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Characterization of Benign and Malignant Thyroid Nodules using high frequency Ultrasound

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High frequency ultrasound is one of the primary imaging modalities for diagnosis of thyroid nodules, unfortunately there is limitation of ultrasound in differentiating benign from malignant nodule, fine needle aspiration (FNA) is required to differentiate benign and malignant thyroid nodules. This was a prospective study conducted in King Fahad Specialist Hospital in Dammam (Kingdom Saudi Arabia), in the period from February 2020 to February 2021, the main aim of the study to characterize thyroid nodules using high frequency ultrasound and to correlate sonographic features with the FNA results. The data collected from 222 patients with clinically suspected thyroid nodule, after taken a written approval of protocol from research Centre (King Khalid Medical City-RC-KKMC)-King Fahad Specialist Hospital in Dammam; RAD0317, then verbal consent was taken from all patients, then analyzed by SPSS version 23. The study showed that thyroid nodules occur commonly in females 76.6%, on FNA results 51.4% are benign. On high frequency ultrasound the malignant nodules are mostly hypoechoic, wider than taller, with presence of macrocalcification, moderate or severe vascularity in Doppler interrogation, while benign nodules are commonly seen as hypoechoic or isoechoic, wider than taller, with no or macrocalcification and a vascular or with mild peripheral vascularity in Doppler. Strong significant difference was found in sonographic features for benign and malignant nodules, $P<0.01$ except for composition of nodule. The study concluded that there is strong significant difference in sonographic features of benign and malignant nodules except for composition of nodule.

Keywords: High frequency ultrasound; FNA; Nodule; Benign; Malignant; Doppler

INTRODUCTION

High frequency ultrasound imaging is one of most important imaging modalities for evaluation of thyroid gland and assessing abnormalities; in addition to that real time ultrasound helps to guide diagnostic and therapeutic procedures in thyroid diseases. The major limitation of ultrasound in thyroid imaging is that it cannot determine thyroid function, to evaluate thyroid function a thyroid function test or radioactive isotope uptake test is generally required. (Chaudhary and Bano, 2013)

The incidence and development of thyroid nodules correlate directly with age of the patient and is regarded as a part of normal maturation process of the thyroid gland. The incidence of thyroid nodules on ultrasound ranged from 50% to

70% which is consider very high. There is some overlapping between ultrasound appearance of benign and malignant nodules, certain USG features are helpful in differentiating the two; Solid appearance, hypo echoic, increased vascularity, micro calcifications, irregular margins, and the absence of a halo are features that have been consistently associated with malignancy, unfortunately ultrasound alone cannot reliably distinguish malignant and benign nodules (Bomeli, LeBeau and Ferris, 2010; Chaudhary and Bano, 2013). Ultrasound imaging studies and cytology from fine-needle aspiration are mainly used by the clinician to decide whether surgical excision of a thyroid nodule is warranted. (Bomeli, LeBeau and Ferris, 2010)

The purpose of this study was to characterize benign and malignant thyroid nodules using ultrasound.

MATERIALS AND METHODS

Methodology:

A prospective study done in King Fahad Specialist Hospital in Dammam (Kingdom Saudi Arabia), in the period from February 2020 to February 2021.The sampling includes 222 patients with clinically suspected thyroid nodules (calculating using Cochran's sample size formula from 525 patients with thyroid nodules. Ultrasound examination done using GE LOGIQ E10, E9, S8 and TOSIBA 1700 ultrasound machines with high frequency probe. The data collected by data collection sheet specifically design for the study purpose containing the patients demographic data, ultrasound features of thyroid nodules and fine needle aspiration results, after taking an written ethical approval written approval of protocol from research Centre (King Khalid Medical City-RC-KKMC)- King Fahad Specialist Hospital in Dammam (Kingdom Saudi Arabia); NUMBER (RAD0317) and verbal consent from all of patients after detailed description of the study purposes, all the patients are followed and fine needle aspiration results is record, then the data were analyzed by SPSS version 23, frequency and percentage are taken then Chi square test was used to correlate between dependent and independent variables, p value consider significant at $p < 0.05$.

