Comparison between ultrasonographic findings and fine needle aspiration cytology in differentiating malignant and benign thyroid nodules

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Abstract

The purpose of research was comparing the ultrasound (US) features and fine-needle aspiration cytology (FNAC) in detecting the thyroid nodules in clinical practice. A cross-sectional analytical study retrospectively reviewed the US and FNAC findings for a total of 170 thyroid nodules. The US features that we compared included echogenicity, calcifications, shape, halo and Doppler, between 2017 and 2018. Totally, 170 nodules of thyroid were studied, which contained 72 (42.4%) benign and 98 (57.6%) malignant thyroid nodules. The sonographic features were significantly associated with malignancy such as microcalcification (97.0%), hyperechogenicity (91.5%), wider than taller shape (98.0%), absent halo (90.9%) and positive Doppler (78.0%) ($P < 0.01$). The altogether accuracies of calcification, echogenicity, shape, halo, and Doppler were 0.96, 0.92, 0.97,0.82 and 0.82, respectively. Our data suggest that US features could be a good sonographic criterion for recommending FNA cytology with follow-up thyroid sonography and FNA.

Key Words: ultrasound, fine-needle aspiration, thyroid, clinical.

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In recent years, fine-needle aspiration cytology (FNAC) has became the gold standard diagnostic procedure for therapy plans for euthyroid patients with thyroid parenchymal nodules.[1-5] FNAC reduces significantly the number of dispensable surgeries of thyroid (thyroidectomy) for patients with benign nodules, because FNAC is growing in detection of malignancy potentials of thyroid nodules.[1-8] The Bethesda System of Reporting Thyroid Cytopathology (TBSRTC) is launched in 2007 by the National Cancer Institute (NCI) that describes uniform terminology and diagnostic criteria for thyroid FNA specimens to communicating with pathologists and clinicians. Of course, in December 2010, the ultimate version of TBSRTC was institutionalized with the publication. TBSRTC categorizes the cytological data in 6 classes composed of nondiagnostic or unsatisfactory (ND/UNS, Bethesda I); benign (Bethesda II); atypia of undetermined significance (AUS, Bethesda III) or follicular lesion of undetermined significance (FLUS, Bethesda III); follicular neoplasm (FN, Bethesda IV) or suspicious for FN; suspicious for malignancy (SM, Bethesda V); and malignant (Bethesda VI).[9-13] Thyroid ultrasound (US) is an extensive tool that is utilized as a first-line diagnostic procedure in thyroid nodules (TNs) and it plays a fundamental role in finding malignant TNs leading to a better prognosis and in selecting TNs for FNA. As compared with FNA, ultrasonography of thyroid has the benefit of a non-invasive nature and is a method with giving quick data. In fact, FNAC is appraised as a procedure of selecting to diagnose TNs, but it is invasive. Afterward, it can be refrained in nodules without suspicious specifications to a less invasive test. Taken together, the main dispute is over the precise recognition malignant TNs and to abstain from unessential methods for benign nodules.[14-22] Therefore, in the current study, we investigated the comparison of results from US features and FNAC on thyroid nodules in clinical practice.

Materials and Methods

Study population

A study with retrospective cross-sectional was conducted at the Research Institute for Cancer diseases, as the main referral center for Cancer patients in Tehran, Iran.

The records of patients referred to the clinic and patients are selected to allow the results of their cytology and

Table1. *Characteristics of the thyroid nodules*

Variables	Frequency (Total=170)	Percent
Calcification		
Eggshell	17	10.0
Coarse	17	10.0
Absent	54	31.8
Macro	16	9.4
Micro	66	38.8
Echogenicity		
Hyper	13	7.6
Hypo	106	62.4
Isoechoic	51	30.0
Shape		
Ovoid to round	5	2.9
Taller than wider	99	58.2
Wider than taller	66	38.8
Halo		
Thin	47	27.6
Incompletely thin	46	27.1
Absent	77	45.3
Doppler central flow		
Negative	43	25.3
Positive	127	74.7

sonography to be available and then their demographic and epidemiological characteristics presented and the diagnostic methods mentioned are compared. Pathological slides and cytology samples and their sonographic findings will be reviewed as well as the number of all patients enrolled in the study will be randomized sampling. Among 170 suspected patients of thyroid cancer, 98 subjects have positive tests results after Pathology and were considered as case and non-cancer patients considered as controls. We use the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), in which (Bethesda initial version in 2009 and the second edition in 2017), there are six main diagnostic groups:[23]

1. Non-diagnostic or unsatisfactory
2. Benign
3. Atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS)
4. Follicular neoplasm or suspicious for a follicular neoplasm (FN/SFN)
5. Suspicious for malignancy
6. Malignant

Statistical analysis

In this study, ordinal regression (ordinal classification) analysis was employed to assess the relation between ultrasound (US) features and fine-needle aspiration cytology (FNAC) and to report odds ratio (OR) and 95% confidence interval (CI). The sensitivity, specificity and predictive values of ultrasound (US) features against (FNAC) were counted by receiver operator characteristics (ROC) analysis and the area under the curve (AUC). To display small variables from the mean ± SD, we will use frequency to display qualitative variables. Significance level is less than 0.05. Statistical analyses were done by using IBM SPSS Statistics for Windows, Version 25.0.

