



REVIEW ARTICLE

Validity of core needle biopsy in diagnosing primary thyroid lymphoma: a systematic-review and meta-analysis

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ABSTRACT

BACKGROUND

Primary thyroid lymphoma (PTL) is a rare thyroid malignancy, accounting for less than 5% of thyroid malignancies. The prognosis of PTL depends on the histologic subtype and stage of disease at diagnosis, hence an effective diagnostic method is needed to ensure prompt treatments. Fine needle aspiration (FNA) is the first test for microscopic examination of a rapidly enlarging thyroid mass, but its limitations and low sensitivity have been observed. After the often “inconclusive” result is known, core-needle biopsy (CNB) should be performed as the natural next diagnostic step. This systematic review and meta-analysis aimed to evaluate the diagnostic value of core needle biopsy (CNB) in diagnosing PTL.

METHODS

This systematic review and meta-analysis follows the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. A PubMed and Embase database search was performed in August 2025. Populations included were patients with final diagnosis of PTL. Pooled sensitivity was calculated using a random-effects model.

RESULTS

This systematic review and meta-analysis of 12 studies comprised a total of 1091 patients. Core needle biopsy proved to be highly effective, with a pooled sensitivity of 91.6% (95% CI: 82.1%–96.3%). The development of tumor-cell seeding following CNB has been a major concern, but this complication is extremely rare. Other potential complications include bleeding and infection.

CONCLUSION

Core needle biopsy demonstrates high diagnostic sensitivity and a favorable safety profile in diagnosing primary thyroid lymphoma, supporting its role as a valuable diagnostic modality, particularly when PTL is clinically suspected or FNA results are inconclusive.

Keywords: Core needle biopsy, primary thyroid lymphoma, thyroid carcinoma, thyroid malignancy diagnosis

INTRODUCTION

Primary thyroid lymphoma (PTL) is a rare thyroid malignancy, accounting for <5% of thyroid cancers and ~2% of extranodal lymphomas, with an estimated annual incidence of approximately 2 cases per million population.^(1,2) While Hashimoto's thyroiditis is a well-established risk factor, only about 0.5% of individuals with Hashimoto's thyroiditis progress to PTL.⁽³⁾ Consequently, PTL is more common in women than in men (approximately 8:1) and typically presents in the sixth to seventh decades of life. Its clinical presentation is often similar to that of anaplastic thyroid carcinoma, typically affecting women aged 60–70 years and manifesting as a rapidly enlarging neck mass over weeks to months, frequently accompanied by compressive symptoms such as neck pain, dysphagia, hoarseness, and stridor. However, despite these similarities in presentation, prognosis and management differ substantially.^(4,5) Urgent management would benefit from an evidence-based strategy excluding unnecessary delays in reaching a precise diagnosis. Unlike thyroid carcinomas that arise from follicular cells, PTL originates from lymphoid tissue, most frequently B lymphocytes; therefore, its management differs substantially from that of other thyroid malignancies, with systemic therapy (e.g., chemotherapy, with or without radiotherapy) as the cornerstone of treatment.^(6,7)

Tissue diagnosis using ultrasound-guided cytology and/or histology is essential for establishing an accurate diagnosis. Fine-needle aspiration (FNA), ideally performed with ultrasound guidance and rapid on-site assessment when available, remains the standard first-line test for evaluating thyroid nodules because it is effective and economical for determining malignancy and guiding the need for surgery.⁽⁶⁻⁸⁾ However, FNA has limited diagnostic accuracy for PTL and often necessitates additional procedures or diagnostic surgery for confirmation.^(9,10) In real-world practice, FNA sensitivity has been reported to be approximately 48% for PTL, and around 50–61% for anaplastic thyroid carcinoma (ATC), highlighting the challenges of cytology-based diagnosis in aggressive or

uncommon thyroid malignancies.⁽¹¹⁾ This may be due to the overlapping features with those of thyroid malignancy in the ultrasound imaging, showing hypoechoic nodules.⁽¹²⁾ Moreover, the results may also show up as non-diagnostic or indeterminate.⁽¹²⁾ Some patients had also been reported to undergo unnecessary thyroidectomy due to atypical findings from FNA.⁽¹¹⁾ Thyroid lymphoma often develops on a background of Hashimoto's thyroiditis (HT), chronic autoimmune stimulation being considered as the main trigger for malignant transformation.⁽¹³⁾ Because of these diagnostic challenges, alternative diagnostic approaches have been explored.

Some experts had suggested that in suspected cases of thyroid lymphoma (TL), core needle biopsy (CNB) may reduce the need for diagnostic surgery and, more importantly, facilitate early diagnosis, allowing timely initiation of chemotherapy as the mainstay of treatment for lymphomas.^(3,11,14,15) Na et al.⁽¹⁶⁾ recommended immediate CNB in patients with thyroid masses with uncommon clinical and radiological features, the recommendation being based on a small number of retrospective cohort studies, not specific for ATC and TL.

However, in general practice setting, CNB itself is still considered an alternative method to evaluate thyroid masses due to the use of a large needle and the need for an experienced operator with specific training. Core needle biopsy has also been associated with several limitations such as bleeding, tumor cell seeding and complications due to technical difficulties in approaching areas close to the carotid artery or trachea.⁽¹⁶⁾ For diagnosing malignant lymphomas in the neck outside the thyroid, as well as for the more common thyroid neoplasms, CNB has yielded satisfactory results with reported sensitivities of up to 100%.⁽¹⁷⁾ In the narrower context of diagnosing ATC and TL, a thorough review of the reliability of CNB is lacking. Hence, our study aims to evaluate the diagnostic value of CNB in diagnosing uncommon thyroid malignancy, specifically in PTL cases.^(16,18,19) This prompted the present systematic review and meta-analysis, to assess the value of CNB in diagnosing primary thyroid lymphoma by calculating sensitivity.

