Diagnostic Efficacy of ^{131}I-SPECT/CT in Detecting Postoperative Residual and Recurrent Lesions in Patients With Differentiated Thyroid Cancer: A Meta-Analysis

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AIM: Single-photon emission computed tomography/computed tomography (SPECT/CT) technology is a promising imaging tool for the detection of postoperative residual and recurrent lesions in differentiated thyroid cancer (DTC). However, existing studies presented mixed results, and the overall diagnostic efficacy of this technology remains unclear. Therefore, this meta-analysis was conducted to systematically evaluate the diagnostic value of ^{131}I-SPECT/CT for identifying residual or recurrent disease in patients with DTC.

METHODS: A systematic literature search was conducted across PubMed, Web of Science, EMBASE, and Cochrane Library from inception to 4 December 2025. The search strategy incorporated relevant keywords and MeSH terms, such as "differentiated thyroid cancer", "thyroidectomy", "SPECT", "SPECT/CT", "SPECT-CT", "metastasis", "recurrence", and "residual". Study selection, data extraction, and risk-of-bias assessment were performed independently by two investigators. The overall diagnostic performance was assessed by calculating the pooled sensitivity (SENS), specificity (SPEC), and summary receiver operating characteristic (SROC) curve. Sensitivity analyses were performed by excluding individual studies to assess the robustness and stability of the pooled results. Subgroup analysis was used to determine the source of heterogeneity.

RESULTS: Six studies involving 800 patients were included. Pooled analysis showed that lesion-level ^{131}I-SPECT/CT had a pooled SENS of 0.59 (0.33–0.81) and a pooled SPEC of 0.92 (0.85–0.96). The pooled diagnostic odds ratio (DOR) was 18 (3–91), and the area under the curve (AUC) was 0.92. Based on patient-level ^{131}I-SPECT/CT, the pooled SENS was 0.89 (0.63–0.98), the pooled SPEC was 0.95 (0.70–0.99), and the DOR was 166 (7–4126). The AUC of the SROC curve was 0.97. The overall diagnostic accuracy of ^{131}I-SPECT/CT was confirmed, regardless of whether it was conducted at the patient or lesion level. To avoid potential patient overlap, we excluded an earlier study for a sensitivity analysis. The results after exclusion remained within reasonable limits, supporting the robustness of the main findings. Subgroup analyses indicated that patient type may be a potential source of heterogeneity in the non-threshold effect. No publication bias was statistically suggested through Deeks' funnel plot.

CONCLUSIONS: ^{131}I-SPECT/CT demonstrates efficacy for the targeted detection of postoperative residual and recurrent lesions in DTC, showing high diagnostic accuracy. However, existing evidence is subject to high heterogeneity, and clinical application should be carefully interpreted in combination with the specific characteristics of patients. Future higher-quality studies conducted using unified standards are needed to further verify its clinical value.

Keywords: ^{131}I-single-photon emission computed tomography/computed tomography; differentiated thyroid cancer; recurrence; lesion detection; diagnosis; meta-analysis

Introduction

Differentiated thyroid cancer (DTC) primarily comprises papillary and follicular carcinomas [1,2]. Although most patients have a favorable prognosis, a subset still develop residual or recurrent lesions after initial treatment, facing a significant risk of a decline in long-term survival and quality of life [2,3]. Accurate identification of the location of residual or recurrent lesions is thus crucial for guiding subsequent treatment decisions [4].

The traditional postoperative monitoring methods rely on the determination of serum thyroglobulin (Tg), cervical ultrasound, and diagnostic whole-body radioactive iodine scan. However, each method has its limitations. Elevated Tg levels often indicate disease recurrence, but such information does not often indicate accurate details concerning the anatomic location of lesions [5,6]. Although cervical ultrasound scans can be quite accurate in detecting cervical lymph node metastasis, they may miss distant metastases or lesions in regions with limited acoustic windows [7]. Although ^{131}I or ^{123}I diagnostic whole-body planar imaging

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remains the cornerstone of functional imaging in DTC, its planar nature lacks precise anatomical detail, which may lead to misdiagnosis [8,9].

In recent years, the combined application of single-photon emission computed tomography/computed tomography (SPECT/CT) has significantly improved the diagnostic efficiency of radioactive iodine imaging. ^{131}I-SPECT/CT provides co-registered functional and high-resolution anatomical information for precise localization. It improves the accuracy of detecting, characterizing, and staging iodine-avid lesions [10]. This hybrid imaging technique has demonstrated substantial clinical value in clarifying suspicious findings on conventional planar imaging, effectively distinguishing physiological from pathological uptake, and detecting small or anatomically complex residual and recurrent foci [11]. Despite increased and broader adoption of ^{131}I-SPECT/CT in clinical practice, its diagnostic efficacy in the detection of residual or recurrence after DTC remains incompletely deciphered through meta-analysis. The sensitivity and specificity reported in previous studies present huge variations, and these metrics are subject to the confounding impacts of patient selection, imaging protocols, and reference standards. Therefore, a comprehensive meta-analysis of existing studies is warranted to clarify the diagnostic value of ^{131}I-SPECT/CT in such clinical scenarios.