Technique

The high frequency gray-scale US performed with the real-time scanner using (9/15 MHz) probe. The US machine settings such as gain, time gain compensation, dynamic range, focus, depth, color gain, wall filter, were optimized until high quality US images obtained. The patients lay supine, with their neck extended, then the thyroid gland and adjacent neck tissues scanned both transversely and longitudinally. For each nodule the description by ultrasound is obtained individually and include the following morphological features; nodule location (left lobe, right lobe, or isthmus); Composition (either mixed or solid); Echogenicity(hyperechoic, hypoechoic, isoechoic ,markedly hypoechoic); Shape (taller than wide , wider than taller); Margin(extra-thyroidal ,lobulated and smooth); Echogenic foci (micro, macro, absent); Doppler evaluation of thyroid nodules perform using the color Doppler gate to identify vascular color signals (a vascular , mild ,moderate or severe vascularity). The measurement of thyroid volume, isthmus and largest diameter of nodules are obtained also.

RESULTS

The study found that the thyroid nodules affected females more than males 76.6%; female to male ratio is 3.3:1, the nodules occur commonly in age group 40-50 years 30.2%, followed by 29-30 years 25.7% then in 51-60 years 21.6%, the least affected age, group was 18-28 years and 62-72 years, respectively, as shown in table 1.

Regarding the location of thyroid nodules, in the left lobe is about 48.6%, then the right lobe 46.8% and only 4.5% occurs in the isthmus. Figure 1

The study found that the mean age of patients with thyroid nodule are 44.37±13.31 years (ranged 18- 85 years), the mean measurement of the thyroid gland volume was 10.05±4.73 ml for right lobe and 10.80±8.41 ml for left lobe, the AP diameter of isthmus is 3.08±1.44 mm and the maximum diameter of nodules ranged (1-11 cm) with mean 2.97±1.44 cm, table 2.

On fine needle aspiration result the study found that more than halves of nodules are benign 51.4%, while 48.6% are malignant, figure 2

The study clarified that more than halve of thyroid nodules are hypoechoic 55.4%, 37.4% are isoechoic, 5% hyperechoic and 2.3 % are very hypoechoic, significant difference are found in the echogenicity in benign versus malignant nodule $P<0.001$ as most of benign nodules appear hyperechoic (10/11), or isoechoic (50/83), while most of malignant nodules appears hypoechoic (71/123) or markedly hypoechoic, (3/5). Concerning margin of thyroid nodules, 94.1% are smooth , 5.4% are lobulated and 0.5% is extra

thyroidal, in benign it is mostly smooth (113/209) nodules, while malignant nodule margin either smooth (96/209) or lobulated (11/12) and extra thyroidal (1/1), p value <0.001, concerning the shape of nodules the percentage of wider than taller is 95% ,mostly benign nodule are wider than taller in shape (113/211) only one patients had taller than wider benign thyroid nodule, mean awhile (10/11) taller than wider nodule are malignant and (98/211) of wider than taller nodule are malignant , also significant difference is found in nodule shape in benign versus malignant nodules , p <0.001. Table 3

Concerning composition of nodule this study found that no significant difference between benign and malignant nodules in tissue composition as (105/205 and 100/205) nodule of benign and malignant respectively are solid in nature, while (9/17 and 8/17) benign and malignant nodules are mixed tissue composition respectively, in all cases the percentage of solid nodule is 92.3%. Table 3

Concerning presence of echogenic foci within the nodules, in more than halve cases there is no presence of echogenic foci 51.4%, while in 37.7% there is micro calcification, in 9.5% the calcification is micro, the malignant nodule usually had associated micro calcification in (64 out of 77 nodule with macro calcification) nodules with micro calcification , and peripheral in (6/10) nodules with peripheral echogenic foci ,while in benign nodules the echogenic foci either macro (12/21) nodules with macro calcification are benign, (4/10) nodules with peripheral calcification are benign , and (85/114) nodules with no echogenic foci are benign , significant difference was found between presence and type of echogenic foci in benign versus malignant nodule , p<0.001.Table 3

In 37.4% of thyroid nodules the flow vascularity is mild , in 27.9% is severe, in 20.3% is moderate and in 14.4% there is no vascularity, furthermore all of nodule that is a vascular in doppler are benign in FNA result (32/32), most of nodules with mild vascularity also are benign (67/83), but most of nodules yield moderate or excessive vascularity are diagnosed as malignant on FNA results (34/45 and (58/62) moderate and severe vascularity nodules are malignant respectively , so the Doppler feature also is one of important parameter to differentiate the benign and malignant nodules, significant correlation was found between the vascularity of nodules and either it was confirmed as benign or malignant nodule, p<0.001. Table 3 and figure 3,4 showed the feature mentioned above for benign and malignant thyroid nodule.

