ORIGINAL ARTICLE

The Accuracy of FNAB as Diagnostic Tool For Thyroid Cancer Compared to Anatomical Pathology Results as Gold Standard at Sanjiwani Hospital, Gianyar

I Nyoman Wawan Tirtayasa[1*], Luh Putu Dewanda Maheswari[2], Ida Bagus Made Suryawisesa[3], Hendry Irawan[3], I Wayan Sudarsa[3], Made Dwi Yoga Bharata[4], I Ketut Tangking Widarsa[2]

[1] Division of Oncology, Department of Surgery, Sanjiwani Hospital, Gianyar/Faculty of Medicine and Health Science, Warmadewa University.
[2] Faculty of Medicine and Health Science, Warmadewa University.
[3] Division of Oncology, Department of Surgery, Prof. dr. IGNG Ngoerah Hospital/Faculty of Medicine, Udayana University.
[4] Division of Digestive Surgery, Department of Surgery, Sanjiwani Hospital, Gianyar/Faculty of Medicine and Health Science, Warmadewa University.

* Correspondence author: nyomanwawan@yahoo.com.

ABSTRACT

Aim: The aim of this study was to assess the accuracy of fine needle aspiration biopsy (FNAB) as a diagnostic tool for thyroid cancer in Sanjiwani Hospital, Gianyar. **Methods:** This study used a diagnostic test method with a retrospective cross-sectional design. A total of 138 cases of thyroid nodules that received FNAB and anatomical pathology examinations were selected consecutively. The level of accuracy was determined from the number of sensitivity, specificity, positive predictive value and negative predictive value. **Results:** The results of this study showed a low sensitivity 11.53%, but high specificity 100%, positive predictive value 100%, and negative predictive value 82.96% of FNAB. The accuracy of FNAB as diagnostic tools of thyroid cancer was 83,3% compared with anatomical pathology results as gold standard. **Conclusion:** FNAB is less accurate to diagnose thyroid cancer, but FNAB examination is accurate in differentiate benign and cancer lesion in thyroid nodule.

Keywords: thyroid cancer, diagnostic test, FNAB.

INTRODUCTION

The thyroid is an endocrine gland located in front of the neck, between the fascia of the media colli and the prevertebral.[1] The functions of thyroid gland are to regulate the process of oxidation and the release of carbon dioxide, affect physical and mental development in children, and also secrete the thyroxine (T4) and triiodothyronine (T3) hormones derived from iodine that enters the body from diet.[1]

Enlargement of the thyroid gland or struma could be an inflammatory disorder or hyperplasia or neoplasm. Sometimes, they are difficult to differentiate clinically.[2] Most strumas (90% to 95%) are benign (non-cancerous), but the malignant types can spread throughout the body sporadically and life-threatening. Struma is less common at a young age, but malignant struma is more common in young men. The prevalence of malignancy in single and multiple strumas is quite similar, 4.1% and 4.7% respectively. Based on type of carcinoma, ± 90% cases were papillary and follicular carcinoma, 5-9% were medullary carcinoma, 1-2% were anaplastic carcinoma, and 1-3% were other types.[3] Thyroid cancer is a malignant tumor in the thyroid gland, the largest endocrine organ in humans. The incidence rate tends to increase rapidly. A study conducted in America reported thyroid cancer had the fastest increase of incidence rate compared to other cancers. It could be

related to the increasing use of diagnostic tools as a supporting examination.[4]

Thyroid nodules can be detected either through physical examination or by using various diagnostic tests such as laboratory and ultrasound examinations, thyroid scanning or thyroid fingerprints, fine needle aspiration biopsy (FNAB) examinations, and histopathological examinations. About 5% of palpable nodules are likely to be malignant, in addition to patient's symptoms such as feeling uncomfortable due to mechanical pressure of nodules on surrounding organs as well as cosmetic problems. Therefore, a specific initial test to detect thyroid malignancy is needed.[5,6] The problem faced by oncology surgeons is to definitively classify a thyroid gland enlargement to benign or malignant struma especially cases with no clearly symptoms of malignancy.

