Original Article

Comparison of the diagnostic performance of ultrasonography with fine-needle aspiration cytology in thyroid nodules

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Abstract

Objective: The aim of the study was to correlate the sonographic (ultrasound [US]) and color flow Doppler findings with the results of US-guided fine-needle aspiration biopsy.

Materials and Methods: This is a cross-sectional study conducted in the ultrasound suite of our hospital, South Western, Nigeria. It is a cross-sectional study on 110 adult patients with clinically palpable thyroid nodule(s) in our hospital. Sonographic scans of 110 thyroid nodules in 110 patients were performed, and characteristics of thyroid nodules that were studied included microcalcifications, an irregular or microlobulated margins, marked hypoechogenicity/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, respectively.

Results: Among 110 solid thyroid nodules, 23 lesions were classified as positive considering the sonographic characteristics and 9 of them were proved to be malignant on histopathology. Of 87 lesions which were classified as negative, none was proved to be malignant. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value based on our sonographic classification method were 100%, 86%, 36%, and 100%, respectively.

Conclusion: This study showed that ultrasound can be sensitive and specific for thyroid nodules but the PPV is low.

Keywords: Diagnostic performance, fine-needle aspiration cytology, thyroid nodules, ultrasonography

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INTRODUCTION

Thyroid nodules occur with relatively high frequency in the general population with prevalence of 4%–7% by palpation alone and 13%–67% by sonographic evaluation.[1,2] However, <7% of thyroid nodules are malignant.[3,4] Imaging modality of choice for the investigation of thyroid nodules is high resolution ultrasound. Ultrasonography is the modality of choice for initial characterization of a thyroid nodule.[5] Ultrasound is helpful in distinguishing malignant from benign thyroid nodules. Although thyroid nodules may be detected at computed tomography and magnetic resonance imaging, these modalities are not useful for characterization of a nodule.[6] Positron emission tomography may occasionally

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help identify thyroid nodules, but it is considered by some authors to have limited utility in differentiating benign from malignant lesions.[1,7,8]

Fine-needle aspiration biopsy (FNAB) is considered to be the most effective and reliable procedure for the diagnosis of malignant thyroid nodules.[9]

As thyroid nodules are shown by US to be present in 30%–50% of the population and fewer than 5.0%–6.5% of these are malignant,[10] US-guided fine-needle aspiration (FNA) has become increasingly popular.[11]

Sonographic features of potentially malignant thyroid nodules include microcalcifications, marked hypoechogenecity, irregular or microlobulated margins, taller than wide shape, and intranodular central vascularity.[1] Although the individual ultrasonic features may be of limited value, when multiple features appear in combination, it is possible to make an accurate prediction and such nodules should be further assessed with FNA.[1,12,13]

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.[14,15]

This study aimed at evaluating the various ultrasound criteria in thyroid nodules and comparing to FNA cytology (FNAC) diagnosis.

MATERIALS AND METHODS

This is a cross-sectional study that was approved by the Institutional Review Board on 110 consenting adults presenting with thyroid nodules.

Previously diagnosed malignant nodules and normal thyroids were excluded.

Clinical assessment of all patients in this study was carried out including history taking and local examination.

All studied participants had ultrasound examination using a high-resolution, 7.5–12 MHz, linear array transducer of Ultrasonix Sonix TOUCH ultrasound machine made in 2010 by Ultrasonic medical corporation in Canada for B-mode and color Doppler characteristics as well as FNAC.

For patients with multiple thyroid nodules, the nodule with the most suspicious sonographic features was evaluated and aspirated for cytology.

A careful evaluation of the following parameters was carried out on all lesions: echogenicity (Hyperechoic, isoechoic, hypoechoic or anechoic), echo structure (solid, spongiform, or cystic), margins (well defined or poorly defined) and presence or absence of hyperechoic spots (macrocalcifications or microcalcifications), shape (taller than wide or wider than tall), presence or absence of halo (thin or thick incomplete), and color flow pattern (peripheral, intranodal, and avascular).

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.