This study aims to assess the diagnostic performance of ^{131}I-SPECT/CT in identifying residual or recurrent lesions in DTC patients after surgery through meta-analysis, with the expectation of providing a basis for formulating evidence-based imaging guidelines and optimizing postoperative monitoring strategies.

Methods

This meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement. The completed PRISMA 2020 checklist is provided in the **Supplementary Material 1**.

Search Strategy

This review was not registered, and no protocol was prepared. Two reviewers independently conducted the literature search and screened studies for eligibility. Any disagreements were resolved through discussion with a third reviewer. Literature search was conducted through PubMed, EMBASE, Cochrane Library, and Web of Science, targeting studies published since the inception of these databases until 4 December 2025. The search strategy was constructed using a three-concept block design with Boolean operators: Concept A (disease): "differentiated thyroid cancer", "thyroidectomy". Concept B (imaging modality): "SPECT", "SPECT/CT", "SPECT-CT". Concept C (target condition): "recurrence", "metastasis", and "residual". Group logic: Concepts were combined as "A" AND "B" AND "C". Terms within each concept were combined with OR. The complete search strategies for all databases are provided in the **Supplementary Materials 2**.

Quality Assessment

The quality of the included study was assessed using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool [12], which evaluates the risk of bias and concerns regarding applicability across four domains: patient selection, index test, reference standard, and flow and timing. Each study was rated as having a high, low, or unclear risk of bias based on a series of questions. Two reviews independently assessed all included studies, with disagreements resolved through discussion or, if necessary, consultation with a third reviewer. No automation tools were used in the risk-of-bias assessment process.

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria: (1) evaluated the role of ^{131}I-SPECT/CT in the locating residual or recurrent DTC after thyroidectomy; (2) used an appropriate reference standard; and (3) provided sufficient data to extract the numbers of true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN). Studies were excluded if they: (1) did not focus on SPECT/CT; (2) used tracers other than ^{131}I (e.g., ^{123}I, ^{18}F-FDG); (3) were animal studies; or (4) were letters, abstracts, reviews, and case reports.

Data Extraction

Data were extracted by two investigators independently, including first author, publication year, study design, country, sample size, patient characteristics (age, sex, type of DTC, number of radioiodine therapy [RAI] received), reference standard, and diagnostic accuracy outcomes (TP/TN/FP/FN). When numerical data were not directly reported but could be derived from sensitivity, specificity, and sample size, we calculated TP/TN/FP/FN values accordingly. If critical data were missing or unclear, the corresponding author was contacted via email (up to two attempts). Studies for which no response was received were excluded from the relevant quantitative analysis. For studies with potential patient overlap (e.g., same institution and overlapping recruitment periods), the larger or more recent study was included, and sensitivity analyses were performed to assess the impact. Based on the unit of analysis, the studies were categorized into patient-level and lesion-level analyses, and a separate meta-analysis was conducted for each level.

Statistical Analysis

Based on their unit of analysis (as pre-specified in the "Methods" section), studies were categorized as either patient-level or lesion-level analyses. Data were analyzed using Meta-Disc 2.0 and Stata 18.0 (manufacturer: Stat-