Histopathological examination on biopsy samples was a gold standard to diagnose thyroid cancer. However, this examination need a quite time, about 3-7 days to get the results and the sampling method is invasive, need anaesthesia, required a lot of facilities and cost, and also skilled surgeon. Therefore, the cheaper (cost-effective), relatively simple and high accuracy diagnostic tools/methods are needed.[7]

The FNAB is the initial diagnostic step to diagnose thyroid nodules, performed by an operator and assessed by an experienced cytologist. The techniques are safe, simple, inexpensive and reliable and can be performed on an outpatient setting with a relative low risk.[8] The FNAB examination has been reported to reduce unnecessary surgery by 25% and increase thyroid cancer diagnosis by 30-40%. However, the FNAB are unable to identify tumor tissue architecture with unclear accuracy in differentiate benign and malignant thyroid nodules.[9] In a study at Dr. H. Abdul Moeloek Hospital Bandar Lampung, the sensitivity and specificity of FNAB for thyroid nodule diagnosis was 94.44% and 100%, respectively.[10] Different study by Rahmadhani et al. reported low accuracy of FNAB (62.2%) with sensitivity 62.1%, specificity 62.5%, positive prediction value 75%, and negative prediction value 47.6%.[11]

The accuracy of examination with FNAB as a diagnostic procedure for thyroid cancer at Sanjiwani Hospital, Gianyar has never been reported. Therefore, the aim of this study was to determine the accuracy of FNAB as a thyroid cancer diagnostic procedure at the Anatomical Pathology Laboratory of Sanjiwani Hospital. The results of this study may provide benefits in terms of cost, accuracy of diagnosis, and convenience for patients.

METHODS

This study was a diagnostic test with a retrospective cross-sectional design. The study was conducted at the Pathology and Surgical Oncology Department of Sanjiwani Hospital. The patients with thyroid nodule and conducted FNAB procedure and histopathological examination in January 2017 – December 2019 was included by consecutive sampling technique. Patients with incomplete medical record or history of other primary cancer were excluded. This study used secondary data from medical record. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated by comparing the results of FNAB and histopathological examination as the gold standard.

The minimum sample size of the study (N) was calculated using the sample size formula for diagnostic study, with the expected sensitivity of FNAB (p) was 90%, deviation (d) for sensitivity was 10%, the prevalence of

thyroid cancer (p_x) was 50%, and the confidence level (α) was set at 95%.

$$N = \frac{(Z_\alpha)^2 p(1-p)}{d^2 p_x^2} = 138 \text{ samples}$$

The data obtained is then collected, processed, and presented in the form of tables and narratives. Data analysis used formulas to calculate sensitivity, specificity, positive and negative predictive values, and accuracy.

RESULTS

During the study period, there was 138 samples included in this study. Majority of samples was 40-60 years old (61.59%) and female (82.6%). The mean age of patients who had undergone FNAB examination followed by histopathology biopsy in this study was 45.85 years, from the age of 14 - 73 years (**Table 1**).

Table 1. Characteristics of Patients with Thyroid Nodule.

Characteristics	N=138	Percentage (%)
Age		
14-39	36	26.08
40-60	85	61.59
>60	17	12.31
Sex		
Female	114	82.6
Male	24	17.3

There were three cases of thyroid carcinoma/malignant and 135 samples were non-thyroid carcinoma/benign based on FNAB examination. Follicular neoplasms are the most types of benign cases (44.44%), followed by thyroid cysts, colloides struma, thyroiditis, and adenomatous struma. Colloid struma, as many as 11 samples. Thyroiditis as many as 5 samples and adenomatous struma as many as 3 samples (**Table 2**). In malignant cases, follicular neoplasms suspected of malignancy are the most types of thyroid malignancy with a total of 2 samples followed by suspected malignant thyroid cyst with 1 sample (**Table 2**).

Table 2. Types of Thyroid Nodule Diagnosis Based on FNAB.

Types of Thyroid Nodule	N=138	Percentage (%)
Benign		
Colloid struma	11	8,14
Adenomatous struma	3	2,22
Follicular neoplasm	60	44,44
Thyroid cyst	56	41,5
Thyroiditis	5	3,7
Malignant		
Suspect malignant follicular neoplasm	2	66,67
Suspect malignant thyroid cyst	1	33,33

Based on histopathological examination, there was 112 benign cases and 26 malignant cases (thyroid carcinoma=18.4%) of thyroid nodule. In benign cases, thyroid cysts were the most diagnosis (58%), followed by follicular neoplasms (5.21%), thyroiditis (2.89%), and oncocytic adenoma (1.45%) samples (**Table 3**).

Table 3. Thyroid Nodule Diagnosis Based on Histopathological Examination.

Types of Thyroid nodule	N = 138	Percentage (%)
Oncocytic Adenoma	2	1.45
Follicular neoplasm	5	3.62
Adenomatous struma	21	15.21
Thyroid cyst	80	58
Thyroiditis	4	2.89
Thyroid Carcinoma	26	18.84

The similarity of thyroid nodule diagnosis based on FNAB examination and histopathological examination were 0% of adenomatous struma, 5% of follicular neoplasms, 69% of thyroid cysts, 10% of thyroiditis. All the diagnosis of malignant nodule in FNAB was similar to histopathological results (**Table 4**).

