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LAMPANG HOSPITAL

ลำปางเวชสาร
LAMPANG MEDICAL JOURNAL



Original Article

Diagnostic Accuracy and Risk of Malignancy of Liquid-Based Thyroid Fine-Needle Aspiration Cytology Compared with Histopathology: A Retrospective Study in Lampang Hospital

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Lampang Med J 2026;47(1): 43-54

Received: 17 Dec 2025
Revised: 12 May 2026
Accepted: 14 May 2026

Keywords:
thyroid,
fine-needle aspiration,
liquid-based cytology,
Bethesda system,
risk of malignancy

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Abstract

Background: Fine-needle aspiration (FNA) is the standard method for preoperative evaluation of thyroid nodules. Liquid-based cytology (LBC) has increasingly been adopted; however, data on its diagnostic performance and risk of malignancy (ROM) in Thailand remain limited.

Objective: To evaluate the diagnostic performance of LBC in thyroid nodules and to determine the ROM across Bethesda categories.

Materials and methods: A retrospective study was conducted on patients who underwent thyroid LBC and subsequent surgery at Lampang Hospital between 2020 and 2024. Diagnostic indices, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy, were calculated using histopathology as the reference standard. ROM was assessed for each Bethesda category.

Results: Of 1,328 cases, 361 underwent surgery, and 226 cases were included in performance analysis. Concordant cytology–histology results were observed in 186 cases, stratified by category. The false-positive and false-negative rates were 6.4% and 37.7%, respectively. Sensitivity was 62.3%, specificity 93.6%, PPV 81.1%, NPV 85%, and overall accuracy 84.1%. The ROM for nondiagnostic, benign, AUS, FN/SFN, suspicious for malignancy, and malignant categories was 11.4%, 8.7%, 32.3%, 14.3%, 96%, and 100%, respectively.

Conclusion: LBC demonstrates high specificity and good overall diagnostic accuracy in evaluating thyroid nodules, although sensitivity remains moderate. Integration with clinical and sonographic findings is essential for optimal management.

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นิพนธ์ต้นฉบับ

ความแม่นยำทางการวินิจฉัยและความเสี่ยงต่อการเกิดมะเร็งของการตรวจเซลล์วิทยาแบบของเหลวจากการเจาะตรวจต่อมไทรอยด์เปรียบเทียบกับผลพยาธิวิทยา: การศึกษาย้อนหลังในโรงพยาบาลลำปาง

สิริอร แดงละอุ่น พ.บ.
กลุ่มงานพยาธิวิทยากายวิภาค โรงพยาบาลลำปาง

รับต้นฉบับ: 17 ธันวาคม 2568
ปรับแก้ไข: 12 พฤษภาคม 2569
รับลงตีพิมพ์: 14 พฤษภาคม 2569

คำสำคัญ:
ต่อมไทรอยด์,
การเจาะดูดเข็มขนาดเล็ก,
เซลล์วิทยาแบบของเหลว,
Bethesda system,
ความเสี่ยงของการเป็นมะเร็ง

บทคัดย่อ

ภูมิหลัง: การตรวจเซลล์วิทยาด้วยการเจาะดูดเข็มขนาดเล็ก (fine needle aspiration) เป็นวิธีมาตรฐานในการประเมินก้อนต่อมไทรอยด์ก่อนผ่าตัด โดยปัจจุบันมีการใช้การเตรียมสไลด์แบบของเหลว (liquid-based cytology : LBC) มากขึ้น อย่างไรก็ตาม ข้อมูลด้านความแม่นยำของการวินิจฉัยเซลล์วิทยาด้วยวิธีการเตรียมเซลล์แบบของเหลวและข้อมูลความเสี่ยงของมะเร็งไทรอยด์ตามการจัดประเภทของเซลล์พยาธิวิทยาด้วยวิธีการเตรียมเซลล์แบบของเหลวยังมีจำกัด

วัตถุประสงค์: เพื่อประเมินประสิทธิภาพของ LBC ในการวินิจฉัยก้อนต่อมไทรอยด์ และศึกษาความเสี่ยงของการเป็นมะเร็ง (risk of malignancy; ROM) ตามระบบ Bethesda

วัสดุและวิธีการ: การศึกษาย้อนหลังในผู้ป่วยที่ได้รับการตรวจ LBC และผ่าตัดต่อมไทรอยด์ ณ โรงพยาบาลลำปาง ระหว่างปี 2563–2567 วิเคราะห์ความไว ความจำเพาะ ค่าพยากรณ์บวก ค่าพยากรณ์ลบ และความแม่นยำ โดยเปรียบเทียบกับผลชิ้นเนื้อหลังผ่าตัด และคำนวณ ROM ในแต่ละกลุ่ม Bethesda