Table2. *Relationship between ultrasound features and fine needle aspiration results*

Sonographic features	Benign [n (%)]	Malignant [n (%)]	Odds Ratio (95% confidence interval)	p value
Calcification				
Absent	50 (92.6%)	4 (7.4%)	0.013 (0.005, 0.038)	<0.001
Eggshell	17 (100.0%)	0 (0.0%)	0.061 (0.028, 0.133)	<0.001
Macro	0 (0.0%)	16 (100.0%)	0.257 (0159, 0.415)	<0.001
Coarse	0 (0.0%)	17(100.0%)	0.566 (0.376, 0.852)	0.006
Micro	2 (3.0%)	64 (97.0%)	-	-
Echogenicity				
Isoechoic	13 (100.0%)	0 (0.0%)	0.018 (0.005, 0.053)	<0.001
Hypo	9 (8.5%)	97 (91.5%)	0.042(0.016, 0.113)	<0.001
Hyper	47 (92.2%)	4 (7.8%)	-	-
Shape				
Ovoid to round	4 (80.0%)	1(20.0%)	0.0001(0.00002, 0.0008)	<0.001
Taller than wider	2 (2.0%)	97 (98.0%)	0.042 (0.015,0.113)	<0.001
Wider than taller	63 (95.5%)	3 (4.5%)	-	-
Halo				
Thin	43 (91.5%)	4 (8.5%)	0.059(0.030,0.116)	<0.001
Incompletely thin	19 (41.3%)	27 (58.7%)	0.432(0.283, 0.659)	<0.001
Absent	7 (9.1%)	70 (90.9%)		
Doppler central flow				
Negative	41 (95.3%)	2 (4.7%)	0.019(0.004, 0.085)	<0.001
Positive	28 (22.0%)	99 (78.0%)	-	-

Results

In this study, we found that men percent in the malignant group (75.6%) are significantly higher than women (51.9%). The mean ± SD age in the malignant group was 61.63 ± 6.80 and in the benign group was 54.92 ± 10.75. The frequency and percentage of ultrasound (US) features are reported in Table 1. Table 2 shows the relation between ultrasound (US) features and fine-needle aspiration cytology (FNAC) results. Significant positive relations were found between all US and FNAC results. For features of calcification; Absent, Eggshell, Macro, Coarse against of Micro we found respectively (OR 0.013, CI 0.005- 0.038), (OR 0.061, CI 0.028- 0.133), (OR 0.257, CI 0159- 0.415) and, (OR 0.566, CI 0.376, 0.852). For features of Echogenicity; Isoechoic and Hyper against of Hypo, respectively we got (OR 0.018, CI 0.005- 0.053) and (OR 0.042, CI 0.016- 0.113).

Table 3. *Sensitivity and specificity of thyroid nodules diagnostic tests*

Ultrasound features' characteristics	sensitivity	specificity	Positive predictive value	Negative predictive value	Accuracy
Calcification	0.960	0.71	0.94	0.98	0.96
Echogenicity	0.960	0.87	0.94	0.91	0.92
Shape	0.960	0.71	0.94	0.98	0.97
Halo	0.960	0.62	0.91	0.79	0.82
Doppler	0.980	0.59	0.95	0.78	0.82

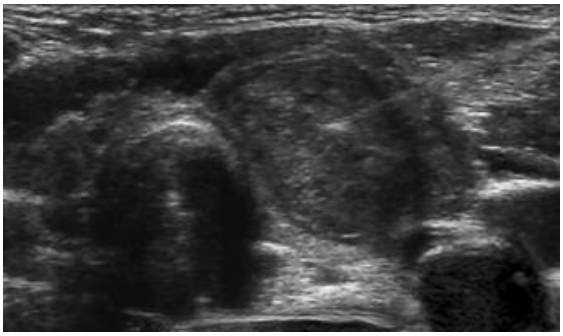

Fig 1. *Fine needle aspiration guided by sonography of a hypoechoic nodule proved as papillary thyroid carcinoma.*

