Youssef et al. The Egyptian Journal of Otolaryngology (2020) 36:23
https://doi.org/10.1186/s43163-020-00025-1

The Egyptian Journal of Otolaryngology

ORIGINAL ARTICLE

Open Access

The diagnostic value of ultrasonography in detection of different types of thyroid nodules

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Abstract

Background: This article discusses the importance of high frequency ultrasonography in detection of different types of thyroid nodules considering only the histopathological examination of the surgical specimens as the final diagnosis. We studied 50 patients referred to ENT clinic with a thyroid nodule. Ultrasonography and ultrasound-guided fine-needle aspiration biopsy were done to all the patients. Thyroid surgery was done according to FNAB results.

Result: From 50 thyroid specimens, the US could predict the malignancy in 18 specimens. By histopathology, only 16 specimens were malignant, and 34 were benign thyroid disease. The sensitivity, specificity, and accuracy of US were 100%, 94.12%, and 96% respectively. The most suspicious ultrasongraphic feature was microcalcification followed by taller than wider (T ˃ W).

Conclusion: High frequency ultrasound is a very important tool to predict the malignant possibility during thyroid nodule evaluation.

Keywords: Ultrasound (US), Fine-needle aspiration biopsy (FNAB), Thyroid nodule, Microcalcification

Background

The thyroid nodule (TN) is a discrete lesion that could be distinct radiologically and pathologically from the normal thyroid parenchyma [1]. It is considered the most common abnormality in the endocrine system. Using ultrasonography (US) in thyroid nodule detection has raised the nodule prevalence to reach 67%. Seven to fifteen percent of thyroid nodules are malignant [2, 3].

The current goal in the TN evaluation is to determine whether it is benign or malignant [4]. Usually, the US is the first choice among the imaging studies during TN assessment followed by ultrasound-guided fine-needle aspiration biopsy (FNAB), and mostly the surgery decision or leaving the nodule alone is dependent on the FNAB result. However, FNAB has several limitations including inadequate sampling, operator dependency, and false negative cytology rates (10–30%) [5–8].

Recently, several studies have been performed using high frequency ultrasonography to determine suspicious features of malignant TN like taller than wider in shape, microcalcifications, solid texture, central vascularity, hypoechogenicity, and irregular margin [4, 9–11].

The purpose of this study is to determine the diagnostic value of US in the evaluation of TN in comparison with the final histopathological examination of thyroid surgical specimen.

Methods

Patients

A total of fifty patients aged from 20 to 50 years old with equivocal or suspicious US/FNAB results underwent

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hemi-thyroidectomy. Malignant TN (proved by FNAB) underwent total thyroidectomy.

High frequency ultrasonography of thyroid gland

High frequency US was performed by radiologist with more than 3 years of experience in thyroid gland ultrasonographic assessment using high-resolution ultrasound equipment using 7–15 MHz linear transducer in transverse and longitudinal planes. Each TN was evaluated according to the site, size, and shape.

The nodular features were classified for:

1. Shape: oval or rounded
2. Taller than wider (T > W) or wider than taller (W˂T)
3. Echogenicity as isoechoic, hypoechoic, hyperechoic, or anechoic
4. Echotexture as solid, mixed, or cystic (if the cystic component occupied an area of less than 25%, it was considered as solid, between 25 and 74% as mixed and 75 and 100% as cystic)
5. Presence of microcalcification as “present” or “absent”
6. Presence of macrocalcification as “present” or “absent”
7. Presence of halo: as “present” or “absent”
8. Regularity of nodule margin as regular or irregular
9. Nodal vascularity: type I was absent vascularity, type II was mixed type (central and peripheral), and type III was central
10. Cervical lymph nodes: shape, size, and presence of hilum

We considered that the nodule was suspicious for malignancy if it had two or more of suspicious malignant features of US (T > W, microcalcifications, central vascularity, solid texture, hypoechogenecity, and irregular or ill-defined margins).