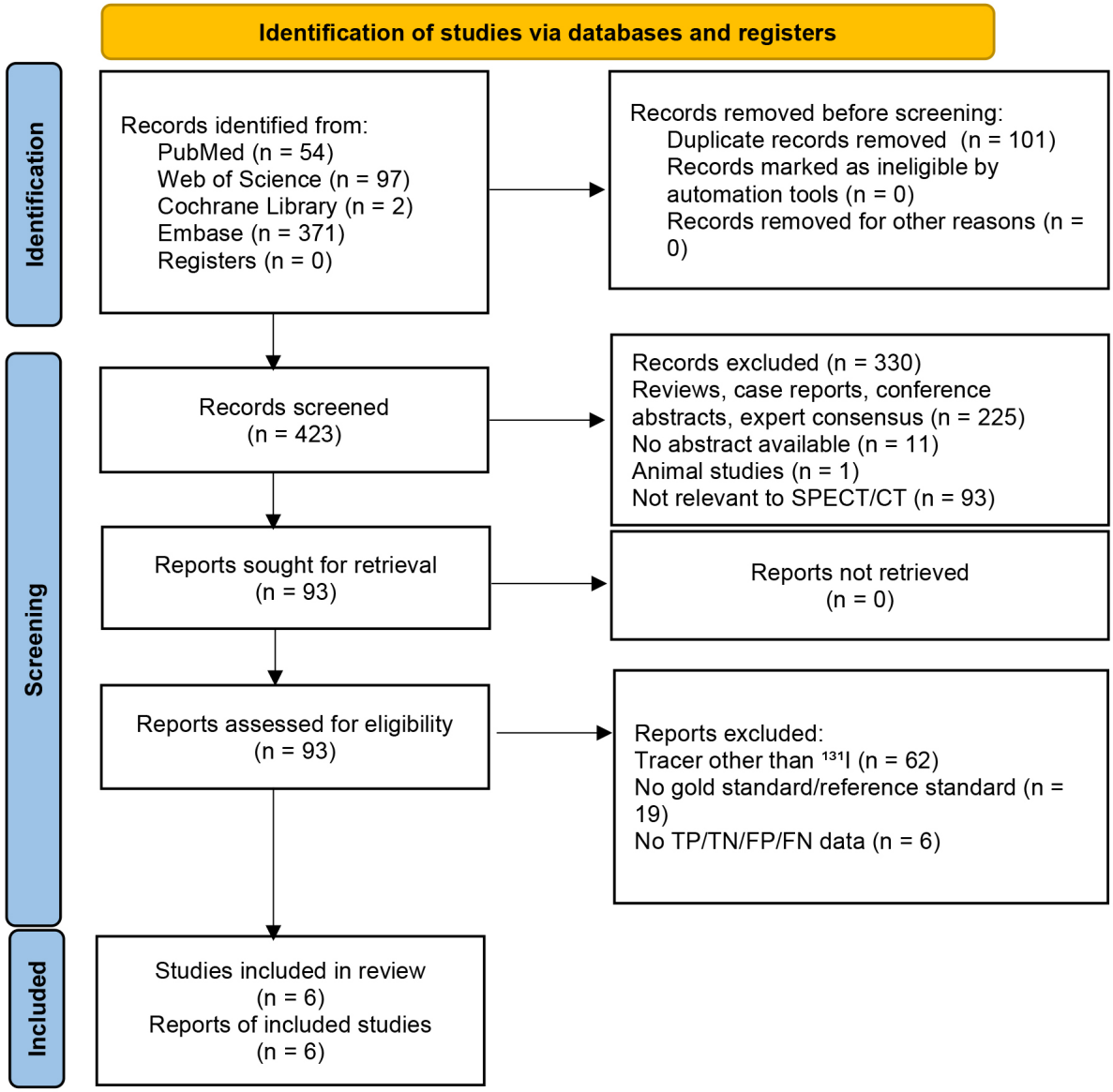

Fig. 1. Flowchart depicting the study screening process. SPECT/CT, single-photon emission computed tomography/computed tomography; TP, true positives; TN, true negatives; FP, false positives; FN, false negatives.

aCorp LLC) software. Summary estimates of sensitivity (SENS), specificity (SPEC), positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR), all with 95% confidence intervals, were obtained with the use of the bivariate random-effects model in Stata 18.0 (midas command). Summary receiver operating characteristic (SROC) curves were generated using Stata 18.0 (midas command) to visually display the overall diagnostic performance. Subgroup analyses were performed using Meta-Disc 2.0 to explore potential sources of non-threshold heterogeneity for the differences in non-threshold effects. Sensitivity analyses were conducted to assess the robustness of the pooled estimates. Publication bias was evaluated using Deeks' funnel plot in Stata 18.0 software, with $p < 0.05$ indicating the presence of bias.

Results

Included Studies

Through systematic retrieval, 524 relevant studies were obtained, including 54 studies in the PubMed database, 97 studies in the Web of Science database, 2 studies in the Cochrane Library database, and 371 studies in the Embase database. After eliminating duplicate studies, 423 studies remained. Six studies were included in the final analysis. The study selection process, including detailed reasons for exclusion at each stage, is illustrated in Fig. 1.

Study Quality Assessment

The results of the QUADAS-2 assessment are shown in Fig. 2. Among the six included studies, three were considered to have a low risk of bias in patient selection for

Table 1. Characteristics of the included studies.

No.	First author	Year	Region	Research type	Sample size	Gender (male/female)	Age (years)	Type of DTC			Number of RAI received	Reference standard
								PTC	FTC	Others		
1	Hongyuan Dai [13]	2023	China	Retrospective	53	25/28	7–69	46	6	1	One time	Pathology
2	Julia V Malamitsi [14]	2019	Greece	Prospective	58	25/33	30–82	58			One time	Pathology, follow-up, imaging, and Tg changes
3	Angela Spanu [15]	2018	Italy	Retrospective	351	77/ 274	18–81	351			One time	Pathology, follow-up, imaging, and Tg changes
4	Jong-Ryool Oh [16]	2011	South Korea	Retrospective	140	30/110	21–81	128	12		One time (101); multiple times (39)	Pathology, follow-up, imaging, and Tg changes
5	Daniela Schmidt [17]	2010	Germany	Retrospective	81	32/49	13–86	73	7	1 (both PTC and FTC were diagnosed)	One time	Pathology, follow-up, and imaging
6	Angela Spanu [18]	2009	Italy	Prospective	117	28/89	21–81	109	7	1 (Hürthle cell carcinoma)	Varying	Pathology, follow-up, imaging, and Tg changes

DTC, differentiated thyroid cancer; FTC, follicular thyroid carcinoma; PTC, papillary thyroid carcinoma; Tg, thyroglobulin; RAI, radioiodine therapy.