Nodules were prospectively classified as positive or negative based on previous studies.[16] 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).

After US examination, an US-guided fine-needle aspiration was performed for all evaluated 110 nodules.

Ultrasound-guided FNAB was performed by the pathologist using a 23-gauge needle with a free hand technique. For a partially cystic nodule, the biopsy sampling was directed to the solid portion of the nodule. In patients with more than one nodule, FNA of the suspicious nodule was retained.

Aspirate was smeared on slides and stained by May–Grunwald–Giemsa stain. The cytological analysis was performed by a single pathologist. Cytological material was defined as adequate when six or more thyroid cell clusters were obtained. Adequate cytological material was classified as benign, malignant, or suspicious.

Based on previous study, cytologic results were classified as benign, suspicious, or malignant.[9]

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.

Cytological variables consisted of malignant, benign, and suspicious cases.

Fisher's exact test was used to determine the association between categorical variables of interest and the dependent variable. Specificity, sensitivity, negative predictive value, and positive predictive value (PPV) of the ultrasound features were also determined. Level of statistical significance was set at <0.05.

RESULTS

The study population of 110 cases obtained comprised 103 females and 7 males with a female to male ratio of 14.7:1. The ages ranged from 22 to 71 years with a mean of 44.05 ± 11.79 years [Table 1]. The majority of the patients 79 (71.8%) had tertiary education. Only 4 (3.6%) had no formal education.

The sonographic findings in malignant and benign nodules are summarized in Table 2.

Most of the nodules 103 (93.6%) were wider than tall, isoechoic 59 (53.6%), mostly spongiform [Figure 1] 83 (75.5%), mostly well-defined 101 (91.8%) with thin surrounding halo 93 (92.1%). Calcification was present in 18 (16.4%) patients, of which 5 (27.8%) were macrocalcifications while 13 (72.2%) were microcalcifications [Figure 2]. Color flow was present in 84 (76.4%) nodules, of which 76 (69.1%) were peripheral while intranodal [Figure 3] were 8 (7.3%).

Among 110 thyroid nodules, 23 nodules were classified as positive considering the sonographic characteristics while 87 nodules were classified as negative as shown in Table 3.

At cytological evaluation, 101 lesions were benign (91.8%) and 9 were malignant (8.2%) as shown in Table 4.

The correlation of ultrasound categories with cytologic findings and the correlation of sonographic features with cytologic findings are shown in Tables 5 and 6, respectively.

Among 110 thyroid nodules, 23 lesions were classified as positive considering the sonographic characteristics and 9 of them were proved to be malignant on FNAC. Of 87 lesions which were classified as negative, none was malignant after FNAC.

Of the 9 confirmed by FNAC to be malignant, 6 had nodal involvement on ultrasound.

In these 110 nodules, our sonographic classification method resulted in a sensitivity of 100% (9/9), specificity of 86% (87/101), PPV of 39% (9/23), and negative predictive value of 100% (87/87). The sensitivity of each sign was ranging from 62% to 86%,

Table 1: Sociodemographic characteristics of participants studied

Variable	Frequency (%)
Age (years)	
≤25	5 (4.5)
26-35	22 (20.0)
36-45	36 (32.7)
46-55	30 (27.3)
>55	17 (15.5)
Mean±SD	44.05±11.79
Sex	
Male	7 (6.4)
Female	103 (93.6)
Height (m), mean±SD	1.61±0.08
Weight (kg), mean±SD	63.39±12.26
BMI (kg/m^2), mean±SD	26.18±4.85
Educational status	
None	4 (3.6)
Primary	5 (4.5)
Secondary	22 (20.0)
Tertiary	79 (71.8)
Tribe	
Yoruba	97 (88.2)
Igbo	12 (10.9)
Hausa	1 (0.9)

