Original Article

Significance of ultrasound features in predicting malignant solid thyroid nodules: Need for fine-needle aspiration

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Abstract

Objective: The purpose of this study was to provide sonographic and colour flow criteria helpful for differentiation between benign and malignant solid thyroid nodules.

Methods: This prospective study was carried out at Sindh Institute of Urology and Transplantation (SIUT), Karachi Pakistan from 01.05.07 to 31.12.08. Sonographic scans of 78 thyroid nodules in 66 patients were performed and characteristics of thyroid nodules that were studied included microcalcifications, an irregular or microlobulated margins, marked hypoechogenicity, a shape that was taller than it was wide and color flow pattern in Color Doppler ultrasound. The presence and absence of characteristics of nodules were classified as having positive or negative findings. If even one of these sonographic features was present, the nodule was classified as positive (malignant). If a nodule had none of the features described, it was classified as negative (benign). The final diagnosis of a lesion as benign (n= 53) or malignant (n= 25) was confirmed by fine needle aspiration biopsy, and patients who were proved to have benign lesions were followed-up for 6 months and malignant lesions which were proved on histopathology after FNA were subjected to surgery. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were then calculated on the basis of our proposed classification method.

Results: Among 78 solid thyroid nodules 35 lesions were classified as positive considering the sonographic characteristics and 23 of them were proved to be malignant on histopatology. Out of 43 lesions which were classified as negative, 2 were proved to be malignant. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy based on our sonographic classification method were 93.8%, 66%, 56.1%, 95.9%, and 74.8%, respectively.

Conclusion: Ultrasound is valuable for identifying many malignant or potentially malignant thyroid nodules. No single ultrasound criterion is reliable in differentiating all benign from malignant thyroid nodules, but many US features aid in predicting the benign or malignant nature of a given nodule. Fine-needle aspiration biopsy should be performed on thyroid nodules classified as positive, regardless of palpability (JPMA 60:848; 2010).

Introduction

Thyroid nodules occur with relatively high frequency in the general population with prevalence of 4-7% by palpation alone[1] and 13% to 67% by Sonographic evaluation.[1,2] However, less than 7% of thyroid nodules are malignant.[3,4] Imaging modality of choice for the investigation of thyroid nodules is High Resolution Ultrasound. Ultrasound is helpful in distinguishing malignant from benign thyroid nodules. Sonographic features of potentially malignant thyroid nodules include Microcalcifications, marked hypoechogenecity, irregular or microlobulated margins and intranodular central vascularity.[4] Although the individual ultrasonic features may be of limited value, but when multiple features appear in combination it is possible to make an accurate prediction and such nodules should be further assessed with FNA.[4-6]

Although the thyroid nodules are a common medical problem and the international literature is available but we have conducted this study so that the ultrasonic features of malignant thyroid nodules can be identified in our population. Most related local research that has been carried out at Jinnah Postgraduate Medical Centre by Dr Toor R[7] about the ultrasonic features of malignant thyroid nodules in grey scale imaging confirms and reassures our results. Color Doppler Ultrasound has become an established imaging technique for assessing thyroid nodules, and many international authors

have shown its ability to identify lesions with more probability of malignancy with good sensitivity and specificity.[8,9] Hence, in our study Color Doppler assessment of the solid thyroid nodules has also been carried out to assess its significance in predicting malignant thyroid nodules in the local population.

Patients and Methods

This prospective study was carried out at Sindh institute of Urology and Transplantation (SIUT), Karachi Pakistan from 01.05.07 to 31.12.08 and included 66 patients. 58 (87.9%) patients were females and 8 (12.1%) were males. Their ages ranged from 18-75 years.

These 66 patients had 78 solid thyroid nodules, fifty nine (89.4%) of them had single thyroid nodule while the remaining 7 (10.6%) patients had multiple solid nodules. Of the 78 nodules, 27 (34.6%) were non palpable when examined by an experienced surgeon, and they were discovered incidentally in patients subjected to US for non thyroid causes e.g. Carotid Doppler ultrasound or sonographic investigation of neck mass.

