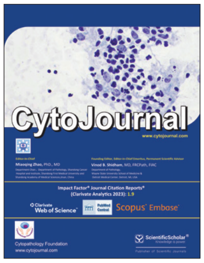

https://www.cytojournal.com/

CytoJournal

Research Article

The impact of anthropometric parameters and sonographic characteristics on the choice of biopsy method for thyroid nodules: Fine-needle aspiration versus non-aspiration biopsy

Muzaffer Serdar Deniz, MD.[1], Nuriye Ozder, MD.[2], Zubeyde Ilke Narli, MD.[3]

[1]Department of Endocrinology, Sincan Education and Research Hospital, Ankara, Turkey, [2]Department of General Surgeon, Karabük University, Faculty of Medicine, Education and Research Hospital, Karabük, Turkey, [3]Department of Pathology, Karabük University, Faculty of Medicine, Karabük, Turkey.

***Corresponding author:**
Muzaffer Serdar Deniz,
Department of Endocrinology,
Sincan Education and Research Hospital, Ankara, Turkey.

md.mserdardeniz@gmail.com

Received: 11 April 2024
Accepted: 28 May 2024
Published: 16 August 2024

DOI
10.25259/Cytojournal_42_2024

Quick Response Code:

ABSTRACT

Objective: The accurate diagnosis of thyroid nodules is crucial for effective management and the detection of malignancy. Fine-needle aspiration biopsy (FNAB) and fine-needle non-aspiration biopsy (FNNAB) are widely used techniques for evaluating thyroid nodules. In this study, we aimed to investigate the impact of anthropometric parameters and sonographic characteristics on the choice between FNAB and FNNAB in terms of diagnostic yield.

Material and Methods: This retrospective and cross-sectional analysis involved 188 cases with a total of 225 thyroid nodules. Each nodule initially underwent either FNAB or FNNAB and if the initial biopsy did not yield a diagnostic result, the nodule was re-biopsied using the alternate technique. Ultrasound was used to evaluate the nodules, with a focus on echogenicity, calcifications, size, vascularity, and the presence of a halo sign. Both FNAB and FNNAB were performed using a 25-gauge needle, with the only difference being the application of suction.

Results: FNAB demonstrated a higher diagnostic rate for nodules with a taller-than-wide shape (anteroposterior-to-transverse ratio ≥1), nodules sized 10–40 mm, nodules with volumes <0.5 cc, and hypoechoic nodules (P < 0.001 for all). FNAB also outperformed FNNAB in the assessment of the right-sided, inferior, and posterior nodules (P < 0.001), nodules with and without calcification (P = 0.041 and P = 0.020, respectively), and nodules with type 1 and type 2 vascularity patterns (P = 0.006 and P = 0.017, respectively). FNAB was effective in obese individuals (Body mass index ≥40 kg/m^2), males with a waist circumference of <94 cm, females with a waist circumference of ≥80 cm, and females with a neck circumference of ≥34 cm (P = 0.011, P = 0.044, P = 0.029, and P = 0.008, respectively).

Conclusion: Anthropometric parameters and sonographic characteristics influenced the diagnostic yield of FNAB and FNNAB, with FNAB generally demonstrating superior results. Given the importance of obtaining an accurate diagnostic result from fine-needle biopsy, clinicians should consider both the sonographic features of the nodule and the anthropometric measurements of the patient when selecting a biopsy technique.

Keywords: Fine-needle aspiration biopsy, Non-aspiration biopsy, Bethesda, Anthropometric parameters, Sonographic characteristics

INTRODUCTION

Determining the nature of thyroid nodules is imperative for selecting the correct treatment strategy and mitigating the risk of overlooking malignant lesions.[1,2] Fine-needle aspiration biopsy (FNAB) and fine-needle non-aspiration biopsy (FNNAB) are two pivotal biopsy techniques employed in nodule assessment.[3] Various demographic and sonographic characteristics influence the choice between these methods, necessitating a comprehensive understanding of their impact on diagnosis and diagnostic yield.[4,5]

Demographic factors such as sex and age impact the prevalence and characteristics of nodules, thereby influencing the choice of biopsy method.[1,6] Similarly, sonographic characteristics, such as nodule size, shape, composition, and vascularity, are integral in the decision-making process.[7] Sonographic criteria have demonstrated excellent diagnostic performance in guiding fine-needle biopsy (FNB) procedures, particularly in females who have a very high likelihood of thyroid abnormalities (up to 42% of screened populations).[8] The sonographic appearance of thyroid nodules provides valuable data that can aid in determining the necessity and the type of biopsy procedure.[9] Ultrasonography-guided FNAB and FNNAB have been compared in various studies regarding efficacy and diagnostic yield.[3,4,8,10] The Bethesda classification, utilized for documenting and classifying thyroid cytopathology, also plays a crucial role when correlated with sonographic features of nodules, aiding in the stratification of nodules based on their malignancy risk.[10,11]

Analyzing Bethesda classification with anthropometric parameters and sonographic characteristics may guide the choice of using FNAB or FNNAB to evaluate thyroid nodules. This study aimed to compare the FNAB and FNNAB techniques by examining anthropometric parameters and sonographic characteristics that may affect the diagnostic yield of the second biopsy among patients in whom initial fine-needle biopsies were non-diagnostic.