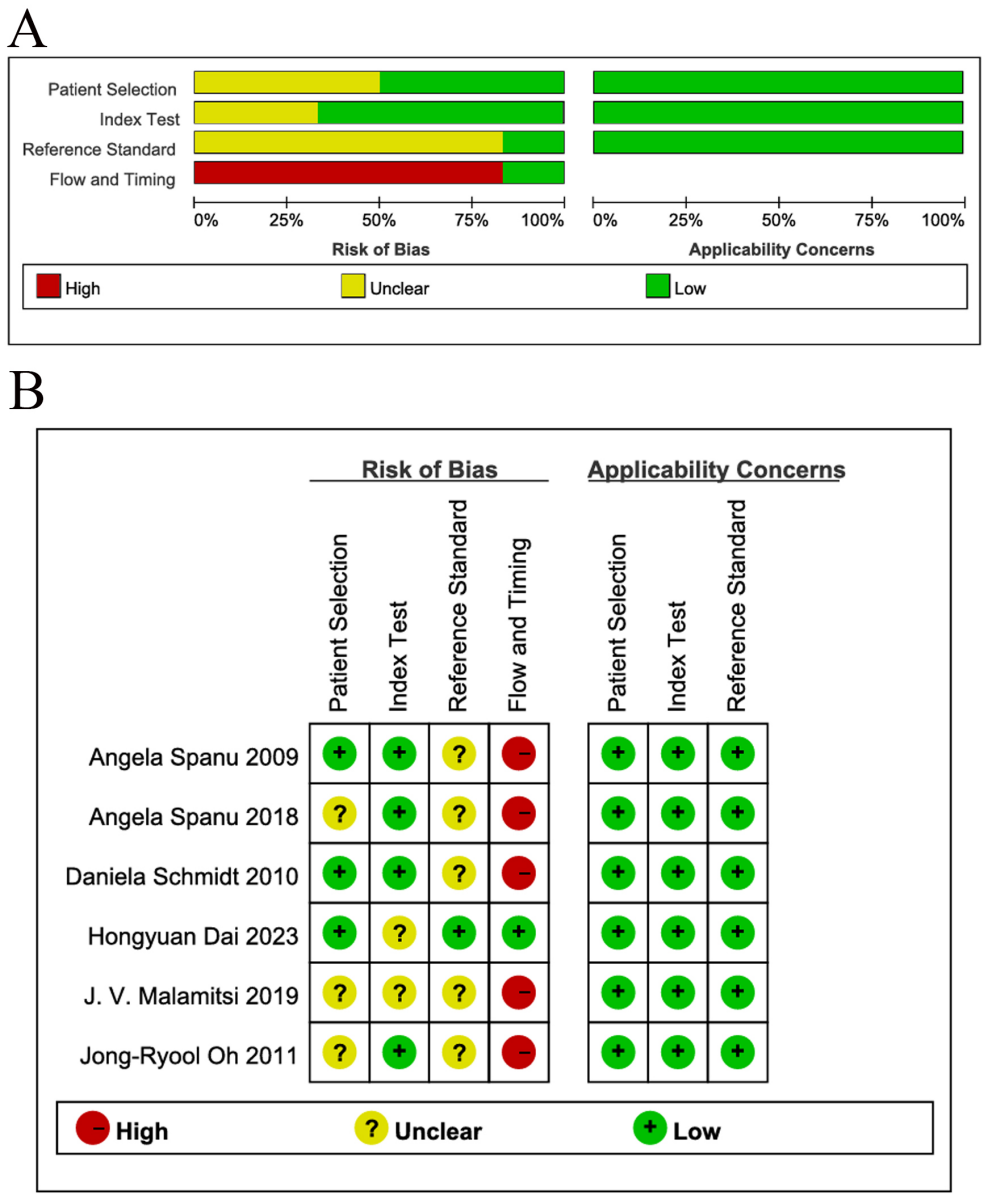

Fig. 2. Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) assessment results of study quality. (A) Proportion of studies with high/low/unclear risk in each domain. (B) Summary of assessments for all studies.