Only solid nodules were included in this study. Cystic and complex cystic lesions with solid components, previously diagnosed malignant nodules and toxic nodules were excluded from this study (local and general examination and thyroid hormonal analysis aided in excluding toxic nodule).

Clinical assessment of all patients in this study was carried out including history taking, general and local examination to exclude toxic and inflammatory goitre. Indirect laryngoscopic examination was done for all patients subjected to surgery.

Laboratory investigations which were carried out included thyroid function tests for all patients to exclude toxic nodule and routine pre-biopsy and preoperative laboratory investigations.

Grey scale Ultrasound and Color Doppler study were preformed with Toshiba Aplio-50 machine using 7.5 MHz linear high resolution probe. Sonographic characteristics suggesting malignancy were defined as microcalcifications, an irregular or microlobulated margins, marked hypoechogenecity, a shape that was taller than it was wide and intranodular vascularity in color Doppler study.

Micro-calcifications suggesting malignancy were defined as tiny, punctate hyperechoic foci which are 10- 100 μm sized, round- laminar crystalline calcific deposits, with or without acoustic shadows.[4] Peripheral eggshell-like or coarse calcifications were not considered malignant. Irregular or microlobulated margins were also considered to be malignant findings.[4,10] Microlobulation was defined as the presence of many small lobules on the surface of a nodule. Marked hypoechogenecity was defined as decreased echogenicity compared with the surrounding strap muscle and is considered to be feature of a malignant nodule.[3,4,10] Normally, the healthy thyroid gland shows homogeneous hyperechogenicity compared with the surrounding muscle. Because most thyroid nodules show hypoechogenicity when compared with the parenchyma of the thyroid, this comparison does not provide much useful information. The strap muscle is uniformly present in all patients; therefore, it was used as the comparative standard for the evaluation of the echogenicity of solid nodules. A nodule with a shape taller than wide was defined as being greater in its anteroposterior dimension than its transverse dimension was considered to be a positive finding for malignancy if any part of the nodule was more tall than wide.[4,11] Vascularity of each nodule was seen in color Doppler ultrasound and ranked from 0 - 4. Type 0 was defined as no visible flow, Type 1 as peripheral flow only, Type 2 as predominantly peripheral with some central flow, Type 3 as extensive internal flow with peripheral flow and Type 4 as central flow only.[8]

Nodules were prospectively classified as positive or negative. If one or more features suggestive of malignancy were present, the nodule was classified as positive. If a nodule had no suspicious features, it was classified as negative (benign).

Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated for individual sonographic characteristics.

After US examination, an US-guided fine-needle aspiration biopsy was performed for all 78 nodules in 66 patients. The aspirated material was evaluated by a cytopathologist. According to Gharib & Goellner,[12] Cytologic results were classified as benign, suspicious, or malignant. Patients with a benign cytodiagnosis had no features suggestive of or diagnostic for malignancy. Patients with a suspicious cytodiagnosis had specimens showing hypercellularity and a pattern suggestive of follicular neoplasms or atypical features suggestive of, but not diagnostic for, malignancy. Patients with a malignant cytodiagnosis had cytologic findings that indicated the presence of malignant cells consistent with thyroid carcinoma.

Among 78 solid thyroid nodules, 35 lesions were classified as positive considering the sonographic characteristics and 23 of them were proved to be malignant on FNA. Of 43 lesions which were classified as negative, 2 had atypical cells (suspicious for being malignant) after FNA evaluation.

Surgery (total thyroidectomy with lateral neck lymph node dissection) was performed for 25 nodules, 2 of them had atypical cells and were suspicious for being malignant and 23

nodules had malignant cytological evaluation after FNA. All these lesions were proved to be malignant on histopathological evaluation after surgery.