MATERIAL AND METHODS

Study settings

This cross-sectionally designed retrospective study was conducted at the Department of Endocrinology at Karabük University Training and Research Hospital in Karabük, Turkey. Between October 2021 and July 2023, 225 thyroid nodules from 188 patients were identified as non-diagnostic. This study included patients who underwent a second biopsy using an alternative technique. Approval was received from the Institutional Ethics Committee in November 2023 (Approval #1424) to confirm that all procedures complied with the ethical standards outlined in the Declaration of Helsinki.

Clinic, demographic, and anthropometric data

Participants' clinical, demographic, and anthropometric data were collected from electronic databases. A comprehensive anamnesis of each participant was conducted to gather information about any previous thyroid surgeries, fine-needle biopsy procedures, and history of neck radiation. The participant's weight was measured using a mechanical platform scale with a maximum capacity of 250 kg and a precision of 100 g. Height was determined with a stadiometer attached to the scale (sensitivity: 0.1 cm). Body mass index (BMI) was calculated by dividing patient weight (in kilograms) by height squared (in meters). BMI (kg/m^2) was categorized as <25, 25–30, 30–35, 35–40, and >40–as the World Health Organization described. Measurements of waist and hip circumferences were made with a measuring tape and noted in centimeters. Waist circumference was classified as below and above 94 cm in males and below and above 80 cm in females. The waist-to-hip ratio was rated below and above 0.9 in males and below and above 0.85 in females.[12] The neck circumference measurement was conducted by positioning the top edge of the measuring tape just below the laryngeal prominence, aligning it perpendicular to the neck's long axis. Typical values considered normal were less than 37 cm for males and <34 cm for females.[13]

Laboratory measurements

Blood samples were collected immediately before the biopsy procedure and included thyroid hormones (free triiodothyronine, free thyroxine, and thyroid-stimulating hormone), along with measurements of thyroglobulin, anti-thyroglobulin antibodies, anti-thyroid peroxidase antibodies, and calcitonin. Data were retrieved from our institution's digital database. All laboratory analyses were conducted in accredited local laboratories on regularly calibrated equipment to ensure accuracy and reliability.

Data inclusion/exclusion

The primary clinical indication for biopsy was the presence of thyroid nodular goiter, with nodules exhibiting uncertain echographic characteristics. For cases with multinodular goiter, selection for sampling was based on either the size of the largest nodule or the presence of suspicious characteristics in ultrasound. Patients were provided a comprehensive explanation of the FNAB and FNNAB procedures before obtaining informed consent. Inclusion criteria were having undergone a single biopsy (FNAB or FNNAB), suspicious ultrasound findings, high risk for malignancy, and the presence of nodules that grew larger during the follow-up phase. Individuals younger than 18 or older than 80 years, those with a history of thyroid ablation, and patients with coagulation abnormalities or pregnancy were excluded from the study.

Ultrasound and biopsy procedures

In all procedures, we utilized a conventional ultrasound with a 10 MHz linear-array transducer (Aloka SSD-4000, Japan).

Each detected nodule was characterized by evaluating its echogenicity, calcification status, vascularity, and size. In cases where multinodular goiter was present, the most suspicious or dominant nodule (if no suspicious nodules were present) was selected for biopsy. The initial biopsy technique was determined based on the preference of the endocrinologist. All biopsies were performed by a single experienced endocrinologist. The patients were divided into two groups based on the order of the secondary biopsy: those who underwent FNAB followed by FNNAB, and those who underwent FNNAB followed by FNAB. The second biopsy was conducted approximately 3 months after the first biopsy.

The FNAB procedure was performed using a conventional method: A 25-gauge needle attached to a 10-mL disposable syringe and secured in a mechanical syringe holder. Briefly, the operator inserted the needle into the nodule, created a vacuum, and maneuvered the needle to obtain the specimen from within the nodule. After stopping the suction, the needle was removed, and the extracted specimen was projected onto glass slides to prepare smears. The FNNAB procedure involved gripping the base of a 25-gauge needle such as a pencil, carefully inserting it into the nodule, and agitating the needle for 5–15 seconds. The specimen was drawn into the needle by capillary force. When the specimen became visible within the needle's hub, the needle was removed, connected to an air-filled syringe, and the content was expelled onto slides. Rapid on-site evaluation was not performed during the procedure.

Statistical analysis

Statistical evaluations were executed with a two-tailed approach, where *P*-value below 0.05 denoted significance. All analyses were performed on the Statistical Package for the Social Sciences version 23 (IBM Corporation / Armonk, New York, USA). Population and sonographic attributes were collated using descriptive statistical methods. Continuous data were summarized with mean ± standard deviation, while categorical data were described through frequencies and percentages. Comparative analyses between FNAB and FNNAB group data employed tests suited to the data type: the Chi-square or Fisher's exact test for categorical variables and the independent samples t-test or Mann–Whitney U-test for continuous variables, selected based on the presence or absence of normal distribution. In addition, multivariate analysis of variance was conducted to assess the impact of multiple independent variables, including sonographic features and anthropometric measurements, on the diagnostic outcomes. This allowed us to determine the combined effect of these variables on the diagnostic accuracy of FNAB and FNNAB methods.

RESULTS

The mean age was 54.2 ± 13.1 years, and 79.8% of the patients were female. A small fraction had a family history of thyroid cancer (4.3%, $n = 8$), and an even smaller percentage had undergone neck radiotherapy (2.7%, $n = 5$) [Table 1].

