DIAGNOSTIC ACCURACY OF COLOR FLOW DOPPLER IN THYROID TUMORS

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ABSTRACT

Objective: To determine the diagnostic accuracy of color flow Doppler in differentiating between benign and malignant thyroid nodules and using FNAC as gold standard.

Study Design: Validation study.

Place and Duration of Study: Radiology Department, Benazir Bhutto and Allied hospital Rawalpindi for a period of six months, from Mar 2013 to Sep 2013.

Material and Methods: The validation study was done at Radiology department, Benazir Bhutto and Allied Hospitals, Rawalpindi for the period of six months from 13th March to 13th September 2013. A total of 130 patients presenting with thyroid swelling with at least one dominant nodule, belonging to either sex were included through non probability consecutive sampling.

Results: Sensitivity, specificity, positive and negative predictive values as well as accuracy of color flow Doppler ultrasonography in detection of malignant thyroid nodule was 93.3%, 97.4%, 82.4%, 99.1% and 96.9% respectively. Area under the curve (AUC) was 0.935 (p=0.0001).

Conclusion: Color flow Doppler was found to be a useful diagnostic modality in the management of thyroid nodules, although the primary means should be FNA Biopsy.

Keywords: Color, Doppler, Fine needle aspiration biopsy, Thyroid nodules, Ultrasonography.

INTRODUCTION

Thyroid nodules are a common clinical finding, being more frequently found in women, in the elderly population and in those exposed in the past to a period of iodine deficiency[1]. Its prevalence in general adult population is about 67%[2]. Clinical importance of thyroid nodules rests with need to exclude thyroid cancer[1]. Prevalence of the thyroid cancer is 36%[3]. Frequency of carcinoma of thyroid is very high in solitary thyroid nodule but markedly low in multi-nodular goitre[4]. Fine needle aspiration of the thyroid nodule is the procedure of choice in diagnosis of thyroid nodule with sensitivity 100%[5] and specificity 100%[6], but it is not feasible to do biopsy of every thyroid nodule. Reasons for limiting thyroid biopsy include small percentage of malignant lesions, economic costs, burden on radiology resources and the patient anxiety incumbent on a potentially malignant diagnosis[7]. Conventional gray scale sonography is primary noninvasive method used for diagnosing thyroid lesion because of its low cost and wide availability but it is not very accurate in differentiating between benign and malignant thyroid nodules[8]. Ultrasound features that have to be found to be associated with increased risk of malignancy include a solid lesion, hypo-echogenicity, calcifications, irregular margins, absence of halo and taller than wide nodule[3]. No single ultrasound criteria is reliable in differentiating benign from malignant thyroid nodules but many ultrasound features aid in predicting benign and the malignant nature of a given nodule[9].

Malignant tumors usually present with high vascularization than the benign ones. Color flow Doppler based on the Doppler phenomenon calculates difference in frequency of emission and reception of an ultrasound beam reflecting moving RBCs inside the vessels and providing color images of vessels[10]. Doppler facilitates screening of thyroid nodules at high risk of

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malignancy with elevated sensitivity 92.3% and specificity 88%[11]; however some studies show variable results with low sensitivity and specificity 70%[3] and 66%[3] respectively. The thyroid nodules are characterized on the basis of vascularity that undertakes following patterns:

Score 0: No visible flow.

Score 1: Minimal internal flow without a peripheral ring.

Score 2: Peripheral ring of flow but minimal or no internal flow.

Score 3: Peripheral ring of flow and a small-to moderate amount of internal flow.

Score 4: Extensive internal flow with or without a peripheral ring. Significantly more benign nodules will have vascularization patterns 1 and 2, and significantly more malignant nodules will have vascularization pattern 3 and 4, and only pattern 4[12].

Color flow Doppler being easily available, cost effective with no radiation exposure and side effects and rapid production of results is still not in practice in differentiating thyroid nodules. Aim of this study was to explore the accuracy of color flow Doppler and results may help in recommending its use locally to screen thyroid nodules with distinguishing high risk of malignancy with subsequent biopsy FNAC. The rationale was to determine the diagnostic accuracy of color flow Doppler in differentiating between benign and malignant thyroid nodules and using FNAC as gold standard.

Table-I: Diagnostic accuracy of colour flow doppler in differentiating between benign and malignant thyroid nodules.

Color flow Doppler U/S	Fine needle aspiration		Total
	Malignant	Benign	
Malignant	14 (TP)	3 (FP)	17
Benign	1 (FN)	112 (TN)	113
Total	15	115	130
Sensitivity	=14/15	=93.3%	
Specificity	=112/115	=97.4%	
PPV	=14/17	=82.4%	
NPV	=112/113	=99.1%	
Accuracy	=14+112/130	=96.9%	

Table-II: Diagnostic accuracy of colour flow doppler in differentiating between benign and malignant thyroid nodules by age groups.

Age Groups (Years)	Color flow DopplerU/S	FNAC		Total	*p*-value by chi-square
		Malignant	Benign		
≤40 Years	MalignantBenign Total	7 (TP) 0 (FN) 7	3 (FP) 57 (TN) 60	10 57 67	<0.0001
>40 Years	MalignantBenign Total	7 (TP) 1 (FN) 8	0(FP) 55 (TN) 55	7 56 63	<0.0001
For Age ≤ 40 Years			**For Age >40 Years**		
Sensitivity	=7/7	=100%	Sensitivity	=7/8	=87.5%
Specificity	=55/60	=95%	Specificity	=55/55	=100%
PPV	=7/10	=70%	PPV	=7/7	=100%
NPV	=57/57	=100%	NPV	=55/56	=98.2%
Accuracy	=7+57/67	=95.5%	Accuracy	=7+55/63	98.4%