ผลการศึกษา: จากผู้ป่วย 1,328 ราย มี 361 รายได้รับการผ่าตัด และ 226 รายถูกนำมาวิเคราะห์ประสิทธิภาพ พบความสอดคล้องระหว่าง cytology และ histology แยกตามแต่ละกลุ่มวินิจฉัยทางเซลล์วิทยา 186 ราย อัตราผลบวกลวง ร้อยละ 6.4 และผลลบลวง ร้อยละ 37.7 ค่าความไวร้อยละ 62.3, ความจำเพาะร้อยละ 93.6, ค่าพยากรณ์บวก ร้อยละ 81.1, ค่าพยากรณ์ลบ ร้อยละ 85 และความแม่นยำร้อยละ 84.1 ค่า ROM ในแต่ละกลุ่ม ได้แก่ nondiagnostic ร้อยละ 11.4, benign ร้อยละ 8.7, AUS ร้อยละ 32.3, FN/SFN ร้อยละ 14.3, suspicious for malignancy ร้อยละ 96 และ malignant ร้อยละ 100

สรุป: LBC มีความจำเพาะสูงและความแม่นยำดีในการวินิจฉัยมะเร็งต่อมไทรอยด์ แต่มีความไวปานกลาง ควรใช้ร่วมกับข้อมูลทางคลินิกและอัลตราซาวด์เพื่อเพิ่มความแม่นยำในการวางแผนการรักษา

Introduction

Thyroid cancer is the most common malignancy of the endocrine system and one of the most prevalent cancers among Thai females. Its incidence has been increasing in both genders, with mean annual rates of 1.5 per 100,000 in males and 5.1 per 100,000 in females.[1] Fine needle aspiration (FNA) is widely used for preoperative evaluation of thyroid nodules, in conjunction with clinical and sonographic findings, to enable appropriate risk stratification for surgical management, as recommended by the National Comprehensive Cancer Network (NCCN).[2] In parallel, the Bethesda System for Reporting Thyroid Cytopathology was developed to standardize cytological interpretation by providing diagnostic categories, associated risks of malignancy, and management recommendations.[3-5] As a simple, safe, and cost-effective procedure, accurate cytopathologic interpretation of FNA specimens facilitates appropriate clinical decision-making.[5] Ultimately, optimal management of thyroid nodules can reduce postoperative complications and overall healthcare costs.

The 2017 Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) is widely adopted for classifying thyroid cytology findings into six categories: nondiagnostic, benign, atypia of undetermined significance (AUS /FLUS), follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN), suspicious for malignancy, and malignant.[3] Each category is associated with a specific risk of malignancy (ROM), which is highest in malignant and suspicious for malignancy categories, and lowest among cases classified as benign nodules.[3,4] Category 2 (benign) is designated for non-neoplastic lesions, such as thyroiditis and hyperplastic nodules. Cases categorized as Bethesda category 4 (FN/SFN) require surgical intervention for definitive histopathological distinction between benign thyroid neoplasms (including follicular adenoma) and malignant lesions such as follicular carcinoma. Repeat FNA is recommended for nondiagnostic (category 1) and AUS/FLUS (category 3) results to obtain a cytological diagnosis. Thyroid nodules classified as category 5 (suspicious for malignancy) and category 6 (malignant) necessitate surgical intervention due to their high correlation with malignancy. However, diagnostic challenges may result in discrepancies, leading to both false-positive and false-negative interpretations.[5] Cytopathology results therefore play a critical role in guiding clinical management, minimizing unnecessary aggressive surgery, and supporting more conservative approaches.

Liquid-based cytology (LBC) has been introduced as an alternative to conventional smears for evaluating thyroid nodules.[6] It provides advantages such as improved cellular distribution, a cleaner background, and the ability to perform ancillary testing.[6] Previous studies have demonstrated that LBC and conventional smears have comparable diagnostic performance in preoperative evaluation.[6,7] In Thailand, LBC has gradually replaced conventional techniques, particularly in cervical cytology screening. However, its application in thyroid fine-needle aspiration cytology remains limited.[8] Moreover, data on the diagnostic performance and risk of malignancy of thyroid LBC in Thailand are still scarce. Therefore, this study aims to evaluate the diagnostic performance and malignancy risk of thyroid LBC at Lampang Hospital.

Materials and Methods

This retrospective study analyzed pathological reports from Lampang Hospital, including cases recorded after the implementation of LBP using the EASYPREP® system (YD Diagnostics Corp., Seoul, Korea) from June 2020 to December 2024.

Thyroid FNA specimens were collected by clinicians and placed in EASYPREP non-gynecologic (non-gyn) preservation solution, then transported to the laboratory without rapid on-site evaluation (ROSE). The LBC process using the EASYPREP® system was performed automatically. In a public hospital setting, cytologic slides were examined by six general pathologists; each case was independently diagnosed by a single pathologist as part of routine services. All thyroid surgical resection specimens performed at Lampang Hospital were also evaluated and reported by general pathologists.

All patients with thyroid nodules, who received FNA during preoperative evaluation and underwent thyroid

surgery, were studied based on available records from the Lampang Hospital Information System. Demographic data, thyroid cytopathology results, and histopathological diagnoses were retrieved from the system, all of which had been reported as part of routine clinical services by general pathologists. Histopathological data were identified using pathology laboratory codes P092, P47, P49, and P490, while thyroid cytopathology data were retrieved using cytology code G08. Data collection covered the period from June 2020 to December 2024, and all data were recorded in Microsoft Excel. Patients with thyroid nodules who underwent preoperative FNA and subsequent thyroid surgery were included. Cases evaluated using conventional smear cytology or lacking corresponding histopathological results from thyroidectomy specimens were excluded.

