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THE ROLE OF CONVENTIONAL ULTRASOUND IN THE ASSESSMENT OF THYROID NODULES IN AL-SULAIMANYIA TERRITORY

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Abstract

A palpable thyroid nodule is a common clinical problem; the ultrasonography (US) and fine needle aspiration biopsy (FNA) are its main diagnostic tools. This article aimed to study the reliability and advantages of ultrasound as a diagnostic aid in predicting malignancy in thyroid nodules and to reduce the number of unnecessary surgery. Two hundreds and thirty three patients were examined by ultrasound, and then fine needle aspiration cytology under ultrasound guidance (US-FNAC) was done for 210 of them. From those 210 patients we obtained the histopathological proof of 58 patients who underwent surgery. We calculated the sensitivity, specificity and accuracy of US-FNAC. There are certain sonographic criteria that suggest malignancy these include microcalcification, irregular margins, and hypoechogenicity of the nodule. The sensitivity, specificity, and accuracy of US-FNAC were 80%, 96%, and 94% respectively. Although ultrasound can not reliably distinguish benign from malignant nodules, but it can identify suspected nodules based on certain sono-graphic criteria.

Introduction

The finding of a palpable thyroid nodule is a common clinical problem and is by far the commonest indication for imaging of the thyroid. The main burden of thyroid imagining in this part of the world falls on the ultrasound as the radionuclide scan is not available.

Current ultrasonographic technology permits high-resolution imaging of thyroid gland that is more accurate than clinical palpation or other imaging techniques. Ultrasonography is safe and sensitive and capable of detecting lesions as small as 1-3 mm in the thyroid parenchyma[1-5].

The vast majority of thyroid nodules are benign. The identification of those minority nodules, which are malignant, is therefore of great importance to avoid unnecessary surgery on the remainder.

It is important to know whether the patient has a solitary or multiple thyroid nodules, as the incidence of malignancy is about 5-30% in solitary thyroid nodules, while this incidence is minimized to less than 1-5% in multinodular goiter[6-9].

The thyroid nodules are three to four times more frequent in women than men[7,10,11].

Although, ultrasound can not reliably distinguish benign from malignant nodules, there are certain sonographic criteria that suggest malignancy. These include microcalcification, irregular margins, and hypoechogenicity of the nodule. On the other hand, there are certain sonographic features that can aid in predicting the benign nature of a given nodule. These include hyperechogenicity and cystic nature of the nodule, well-marginated nodules, coarse and eggshell calcifications, intact thin halo, and comet-tail sign.

Aim of the study

This work has been undertaken to study the reliability and advantages of ultrasound as a diagnostic aid in thyroid nodules, by correlating sonographic characteristics of the thyroid nodules with US-FNAC results and histopathological proofs (where available), to establish the relative importance of these features in predicting for malignancy. This will avoid unnecessary surgery on the majority of the thyroid nodules which are benign.

Materials and methods

This study was carried out in the Department of diagnostic imaging at AL-Sulaimanyia Teaching Surgical Hospital from June 2003 to May 2006.

In a prospective study, over 300 patients were examined by high-resolution real time sonography.Two hundred thirty three patients with thyroid nodules were included in the study, with the age ranging from 7 to 81 years. The rest of the patients were either normal or just have diffuse enlargement of the gland without nodularity. These were not included in the study.

All the patients were examined using the available Sonoline Omina real time scanner with 7.5MHz linear array transducer. No specific preparation was needed. All the patients were examined in supine position with the neck slightly hyperextended, by putting a pillow under the shoulders. A liberal amount of ultrasound gel was applied to the neck. The scan was done in the standard transverse and longitudinal, as well as multiple oblique positions.

The average examination time was 10 minutes.

US-FNAC was obtained for 210 out of those 233 patients with nodules, excluding those nodules that were less than 10mm. Regarding this last group of patients with micronodules (less than 10mm), it is rare for one of these lesions to represent an occult thyroid cancer and rarer still for one to become a clinically significant malignancy, indiscriminate surgery, which has an exceedingly small yield of cancer, seems ill-advised. Rather, periodic sonographic re-assessment for possible growth of the nodule appears preferable to dismissal of the problem as unimportant[12]. So we decided to follow this group of patients sonographically and not to do FNAC as there was no history of exposure to therapeutic x-ray and no family history of thyroid cancer in our cases.

