Role of sonographic features in predicting the malignant potential of thyroid nodules

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Abstract

However, while thyroid nodules are common, thyroid malignancy is relatively rare, constituting about 1% of all malignancies. The main point of the approach of the thyroid nodule is the detection of the malignant nodules and deciding for the surgical treatment. Ultrasonography (US) plays a crucial role in the diagnostic management of thyroid nodules. The aim was to assess the reliability of using hypoechoic, solid and ill-defined margin as independent predictors for the identification of malignant thyroid nodules on US. We retrospectively analysed the three suspicious US features of malignancy for 145 patients with 255 thyroid nodules who underwent thyroid resection. We used histological results as gold standard reference test. Of the 255 surgical resected nodules; hypoechoic nodules had a sensitivity of 66.7%, and positive predictive value (PPV) of 8.7%. Solid nodules had a sensitivity of 33.3% and PPV of 3.7%. Ill-defined margins nodules had a sensitivity of 66.7% and PPV of 6.9% in predicting malignancy. The present study adds further evidence on the poor PPV in our results, indicated, that individual US features are not reliable used as independent predictors for the identification of malignant potential thyroid nodules on US.

Key words: Thyroid ultrasound. Thyroid nodules. Thyroid malignancy

Introduction

Thyroid nodules are common in clinical practice [2, 3, 17, 21, 23, 28]. Their clinical importance is primarily related to the need to exclude a thyroid malignancy [6, 21, 22, 28]. The risk of malignancy is similar for solitary nodules and multinodular goiters [18]. The overall risk of malignancy in a thyroid nodule is 5 – 15% [1, 3, 5, 6, 16, 21, 23 – 25, 28]. It is important to diagnose thyroid cancer at an early stage, because it may reduce the risk of disease recurrence and possible mortality [2].

US is an important diagnostic tool in predicting thyroid malignancy and selecting thyroid nodules that should be evaluated by fine needle aspiration cytology (FNAC) [2, 3, 22 – 24]. Thus, preoperative neck US has a role in surgical planning [23]. It is safe, non-invasive and cost effective diagnostic tool for preoperative assessment of patients with thyroid nodules to help the surgeon in the management of these nodules [1, 4, 8, 13, 14, 16, 25]. The purpose of our study was to evaluate the reliability of using the US features, such as hypoechoic, solid and ill-defined margin, in predicting thyroid malignancy in our clinical practice.

Methods

This study is a retrospective carried out at three main hospitals; Al-Gamhouria Modern General Hospital, Basuheeb Military General Hospital and 22 May Hospital in Aden city, Yemen, for two years (2014 and 2016). We reviewed the three suspicious US features of malignancy for 255 nodules in 145 patients. We wanted to test the hypothesis that preoperative these three US features were independent predictors of malignancy.

The criteria for these three US features that we used in this study are based on previous studies [3, 5, 13, 14, 23 – 25]. Thyroid nodule is defined as a discrete lesion within the normal thyroid parenchyma [3, 5, 23, 24]. Hypoechoic nodule is defined as lower echogenicity (darker) when compared to the surrounded thyroid parenchyma or the adjacent strap muscles [3, 13, 14, 24, 25]. Solid nodule is defined as no obvious cystic component or cystic component accounting for ≤ 10%

of the nodule volume [3, 5, 24]. Ill-defined margin nodule as is defined as poorly demarcated margin which cannot be obviously differentiated from adjacent thyroid tissue [3, 5, 13, 24]. According to these definitions, sonographically, the nodules were assessed on the basis of hypoechoic, solid and ill-defined margin US features were considered malignant. Nodule size was recorded as the largest of the three dimensions: length, width, and depth. We looked in each report for these three features that matched our definitions.

All patients underwent surgery for the suspicion of malignancy; information on patient demographics, US characteristics, FNAC and final histology of the nodules were collated. All the cases of thyroiditis were excluded. We considered histopathological diagnosis of resected thyroid gland tissue after surgery to be the gold standard reference test.

Statistical Analysis

The US diagnosis was compared with cytology reports and the histological diagnosis. The sensitivity, specificity, PPV and diagnostic accuracy of US were calculated based on combination of those three US features that were exhibited in 115 thyroid nodules. Each US feature was also compared with its pathology results. Outcomes of interest were the sensitivity and PPV of each US feature of thyroid nodules. The sensitivity, specificity and PPV for each feature were calculated independently in predicting malignancy.

The data were analysed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Baseline continuous data (age and tumor diameter [nodule size]) were expressed in mean ± standard deviation (SD) with confidence interval (95% CI), and categorical data were expressed as percentages. Univariate associations between the presence of malignancy and discrete variables were evaluated using Pearson Chi – Square test (χ^2). Independent sample Student's t – test was used to compare between categorical and continuous variables. $P \leq 0.05$ was considered statistically significant.