Fifty three nodules with benign cytological findings did not receive surgical treatment and were followed up for 6 months. They underwent repeated clinical and US examinations, and thyroid-stimulating hormone and thyroid hormone tests to evaluate nodule progression. During the observation period, none of these patients had any findings suspicious for malignancy.

Results

Among 66 patients, 78 solid thyroid nodules were evaluated. Fifty nine (89.4%) patients had single thyroid nodule while the remaining 7 (10.6%) patients had multiple solid nodules. Sonographic criteria of malignant nodules included microcalcifications, irregular or microlobulated margins, marked hypoechogenecity, nodule that is taller than wide, and intranodular color flow pattern in color Doppler ultrasound.

If one or more features suggestive of malignancy were

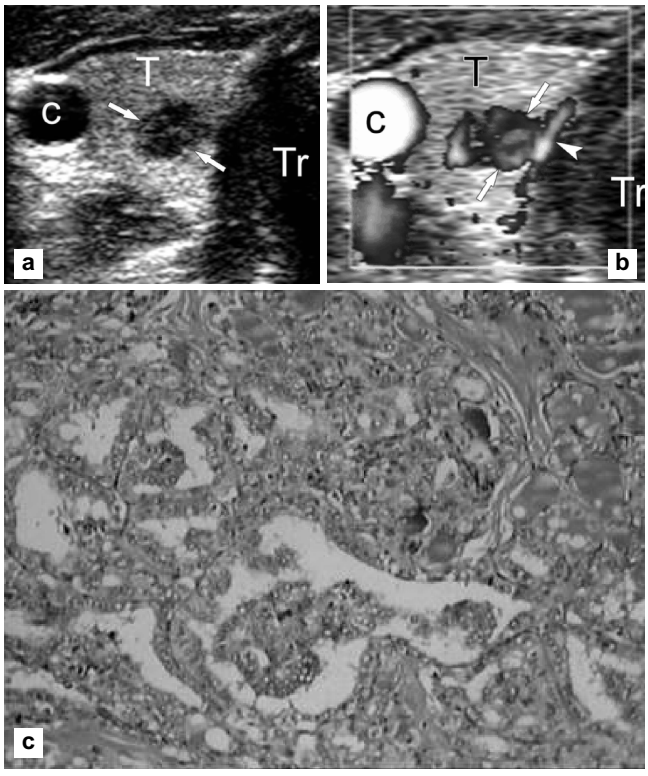

Figure-1: 45 years old female with incidentally discovered thyroid papillary carcinoma. (a) Grey-scale image shows 7-mm sized hypoechoic nodule (arrows) with irregular margins. Note microlobulations on medial aspect of the lesion. (b) Transverse power Doppler US of the same nodule (arrows) demonstrates noticeably increased intranodular vascularization (type 3). C = carotid artery, T = thyroid gland, Tr = trachea, arrowhead in b = inferior thyroid artery. (c) Histopathologic examination shows Papillary structures with thin fibrovascular cores covered by atypical epithelial cells. There is nuclear grooving and ground glass pattern. H&E. X 40.

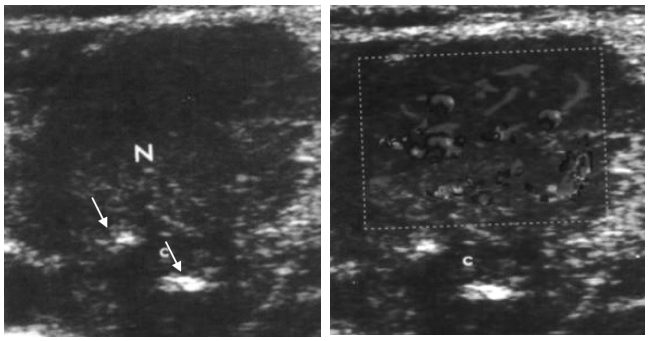

Figure-2: Sixty five years old female with papillary carcinoma right thyroid lobe. (a) Grey scale image shows microcalcifications (white arrows), markedly hypoechoic solid nodule (N) with irregular microlobulated margin on medial aspect of the nodule, more tall than wide. (b) Color power Doppler image shows intra-nodular flow signals (type 3).