We did not face any serious complications from the FNAC. Needle puncture caused slight pain and discomfort in some patients.

Fifty eight patients out of those 210 patients with US-FNAC results underwent excisional surgery. The histopathological results were obtained. Correlation was made directly between the biopsy and pathologic specimen and the ultrasound study.

Data collection regarding the sex, age, sonographic findings, FNAC and histopathology (where available) about each case, were obtained and recorded on a special form.

The established method for evaluating the efficacy (accuracy) of an assessment test is to determine its sensitivity and specificity compared to an adequate reference standard[13,14]. So we estimated the sensitivity and specificity of US-FNAB by comparing the results of US-FNAB to histopathological results, using the following formula:

Diagrammatic representation of the concepts sensitivity, specificity and accuracy[15]

	DISEASE		
TEST	**present**	**absent**	
Positive	**a**	**b**	**a+ b, All subjects with positive test**
Negative	**c**	**d**	**c + d, All subjects with negative test**
	a + c	**b + d**	
	All diseased	**All normal**	

Sensitivity: Proportion of subjects with disease that have positive test (positive in disease) a/a+c
Specificity: Proportion of normal that have negative test (negative in health) d/b+d
Accuracy: Proportion of all test results, both positive and negative, that is correct. a + d a + b+ c+ d

Results

We examined 233 patients (182 females & 51 males) ranging from 7-81 years of age. Ninety four patients (40.3%) were found to have solitary thyroid nodules, and 139 patients (59.7%) were found to have multiple nodules .US-FNAC was done for 210 out of those 233 patients (90 patients with solitary and 120 patients with multiple nodules). The FNA was done for all the solitary nodules and for the dominant nodules, and any nodule(s) with suspicious sonographic criteria in multinodular cases. We did not perform US-FNAC for the remaining 23 patients with nodules less than 10mm (micronodules) as there was no suspicious finding of malignancy in the sonographic examination of the nodules & none of the patients had history of previous therapeutic irradiation of the head & neck & none had family history of thyroid malignancy.

From those 210 patients with US-FNAC, we obtained the histopathological results of 58 patients who underwent surgery. Tables I, II & III.

Table I: The sex distribution in all the cases of nodular thyroid disease

	Females	%	Males	%	Total
Nodular thyroid disease	182	78.1 %	51	21.8 %	233

Table II: The total number of cases with nodular thyroid disease.

Thyroid nodular disease	FNAC done	FNAC not done	Histopathology	
			available	Not available
Solitary thyroid nodule	90	4	32	58
Multinodular thyroid	120	19	26	94
Number of the cases	210	23	58	152

Table III: US appearances of micronodules (23 cases) for whom no FNAC was done

Uncomplicated Cysts	Solid hyperechoic	Outline well-defined	halo sign
17	6	23	3

From those 210 patients, for whom FNA was done, we obtained the histopathological results of only 58 patients (32 patients with solitary thyroid nodules and 26 patients with multinodular thyroid) who underwent surgery. The results of FNAC and histopathological examination are shown in tables IV & V.

In those 32 cases of solitary thyroid nodules, 26 cases were benign by both (FNA and histopathology), 2 were malignant by both, and one case was suspicious for malignancy by FNAC & confirmed by histopathology. We had one false positive and one false negative results by FNAC in comparison with the final histopathological examination. We had only one case in which the FNA was inadequate and proved to be benign by histopathology.

In those 26 cases of multinodular thyroid disease, 23 cases were benign by both (FNAC and histopathology), and one case was malignant by both. One case was false positive by FNAC compared to the histopathological result, and one case was inadequate by FNA and proved to be benign by histopathological diagnosis

Table IV: FNAC & histopathological results cross tabulation of the (32) solitary thyroid nodule cases

	Results of Histopathology		
	Benign	Malignant	Total
Results of FNAC			
Benign	26	1	27
Malignant	1	2	3
Suspcious		1	1
Inadequate	1		1
Total	28	4	32

Table V: FNAC & histopathological results cross tabulation of the (26) Multinodular thyroid cases.

