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Characterization of malignant solid thyroid nodules by Ultrasound and Doppler

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Abstract: *This is a prospective, consecutive study of thyroid patients referred for ultrasound for the period of 2012 to 2014 m at King Abdulaziz University hospital.*

Problem of the study lies in the interest or inadequate research that have been made about the role of ultrasound imaging in monitoring and predicted differentiate benign from malignant thyroid nodule and lack of diagnosis to see which should be subjected to histopathological examination and any of them need to medical follow up only.

Importance of the study is to take advantage of the use of ultrasound system plasticity in description Thyroid disease monitoring predicted characteristics that indicate the presence of slag between thyroids nodules among patients in the study sample and comparing the results of science high aspiration needle cells and results of histology.

Study aimed to take advantage of the characteristics of the ultrasound description Thyroid disease and take advantage of the elastography ultrasound to distinguish and identify and evaluate thyroid nodule. The study monitored a sample of 100 patients. Out of 100 nodules in100 patient examined by B-mode Ultrasound and color flow doppler (CFD), 29 (29%) presented inadequate cytological specimens and were excluded from the study (table 17).The remaining 71(71%) , histology diagnosed 11(15%) as malignant (MN) and 60(85%) as benign nodules (BN). On Ultrasound, 7 nodules were diagnosed as malignant (MN) and 74 as benign nodules (BN), with sensitivity of 55%, specificity of 98%, a positive predictive value of 85%, a negative predictive value of 92% and the accuracy of 91%.

50 patients from the total 100 patients were also examined by ultrasound elastography. Final diagnoses were obtained from fine needle aspiration. Out of 50patients 28 patients were excluded due to insufficient diagnosis in histology .From the remaining 22 nodule elastography showed four malignant nodules and 18 were benign. Sensitivity and specificity of the Ultrasound elastography for thyroid cancer diagnosis were 80% (4/5) and 100% (17/17), respectively. The positive and negative predictive values were 100% (4/4) and 94% (17/18), respectively. The accuracy of the technique was 95%.

I. Introduction

Ultrasonography (US) has become the imaging modality of choice for diagnosing different thyroid diseases. One of the commonest thyroid problems is thyroid nodules. They are found in 4%–8% of adults by palpation, in 10%–41% by US examination [1, 2] and in 50% by histo-pathologic examination at autopsy [3, 4, 5]. It is known that the prevalence of thyroid nodules increases with age [5]. Although thyroid nodules are commonly encountered problem in medicine, however, most of them are benign and the incidence of malignancy is low, about 3-7% [6, 7]. The continuous advancement of high resolution US machines has resulted in discovery of a large number of obscured, non palpable, tiny thyroid nodules [8]. Fine needle aspiration biopsy (FNAB) is frequently requested for suspicious thyroid nodules to exclude underling malignancy. Diagnostic accuracy of FNAB increases when guided by US. This ensures that the sample is obtained from the specific nodule in question and allows direction of the needle into the solid portions of partially cystic nodules to avoid inefficient sample, which will improve the diagnostic accuracy [9, 10]. Since the late 1990s, several studies have been conducted to investigate the relation between certain US features of thyroid nodules and malignancy [5, 11, 12]. These studies show persistent limitation of specificity and sensitivity of certain ultrasound features in the prediction of malignancy [13]. Some authors [14, 15] support a changed approach of recognition of specific patterns rather than individual US features in characterizing benign and malignant nodules that warrants biopsy.
Many studies have been published in which the US ability to predict whether a thyroid nodule is benign or malignant was assessed [16, 17, 8, 18, 19, 20, 21, 22, 23, 24, 25] There are certain criteria in the US differentiation of benign and malignant thyroid nodules, however, there is also some overlap in their appearances[5]. For that reason, FNAB and cytopathologic evaluation of a thyroid nodule are usually asked for before a patient undergoes surgical resection for a suspicious thyroid malignancy [5].unexpectedly, the large size of the nodule is not in favour of malignancy. The possibility of a thyroid nodule to be malignant has been shown to be the same whether it is large or small on US basis [17.*8, 19, 22]*. Several US features have been

found to be associated with an increased risk of thyroid malignancy ,including completely or premoninantly solid consistency, hypoechoic texture, irregular and ill defined margins, absent halo sign, presence of calcifications, and intranodule abnormal vascularity. However, no US feature has both a high sensitivity and a high positive predictive value for thyroid cancer. The sensitivities, specificities, and negative and positive predictive values for these criteria are extremely variable from study to study [5] Color Doppler US has also been studied as a diagnostic tool for prediction of thyroid malignancy. Although color Doppler US finding of abnormal central blood flow within the nodule appears to increase the chance that a nodule is malignant, however, it cannot be used to prove or exclude malignancy with a high degree of confidence [5]. Solid or predominantly solid nodules have a higher risk of malignancy than do mixed or predominantly cystic nodules. cystic nodules have a very low possibility of being malignant. Nodules with mixed composition have an average risk of malignancy. US greatly help localizing the solid component of mixed nodules during FNAB [5].