consecutive patient groups, while the risk remained unclear in the other three. Four studies were considered as having a low risk of bias for index test interpretation, as ^{131}I-SPECT/CT results were assessed without knowledge of the reference standard, whereas the risk was unclear in two studies. Establishing a consistent reference standard remains a challenge in studies evaluating the diagnostic performance of different techniques. Because DTC is highly associated with multiple local or distant metastases, it is difficult to obtain a histopathological analysis of all lesions. Therefore, in addition to histopathological data, clinical and imaging follow-up data or serum thyroglobulin (Tg) levels were also used as the reference standard. One study utilized histopathology as the reference standard. In the five studies, a comprehensive reference standard combining histopathology, clinical follow-up, imaging findings, and Tg levels was used. Therefore, regarding the reference standard, one study was considered as having a low risk of bias, and the risk in five studies remained unclear due to the use of composite reference standards. Regarding flow and timing, one study was rated as a low risk of bias, while the remaining studies were rated as high risk. In terms of clinical applicability, all six studies were considered to have a low risk of bias for patient selection, the clinical relevance of ^{131}I-SPECT/CT, and the applicability of the reference standard.

Characteristics of the Included Studies

As shown in Table 1 (Ref. [13–18]), the six studies included in this analysis were published between 2009 and 2023. Among them, two were prospective studies, while the re-

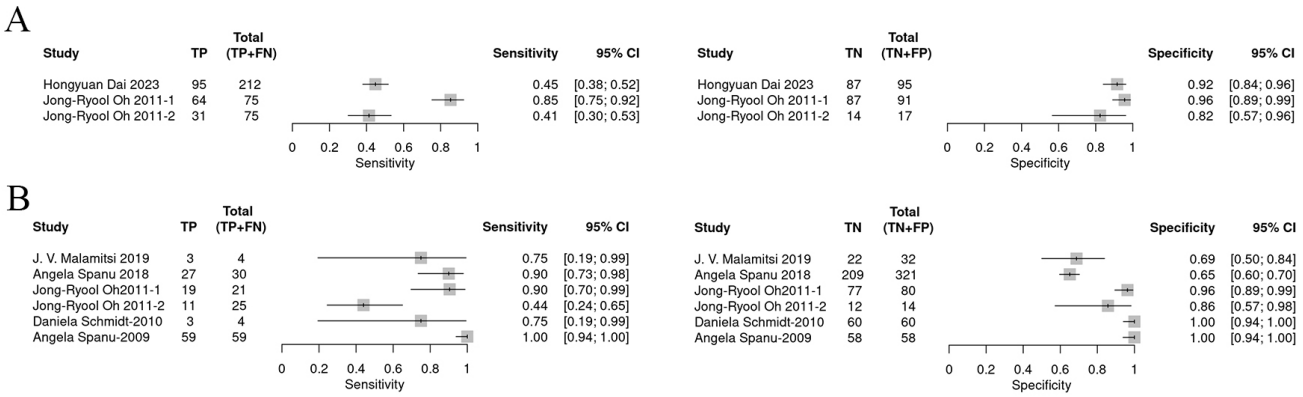

Fig. 3. Forest plots of sensitivity and specificity for ^{131}I-SPECT/CT in detecting residual/recurrent differentiated thyroid cancer (DTC). (A) Lesion-level analysis, and (B) patient-level analysis.

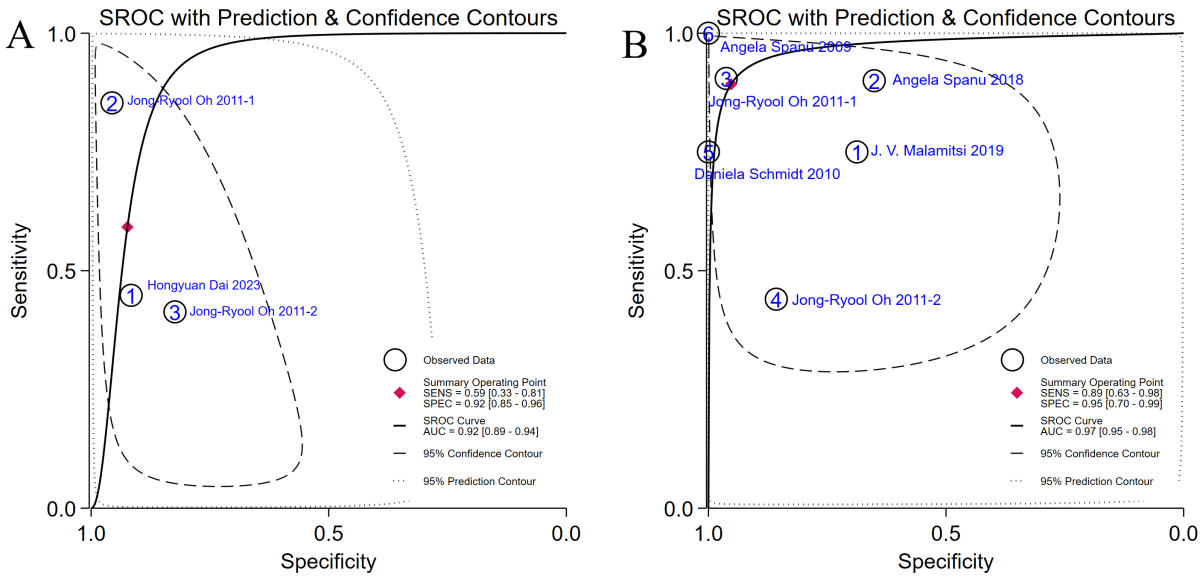

Fig. 4. Summary receiver operating characteristic (SROC) curve based on the diagnostic accuracy of lesion-level and patient-level ^{131}I-SPECT/CT. (A) Lesion-level analysis, and (B) patient-level analysis. SENS, sensitivity; SPEC, specificity; AUC, area under the curve.