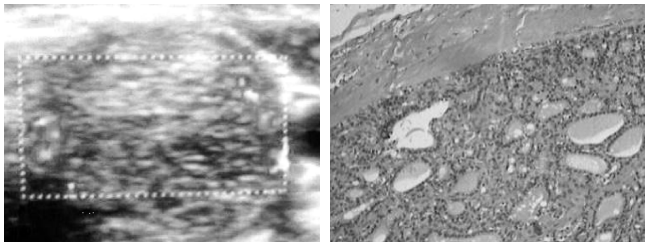

Figure-3: Male patient 35 years old with follicular adenoma left thyroid lobe. (a) Grey scale and color Doppler US shows an isoechoic, solid nodule with rounded shape and type 2 color flow signals (peri-nodular without intranodular flow signals). No microcalcifications. (b) Histopathological examination shows Capsulated tumor tissue with mostly large size follicles. The capsule is intact. H&E. X 40.

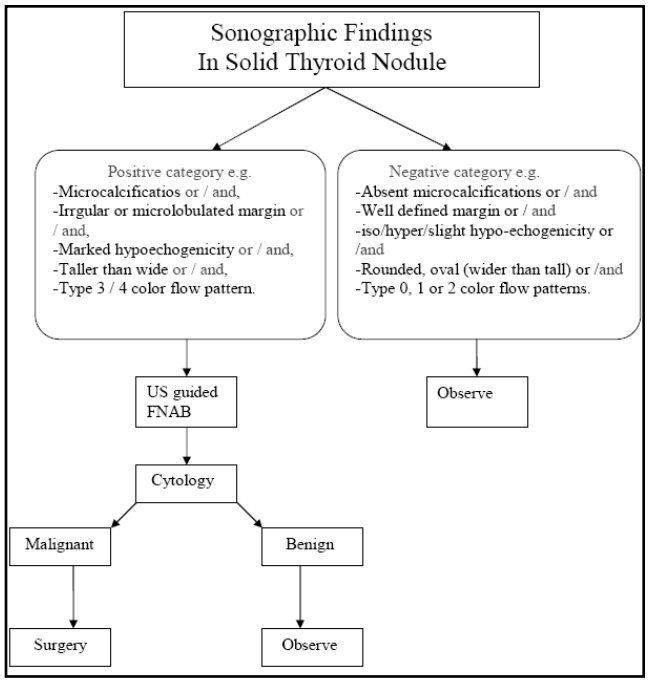

Figure-4: An algorithm for evaluation of solid thyroid nodules according to US characteristics of the nodule.

Table-1: Sonographic findings in malignant and benign thyroid nodules.

Sonographic Characteristics N=53	Malignant nodules N=25	Benign nodules (%)
Microcalcifications	14 (56%)	7 (13.2%)
Irregular or microlobulated margin	13 (52%)	14 (26.5%)
Marked hypoechogenicity	6 (24%)	3 (5.6%)
More tall than wide	8 (32%)	4 (7.5)
Type III color flow pattern	21 (84%)	5 (9.4%)

Table-2: Comparison of sonographic and final histologic findings.

Sonographic Category	Histopathologic Findings		
	Malignant	Benign	Total
Malignant	23	12	35
Benign	2	41	43
Total	25	53	78

present, the nodule was classified as positive. If a nodule had no suspicious features, it was classified as negative.

Color flow pattern of nodules on Doppler ultrasound study was ranked 0-4 (as described in methods) and according to that classification, 20 nodules had type 0 pattern, 14 nodules had type 1 pattern, 23 had type 2 pattern, 21 nodules had type 3 pattern, while none of patients had type 4 pattern (Figures-1,2,3).

