MEDS Clinical Medicine (2024)
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2024.050411
ISSN 2616-1907 Vol. 5 Num. 4

The Application Value of C-TIRADS and ACR-TIRADS in the Diagnosis of Thyroid Nodules: A Meta-Analysis

Chaoip Ng[1], Claudia Gabriela Ho Cambeta[2], Yanting Ip[3,*]

[1]Xiangya School of Medicine, Central South University, Changsha, 410083, China
[2]The Affiliated School of the University of Macau, Macao, 999078, China
[3]School of Stomatology, Jinan University, Guangzhou, 510632, China
xtye1996@163.com
[*]Corresponding author

Keywords: C-TIRADS, ACR-TIRADS, Thyroid Nodules, Meta-analysis

Abstract: To study the diagnostic value of C-TIRADS and ACR-TIRADS for benign and malignant thyroid nodules. This study searched the Chinese databases CNKI, Wanfang, and VIP database for literature regarding the diagnosis of benign and malignant thyroid nodules by C-TIRADS and ACR-TIRADS, covering the period from June 2020 to June 2024. After screening, a total of 13 literature pieces were included, containing 5849 patients. The Cochrane bias risk assessment tool of RevMan5.3 software was used to assess the quality of the included literature. The combined sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, odds ratio, and heterogeneity were measured by Stata16.0 and RevMan5.3 software. The summary receiver operating characteristic (SROC) curve was drawn and the area under the curve (AUC) was calculated. Among the included cases, 7514 lesions were discovered 4329 were malignant (57.61% positive rate) and 3185 were benign (42.39% negative rate). The calculated C-TIRADS sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 0.91 (95%CI: 0.87-0.94), 0.80 (95%CI: 0.71~0.86), 4.5 (95%CI: 3.2-6.5), 0.11 (95%CI: 0.07-0.06), 42 (95%CI: 28-63), and the AUC was 0.93. The ACR-TIRADS sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 0.89 (95%CI: 0.82-0.93), 0.71 (95%CI: 0.61-0.79), 3.1 (95%CI: 2.3-4.1), 0.16 (95%CI: 0.10-0.26), 19 (95%CI: 11-35), and the AUC was 0.88. The heterogeneity test result for sensitivity was Q=182.52, df=12.00, P<0.00001, I2=93.43%, 95%CI(2.70,3.57). In Conclusion, compared to ACR-TIRADS, C-TIRADS technology has higher diagnostic performance for the judgment of benign and malignant thyroid nodules and is worth promoting in clinical practice.

1. Introduction

Thyroid nodules represent an abnormal proliferative mass within the thyroid gland, being one of the common diseases in the endocrine system[1]. In recent years, the global incidence of thyroid nodules has shown an upward trend[2], with the current rate of affliction reaching 72%[3]. Research indicates that, in China, the prevalence of thyroid nodules, exceeding 0.5cm in diameter, discovered through ultrasonography among adult populations is up to 20.43%, with 8-14.8% of these nodules

diagnosed as thyroid cancer[4]. Although patients with thyroid cancer have great opportunities to recover, the risk of cancer cell metastasis and the potential harm cannot be ignored. Therefore, the early discovery of thyroid nodules can greatly reduce the patient's risk [5].

Histopathological results are generally accepted as the gold standard for the diagnosis of thyroid nodules. However, as this technique is invasive and substantial medical resources are required, it is hardly accepted by patients. Hence, its application on a large scale is impractical. Consequently, clinicians prefer employing non-invasive, external diagnostic techniques for diagnosing thyroid nodules. These techniques mainly include palpation, computed tomography (CT) scans, magnetic resonance imaging (MRI), and ultrasound examinations. Among these, ultrasound examination is considered the most widely used diagnostic technique for thyroid nodules in current clinical practices. Two advantages of ultrasound are as follows: 1. High detection rates. Previous clinical studies have demonstrated a detection rate of 50%-67% for ultrasound examinations[6], notably higher than the other methods. 2. Lower medical costs. The cost of ultrasound examinations is significantly lower than CT scans and MRIs. In addition, its' required equipment is portable and, thereby, facilitates a broader population screening. Accordingly, thyroid sonography holds great potential for the assessment and management of thyroid nodules and is routinely employed as a diagnostic tool in many domestic hospitals.