The comparative analysis between FNAB and FNNAB

Each of the 225 nodules underwent an initial biopsy with FNAB or FNNAB followed by the alternate technique for non-diagnostic results. Bethesda I (non-diagnostic) was prevalent in both FNAB and FNNAB, although more pronounced in the latter, with 170 (76%) nodules in FNNAB compared to 141 (63%) in FNAB ($P = 0.159$). Conversely, the diagnostic categories (Bethesda II-IV, VI) were more frequently detected with the FNAB technique. Notably, no nodules were classified as Bethesda IV or VI in either group [Table 2]. Initially, thyroid nodules were biopsied using two different techniques: 101 nodules with FNAB and 124 nodules with FNNAB. For the 101 nodules reported as non-diagnostic FNAB, FNNAB was performed. Of these, 55 were found to be diagnostic, while 46 were found to be non-diagnostic. For the 124 nodules reported as non-diagnostic FNNAB, FNAB was performed. Of these, 84 were found to be diagnostic, while 40 were found to be non-diagnostic [Table 3].

Sonographic findings and biopsy

When the index nodule's anteroposterior-to-transverse ratio (AP/T) was one or higher, the FNAB technique had a higher diagnostic yield compared to the FNNAB ($P < 0.001$). The longitudinal diameter of the nodule also demonstrated notable differences between the two methods. Nodules measuring 10–40 mm showed a higher diagnosis rate with FNAB than with FNNAB ($P < 0.001$). In terms of nodule volume, FNAB demonstrated a higher diagnostic yield than FNNAB for nodules smaller than 0.5 cc ($P = 0.012$), as well as for those ranging from 0.5 to 2 cc and those larger than 2cc ($P < 0.001$). Echogenicity, another critical sonographic parameter, was diagnosed more frequently when nodules were detected hypoechoic using FNAB versus FNNAB ($P < 0.001$). Isoechoic, hyperechoic, and mixed echogenicity showed no diagnostic differences between the two methods [Table 4].

The localization of the nodule yielded mixed results. Right-sided, inferior, posterior ($P < 0.001$) and anterior nodules ($P = 0.015$) were diagnosed more frequently with FNAB. However, other localizations (such as left-sided, isthmus, superior, and middle placement) showed no differences ($P > 0.05$). In evaluating nodule calcification, FNAB had a higher diagnostic rate in cases with ($P = 0.041$) and without

Table 1: Summary of clinical and laboratory values.

Variables	Value
Age, years	54.22±13.14
Gender distribution	
Male	38 (20.2)
Female	150 (79.8)
Thyroid cancer history	
No	180 (95.7)
Yes	8 (4.3)
Neck radiotherapy status	
No	183 (97.3)
Yes	5 (2.7)
History of thyroid surgery	
No	165 (87.8)
Yes	23 (12.2)
History of FNB	
No	114 (60.6)
Yes	74 (39.4)
Solitary/multiple status	
Solitary	24 (12.8)
Multiple	164 (87.2)
Thyroid function status	
Euthyroid	109 (58)
Hyperthyroid	35 (18.6)
Hypothyroid	44 (23.4)
Laboratory values	
FT_3, pg/mL	3.43±1.54
FT_4, ng/dL	1.35±1.15
TSH, μIU/mL	2.76±3.93
TG, ng/mL	58.2±108.76
A-TG, IU/mL	26.3±122.5
A-TPO, IU/mL	228.4±429.5
Calcitonin, pg/mL	3.1±4.3

FNB: Fine-needle biopsy, FT_3: Free triiodothyronine, FT_4: Free thyroxine, TSH: Thyroid-stimulating hormone, TG: Thyroglobulin, A-TG: Anti-thyroglobulin antibody, A-TPO: Anti-thyroid peroxidase antibody. The percentage in the table represents the ratio of the number of individuals in the respective category to the total number of individuals. The "±" sign in laboratory values represents the standard deviation of the mean value

calcification (P = 0.02). In thyroid nodules with type 1 and type 2 vascularity patterns, FNAB was found to be more diagnostic (P = 0.006 and P = 0.017, respectively), while in nodules with type 2 + 3 and type 3 vascularity patterns, no significant difference in diagnostic efficacy was detected between the biopsy techniques (P = 0.342 and P = 0.126, respectively). While the diagnostic yield of the FNAB technique was higher in the absence of a halo sign (P = 0.005), the presence did not influence diagnostic yield (P = 0.299). Based on the classifications established by thyroid imaging reporting and data system (TIRADS), there was no disparity in the diagnostic effectiveness between FNAB and FNNAB for nodules rated as TIRADS 2, 3, 4, and 5 [Table 4]. The impact of the sonographic findings of thyroid nodules on diagnostic accuracy was analyzed using multivariate analysis. According to the results for sonographic findings of thyroid nodules, when the dependent variables were considered separately, there are differences between the non-diagnostic thyroid nodules on index nodule volume ($F(1,2) = 7.852$; $P < 0.001$), non-diagnostic thyroid nodules on index nodule localization ($F(1,11) = 7.768$; $P < 0.001$), diagnostic thyroid nodules on index nodule calcification ($F(1,1) = 9.274$; $P < 0.001$), and lastly diagnostic thyroid nodules on index nodule halo sign ($F(1,1) = 5.326$; $P < 0.001$).