Results

A total of 145 patients with 255 nodules were eligible for the study. Of the 255 nodules, 15 (5.9%) were malignant and 240 (94.1%) were benign. There were 15 (10.3%) male and 130 (89.7%) female patients. The mean age of patients was significantly higher in the malignant nodules, compared with the benign nodules (45.66 ± 10.63 years; 95% CI, 39.77 – 51.55 versus (vs.) 37.11 ± 15.87 years; 95% CI, 34.36 – 39.86; P = **0.000**). The malignant nodules had a significantly larger nodule size (mean, 4.23 ± 2.81 cm; 95% CI, 2.67 – 5.79) than the benign nodules (mean, 1.61 ± 1.88 cm; 95% CI, 1.28 – 1.94) (P = **0.000**).

Table 1: Comparison of patients demographics and sonographic characteristics

Characteristic	Histological diagnosis		P – value
	Malignant n = 15 (%)	Benign n = 240 (%)	
Male	5 (3.4)	10 (6.9)	**0.002***
Female	10 (6.9)	120 (82.8)	
Mean age (yr)	45.66 ± 10.63	37.11± 15.87	**0.000***
Nodule size (cm)	4.23 ± 2.81	1.61 ± 1.88	**0.000***
Hypoechoic	10 (8.7)	105 (91.3)	**0.000***
Solid	5 (3.7)	130 (96.3)	**0.008***
Ill defined	10 (6.9)	135 (93.1)	0.072
*Significant p – value <0.01			

Of the 115 malignant nodules diagnosed by US; 5 nodules were cytological confirmed as malignant. The diagnostic parameters of US are summarized in Table (2).

Table 2: Comparison of sonographic of with cytology

	Cytological diagnosis			
		Malignant (+)	Benign (-)	Total
US	Malignant (+)	5	110	115
	Benign (-)	0	140	140
Total		5	250	255
Sensitivity: 100%(5/5) Specificity: 56% (140/250) Positive predictive value: 4.3% (5/115) Accuracy: 56.9% (5+140/225)				

Of the 255 surgical resected nodules, 115 nodules were diagnosed as malignant on US; final histological diagnosis was proved malignancy in 10 nodules vs. 5, out of 140 nodules, were diagnosis as benign on US. All of the 15 malignant nodules were confirmed at pathology as papillary carcinoma. In comparison with histopathological results, US had a sensitivity of 66.7%, specificity of 56.3%, PPV 8.7% and an accuracy of 56.9% in predicting malignancy.

Table 3: Comparison of sonographic of with histopathology

	Histological diagnosis			
		Malignant (+)	Benign (-)	Total
US	Malignant (+)	10	105	115
	Benign (-)	5	135	140
Total		15	240	255
Sensitivity: 66.7% (10/15) Specificity: 56.3% (135/240) Positive predictive value: 8.7% (10/115) Accuracy: 56.9% (10+135/255)				

Each US characteristic and its corresponding pathology results are presented in Table (4). Of the 255 surgical resected nodules, hypoechoic was found in 10/15 malignancies and in 105/240 benign nodules. Of the 115 nodules that were hypoechoic, 8.7% (10/115) were malignant vs. 91.3% (105/115) were benign ($P = $ **0.000**). Hypoechoic nodules had a sensitivity of 66.7%, specificity of 56.3%, and PPV of 8.7% in predicting malignancy. Solid was found in 5/15 malignancies and in 130/240 benign nodules. Of the 135 nodules that were solid, 3.7% (5/135) were malignant vs. 96.3% (130/135) were benign ($P = $ **0.000**). Solid nodules had a sensitivity of 33.3%, specificity of 45.8% and PPV of 3.7% in predicting malignancy. Ill-defined margin was found in 10/15 malignancies and in 135/240 benign nodules. Of the 145 nodules that were ill-defined margins, 6.9% (10/145) were malignant vs. 93.1% (135/145) were benign ($P = $ **0.000**). Ill-defined margins nodules had a sensitivity of 66.7%, specificity of 43.8% and PPV of 6.9% in predicting malignancy.