In 2009, Horvath put forth the Thyroid Imaging Reporting and Data System (TIRADS)[7,8], which established a standard, based on thyroid ultrasound results, to classify benign and malignant thyroid nodules. The most popular standard presently in use domestically is the American College of Radiology's ACR-TIRADS[9]. However, ACR-TIRADS is used in conjunction with fine-needle aspiration biopsy (FNAB)[10], and FNAB has not been widely adopted domestically. Hence, some research considers the diagnostic capacity of ACR-TIRADS's diagnostic capacity is not as fascinating as we thought [11]. In response to these limitations, in 2020, the China Ultrasonography Expert Committee established the China-specific C-TIRADS (Chinese Guidelines for Malignancy Risk Stratification of Thyroid Nodules by Ultrasound, 2020), to replace the current ACR-TIRADS standard. However, although clinical research supports the effectiveness of C-TIRADS and ACR-TIRADS in diagnosing thyroid nodules, a comprehensive systematic evaluation is lacking. Therefore, this study undertakes a systematic review and Meta-analysis of clinical research concerning the diagnostic capacity of C-TIRADS and ACR-TIRADS for thyroid nodules, comparing the efficacy of C-TIRADS and ACR-TIRADS in diagnosing clinical cases, thereby providing suggestions for diagnosing thyroid nodules in clinical.

2. Materials and Research Methods

2.1 Literature Search Strategy

Chinese databases, CNKI, Wanfang, and VIP were searched for relevant literature published between June 2020 and June 2024. The keywords in literature searching include: "thyroid nodules, ultrasound, malignant risk, thyroid imaging recording and data systems, diagnostic capacity, Chinese Ultrasound Thyroid Imaging Reporting System, American Radiological Society Thyroid Imaging Reporting and Data System". No limitations were made regarding the region or study features, such as participant race or age. Manual secondary searches were conducted on the reference and similar literature of the included studies.

2.2 Inclusion and Exclusion Criteria for Literature

Inclusion Criteria include: (1) Currently published Chinese literature; (2) Literature must cover multiple types of malignant and benign thyroid nodules; (3) Clinical research literature; (4) Literature

with a clear gold standard(pathology, clinical follow-up, or imaging examination); (5) Literature that can provide sufficient data to calculate combined sensitivity and specificity, and can directly or indirectly derive true positive (TP), false positive (FP), false negative (FN), and true negative (TN) values; (6) Literature that uses both the 2017 version of ACR-TIRADS and the 2020 version of C-TIRADS as diagnostic tools; (7) Literature with clear C-TIRADS and ACR-TIRADS diagnostic effectiveness for both benign and malignant thyroid nodules in the same patient population.

Exclusion criteria include: (1) Duplicate publications; (2) Reviews, Meta-analyses, conference abstracts, and case analyses; (3) Studies that do not provide sufficient data to calculate effect sizes or lack other important information;(4) Animal experiments; (5) Literature that does not use both the 2017 ACR-TIRADS and the 2020 C-TIRADS versions as diagnostic tools; (6) Studies comparing the diagnostic effectiveness of C-TIRADS or ACR-TIRADS alone with other TIRADS in diagnosing benign and malignant thyroid nodules; (7) Literature that includes other TIRADS diagnostic indicators; (8) The literature for the individual diagnosis of benign and malignant thyroid nodules by C-TIRADS and ACR-TIRADS; (9) Literature in languages other than Chinese.

2.3 Data Extraction

Two researchers independently extracted information and data from the determined studies by searching the title and the abstract, using a standardized Excel data extraction table. The researchers checked the first author's name, publication year, gender ratio, sampling and testing methods, gold standards, true positive values, false positive values, false negative values, and true negative values of the included articles. After the extraction of detailed information and data, another researcher conducted a secondary review, to ensure the completeness and accuracy of the data, then combined and sorted the collected data, finally generating a complete data view. In the event of disagreement between the two researchers, a conclusion was reached after consultation with a third researcher.

2.4 Literature Quality Assessment

The Cochrane bias risk assessment tool of the RevMan5.3 software was used to evaluate the quality of the included literature, that is, to assess the risk of bias and applicability of each article.

