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Original

Comparing ultrasound to fine needle aspiration in differentiating between benign and malignant thyroid masses

Ladan Hajiabdolrrasouli[1], Hamid Reza Samimagham[1], Saeed Hosseini Teshnizi[2], Ali Salimi Asl[3], MohammadHosein Sheybani-Arani[3], Soroush Jaberansari[3], Mitra Kazemi Jahromi[4*]

Abstract

Introduction: Due to the possibility of malignancy of thyroid nodules, it is necessary to identify the type of thyroid nodule to choose the most accurate treatment possible.

Objectives: Considering that there is no standard diagnostic method for masses with intermediate suspicion of malignancy, the present study was conducted to investigate the diagnostic value of ultrasound in differentiating between benign and malignant thyroid masses compared with fine needle aspiration (FNA).

Patients and Methods: In this cross-sectional study, 150 patients who had been referred to an endocrinologist's office in Bandar Abbas with a complaint of thyroid mass in 2019-2020 and had undergone ultrasound and FNA were included in the study by census. After obtaining their informed consent, the patient's information was collected by reviewing their ultrasound and FNA reports and analyzed with descriptive and analytical tests in SPSS software version 26.

Results: The sensitivity and specificity of ultrasound in detecting malignant and benign masses were 56.25% and 85.07%, respectively. The positive and negative predictive values of ultrasound were 60% and 98.27%, respectively. The number of malignant FNA reports was significantly higher in the intermediate suspicion category of patients than in patients with ultrasound results showing high suspicion of malignancy.

Conclusion: Performing further diagnostic measures such as FNA and core needle biopsy after noticing an intermediate suspicion in a patient's ultrasound seems necessary.

Keywords: Thyroid mass, Ultrasound, Fine needle aspiration

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Introduction

Thyroid nodules, which are defined as "any abnormal growth in the thyroid tissue that causes a mass in the thyroid gland," have a high prevalence of about 5% in the general population as estimated by examinations and touching the gland and about 50% based on ultrasound or autopsy (1,2). Thyroid nodules are more common in some people and may be noticed by physicians due to the pressure exerted on the surrounding organs, gland hyperactivity, and suspicion of malignancy (3, 4). Although thyroid nodules can be considered a common disease, less than 5% of cases are malignant, and their diagnosis is of clinical importance (1).

Over the past two decades, dealing with thyroid nodules has significantly changed due to the widespread use of modern diagnostic methods such as ultrasound and fine needle aspiration (FNA). Despite these advances, however, there still needs to be a complete consensus on appropriate and practical diagnostic strategies, and clinical evaluation still plays a critical role in diagnosing these nodules (5-7).

Several studies have been conducted to prove ultrasound's capacity to differentiate benign from malignant nodules (8). For instance, in a study by Shuler et al, the diagnostic accuracy of ultrasound for differentiating between benign and malignant nodules was reported to be low (9). In addition to ultrasound, FNA is an inexpensive and common method for preoperatively diagnosing thyroid nodules (10). Some researchers believe that cytopathologic examination alone can differentiate benign from malignant nodules due to its high sensitivity (93%-100%)

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[1]Clinical Research Development Center, Shahid Mohammadi Hospital, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
[2]Nursing and Midwifery School, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
[3]Student Research Committee, Faculty of Medicine, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
[4]Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran.
***Corresponding author:** Mitra Kazemi Jahromi, Email: mitra.kazemijahromi@gmail.com

Implication for health policy/practice/research/ medical education

Health practitioners can use the findings of this study to improve the diagnosis of thyroid nodules and choose the most accurate treatment possible. Health policymakers can use the study's findings to develop guidelines for diagnosing and treating thyroid nodules. Researchers can use the study's findings to conduct further research on the diagnostic value of ultrasound in differentiating between benign and malignant thyroid masses. Medical educators can use the study's findings to develop training programs for health practitioners on the use of ultrasound in diagnosing thyroid nodules..

and specificity (86%-100%) and low negative predictive value (3%-6%) (11). The American Thyroid Association has recommended FNA as the first preliminary measure for thyroid nodules larger than 1 centimeter (12). There is consensus about the most standard diagnostic methods for high and low suspicion masses in valid thyroid nodules guidelines, but not intermediate suspicion nodules.