METHODS

Protocol registration and reporting

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.⁽²⁰⁾ The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD420261324472 (available at: <https://www.crd.york.ac.uk/PROSPERO/view/CRD420261324472>).^(21,22)

Search strategy

A systematic literature search was conducted in PubMed, ProQuest, Scopus, and ScienceDirect. The search strategy combined relevant keywords and Boolean operators as follows: (“core needle biopsy”) AND (“primary thyroid lymphoma” OR “thyroid lymphoma”). Records were exported to Microsoft Excel 2020 for management and screening. As this was a systematic review of published data, ethics approval and informed consent were not required. The study selection process is summarized in a PRISMA flow diagram (Figure 1).

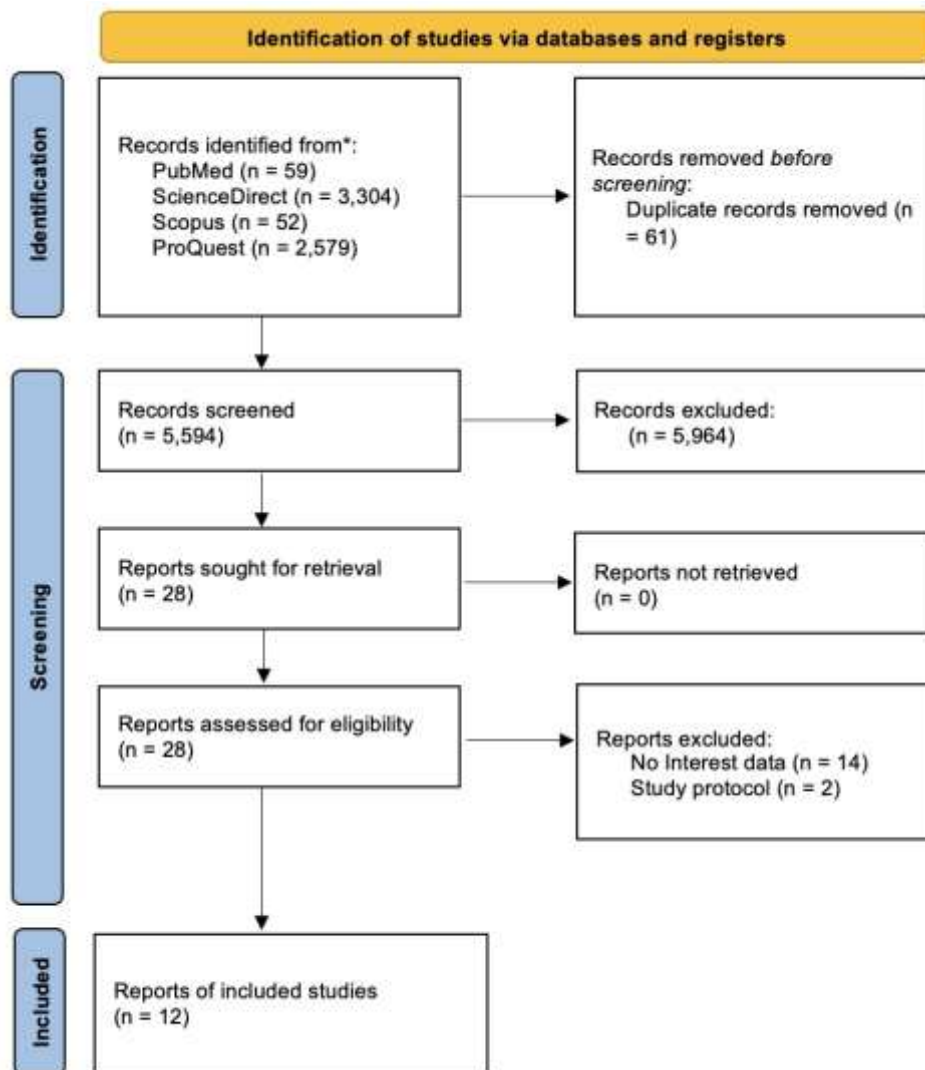


Figure 1. PRISMA flow diagram of the literature search

Inclusion and exclusion criteria

We included published randomized controlled trials, cohort studies, cross-sectional studies, case-control studies, and case series that reported the use of core needle biopsy to diagnose primary thyroid lymphoma, or studies in which data for primary thyroid lymphoma could be clearly extracted. We excluded duplicate records, studies with insufficient data to derive diagnostic accuracy measures, review articles, technical reports, editorials, commentaries, and letters.

Data extraction and study appraisal

Independent data extraction was performed by the authors using a standardized form, including the study characteristics, patient characteristics, and outcomes. Risk of bias was assessed using tools appropriate to each study design: randomized controlled trials were appraised using the Cochrane Risk of Bias tool,⁽²³⁾ while cohort and other observational studies were assessed using the Newcastle–Ottawa Scale (NOS),⁽²⁴⁾ including evaluation of selection, comparability, and outcome assessment.