US-guided fine-needle aspiration biopsy (US-FNAB)

All patients signed the informed consent after the explanation of the US-FNAB procedure. It was done by experienced radiologist using 22-gauge needle. The specimen was smeared and fixed by alcohol. The cytological analysis was classified according to Bethesda category (Table 1) [12].

Histopathology

Patients with FNAB results with Bethesda 4 and 5 underwent hemi-thyroidectomy. Patients with Bethesda 6 underwent total thyroidectomy. The surgical specimens were embedded in paraffin blocks and sectioned. The sections were stained by hematoxylin and eosin stain and examined under light microscope.

Table 1 Bethesda system for cytological diagnosis of thyroid nodules [12]

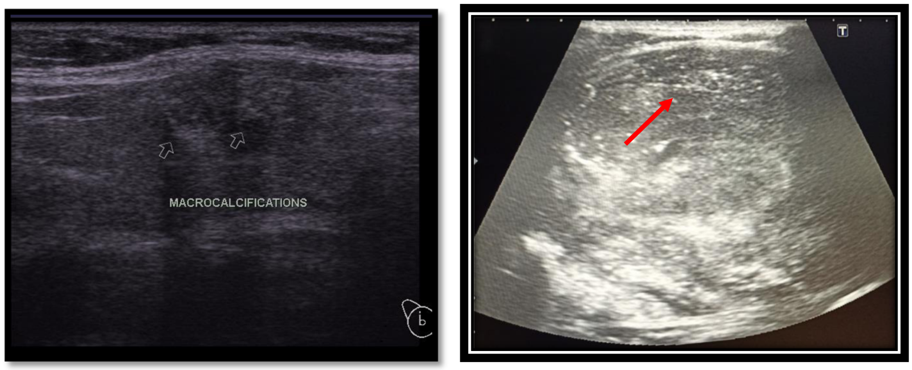
Category	Category name	Cytologic features	Malignancy risk (%)
I	Non-diagnostic or Unsatisfactory (ND)	Insufficient cellularity, obscuring blood	5–10
II	Benign	Normal-appearing follicular cells arranged in sheets or macrofollicls, abundant colloid	0–3
III	Atypical of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS)	Sparsely cellular, microfollicles, mild nuclear changes	10–30
IV	Follicular lesion/ suspicious for follicular lesion (FN/SFN)	Hypercellular, crowding, microfollicles, scant colloid	25–40
V	Suspicious for malignancy (SFM)	Some features that suggest but not definitive for malignancy	50–75
VI	Malignant	Papillary architecture, definitive nuclear changes	97–99

Statistical analysis

Data were fed to the computer and analyzed using the IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation, and median. Significance of the obtained results

Table 2 Distribution of the studied cases according to histopathology (n = 50)

Histopathology	No.	%
Benign	**34**	**68.0**
Micro nodular goiter	5	14.7
Micro follicular adenoma	16	47.1
Hyperplastic thyroid nodule	2	5.9
Early thyroiditis	1	2.9
Colloid nodule with hyperplastic changes	7	20.6
Colloid cyst	3	8.8
Malignant	**16**	**32.0**
Sarcoid scarcoma of thyroid gland	1	6.3
Papillary micro carcinoma	12	75.0
Follicular variant of papillary carcinoma	2	12.5
Follicular thyroid carcinoma	1	6.3



(A) (B)

Fig. 1 a Thyroid nodule US picture showing macrocalcification in benign TN (arrow). **b** US picture shows microcalcification in malignant TN (red arrow)

was judged at the 5% level. The used tests were chi-square test, Fisher's exact test, *F* test (ANOVA), and Kruskal-Wallis test.

Results

Demographic data

Fifty patients ranged in age between 22.0 and 50.0 years with a mean age of 38.60 ± 7.43 years. Studied cases were 14 (28.0%) males and 36 (72.0%) females.

Histopathological result

Fifty patients were operated. The result was benign in 34 patients and malignant in 16 patients with different histopathological types (Table 2).

US suspicious features of thyroid nodule

There was solitary thyroid nodule in the 50 patients, 34 nodules were in the right thyroid lobe, 2 nodules in the isthmus, and 14 nodules in the left lobe. Microcalcification was the most suspicious US features, and Fig. 1 displays the difference of microcalcification and macrocalcification.

