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The Value of Ultrasound and Color-Doppler Features in the Assessment of Single Solid Thyroid Nodule

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Abstract

Background The use of ultrasound (US) in the assessment of thyroid disease has greatly increased the detection of small thyroid nodules unrecognized at clinical examination.

Objective To determine the accuracy of the diagnosis of the nature of solitary thyroid nodule by ultrasound in comparison with histopathological findings and to correlate the different sonographic and color-Doppler (CFD) findings with the results of histopathology of resected nodules.

Methods The nodule size, echogenicity, presence/absence of calcification, lesion margins and vascular pattern of 63 patients with solitary thyroid nodule referred for US assessment).

Results Twenty four patients (38.1%) had malignant thyroid nodules and 39 patients (61.9%) had benign nodules as confirmed by histopathology. The large nodules show benign histopathological finding more than the small nodules (no significant difference; 56.5% vs. 25.4%, respectively). Histologically-confirmed malignant lesions show hypoechoic appearance and calcification more than benign nodules. The Malignant lesions presented more frequently than did benign nodules as solid hypoechoic appearance and irregular or blurred margins (52.2% *vs.* 47.8%;), and intranodular vascular pattern with calcification (63.3% *vs.* 36.4%) and the sensitivity and specificity by ultrasound in the evaluation of these nodules will be more and have highly diagnostic accuracy (58.3%, 79.49%, 71.5% respectively) in comparison to the former feature (50%, 71.79%, 63.5% respectively).

Conclusion We conclude that the typical appearance of nodules in thyroid carcinoma is irregular hypoechoic mass with internal vascularity and calcifications. Uncommon appearances of carcinoma include hyperechoic texture, intrinsic hypovascularity, and sharp regular contours. Uncommon sonographic features were found to occur more often than expected.

Keywords Thyroid nodule, ultrasound, color Doppler

Introduction

The thyroid gland is an endocrine gland; this means that it manufactures hormones that are released into the bloodstream, which then act as messengers to affect cells and tissues in other parts of the body [(1)] The use of US in the assessment of thyroid disease has greatly increased the detection of small thyroid nodules unrecognized at clinical examination [(2).]

Thyroid nodules are common, but thyroid cancer is rare. Palpable nodules (usually >1.5 cm) are found in approximately 5% of the population. The prevalence of non-palpable nodules is even higher, occurring in an estimated 40% to 50% of the population. In contrast, the American Cancer Society estimated that there were only 19,500 new cases of thyroid cancer in 2001, representing 1.5% of all new cancers [(3)]. During the past decade, the use of high-resolution sonography has resulted in high rates of detection of thyroid nodules, but character-ization of nodules as either benign or malignant remains problematic because of considerable overlap in sonographic features [(4)].

Ultrasonography is often the first imaging modality employed to evaluate a thyroid nodule since it is readily accessible, inexpensive, and noninvasive, and it requires no radiation exposure. Ultrasonography is effective at delineating intrathyroidal architecture, distingui-shing cystic from solid lesions, determining if a nodule is solitary or part of a multinodular gland, and accurately locating and measuring a nodule [(5)]. It has the added advantage of demonstrating any associated lymphadenopathy in the para-tracheal region, the most commonly involved lymph node region for metastasis [(6)].

The first use of thyroid ultrasonography was more than 30 years ago to differentiate solid and cystic thyroid lesions [(7)]. Ultrasonography relies on the emission of high-frequency sound waves that are reflected as they pass through tissue of various impedances. The current technology of high-resolution ultra-sonography uses sound frequencies between 7.5 and 14 MHz, allowing visualization of solid or cystic nodules as small as 2 mm. With improvements in technology, high-resolution ultrasonographic equipment has become more affordable and available so that many endocrinologists are now well trained in its applications and use office-based equipment for evaluation of thyroid nodules [(7)].

Our aim is determine the accuracy of the diagnosis of solitary thyroid nodule with ultrasonographic findings in comparison with histological finding and to correlate the sonographic ultrasound (US) and color-Doppler (CFD) findings with the results of histopathology of resected nodules to establish:

1) The relative importance of US features as risk factors of malignancy; and

2) A cost-effective management of thyroid nodules.

Methods

From January 2011 to May 2011, sixty three patients (from 20 to 70 yr old, mean age: 38.2±14.7 year; (males 17 and females 46), with solitary thyroid nodule were referred from US department in Baghdad Teaching Hospital to Baghdad hospital surgical center for further assessment.