Statistical analysis

The authors performed diagnostic test accuracy meta-analysis. When available, true-positive, false-negative, true-negative, and false-positive values were extracted from each study. A random-effects model (DerSimonian and Laird method) was applied.^(25,26) Statistical heterogeneity was assessed using the I^2 statistic, with values of 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively.⁽²⁷⁾ Forest plots were generated to visually display pooled sensitivity estimates. All statistical analyses were conducted using R Studio. A p -value <0.05 was considered statistically significant.^(28,29)

RESULTS

Study selection and characteristics

Twelve studies met the inclusion criteria and were included in the qualitative and quantitative synthesis. The included studies comprised predominantly retrospective cohort studies and case series, with one prospective cohort study. Geographically, most studies were conducted in Asia (Korea, China, Taiwan, Malaysia), followed by Europe (Italy, Spain) and the United States.

Across the included reports, CNB was almost uniformly performed under ultrasound guidance in patients with suspected or confirmed PTL. In

several cohorts, CNB was used following inconclusive FNA, while in others it was implemented as a first-line diagnostic modality when aggressive thyroid malignancy was clinically suspected.

Patient profile at presentation

A total of 1091 patients were included across all studies. Individual study sample sizes ranged from 6 to 95 patients. Female predominance was consistently observed. Diffuse large B-cell lymphoma (DLBCL) was the most frequently reported histologic subtype, followed by mucosa-associated lymphoid tissue (MALT) lymphoma.

Table 1 summarizes the clinical characteristics at presentation. The predominant presenting feature across studies was a rapidly enlarging neck mass. In cohorts that reported symptom frequency, approximately 80–100% of patients presented with progressive thyroid enlargement. Compressive symptoms were frequently described, including dysphagia (up to 65%), dyspnea (up to 53%), and hoarseness (up to 37%). Some studies also reported neck discomfort and constitutional symptoms. The rapid growth pattern and compressive manifestations often prompted urgent diagnostic evaluation. Overall, these findings are consistent with the characteristic presentation of PTL as a fast-growing thyroid mass, frequently arising in the context of chronic lymphocytic thyroiditis and requiring timely histopathologic confirmation.

Meta-analysis

Twelve studies provided sufficient data and were eligible for quantitative pooling in the meta-analysis. The forest plot of the random effects meta-analysis of core needle biopsy in diagnosing primary thyroid lymphoma is shown in Figure 2. Core needle biopsy proved to be highly effective with a pooled sensitivity of 91.6% (95% CI: 82.1%–96.3%). These results support the high diagnostic yield of CNB in real-world settings where PTL is suspected after clinical and sonographic evaluation.

Safety

No major procedure-related adverse events were reported. Minor complications were uncommon and limited to isolated hematomas or superficial biopsy-site infections in older series; no cases of tumor-tract seeding were documented in the included cohorts. Overall, the safety profile observed across studies is favorable and comparable to CNB in other thyroid indications.

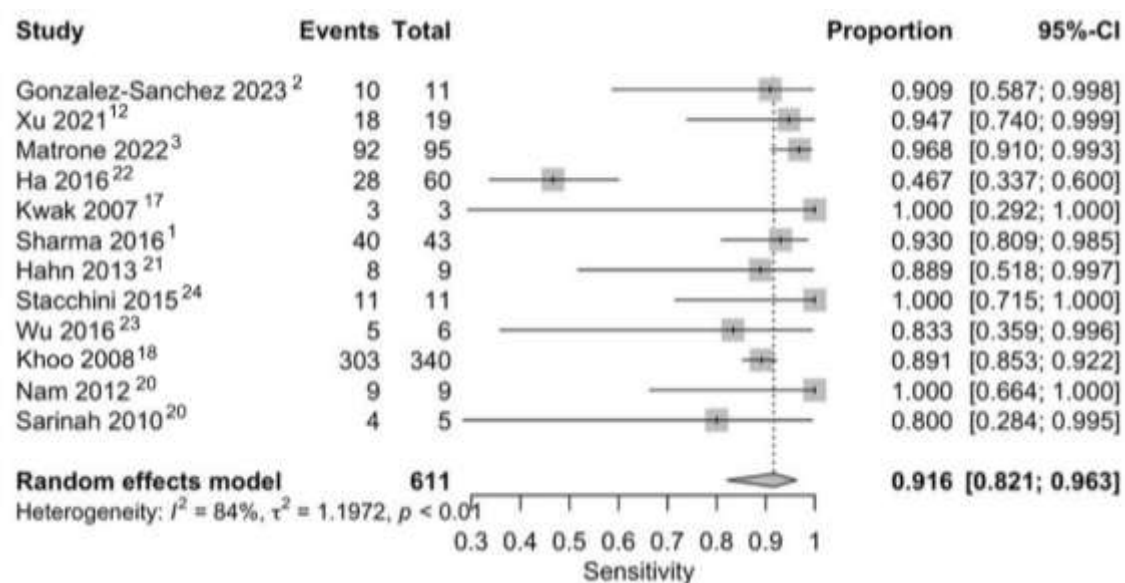


Figure 2. Forest plot of core needle biopsy sensitivity in diagnosing primary thyroid lymphoma

Critical appraisal

Quality assessment used the Joanna Briggs Institute (JBI) checklist for case series and the Newcastle-Ottawa Scale (NOS) for cohort/case-control studies.^(30,31) Overall, reporting quality was heterogeneous and most studies were retrospective.