maining four were retrospective. All patients surveyed in these studies had DTC and had received at least one RAI treatment. The inclusion of these six studies contributed a total of 800 patients for the analysis.

Overall Analysis

In lesion-level analysis, two studies (providing three datasets) were included, with the sensitivity and specificity of individual studies presented in Fig. 3A. Five studies (providing six datasets) were included in the patient-level analysis, and the sensitivity and specificity of individual studies are shown in Fig. 3B. Malamitsi *et al.* [14] categorized patients into single-treatment and multiple-treatment groups. In the present analysis, we applied the same classification approach as described in the study of Malamitsi *et al.* [14]. For lesion-level analysis, the pooled SENS was 0.59 (0.33–0.81), the pooled SPEC was 0.92 (0.85–0.96), the pooled PLR was 7.7 (2.8–21.3), and the pooled NLR was 0.44 (0.22–0.87). The pooled DOR was 18 (3–91), and the area under the SROC curve was 0.92 (Fig. 4A). All these metrics indicate that the SPECT/CT has a high level of diagnostic performance, without significant statistical heterogeneity ($p = 0.191$). Since the analysis included only three studies, the stability of pooled estimates may be limited; therefore, these findings should be considered preliminary and exploratory, and their reliability remains to be confirmed by additional studies.

The patient-level analysis yielded a pooled SENS of 0.89 (0.63–0.98), a pooled SPEC of 0.95 (0.70–0.99), a pooled PLR of 18.7 (2.3–153.8), a pooled NLR of 0.11 (0.03–0.49), and a pooled DOR of 166 (7–4126). The area under the SROC curve, used to assess the overall accuracy of the diagnostic test, for the patient-level analysis was 0.97 (Fig. 4B), suggesting favorable diagnostic performance within the in-

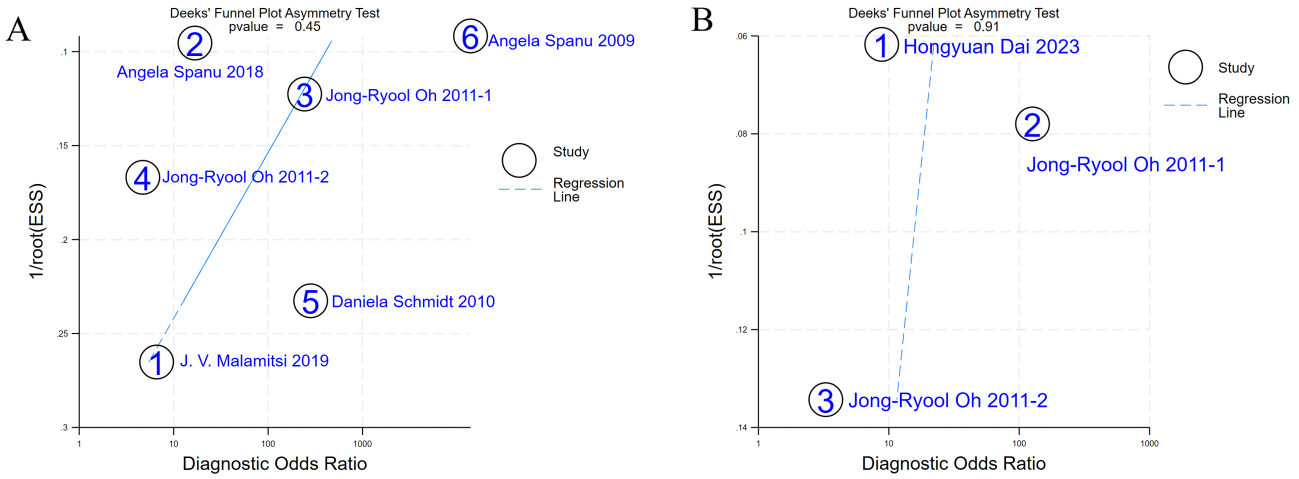

Fig. 5. Deeks' funnel plots for the assessment of publication bias. (A) Patient-level analysis, and (B) lesion-level analysis. ESS, effective sample size.

Table 2. Subgroup analyses based on the patient level.