The primary outcome was the diagnostic performance of thyroid liquid-based cytology, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy, compared with final histopathological diagnosis. The secondary outcome was the risk of malignancy (ROM) for each Bethesda category, defined as the proportion of malignant nodules among all surgically resected nodules within each category.

Statistical analysis

Statistical analyses were performed using Microsoft Excel. Demographic characteristics were summarized using descriptive statistics, including mean, median, frequency, and percentage. Thyroid cytology results were classified according to TBSRTC. Nondiagnostic cases were reported as percentages. Histopathological outcomes of category 3 (AUS) were also summarized as percentages.

The ROM for each Bethesda category was calculated as the proportion of malignant cases among all surgically resected nodules in that category. LBC performance was assessed in correlation with final histopathological findings.

Based on TBSRTC recommendations, cytology categories of FN/SFN, suspicious for malignancy, and malignant were classified as positive test results, whereas benign cytology was considered negative. Positive outcomes were defined as a histologically confirmed thyroid carcinomas or benign thyroid neoplasms that necessitated surgical resection for definitive diagnosis, while non-neoplastic lesions (nodular goiter, chronic lymphocytic thyroiditis) were defined as negative outcomes. Tumors of uncertain malignant potential were considered as positive outcomes. Results were categorized as true positive (TP), true negative (TN), false positive (FP), and false negative (FN). Diagnostic indices, including sensitivity, specificity, PPV, NPV, and accuracy, were calculated using a standard 2×2 contingency table. Corresponding 95% confidence intervals were estimated using binomial proportion methods. Nondiagnostic and AUS categories were excluded from diagnostic performance analysis, as repeat FNA is recommended for these categories.

Histopathological results were correlated with preoperative liquid-based cytology findings to assess diagnostic concordance. Discordant cases were reviewed, and corresponding histopathological findings were summarized in a table. This study was approved by the Ethics Committee of Lampang Hospital (EC029/68).

Results

Among 1,328 cases that underwent liquid-based thyroid FNA cytology, 361 cases proceeded to surgical resection, yielding a surgery rate of 27.2%. Ultrasound-guided aspiration was performed in 1,224 cases (92.2%), while 89 cases underwent aspiration without ultrasound guidance; procedure details were unavailable for 15 cases. Of the surgical cohort, 308 patients (85.3%) were female and 53 (14.7%) were male, with a female-to-male ratio of 5.8:1. Patient age ranged from 17 to 94 years, with a median age of 57 years.

Of the 361 final histopathological cases, 238 were non-neoplastic lesions, 42 were benign neoplasms, 78 were malignant, and 3 were tumors of uncertain malignant potential. Among female patients, 64 cases (20.8%) were diagnosed as malignant, 208 cases (67.5%) as non-neoplastic lesion, 33 cases (10.7%) as benign neoplasm, and 3 cases (1.0%) as tumor of uncertain malignant potential. In male patients, 14 cases (26.4%) were