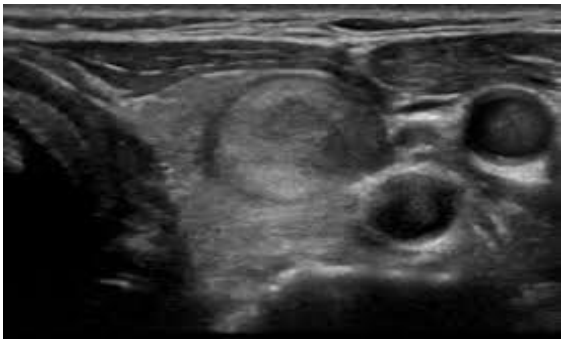

Fig 2. *Ultrasound features shown in the figure of hypoechoic thyroid nodules proved as papillary carcinoma by cytology*

Ovoid to round and Wider than taller against of Taller than wider we were (OR 0.0001, CI 0.00002- 0.0008) and (OR 0.042, CI 0.015- 0.113), For features of Halo; thin and Incompletely thin against of Absent, we got respectively (OR 0.059, CI 0.030- 0.116) and (OR 0.432, CI 0.283- 0.659) and for features of Doppler central flow; negative against of positive we received at (OR 0.019, CI 0.004- 0.085). Table 3 suggests the calculated sensitivity, specificity, predictive vales and accuracy of thyroid nodules by ultrasound features. Figure 1 shows the ROC curve for the sensitivity and specificity of US, shape had the greatest predictive ability (AUC= 0.962), and then respectively calcification (AUC= 0.956), echogenicity (AUC= 0.911), halo (AUC= 0.871) and, Doppler central flow (AUC= 0.787). Figure 2 and 3 indicate the thyroid nodules ultrasound characteristics' and the process of which the nodules are gone under aspiration by the fine needle.

Discussion

In this study, the prevalence of malignancy in men was 75.6% and in women was 51.9%, but comparing to other studies this difference was significant. But, Razmpa et al., 2002 reported the incidence of malignancy in men

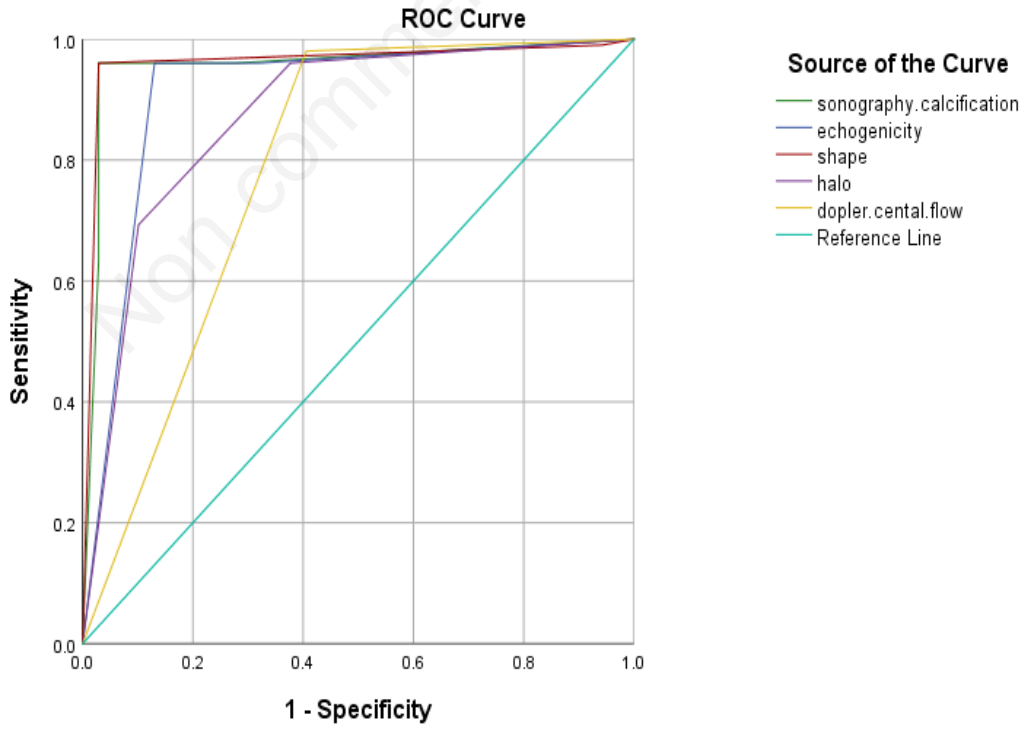

Fig 3. *Receiver operating characteristic curve estimates the ability of ultrasound to diagnose malignant nodules*