Table 1: Patients' demographic data

Demographic data	Frequency	Percent	Valid Percent	Cumulative Percent
Gender				
Female	170	76.6	76.6	76.6
Male	52	23.4	23.4	100.0
Age group				
18-28	26	11.7	11.7	11.7
29-39	57	25.7	25.7	37.4
40-50	67	30.2	30.2	67.6
51-61	48	21.6	21.6	89.2
62-72	19	8.6	8.6	97.7
Total	222	100.0	100.0	

Table 2: Descriptive statistic for age, measurement of thyroid gland and maximum diameter of nodule

Variables	N	Minimum	Maximum	Mean ± Std. Dev
Age/ years	222	18	85	44.73±13.31
RT lobe volume in ml	222	3.8	53.0	10.05±4.73
LT lobe volume in ml	222	4.0	90.0	10.80±8.41
Isthmus AP in mm	222	2	10	3.08±1.44
Maximum diameter of nodule in cm	222	1.00	11.00	2.97±1.44

Table 3: Sonographic feature of benign and malignant nodule (correlation between ultrasound features and histopathology)

FNA result	Echogenicity				Total	P value
	Hyper echoic	Hypo echoic	Iso echoic	Very hypo echoic		
Benign	10	52	50	2	114	0.003
Malignant	1	71	33	3	108	
Total	11(5%)	123(55.4%)	83 (37.4%)	5 (2.3%)	222	
FNA result	Margin				Total	0.005
	Extrathyroidal	Lobulated	Smooth			
Benign	0	1	113		114	
Malignant	1	11	96		108	
Total	1(0.5%)	12(5.4%)	209(94.1%)		222	
FNA result	Shape				Total	0.004
	Taller than wider		Wider than taller			
Benign	1		113		114	
Malignant	10		98		108	
Total	11(5%)		211(95%)		222	
FNA result	Composition				Total	0.547
	Solid		Mixed			
Benign	105		9		114	
Malignant	100		8		108	
Total	205(92.3%)		17(7.7%)		222	
FNA result	Echogenic foci				Total	0.000
	Macro	Micro	None	Peripheral		
Benign	12	13	85	4	114	
Malignant	9	64	29	6	108	
Total	21(9.5%)	77(37.7%)	114(51.4%)	10(4.5%)	222	
FNA result	Vascularity				Total	0.000
	A vascular	Mild	Moderate	Severe		
Benign	32	67	11	4	114	
Malignant	0	16	34	58	108	
Total	32 (14.4%)	83(37.4%)	45 (20.3%)	62(27.9%)	222	