The relative ease and safety of FNAB compared with surgery and the increased frequency and quality of imaging studies has resulted in more detection of thyroid nodules which is referred to as an epidemic of thyroid nodules by some authors [6, 26]. For many reasons, it is not practicable to biopsy every thyroid nodule discovered with ultrasound. Reasons for limiting thyroid biopsy include the small percentage of expected malignant nodules, the small number of cases of thyroid cancer in which early diagnosis may actually have an effect, the economic and community costs, , the patient anxiety for the possibility of having thyroid malignancy and the load on radiology machines and staff. so, reliable guidelines for selecting nodules that need and that don't need biopsy have become essential [13].

The aim of this study is to evaluate the sensitivity and specificity of US and Doppler in predicting malignancy of solid thyroid nodules that warrants biopsy.

II. Patients and methods

Patients:

Prospective hospital-based study was done after obtaining ethical approval from the medical research ethical committee. The study included 100 patients with thyroid nodules referred to the Ultrasound unit at the diagnostic radiology department, at a university hospital between February, 2012 and October, 2012. The patients were 87females and 13 males ranging in age from 19 - 80 years with the mean age is 49.5 years. The exclusion criteria included; diffuse thyroid diseases and purely cystic nodules.

Ultrasound technique:

After obtaining verbal consent from patients,Ultrasound examination was done by an expert sonographer and radiologist using high-frequency linear array transducer (5 to 12 MHz) with spatial digital iU22 Philips compounded B-mode, color and power Doppler US.

Images of each lobe were obtained in transverse and longitudinal planes. The size of the thyroid gland was measured. Thyroid nodules were evaluated regarding their location, size, echogenicity, margin, halo sign and the presence of calcification. Doppler application was done to detect any abnormal peripheral or central blood flow within the thyroid nodules.

Image interpretation:

Thyroid nodules were classified into benign or malignant based on US and Doppler criteria by an expert radiologist.

Fine Needle Aspiration biopsy:

FNA biopsy could be done for only 71 cases of suspicious thyroid nodules by expert radiologists at the Diagnostic Radiology department. Written consent was obtained from the patient prior to biopsy. "Fine" or "thin" (22- to 27-gauge) needles; most commonly 25-gauge needle were used under strict aseptic conditions. Aspirate was sent for histopathology study at the main laboratory of the hospital. Results of FNAB were correlated with those of US & Doppler. Twenty-nine patients were either missed for biopsy, refused biopsy or the sample of biopsy was insufficient for histopathologic analysis.

Data analysis :

Demographic patients data including their age and sex associated with detailed US & Doppler criteria of the thyroid nodules were collected and correlated with histopathologic results of cases subjected to FNAB. All these data were statistically analyzed using SPSS 16 program. Data results in number and percentage were described. The sensitivity, specificity, positive predictive value, and negative predictive value were defined for each individual sonographic feature of benign or malignant nodules. The P value was considered to be significant if it was <0.05.

III. Results :

Ultrasound criteria of benignity or malignancy included, internal nodule echogenicity, halo sign, microcalcification within the nodule, nodule shape (taller than wide), margin and peripheral or intranodular vascularity relative to the rest of the thyroid gland.

Our results showed the superior detection of thyroid nodules in females more than in males (87% and 13% respectively).

Figure 1showed the age group distribution of thyroid nodules, where the highest percentage was in the age of 45-55 years (38%).