Table 4. Comparison of FNAB and Histopathological Examination Based on Types of Thyroid Neoplasm.

		Histophatological Examination					
		OA	FS	AS	KT	T	CT
F N A B	CS			4	6		1
	AS				3		
	FS	1	3	9	30	3	14
	TC	1	2	7	39		7
	T			1	2	1	1
	MFN						2
	MTC						1

Abbreviation:

CS: colloid struma	MFN: suspect malignant follicular neoplasm
AS: adenomatous struma	MTC: suspect malignant thyroid cyst
FS: follicular struma	OA: oncocytic adenomatous
TC: thyroid cyst	CT: carcinoma thyroid
T: thyroiditis	

The calculation of sensitivity, specificity, negative and positive predictive values, and accuracy were based on 2x2 table. The accuracy of FNAB as diagnostic tool of thyroid nodule was 83.33%, with low sensitivity was 11.53%, but high specificity (100%), positive predictive value (100%), and negative predictive value (82.96%) (**Table 5**).

Table 5. thyroid nodules with FNAB and PA biopsy using 2x2 table.

FNAB	Histopathological Examination		Total
	(+) Malignant	(-) Malignant	
(+) Malignant	3	0	3
(-) Malignant	23	112	135
Total	26	112	138

a. Sensitivity : $\frac{3}{26}$ x 100% = 11,53%

b. Specificity : $\frac{112}{112}$ x 100% = 100%

c. Positive predictive value : $\frac{3}{3}$ x 100% = 100%

d. Negative predictive value : $\frac{112}{135}$ x 100% = 82,96%

e. Accuracy : 115: 138 x 100 % = 83,33 %

DISCUSSION

The result of this study reported a low sensitivity of FNAB to detect thyroid cancer. Incomplete diagnosis writing in medical record, improper cytological aspiration collection sites, less experience and foresight of pathologists are several factors contribute to this result. Meanwhile, several similar studies that have been published reported the higher results. Study conducted at Hasanuddin University Hospital Makassar by Ayub reported the sensitivity of FNAB to diagnose thyroid nodule was 47.62%.[12] A study by Sinna et al.[13] reported a sensitivity of 92.8% and study by Prasetyo et al.[14] at Dr. Kariadi Hospital Semarang reported the sensitivity of 100%.[14]

The level of specificity indicates the ability of the diagnostic test to detect the possibility that the diagnostic test result will be negative (true negative). The result of this study reported that all patients who were not thyroid cancer based on FNAB examination could be declared not thyroid cancer (specificity 100%). The high specificity results were also reported in several previous studies, range from 94.12% to 94.2%.[12,13] There was a slight difference with the research at Dr. Kariadi Hospital Semarang which reported specificity of 84%, due to fewer samples.[14]

A positive predictive value (PPV) indicates the probability of a person suffering from the disease if the diagnostic test result is positive. These results showed that patients with positive FNAB results were all thyroid cancer patients, so the false positive values were nil or very low (PPV was 100%). Compared to other studies, the positive predictive value of FNAB were quite high, ranging from 69.2%-94.9%.[12-14] A negative predictive value (NPV) indicates the probability of a person not suffering from the disease if the diagnostic test result is negative. The result of this study showed that patients who did not suffer from cancer, based on the results of FNAB examination as many as 82.96% were declared not malignant lesion. The other studies also reported high NPV. Sinna et al.[13] reported NPV of 91.8% and Prasetyo et al. reported NPV was 100%.[14] Lower NPV was reported by Ayub, which was 74.42%.[12]

Misinterpretation of FNAB can occurred due to inadequate samples, punctured surrounding tissue, and incorrect locations, as well as human-error by anatomical pathologists. The diagnosis of cytology cannot be established if the preparation and handling of specimens are scant or if the cellular material is inadequate.[13] Ultrasound-guided FNAB may increase the precision of

aspiration area.[15] The most common misinterpretation of FNAB in this study was in follicular neoplasms, which was 14 out of 26 cases of thyroid malignancy. The cytological features of edematous goiter, follicular edematous, and follicular adenocarcinoma are similar, therefore differentiate them based on FNAB is quite difficult. Those differentiation depend on the description of invasion to the capsule and vascular which can only be seen from histopathological examination. This can increase false negative values and reduce the sensitivity rate in the study.[4]

Cytological diagnosis is helpful in papillary carcinomas with adequate specimens. FNAB examination is recommended at normal and elevated TSH levels. The results of thyroid nodule examination by FNAB were divided into four categories: non-diagnostic, malignant, indeterminate or suspected malignancy, and benign.[15] In this study, FNAB examination require other supporting examinations for better diagnosis of thyroid malignancy.