Ultrasound investigations used an ultra-sonographic scanner (Philips HD11) equipped with a 7.5-10 MHz linear transducer for morphological studies 4.5-7 MHz for color flow Doppler evaluation. The CFD examinations were performed with biplanar scanning. Examinations were conducted and recorded by two skilled sonographers according to a standard procedure; the amplifier gain was adjusted in each case at a level to block the appearance of random color noise.

The following ultrasound parameters were assessed in all nodules:

- Nodule diameter (maximum diameter as evaluated by sagittal and transverse scans)
- echogenicity (iso-, hyper- or hypoechoic)
- presence/absence of calcification
- lesion margins: well-defined or blurred
- vascular pattern (along the maximum diameter of the nodule:

Type 0, absence of flow signals

Type 1, vascular flow in peripheral position

Type 2, intranodular flow with multiple vascular images.

All cases were confirmed pathologically by FNA, thyroidectomy, or both.

Adequate cytological material was classified as benign (colloid nodules, lymphocytic thyroiditis, cystic goiters), malignant (papillary carcinoma, medullary carcinoma, anaplastic carcinoma) or suspicious (including follicular or Hurthle cell neoplasms). Cases with benign cytology (or repeated inadequate smears) underwent clinical and biocmeical control; to rule out overlooked malignancies. All patients with suspicious or malignant cytology underwent surgery

Statistical Analysis: Clinical, ultrasound, cytological and histological findings were separately recorded and blind-processed for statistical evaluation. Comparison of frequency distributions used the $\chi//^2$ test. Univariate and multivariate (logistic regression analysis) with 95% confidence interval were calculated to assess the relationships between ultrasound criteria and histological outcomes.

The diagnostic value of ultrasound criteria was also assessed in terms of sensitivity, specificity, likelihood ratio, positive/negative predictive value and efficiency. The relative risk of malignancy was evaluated by logistic regression analysis. The significance level was set at *P* less than 0.05.

Overall, 63 nodules were examined by US, of which 25 (39.7%) were <1 cm in diameter, and 38 (60.3%) were >1 cm in diameter. After the assessment of sonographic features, patients were referred thus, there were a total of 24 thyroid nodules representing carcinoma. Patients with treated thyroid disease without surgery were excluded from this study.

Those patients complaining from hyper-thyroidism have increase in thyroid function test (increase in T4 and/or increase T3) with decrease TSH, Each patient underwent a physical examination have a characteristic feature which elicited in table 1.

Table 1. Characteristic feature of patient with thyroid nodules and laboratory finding

Patients		Benign N = 39	Malignant N = 24
Laboratory investigation	T3	1.6662±0.482	1.284±0.292
	T4	87.85±21.81	78.9±17.12
	TSH	2.88±0.11	4.17±1.9
Age		39.48±15.05	36.33±14.20

Results

Sixty three patients (from 20 to 70 year old, mean age: 38.2±14.7 year; (46 females and 17 males) with solitary solid thyroid nodule underwent US / CDI examination for evaluation

Ultrasound investigations

The sonographic features of the nodules are given in Table 2. The solitary thyroid nodule was identified and sonographically characterized in each patients, which show that there is no significant difference between groups of small nodules and large nodules in the sonographic features (p<0.05).

Table 2. Sonographic features of the nodules

Sonographic Finding		Small nodule <1cm N= 25	Large nodule ≥1cm N = 38	Total
Echoic	Hyper	4 (6.3%)	7 (11.1%)	11 (17.5%)
	Iso	7 (11.1)	11 (17.5%)	18 (28.6)
	Hypo	14 (22.2%)	20 (31.7%)	34 (54%
Calcification	No	12 (19%)	19 (30.2%)	25 (49.2%)
	Yes	13 (20.6%)	19 (30.2%)	38 (50.2%)
Margin	Define	14 (22.2%)	17 (27%)	31 (49.2%)
	Blurred	11 (17.5%)	21 (33.3%)	32 (50.8)
Vascularity	type 0	5 (7.9%)	9 (14.3%)	14 (22.2%)
	type1	5 (7.9%)	9 (14.3%)	14 (22.2%)
	type2	15 (23.8%)	20 (31.7%)	35 (55.6%)

Histological features

Twenty four patients (38.1%) were histologically confirmed to have malignant nodule. The remaining 39 had benign nodules (61.9%). The prevalence of malignancy was lower in small vs. large nodules (14.0% vs. 23.8%, $p < 0.05$). However, the benign histopathological finding were more common in large than in small nodules also but there is no significant difference (56.5% vs. 25.4% respectively, $p > 0.05$).