Table 2: The Bethesda classification for thyroid nodules according to aspiration and non-aspiration fine-needle biopsy techniques.

Index nodule Bethesda	FNAB (*n*: 225)	FNNAB (*n*: 225)
Non-diagnostic		
I	141 (63)	170 (76)
Diagnostic		
II	54 (24)	35 (16)
III	30 (13)	18 (8)
IV	0	0
V	0	2 (1)
VI	0	0

FNAB: Fine-needle aspiration biopsy, FNNAB: Fine-needle non-aspiration biopsy. Values in the table are presented as counts (percentages)

Anthropometric measurement parameters and biopsy choice

FNAB was superior to FNNAB in evaluating nodules among cases with a BMI of ≥40 kg/m^2 (P = 0.011). In males with a waist circumference of <94 cm, the aspiration technique proved more effective for nodule assessment than the non-aspiration technique (P = 0.044). In addition, in females with a waist circumference of ≥80 cm, the aspiration method was superior to the non-aspiration method in evaluating nodules (P = 0.029). Furthermore, a waist-to-hip ratio of >0.9 in males was associated with greater diagnostic yield with FNAB (P = 0.017). In female patients with a neck circumference

Table 3: Comparative diagnostic analysis of thyroid nodules depending on the initial choice between FNAB and FNNAB technique.

Biopsy technique	Number of nodules	Diagnostic (D)	Non-diagnostic (ND)
1st FNAB	101	-	101
1st FNNAB	124	-	124
2nd FNNAB (After ND FNAB)	101	55 (54)	46 (46)
2nd FNAB (After ND FNNAB)	124	84 (68)	40 (32)
FNAB Total	225	84 (37)	141 (63)
FNNAB Total	225	55 (24)	170 (76)

FNAB: Fine-needle aspiration biopsy, FNNAB: Fine-needle non-aspiration biopsy. The values presented in the table are represented as counts (percentages).

of ≥34 cm, the FNAB was more diagnostic than FNNAB (P = 0.008). These findings suggest that anthropometric factors such as waist-circumference, BMI, waist-to-hip ratio, and neck circumference may impact the diagnostic yields of the FNAB and FNNAB techniques used to evaluate thyroid nodules [Table 5].

The impact of the patient's anthropometric measurements on diagnostic accuracy was analyzed using multivariate analysis on diagnostic accuracy that was analyzed using multivariate analysis. According to the results for the patient's anthropometric measurements, when the dependent variables were considered separately, there was a difference between diagnostic thyroid nodule and waist circumference for male ($F(1,1) = 14.629$; $P < 0.001$), non-diagnostic thyroid nodule and waist circumference for male ($F(1,1) = 16.615$; $P < 0.001$), diagnostic thyroid nodule and waist-hip ratio for male ($F(1,1) = 7.880$; $P < 0.001$), non-diagnostic thyroid nodule and waist-hip ratio for female ($F(1,1) = 20.407$; $P < 0.001$), and lastly diagnostic thyroid nodule and neck circumference for female ($F(1, 1) = 12.843$; $P < 0.001$). The reasons for non-diagnostic FNB results, apart from biopsy technique, sonographic characteristics of the nodule, and anthropometric measurements, were categorized into four groups: Insufficient cell count, blood or fibrin contamination, cystic nature of the nodule, and crushing or other technical issues. Among the 141 non-diagnostic thyroid nodules using the FNAB method, 80 (56.7%) were due to insufficient cell count, 25 (17.7%) were due to blood or fibrin contamination, 20 (14.2%) due to the cystic nature of the nodule, and 16 (11.4%) due to crushing or other technical issues. Among the 170 non-diagnostic thyroid nodules using the FNNAB, 95 (55.9%) were due to insufficient cell count, 45 (26.5%) were due to blood or fibrin contamination, 20 (11.8%) due to the cystic nature of the nodule, and 10 (5.9%) due to crushing or other technical issues. Of the 86 thyroid nodules that were non-diagnostic with both FNAB and FNNAB methods, 50 (58.1%) were due to insufficient cell count, 20 (23.3%) were due to blood or fibrin contamination, 10 (11.6%) due to the cystic nature of the nodule, and 6 (7.0%) due to crushing or other technical issues.

DISCUSSION

In contemporary endocrinological practice, when faced with a non-diagnostic fine-needle biopsy result, clinicians are inclined to recommend a repeat biopsy, typically scheduled 3 months after the initial procedure. This protocol, while standard, poses considerable inconvenience and discomfort to the patient due to the invasive nature of the process, not to mention the delay, it imposes on both the patient and the clinician. We analyzed the approach to repeat biopsy by considering anthropometric measures such as obesity and the sonographic characteristics of thyroid nodules, aiming to discern the optimal technique for a second biopsy after a non-diagnostic initial FNB. According to our findings, the FNAB approach outperformed the FNNAB approach in terms of diagnostic yield for thyroid nodules that were located posteriorly and inferiorly without the halo sign, had volumes ranging from 0.5 cc to 2 cc, hypoechogenicity, and a right-sided localization (potentially due to right-hand dominance).