Across the case series (Table 2), lymphoma diagnosis was generally established using valid methods and key clinical information was usually described. However, consecutive/complete inclusion was rarely stated, site/center characteristics were consistently not reported, and follow-up reporting was variable, suggesting potential selection bias and incomplete reporting.

For the cohort (Table 3) and case-control studies (Table 4), NOS star ratings suggested overall low-to-moderate methodological quality. Most studies clearly documented the index/comparator procedures and verified diagnoses using pathology or other reference standards. However, several NOS domains were frequently not met, mainly due to the diagnostic-pathway nature of the studies: comparator cohort definitions were sometimes suboptimal, confounding was rarely addressed (limited matching/adjusted analyses), and follow-up items were inconsistently reported or not directly applicable to diagnostic endpoints. Collectively, these limitations suggest a moderate-to-high risk of bias, and the findings should be interpreted with appropriate caution when considering diagnostic accuracy and downstream clinical impact outcomes.

DISCUSSION

In this systematic review and meta-analysis of 12 studies (1091 patients), ultrasound-guided CNB demonstrated high diagnostic yield for PTL, with a pooled sensitivity of 91.6% (95% CI, 82.1–96.3%). This performance aligns with the biological and clinical context of PTL, a disease frequently arising on a background of chronic autoimmune thyroiditis and exhibiting distinctive histopathology that often requires architectural assessment and immunophenotyping for definitive classification. CNB provides preserved tissue cores suitable for such work-up, explaining the consistent sensitivity observed across centers.^(14,18)

Our pooled sensitivity of 91.6% is consistent with contemporary evidence evaluating diagnostic strategies for thyroid lymphoma. A recent systematic review by Zhang et al.⁽¹¹⁾ demonstrated that FNA alone may have suboptimal sensitivity for PTL, particularly in cases requiring architectural assessment and immunophenotypic confirmation. Similarly, Vander Poorten et al.⁽¹²⁾ reported that core needle biopsy significantly improves diagnostic adequacy in suspected thyroid lymphoma and anaplastic thyroid carcinoma compared with cytology-based approaches alone. Prospective data from Matrone et al.⁽³⁾ further support the early use of CNB in large or rapidly growing thyroid masses, showing that preserved tissue cores facilitate definitive histologic classification and reduce diagnostic delay.

Table 1. Patient characteristics

Authors	Study design	Study period	Country	Follow-up	Subjects	M/F	Symptoms at presentation	Histologic subtype
Kwak et al. (32)	Case series	January 2003 – December 2005	Korea	Not reported	6	2/4	Enlarged neck mass (100%)	DLBCL (5/6); follicular (1/6)
Kho0 et al. (33)	Retrospective case-control	January 1999 – December 2001	USA	Not reported	FNAB+core: 320 pts (340 episodes); FNAB-only: 311 pts (340 episodes)	FNAB+core: 90/230; FNAB-only: 80/231	Not reported	Not reported
Sarinah and Hisham (34)	Case series	October 1998 – March 2006	Malaysia	19 months	17	6/11	Rapidly enlarging neck mass (88%); dyspnea (65%); dysphagia (53%); hoarseness (35%); pain (12%); constitutional symptoms (n=6)	B-cell NHL (16/17); T-cell NHL (1/17)
Nam et al. (35)	Case series	January 1995 – October 2010	Korea	Not reported	16 (13 primary; 3 secondary)	Primary: 3/10; Secondary: 1/2	Neck swelling/mass sensation: primary 84.6%; secondary 33.3%	Primary: MALT 61.5%, DLBCL 30.8%, mixed 7.7%
Hahn et al. (36)	Retrospective cohort	April 2006 – December 2010	Korea	Follow-up imaging ≥ 12 months in 69.3% (range 18–72 mo; mean 38.1 mo)	88	16/72	Rapidly growing mass	Lymphoma (8/10), Hashimoto (1/10), inconclusive (1/10)
Ha et al. (37)	Retrospective cohort	January 2000 – March 2012	Korea	Not reported	40	12/28	Rapidly growing tumor (33/40)	Not reported
Wu et al. (38)	Case series	1992 – 2015	Taiwan	Mean follow-up 58.1	10	4/6	Rapidly growing neck mass (100%)	DLBCL (8/10); MALT (2/10)

				months (range 5– 123)				
Sharma et al. ⁽¹⁾	Retrospective cohort	January 2000 – December 2014	USA	Not reported	75	38/37	Neck mass (88%); dysphagia (45.3%); hoarseness (37.3%); dyspnea (24%); median symptom duration 4 weeks	DLBCL (72%); MALT (12%); follicular (5.3%); mixed MALT/DLBCL (4%); others (incl. T-cell, Hodgkin)
Stacchini et al. ⁽³⁹⁾	Case series	2001 – 2013	Italy	Not reported	35	Not reported	Diffuse thyroid enlargement ± nodules	MALT and DLBCL
Xu et al. ⁽¹⁴⁾	Case series	January 2013 – June 2018	China	Not reported	24	5/19	Not reported	Not reported
Matrone et al. ⁽³⁾	Prospective cohort	April 2014 – January 2020	Italy	Not reported	95	40/55	Rapidly enlarging thyroid mass	Not reported
González-Sánchez et al. ⁽²⁾	Retrospective cohort	From 1990 (earliest) to June 2018	Spain	Median follow-up 29.5 months (IQR 10–75)	54	8/46	Fast-growing neck mass common; compressive symptoms reported	DLBCL most common; MALT and mixed/other also reported