2.5 Statistical Methods

RevMan5.3 and Stata16.0 were used to conduct heterogeneity tests and meta-analyses on the included studies. The fixed effect model was applied if $P > 0.05$, $I2 \leq 50\%$, indicating low heterogeneity among studies. If $P \leq 0.05$, $I2 > 50\%$, indicating significant heterogeneity among studies, the random effect model was used. Further, sensitivity analysis and subgroup analysis were conducted to identify the source of heterogeneity. Meta-analysis was conducted to measure the combined effect size and the summary receiver operating characteristic curve (SROC) and the area under the curve (AUC), comparing the diagnostic effectiveness of CTIRADS and ACRTIRADS for benign and malignant thyroid nodules analyzing and evaluating the clinical value.

2.6 Publication Bias Analysis

Deeks' funnel plot test of the Stata16.0 was used to check for publication bias.

3. Result

3.1 Literature Search and Inclusion Results

A total of 258 related articles were included in this study. The number of articles retrieved from each database was as follows: CNKI (37 articles), Wanfang Data (45 articles), and VIP Information (175 articles). After removing duplicates, 225 articles were obtained. After excluding reviews and academic dissertations (19 articles), case reports and studies (20 articles), diagnostic efficiency tools that did not match (55 articles), comparative diagnostic tools with inconsistent related diseases (24 articles), and non-comparative studies (40 articles), a total of 158 articles were excluded. The remaining 67 articles were further screened by reading the full text. Finally, 13 articles that met the inclusion criteria were selected. The specific screening process is shown in Figure 1.

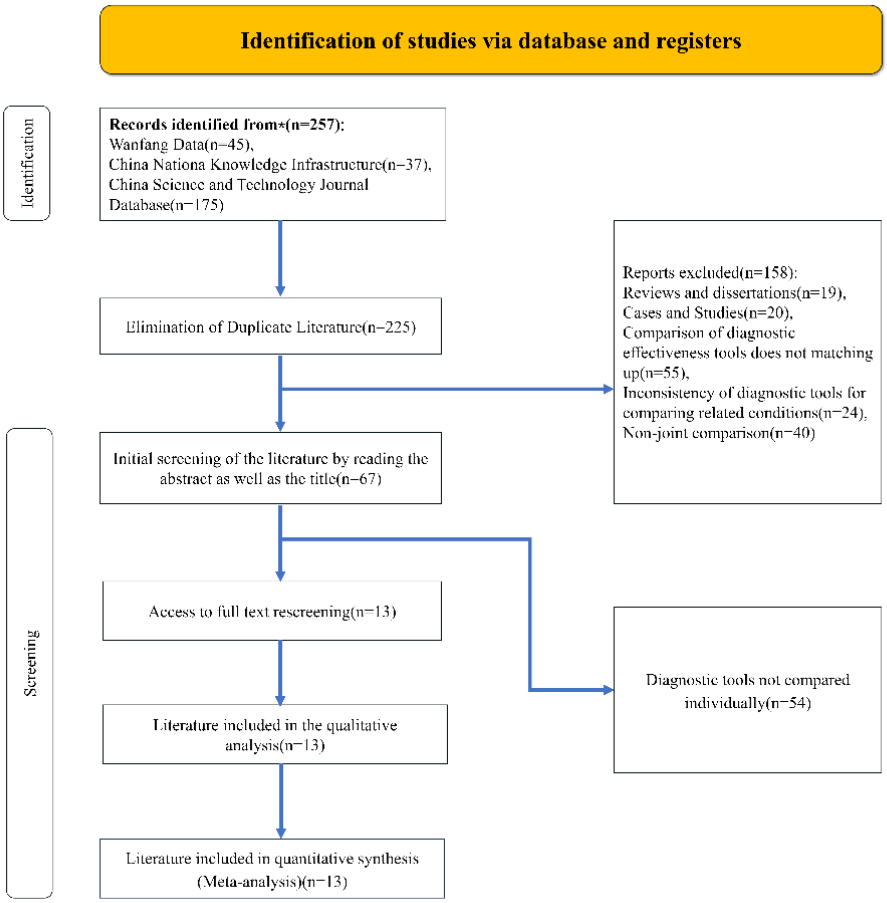

Figure 1: Process and outcome of the study selection strategy

3.2 Baseline Characteristics and Quality Evaluation of the Included Studies

A total of 13 studies were included, which consisted of 5,849 patients, including 7,514 lesions. Among these, 4,329 were malignant, and 3,185 were benign. The diagnosis of thyroid nodules in all included studies was confirmed by pathological results. The basic information of the included studies is shown in Table 1. The quality evaluation of the included studies was conducted using the Cochrane Bias Risk Assessment Tool and the results are displayed in Figure 2.