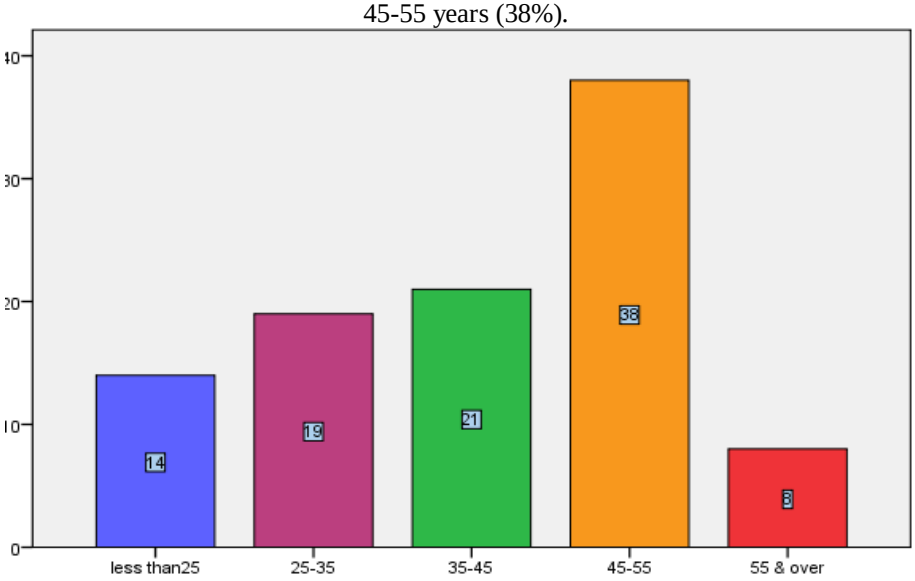

Figure 1: Distribution of thyroid nodules among different ages of the study population

Results of 71 patients subjected to FNAB were correlated with those of US characterization of thyroid nodules. Significant individual US criteria for detection of malignancy (with the p value < 0.05) included; hypoechogenicity (figure 2) with the sensitivity and specificity of hypoechogenicity to malignancy was 56% and 94% respectively, absent halo sign (sensitivity and specificity were 0% and 94% respectively), presence of intranodularmicrocalcification (figure 3) (sensitivity and specificity were 13% and 98% respectively), height to width ratio > 1 (sensitivity 63% and specificity 65% respectively), presence of intranodular abnormal blood flow (figure 4) showed 57% sensitivity and 95% specificity, blurred margin showed 9% sensitivity and 100% specificity for malignancy. The highest positive predictive value was for hypoechogenicity and nodular shape (94% and 90% respectively). Table 1 showed the details of US features for benign and malignant lesions.

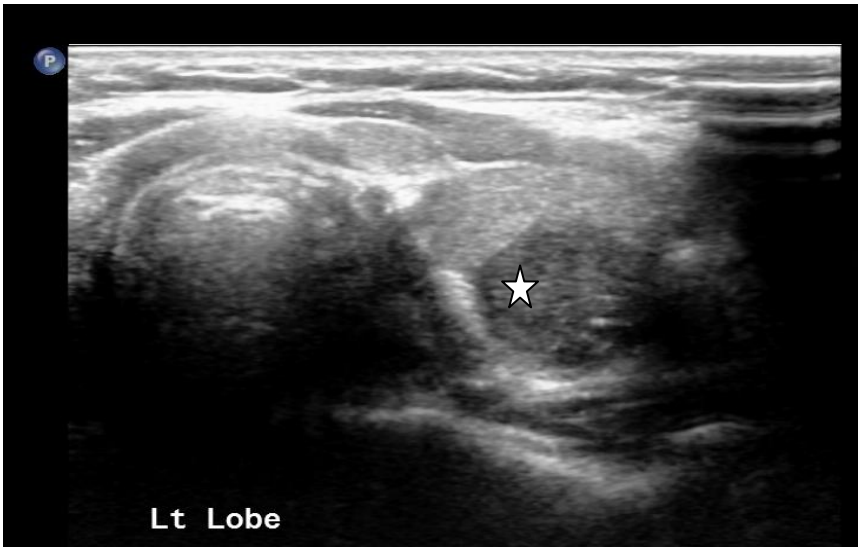

Figure 2: axial US of the thyroid gland shows a well definedhypoechoic nodule of the left lobe (star).FNAB revealedfollicular carcinoma.