Due to the lack of iodine in diets in most areas of Iran, thyroid nodules are also relatively common diseases of the thyroid gland and endemic goitre. Due to the possibility of malignancy, identifying the type of thyroid nodules to adopt the most accurate treatment protocols is highly important. Given the lack of consensus on the most superior diagnostic method for masses with intermediate suspicion of malignancy, the present study was conducted to investigate the diagnostic value of ultrasound in comparison with FNA in differentiating between benign and malignant thyroid masses and to compare the results of FNA with ultrasounds showing an intermediate suspicion of malignancy.

Patients and Methods

Study design

This cross-sectional study's population consisted of all the patients referred to an endocrinologist's office or endocrinology clinic in Bandar Abbas with complaints of a thyroid mass in 2019-2020.

The subjects were selected by census sampling, and all the eligible patients in 2019-2020 who signed informed consent forms were recruited.

Inclusion criterion

- Patients with thyroid nodules with a high or intermediate suspicion of malignancy based on ultrasound who underwent FNA.

Exclusion criteria

- Patients whose cytology samples were reported to be insufficient;
- Patients with a history of receiving radioactive iodine or any history of thyroid surgery;
- Patients who were not interested in participating in the study and did not sign the informed consent form.

Data collection and study design

At first, patients referred to an endocrinologist's office or endocrinology clinic in Bandar Abbas with complaints of a thyroid mass underwent a thyroid examination. Then those suspected of having thyroid nodules were referred to a radiologist for a thyroid ultrasound. Then, according to the previous definitions, lesions with a high and intermediate suspicion of malignancy were referred to an experienced pathologist for FNA.

For the cytopathological examination of the nodules, FNA was performed in the standard way (without anesthesia and using a #23 needle connected to a 10-cc plastic syringe). After the biopsy, the samples were spread on glass slides and sent to the laboratory after fixing them with 95% alcohol. Finally, the selected slides were stained by Papanicolaou and Giemsa method. A radiologist performed all the ultrasound examinations, and a pathologist carried out the FNA to reduce errors. Then, the thyroid nodules were classified according to the Bethesda system: non-diagnostic, benign, atypia (or follicular lesions) of uncertain significance, follicular neoplasms or suspicious of follicular neoplasms, suspicious of malignancy, and malignant (13).

Then, the sensitivity, specificity, positive predictive value, and negative predictive value of the ultrasound results were calculated in the sample size.

Measurement tool

The research tool in this study was a researcher-made checklist including the subjects' demographic, ultrasound, and FNA sample information.

Statistical analysis

Sensitivity, specificity, and positive and negative predictive values were used to investigate the research objectives. After collecting the data, the quantitative data were described using mean and standard deviation, and the qualitative variables were defined using frequency and percentage with SPSS software version 26. The chi-square test was also used to examine the relationship between the qualitative variables. In all the tests, $P<0.05$ was taken as the level of statistical significance.

Results

A total of 150 patients participated in this study, including 139 female (92.7%) and 11 male (7.3%) participants, with a mean age of 44.49±9.81 years.

This study examined six characteristics from the ultrasounds of 150 patients, including the number, type, echogenicity, margin symmetry, size, and calcification of nodules. The ultrasound showed that most nodules were hyper/isoechoic, multinodular, with regular margins and more than 15 mm in size (Table 1). Also, the most common FNA results were related to adenomatous goitre, followed by cysts, papillary carcinoma, and thyroiditis, respectively (Table 2).

Table 1. Frequency distribution and percentage of ultrasound findings in the subjects

Variable		No. (%)
Number of nodules	Single	29 (19.3)
	Multi	121 (80.7)
Type of nodules	Solid	81 (54)
	Cystic/solid	69 (46)
Echogenicity of nodules	Hypoechoic	32 (25.3)
	Hyper/isoechoic	118 (74.7)
Margin of nodules	Irregular	31 (20.7)
	Regular	119 (79.3)
Size of nodules	<15 mm	24 (16)
	>15 mm	126 (84)
Calcification of nodules	+	77 (57.3)
	-	73 (42.7)

Table 2. Frequency distribution and percentage of FNA results in the subjects

	Variable	No. (%)
FNA results	Adenomatous goiter	97 (64.7)
	Thyroiditis	7 (4.7)
	Cysts	30 (20)
	Suspicious of papillary carcinoma	1 (0.7)
	Papillary carcinoma	13 (8.7)
	Follicular carcinoma	2 (1.3)

FNA, Fine needle aspiration.