	Results of Histopathology		
	Benign	Malignant	Total
Results of FNAC			
Benign	23		23
Malignant	1	1	2
Inadequate	1		1
Total	25	1	26

Tables IV&V show that, we had 49 benign nodules, 4 malignant nodules, 1 false negative, and 2 false positive cases. We calculated the sensitivity, specificity, and accuracy of US-FNA (excluding the inadequate specimens), and they were 80%, 96% and 94% respectively.

The age and sex of the five cases of malignant thyroid diseases with their detail sonographic criteria are shown in table VI.

Table VI: The age, sex, and the detail sonographic criteria of the 5 malignant thyroid diseases.

	Sonographic criteria of the malignant nodules								
Pathology	Age years	Sex	Site	Size (mm)	Solid echog*	Outline	Halo sign	Calci*	Ipsi* LAP
1- Papillary Ca.	47	M	Rt.	15	Hypo	Irregular	No	Pun.*	-ve
2- Papillary Ca.	45	M	Rt.	22	Hypo	Irregular	No	Pun	+ve
3- Papillary Ca.	50	F	Lt.	35	Hypo	Irregular	No	No	-ve
4- Papillary Ca.	53	F	Lt.	20	Isoech	irregular	Blur*	No	+ve
5- Metastatic Ca.	60	F	Rt.	25	Hypo	Regular	No	No	-ve

Note: The first four cases were primary carcinomas of the thyroid (papillary type) & they presented as solitary thyroid nodules. The fifth case was a metastatic carcinoma and presented as a dominant nodule in a multinodular goitre. The rest of the nodules were hyperechoic. Echo*=echogenicity Hypo=hypoechoic Isoech=isoechoic Calcif*=calcification. Pun.*=Punctate calcification(microcalcification) M=Male F=Female. Blurred*= Blurred halo Ipsi. LAP=Ipsilateral lymphadenopathy.

Table VII shows the sex incidence in all those 58 patients whom submitted to surgery, with the number of benign and malignant cases and percentage of benign and malignant nodules to the total number of the nodules in each sex .

Table VII: Sex incidence in the thyroid nodules submitted to surgery with the results of histopathology.

Sex	no. of benign nodules	% to the total nodules	no. of malign. nodules	% to the total nodules
35 females	32	91.4 %	3	8.5 %
23 males	21	91.3 %	2	8.6 %
58 cases	53	91.3 %	5	8.6 %

The histopathological results of those 58 patients, whom underwent surgery, with their sonographic appearances are shown in tableVIII.

Table VIII: Analysis of US appearances of various thyroid nodular pathology.

Pathology		No.	Percent	Solid	Cystic	Mixed
Carcinoma		5	8.6 %	5	0	0
Benign	adenoma	6	10.3 %	5	0	1
Nodules	Others*	47	81.1 %	30	6	11
Total		58	100.0	40	6	12

*Others; include other benign nodular thyroid diseases (hyperplastic adenomatounodules, degenerated thyroid nodules, hemorrhagic cysts, and Hashimoto's thyroiditis cases).

Analysis of the echo pattern of the thyroid nodules with other associated sonographic signs in those 58 patients with histopathological proof, are summarised in table IX with their frequencies in both benign and malignant nodules and percentage of each sign to the total benign and malignant nodules in our study.

Table IX: Distribution and percentage of sonographic criteria of thyroid nodules and other associated sonographic signs among the benign and malignant lesions by histopathological proof (58 cases).