Note : DLBCL : diffuse large B-cell lymphoma; FNAB : fine-needle aspiration biopsy; IQR : interquartile range; MALT: mucosa-associated lymphoid tissue; NHL : non-Hodgkin lymphoma; mo : months; M : male; F : female

Table 2. Critical appraisal of case series studies

Question	Kwak et al. ⁽³²⁾	Sarinah et al. ⁽³⁴⁾	Nam et al. ⁽³⁵⁾	Wu et al. ⁽³⁸⁾	Stacchini et al. ⁽³⁹⁾	Xu et al. ⁽¹⁴⁾
Were there clear criteria for inclusion in the case series?	Unclear	Yes	Yes	Unclear	Unclear	Unclear
Was the condition measured in a standard, reliable way for all participants included in the case series?	Yes	Yes	Yes	Yes	Yes	Unclear
Were valid methods used for identification of the condition for all participants included in the case series?	Yes	Yes	Yes	Yes	Yes	Yes
Did the case series have consecutive inclusion of participants?	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Did the case series have complete inclusion of participants?	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Was there clear reporting of the demographics of the participants in the study?	Yes	Yes	Yes	Yes	No	No
Was there clear reporting of the clinical information of the participants?	Yes	Yes	Yes	Yes	Unclear	Unclear
Were the outcomes or follow-up results of cases clearly reported?	Unclear	Yes	Unclear	Yes	Unclear	Unclear
Was there clear reporting of the presenting sites'/clinics' demographic information?	No	No	No	No	No	No
Was statistical analysis appropriate?	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

Table 3. Critical appraisal of cohort studies

Authors	S1	S2	S3	S4	C1	O1	O2	O3	Total	Quality
Hahn et al. ⁽³⁶⁾	★		★	★	★	★	★	★	7	Good
Ha et al. ⁽³⁷⁾	★	★	★	★	★	★	★	★	8	Good
Sharma et al. ⁽¹⁾	★	★	★	★	★	★	★	★	8	Good
Matrone et al. ⁽³⁾	★	★	★	★	★★	★	★	★	9	Good
González-Sánchez et al. ⁽²⁾	★	★	★	★	★	★	★	★	8	Good

S: selection, C: comparability, O: outcome

S1: Representativeness of the exposed cohort; S2: Selection of the non-exposed cohort; S3: Ascertainment of exposure; S4: Demonstration that outcome was not present; C1: Comparability of cohorts; O1: Assessment of outcome; O2: Follow-up duration; Adequacy of follow-up

Conversion to Agency for Healthcare Research and Quality (AHRQ) standards:

- Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
- Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Table 4. Critical appraisal of case control study

Authors	S1	S2	S3	S4	C1	E1	E2	E3	Total	Quality
Khoo et al. ⁽³³⁾	★	★			★★	★	★		6	Fair

S: selection, C: comparability, O: outcome

S1: Representativeness of the exposed cohort; S2: Selection of the non-exposed cohort; S3: Ascertainment of exposure; S4: Demonstration that outcome was not present; C1: Comparability of cohorts; E1: Ascertainment of exposure; E2: Measurement of exposure similarity; E3: Non-response/follow-up rate

Conversion to Agency for Healthcare Research and Quality (AHRQ) standards:

- Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
- Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

These findings reinforce the role of CNB not merely as a salvage technique after inconclusive FNA, but as a valuable first-line diagnostic modality in selected high-risk clinical scenarios. A single-center thyroid lymphoma series by Lee et al.⁽⁴⁰⁾ also reported that core biopsy had a higher positive predictive value than FNA (93% vs 82%, $p=0.006$), and the authors recommended core biopsy as the first diagnostic test in patients with a rapidly enlarging thyroid mass suspicious for lymphoma.

Our findings are directionally concordant with prior evidence suggesting CNB's value when lymphoma is in the differential for a rapidly enlarging, hypoechoic thyroid mass.⁽¹⁵⁾ Studies comparing biopsy strategies have shown that CNB can reduce non-diagnostic results and subsequent diagnostic surgery in suspected aggressive thyroid tumors, including PTL and ATC.⁽⁴¹⁾ The 2016 European Radiology cohort and several institutional series reported fewer indeterminate results and more frequent definitive histologic subtyping when CNB was used up front or after an inconclusive FNA.^(12,16) This is clinically important because rapidly progressive thyroid masses often require treatment decisions within a short time window, and avoiding repeated non-diagnostic sampling may expedite initiation of chemotherapy rather than unnecessary diagnostic thyroidectomy.^(3,42)

The CNB's practical role is further supported by consensus recommendations that position it as a complementary technique to FNA when malignancies requiring architecture and ancillary studies are suspected.^(43,44) By contrast, FNA alone may be limited for PTL because cytology can be non-specific or indeterminate, and clonality/immunophenotyping on scant material is challenging. Large historical cohorts of thyroid FNA demonstrate meaningful indeterminate rates and false-negatives for uncommon malignancies, which is consistent with clinicians' experience in PTL work-ups.^(43,45) The CNB mitigates these shortcomings by yielding cores that facilitate immunohistochemistry and, when available, flow cytometry, thereby accelerating definitive diagnosis and treatment planning. In addition, methodological work on lymphoma diagnosis has shown that CNB specimens can be processed for flow-cytometric immunophenotyping while preserving tissue for morphology, further strengthening the suitability of CNB for lymphoma subclassification. This added value is especially relevant in PTL, where distinction

between diffuse large B-cell lymphoma, MALT lymphoma, and reactive lymphoid infiltrates may directly influence first-line treatment selection and urgency.⁽¹⁷⁾