The management and assessment of thyroid nodules have been subjects of extensive research and clinical debate.[14] In a study by Wang *et al.*, the comparative efficacy of FNAB and FNNAB under ultrasound guidance was investigated, providing critical insights into the optimization of diagnostic procedures for thyroid nodules.[9] The results highlighted superior diagnostic performance in specimens obtained through FNAB compared to FNNAB, particularly in nodules displaying hypovascularity and macrocalcifications. These findings underscore the importance of technique selection based on nodule characteristics. Indeed, the selection of the biopsy method remains a point of contention in clinical practice. Our study found that for nodules with an AP/T ratio of >1, the diagnostic utility of aspiration techniques surpassed that of FNNAB. Contrary to initial expectations that a nodule with a larger AP diameter would have more excellent proximity to the surface, the anatomical localization of the nodule proved more important in this context. The aspirate technique was deemed superior diagnostically for nodules measuring 10–40 mm on their longest axis compared to the

Table 4: Comparison of the diagnostic efficacy of aspiration and non-aspiration fine needle biopsy techniques in conjunction with sonographic findings.

Variables	FNAB (*n*: 225)		FNNAB (*n*: 225)		*P*-value
	D	ND	D	ND	
Index nodule AP/T ratio					
<1	67 (80)	123 (87)	52 (95)	138 (81)	0.096
≥1	17 (20)	18 (13)	3 (5)	32 (19)	<0.001
Index nodule longitudinal diameter, mm					
<10	5 (6)	17 (12)	7 (13)	15 (8)	0.497
10–40	78 (93)	119 (84)	47 (85)	150 (89)	<0.001
≥40	1 (1)	5 (4)	1 (2)	5 (2)	0.990
Index Nodule Volume, *cc*					
<0.5	26 (31)	39 (28)	13 (24)	52 (31)	0.012
0.5–2	38 (45)	53 (38)	19 (35)	72 (42)	<0.001
≥2	20 (24)	49 (34)	23 (41)	46 (27)	0.580
Index nodule echogenicity					
Hypoechoic	40 (47.6)	45 (31.9)	21 (38.1)	64 (37.6)	<0.001
Isoechoic	32 (38.1)	77 (54.6)	23 (41.8)	86 (50.6)	0.178
Hyperechoic	9 (10.7)	5 (3.55)	6 (10.9)	8 (4.7)	0.255
Mixed	3 (3.6)	14 (9.9)	5 (9)	12 (7.1)	0.686
Index nodule localization					
Right	48 (57)	66 (47)	26 (47)	88 (52)	<0.001
Left	32 (38)	66 (47)	25 (45)	73 (43)	0.270
Isthmus	4 (5)	9 (6)	4 (8)	9 (5)	0.990
Index nodule localization					
Superior	14 (16.6)	23 (16.3)	12 (21.8)	25 (14.7)	0.626
Middle	21 (25)	47 (33.3)	15 (27)	53 (31.2)	0.242
Inferior	42 (50)	62 (44)	22 (40)	82 (48.3)	<0.001
Completely	7 (8.3)	9 (6.3)	6 (11)	10 (5.9)	0.718
Index nodule localization					
Not defined	38 (45)	81 (57)	41 (75)	78 (46)	0.679
Anterior	16 (19)	23 (16)	5 (9)	34 (20)	0.015
Middle	6 (7)	11 (8)	2 (4)	15 (9)	0.107
Posterior	19 (23)	18 (13)	4 (7)	33 (20)	<0.001
Completely	5 (6)	8 (6)	3 (5)	10 (5)	0.456
Index nodule calcification					
No	65 (77)	107 (76)	45 (82)	127 (75)	0.020
Yes	19 (23)	34 (24)	10 (18)	43 (25)	0.041
Index nodule vascularity					
Type 1	61 (73)	85 (60)	39 (70)	107 (63)	0.006
Type 2	13 (15)	43 (30)	4 (7)	52 (30)	0.017

(Contd...)

Table 4: *(Continued).*

Variables	FNAB (*n*: 225)		FNNAB (*n*: 225)		*P*-value
	D	ND	D	ND	
Type 2+3	6 (7)	3 (2)	4 (7)	5 (3)	0.342
Type 3	4 (5)	10 (8)	8 (16)	6 (4)	0.126
Index nodule halo sign					
No	57 (68)	97 (69)	35 (64)	119 (70)	0.005
Yes	27 (32)	44 (31)	20 (36)	51 (30)	0.299
TIRADS					
2	6 (7)	7 (5)	3 (5)	10 (6)	0.201
3	39 (47)	63 (45)	29 (53)	73 (43)	0.135
4	27 (32)	53 (38)	18 (33)	62 (36)	0.110
5	12 (14)	18 (13)	5 (9)	25 (15)	0.704

The table compares aspiration (FNAB) and non-aspiration (FNNAB) biopsy in fine needle cytology of thyroid nodules, focusing on sonographic findings. Values in the table are presented as counts (percentages). "*P*" values represent the significance of the differences observed between each variable's aspiration and non-aspiration techniques. FNAB: Fine-needle aspiration biopsy, FNNAB: Fine-needle non-aspiration biopsy, AP/T: Anteroposterior to the transverse ratio of the index nodule, TIRADS: Thyroid imaging reporting and data system, D: Diagnostic, ND: Non-diagnostic, mm: millimeters and cc: cubic centimeters

FNNAB. This may be attributed to the tremendous negative pressure achievable with aspiration, allowing for more efficient transmission of force over the surface area and the potential for collecting more cellular material without damaging the surrounding nodule tissue. The number of samples in our study is insufficient to compare the diagnostic accuracies of FNAB and FNNAB in nodules with a longitudinal diameter of >40 mm. In nodules measuring <10 mm in diameter, accurate needle placement may be challenging, suggesting a diagnostic advantage for aspiration techniques; nonetheless, the similarity in diagnostic performance in the two approaches may be associated with other nodule characteristics and specific patient circumstances.