Table 1: Studies Baseline Characteristics.

The First Author	Year	Gender		C-TIRADS				ACR- TIRADS				Benign Tumors	Malignant Tumors	Number of Lesions	Gold Standard
		Female	Male	TP	FN	TN	FP	TP	FN	TN	FP				
Yan M.[11]	2022	523	121	646	31	289	48	603	74	301	36	337	677	1014	a
Bo G.[12]	2022	213	76	86	19	214	5	62	1	218	43	219	105	324	a
Yang S.[13]	2024	190	36	60	26	117	23	63	23	99	41	140	86	226	a
Linlin Z.[14]	2021	196	70	201	10	39	33	207	4	24	48	72	211	283	a
Shen M.[15]	2021	1422	328	1131	56	543	299	768	419	546	296	842	1187	2029	a
Miaomiao C.[16]	2023	1302	325	1180	67	667	150	1120	127	621	196	817	1247	2064	a
Wei L.[17]	2021	93	27	63	4	39	17	58	9	38	18	56	67	123	a
Jianfeng J.[18]	2022	95	52	124	17	94	23	99	42	105	12	117	141	258	a
Wenbin L.[19]	2022	200	38	125	12	103	25	129	8	68	60	128	137	265	a
Guixia W.[20]	2022	212	89	99	22	169	32	99	22	120	80	200	121	321	a
Shiyue D.[21]	2021	160	35	102	28	92	13	116	14	68	37	105	130	235	a
Lulu Z.[5]	2023	86	31	62	2	36	40	61	3	41	35	76	64	140	a
Li L.[22]	2022	145	50	148	8	61	15	132	24	64	12	76	156	232	a

a: Pathological results; TP:True positive; FN:False Negative; TN:True Negative; FP:False positive

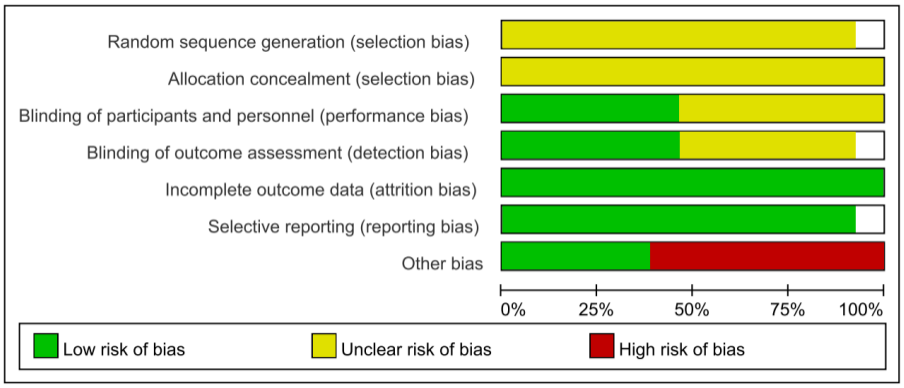

Figure 2: The risk of bias graph

3.3 Heterogeneity Test

The results of the heterogeneity test on the combined sensitivity of the C-TIRADS system showed Q=182.52, df=12.00, P<0.00001, and I^2=93.43%, suggesting the existence of heterogeneity.