Safety signals in the included studies were favorable. Across cohorts, major complications were rare; minor events were limited to small hematomas or self-limited bleeding. These observations align with broader CNB experience in large thyroid masses and institutional series in which CNB was performed under ultrasound guidance with appropriate needle gauge selection and operator expertise.⁽⁴⁶⁾ While theoretical risks such as tumor-tract seeding are often cited, the reviewed literature and consensus statements suggest that this event is exceedingly uncommon when standard technique is followed.⁽⁴⁷⁾ More recent single-center experience in rapidly growing thyroid tumors by Bakula-Zalewska et al.⁽⁴⁸⁾ likewise reported accurate CNB results with minimal complications, supporting its feasibility when performed in appropriately selected patients and experienced centers.

Clinical implications are immediate. In patients with clinical and sonographic features suggestive of PTL, often on a background of Hashimoto thyroiditis, ultrasound-guided CNB should be considered early, particularly when FNA is non-diagnostic or when rapid histologic subtyping (e.g., DLBCL vs MALT) will change initial therapy. An algorithmic approach that integrates grayscale ultrasound, early CNB for architecture-dependent diagnoses, and obligatory immunohistochemistry can shorten the time to first treatment and avoid unnecessary diagnostic thyroid surgery. This approach may be particularly valuable in elderly or frail patients with compressive symptoms, in whom a rapid minimally invasive diagnosis can guide prompt non-surgical treatment and reduce the burden of repeated procedures.^(49,50)

Strengths and Limitations

A major strength of this study is that it specifically evaluates the diagnostic performance of CNB in PTL, a rare but clinically important thyroid malignancy for which evidence remains limited. By synthesizing data from 12 studies with a total of 1091 patients, this review provides a more comprehensive estimate of CNB sensitivity than any single-center report alone. In addition, the study addresses a clinically relevant question, namely whether CNB can facilitate earlier and more accurate diagnosis in a disease where

delayed recognition may significantly affect management.

However, several limitations should be acknowledged. First, most included studies were retrospective, which increases the risk of selection bias and heterogeneity in patient selection, biopsy technique, and pathology workflow. Second, many studies included only patients with a final diagnosis of PTL, limiting the ability to evaluate specificity and other diagnostic accuracy parameters comprehensively. Third, reporting quality across studies was variable, with incomplete information on operator experience, needle size, number of passes, ancillary testing, and follow-up. Fourth, heterogeneity across studies was considerable, which may affect the precision and generalizability of the pooled estimate. Finally, because PTL is rare, the available evidence remains based largely on observational studies and case series rather than large prospective multicenter diagnostic studies. Therefore, the findings should be interpreted with appropriate caution.

CONCLUSION

The utilization of CNB in the diagnosis of primary thyroid lymphoma has been found to be highly effective, with very few complications. For patients presenting with a rapidly growing thyroid mass, especially in the setting of suspected thyroid lymphoma, CNB offers higher diagnostic sensitivity than cytology-based evaluation alone and provides tissue adequacy for definitive histopathologic classification. Accordingly, CNB should be considered early in the diagnostic pathway to minimize delay, avoid unnecessary thyroid surgery, and expedite appropriate lymphoma-directed therapy.

Conflict of Interest

The authors declare that there is no competing interest regarding the making and the publication of this article.

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Authors' Contributions

NPS, KVM: Concept and design of case report, data collection, drafting, revision, approval of final manuscript. ISS: Concept and design of case report, revision, approval of final manuscript. KK: Data collection, revision, approval of final

manuscript. HN: Data collection, revision, approval of final manuscript. All authors have read and approved the final manuscript

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Data Availability Statement

Available upon request.

Declaration of AI Usage in Scientific Writing

Nothing to declare

REFERENCES

1. Sharma A, Jasim S, Reading CC, et al. Clinical presentation and diagnostic challenges of thyroid lymphoma: a cohort study. *Thyroid* 2016;26:1061–7. doi: 10.1089/thy.2016.0095.
2. González-Sánchez C, Salvador-Egea MP, Glückmann-Maldonado E, et al. Diagnosis and treatment of primary thyroid lymphoma from a surgical perspective: a multi-institutional study. *Langenbecks Arch Surg* 2023;408:1-5. doi: 10.1007/s00423-023-02945-x.
3. Matrone A, De Napoli L, Torregrossa L, et al. Core needle biopsy can early and precisely Identify large thyroid masses. *Front Oncol* 2022;12:854755. doi: 10.3389/fonc.2022.854755.
4. Ahmed S, Ghazarian MP, Cabanillas ME, et al. Imaging of anaplastic thyroid carcinoma. *AJNR Am J Neuroradiol* 2018;39:547–51. doi: 10.3174/ajnr.A5487.
5. Bible KC, Kebebew E, Brierley J, et al. 2021 American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. *Thyroid* 2021;31:337–86. doi: 10.1089/thy.2020.0944.
6. Xiang N, Dong F, Zhan X, et al. Incidence and prognostic factors of primary thyroid lymphoma and construction of prognostic models for post-chemotherapy and postoperative patients: a population-based study. *BMC Endocr Disord* 2021;21:68. doi: 10.1186/s12902-021-00732-7.
7. Stein SA, Wartofsky L. Primary thyroid lymphoma: a clinical review. *J Clin Endocrinol Metab* 2013;98:3131–8. doi: 10.1210/jc.2013-1428.
8. Bayrak BY, Paksoy N. Diagnostic accuracy of fine-needle aspiration cytology for extrathyroidal head-and-neck lesions performed by a cytopathologist with the assistance of radiologist: a single-center study. *Cytojournal* 2025;22:57. doi: 10.25259/Cytojournal_247_2024.
9. Hrizat AS, Doxzon KA, Post RP, et al. Diagnostic accuracy and clinical utility of fine-needle aspiration in breast lesions: a correlation with