Contrary to Zhou *et al.*'s findings which suggested technique suitability based on nodule size,[15] Wang *et al.* found no difference between FNAB and FNNAB across different nodule sizes.[9] These conflicting results are potentially attributable to differences in study design, sample sizes, and needle diameter. In our analysis of nodule echogenicity, we found that compared to FNNAB, FNAB had a more remarkable ability to provide diagnostic classification in hypoechoic nodules. This could be due to increased tissue density in lower echogenicity, which causes more excellent resistance to needle manipulation. Nodules located on the right were better diagnosed using aspiration techniques, potentially because predominantly right-handed clinicians may find it easier to biopsy nodules on the right side. For nodules situated inferiorly within the thyroid, FNAB was superior, possibly due to the ease of aspiration when the patients were in a supine position with neck extension. Anteriorly positioned thyroid nodules were also better diagnosed with aspiration techniques, which might be attributed to the closer proximity of the nodules to the skin surface, making aspiration less challenging. Consequently, FNAB could enhance diagnostic efficiency in anteriorly located nodules. Although posteriorly-located thyroid nodules are farther from the surface, they are better diagnosed using FNAB; the depth of these nodules might hinder needle manipulation with FNNAB, potentially increasing the diagnostic yield of FNAB.

In our study, nodules with a volume lower than 0.5 cc demonstrated greater diagnostic yield with the FNAB technique than the FNNAB. The increased diagnostic potential of FNAB over FNNAB in smaller nodules might be due to the difficulty in needle positioning and the need for more significant negative pressure. Given the correlation between volume and longitudinal diameter, these factors can also explain the greater diagnostic yield with FNAB in nodules with a volume of 0.5–2 cc. In thyroid nodules with no (type 1) or peripheral vascularity (type 2), FNAB was more diagnostic. However, as the vascularity pattern increases (type 2 + 3, type 3), there is no difference in diagnostic efficacy between the two biopsy techniques. This could be attributed to nodules with higher vascularity patterns being harder and denser, making tissue sampling with FNAB more challenging. Even though the number of thyroid nodules with halo signs was small, the diagnostic effectiveness of FNAB was more incredible because the thyroid nodule is sharply delineated from the surrounding thyroid parenchyma. While the absence of a halo sign typically makes it difficult to distinguish the nodule from the surrounding tissue, our study found that FNAB's effective collection of cellular samples, its higher negative pressure,

Table 5: Comparison of the diagnostic efficacy of aspiration and non-aspiration fine needle biopsy techniques in conjunction with anthropometric measurements.

Variables	FNAB (*n*: 225)		FNNAB (*n*: 225)		*P*-value
	D	ND	D	ND	
BMI-kg/m^2					
18–25	5 (6)	23 (16)	9 (16)	19 (11)	0.210
25–30	33 (40)	45 (32)	14 (25,4)	64 (38)	0.697
30–35	19 (23)	38 (27)	15 (27)	42 (25)	0.913
35–40	12 (14)	26 (18)	14 (25.4)	24 (14)	0.628
≥40	15 (18)	9 (6)	3 (6)	21 (12)	0.011
WC-cm (Male)					
<94	3 (20)	4 (13.8)	0 (0)	7 (27)	0.044
≥94	12 (80)	25 (86.2)	7 (100)	30 (73)	0.182
WC-cm (Female)					
<80	3 (4)	6 (5)	2 (4.2)	7 (5.3)	0.598
≥80	66 (96)	106 (95)	46 (95.8)	126 (94.7)	0.029
WHR-(Male)					
≤0.9	1 (7)	4 (14)	1 (17)	4 (11)	0.990
>0.9	14 (93)	25 (86)	5 (83)	34 (89)	0.017
WHR-(Female)					
≤0.85	17 (25)	29 (26)	11 (22.5)	35 (27)	0.176
>0.85	52 (75)	83 (74)	38 (77.5)	97 (73)	0.071
Neck circumference-cm (Male)					
<37	4 (27)	5 (17)	2 (29)	7 (29)	0.620
≥37	11 (73)	24 (83)	5 (71)	30 (81)	0.153
Neck circumference-cm (Female)					
<34	7 (10)	11 (10)	9 (18.8)	9 (6.8)	0.738
≥34	62 (90)	101 (90)	39 (81.2)	124 (93.2)	0.008

The table presents the analysis of aspiration (FNAB) and non-aspiration (FNNAB) techniques in fine-needle cytology of thyroid nodules, focusing on demographic features, with groups of 225 samples each. The data in the table are expressed as counts (percentages), and "*P*" values indicate the statistical significance of the observed differences between the aspiration and non-aspiration techniques across various demographic variables. The variables analyzed include body mass index (BMI), categorized according to the World Health Organization's classification, and waist circumference and waist hip ratio, further categorized by gender. FNAB: Fine-needle aspiration biopsy, FNNAB: Fine-needle non-aspiration biopsy, D: Diagnostic, ND: Non-diagnostic, kg/m^2: Kilograms per square meter, cm: Centimeters, WHR: Waist hip ratio, WC: Waist circumference, BMI: Body mass index

and the biological behaviors of the nodule may have resulted in greater diagnostic yield in the absence of the halo sign.