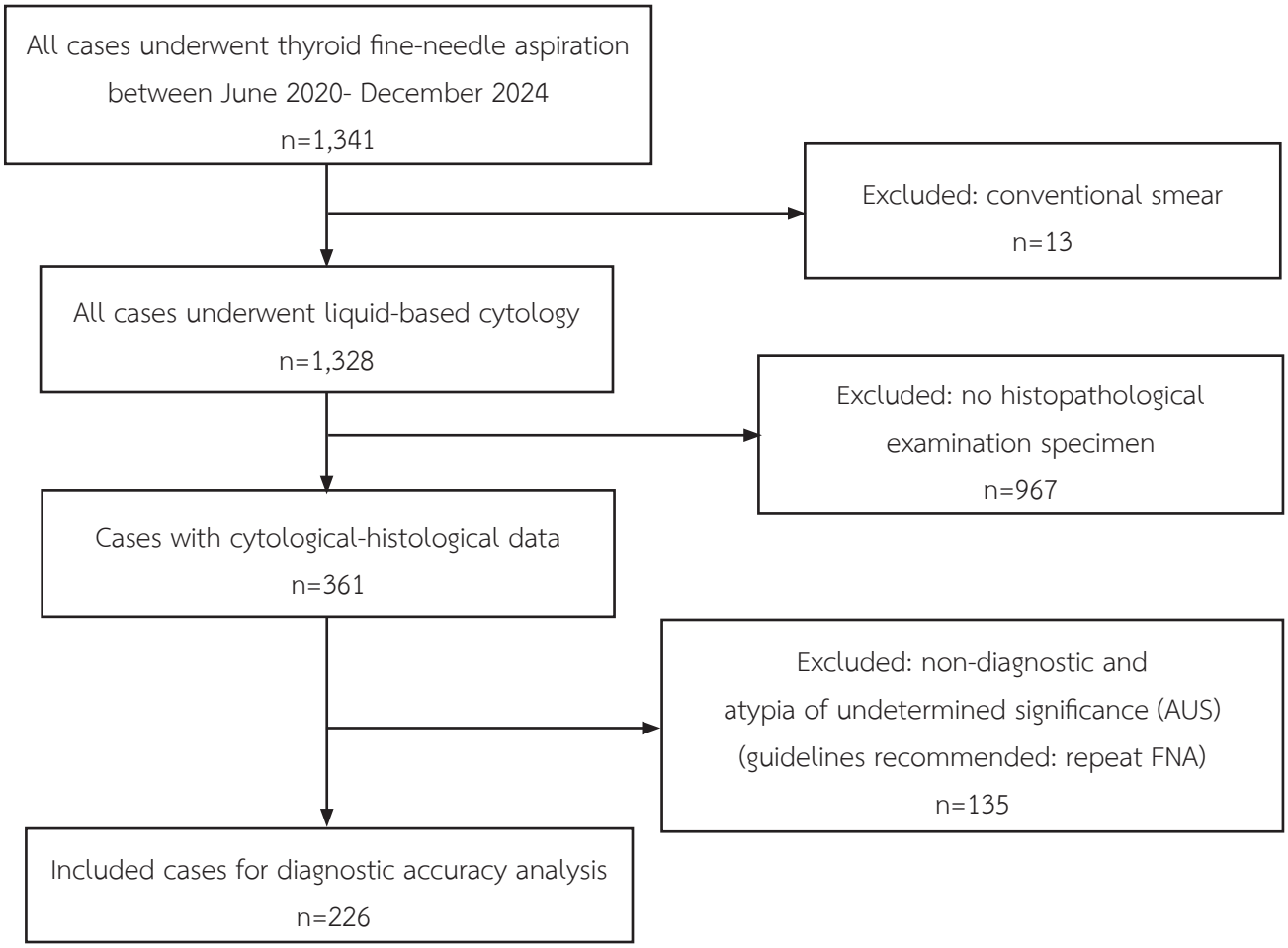


Figure 1 : Diagram of selection of study

malignant, 30 cases (56.6%) were non-neoplastic lesion, and 9 cases (17%) were benign neoplasm. Overall, females accounted for the majority of malignant cases (64 cases, 82.1%) compared with males (14 cases, 17.9%), with a female-to-male ratio of 4.6:1. However, the proportion of malignancy was higher in males (26.4%) than in females (20.8%). The age of patients with malignancy ranged from 17 to 94 years, with a median age of 54 years.

Among benign lesions, nodular goiter was the most common diagnosis, accounting for 226 cases (80.7%). Among malignant tumors, papillary thyroid carcinoma was the most frequent, comprising 64 cases (82.1%). Other malignancies included 9 follicular thyroid carcinomas, 3 poorly differentiated thyroid carcinomas, and 2 anaplastic thyroid carcinomas. In lobectomy specimens, final histopathology demonstrated 35 malignant cases (14%), 213 benign cases (85.2%), and 2 cases (0.8%) with uncertain cases (38.7%) were malignant, 67 (60.3%) were benign, and 1 case (0.9%) was classified as uncertain malignant potential.

Table 1 shows the distribution of thyroid cytology according to TBSRTC. Among the 361 cases, 70 (19.4%) were nondiagnostic, 173 (47.9%) benign, 65 (18.0%) AUS, 21 (5.8%) FN/SFN, 25 (6.9%) suspicious for malignancy, and 7 (1.9%) malignant.

As shown in Table 2, the rate of nondiagnostic cytology was 70 of 361 cases (19.4%). Of these, 61 cases (87.1%) were benign on histology, including 49 nodular goiters, 8 follicular adenomas, 2 noninvasive follicular thyroid neoplasms with papillary-like nuclear features (NIFTP), 1 chronic lymphocytic thyroiditis, and 1 oncocytic adenoma. Eight cases (11.4%) were malignant, including 6 papillary thyroid carcinomas, 1 follicular carcinoma, and 1 anaplastic thyroid carcinoma. The remaining case was diagnosed as a follicular tumor of uncertain malignant potential. Most common cause of nondiagnostic results

Table 1 Distribution of thyroid cytology cases by TBSRTC category (n=361)

Cytology diagnostic category	Number of cases (%)
Nondiagnostic	70 (19.4)
Benign	173 (47.9)
Atypia of undetermined significance (AUS)	65 (18)
Follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN)	21 (5.8)
Suspicious for malignancy	25 (6.9)
Malignancy	7 (1.9)

was cyst fluid only. Among 173 cases diagnosed as benign on cytology, 156 cases (90.2%) were confirmed as benign on histology, consisting of 147 non-neoplastic cases and 9 benign thyroid neoplasms, while 15 cases (8.7%) were malignant and 2 cases (1.2%) were of uncertain malignant potential. For cytological diagnoses of FN/SFN, 10 of 21 cases (47.6%) were non-neoplastic lesions (9 nodular goiter, 1 chronic lymphocytic thyroiditis). 8 cases (38.1%) were benign thyroid neoplasm (5 follicular adenoma, 2 oncocytic adenoma and 1 NIFTP). Remaining 3 cases (14.3%) were malignant (2 papillary thyroid carcinomas and 1 follicular carcinoma). Among 25 cases categorized as suspicious for malignancy, 24 cases were confirmed malignant, with only 1 benign thyroid neoplasm diagnosed as follicular adenoma. All cases diagnosed as malignant on cytology were confirmed as malignant on final histopathology.