The suspicious malignant US features and their statistical analysis are shown in Table 3 and Fig. 2 in comparison to the final histopathological results.

In comparison to the final histopathological results, we could summarize sensitivity and specificity the of US decision in Table (4).

US-guided FNAB results

The results of FNAB were classified according to Bethesda category in comparison to the histopathological results as follow:

Table 5 summarizes the relation between histopathology and Bethesda system. There was a significant relation between histopathology and Bethesda system.

Table 6 summarizes sensitivity and specificity for Bethesda system. The sensitivity of Bethesda system in detecting different types of thyroid nodules was 37.50%, with specificity100.0% and accuracy 80.0%.

Comparison of US findings and FNAB results

The review of all results revealed that the US decision was compatible with the FNAB result in 72% of cases (*n*

Table 3 Summarizes sensitivity, specificity, PPV, NPV, accuracy and *p* value of suspicious US finding of TN

Suspicious US finding	Histopathology				Sensitivity	Specificity	PPV	NPV	Accuracy	***P*** value
	Benign (***n*** = 34)		Malignant (***n*** = 16)							
	No.	%	No.	%						
Taller than wider	3	8.8	15	93.8	93.75	91.18	83.33	96.88	92.0	0.001
Oval shape	24	70.6	16	100	100.0	29.41	40.0	100.0	52.0	0.020
Hypoechoic	13	38.2	14	87.50	87.50	61.76	51.85	91.30	70.0	0.001
Ill-defined halo	0	0.0	4	25.0	25.0	100.0	100.0	73.91	76.0	0.008
Solid echotexture	30	88.2	16	100	100.0	11.76	34.87	100.0	40.0	0.292
Central vascularity	1	2.9	8	50.0	50.0	97.06	88.89	80.49	82.0	0.001
microcalcification	1	2.9	16	100	100.0	97.06	94.12	100.0	98.0	0.001

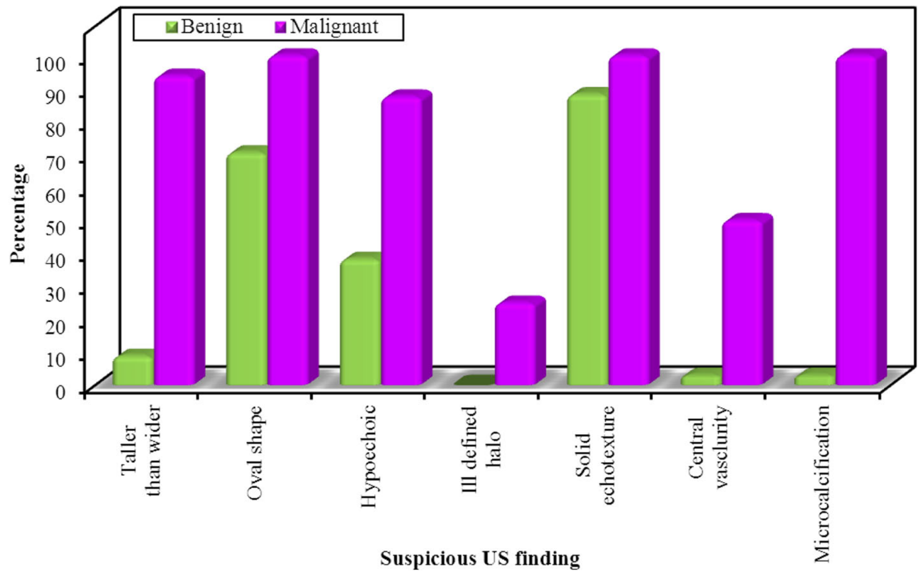


Fig. 2 Distribution of suspicious US features in thyroid nodules

= 36). On the other hand, the US was more accurate in 24% cases (*n* = 12). The FNAB could predict the final histology types in 2 cases better than US (Table 7).

One of the cases was benign (Bethesda II) with microcalcifications and T > W features on ultrasonography, and hemi-thyroidectomy was done. The final histopathology report was papillary thyroid carcinoma.