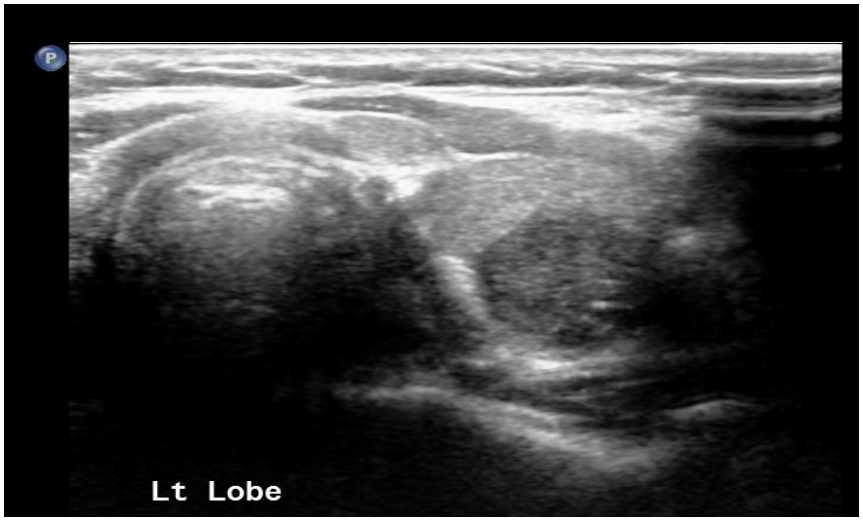

Figure 3: US of the thyroid gland shows lobulated nodule with foci of microcalcification (Papillary carcinoma).

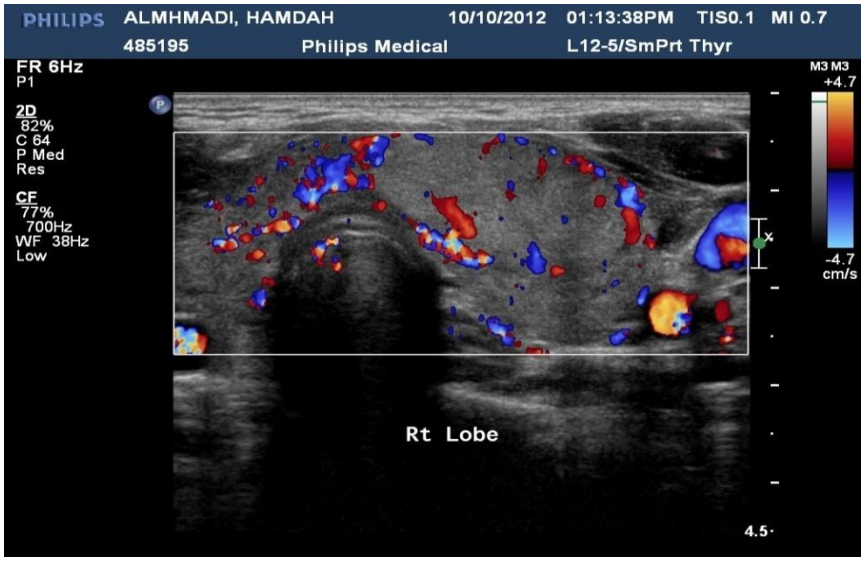

Figure 4: Doppler US of the thyroid gland shows a large solid mass with intranodular abnormal vascularity. FNAB proved follicular carcinoma.

Table 1: US criteria of benign and malignant thyroid nodules in correlation with FNAB

Feature	Benign, n (n = 84)	Malignant n (n = 16)	Sensitivity %	Specificity %	PPV %	NPV %	P
Hypoechogenicity	5	11	56	94	64	94	0.000
Halo Sign	5	0	0	94	0	85	0.000
microcalcifications	1	3	13	98	67	86	0.015
Intranodular blood flow	9	11	57	95	64	89	0.000
*H/T ≥1	10	55	63	65	27	90	0.007
Blurred margins	0	1	9	100	100	85	0.021

Comparing the overall criteria of US for detection of malignancy gathered together to FNAB showed increased its sensitivity and specificity to 55% of 98% respectively with a negative predictive value of 92% and positive predictive value of 85% as shown in **table 2**

		F.N.A Result		Sensitivity%	Specificity%	PPV %	NPV%	P
		M	B					
U.S. Result	M	6	1	55	98	85	92	0.000
	B	5	59					
Total		11	60					

Table 2: correlation of US and FNAB findings for malignant and benign lesions.