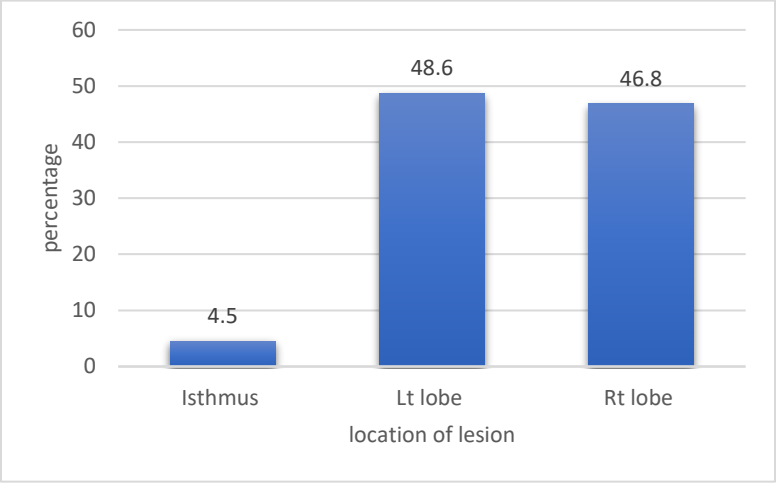

Figure 1: Location of nodule

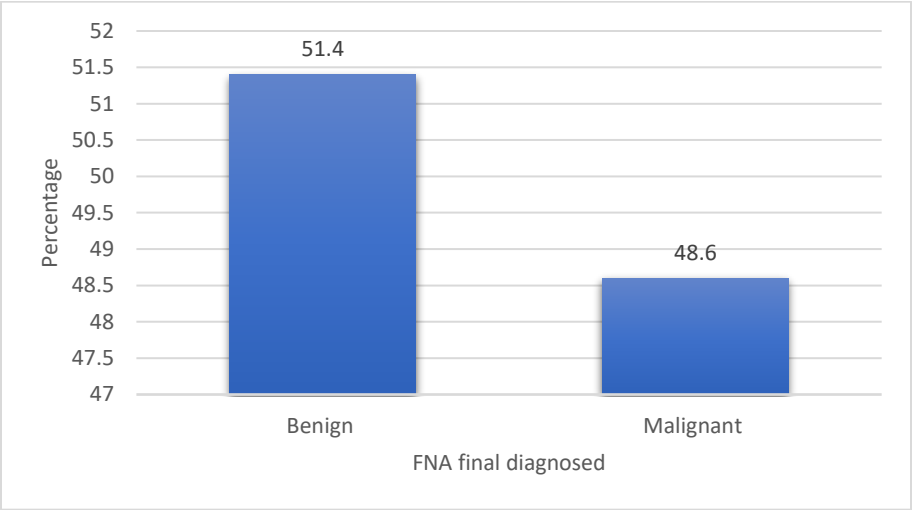

Figure 2: Frequency distribution of final diagnosed of nodule based on FNA

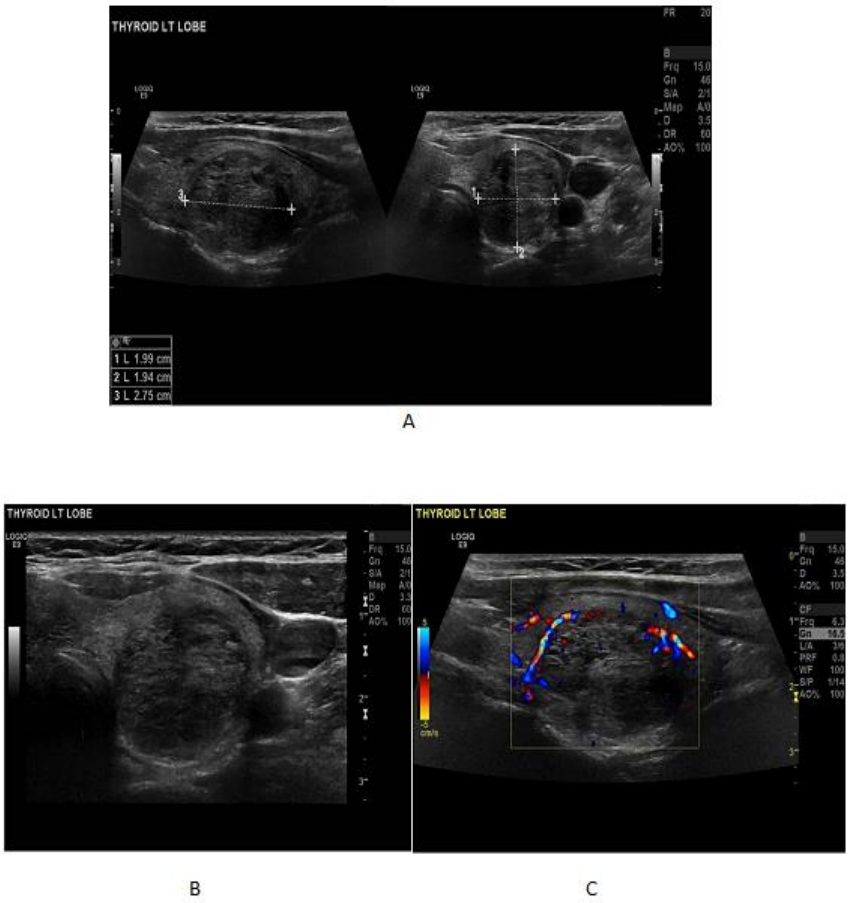

Figure 3: A, B & C. (A) Shows left thyroid nodule 2.75 cm in diameter solid, hypoechoic, (B) wider than tall, smooth margin with no echogenic foci and (C)peripheral vascularity on FNA is benign