BMI - Body mass index; SD - Standard deviation

Table 2: Ultrasound features of thyroid nodules of participants

Features	Frequency (%)
Shape	
Wider than tall	103 (93.6)
Taller than wide	7 (6.4)
Internal content	
Cystic	12 (10.9)
Spongiform	83 (75.5)
Predominantly solid	15 (13.6)
Halo	
Present	101 (91.8)
Absent	9 (8.2)
Presence of halo (*n*=101)	
Thin halo	93 (92.1)
Thick incomplete halo	8 (7.9)
Margin	
Well defined	101 (91.8)
Poorly defined	9 (8.2)
Spiculated	0 (0.0)
Calcification	
Present	18 (16.4)
Absent	92 (83.6)
Present calcification	
Macrocalcification	5 (27.8)
Microcalcification	13 (72.2)
Echogenicity	
Hypoechoic	19 (17.3)
Isoechoic	59 (53.6)
Hyperechoic	20 (18.2)
Anechoic	12 (10.9)
Color flow	
Peripheral	76 (69.1)
Intranodal	8 (7.3)
Avascular	26 (23.6)

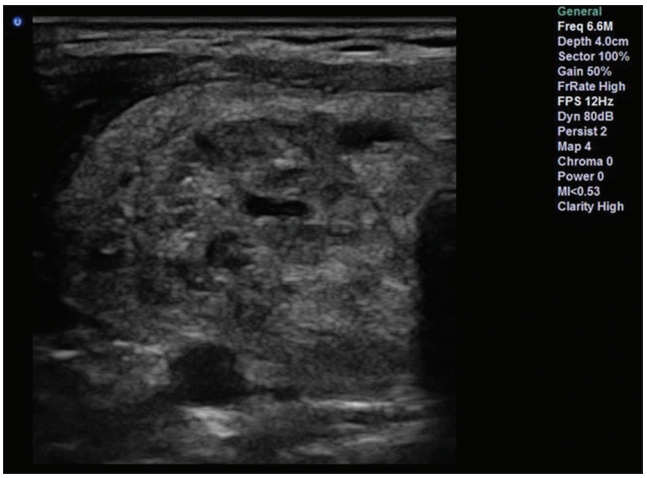

Figure 1: Transverse USS of the thyroid gland showing a huge fairly oval-shaped isoechoic nodule with mixed solid and cystic components (spongiform) which was confirmed to be benign with fine-needle aspiration cytology

Figure 2: Transverse USS of the thyroid gland showing a huge isoechoic nodule with both microcalcifications and macrocalcification which was confirmed to be malignant with fine-needle aspiration cytology

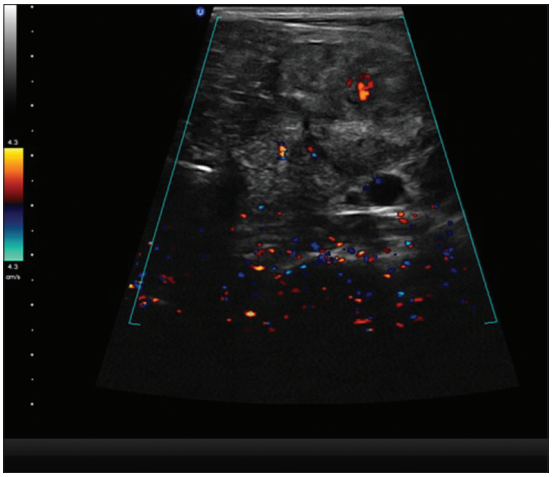

Figure 3: Transverse USS of the thyroid gland with color Doppler interrogation showing a lobulated, poorly defined, isoechoic nodule with intranodal flow and incomplete thick halo which was confirmed to be malignant with fine-needle aspiration cytology

Table 3: Categories of the thyroid nodules studied

Ultrasound	Frequency (%)
Negative	87 (79.1)
Positive	23 (20.9)

Table 4: Cytological findings in the thyroid samples studied

Cytological findings	Frequency (%)
Benign	101 (91.8)
Malignant	9 (8.2)

Table 5: Ultrasound categories and the cytological findings

Variable	Cytological findings	
	Benign (%)	Malignant (%)
Categories		
Negative (*n*=87)	87 (100)	0
Positive (*n*=23)	14 (60.8)	9 (39.1)

but the specificity was from 97% to 100%. These are illustrated in Table 7.