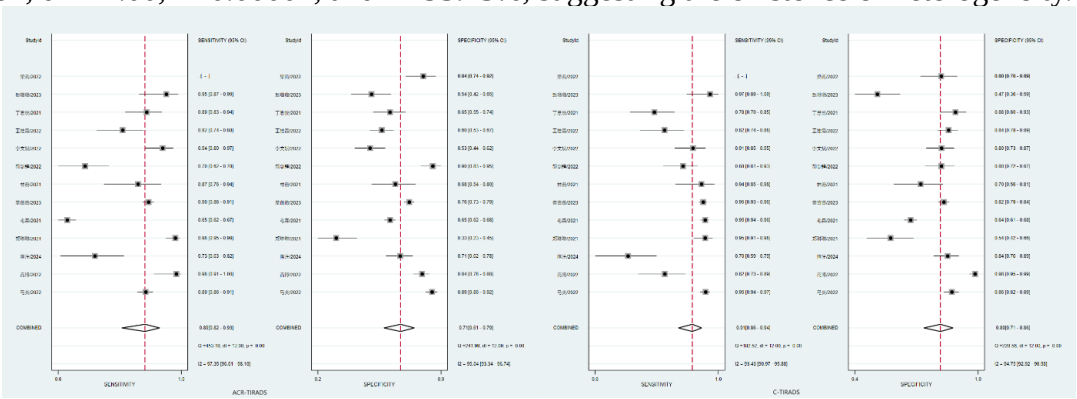

Figure 3: Forest Plot of Sensitivity and Specificity

3.4 Combined effect size results

According to the evaluation results of the heterogeneity, a meta-analysis was conducted using a random-effects model. The sensitivity and specificity of the C-TIRADS diagnostic method compared with the ACR-TIRADS were shown in Figure 3 as 0.91(95%CI: 0.87--0.94), 0.80(95%CI:0.71-0.86), while the sensitivity and specificity of the ACR-TIRADS were shown as 0.89 (95%CI:0.82-0.93), 0.71(95%CI:0.61-0.79), respectively. The positive likelihood ratios, negative likelihood ratios, and diagnostic odds ratios for C-TIRADS and ACR-TIRADS are displayed in Figure 4 as 4.5(95%CI:3.2-6.5), 0.11(95%CI:0.07-0.06), 42(95%CI:28-63) and 3.1(95%CI:2.3-4.1), 0.16(95%CI:0.10-0.26), 19(95%CI:11-35), respectively. By using the true positive rate as the y-axis and the false positive rate as the x-axis, the ROC curves of the two diagnostic tools were plotted and the AUC area was calculated. The AUC for ACR-TIRADS is 0.88 and C-TIRADS is 0.93 (Figure 5). Since getting approached 1 on AUC illustrates the better the diagnostic performance, it is reasonable to conclude that C-TIRADS appears a superior performance to ACR-TIRADS.