Variables	Subgroup	Sensitivity (95% CI)	*p*	Specificity	*p*
Study type	Prospective	0.977 (0.690–0.999)	0.195	0.818 (0.485–0.956)	0.759
	Retrospective	0.968 (0.422–0.999)		0.940 (0.607–0.994)	
DTC type	PTC	0.886 (0.385–0.990)	0.871	0.654 (0.437–0.821)	0.017
	Other than PTC	0.910 (0.588–0.986)		0.976 (0.929–0.992)	

cluded studies. However, significant heterogeneity was detected ($p = 0.001$), and the small number of studies limits the generalizability of this finding. Therefore, the result should be interpreted as exploratory rather than conclusive.

Sensitivity Analysis

We performed sensitivity analyses to assess possible patient overlap between the two studies by Spanu *et al*. (2009 and 2018) [15,18], because the studies were conducted by the same research group and may have included patients from similar clinical settings. We excluded older study (Spanu *et al*., 2009 [18]) and repeated the meta-analysis using the remaining studies. After exclusion, ^{131}I-SPECT/CT had a pooled SENS of 0.79 (0.56–0.92), a pooled SPEC of 0.91 (0.67–0.98), and a DOR of 36.30 (5.76–228.70). These estimates were generally consistent with the results of the primary analysis, but there were some expected variations given the limited number of included studies.

Subgroup Analysis

As shown in Table 2, to explore potential sources of heterogeneity, subgroup analyses were performed based on study design and DTC type, respectively. There was no significant difference in the pooled sensitivity and pooled specificity between the prospective studies and the retrospective studies ($p > 0.05$), suggesting that study design was not the main source of heterogeneity. The pooled specificity of papillary thyroid carcinoma (PTC) was 0.654 (0.437–0.821), which was significantly lower than 0.976 (0.929–0.992) of the other than PTC category ($p = 0.017$). There was no significant difference in the pooled sensitivity between the two groups ($p = 0.871$). DTC type may be a potential source of heterogeneity. However, given the limited number of studies included in each subgroup, these findings should be interpreted with caution and are considered hypothesis-generating rather than definitive. Further validation in larger, well-designed studies is warranted.

Bias of Publication

As shown in Fig. 5, publication bias was evaluated through the Deeks' funnel plot. For the combined analyses at the patient ($p = 0.45$) (Fig. 5A) and lesion levels ($p = 0.91$) (Fig. 5B), no evidence of publication bias was detected. However, due to the very small number of included studies, the power of Deeks' test is limited, and the possibility of publication bias cannot be excluded.

Discussion

Patients with DTC often face the risk of residual disease and recurrence after surgery, and its accurate detection is very crucial for the development of individualized treatment strategies and prognosis evaluation. Postoperative ^{131}I whole-body scan is a conventional functional imaging method to evaluate residual and recurrent lesions, but it exhibits limited capability in accurately locating and qualitatively identifying lesions, especially in complex regions such as cervical lymph nodes, mediastinum, and bone

metastases [19]. By combining functional information with fine anatomical structure, ^{131}I-SPECT/CT serves as a potential tool for improving diagnostic accuracy in DTC contexts.

In this meta-analysis, we evaluated the diagnostic efficacy of ^{131}I-SPECT/CT in the detection of postoperative residual and recurrent DTC lesions. The results showed that ^{131}I-SPECT/CT demonstrated favorable diagnostic performance for the detection of postoperative residual and recurrent DTC lesions at both the patient and lesion levels. In this study, heterogeneity was observed at both patient- and lesion-level analyses. No threshold effect was identified at the patient level. Subsequently, we conducted a subgroup analysis and found that the heterogeneity at the patient level stemmed from the type of DTC; specifically, a study included all patients with PTC, while another study encompassed those other than PTC, leading to fundamental analytical differences in ^{131}I-SPECT/CT [20]. Due to the small number of studies included in each subgroup, these analyses should be considered exploratory in nature. There was significant heterogeneity of the threshold effect at the lesion level, but subgroup analysis was not performed due to the small number of included studies.

Despite the heterogeneity, the pooled results of the random-effects model showed that the areas under the patient-level and the lesion-level SROC curves were 0.97 and 0.92, respectively, suggesting favorable overall diagnostic performance within the included studies. Early and accurate identification of postoperative residual and recurrence is of great clinical significance for initiating intervention and improving the prognosis of patients. According to the results of this study, ^{131}I-SPECT/CT demonstrates high specificity in clinical diagnosis of lesions, precluding patients from unnecessary treatments. Meanwhile, its relatively limited sensitivity indicates that negative results cannot reliably exclude the presence of small or low-iodine-uptake lesions. Therefore, interpretation should be made comprehensively in combination with serum Tg levels and other indicators.