	Sonographic Criteria	No.	Ben.	%	% to total bengin cases (53)	Malig.	%	% to total malign cases (5)
Solid Nod	Isoechoic	12	11	91.6	20.7	1	8.3	20.0
	Hyperechoic	7	7	100.0	13.2	0	0.0	0.0
	Hyperechoic	21	17	80.9	32.0	4	19.0	80.0
Cystic nodules		6	6	100.0	11.3	0.	0.0	0.0
Mixed nodules		12	12	100.0	22.6	0	0.0	0.0
Outline	Regular	54	53	98.1	100.0	1	1.8	20.0
	Irregular	4	0	0.0	0.0	4	100.0	80.0
Halo	Intact	12	12	100.0	22.6	0	0.0	0.0
Sign	Blurred	1	0	0.0	0.0	1	100.0	20.0
	Punctate	2	0	0.0	0.0	2	100.0	40.0
Calcif.	Coarse	17	17	100.0	32	0	0.0	0.0
	Eggshell	2	2	100.0	3.7	0	0.0	0.0
Comet tail		1	1	100.0	1.8	0	0.0	0.0
Lap		2	0	0.0	0.0	2	100.0	40.0

Note that hyperechoic nodules, cystic and mixed nodules with regular outline and intact halo sign, coarse and eggshell calcification and comet tail sign, all are signs which are highly predominate in benign lesions, while hypoechoic nodules, irregular outline, blurred halo, punctuate calcification and lymph node enlargement, all are signs which are highly predominate in malignant lesions. Lastly, as the main pitfall of FNAB is that it could not differentiate between follicular adenoma and carcinoma, so all the cases that were diagnosed as follicular adenoma submitted to surgery, and fortunately all confirmed to be adenomas.

Discussion

Analysis of Sonographic Sings of Nodular Thyroid Disease: The incidence of nodular thyroid disease was higher in females than males (table I), with the female/male ratio; 3.5/1. This ratio agrees with all the other literatures.

The high sensitivity of ultrasound was clearly seen in our study, as we were able to detect nodules as small as 3mm, and we subdivided the thyroid nodules, on the basis of ultrasonic morphological findings, into solitary and multiple thyroid nodules (table II); 40.3% of the cases were solitary, and 59.6% were multiple nodules. This observation has an outstanding practical significance since the incidence of carcinoma in thyroid nodules is much higher in solitary thyroid nodules than in multinodular goiter. This point is clearly evident in our study, as we have four cases of thyroid carcinoma out of 32 cases of solitary thyroid nodules (12.5%) (Table IV), while we have only one case of thyroid carcinoma out of 26 cases of multinodular thyroid (3.8%) (Table V).

The incidence of malignancy was slightly higher in females than males (Table 6)

(3 females & 2 males) with the female to male ratio; 1.5/1, which indicates that although the thyroid nodular disease is more common in females, thyroid cancer is nearly equally common in males and females; a fact which puts males with thyroid nodules at risk even more than females[(16-18)]. This observation is quite obvious in the table VII, which shows that 8.6% of the nodules, in the male patients, were malignant, while 8.5% of the nodules, in the female patients, were malignant.

The age of the patients with nodular thyroid disease ranged from 7 years to 81 years. Regarding the age of the patients with thyroid carcinomas, table 6 shows that all the 5 cases were between 45-60 years of age. No malignancy was found below 45 years. This result is consistent with what Nidhal M. Mousa had noticed in her dissertation[19]. None of the patients was exposed to therapeutic irradiation of head and neck, and none had family history of thyroid malignancy.

The incidence of malignancy in our study was 8.6% of the nodules (5 out of 58 cases) (table VIII), which is higher than any Iraqi studies[19-23]. This is due to the limited number of the cases who underwent surgery, because of the performing of FNAC for each case preoperatively, which is the main aim of our study. Another reason for the limited number of surgery is the selective referring of the patients to surgery based on certain sonographic criteria which will be mentioned later[24,25].

As one of the main goals of thyroid ultrasonography is to determine the nature of thyroid nodules, and to predict the potential for malignancy, attempts have been made to find the characteristic signs that are specific enough to identify a nodule as either benign or malignant:

1-Our study did not show any relation between the size of the nodules, detected by ultrasound and the final pathological diagnosis; with small and large nodules were found in both benign and malignant lesions (Table VI).

This agrees with the answer of Dr. Maher, in the Interventional Radiology Case Conference Massachusetts General Hospital, who stated that size is not a reliable indicator of a benign or malignant nature of a thyroid nodule[26].