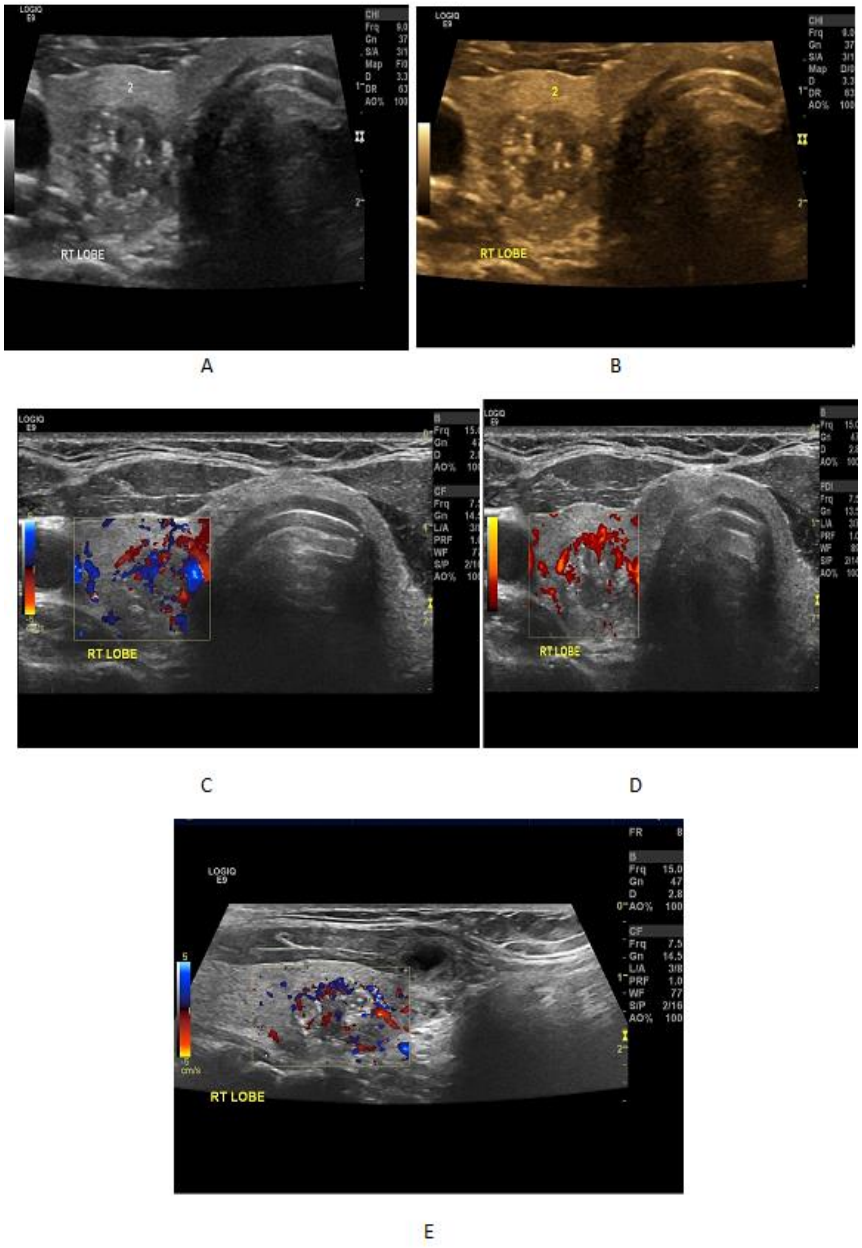

Figure 4: A, B is gray scale ultrasound shows nodule about 1.5 cm in maximum diameter, with punctate echogenic foci, solid, hypoechoic; C, D and E shows central and peripheral marked vascularity, on FNA is malignant.