Discussion

Due to the expanding use of ultrasonography and other imaging modalities, the incidence of thyroid nodule was increased up to 67%. Most of thyroid lumps are benign; malignancy is quite low (3–7%) [13–19]. Although the thyroid cancer incidence has increased about 2.4-fold over the last three decades by applying the US as a preliminary assessment tool of thyroid gland lesions, this malignancy rate may be not actually estimated because there is an overlap between the gold standard investigation in the diagnosis of primary thyroid malignancy [8, 20–24].

The conflict is always between FNAB and US. Although the FNAB is simple, economic and available way, it has limitations. It causes physical and psychological discomfort because of its invasiveness [8]. The most relevant restriction is the intermediate result in 10 to 30% of cases [25]. Non-diagnostic FNAB or false negative results may be to low cellularity, small sized nodules, and cystic nature of nodules or due to inexperience of the aspirator or the cytologist [26]. Also, the FNAB failed in distinguishing between follicular adenoma and follicular carcinoma, which will not be achieved without intracapsular or intravascular invasion proof. The only tool to prove this invasion is the final histopathological analysis after surgical removal of thyroid specimen [27–29].

About the ultrasonographic assessment of thyroid nodule, it is well established that no single sonographic feature has adequate diagnostic accuracy in reliably discrimination between malignant nodules from benign ones. Many studies emphasize on the recognition of complex pattern [8, 19, 24, 30, 31]. In this study, we

Table 4 Sensitivity and specificity for ultrasound decision in relation to the histopathological results

Ultrasound decision	Histopathology				Sensitivity	Specificity	PPV	NPV	Accuracy
	Benign (***n*** = 34)		Malignant (***n*** = 16)						
	No.	%	No.	%					
Non-suspicious	32	94.1	0	0.0	100.0	94.12	88.89	100.0	96.0
Suspicious	2	5.9	16	100					
χ^2(*p*)	41.830[a] (< 0.001[a])								

NPV negative predictive value, *PPV* positive predictive value, c^2 chi-square test, *p* p value for comparing between the studied groups
[a]Statistically significant at $p \le 0.05$

Table 5 Relation between histopathology and Bethesda

Bethesda	Histopathology				χ^2	^{MC}p
	Benign (***n*** = 34)		Malignant (***n*** = 16)			
	No.	%	No.	%		
Non-diagnostic (I)	1	2.9	0	0.0	17.410[a]	< 0.001[a]
Benign (II)	0	0.0	1	6.3		
Atypia of unknown origin (III)	2	5.9	2	12.5		
Suspicious for follicular neoplasm (IV)	31	91.2	7	43.8		
Suspicious for malignancy (V)	0	0.0	4	25.0		
Malignant (VI)	0	0.0	2	12.5		

c^2 chi-square test, *MC* Monte Carlo test, *p p* value for comparing between the studied groups
[a]Statistically significant at $p \leq 0.05$

tried to search about the most sensitive suspicious US character of thyroid nodule to avoid unnecessary surgeries or overlooked malignant nodules without definite treatment. The US can see the intanodular structures and compare it to the surrounding neck parts [26].

On reviewing in the literatures, there are some suspicious ultrasongraphic features of thyroid nodule, namely, tall than wider nodules, solid texture, microcalcification, intranodal vascularity, hypoechogenicity, and irregular margin with different statistical accuracy [4, 9–11]. The present study results revealed that microcalcification is the best suspicious US thyroid feature that should be relied on during examination. The microcalcification represents the Psammoma body that is very specific for thyroid carcinoma and, especially, for papillary thyroid cancer, and the microcalcification is considered malignant if it is present without posterior shadowing and if it is appeared in the solid part of the TN. The calcification appears in the cystic part which it is considered the comet-tail artifact that is benign feature. Yunus et al. [11] and Salmaslıoğlu et al. [32] found that microcalcification was one of the best specific characters of thyroid malignancy.

