dependent on the concluding remark of the experienced trained radiologists and the medical team.

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Footnotes

Conflicts of Interest: The authors declared that there were no conflicts of interest.

Author Contribution: All authors contributed equally to the research design, conduction of the experiment, analysis of the results, and preparation of the manuscript.

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Ethical Statements: Not applicable.

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