Comparison of thyroid FNA cytology with final histopathology for AUS cases is shown in Table 2. Among these, 31 cases (47.7%) were non-neoplastic lesion, including 28 nodular goiters, 3 chronic lymphocytic thyroiditis). 13 cases (20%) were benign thyroid neoplasm, consisting of 7 follicular adenomas, 4 oncocytic adenomas, and 2 NIFTP. The remaining 21 cases (32.3%) were malignant, comprising 17 papillary thyroid carcinomas, 3 follicular carcinomas, and 1 poorly differentiated thyroid carcinoma. The ROM for each category (nondiagnostic, benign, AUS,

Table 2 Comparison of thyroid FNA cytology and final histopathology results (n=361)

Cytology diagnostic category	Cytology results (n)	Non-neoplastic (n, %)			
		Non-neoplastic (n, %)	Benign neoplasm (n, %)	Malignancy (n, %)	uncertain malignant potential (n, %)
Nondiagnostic	70	50 (71.4)	11 (15.7)	8 (11.4)	1 (1.4)
Benign	173	147 (85)	9 (5.2)	15 (8.7)	2 (1.2)
Atypia of undetermined significance (AUS)	65	31 (47.7)	13 (20)	21 (32.3)	0
Follicular neoplasm or suspicious for a follicular neoplasm	21	10 (47.6)	8 (38)	3 (14.3)	0
Suspicious for malignancy	25	0	1 (4)	24 (96)	0
Malignancy	7	0	0	7(100)	0

Table 3 Comparison of risk of malignancy (ROM) of this study results with TBSRTC.

Bethesda Category	ROM in the Bethesda system	Number of cases (n)	Malignant cases (n)	ROM in this study (%)
I (ND/UNS)	5-10%	70	8	11.4 %
II (Benign)	0-3%	173	15	8.7%
III (AUS/FLUS)	10-30%	65	21	32.3 %
IV (FN/SFN)	25-40%	21	3	14.3 %
V (Suspicious for malignancy)	50-75%	25	24	96 %
VI (Malignant)	97-99%	7	7	100 %

Table 4 Diagnostic performance metrics of the LBC results with the final histology diagnoses. (n=226)

Cytology diagnosis	Histology diagnosis (n)		
	Malignancy	Benign neoplasm	Non-neoplastic
Category 2	17 (false negative)	9 (false negative)	147 (true negative)
Category 4	3 (true positive)	8 (true positive)	10 (false positive)
Category 5	24 (true positive)	1 (true positive)	-
Category 6	7 (true positive)	-	-

Table 5 The diagnostic performance of thyroid LBC (n=226)

Cytology diagnosis	Histology diagnosis		Total	Diagnostic Metrics (95% CI)
	Malignancy and benign neoplasm	Non-neoplastic		
Malignancy	True positive = 43	False positive = 10	53	PPV: 81.1% (76%– 86.2%)
Benign	False negative = 26	True negative = 147	173	NPV: 85% (80.3% – 89.6%)
Total	69	157	226	
Diagnostic Metrics (95% CI)	Sensitivity: 62.3% (56% – 68.6%)	Specificity: 93.6% (90.4% – 96.8%)		Overall Accuracy: 84.1% (79.3% – 88.8%)

follicular neoplasm/suspicious for follicular neoplasm, suspicious for malignancy, and malignant) was 11.4%, 8.7%, 32.3%, 14.3%, 96%, and 100%, respectively. The ROM for each TBSRTC category in this study, compared with the ROM defined by the TBSRTC, is shown in Table 3.

After excluding nondiagnostic and AUS categories, 226 cases were included. Of the 226 cases as shown in

Table 6 Summary of discordant cases between cytology and histopathology (n=40)