According to de Siqueira *et al.*,[16] in obese individuals, thyroid tissue exhibits less echogenicity, and thyroid nodules are frequently observed during ultrasonographic assessment. Some studies compared the properties of adipose tissue gathered through needle aspiration.[17,18] In our analysis, nodules in obese cases demonstrated a superior diagnostic yield with FNAB compared to FNNAB. This could be attributed to the greater distance of the nodule from the skin surface and the increased coverage by subcutaneous fat layers in obese individuals. However, the sample size was limited. In males with a waist circumference of <94 cm, the diagnostic efficacy of FNAB was more significant than FNNAB's. The number of patients was not optimal for a robust diagnostic comparison between the two techniques. Especially, since obesity is a crucial risk factor for nodules.[19] In females with a waist circumference of ≥80 cm, FNAB was more effective than FNNAB. Although the waist indicated abdominal adiposity, there was a high probability of fat accumulation in the neck area. Therefore, the nodule was likely to be situated deeper under the skin and obscured by a thicker subcutaneous fat layer. Our study supported this observation, finding that in female patients with a neck circumference of ≥34 cm, the FNAB was more diagnostic. Another reason may be the increased difficulty in directing the needle to target the FNNAB as the neck circumference increases. In males with a waist-to-hip ratio of >0.9, FNAB was superior to FNNAB. A higher waist circumference can challenge patient positioning, compromising the procedure. Hence, FNAB, which allows for more precise stabilization, may enhance diagnostic accuracy.

The present study has several strengths and some limitations. Unlike previous studies, we assessed sonographic characteristics and incorporated anthropometric parameters to determine their influence on accuracy. Our findings provide a nuanced understanding of factors contributing to biopsy success among patients whose initial biopsy yielded indeterminant results. These data can guide clinicians in the decision-making process for the biopsy technique. In addition, one of the most significant aspects of our study, setting it apart from others in the literature, is that different biopsy techniques were applied to the same thyroid nodule, ensuring sample set uniformity. As a limitation, the sample size was relatively small for nodules that were more prominent than 40 mm. This limitation restricts the generalizability of our findings to larger nodules and would have influenced the comparisons between the aspiration and non-aspiration techniques. One of the other limitations of the study is whether the second biopsy with the same technique would be diagnostic without changing the first biopsy technique. Since the study was retrospective, such a group could not be created. It would not be the same sample set if it were because different nodules would be selected. A more effective diagnostic comparison would have been possible if the same thyroid nodule had been biopsied simultaneously with both aspiration and non-aspiration techniques. However, since our study was retrospective, we could not perform such an application. In addition, thyroid sampling relies greatly on operator expertise and technique consistency, which may have introduced variability in the results. Finally, our study focused solely on the technical aspects of the biopsy procedures and did not delve into the cost-effectiveness or patient experience associated with each technique.

SUMMARY

Our results indicate that for thyroid nodules with an anteroposterior/transverse diameter ratio of ≥1, volumes ranging from 0.5 to 2 cc, hypoechogenicity, and a right-sided localization, especially in clinicians who are right-hand dominant, and those situated posteriorly and inferiorly without the halo sign, nodules with type 1 and type 2 vascularity patterns, the FNAB proved superior in diagnostic yield compared to the FNNAB approach. From an anthropometric perspective, in cases with a BMI of ≥40 kg/m^2, a waist circumference of ≥80 cm (in females), and a waist-to-hip ratio of >0.9 (in males), neck circumference of ≥34 cm (in females) FNAB demonstrated greater diagnostic efficacy over FNNAB. Opting for the appropriate biopsy in such patients can diminish the risk of additional invasive procedures and complications, thereby shortening the diagnostic process. In the repeat biopsy of thyroid nodules with a non-diagnostic initial FNB, the clinician should consider both the sonographic features of the nodule and the patient's anthropometric characteristics when selecting the appropriate biopsy technique. The present study's findings can be used to create evidence-based guidelines for selecting either FNAB or FNNAB biopsy techniques in repeat biopsies of thyroid nodules with a non-diagnostic initial FNB result.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

ABBREVIATIONS

FNAB - Fine-needle aspiration biopsy
FNNAB - Fine-needle non-aspiration biopsy
BMI - Body mass index
WC - Waist circumference
WHR - Waist-to-hip ratio
FT_3 - Free triiodothyronine
FT_4 - Free thyroxine
TSH - Thyroid-stimulating hormone
TG - Thyroglobulin
A-TG - Anti-thyroglobulin antibody
A-TPO - Anti-thyroid peroxidase antibody
TIRADS - Thyroid imaging reporting and data system
AP/T - Anteroposterior to transverse ratio.