Ultrasound finding and histological features:

The relationships between ultrasound findings and histological features show that hypoechoic appearance was more common in histologically-confirmed malignant lesions than in benign nodules but without significant difference (54.2% vs. 53.8%)

calcifications were more common in histologically-confirmed malignant lesions than in benign nodules (70.8% vs. 38.7%; 0.13: p < 0.05; OR 2.1, 95% CI 1.8-2.3), as were blurred margins (66.7% vs. 41%; 0.42: p < 0.05; OR 7.1, 95%CI 6.6-7.6), and highly significant difference in central vascularity type 2 (62.5% vs. 25.6%; 0.007: p < 0.01; OR 3.2, 95% CI 3.1–3.4) in malignant lesion versus benign one (Figures 1-4).

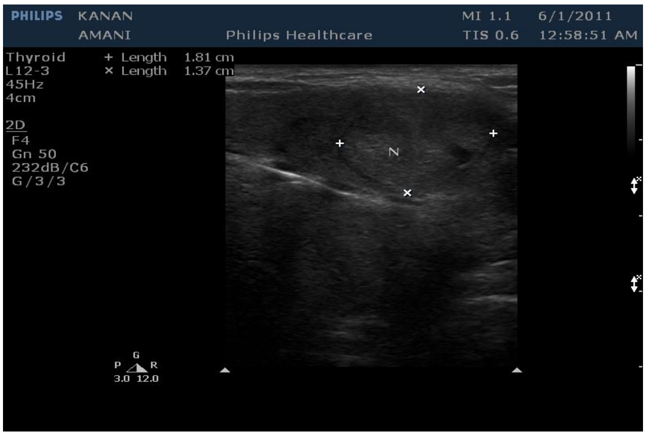

Figure 1. Longitudinal sonogram of a typical hypoechoic, well-defined, round lesion with a thyroid adenoma

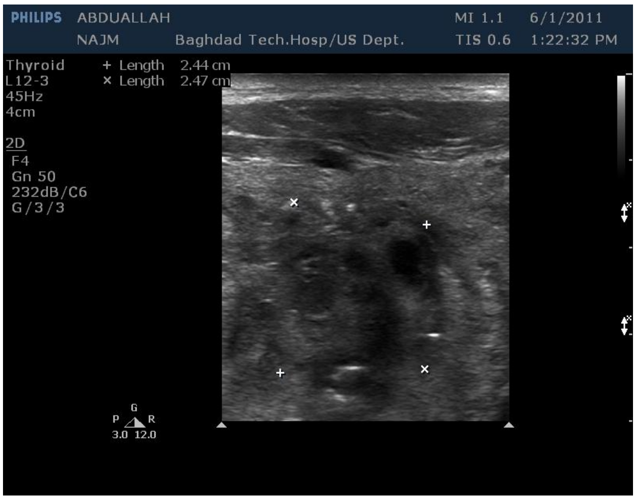

Figure 2. Longitudinal sonogram of a papillary carcinoma with coarse calcifications.

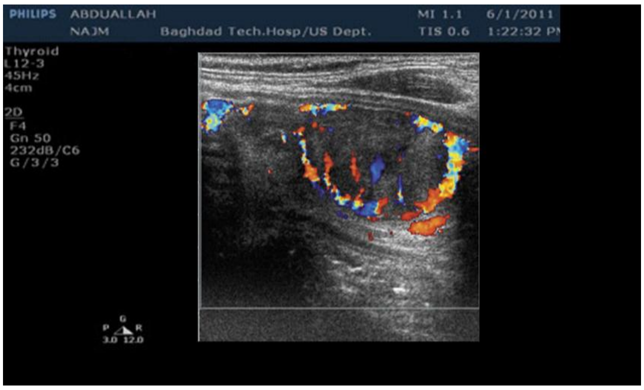

Figure 3. Showing peripheral vascularity in a thyroid nodule on Color Doppler

Figure 4. Showing central vascularity in a thyroid nodule on Color Doppler

Ultrasound finding and nodule malignancy:
Table 3 shows the sensitivity and specificity of ultrasound in the evaluation of malignant thyroid nodules and this show that central vascularity will be more specific and highly diagnostic accuracy (48.7%, 53.97%, respectively).