Table 4: Value of each US features as independent predictors of malignancy

The US nodule features	Sensitivity	Specificity	PPV
Hypoechoic	66.7%	56.3%	8.7%
Solid	33.3%	45.8%	3.7%
Ill-defined margin	66.7%	43.8%	6.9%

Table 5: In summary, combination data from literature with present study

The US nodule features	Studies	Sensitivity	specificity	PPV
Hypoechoic	Present study	66.7%	56.3%	8.7%
	Literature	26.5% – 87.1%	43.4 – 94.3%	11.4 – 68.4%
Solid	Present study	33.3%	45.8%	3.7%
	Literature	69% – 75%	52.5 – 55.9%	15.6 – 27%
Ill-defined margin	Present study	66.7%	43.8%	6.9%
	Literature	17.4% – 77.5%	38.9 – 85%	9.3 – 60%

In contrast to the literature, our results showed lower PPV.

Discussion

Thyroid nodules constitute a diagnostic challenge mainly because of the need to exclude thyroid malignancy [21]. US was first used to diagnose thyroid nodules in 1967 by Fujimoto [21, 23]. The high-resolution US is recommended as the best first-line diagnostic tool in the evaluation of thyroid nodules [10]. US has been widely used to differentiate benign from malignant nodules [1, 14, 24].

This article provides an important analysis in the effort to refine the three of US features using in diagnosis of thyroid malignant nodules. In our study, the malignancy rate in thyroid nodules was 5.9%. In the literature, the malignancy rate in thyroid nodules is reported in various series as 5 – 15% [4, 5, 15, 19, 20, 24, 25], our results confirmed this series in the literature.

In our study, US was able to correctly identify 10 out of 15 malignancies, and 135 out of 240 benign nodules. The diagnostic yield of US for malignant thyroid nodule, including sensitivity, specificity, PPV and accuracy, were 66.7%, 56.3%, 8.7% and 56.9% respectively. According to the literature, the diagnostic yield of US has different values ranging from 20% to 96% for sensitivity, 59% – 100% for specificity, 15 – 100% for PPV and 59 – 94% for accuracy [4 – 6, 11, 13, 16, 26, 27]. Our results concur with currently data in the literature for sensitivity and nearly similar to data in the literature for specificity and accuracy.

In evaluating thyroid nodules, we analysed three individual US characteristics of nodules in predicting malignancy included hypoechogenecity, solid component and ill-defined margins. We compared these characteristics to their respective pathology.

Although most malignancies tend to be hypoechoic, benign nodules may be hypoechoic too [21]. Therefore, many thyroid cancers would be missed if only the hypoechoic nodules underwent FNAC [2, 3]. In our study, 8.7% of malignant nodules were hypoechoic, compared with 91.3% of benign nodules. Hypoechoic nodules had a sensitivity of 66.7%, specificity of 56.3% and PPV of 8.7% in predicting malignancy. In the literature, the hypoechoic nodules had various values ranging from 26.5% to 87.1% for sensitivity, 43.4 – 94.3% for specificity and 11.4 – 68.4% for PPV [1, 4, 9, 11, 13, 14, 20, 24]. Our findings agree with the currently data in the literature for sensitivity and specificity. In contrast to the literature, our results showed lower PPV.

Thyroid malignant nodules are most commonly solid or nearly entirely solid and are more likely to be solid than benign nodules [10, 14, 24]. In our study, 3.7% of malignant nodules were solid, compared with 96.3% of benign nodules. Solid nodules had a sensitivity of 33.3%, specificity of 45.8% and PPV of 3.7% in predicting malignancy. In the literature, the solid nodules had various values ranging from 69% to 75% for sensitivity, 52.5 – 55.9% for specificity and 15.6 – 27% for PPV [1, 4, 8, 9, 14, 24, 25]. In contrast to the literature, our results showed lower values for sensitivity, specificity and PPV respectively.

When more than 50% of the margin of a thyroid nodule is not clearly defined, it is considered as poorly defined [3, 24]. In fact, malignant nodules tend to have ill-defined margins due to the infiltration of the surrounding thyroidal parenchyma [23, 24]. Therefore, irregular margins are finding highly suggestive of malignancy [1, 3, 23]. Unfortunately, this finding is also reported in benign conditions such as thyroiditis [4, 8, 14, 22, 25] or in some benign thyroid nodules incompletely encapsulated that can merge with normal tissue [23, 24]. In our study, 6.9% of

malignant nodules were ill-defined margins, compared with 93.1% of benign nodules. Ill-defined margins nodules had a sensitivity of 66.7%, specificity of 43.8% and PPV of 6.9% in predicting malignancy. In the literature, the ill-defined margins nodules had various values ranging from 17.4% to 77.5% for sensitivity, 38.9 – 85% for specificity and 9.3 – 60% for PPV [1, 4, 7, 9, 12, 13, 20, 22, 24]. Our results agree with the currently data in the literature for sensitivity and specificity.