AUTHOR CONTRIBUTIONS

MSD: Contributed substantially to the conception and design of the study, data curation, formal analysis, methodology, project administration, writing the original draft, and reviewing and editing the manuscript; NO: Contributed to the investigation, resources, validation, and reviewing and editing the manuscript; ZIN: Contributed to data curation, formal analysis, visualization, and manuscript review and editing. All authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Responsibility for the origination and design of the study, the acquisition and examination of data, the interpretation of findings, and the composition of the manuscript rests entirely with the authors.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This cross-sectionally designed retrospective study was conducted at the Department of Endocrinology at Karabük University Training and Research Hospital in Karabük, Turkey. Approval was received from the Karabük University, Ethics Committee in November 2023 (Approval #1424). Participants provided informed consent, with voluntary participation, the right to withdraw at any time, and confidentiality of all data used solely for research purposes.

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

EDITORIAL/PEER REVIEW

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a **double-blind model** (authors are blinded for reviewers and vice versa) through an automatic online system.

REFERENCES

1. Deniz MS, Özdemir D, İmga NN, Başer H, Çuhacı Seyrek FN, Altınboğa AA, *et al*. Investigation of pre-operative demographic, biochemical, sonographic and cytopathological findings in low-risk thyroid neoplasms. Clin Endocrinol (Oxf) 2023;99:502-10.
2. Wang D, Fu HJ, Xu HX, Guo LH, Li XL, He YP, *et al*. Comparison of fine needle aspiration and non-aspiration cytology for diagnosis of thyroid nodules: A prospective, randomized, and controlled trial. Clin Hemorheol Microcirc 2017;66:67-81.
3. Romitelli F, Di Stasio E, Santoro C, Iozzino M, Orsini A, Cesareo R. A comparative study of fine needle aspiration and fine needle non-aspiration biopsy on suspected thyroid nodules. Endocr Pathol 2009;20:108-13.
4. Liu X, Zhu L, Wang Z, Cui D, Chen H, Wei L, *et al*. Comparison of two different standards of care in detecting malignant thyroid nodules using thyroid fine-needle aspiration. Mol Clin Oncol 2015;3:682-6.
5. Chowhan AK, Babu KV, Sachan A, Rukmangdha N, Patnayak R, Radhika K, *et al*. Should we apply suction during fine needle cytology of thyroid lesions? A prospective study of 200 cases. J Clin Diagn Res 2014;8:FC19-22.
6. Jayaram G, Basu D. Cytology in the diagnosis of thyroid lesions--a review. J Assoc Physicians India 1993;41:164-9.
7. Wickramaratne D, Wilkinson P, Rao J, Ragavendra N, Sharma S, Gimzewski JK. Fine Needle Elastography (FNE) device for biomechanically determining local variations of tissue mechanical properties. J Biomech 2015;48:81-8.
8. Shimode Y, Tsuji H, Fukuhara T, Kawakami O, Tsutsumiuchi T, Noda T, *et al*. Examination of selective low-pressure fine needle aspiration cytology under ultrasound guidance. Yonago Acta Med 2017;60:209-12.
9. Wang MM, Beckett K, Douek M, Masamed R, Patel M, Tseng CH, *et al*. Diagnostic value of molecular testing in sonographically suspicious thyroid nodules. J Endocr Soc 2020;4:bvaa081.
10. Triantafillou E, Papadakis G, Kanouta F, Kalaitzidou S, Drosou A, Sapera A, *et al*. Thyroid ultrasonographic characteristics and Bethesda results after FNAB. J BUON 2018;23:139-43.
11. Deniz MS, Dindar M. Examining the impact of several factors including COVID-19 on thyroid fine-needle aspiration biopsy. Diagn Cytopathol 2024;52:42-9.
12. World Health Organization. Waist circumference and waist-hip ratio: Report of a WHO expert consultation, Geneva; 2011.
13. Ben-Noun L, Sohar E, Laor A. Neck circumference as a simple screening measure for identifying overweight and obese patients. Obes Res 2001;9:470-7.
14. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Thyroid 2009;19:1159-65.
15. Zhou JQ, Zhang JW, Zhan WW, Zhou W, Ye TJ, Zhu Y, *et al*. Comparison of fine-needle aspiration and fine-needle capillary sampling of thyroid nodules: A prospective study with emphasis on the influence of nodule size. Cancer Cytopathol 2014;122:266-73.
16. deSiqueiraRA,RodriguesA,MiamaeLM,TomimoriEK,SilveiraEA. Thyroid nodules in severely obese patients: Frequency and risk of malignancy on ultrasonography. Endocr Res 2020;45:9-16.
17. Mutch DM, Tordjman J, Pelloux V, Hanczar B, Henegar C, Poitou C, *et al*. Needle and surgical biopsy techniques differentially affect adipose tissue gene expression profiles. Am J Clin Nutr 2009;89:51-7.
18. Siqueira RA, Noll M, Rodrigues AP, Silveira EA. Factors associated with the occurrence of thyroid nodules in severely obese patients: A case-control study. Asian Pac J Cancer Prev 2019;20:693-7.
19. Demetriou E, Fokou M, Frangos S, Papageorgis P, Economides PA, Economides A. Thyroid nodules and obesity. Life (Basel) 2023;13:1292.

How to cite this article: Deniz MS, Ozder N, Narli ZI. The impact of anthropometric parameters and sonographic characteristics on the choice of biopsy method for thyroid nodules: Fine-needle aspiration versus non-aspiration biopsy. CytoJournal. 2024; 21:27. doi: 10.25259/Cytojournal_42_2024

HTML of this article is available FREE at:
https://dx.doi.org/10.25259/Cytojournal_42_2024