No	Age	Gender	Liquid-based cytology	Histologic follow-up results	Size (cm)
1	65	F	Benign (non-neoplastic)	Papillary carcinoma	1.3
2	57	F	Benign (non-neoplastic)	Follicular adenoma	4
3	46	F	Benign (non-neoplastic)	Minimally invasion follicular carcinoma	8
4	46	F	Benign (non-neoplastic)	Follicular tumor of uncertain malignant potential	5
5	43	F	Benign (non-neoplastic)	Follicular adenoma	3
6	50	M	Benign (non-neoplastic)	Follicular adenoma	6.5
7	39	F	Benign (non-neoplastic)	Papillary carcinoma	1.4
8	24	F	Benign (non-neoplastic)	Minimally invasion follicular carcinoma	2.5
9	40	F	Benign (non-neoplastic)	Minimally invasion follicular carcinoma	4.5
10	62	F	Benign (non-neoplastic)	Papillary carcinoma	0.6
11	24	F	Benign (non-neoplastic)	Follicular adenoma	4.5
12	56	F	Benign (non-neoplastic)	Follicular adenoma	2.5
13	53	F	Benign (non-neoplastic)	Follicular adenoma	4.5
14	73	M	Benign (non-neoplastic)	Papillary carcinoma	2.5
15	78	F	Benign (non-neoplastic)	Papillary carcinoma	0.5
16	61	F	Benign (non-neoplastic)	NIFTP	3.5
17	57	F	Benign (non-neoplastic)	Oncocytic adenoma	4.8
18	62	F	Benign (non-neoplastic)	Follicular adenoma	4
19	50	F	Benign (non-neoplastic)	Papillary carcinoma	0.2
20	40	F	Benign (non-neoplastic)	Papillary carcinoma	4
21	55	F	Benign (non-neoplastic)	Papillary carcinoma	4.3
22	48	F	Benign (non-neoplastic)	Papillary carcinoma	1
23	69	F	Benign (non-neoplastic)	Poorly differentiated carcinoma	6
24	47	F	Benign (non-neoplastic)	Papillary carcinoma	0.3
26	68	F	Benign (non-neoplastic)	Papillary carcinoma	0.3
27	56	F	Benign (non-neoplastic)	Follicular tumor of uncertain malignant potential	4
28	37	M	Suspicious of follicular neoplasm	Papillary carcinoma	3.2
29	78	F	Suspicious of follicular neoplasm	Nodular goiter	-
30	61	F	Suspicious of follicular neoplasm	Nodular goiter	-
31	63	F	Suspicious of follicular neoplasm	Chronic lymphocytic thyroiditis	-
32	64	F	Suspicious of follicular neoplasm	Nodular goiter	-
33	66	F	Suspicious of follicular neoplasm	Papillary carcinoma	3.5
34	65	F	Follicular neoplasm	Nodular goiter	-
35	39	F	Suspicious of follicular neoplasm	Nodular goiter	-
36	51	F	Follicular neoplasm	Nodular goiter	-
37	70	F	Suspicious of follicular neoplasm	Nodular goiter	-
38	46	F	Suspicious of follicular neoplasm	Nodular goiter	-
39	67	F	Follicular neoplasm	Nodular goiter	-
40	34	F	Suspicious of malignancy	Widely invasive follicular carcinoma	3.5