The second most appreciated feature is taller than wider nodule. A recent study by Yoon et al. [33] explained this that a taller than wide shape in malignant thyroid nodules and a wider than tall shape in benign nodules are related to the ability of the probe to compress the thyroid nodule during the US examination. Since the benign nodules and cystic nodules are softer and infiltrate less into the surrounding tissue, benign nodules are more easily compressed than malignant nodules [33–36].

The ill-defined margin was very specific but it showed low sensitivity as it occurred only in 4 cases from 16 malignant nodules. According to Grant et al. [9], this controversy about the ill-defined feature is due to entangled definitions and observer variability. This was on the contrary with Gul [37] who found that the most important US feature to predict malignancy was found to be margin irregularity (with sensitivity 90.2%, specificity 87.3%) followed by hypoechoic pattern.

Central (type 3) vascularity was approved by Doppler US in 8 nodules. The sensitivity of vascularity in detecting different types of thyroid nodules was 50.0%. This result is quite different from Frates' [38] opinion, which showed that more than 50% of hyper vascular thyroid nodules were benign. Additionally, some malignant might lack central vascularity due to fibrosis according to Moon et al. [39]. Also, the new Doppler US equipment could detect the very minute vessels in thyroid nodule and not only large central ones [40].

The sensitivity of ultrasound in detecting different types of thyroid nodules was 100.0%, with specificity 94.12% and accuracy 96.0%. Also, sensitivity of Bethesda system of FNAB in detecting different types of thyroid nodules was 37.50%, with specificity 100.0% and accuracy 80.0%. Both of FNAB and US results were statistically significant, but the US had better preference than FNAB in diagnosis of 12 malignant cases (Table 7).

Small sample size was a limitation of our study but we tried to overcome this obstacle through that all the subjects underwent hemi or total thyroidectomy. So, the final histopathology was the cut point of diagnosis and not the fine-needle aspiration biopsy that has a lot of

Table 6 Sensitivity and specificity for FNAB

Bethesda	Histopathology				Sensitivity	Specificity	PPV	NPV	Accuracy
	Benign (***n*** = 34)		Malignant (***n*** = 16)						
	No.	%	No.	%					
Benign (I:IV)	34	100	10	62.5	37.50	100.0	100.0	77.27	80.0
Malignant (V + VI)	0	0.0	6	37.5					
χ^2 (^{FE}p)	14.489[a] (0.001[a])								

c^2 chi-square test, *FE* Fisher's exact test, *p p* value for comparing between the studied groups, *NPV* negative predictive value, *PPV* positive predictive value
[a]Statistically significant at $p \leq 0.05$

Table 7 Distribution of the studied cases according to final results (n = 50)

Final results	No.	%
Similar US and FNAB results compared to histopathology	36	72.0
US positively correlated to histopathology better than FNAB	12	24.0
FNAB positively correlated to histopathology better than US	2	4.0

debate as being the gold standard diagnostic tool of thyroid nodule.

Conclusion

Ultrasonography is a very essential sensitive tool in detection of thyroid nodule type, especially if it is done by well-experienced radiologist. It has a paramount importance in the successful management of thyroid nodules.

Abbreviations
US: Ultrasound; FNAB: Fine-needle aspiration biopsy; TN: Thyroid nodule

Acknowledgements
Not applicable

Authors' contributions
A Y: corresponding author, surgical procedures, and data review. M H: Supervisor of research, surgical procedures, and data review. R G: Principal investigator, conduct of study, and data collection. M E: Radiological data analysis and review and conduct of study. M Z: Review of literature and statistical analysis. The authors read and approved the final manuscript.

Funding
The source of funding for this research is the authors' personal funding.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
Consent to participate was waived by an IRB (Ethics Committee, Faculty of Medicine Alexandria University (IRB No. 00012098 (Expire on June 10, 2022), FWA No. 00018699 (Expire on April 2, 2021) https://www.hhs.gov/ohrp/irbs-and-assurances.html). Serial number of ethical committee acceptance is 0105764. Date of acceptance is November 16, 2018.

Consent for publication
Not applicable.

Competing interests
We have no competing interests.

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Received: 11 April 2020 Accepted: 22 July 2020
Published online: 19 October 2020

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