2-Looking at the tables 6, 8 & 9 we can get useful information from analysis of the relations of various sonographic criteria to the final pathological diagnosis.

The commonest echo-pattern in our study was solid nodules (40 out of 58) (68.9%) (Table 8), with all the five malignant nodules (100%) being solid, while 35 benign nodules were solid (60.3%). The second common pattern was mixed echo-pattern (12 out of 58) (20.6%), and the least was cystic (6 nodules) (10.3%). These observations and percentages are in accordance with other literatures[27-30].

The incidence of malignancy in different echo-pattern of solid nodules provides interesting data (tables VI, VIII, and IX):

i- the most striking observation is that 4 out of 5 malignant cases were hypoechoic nodules (80%) (Table VI). The table IX shows that out of 21 hypoechoic nodules, 4 were malignant and the remaining 17 were benign. These data agree with the all other literatures, that most of the malignant nodules are hypoechoic, however most of the hypoechoic nodules are benign[17,28,31,32].

ii- We had 12 isoechoic nodules; one case only proved to be malignant, the rest were benign. So one case out of 5 malignant cases, was isoechoic. This agrees with the other literatures in considering isoechoic nodules of significant value in suggesting malignancy[2,17,31].

iii- We had 7 hyperechoic nodules, all were proved to be benign. This result agrees with Solbiati L. et al series who concluded that hyperechoic malignant lesions are rare[2,33].

We had 6 cystic lesions and 12 mixed nodules (table 9), all of them proved to be benign. Mixed solid and cystic lesions are mostly benign, owing usually to colloid degeneration or degeneration in a follicular adenoma, although cystic degeneration can occur in a carcinoma[6,31].

Regarding the cystic lesions, our results were similar to other literatures which consider the incidence of malignancy in cystic lesions is negligible[2,6,19,34].

3-Table 6 shows that the outline of the nodules can be a very useful sign in predicting malignancy, as 4 out of 5 nodules (80%) exhibit irregular margins. On the other hand, all the benign nodules showed well-defined margins. We had only one case out of the remaining 54 cases (1.8%) with well-defined outline (table 9), proved to be malignant. These observations are compatible with the other literatures[17,24,26].

4-Concerning the echolucent halo sign surrounding the nodules, we found that none of the 5 malignant cases was surrounded by an intact halo (table VI). Only one malignant nodule showed a blurred incomplete halo.

Twelve patients had intact halo sign (table IX), all of them proved to be benign. Although Richard A. Propper et al concluded that the halo sign is not specific[35], however blurred halo can be regarded as a suspicious finding[24,26].

5-We found that the detection of thyroid calcifications by sonography is diagnostically valuable. Table 6 shows that 2 nodules out of the 5 malignant cases showed punctate calcification (40%). This finding is in accordance with the other literatures[28,36,37].

In all our cases (the total 233), we had only 2 nodules with punctate calcifications (microcalcifications), both proved to be malignant. This is an outstanding point especially when we notice this else where[24-26,28,36-40].

On the other hand, we have 17 nodules with coarse calcifications and 2 nodules with eggshell calcifications (table IX), all proved to be benign, consistent with other literatures that see peripheral coarse and eggshell calcifications are more frequently seen in benign nodules[17,31,41].

6-The presence of a comet tail artifact sign has been said to be a highly specific sign of a benign colloid nodule[31]. A. Ahuja et al documented its presence in 100 patients who underwent ultrasound examinations of the neck and thyroid, and they found none of the thyroid nodules showed any evidence of malignancy on repeated FNAC [42]. We had only one case (out of the 58 patients who underwent surgery) with comet tail sign proved to be benign (table IX). The cause of having just one case is attributed to the proper selection of the patients to surgery by suggesting the benignity of the nodules from the ultrasound appearances and confirmation by FNAC. This nodule was not the only one in our series of 233 patients. We had originally 9 cases with comet tail sign, from which only one case had been submitted to surgery, fulfilling the chief aim of our study to reduce the number of unnecessary operations.