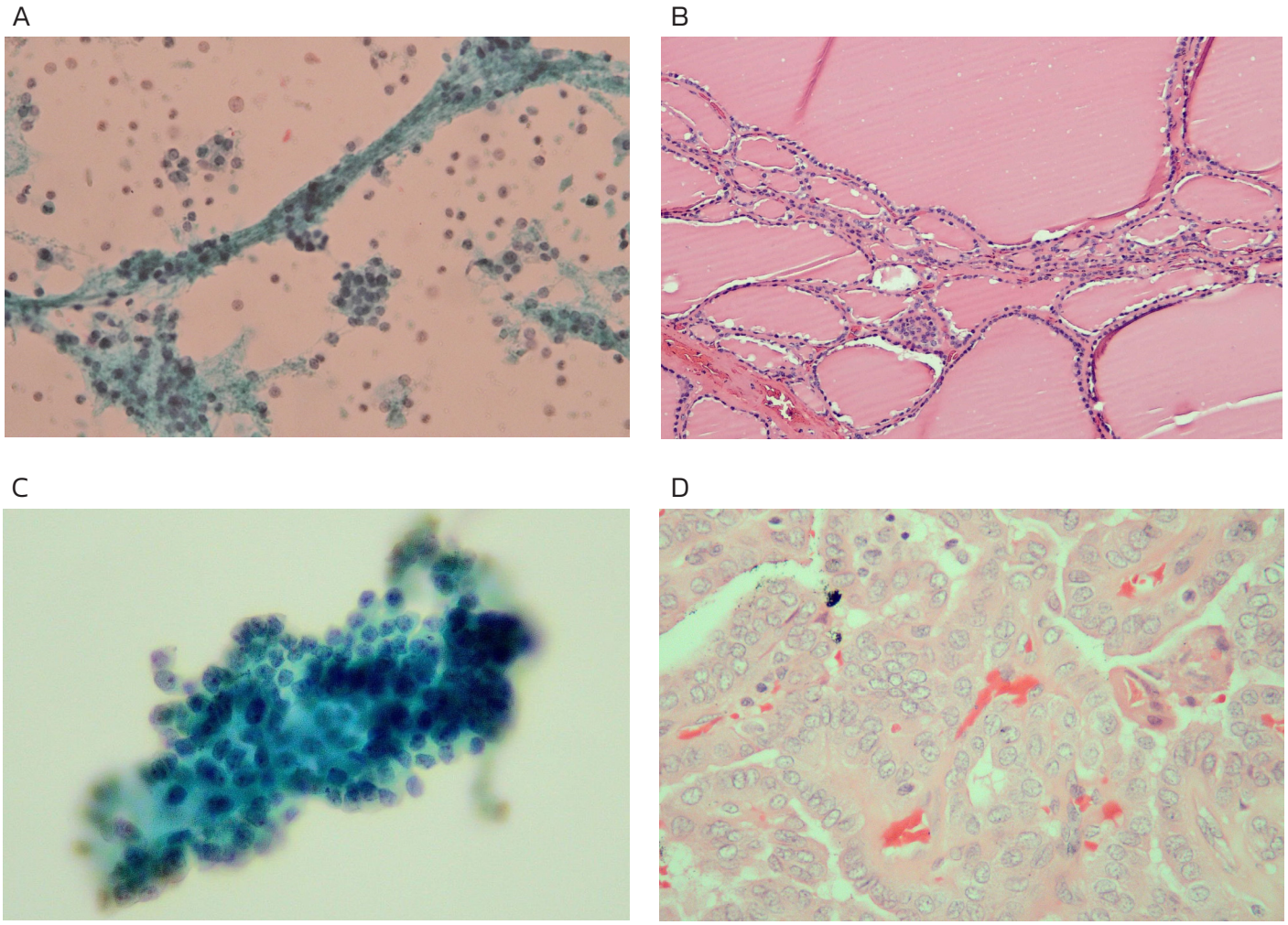


Figure 2 Cytologic findings in cases presenting with discordant diagnoses. The first case was initially interpreted as suspicious for a follicular neoplasm on liquid-based cytology (LBC), whereas the histologic diagnosis was nodular goiter (A, B). The second case was cytologically diagnosed as suspicious for a follicular neoplasm, whereas final histology revealed papillary carcinoma (C, D).

table 4, 147 cases revealed true negative, 43 cases showed true positive, 10 cases were false positive, and 26 cases were false negative. The false-positive and false-negative rates were 6.4% and 37.7%, respectively (Table 4). The diagnostic performance of thyroid LBC was evaluated by comparison with histological diagnosis (Table 5).

Liquid-based thyroid FNA cytology demonstrated a sensitivity of 62.3% (95% CI, 56%–68.6%) and a specificity of 93.6% (95% CI, 90.4%–96.8%). The PPV was 81.1% (95% CI, 76%–86.2%), and the NPV was 85% (95% CI, 80.3%–89.6%). The overall diagnostic accuracy was 84.1% (95% CI, 79.3%–88.8%).

Of 226 cases, 186 showed concordant cytology–histology results, stratified by category. The remaining 40 discordant cases are presented in Table 6.

Discussion

In this study, thyroid nodules occurred predominantly in females, consistent with previous reports[1,7–12], with a female-to-male ratio of 5.8:1. The patient age distribution was comparable to other studies, with thyroid cancer most frequently diagnosed in the fifth decade, as also reported by Nakrangsee.[10] Overall demographics were similar to Thai-based studies.[1,8–12] Nodular goiter was the most common benign lesion[9,10], while papillary thyroid carcinoma was the most frequent malignancy.[9–11] Although the prevalence of papillary thyroid carcinoma was 17.7%, lower than prior studies[9–11], it accounted for

82.1% of all thyroid cancers. Thus, surgical cases were likely selected based on cytological findings.

In this study, 70 cases (19.4%) were nondiagnostic, within the range of 8.1–47.6% reported in Thailand.[8–12] Among these, 87% were benign (non-neoplastic lesions and benign neoplasms), predominantly nodular goiter 80.3% (49 out of 61 benign cases). Malignancy was identified in 11.4% of nondiagnostic cases, lower than previous reports (14.3–28.4%)[8–10,12], though still higher than the TBSRTC estimate.[3] Cyst fluid only was the most common finding, reflecting the predominance of cystic benign nodules with low follicular cellularity.[3] The relatively high nondiagnostic rate observed in this study may be attributed to several factors, including unequal sample splitting during the manual processing steps of the EASYPREP® system, a high proportion of cystic nodules, absence of ROSE, operator variability, and incomplete use of ultrasound guidance.[13, 15-16]

In the benign category, 8.7% were malignant on final histology, exceeding the expected ROM of 0–3% in TBSRTC.[3] However, this rate was lower than in several Thai and Asian studies.[4,8,9,11,12] Clinical and ultrasound follow-up is recommended[3,4], while surgery was mainly performed for large nodules or compressive symptoms.[8] Selection bias may have increased the observed ROM, as only indicated cases underwent surgery.[4]

AUS accounted for 18% of cases, within the reported 1–22% range.[3,5] An AUS-to-malignancy ratio of 3.1 was observed, indicating potential underdiagnosis of more definitive categories or overdiagnosis of AUS, relative to the TBSRTC threshold of 3.0. The malignancy rate was 32.3%, slightly higher than the TBSRTC range of 10–30%, consistent with higher ROM reported in Asian practice[4] and comparable to Thai studies.[8–12] Papillary thyroid carcinoma was found in 17 AUS cases (26.2%), lower than the TBSRTC range of 28–56%. Diagnostic limitations may relate to low cellularity and specimen quality.[4,10] The ROM for FN/SFN was 14.3%, consistent with the TBSRTC range of 10–40% when considering NIFTP. The ROM values for the suspicious for malignancy and malignant categories exceeded the TBSRTC and previous studies.[3,8–12]

