

## Short Communication

# Comparative analysis of accuracy between fine-needle aspiration biopsy and postoperative histopathology for detecting large thyroid nodules: A retrospective observational study

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## Abstract

To avoid unnecessary surgeries, ultrasound-guided fine-needle aspiration biopsy (FNAB) is an effective and reliable procedure for the preoperative evaluation of thyroid nodules. However, there have been only a limited number of studies exploring the ability of preoperative FNAB to distinguish malignancy compared to postoperative histopathology in thyroid nodules larger than 4 cm. The aim of this study was to investigate the diagnostic accuracy of FNAB compared to postoperative histopathology in distinguishing malignancy in thyroid nodules larger than 4 cm. A single-center retrospective observational study was conducted at Dr. Zainoel Abidin Hospital, Banda Aceh, Indonesia, between January 2014 and December 2018. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated. A total of 83 patients were included in the study. The results showed that preoperative FNAB may have the ability to distinguish malignancy compared to postoperative histopathology. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were 42.85%, 98.38%, 90.00%, 83.56%, and 84.33%, respectively. These data suggested that ultrasound-guided preoperative FNAB is a reliable diagnostic tool in the preoperative evaluation of thyroid nodules larger than 4 cm, but it has limited capability in distinguishing malignancies. In conclusion, although FNAB may be useful in reducing unnecessary surgeries, histopathology remains the preferred method for confirming malignancy in thyroid nodules.

**Keywords:** Fine-needle aspiration biopsy, histopathology, thyroid nodule, accuracy, sensitivity



## Introduction

The availability of ultrasound-guided techniques allows the detection and aspiration of smaller and deep-seated thyroid nodules [1-3]. Although most thyroid nodules are benign, the prevalence

of thyroid malignancy has recently increased dramatically up to a rate of 5%–20% [4]. The rising rates of thyroid nodules highlight the importance and urgency of identifying the malignancy precisely [5].

Fine-needle aspiration biopsy (FNAB) has long been considered the most important primary diagnostic tool in the evaluation of thyroid nodules due to its advantages, including simplicity, safety, cost-effectiveness, and high diagnostic specificity [2,6,7]. Reported sensitivity and specificity of thyroid FNAB typically range between 80% and 100% [2,3,8-10]. However, there is ongoing controversy regarding the accuracy of FNAB to exclude malignancy in nodules larger than 4 cm [5]. Studies have reported a high false negativity rate for FNAB, ranging from 10% to 50% [11]. Some studies recommend surgery for nodules larger than 4 cm regardless of FNAB results [5,11-17], while others assert the reliability of FNAB even in larger nodules [18-23].

Larger thyroid nodules are well-established to have a higher risk of cancer [12]. The gold standard for diagnosing malignancy status is a histological assessment of the surgically excised thyroid nodule, although it has inherent surgical risks [24]. FNAB aids clinicians in diagnosing the malignancy and deciding on thyroidectomy. Nevertheless, the increased morbidity and costs associated with unneeded thyroidectomy must be considered [25].

While FNAB is widely accepted and utilized for diagnosing thyroid nodules, the conflicting evidence has been reported in several studies [5,11-23], necessitates a comprehensive investigation into the diagnostic accuracy of FNAB compared to postoperative histopathology for large thyroid nodules. Therefore, this study aimed to provide diagnostic accuracy of FNAB compared to postoperative histopathology in detecting malignancy in thyroid nodules larger than 4 cm. The findings will aid therapeutic decision-making and could potentially decrease avoidable surgical procedures, morbidity, and costs.

## Methods

### Study design and setting

A single-center retrospective observational study was conducted at Dr. Zainoel Abidin Hospital, a tertiary hospital in Banda Aceh, Indonesia between January 2014 and December 2018. The study investigated the medical records of 567 patients who underwent both ultrasound-guided preoperative FNAB and postoperative histopathology. Total sampling was adopted, based on eligibility criteria, resulting in 83 qualified medical records. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were determined using a fourfold table and the receiver operating characteristic (ROC) curve.

### Eligibility criteria

The inclusion criteria are as follows: (1) diagnosed solid thyroid nodules larger than 4 cm based on histopathological and grayscale thyroid ultrasonography assessment; (2) normal thyroid stimulating hormone (TSH) serum level (0.25–5  $\mu$ IU/mL); (3) age range 17–70 years old based on the medical record; and (4) had complete preoperative FNAB record. All patients who had undergone radioiodine therapy and recurrent or relapse thyroid carcinoma were excluded.

### Data collection

FNAB cytology results were categorized using the Bethesda system for the classification of thyroid cytopathology [26]. Cytology classifications were compared to histologic diagnoses of the surgical specimens made by an anatomical pathologist with over ten years of expertise (R.K.K).