Table 3 the predictive value of ultrasound for detection of malignant thyroid nodules

Finding	Sensitivity	Specificity	PPV	NPV	LR	Diagnostic accuracy
Size ≥ 10mm	66.7%	41.1%	41.1%	66.6%	1.13	50.79%
Hypoechoic	54.2%	46.2%	38.2%	62.1%	1.01	49.2%
Calcification	66.7%	48.46%	40%	65.2%	1.08	49.21%
Blurred margin	67.1%	42.2%	39.5%	65.7%	1.21	50.8%
Vascularity type 2	62.5%	48.72%	42.9%	67.8%	1.22	53.97%

PPV: positive predictive value, NPV: negative predictive value, LR: likelihood ratio

In Table 4 the malignant nodules presented more frequently than did benign nodules as a solid hypoechoic appearance and irregular or blurred margins (52.2% *vs.* 47.8%), and intranodular vascular pattern with calcification (63.3% *vs.* 36.4%) and there sensitivity and specificity by ultrasound in the evaluation of these nodules will be more, and have highly diagnostic accuracy (58.3%, 79.49%, 71.5% respectively) in comparison to the former features (50%, 71.79%, 63.5%, respectively).

Table 4 the predictive value of ultrasound for detection of malignant thyroid nodules with combination of feature.

Finding	Sensitivity	Specificity	PPV	NPV	LR	Diagnostic accuracy
Calcification + Vascularity type 2	58.33%	79.4%	63.6%	75.6%	2.84	71.43%
Hypoechoic + Blurred margin	50%	71.79%	52.2%	70%	1.77	63.5%

PPV: positive predictive value, NPV: negative predictive value, LR: likelihood ratio

Discussion

The use of US in the assessment of thyroid disease has greatly increased the detection of small thyroid nodules unrecognized at clinical examination [(2)]. Thyroid nodules are shown by US to be present in 30-50% of the population [(8)]. Although most thyroid “incidentalomas” are benign, approximately 5% to 6.5% may be malignant [(9)]. In our study we concentrate on the finding of Grey scale, color and power Doppler of thyroid nodule and exclude other associated findings like cervical lymph-adenopathy.

Value of US and CFD findings as predictors of malignancy

US findings are important in predicting malignancy in non-palpable lesions. Although previous reports have denied that US findings have a predictive role, in our series sensitivity and specificity analysis confirmed that irregular or blurred nodular margins, an intranodular vascular pattern and microcalcifications were closely linked to neoplastic lesions [(10)]. On the other hand, a hypoechoic appearance or the presences of small lesions were not independent risk factors for malignancy in nonpalpable thyroid nodules.

The presence of calcifications and internal vascularity presented a higher specificity for malignancy (79%) than the findings of hypoechoic and irregular margins (71%) but the predictive value of calcifications and internodal vascularity was blunted by their low sensitivity (58%). Our results also confirm that thyroid cancer tends to be hypervascular. Most commonly, we found a pattern of intrinsic hypervascularity (62.5%) within the malignant nodule rather than perinodular flow (16.7%). Although the perinodular flow pattern or “color halo sign” is a less common pattern of vascularity, our findings suggest that it occurs twice as often as previously thought [11]. Although the hypovascular intrinsic flow pattern was uncommon (20.8%), no lesions were found to be completely avascular. This result differs somewhat from the recent findings of Frates et al [12] because their series included 2 malignant nodules with no detectible intrinsic flow. However, their methods involved only color Doppler sonography, whereas in our series, both color Doppler sonography and power Doppler sonography were used. It is possible that the greater sensitivity to low flow of power Doppler sonography enabled us to detect even very weak signals in hypovascular nodules that might have appeared avascular on color Doppler sonography. Apart from its value in isolation, vascularity assessment was particularly useful in combination with other gray scale features. There is almost unanimous agreement that the presence of calcifications within a nodule is associated with thyroid cancer. Recently, two retrospective studies with 799 and 1475 nodules, respectively, have suggested that this is the only ultrasonographic finding predicting histological malignancy [13,14]. Our data also indicate that intermodal vascularity with intrinsic calcification is the strongest criterion for cancer (2.84, 71.5%). Blurred margins, hypoechoic pattern and size ≥10mm have also been associated with malignant lesions in some (but not all) investigations [14] our results confirm the predictive value of these features, with a stronger association for hypoechoic and blurred margins.

In conclusion, the present study showed that the typical appearance of thyroid carcinoma is irregular hypoechoic mass with internal vascularity and calcifications. Uncommon appearances of carcinoma include hyperechoic texture, intrinsic hypovascularity, and sharp regular contours. Uncommon sonographic features were found to occur more often than expected. Finally, a cost-effective approach to the use of sonographic examination with specific ultrasound patterns (internal vascularity, calcifications, blurred margins and hypoechoic appearance) appear to be useful indicators.

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