Nodular goiter was frequently observed in false-positive FN/SFN cases, consistent with prior reports.[9,10,14] Figure 2A and 2B illustrate the cytologic findings of a discordant case where a nodular goiter was misclassified as suspicious of follicular neoplasm. Cytologic–histologic correlation in follicular-patterned lesions remains challenging due to diagnostic variability among entities such as nodular goiter, follicular adenoma, follicular carcinoma, follicular variant of papillary carcinoma, and NIFTP.[3,5,7] Some follicular neoplasms may be misclassified as benign. Features favoring follicular neoplasm include moderate cell crowding and microfollicular architecture. In this study, 52.4% of FN/SFN cases were confirmed neoplastic; thus, surgical excision is recommended for definitive diagnosis.[3,5] Approximately one-third of false-negative papillary thyroid carcinomas measured ≤1 cm. Small lesions may be difficult to sample cytologically and may also represent incidental findings during treatment of benign nodules.[4,9] In addition, when the classic nuclear hallmarks of papillary carcinoma are indistinct in LBC, the conspicuous follicular architecture can mask the diagnosis, leading pathologists to favor a diagnosis of follicular neoplasm.[14,16] In the discordant case, LBC showed subtle nuclear details, potentially resulting in the misdiagnosis of papillary carcinoma as a follicular neoplasm (Figures 2C and 2D).

The sensitivity of LBC in this study was lower than that reported for conventional smears (Table 7).[10,12] This may be influenced by specimen quality, technique, and pathologist experience.[13-16] Nonetheless, LBC demonstrated good performance in detecting malignancy, with high specificity reducing unnecessary surgery. Diagnostic accuracy was also high, with correspondingly elevated PPV and NPV. Overall, these findings align with prior studies showing high specificity but moderate sensitivity for LBC.[6–7,9–12] The sensitivity observed in this study is comparable to prior reports in similar settings.[10,12] Meta-analyses report no significant difference in accuracy between conventional smear and LBC.[6] Compared to SurePath (a first-generation liquid-based preparation method), EasyPrep yields statistically similar cytomorphologic results.[16] LBC remains reliable; however, improved

Table 7 Previously reported diagnostic performance of thyroid cytology.

Author, year	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Nakrangsee S. 2018 [10]	74.7	90.3	84.6	81.5	86.2
Suwatthanarak T, et al. 2021 [12]	77.8	65.4	69	47.7	87.9
This study	62.3	93.6	84.1	81.1	85

sample adequacy and repeated processing may enhance sensitivity.[16] Integration of clinical and ultrasound findings is essential for optimal management.

Meta-analyses, which have shown that LBC, provides high specificity but only moderate sensitivity in the diagnosis of thyroid malignancy.[13,14] In particular, the meta-analysis by Bongiovanni et al. reported pooled sensitivities range from approximately 65% to 75%, the present study yielded a slightly lower sensitivity of 62.3%. However, the specificity exceeded 90%, which aligns closely with established literature.[13] Similarly, studies from other settings, such as Wu et al.[14], have reported sensitivity values ranging from 68% to 78% and specificity between 92% and 96%. Although the sensitivity in the present study was marginally lower at 62.3%, the observed specificity of 93.6% falls well within the reported range. The comparable diagnostic performance suggests that LBC is a reliable diagnostic modality across different clinical settings. The high specificity observed in this study indicates that LBC is particularly useful for confirming malignancy, especially in cases categorized as suspicious for malignancy or malignant according to the Bethesda system.

However, the moderate sensitivity observed highlights an important limitation of LBC in detecting all malignant cases. False-negative results may occur, particularly in small nodules, cystic lesions, or tumors with overlapping cytological features. Several factors may contribute to this limitation, including sampling error, inadequate cellularity, and operator-dependent variability. In addition, the absence of ROSE in this study may have contributed to both the moderate sensitivity and the relatively high nondiagnostic rate, as ROSE has been shown to improve specimen adequacy and diagnostic yield.[15]

This study has several limitations. First, this study included only patients who underwent surgical resection, study may be overestimated compared to the general population. Second, incomplete pre-analytical data—such as needle size, operator technique, and ultrasound guidance—may affect nondiagnostic rates and sensitivity. Third, the exclusion of non-diagnostic and AUS/FLUS results ensures high specificity, as potential malignant cases within these groups are omitted from the calculation. Finally, although specificity was high, moderate sensitivity limits malignancy detection; thus, cytologic results should be interpreted alongside clinical and sonographic findings. To address these limitations, future research should employ a multi-observer design to assess inter-observer reliability, supported by documented quality assurance procedures. To date, no studies have evaluated thyroid LBC accuracy and ROM in Thailand. Given the small sample size, further studies are needed to validate these findings.

Conclusion

LBC demonstrates good diagnostic performance in evaluating thyroid nodules, with high specificity and overall accuracy, making it reliable for confirming malignancy and reducing unnecessary surgery. However, its moderate sensitivity indicates limitations in detecting all malignant lesions. The risk of malignancy across Bethesda categories was generally consistent with previous studies, supporting its clinical applicability. Therefore, LBC should

be interpreted in conjunction with clinical and ultrasonographic findings to optimize patient management.

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