In our study, a hypoechoic, ill-defined margins and solid nodules had very low PPV indicating that many of the positive results from this testing procedure are false positives. These findings make a hypoechoic, solid and ill-defined margins as a poor reliable and single predictors of malignancy in a thyroid nodule on US in our study. Our findings support previous study results [1, 4, 5, 8, 14, 25]. Thus it will be necessary to follow up any positive result with a more reliable test (Histopathology) to obtain a more accurate assessment as to whether cancer is presented.

The literature reveals great variability in the findings of studies. First of all, US is an observer – dependent method. Interobserver variability are reported, particularly on descriptions of echogenicity and margins features of thyroid nodules [3]. Second, the difference can be explained by the fact that they considered presence of even one US criterion suggestive of malignancy is categorized as malignant nodule. Third, likely due to the differing methodologies.

Although US features utility in predicting malignancy has caused profound changes in the management of thyroid nodules. Finally, in the literature , there is consensus on no single US feature or combinations of features are adequately sensitive to identify all malignant nodules [7 – 17, 19 – 28]. Thus, the goal of management should be to avoid extensive and costly evaluations in most patients with benign disease without missing the minority of patients who have thyroid cancer.

To our knowledge, our study is the first to report on three specific US characteristics of thyroid nodule malignancy that have been published to date in Aden –Yemen. The strength of our study was that the US examinations were performed by the same radiologist, which reduced diagnostic variability. All the results of US features in this study were compared with the gold standard criterion (histology). Our study is primarily limited by its retrospective nature.

Conclusions

In spite of thyroid US can be helpful in the differentiation of benign from malignant lesions. The fact that no US features were pathognomonic for malignancy. In this study, we have found that a hypoechoic and ill-defined margins nodules had moderate sensitivity while solid nodules had low sensitivity. All these features had very low PPV in predicting malignancy on US. Thus, it should not be used as a reliable sole predictors for the identification of malignant potential thyroid nodules in our clinical practice. The diagnosis of thyroid cancer is a major obstacle that needs to be overcome in the future. We emphasized that careful analysis of any features is imperative to identify the thyroid cancer.

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دور الصفات المُميَزة في صور الموجات فوق صوتية في إمكانية التنبؤ بالأورام الخبيثة لعُقَد الغدة الدرقية

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الملخص

إن الغاية الرئيسية من إثارة الاهتمام بعُقَد الغدة الدرقية هي كَشْف العُقَيْدات ذوات الأورام الخبيثة وأتخاذ القرار الحاسم بشأن المعالجة الجراحية. إن الموجات فوق صوتية تقوم بدور حاسم في الإدارة التشخيصية للعُقَيْدات الدرقية. كان الهدف أن تُقَيَم الثِقَة باستعمال صفات الصدى الأقل، والبِنْية الصلبة، والحد الصعب تعينه كمُتنبئات مُستقلة لتميز العُقَيْدات الدرقية ذوات الأورام الخبيثة في صور الموجات فوق صوتية. حللنا الثلاث الصفات المُميَزة لخُبث عُقَيْدات الغدة الدرقية في صور الموجات فوق صوتية بمنهج استرجاعي لبيانات 145من المرضى بـ255 عُقَدة درقية الذين خضعوا لاستئصال الغدة الدرقية. استعملنا نتائج فحص البِنْية النسيجية للعُقَد المُسْتأصلة كقاعدة اختبار مرجعية. من العُقَد المُسْتأصلة جراحياً لـ255 عُقَدة درقية ؛ العُقَيْدات ذوات صدى أقل في صور الموجات فوق صوتية كان لديها حساسية بنسبة 66.7% و قيمة تنبؤية إيجابية بنسبة 8.7% . بينما العُقَيْدات ذوات بِنْية صلبة في صور الموجات فوق صوتية كان لديها حساسية بنسبة 33.3% و قيمة تنبؤية إيجابية بنسبة 3.7%. أما العُقَيْدات ذوات حد صعب تعينه في صور الموجات فوق صوتية كان لديها حساسية بنسبة 66.7% و قيمة تنبؤية إيجابية بنسبة 6.9% بالتنبؤ بالأورام الخبيثة لعُقَيْدات الغدة الدرقية في صور الموجات فوق صوتية. ضئيل القيم التنبؤية الإيجابية برهان يُشير بأن الثلاث الصفات المُميَزة في صور الموجات فوق صوتية لا يُعَوّل على استعملها كمُتنبئات مُستقلة لتميز أورام العُقَد الدرقية الخبيثة المحتملة.

الكلمات المفتاحية: الموجات فوق صوتية للغدة الدرقية. العُقَيْدات الدرقية. ورم الغدة الدرقية الخبيث.