- surgical pathology. *Acta Cytol* 2025;69:114–21. doi: 10.1159/000542811.
10. Facciorusso A, Crinò SF, Muscatiello N, et al. Endoscopic ultrasound fine-needle biopsy versus fine-needle aspiration for tissue sampling of abdominal lymph nodes: a propensity score matched multicenter comparative study. *Cancers (Basel)* 2021;13:4298. doi: 10.3390/cancers13174298.
 11. Zhang L, Castellana M, Virili C, et al. Fine-needle aspiration to diagnose primary thyroid lymphomas: a systematic review and meta-analysis. *Eur J Endocrinol* 2019;180:177–87. doi: 10.1530/EJE-18-0672.
 12. Vander Poorten V, Goedseels N, Triantafyllou A, et al. Effectiveness of core needle biopsy in the diagnosis of thyroid lymphoma and anaplastic thyroid carcinoma: A systematic review and meta-analysis. *Front Endocrinol (Lausanne)* 2022;13:971249. doi: 10.3389/fendo.2022.971249.
 13. Kakkar A, Purkait S, Agarwal S, et al. Primary thyroid lymphoma: a series from a tertiary care center in Northern India. *J Cancer Res Ther* 2019;15:669–75. doi: 10.4103/jert.JCRT_135_17.
 14. Xu L, Li S, Zhu J, et al. [High frequency ultrasound combined with ultrasound-guided core needle biopsy for the diagnosis of primary thyroid lymphoma]. *Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2021;56:858–62. doi: 10.3760/cma.j.cn115330-20201201-00901. Chinese.
 15. Cunha C, Mousinho F, Saraiva C, Duarte JS. Follicular lymphoma of the thyroid and the role of core needle biopsy. *Endocrinol Diabetes Metab Case Rep* 2023;2023: 21-019. doi: 10.1530/EDM-21-0196.
 16. Na DG, Baek JH, Jung SL, et al. Core needle biopsy of the thyroid: 2016 consensus statement and recommendations from Korean Society of Thyroid Radiology. *Korean J Radiol* 2017;18:217. doi: 10.3348/kjr.2017.18.1.217.
 17. Jung CK, Baek JH. Recent advances in core needle biopsy for thyroid nodules. *Endocrinol Metab* 2017;32:407–12. doi: 10.3803/EnM.2017.32.4.407.
 18. Pantanowitz L, Thompson LDR, Jing X, Rossi ED. Is thyroid core needle biopsy a valid compliment to fine-needle aspiration? *J Am Soc Cytopathol* 2020;9:383–8. doi: 10.1016/j.jasc.2020.06.003.
 19. Hasannia MA, Pourghorban R, Asefi H, et al. Diagnostic yield of fine needle aspiration with simultaneous core needle biopsy for thyroid nodules. *J Pathol Transl Med* 2025;59:180. doi: 10.4132/jptm.2025.03.04.
 20. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71.
 21. Schiavo JH. PROSPERO: an international register of systematic review protocols. *Med Ref Serv Q* 2019;38:171–80. doi: 10.1080/02763869.2019.1588072.
 22. Booth A, Mitchell AS, Mott A, et al. An assessment of the extent to which the contents of PROSPERO records meet the systematic review protocol reporting items in PRISMA-P. *F1000Res* 2020;9:773. doi: 10.12688/f1000research.25181.2.
 23. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;366: 366:14898. doi: 10.1136/bmj.l4898.
 24. Gualdi-Russo E, Zaccagni L. The Newcastle–Ottawa scale for assessing the quality of studies in systematic reviews. *Publications* 2026;14:4. doi: 10.3390/publications14010004.
 25. Guolo A, Varin C. Random-effects meta-analysis: the number of studies matters. *Stat Methods Med Res* 2017;26:1500–18. doi: 10.1177/0962280215583568.
 26. McKenzie JE, Veroniki AA. A brief note on the random-effects meta-analysis model and its relationship to other models. *J Clin Epidemiol* 2024;174:111492. doi: 10.1016/j.jclinepi.2024.111492.
 27. Migliavaca CB, Stein C, Colpani V, et al. Meta-analysis of prevalence: I² statistic and how to deal with heterogeneity. *Res Synth Methods* 2022;13:363–7. doi: 10.1002/jrsm.1547.
 28. Shim SR, Kim SJ, Lee J. Diagnostic test accuracy: application and practice using R software. *Epidemiol Health* 2019;41:e2019007. doi: 10.4178/EPIH.E2019007.
 29. Giorgi FM, Ceraolo C, Mercatelli D. The R language: an engine for bioinformatics and data science. 2022;12:648. doi: 10.3390/life12050648.
 30. Hilton M. JBI Critical appraisal checklist for systematic reviews and research syntheses. *J Can Health Libr Assoc* 2024;45:180. doi: 10.29173/jchla29801.
 31. Moskalewicz A, Oremus M. No clear choice between Newcastle–Ottawa Scale and Appraisal Tool for Cross-Sectional Studies to assess methodological quality in cross-sectional studies of health-related quality of life and breast cancer. *J Clin Epidemiol* 2020;120:94–103. doi: 10.1016/j.jclinepi.2019.12.013.
 32. Kwak JK, Kim EK, Ko KH, et al. Primary thyroid lymphoma: role of ultrasound-guided needle biopsy. *J Ultrasound Med* 2007;26:1761–5. doi: 10.7863/jum.2007.26.12.1761.
 33. Khoo TK, Baker CH, Hallanger-Johnson J, et al. Comparison of ultrasound-guided fine-needle aspiration biopsy with core-needle biopsy in the