7-Cervical lymph node enlargement was a significant clue to malignancy, in 2 out of the 5 cases, due to nodal metastasis (table VI). Solbiati L. et al considered cervical lymphadenopathy significant in directing attention toward malignant lesions and moreover in staging malignancy[2].

Table VI shows that 4 out of 5 malignant cases (80%) were papillary carcinomas.

This corroborates all the other literatures in regarding papillary carcinoma the most common thyroid malignancy. The fifth case was a lady with metastatic carcinoma. We could not find the primary tumor.

We did not perform FNAC for the 23 cases in the table III, as there was no suspicious finding of malignancy in the sonographic examination of the nodules. All having regular outline; 17 uncomplicated cysts & 6 hyperechoic nodules.

Analysis of Ultrasound-guided FNAB results: The sensitivity, specificity, and accuracy of US-FNAB in our study were 80%, 96% & 94% respectively. These percentages are almost similar to their corresponding in the other studies[43-45], except the sensitivity which was a bit low in our study. The cause of this relatively low sensitivity, in our study, is attributed to the limited number of the cases, as we had only 5 malignant nodules; we missed one of them by FNAB, thus reducing the sensitivity by 20%.

As we mentioned earlier we did US-FNAB for 210 cases. We obtained the histopathological proof of 58 cases. The remaining 152 cases were all benign by US-FNAB; hyperplastic adenomatous nodules, degenerated nodules, and hemorrhagic cysts. None of these 152 cases was adenoma. So we will discuss the results of those 58 cases that we got their histopathological proof.

The results of US-FNAB in our study were as follows: (tables IV & V)

Benign cytology	49	84.4%
Malignant cytology	3	5.1%
Suspicious cytology	1	1.7%
False-negative diagnosis	1	1.7%
False-positive diagnoses	2	3.4%
Nondiagnostic cytology	2	3.4%

Diagnostic cytology; an adequate specimen of good technical quality is considered diagnostic or satisfactory and may be "benign," "suspicious" or "malignant ". A satisfactory biopsy rate for US-FNA ranges from 80% to 95%[46-50]. Our satisfactory biopsy rate is 91.2%.

We have 1 false negative and 2 false positive results, accounting for 1.7% and 3.4% respectively, which are within the usual range of misdiagnoses mentioned elsewhere[49-52].

Interpretive or sampling errors account for false diagnoses[50,53-55]. In our study the cause of the only false negative case is mostly due to inadequate or improper sampling due to the small size of the nodule which was (15mm) (the first case of the table VI).

The two false positive results were due Hashimoto's thyroiditis, which is the most common cause of false-positive cytology[12].

The 2 nondiagnostic or inadequate specimens accounting for 3.4% of specimens is quite acceptable compared to the other literatures[49,50,52]. The explanation for inadequate sampling was mostly due to defect in our skill (in the beginning of the study), and the cystic components of the nodules[56-59].

Conclusion

Ultrasound can alter the clinical management of patients with nodular thyroid disease. It can show that a suspected nodule is not solitary but one of several nodules in a multinodular goitre, thus minimizing the likelihood of malignancy.

Although ultrasound can not reliably distinguish benign from malignant nodules, we think that sonography can be helpful in this differentiation.

There are certain sonographic criteria that suggest malignancy. These include microcalcification, irregular margins, and hypoechogenicity of the nodule. On the other hand, there are certain sonographic features that can aid in predicting the benign nature of a given nodule. These include hyper-echogenicity and cystic nature of the nodule, well-marginated nodules, coarse and eggshell calcifications, intact thin halo, and comet tail sign.

Although our series was restricted with a small number of patients, the results were in concordance with those of other more comprehensive series.

In addition, ultrasound can guide FNAB for more proper placement of the needle inside the nodule.

Regarding FNAB we think that the patient would be poorly served if all the nodules are biopsied, so we can suggest biopsy of those nodules with suspicious sonographic features.

Thus by ultrasound examination of thyroid gland and by proper selection of the patients for FNAB, we can reduce not only the number of thyroid surgery but the number of FNABs as well.

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