DISCUSSION

There are many USS criteria for differentiating benign from malignant thyroid nodules. Such differentiation is important for selecting patients for further FNAC in cases in which malignancy is suspected and to avoid unnecessary biopsy for those with benign criteria. It has been found in literature that no single criteria can predict malignancy, and combination of the known criteria of malignancy gives higher sensitivity and specificity than depending on single ultrasound feature.[8]

The female to male ratio of 14.7:1 in this study concurs with 10:1, 11.1, and 14.1 recorded for Port-Harcourt, Kano, and Enugu from Southern, North East, and South Eastern parts of Nigeria, respectively.[17-19] It however differs slightly with the reports from Lagos and Ife, both from Western Nigeria, which recorded ratio of 7:1 and 6:1, respectively,[20,21] as well as reports from the United States of America, Saudi Arabia, and Pakistan, which recorded female to male ratios of 7:1, 6.2:1, and 4.5:1, respectively.[22-24]

Ijomone *et al*.[17] gave reasons that the difference was probably due to geographical and socioeconomic variation in these areas; however, this reason is not in agreement with this work as this index study is also from Western part of Nigeria where it was claimed to have a relatively low female to male ratio.

The mean age of patients in this study was 44 years with a range of 22–71 years. The age group 36–45 had the highest prevalence of thyroid nodules 36 (32.7%). This is similar to the findings in other studies from Southern Nigeria where the majority of cases were found in the age group 30–39

Table 6: Correlation of the cytology findings with ultrasound features

Variable	Cytological finding		*P*
	Benign (%)	Malignant (%)	
Shape			
Wider than tall (*n*=103)	100 (97.0)	3 (3.0)	<0.001
Taller than wide (*n*=7)	1 (14.3)	6 (85.7)	
Internal content			
Cystic (*n*=12)	12 (100)	0	<0.001
Spongiform (*n*=83)	83 (100)	0	
Predominantly solid (*n*=15)	6 (40.0)	9 (60.0)	
Halo			
Thin halo (*n*=93)	90 (96.8)	3 (3.2)	<0.001
Thick incomplete halo (*n*=8)	2 (25.0)	6 (75.0)	
Margin			
Well defined (*n*=101)	99 (98.0)	2 (2.0)	<0.001
Poorly defined (*n*=9)	2 (22.2)	7 (77.8)	
Calcification			
Macrocalcification (*n*=5)	5 (100)	0	<0.001
Microcalcification (*n*=13)	5 (38.5)	8 (61.5)	
Echogenicity			
Hypoechoic (*n*=19)	13 (68.4)	6 (31.6)	0.001
Isoechoic (*n*=59)	56 (94.9)	3 (5.1)	
Hyperechoic (*n*=20)	20 (100)	0	
Anechoic (n=12)	12 (100)	0	
Color flow			
Peripheral (*n*=76)	75 (98.7)	1 (1.3)	<0.001
Intranodal (*n*=8)	2 (25.0)	6 (75.0)	
Avascular (*n*=26)	24 (92.3)	2 (7.7)	
Size, mean±SD (cm)	1.75±0.89	1.96±0.76	0.46
<1 (*n*=15)	15 (100)	0	0.61
≥1 (*n*=95)	86 (90.5)	9 (9.5)	
Lymph node involvement			
Present (*n*=8)	2 (25.0)	6 (75.0)	<0.01
Absent (*n*=102)	99 (97.1)	3 (2.9)	

SD - Standard deviation

Table 7: Sensitivity and specificity of ultrasound features

Ultrasound features	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Taller than wide	86	97	67	99
Thick incomplete halo	75	97	67	98
Poorly defined margin	78	98	78	98
Microcalcifications	62	100	100	50
Intranodular flow	67	98	75	97
Hypoechogenicity	67	87	32	97
Overall	100	86	36	100

PPV - Positive predictive value; NPV - Negative predictive value

from Lagos and 31–40 from Port-Harcourt.[20,25] Tsegaye and Ergete[26] found out that 85% of thyroid diseases were found in the age group 20–59. This shows that thyroid diseases are not common in extremes of age.