IV. Discussion:

There are many US criteria for differentiating benign from malignant thyroid nodules. Such differentiation is important for selecting patients for further FNAB in cases with suspicious of malignancy, or to avoid unnecessary biopsy for those with benign criteria. It has been found in literature that no single criteria is sure of malignancy, and combination of the known criteria of malignancy gives higher sensitivity and specificity than depending on single individual one [13,5,27]. There are multiple US features that are highly suggestive of malignancy in a thyroid nodule including presence of calcifications, hypoechogenicity, irregular margins, absence of a halo sign , predominantly solid composition, and intranodule abnormal vascularity. However, the sensitivities, specificities, and negative and positive predictive values for these criteria are extremely variable from study to study, and no US feature has both a high sensitivity and a high positive predictive value for thyroid malignancy [5]. It has been shown that the possibility of cancer in a thyroid nodule has been shown to be the same regardless of the size of the nodule [17, 8, 19,22].The nodule size and multiplicity have not been shown to affect the likelihood of malignancy [8, 17, 12, 28]. In the current study, the sensitivity and specificity of hypoechogenicity to malignancy was 56% and 94% respectively. Out of the 16 cases with hypoechoic nodules,11 of them proved to be malignant by FNAB. These results are matching with the results of some authors [8, 17, 12, 29], where they found that marked hypoechogenicity has been a characteristic that is suggestive of malignancy. Studying the margin of a nodule is an important part of the examination. A hypoechoic or anechoic rim encircling a nodule, known as the halo sign is highly predictive of benignity [8, 17, 12, 29]. However, this sign may be absent in more than 50% of benign nodules and present in up to 20% of malignant nodules [11].In our study, all nodules that show halo sign on US are proved to be benign on FNAB. Halo sign is not a criteria of any malignant nodule in our study population. Blurred margin is an indicator to malignant lesions that invade the surrounding tissues. In the current study, blurred margin is a strong indicator of malignancy with 100% specificity. The presence of calcification within the nodule raises the probability of malignancy. Microcalcifications and macrocalifications in a solid nodule are associated with an approximately threefold and twofold increase in cancer risk respectively, as compared with predominantly solid nodules without calcifications [19].

The sensitivity and specificity of microclcification detected by US as a predictor to malignancy is 13% and 98% respectively. Out of the four nodules that show microcalcification by US, three were proved to be malignant and the remaining one is benign on FNAB. Supporting our results are those of [8], where the specificity of microcalcification to papillary carcinoma is 95% with a relatively low sensitivity 29%. in another study of[19] ,although microcalcifications carry low sensitivity 26.1%–59.1%, they show the highest positive predictive value (41.8%–94.2%) for malignancy. A shape that is taller than wide is highly suggestive of malignancy [8, 17, 12, 29]. In the current study, The ratio of the nodular height to width of > 1 is found in 55 malignant and only 10 benign nodules. Color Doppler US has also been evaluated as a diagnostic tool for

Predicting thyroid malignancy, where peripheral nodular flow is suggestive of a benign nodule, while flow predominantly in the central portion of the nodule is suggestive of malignancy. The results of these studies are controversial, with some reporting that Doppler US is helpful in differentiating benign from malignant lesions [8, 20] and others reporting that it did not improve diagnostic accuracy of thyroid nodules [21, 25]. In one study[29] central flow was seen in a higher percentage of malignant nodules than benign nodules (42% vs 14%). However, like other US features, color Doppler US cannot be used to diagnose or exclude malignancy with a high degree of confidence; rather, the color Doppler US finding of predominantly internal or central blood flow appears to increase the chance that a nodule is malignant[5].out of the 20 cases showing intranodular abnormal vasculature, 11 are malignant and 9 are benign on FNAB. intranodular abnormal blood vessels carry a 57% sensitivity and 95% specificity for malignancy.Putting the whole previous criteria together increases the likelihood of malignancy with confidence. Combining the hypoechogenicity, absent halo sign, intranodularmicrocalcification, increased height than width and presence of intranodule vascularity increase the sensitivity and specificity of US for malignant lesions to 55% and 98% respectively. As mentioned by some authors[8, 18] , the combination of features improves the positive predictive value of US to some extent. In particular, a predominantly solid nodule (<25% cystic) with microcalcifications has a 31.6% likelihood of being

cancer, as compared with a predominantly cystic nodule (>75% cystic) with no calcification, which has a 1.0% likelihood of being cancer [19].

In conclusion, US is the modality of choice in evaluation of thyroid nodules. No single criteria is sure of malignancy, however, combination of some criteria- in particular- hypoechogenicity, microclcification and intranodular vascularity increases the likelihood of malignancy that warrants biopsy.

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