In our study, the pooled sensitivity at the patient level (0.89) was significantly higher than that at the lesion level (0.59), with the pooled specificity also outperforming at the patient level than at the lesion level (0.95 vs. 0.92). This difference may be attributed to the following reasons: in patient-level analysis, the presence of any recurrent or residual lesion is considered a positive finding. In contrast, lesion-level analysis requires individual evaluation of each suspicious site, making it more susceptible to the effects of small lesions, low-iodine-uptake lesions, and complex anatomical regions, which can increase the likelihood of false-negative results. Secondly, the detection of some lesions was realized without a pathological reference standard and relied on imaging, Tg changes, and follow-up instead, which may lead to an underestimation of sensitivity at the lesion level. Therefore, patient-level analysis may be more appropriate for assessing overall recurrence status, whereas lesion-level analysis may help guide local treatment decisions in clinical practice.

The above findings suggest that ^{131}I-SPECT/CT demonstrates promising diagnostic accuracy, but we note that the two included articles published by Spanu's *et al*. group (2009 and 2018) [15,18] may present overlapping patient populations, which may affect the confidence of the results if the same patients were included twice. To determine whether this affected our main conclusions, we removed the earlier article (2009) and conducted sensitivity analyses, which showed that sensitivity, specificity, and diagnostic odds ratios varied slightly compared with the primary analyses but remained within acceptable ranges. These results suggest that our primary findings are relatively robust, although the potential overlap cannot be completely ruled out. This finding supports the incremental value of SPECT/CT fusion technology in providing precise anatomical localization and enhanced characterization of equivocal foci, as suggested by previous studies [10,11].

Several limitations of this study should be acknowledged. (1) With a small sample of included studies, the findings of this study could be subject to some biases in terms of diagnostic efficacy. (2) Due to the inadequacy of details reported in the original studies, all potential sources of heterogeneity, such as detailed CT slice thickness and iterative reconstruction algorithm, could not be further analyzed in subgroup analysis. (3) Due to the lack of studies at the lesion level, subgroup analysis was not performed. (4) Regarding the review process, although we conducted a comprehensive search across four major databases, the exclusion of non-English studies may have introduced publication or language bias. (5) The subgroup analyses were based on a limited number of studies, and the results should therefore be regarded as exploratory. Thus, caution is warranted when interpreting these findings. (6) Two studies (Spanu *et al*., 2009 and 2018 [15,18]) originated from the same research group and may include overlapping patient populations. Although sensitivity analysis excluding the earlier study yielded generally consistent results, partial overlap cannot be completely ruled out and may have influenced the pooled estimates. These findings should therefore be interpreted with caution. (7) This study did not account for tumor dedifferentiation over time, which may reduce iodine avidity and lower the sensitivity of ^{131}I-SPECT/CT. In such cases, detection via ^{18}F-FDG PET/CT may be more appropriate. Additionally, serum Tg levels provide critical information for recurrence detection but were not consistently reported in the original studies. These shortcomings should be considered when interpreting the results. In the future, more well-designed prospective multicenter studies with standardized protocols are needed to further consolidate the evidence base and clarify the optimal application of ^{131}I-SPECT/CT in DTC patients across different risk stratifications.

Taken together, this meta-analysis suggests that ^{131}I-SPECT/CT is a promising imaging tool for the detection of postoperative residual and recurrent lesions in patients with DTC. Its high specificity and accurate anatomical localization capability may offer added value in differential diagnosis and clinical decision-making, particularly when conventional imaging findings are inconclusive. However, due to the limited number of available studies and their inherent heterogeneity, the current evidence is insufficient to support firm conclusions regarding its routine clinical application. In addition, the biological behavior of differentiated thyroid cancer may evolve over time, with some tumors becoming less iodine-avid and more aggressive, which may affect the diagnostic performance of ^{131}I-SPECT/CT. In such cases, other imaging modalities, such as PET/CT, may be more sensitive. Furthermore, serum thyroglobulin levels remain an important adjunct for detecting disease recurrence. Further high-quality studies are warranted to validate these findings.

Conclusions

This meta-analysis suggests that ^{131}I-SPECT/CT is a promising imaging modality for detecting postoperative residual and recurrent lesions in patients with DTC. This fusion technology demonstrates excellent diagnostic performance, providing a reliable basis for disease confirmation. By combining functional and anatomical information, this strategy holds high application value in clarifying suspicious findings on planar imaging and guiding clinical decision-making. However, given the limited number of included studies, substantial heterogeneity, and methodological limitations, the current evidence should be considered preliminary, and no definitive recommendations for clinical practice can be made at this stage. Future studies should focus on well-designed prospective multicenter studies with standardized protocols to validate these findings, optimize imaging strategies for different risk groups, and further clarify the role of ^{131}I-SPECT/CT in postoperative monitoring of DTC.

Availability of Data and Materials

All data supporting this study are included in this article. The data analyzed are available from the corresponding author upon reasonable request.

Author Contributions

WPL and RZL designed the research study. YXZC and QGG performed the research. JJZ analyzed the data. WPL drafted the article. All authors have been involved in revising the manuscript critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.62713/aic.4495.

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