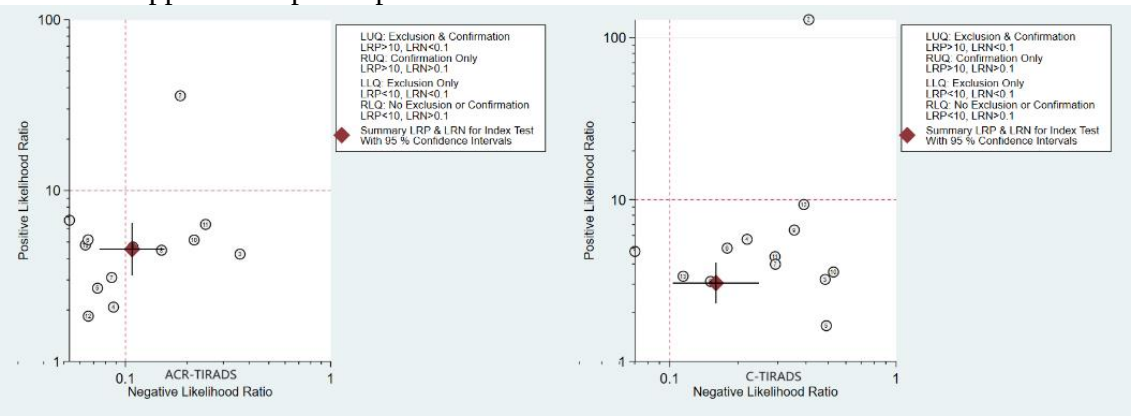

Figure 4: Negative likelihood ratio

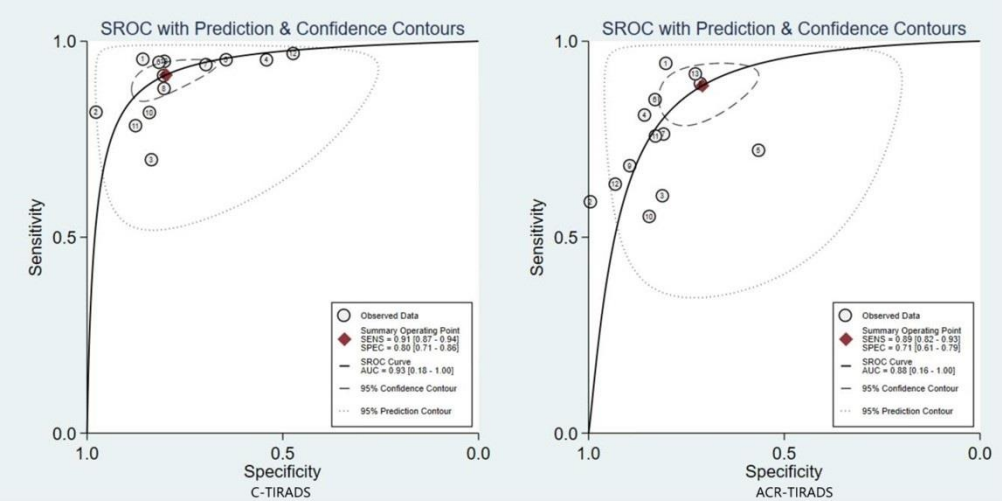

Figure 5: SROC & AUC

3.5 Evaluation of Publication Bias

Publication bias was evaluated using a Deek's funnel plot produced via Stata 16.0. As shown in Figure 6, the results indicate a uniform distribution on both sides and a roughly symmetric representation, suggesting a relatively minor publication bias in the present study.

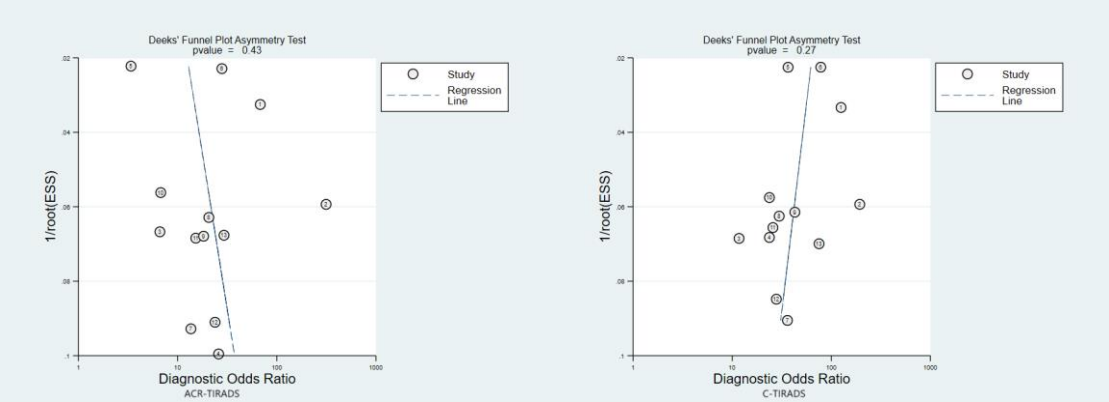

Figure 6: Deeks Funnel Plot

3.6 Assessment of Clinical Diagnostic Value

The clinical utility of C-TIRADS and ACR-TIRADS in diagnosing malignant thyroid nodules was evaluated through Fagan's nomogram. As depicted in Figure 7, the pre-test probability of an ACR-TIRADS diagnosis was set at 70%, which decreased to 40% post-test. When employing the C-TIRADS diagnostic approach, the pre-test probability was set at 40%, and it escalated to 66% post-test. These findings demonstrate that C-TIRADS holds superior diagnostic value in clinical practice.