Thirty five lesions were classified as positive considering the sonographic characteristics and 23 of them were proved to be malignant on FNA and later on histopatology after surgery (Figures-1,2). Of 43 lesions which were classified as negative, 2 had atypical cells (suspicious for being malignant) on FNA and after surgery were proved to be malignant.

Diagnoses of malignancy at histopathology included papillary carcinoma (24) and metastasis from carcinoma of the breast (1) while benign lesions included follicular adenoma (33) and simple nodule (20).

The sonographic findings in malignant and benign nodules are summarized in Table-1. The correlation of sonographic categorization with histopathologic findings is shown in Table-2, and Table-3 summarizes the diagnostic index for individual sonographic criteria of malignant nodules. Most malignant nodules had multiple sonographically suspicious findings.

In these 78 nodules, our sonographic classification method resulted in a sensitivity of 92% (23/25), specificity of 77.3% (41/53), positive predictive value of 65.7% (23/35), negative predictive value of 95.3% (41/43), and accuracy of 80.7% (63/78).

The accuracy of each sign was ranging from 66.7 to 88.4%, but the sensitivity was from 32% to 84.

Discussion

Many thyroid diseases present clinically with one or more thyroid nodules. Such nodules represent common clinical problems. Palpable thyroid nodules occur in 4 to 7% of population,[1] but nodules found incidentally on sonography suggest a prevalence of 13-67%.[1,2] Majority of thyroid nodules are asymptomatic.[13] Hence, incidental abnormalities of the thyroid gland are commonly encountered by the radiologist at the rate of 16% on cross-sectional study and 27% on sonography among imaging studies performed for other purposes.[14,15]

Table-3: Diagnostic Index for Individual Sonographic Criteria of Malignant Thyroid Nodules.

Sonographic Criteria	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Accuracy (%)
Microcalcification	14/25 (56)	46/53 (86.8)	14/21 (66.7)	46/57 (80.7)	60/78 (76.9)
Irregular or microlobulated	13/25 (52)	39/53 (73.6)	13/27 (48.1)	39/51 (76.5)	52/78 (66.7)
Marked hypoechogenicity	6/25 (24)	50/53 (94.3)	6/9 (66.7)	50/73 (68.5)	56/78 (71.7)
More tall than wide	8/25 (32)	49/53 (92.5)	8/12 (66.7)	49/66 (74.2)	57/78 (73)
Type III color flow pattern	21/25 (84)	48/53 (90.5)	21/26 (80.7)	48/76 (63.2)	69/78 (88.4)

The goal of conducting this study was to avoid extensive and costly evaluations in most patients with benign disease without missing the minority of patients who have thyroid carcinoma. Several studies have been performed to establish the ability of US to differentiate benign from malignant thyroid nodules and their results compared with FNA, thyroid ultrasound has the advantage of being a non invasive procedure and giving immediate information.[16] The aim of this study was to assess various ultrasound criteria including microcalcifications, marked hypoechogenicity, tall shape, irregular margins and intranodular pattern of color flow in predicting malignant nature of these lesions.

Calcifications occurring in thyroid nodules includes microcalcifications, coarse calcifications and peripheral calcifications. Thyroid microcalcifications are psammoma bodies which in ultrasound, appear as punctuate hyperechoic foci, usually without acoustic shadowing.[4] They are one of the most specific features of thyroid malignancy.[17] In our study its specificity is 86%, which correlates with other studies where it is stated as 85.8% to 95%[3,18] and positive predictive value is 66.7% in current study which is in agreement with other studies where it has been 4.8% to

94.2%.[6] Microcalcifications are found in 24% to 59% of all primary thyroid carcinomas,[3,4] most commonly in papillary thyroid carcinomas but their occurrence has been describes in follicular and anaplastic thyroid carcinomas as well as benign conditions such as follicular adenomas and Hashimoto's thyroiditis.[19] In contrast to microcalcifications, coarse and peripheral calcifications are commonly present in multinodular goiter.[4]