The ultrasound results were divided into three categories according to the guidelines of the American Thyroid Association (ATA) (14): Intermediate suspicion, low suspicion, and high suspicion.

Based on this guideline, 15 ultrasounds were in the high suspicion category, 19 in the intermediate class, and 116 in the low suspicion category. Among the 19 patients with intermediate suspicion ultrasound results, 14 had benign FNA and five malignant FNA results. The overall findings were calculated as specificity, sensitivity, positive predictive value, and negative predictive value. The sensitivity of FNA was 56.25% according to the respective formula (TP/TP+FN); in other words, this table shows the probability of high-suspicion ultrasound results in malignant people (Table 3).

The specificity of this test was 85.07% according to the related formula (TN/TN+FP); this table shows the probability of low-suspicion ultrasound results in benign cases. Also, the positive predictive value or the degree of malignancy of the mass in patients with high suspicion ultrasounds was 60%, and the negative predictive value or the degree of the benignity of the mass in patients with low suspicion was 98.27%.

Table 3. Malignancy or benignity of the mass according to the ultrasound and FNA

		FNA		Total
		Benign	Malignant	
Ultrasound	(-) Low Suspicion	114 (TN)	2 (FN)	116
	Intermediate suspicion	14	5	19
	(+) High suspicion	5 (FP)	9 (TP)	15
	Total	134	16	150

FNA, Fine needle aspiration.

Assessing the ultrasound findings of the patients based on whether the masses were benign or malignant was performed after running the cross-tab command using the chi-square test. The chi-square test results showed that the three ultrasound findings had a significant relationship with whether the mass was benign or malignant ($P<0.05$). Consequently, malignant masses were significantly hypoechoic, single, and irregular. The following table explains the results in detail (Table 4).

The FNA results of patients with low and high-suspicion ultrasounds (i.e., patients with definitive ultrasound results) were compared with the FNA results of intermediate-suspicion patients after running the cross-tab command and were analyzed using the chi-square test. The findings showed a significant difference in FNA between these two groups ($P=0.018$). As in Table 5, the number of malignant FNA was significantly higher in the intermediate suspicion patients compared to those with low suspicion and high suspicion ultrasounds. Performing further diagnostic measures such as FNA and core needle biopsy after noticing an intermediate suspicion in a patient's ultrasound seems necessary (Table 5).

Discussion

This study examined the diagnostic value of ultrasound in differentiating between benign and malignant thyroid masses compared to FNA. Furthermore, FNA results were compared with ultrasound diagnoses with an intermediate suspicion of malignancy.

In this study, the assessment of six ultrasound characteristics in 150 patients, including the number, type, echogenicity, margin symmetry, size, and calcification of nodules, showed that most nodules were hyper/isoechoic, multinodular, with a regular margin and size larger than 15 mm; also, the most common FNA result was an adenomatous goitre diagnosis. In the study by Rahimi et al, most of the malignant nodules were single, solid, and hypoechoic, with irregular margins and calcification. According to their results, malignant masses are significantly correlated with irregular margins, hypoechoic nodules, and singularity (15). Other studies showed that malignancy of a nodule is independent of nodule number (16,17). Therefore, we conclude that nodule number alone cannot be a good predictor of mass malignancy.

Rahimi et al also found no significant relationship between malignancy and a nodule size greater than 15 mm ($P>0.05$)(15), which is consistent with the findings of the present study, and the other findings were consistent with the results reported by Samiee Rad et al (18). On the other

Table 4. Ultrasound findings of patients based on the malignancy or benignity of the mass

Variable		FNA		df	*P* value
		Malignant	Benign		
Number of nodules	Single	8	21	1	0.001
	Multi	8	113		
Type of nodules	Solid	12	69	1	0.075
	Cystic/solid	4	65		
Echogenicity of nodules	Hypoechoic	12	20	1	0.000
	Hyper/isoechoic	4	114		
Margin of nodules	Irregular	8	23	1	0.002
	Regular	8	111		
Size of nodules	<15 mm	0	24	1	00.065
	>15 mm	16	110		
Calcification of nodules	+	9	68	1	0.677
	-	7	66		

FNA, Fine needle aspiration.