DISCUSSION

Ultrasonography is the imaging study of choice for thyroid nodules. It can determine the nodule that is unpalpable, provides precise measurements of nodule diameter for interval monitoring and also it allows characterization of nodules by sono graphic features which suggest malignancy. (Bomeli, LeBeau and Ferris, 2010)

According to the American College of Radiology, the American Thyroid Association, and the European Thyroid Association, ultrasound features that strongly suggest malignancy include hypo echoic, solid, irregular margins, micro calcifications, height greater than width, extra thyroidal extension, disrupted rim calcification, and cervical lymph nodes with suspicious features. FNA should not be performed on nodules smaller than 1 cm. (Haugen et al. 2016; Russ et al. 2017; Tessler et al. 2017) The present

study found that the thyroid nodules affected females more than males 76.6%; female to male ratio is 3.3:1, the mean age was 44.73 years,other studies found that found that thyroid nodule affected female more than male (Manoj and Prasad., 2019), (Kalantari, 2018) . Fukunari et al. 2004 mention that 87% and 85 % of patients with thyroid nodule were female. (Fukunari et al. 2004). In this study the percentage of malignant nodule is about 48.6%, in study done by Manoj and Prasad, 2019 is about 16.18% only. (Manoj and Prasad, 2019)

This study found that the features of malignant nodule are mostly hypo echoic 66%, the remaining are iso echoic and markedly hypo echoic, 88.8% smooth, 10.1% lobulated, 90.7% wider than taller ,9.3% taller than wider, 92.6% solid, 59.3% had micro calcification and 53.7% had severe Doppler vascularity. (Kalantari, 2018) mention the similar feature for prediction of malignancy, Manoj and Prasad, 2019 mention that all malignant nodule is hypo echoic 100%. (Manoj and Prasad, 2019). Malignant nodule is solid in 82%, hypo echoic in 51.4%, fine calcification 31.8%; margin, shape, echo structure, echogenicity, and calcification were statistically significant for predicting malignancy in non-follicular neoplasms, (Koike et al. 2001), while this study found that margin, shape, echogenicity, calcification and vascularity were statistically significant for differentiating benign from malignant neoplasms, except the tissue composition which was insignificant to differentiate benign from malignant neoplasm. Our result also consistent with (Shen Y, et al. 2019) who found that the malignant nodules were more likely to have a solid composition, hypo echogenicity, taller-than-wider in shape, lobulated or irregular margins, with extra thyroidal extension, micro calcifications in correlation to benign nodules. (Shen Y, et al. 2019)

Rago and Vitti, 2008 stated that features associated of malignancy nodule in thyroid gland are in are micro-calcifications, hypo echogenicity, irregular margins or absent halo sign, solid aspect, intranodular vascularization, and shape (taller than wide), our study similar to them as it found that the ultrasound features of malignancy nodules in thyroid gland is mostly hypoechoic, solid component with Prescence of microcalcification or peripheral echogenic foci and marked doppler vascularity. (Rago and Vitti, 2008) Macrocalcifications in thyroid nodules increase the risk of malignancy. (Moon, Kwag and Na, 2009; Seo et al. 2015), but they are not specific for malignancies, with malignancy risk 23.9–64.8%. (Moon, Kwag and Na, 2009; Lu et al. 2011; Na et al. 2016)

This study found that the most common sono graphic feature of benign nodules is hypo echoic and isoechoic 45.6%, 43.8% respectively,99.1% smooth in outline,99.1%wider than taller ,92.1% solid, 74.6% no presence of calcification, 58.7% mild vascularity and 28.1% a vascular , Wienke, Jeffrey R et al. 2003 clarified that 60% of benign nodules are solid, 54% are hypo echoic, 59% are micro-lobulated or macro-lobulated, 47% had central vascularity,24% contained calcifications and 82% were elliptical in shape.(Wienke et al. 2003). There were significant differences in sono graphic feature of benign versus malignant nodules, except for composition of nodule, in this study, both malignant and benign nodule mostly are solid.

High frequency ultrasound is helpful to differentiate benign and malignant thyroid nodule, there is overlapping in some sono graphic features such as composition and shape, on the other hands some sonographic features help in prediction of malignancy such as taller than wider, presence of micro calcification, extra thyroidal extension and severe Doppler vascularity.

CONCLUSION

The study concluded that on high frequency ultrasound the malignant thyroid nodule is mostly appears as hypoechoic nodule, wider than taller or taller than wider, with presence of micro calcification, moderate or severe vascularity in doppler, benign nodules is appearing as hypoechoic or isoechoic, wider than taller, with no or macro calcification and a vascular or with mild peripheral vascularity on Doppler. In this study Strong significant difference in ultrasound features for benign and malignant nodules, except for nodule composition.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

MO designed the study, MO, MA, AA performed investigation and collect the data, AG and AC

wrote the manuscript, AG did the data analysis. AG, AC and EA reviewed the manuscript. All authors read and approved the final version.

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