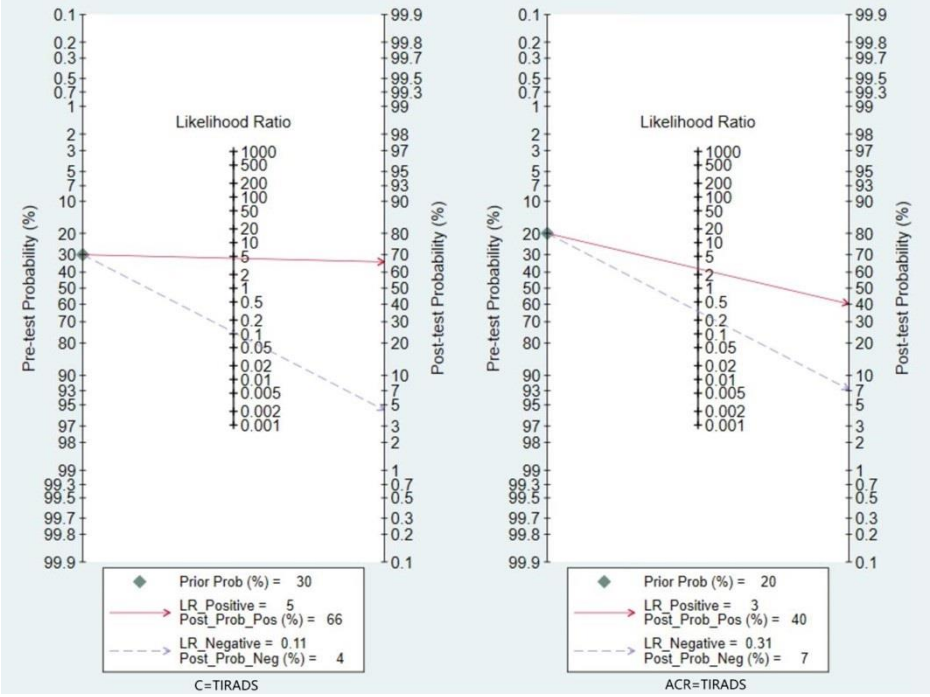

Figure 7: Fagan's nomogram and probability-modified plot

4. Discussion

The key point in diagnosing thyroid nodules is to distinguish between benign and malignant lesions, with benign ones either being monitored or surgically removed and malignant ones requiring surgery. The use of high-resolution ultrasound has made it easier to detect small thyroid nodules, and ultrasound-guided biopsies have led to more diagnoses of tiny thyroid cancers[21]. Considering the healthcare situation in China, A unified ultrasound grading system, specifically using C-TIRADS

instead of ACR-TIRADS, is critical in improving accuracy in diagnosing the nature of thyroid nodules.

The heterogeneity test result of this study was I^2=93%, indicating high heterogeneity. A narrative analysis of the included retrospective literature suggests that the major sources of heterogeneity might be some studies having an unusually high sensitivity of ACR-TIRADS [13,14,22]. Consequently, the study did not conduct subgroup analysis or meta-regression analysis due to the identified heterogeneity. Other potential sources of heterogeneity may arise from differences in the size of thyroid nodules, whether there was a size group, different ultrasound equipment, different operating doctors, and varying amounts of contrast agent. This study concludes that C-TIRADS is more accurate than ACR-TIRADS in assessing thyroid nodules, as it better suits China's healthcare context. The meta-analysis results show that C-TIRADS has a superior ability to distinguish between benign and malignant thyroid nodules.

However, there are several potential limitations to this meta-analysis: (1) Only Chinese databases were searched, which might have led to language bias; (2) Only 13 articles were incorporated, and as research comparing the diagnostic efficacy of C-TIRADS and ACR-TIRADS in distinguishing benign and malignant thyroid nodules is ongoing, the small sample size could lead to bias, and the number of articles that meet the inclusion criteria is limited; (4) Other confounding factors, such as the size of the thyroid nodules included, the analysis of the types of thyroid nodules, and the shape of the thyroid nodule borders, could potentially affect the stronger diagnostic efficacy of C-TIRADS than ACR-TIRADS; (5) This study did not compare the diagnostic efficacy of C-TIRADS with other TIRADS currently used in China, so comprehensive conclusions about the superiority of C-TIRADS in diagnostic efficacy cannot be drawn. Further studies on this aspect will be continued.

In summary, C-TIRADS is more effective than ACR-TIRADS in diagnosing thyroid nodules and aligns better with national conditions. It shows excellent overall performance, helping clinicians make better decisions and reduce unnecessary biopsies. The study recommends its clinical use, though further research is needed to evaluate its potential as the sole diagnostic tool for thyroid nodules in the country and to clarify its overall diagnostic value.

5. Conclusion

This research indicated that for Chinese patients, C-TIRADS demonstrates both higher sensitivity and specificity, is more effective than ACR-TIRADS in diagnosing thyroid nodules, and aligns better with China's social and economic conditions. It shows excellent overall performance, helping clinicians make better decisions and reduce unnecessary biopsies. The result of this study recommends its greater diagnostic effectiveness and clinical application value, though further research is needed to evaluate its potential as the sole diagnostic tool for thyroid nodules in the country.

References

[1] Bo L., Zixiang K., & Baogui C. An Analysis of Professor Chen Baogui's Treatment Approaches for Thyroid Nodules[J]. Journal of Tianjin Traditional Chinese Medicine, 2021, 39(1): 8-10.

[2] Subramanian K. Molecular markers in the diagnosis of thyroid cancer in indeterminate thyroid nodules[J].Indian J Surg Oncol, 2022, 13(1): 11-16.

[3] Paschou SA, Vryonidou A, Goulis DG. Adrenal incidentalomas: a guide to assessment, treatment and follow-up [J].Maturitas, 2016, 92: 79-85.