Table 5. Ultrasound results of patients based on the malignancy or benignity of the mass

Ultrasound	FNA		Chi-square test statistic	*P* value
	Benign	Malignant		
Intermediate suspicion	14 (73.7%)	5 (26.3%)	5.591	0.018
Low or high suspicion	120 (91.6%)	11 (8.4%)		

FNA, Fine needle aspiration.

hand, a study conducted by Cavallo et al in University of Chicago Medical Center also demonstrated that as the malignancy rates decreased, size of the nodules increased; concluding that size at ultrasound alone should not be considered as an independent risk factor (19). Other studies also concluded that nodule size and malignancy cannot be statistically related, and their relationship is poor predicator (16,17,20). Also, a meta-analysis study found that nodules > 2 cm no longer influence malignancy risk (21).

The positive and negative predictive values of ultrasound were 60% and 98.27% in the present study and 65% and 89.6% in the study by Samee Rad et al (18). Another study reported ultrasound had sensitivity, specificity, and positive predictive values of 74%, 83%, and 51%, respectively (22); the numbers in previous studies are pretty similar to ours and therefore, approving our study in revealing the sensitivity and specificity of ultrasound in diagnosing malignant masses as 56.25% and 85.07%, respectively. Another study on the Iranian population reported the sensitivity and specificity of ultrasound as 56.25% and 95.9%, respectively. Indicating the same result might be due to conducting the study in almost the same population (23). Kaur et al reported the sensitivity and specificity of ultrasound as 73% and 89%, respectively (24). A comparison of these findings reveals the lower sensitivity of ultrasound in the present study, while the specificity was almost the same in both studies. On the other hand, the overall sensitivity of ultrasound in the study of Alshoabi et al in the diagnosis of benign thyroid lesions was 98.38%, with a specificity of 71.42% and positive and negative predictive values of 98.38% and 55.55%, respectively; which can be due to the small sample size of both studies and radiologists' skills (25). Moreover, in a multi-center study, the ultrasound finding had a sensitivity of 83.3% and specificity of 74.0% (26); in the end, due to the variety of numbers among studies, we find a need for a comprehensive systematic review and meta-analysis of present studies in the matter, to determine the exact number and range of specificity and sensitivity.

Conclusion

The number of malignant FNA was significantly higher in the intermediate suspicion patients than those with low suspicion and high suspicion ultrasounds. Performing further diagnostic measures such as FNA and core needle biopsy after noticing an intermediate suspicion in a patient's ultrasound seems necessary. Overall, the present findings showed that the use of core needle biopsy could be helpful for better determining whether masses, especially the intermediate ones are benign or malignant. The present study is limited in having a small number of participants, which must be considered when interpreting its findings. All to say, studies with larger statistical populations and more extended follow-up periods are needed to achieve more accurate results. Further research is suggested using permanent pathology instead of FNA and thyroid imaging reporting and data system (TI-RADS) classification (27) instead of ATA.

Limitations of the study

The study may have a small sample size, which could limit the generalizability of the findings to a broader population. The study may indicate a need for further research with larger sample sizes and longer follow-up periods to confirm the effectiveness of the diagnostic methods being compared.

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Authors' contribution

Conceptualization: Ladan Hajiabdolrrasouli.
Data curation: Ladan Hajiabdolrrasouli.
Formal analysis: Saeed Hosseini Teshnizi.
Funding acquisition: Hamid Reza Samimagham.
Investigation: Ladan Hajiabdolrrasouli.
Methodology: Mitra Kazemi Jahromi.
Project administration: Mitra Kazemi Jahromi.
Resources: Ali Salimi Asl.
Software: Saeed Hosseini Teshnizi.
Supervision: Mitra Kazemi Jahromi.
Validation: Hamid Reza Samimagham.
Visualization: Ali Salimi Asl.
Writing–original draft: MohammadHosein Sheybani-Arani & Soroush Jaberansari.
Writing–review & editing: MohammadHosein Sheybani-Arani & Soroush Jaberansari.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki and was approved Hormozgan University of Medical Sciences Ethical Committee under the ethical code IR.HUMS.REC.1398.383. Prior to any intervention, all participants provided written informed consent. The authors have fully complied with ethical issues, such as plagiarism, data fabrication, and double publication.

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