The limitation of this study was the low number (only 3 samples) of thyroid malignancy samples diagnosed with FNAB and histopathology examination in 3 years. Therefore, the further research needs a longer period to get more cases of thyroid malignancy.

CONCLUSION

FNAB as diagnostic tool of thyroid nodule has a low sensitivity 11.53%, but high specificity 100%, positive predictive value 100%, negative predictive value 82.96%, and accuracy 83,3% compared to histopathological examination as gold standard. The low sensitivity value makes FNAB examination not feasible to diagnose thyroid cancer accurately. However, FNAB examination is accurate in separating benign and malignant lesion of thyroid nodule.

REFERENCES

1. Haznam MW. *Endokrinologi*. Bandung: Penerbit Angkasa Offset Merdeka; 1991.

2. Maulinda JR. *Goiter*. 2018. [cited at 13 March 2023]. Available at: https://emedicine.medscape.com/article/120034-overview?form=fpf.

3. Sudoyo AW, Alwi I, Simadibrata M, et al. *Buku Ajar Ilmu Penyakit Dalam*. 4th edition. Jakarta: FK UI; 2006. p.1959-1963.

4. Cabanillas ME, McFadden DG, Durante C. Thyroid cancer. *Lancet*. 2016: 388(10061):2783-2795.

5. http://www.cancersupportivecare.com/fna.html.

6. Masjhur JS. Nodul Tiroid. In: Sudoyo AW, Setiyohadi B, Alwi I, et al, editors. *Buku Ajar Ilmu Penyakit Dalam Jilid III*. 5th Edition. Jakarta: Interna Publishing Perhimpunan Dokter Spesialis Penyakit Dalam Indonesia; 2009. p.2022-2023.

7. Mathur R. *Fine needle aspiration biopsy of the thyroid*. [cited at 20 May 2023]. Available at: https://www.medicinenet.com/fine-needle_aspiration_biopsy_of_the_thyroid/article.htm.

8. Subekti I. Karsinoma Tiroid. In: Sudoyo AW, Setiyohadi B, Alwi I, et al, editors. *Buku Ajar Ilmu Penyakit Dalam Jilid III*. 5th Edition. Jakarta: Interna Publishing Perhimpunan Dokter Spesialis Penyakit Dalam Indonesia; 2009. p.2031-2037.

9. Orell RS, Sterett FG, Whitaker D. *Fine Needle Aspiration Cytology*. 5th Edition. Philadelphia: Elsevier; 2012. p.119-149.

10. Wardani YA. Studi diagnostik Fine Needle Aspiration Biopsy (FNAB) dalam menegakkan diagnosis nodul tiroid di Instalasi Patologi Anatomi Rumah Sakit Umum Daerah Dr. H. Abdul Moeloek Bandar Lampung. [*skripsi*]. Bandar Lampung: FK Universitas Negeri; 2015.

11. Rahmadhani S, Asri A, Tofrizal. Akurasi Fine Needle Aspiration Biopsy sebagai Prosedur Diagnostik Nodul Tiroid di Laboratorium Patologi Anatomi Rumah Sakit Umum Pusat DR M Djamil Padang. *Jurnal Kesehatan Andalas.* 2018.

12. Ayub AD. Korelasi Aspirasi Jarum Halus dengan Histopatologi Akhir pada Neoplasma Tiroid di Bagian Patologi Anatomi Rumah Sakit Universitas Hasanuddin Makassar Periode 2015-2016. [*skripsi*]. Makassar: FK Universitas Hasanuddin; 2017.

13. Sinna EA, Ezzat N. Diagnostic accuracy of fine needle aspiration cytology in thyroid lesions. *J Egypt Natl Canc Inst.* 2012;24(2):63-70.

14. Prasetyo ZA, Nugroho H, Hapsari R. Uji Diagnostik FNAB (Fine Needle Aspiration Biopsy) Dibandingkan Dengan Biopsi Patologi Anatomi Dalam Mendiagnosis Karsinoma Tiroid. *Jurnal Kedokteran Diponegoro*. 2012;1(1).

15. Lai SW, Roberts DJ, Rabi DM, et al. Diagnostic accuracy of fine needle aspiration biopsy for detection of malignancy in pediatric thyroid nodules: protocol for a systematic review and meta-analysis. *Syst Rev*. 2015;4:120.