### Statistical analysis

Sensitivity, specificity, PPV, NPV, and diagnostic accuracy were determined by comparing cytology results to histology results, which serve as the gold standard for malignancy detection. The fourfold table analysis and ROC curve were employed for these calculations.

## Results

### Characteristics of patients

The basic characteristics of the 83 patients with thyroid nodules larger than 4 cm are presented in **Table 1**. There were different proportions between gender and age between patients; the majority of patients (83.13%) were male, and the mean age was approximately 46–55 years old.

**Table 1. Characteristics of patients with thyroid nodules larger than 4 cm included in the study**

Patient characteristic	Total	
	n	%
Sex		
Male	69	83.3
Female	14	16.86
Age (year)		
17–25	5	6.02
26–35	10	8.30
36–45	20	16.60
46–55	21	25.30
56–65	21	25.30
>65	6	7.22

### Characteristics of thyroid nodules based on FNAB and histopathology

Thyroid nodules were histopathologically detected following surgery. The outcome was classified as non-malignancy, non-neoplasm, or malignancy based on FNAB thyroid nodule characteristics and histopathologic examination. The details are presented in **Table 2**. As shown, there are differences between FNAB and histopathologic results for each diagnosis.

**Table 2. Comparison of nodule characteristics based on FNAB and histopathology**

Diagnosis	Classification	Fine-needle aspiration biopsy	Histopathology
		Number of cases (n)	Number of cases (n)
Non-malignance	Follicular neoplasm	5	0
	Follicular adenoma	1	19
	Papillary adenoma	0	1
Non-neoplasm	Adenomatous goiter	31	27
	Colloid goiter	15	9
	Cystic disease	18	1
	Hashimotos thyroiditis	0	2
	Nodular goiter	0	1
	Simple goiter	1	0
	Thyroglossal cyst	0	1
	Reactive hyperplasia	1	0
Malignance	Papillary adenocarcinoma	5	9
	Follicular adenocarcinoma	3	3
	Papillary carcinoma	1	4
	Follicular carcinoma	1	3
	Invasive papillary adenocarcinoma	0	2
	Metastasis follicular	0	0

### Diagnostic ability of FNAB compared to histopathology

The sensitivity, specificity, PPV, and NPV were calculated using a fourfold table analysis (**Table 3**). Slight inconsistencies exist between FNAB and histopathologic results. Nine out of ten positive carcinoma results in FNAB and histopathology were confirmed, while one turned negative in histopathology. Surprisingly, 12 negative results from FNAB were positive in histopathology, while the majority of cases (n=61) showed consistent negative results in both FNAB and histopathology (**Table 3**).

Table 3. Fourfold analysis of diagnostic accuracy of FNAB and histopathology

		Histopathology	
		Positive thyroid carcinoma (n)	Negative thyroid carcinoma (n)
FNAB	Positive thyroid carcinoma (n)	9	1
	Negative thyroid carcinoma (n)	12	61

Based on a fourfold analysis of FNAB compared to histopathology examination, the sensitivity, specificity, PPV, and NPV were 42.85%, 98.38%, 90.00%, and 83.56%, respectively. The ROC curve was calculated, and results showed a diagnostic accuracy of 84.33% from comparing FNAB to histopathologic examination (**Figure 1**).