- evaluation of thyroid nodules. *Endocrine Practice* 2008;14:426–31. doi: 10.4158/EP.14.4.426.
34. Sarinah B, Hisham AN. Primary lymphoma of the thyroid: diagnostic and therapeutic considerations. *Asian J Surg* 2010;33:20–4. doi: 10.1016/S1015-9584(10)60004-8.
 35. Nam M, Shin JH, Han BK, et al. Thyroid lymphoma: correlation of radiologic and pathologic features. *J Ultrasound Med* 2012;31:589–94. doi: 10.7863/jum.2012.31.4.589.
 36. Hahn SY, Shin JH, Han BK, et al. Ultrasonography-guided core needle biopsy for the thyroid nodule: does the procedure hold any benefit for the diagnosis when fine-needle aspiration cytology analysis shows inconclusive results? *Br J Radiol* 2013;86. doi: 10.1259/bjr.20130007.
 37. Ha EJ, Baek JH, Lee JH, et al. Core needle biopsy could reduce diagnostic surgery in patients with anaplastic thyroid cancer or thyroid lymphoma. *Eur Radiol* 2016;26:1031–6. doi: 10.1007/s00330-015-3921-y.
 38. Wu SY, Chu CH, Duh QY, Hsieh CB, Yu JC, Shih ML. Management for primary thyroid lymphoma: Experience from a single tertiary care centre in Taiwan. *Formos J Surg* 2016;49:201–7. doi: 10.1016/j.fjs.2016.07.001.
 39. Stacchini A, Pacchioni D, Demurtas A, et al. Utility of flow cytometry as ancillary study to improve the cytologic diagnosis of thyroid lymphomas. *Cytometry B Clin Cytom* 2015;88:320–9. doi: 10.1002/cyto.b.21204.
 40. Lee JS, Shin SJ, Yun HJ, et al. Primary thyroid lymphoma: A single-center experience. *Front Endocrinol (Lausanne)* 2023;14:1064050. doi: 10.3389/fendo.2023.1064050.
 41. Karki SS, Pandey S, Karki S, et al. Diffuse large B-cell lymphoma of the thyroid in a patient with Hashimoto thyroiditis: a diagnostic dilemma. *Clin Case Rep* 2025;13:e71346. doi: 10.1002/ccr3.71346.
 42. Kim SY, Lee HS, Moon J, et al. Fine-needle aspiration versus core needle biopsy for diagnosis of thyroid malignancy and neoplasm: a matched cohort study. *Eur Radiol* 2017;27:801–11. doi: 10.1007/s00330-016-4424-1.
 43. Jung CK, Baek JH, Na DG, et al. 2019 Practice guidelines for thyroid core needle biopsy: a report of the Clinical Practice Guidelines Development Committee of the Korean Thyroid Association. *J Pathol Transl Med* 2020;54:64. doi: 10.4132/jptm.2019.12.04.
 44. Kim SY, Chung HW, Oh TS, et al. Practical guidelines for ultrasound-guided core needle biopsy of soft-tissue lesions: transformation from beginner to specialist. *Korean J Radiol* 2017;18:361. doi: 10.3348/kjr.2017.18.2.361.
 45. Misiakos EP, Margari N, Meristoudis C, et al. Cytopathologic diagnosis of fine needle aspiration biopsies of thyroid nodules. *World J Clin Cases* 2016;4:38. doi: 10.12998/wjcc.v4.i2.38.
 46. Mancia G, Kreutz R, Brunström M, et al. 2023 ESH Guidelines for the management of arterial hypertension the task force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association. *J Hypertens* 2023;41:1874–2071. doi: 10.1097/HJH.0000000000003480.
 47. Yim Y, Baek JH. Core needle biopsy in the management of thyroid nodules with an indeterminate fine-needle aspiration report. *Gland Surg* 2019;8:S77–85. doi: 10.21037/gs.2018.09.07.
 48. Bakuła-Zalewska EB, Kwapisz MI, Góralski P, et al. Core needle biopsy: an efficacious adjunct to cytological diagnosis in thyroid tumours suspected of anaplastic carcinoma - single-centre experience. *Contemp Oncol (Pozn)* 2024;28:167–71. doi: 10.5114/wo.2024.142468.
 49. Marcy PY, Bauduer F, Thariat J, et al. Fast track management of primary thyroid lymphoma in the very elderly patient. *Curr Oncol* 2023;30:5816–27. doi: 10.3390/curroncol30060435.
 50. Iskra I, Tomaš MI, Crnčić TB, et al. Two lymphoma histotypes and papillary thyroid carcinoma coexisting on Hashimoto ground: a case report and review of the literature. *Diagn Pathol* 2024;19:15. doi: 10.1186/s13000-024-01472-7.



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