The incidence of malignant nodules was 8.2% in this study which is significantly lower than benign nodules; this is in agreement with findings by Abdulkareem *et al*.[20] and Anidi *et al*.[18] who got an incidence of 7% and 8.3%, respectively, although findings by Papini *et al*.,[27] Hegedüs *et al*.,[28] and Kunreuther *et al*.[29] however showed higher percentage of malignancy (9.2%–13.0%) which is slightly higher than the findings in this index study.

Calcifications occurring in thyroid nodules include microcalcifications, coarse calcifications, and peripheral calcifications. Thyroid microcalcifications are psammoma bodies which in ultrasound appear as punctuate hyperechoic foci; usually without acoustic shadowing.[1] The presence of microcalcification is one of the most specific features of thyroid malignancy.[30] In this study, its specificity is 100%, which is in agreement with other studies where it is stated as 85.8%–95%[8,31] and its PPV is 100% which is also in agreement with other studies where it has been 4.8%–94.2%.[13] The presence of poorly defined margin was considered a feature for a malignant nodule. In our study, it was about 78% sensitive and 98% specific. The reported sensitivity of poorly defined margins ranges widely (53%–89%).[31] Results of current study were similar with the one reported by Papini *et al*.[27] The difference in the range may be due to their larger patient sample size.

Since poorly defined margins may also be demonstrated in 15%–59% of benign nodules,[8,32] Hoang *et al*.[1] state that 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.

Hypoechogenicity in solid thyroid nodules was considered a finding suggestive of malignancies such as carcinomas and lymphomas. However, 55% of benign nodules are also solid and hypoechoic.[1,27] In this study, no attempt was made to differentiate markedly hypoechoic lesions from other hypoechoic lesions, and both were considered a finding indicative of malignancy. The specificity for detection of a malignancy in hypoechoic solid nodule is 87%, but sensitivity is 67% and is described in other studies as well.[1,8,27]

A nodule shape taller than wide is regarded as a potentially useful ultrasound feature suggestive of malignancy[1] signifying that the lesion is aggressive and is growing against the soft tissue planes. This feature has been described by Kim *et al*.[3] and has high specificity for malignancy (93%), which is in agreement with this study (97%) which also has high sensitivity value (86%). Color Doppler US 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 have been proven to be statistically significant criteria when deciding for FNA.[14,15] In this study, predominantly central color flow pattern in solid nodules is predictive of malignancy with 67% sensitivity and 98% specificity with 75% PPV and 97% negative predictive value. De Nicola *et al*.[14] and Cerbone

et al.[33] state that most thyroid carcinomas have exuberant central vascularization which is described as having chaotic and irregular pattern.

In this study, of the 101 nodules that showed halo sign, 93 had thin halo while 8 showed thick incomplete halo. Ninety-six percentage of the nodules with thin halo were proven to be benign while 75% (60) of nodules with thick incomplete halo were malignant. This was in agreement in previous studies of Papini *et al*.[27] in Italy, Kim *et al*.[3] in Korea, and Frates *et al*.[34] in USA where thin halo sign was found to be highly predictive of benignity. Papini *et al*.[27] found no benign nodule with thick incomplete halo.

This study confirms that gray scale ultrasound features are helpful in differentiating the malignant from benign lesions, but we found that there is no single gray scale ultrasound criterion that could distinguish benign from malignant thyroid nodules with 100% reliability. However, the presence of microcalcifications within a nodule is associated with thyroid cancer among the rest of the ultrasonic features which buttress the point of view of Cappelli *et al*.[35] and Lyshchik *et al*.[36] that intrinsic microcalcification is the strongest criterion predicting malignancy.

CONCLUSION

USS is highly sensitive than specific for diagnosis of thyroid masses in this study. However, its PPV is very low.

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Conflicts of interest
There are no conflicts of interest.

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