[4] Yanjuan T., Lingyun B., Anqi H., et al. Application of Ultrasonographic Time-Intensity Curves in Thyroid Nodules[J]. Medical Imaging Journal, 2013, 23: 678-681.

[5] Ying Z., Guanghui Y., Yan Z., et al. Value and Accuracy Analysis of Ultrasound-Guided Thyroid Coarse Needle Aspiration Biopsy in Differential Diagnosis of Benign and Malignant Thyroid Nodules[J]. Modern Drug Application in China, 2022, 17(2): 50-53.

[6] Shipeng Y. Standardized Evaluation and Treatment of Thyroid Nodules. Chinese Society of Endocrinology, 2009-12-

13.
[7] Park JY, Lee HJ, Jang HW, et al. A proposal for a thyroid imaging reporting and data system for ultrasound features of thyroid carcinoma[J].Thyroid, 2009, 19(11): 1257–1264.
[8] Tessler FN, Middleton WD, Grant EG, et al. ACR Thyroid Imaging, Reporting and Data System=(TI-RADS): white paper of the ACR TI-RADS Committee[J]. J Am Coll Radiol, 2017, 14(5): 587-595.
[9] Moon WJ, Baek JH, Jung SL, et al. Ultrasonography and the ultrasound-based management of thyroid nodules: consensus statement and recommendations[J]. Korean J Radiol, 2011, 12(1): 1-14.
[10] Russ G., Royer B., Bigorgne C., et al. Prospective evaluation of thyroid imaging reporting and data system on 4550 nodules with and without elastography[J]. Eur J Endocrinol, 2013, 168(5): 649–655.
[11] SHIN JH, BAEK JH, CHUNG J, et al. Ultrasonography Diagnosis and Imaging-Based Management of Thyroid Nodules: Revised Korean Society of Thyroid Radiology Consensus Statement and Recommendations[J]. Korean J Radiol, 2016, 17(3): 370-395.
[12] Tessler FN, Middleton WD, Grant EG, et al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): white paper of the ACR TI-RADS Committee[J]. J Am Coll Radiol, 2017, 214(5): 587-595.
[13] Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines task force on thyroid nodules and differentiated thyroid cancer[J]. Thyroid, 2016, 26(1):1-133.
[14] Cox AE, LeBeau SO. Diagnosis and treatment of differentiated thyroid carcinoma[J]. Radiol Clin North Am, 2011, 49(3): 453-462.
[15] Guth S., Theune U., Aberle J., et al. A very high prevalence of thyroid nodules detected by high frequency(13 MHz) ultrasound examination[J]. Eur J Clin Invest, 2009, 39(8): 699-706.
[16] Bingyin S. Thyroid Nodules: From Confusion to Clarity [J]. International Journal of Endocrinology and Metabolism, 2022, 42(2): 93-95.
[17] Yang S., Bing W., Yixue S. Comparative Study of Three Thyroid Nodules Risk Stratification Systems C-TIRADS, ACR-TIRADS, and KTA/KSThR-TIRADS [J]. Journal of Bengbu Medical College, 2024, 49(3): 381-385.
[18] Linlin Z., Shiyan L., Lilong X., et al. Comparative Study of Thyroid Nodule Malignancy Risk Stratification: C-TIRADS, ACR-TIRADS and KTA/KSThR-TIRADS [J]. Chinese Journal of Ultrasonography, 2021, 30: (09): 785-791.
[19] Miaomiao C. Comparative Diagnostic Value of C-TIRADS and ACR-TIRADS in Malignancy Risk Stratification of Thyroid Nodules [D]. Jilin University, 2023.
[20] Wenbin L., Jinyan Q., Zhengren O. Diagnostic Value of ATA, ACR-TIRADS and C-TIRADS Classification Standards for Thyroid Nodules [J]. Central South Medical Science Journal, 2022, 50(6): 879-882.
[21] Siyue D., Quanquan D., Yan W., et al. Comparative Study on the Diagnostic Performance of C-TIRADS and ACR TI-RADS in Thyroid Nodules [J]. Chinese Journal of Ultrasonic Medicine, 2021, 37(9): 964-969.
[22] Li L. A Comparative Study on the Clinical Diagnosis and Management Value of C-TIRADS and ACR-TIRADS Classification for Thyroid Nodules [D]. Guangxi Medical University, 2022.