In our study, the presence of irregular or microlobulated margin was considered positive index for a malignant lesion that requires further evaluation although; it was about 52% sensitive and 66.7% accurate. The reported sensitivity of irregular margins ranges widely (53% to 89%).[18] Results of current study were lower than reported by Papini et al 2002.[10] The difference may be due to the fact that their study was on nonpalpable nodules only and other factor could be due to their larger patient sample size. 15%-59% of benign nodules may have poorly defined margins with micro or macrolobulations,[3,20] therefore unless frank invasion beyond capsule is demonstrated the ultrasound appearance of margins of thyroid nodule alone is an unreliable basis for determining malignancy or benignity.[4]

Hypoechogenecity in solid thyroid nodules was considered a finding suggestive of malignancies like carcinomas and lymphomas. However, 55% of benign nodules are also solid and hypoechoic.[4,10] In this study, it was attempted to differentiate markedly hypoechoic lesions from other hypoechoic lesions, and only markedly hypoechogenic lesions were considered a finding indicative of malignancy. In this study the specificity for detection of a malignancy in markedly hypoechoic solid nodule reaches 94%, but sensitivity is reduced to 24% and is described in other studies as well.[3,4,10]

A nodule shape taller than wide is regarded as a potentially useful ultrasound feature suggestive of malignancy,[4] signifying that the lesion is aggressive and is growing against the soft tissue planes. This feature has been described by Kim et al[11] and has high specificity for malignancy (93%), which is in agreement with this study (92.5%) although it is less sensitive (32%).

Color Doppler US is widely availalable and is more feasible to apply in our practice and has become an established imaging technique for assessing thyroid nodules, and many authors have shown its ability to identify lesions with more probability of malignancy with good sensitivity and specificity and has been proven to be statistically significant criteria when deciding for FNA and surgery.[8,9] In this study predominantly central color flow pattern in solid nodules is predictive of malignancy with 84% sensitivity and 90% specificity with 80% positive predictive value and 88% accuracy.

Researchers from Nagoya University (Japan)[21] have concluded that the use of Power Doppler imaging considerably improves the characterization of the intranodular flow and that it might assist in distinguishing between malignant and benign nodules. In most recent reviews there has been consensus that most differentiated thyroid carcinomas have exuberant central vascularization which is described as having chaotic and irregular pattern.[8,22]

This study confirms that grey scale Ultrasound features that are helpful in differentiating the malignant from benign lesions and this is further reassured by other studies conducted locally at Jinnah Postgraguate Medical Centre[7] but we found no single grey scale ultrasound criterion that could distinguish benign from malignant thyroid nodules with 100% reliability. However, there is almost unanimous agreement that the presence of microcalcifications within a nodule is associated with thyroid cancer among rest of the ultrasonic features intrinsic microcalcifications is the strongest criterion predicting malignancy.[23,24]

The combination of each individual grey scale sonographic criterion with type 3 or 4 color flow pattern will increase the specificity for malignancy but unfortunately, this gain in specificity occurred at the expense of sensitivity.

A proposed algorithm for management of solid thyroid nodules according to US and color flow pattern is shown in Figure-4.

Conclusion

Ultrasound is the most sensitive method for diagnosing intrathyroid lesions, and is valuable for identifying many malignant and potentially malignant thyroid nodules. Ultrasound features that are helpful in differentiating the two includes microcalcifications, irregular or microlobulated margins, marked hypoechogenecity, a lesion that is taller than wide, and intranodular vascularity within a solid thyroid nodule.

Despite clear identification, no single Ultrasound criterion is reliable in differentiating benign from malignant thyroid solid nodules, but many combined US features may aid in predicting the benign or malignant nature of a given nodule. However, the predictive value of these combinations increases at the expense of their sensitivity. FNAB should be performed for any solid nodule categorized as positive for malignancy, regardless of being palpable on nonpalpable.

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