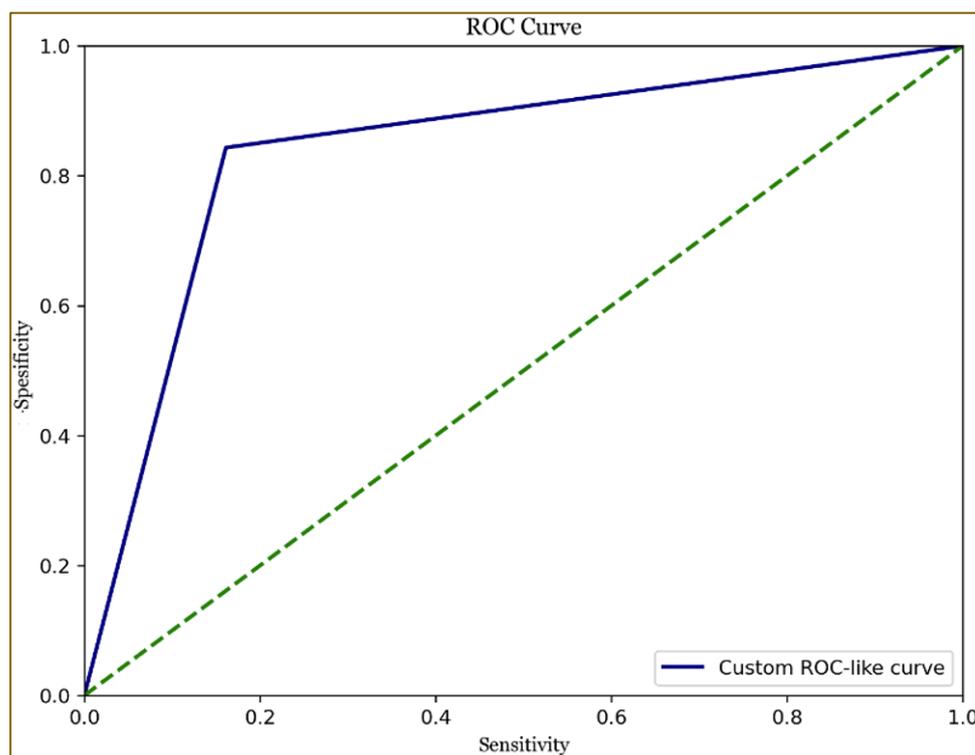


Figure 1. The receiver operating characteristic (ROC) curve shows diagnostic accuracy by comparing FNAB to histopathology.

## Discussion

Thyroid nodules larger than 4 cm present a significant challenge in terms of diagnostic accuracy for appropriate management, given the fact that this study showed conflicting results from comparing FNAB to postoperative histopathology in detecting malignancy. This and previous studies [2,5,11,18,24,27,28] have demonstrated that FNAB may have the ability to distinguish malignancy in thyroid nodules larger than 4 cm, with varying sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy values.

The results from preoperative FNAB in this study are in line with previous studies, highlighting the lower sensitivity and higher false negativity rate of FNAB in larger nodules [2,18,24,27,28]. A study conducted found that there was an overall discrepancy rate of 15.3% between cytologic and histologic diagnoses [3]. Although FNAB can accurately detect large thyroid nodules, it has limited capability in distinguishing malignancies.

Previous studies have shown false negativity rates ranging from 7.7% to as high as 50% in nodules larger than 4 cm [2,3,5,12,15,24,27,28]. Three studies reported that the false negativity rates of 10.4% to 20% [5,11,13]. McCoy *et al.* demonstrated an unacceptably high false negativity rate of 13%, which increased to 16% when multifocal micropapillary carcinomas were included [12]. In addition, an unexpected finding by Koo *et al.* revealed a remarkably high false negativity

rate of 50% in thyroid nodules larger than 4 cm [15]. These findings suggest that relying solely on FNAB results may lead to missed malignancies, necessitating the consideration of thyroidectomy even in cases with benign biopsy results.

Despite the reported high false negativity rates, conflicting studies have presented alternative perspectives. Kuru *et al.* reported similar false negativity rates for nodules smaller and larger than 4 cm (1.3% and 4.3%, respectively), indicating that the size of the nodule may not significantly influence FNAB accuracy [18]. Additionally, Albuja-Cruz *et al.* also found that the diagnostic reliability of FNAB is not affected by nodule size [22]. Rosario *et al.* suggested that the false negativity rate of 3.6% in nodules  $\geq 4$  cm does not justify routine surgery [19]. These distinct findings emphasize the need for a thorough assessment of various factors before deciding on thyroidectomy.

It is important to note that the accuracy of FNAB results can be influenced by various factors, including sample volume sufficiency, sampling from the correct site, and the accurate interpretation of the results [2,14,23,29]. Furthermore, the sensitivity of FNAB can be considerably impacted by pathologists' competence in high-volume centers, as well as the quality of training and experience of operators at a particular facility [30]. Therefore, when advising patients about the necessity of thyroidectomy for large nodules, these factors should be taken into consideration and thoroughly discussed to ensure informed decision-making.

The recommendation of thyroidectomy can pose challenges for certain patients with large nodules, particularly those who have reduced life expectancies due to age or comorbidities, or for whom surgery may present significant health risks or financial burdens [24]. It is important to acknowledge that thyroid surgery is a complex procedure associated with potential complications. The extent of surgery and the surgeon's experience both contribute to determining the risk of surgical complications, with total thyroidectomy carrying a higher risk compared to unilateral lobectomy [24]. The decline in quality of life after surgery can be impacted by a variety of factors, including the requirement for long-term medication, hypoparathyroidism, dysphagia, and dysphonia, which can be temporary or permanent [31]. Hence, the decision to remove large thyroid nodules should be carefully evaluated, taking into account individual patient factors and considerations.

## Conclusion

Preoperative FNAB is a reliable diagnostic tool in the preoperative evaluation of thyroid nodules larger than 4 cm. Although FNAB can accurately detect large thyroid nodules, it has limited capability in distinguishing malignancies. Our results suggest that FNAB may be useful in reducing unnecessary surgeries; however, histopathology remains the preferred method for confirming malignancy in thyroid nodules.

## Ethics approval

This study was approved by the Health Research Ethics Committee of Dr. Zainoel Abidin Hospital Banda Aceh, Indonesia (No 312/EA/FK-RSUDZA/2019).

## Competing interests

The authors declare that there is no conflict of interest.

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## Underlying data

Derived data supporting the findings of this study are available from the first author on request.

## How to cite

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