was 76% and in women was 71%, which shows this difference was no significant,[20] in contrast with present research. However, it may be due to the average patients' age who had malignant nodules was notably higher than people with benign nodules such as findings from Lin et al.,1997 and Danese et al.,1998.[21,22] On the other hand, the malignant portion of thyroid nodules was 57.6%, which is seemingly higher than in most previous reports from Nam-Goong et al., 2004, Izquierdo et al., 2006, and Frates et al., 2006, which might result from selection bias based on sonographic findings of the people who had undergone surgery.[23-25] In parallel, Ishida et al.,1988 suggested that 0.14% of the general Japanese population had malignant thyroid nodules.[26] a range that is lower than our report. Moreover, Park et al., 2011 reported that the malignancy rate for the nodules identified as benign was 2.8%, and 68.7% for nodules suspicious for malignancy.[27] In the present study, hypoechogenicity as one of sonographic characteristics was the most worth measure to predict malignancy (91.5%), with 0.96% sensitivity, 87% specificity and 92% accuracy. Other studies by Nabahati et al.,[14] and Alam et al.,[28] have reported that hypoechogenicity was most anticipated scale for malignancy, these rates were observed, (53% sensitivity, 77% specificity), (42% sensitivity and 75% specificity), respectively, which were in contrast to our data. Furthermore, in conflict with our results, in another study by Sankhla et al., 2001, found 33% of hypoechoic malignant nodules and 11% of hyperechoic malignant nodules.[29] Calcifications are seen in both malignant nodules and benign ones. According to our results, calcification was related to low specificity (0.71%), but high sensitivity (0.96%), which was in contrast with the previously published data like, Alam et al., 2014, Kim et al., 2002, Papini et al., 2002 and Nabahati et al., 2019.[14,28,30,31] Of course, some studies are in agreement with our results, which showed a higher rate of sensitivity such as Xu et al.,2017,[32] moreover, microcalcification was associated with malignancy (97.0%) and benign (3.0%), but there were conflicting data about absent, eggshell, coarse, and macrocalcification such as studies published from Petrone et al., 2012, Kim et al., 2013, and Park et al., 2014.[33-35] A study by Koike et al., 2001,[36] indicated that calcification had a sensitivity of 88.7% and Ram et al., 2015 showed a high sensitivity (80%) and a relatively lower specificity (68%) for calcification,[19] results of these two studies are relatively close to our findings for calcification (both micro as well as macro). On the other hand, our data have clearly demonstrated that taller than wider shape was the other predicting feature of malignancy with high sensitivity but low specificity. These results were in contrast with Kwak et al., 2011, Ram et al., 2015, and Wang et al., 2017, and also, consistent with, Ren et al., 2015, Nabahati et al., 2019 and Moon et al, 2011, who demonstrated a taller-than-wide shape can be of a good help in predicting malignant nodules.[19,37-40] Our results revealed that difference between isoechoic nodules (0.0%), hypoechoic nodules (91.5%) and hyperchoic nodules (7.8%), was statistically significant, the research by Degirmenci et al.,[41] reported the hypoechoic nodules (35.9%), isoechoic nodule (28.6%) or hyperechoic nodules (33.3%) were no different in number. The study by Leenhardt et al.,[42] showed the hypoechoic and isoechoic nodules (20% and 21%, respectively) compared with hyperechoic nodules (7%). Our data showed relatively higher rates of nondiagnostic cytology and one feasible statement is nodules with hypoechogenecity are associated with more fibrosis that might lead to a higher contingency of nondiagnostic report of cytology. In conclusion, our data suggest that US features like microcalcification, hypoechogenicity, taller than wider shape, and absent halo could be a good sonographic criterion for recommending FNA cytology, the US as useful approach might help to facilitate the diagnosis in patients with thyroid nodules, and finally, it can be proposed that the FNA utilize on planning of surgery for thyroid nodules and especially for follow-up of the patients. However, further studies containing a greater study population are necessary to confirm our study findings.

List of acronyms

AUS - Atypia of undetermined significance
interval
BMI - Body Mass Index AUC - area under the curve
CI - Confidence interval
FLUS - follicular lesion of undetermined significance
FN - Follicular neoplasm
SFN - suspicious for a follicular neoplasm
FNAC - fine-needle aspiration cytology
NCI - National Cancer Institute
OR - Odds ratio
ROC - receiver operator characteristics
TBSRTC - Bethesda System for Reporting Thyroid Cytopathology
TNs - thyroid nodules
US - ultrasound

Authors contributions

All named authors played a substantial role in the conception and/or study design, data acquisition and/or analysis, as well as drafting of the manuscri agree the accountability for all aspects of accuracy and integrity of the work.

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Conflict of Interest

The authors declare they have no conflicts of interest..

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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