MATERIAL AND METHODS

This validation study was carried out in the radiology dept of BBH and Allied hospitals

Rawalpindi from 13th March 2013 to 13th March 2013. A total of 130 patients calculated through GPower 3.1.16 software (alpha error probability =0.05, effect size = 0.3, degree of freedom = 1 and power as 0.90) presenting with thyroid swelling with at least one dominant nodule, belonging to either sex were included through non probability consecutive sampling. Exclusion criteria were old proven cases, patients on chemo or radiotherapy, patients who had undergone FNAC directly before ultrasonography and finally those cases where there was some contraindication for FNAC. Informed consent of the patients was obtained for conducting the tests and using their data in the research. Patients were counseled about the FNAC results and the follow-up. The demographic data like name, age, sex, address and telephone numbers were obtained. The tilted in hyper extended position for thyroid ultrasound. Patient then underwent conventional ultrasound using high frequency linear probe of 7.5 MHz for number of nodules, size, consistency, echogenicity, calcifications, dimensions (taller than wide) and the presence of the halo sign. The color flow Doppler ultrasound (TOSHIBA PLN-703 AT) using high frequency linear probe of 7.5 MHz was performed to check for vascularity of the nodule that may have anyone of the above mentioned four scores. FNAC was performed after the ultrasound by taking samples from three different sites of the nodule using a 25G needle on a 10 ml syringe and preparing slides for cytological examination. FNAC results were presented in terms of "benign, malignant and non diagnostic". FNAC results were taken as gold standard. Finding of the color flow Doppler

Table-III: Diagnostic accuracy of colour flow doppler in differentiating between benign and malignant thyroid nodules by gender.

Gender	Color flow DopplerU/S	FNAC		Total	*p*-value by chi square
		Malignant	Benign		
Female	Malignant	4 (TP)	2 (FP)	6	<0.0001
	Benign	1 (FN)	96 (TN)	97	
	Total	5	98	103	
Male	Malignant	10 (TP)	1 (FP)	11	<0.0001
	Benign	0 (FN)	16 (TN)	16	
	Total	10	17	27	
For Female			**For Male**		
Sensitivity	=4/5	80%	Sensitivity	=10/10	100%
Specificity	=96/98	98%	Specificity	=16/17	94.1%
PPV	=4/6	66.7%	PPV	=10/11	90.9%
NPV	=96/97	99%	NPV	=16/16	100%
Accuracy	=4+96/103	97.1%	Accuracy	=10+16/27	96.3%

diagnostic criteria was history of present illness for symptoms and their duration and physical examination for palpable nodules, their size and other relevant signs. Specific investigation like thyroid function tests i.e. TSH, T3 and T4 were also done for all the patients. Confounding variables such as expertise of radiologist were controlled by having ultrasound performed by the single experienced sonologist. Patient was layed his on back, a rolled towel was placed below shoulders and upper back and head was ultrasound was noted and was compared with the FNAC. No ethical or cost involvement procedures were affecting the study. All this information was collected through a special designed proforma.

Data were entered and analyzed through SPSS (version 20). Mean and ± standard deviation for numerical variables like age, and number of nodules were presented. The qualitative variables like echogenicity, calcifications, halo sign and vascularity patterns were presented as frequency,

percentage and proportions. A 2x2 table was generated to calculate sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of colour flow Doppler ultrasound, taking FNAC as gold standard. Stratification was done with respect to age and gender to observe an accuracy of color flow Doppler ultrasound. Chi square test was applied on categorical variables. A *p*-value <0.05 was taken as significant.

RESULTS

A total of 130 patients presenting with thyroid swelling with at least one dominant nodule, belonging to either sex were included in this study. Most of the patients were 31 to 50 years of age. The average age of the patients was 40.75 ± 9.77 years. Mean (SD) number of nodules were 7.06 (2.14) while the median (IQR) number of nodules was 8 (3). There were 103 (79.23%) females and 27 (20.77%) males.

Most of the cases were multi-nodular 59.23% while 40.77% had single nodule. Hyper-echoic were observed in 64 (49.23%) cases, hypoechoic 32 (24.62%), anechoic 25 (19.23%) and mixed echogenicity were 9 (6.92%) cases. Regarding calcification, 82 (63.08%) had micro-calcification and 48 (36.92%) had coarse calcification. Halo sign was present in 20 (15.38%) cases.

Rate of malignant solitary thyroid nodule was 11.5% cases and benign 88.5% cases confirmed by FNAC while color flow Doppler ultrasound diagnosed 13.7% malignant and 86.9% benign as given in table-I. Sensitivity, specificity, positive and negative predictive values as well as accuracy of color flow Doppler ultrasonography in detection of malignant thyroid nodule was 93.3%, 97.4%, 82.4%, 99.1% and 96.9% respectively. Accuracy of color Doppler ultrasonography was above 90% as presented in table-II. Similarly accuracy of color flow Doppler ultrasonography was 97.1% for female patients and 96.3% observed in male cases (table-III). Receiver operating characteristic Curve (ROC) of colour Dopplers showed AUC of 0.935 (*p*=0.0001) (figure).

DISCUSSION

It is of utmost importance to recognize reliable criteria for malignancy when using imaging methods[13]. The use of ultrasonography in the assessment of thyroid disease has greatly increased the ability to detect small thyroid nodules, which were unrecognized by clinical examinations[14]. During the past decade the application of colour flow Doppler sonography has greatly increased in the differential diagnosis of benign and malignant tumors[15]. Reports in literature underline the usefulness of colour flow Doppler and power Doppler sonography in the diagnosis of certain forms of malignant tumors in various organs, such as liver, breast, ovary, kidney and prostatic tumors, as well as in the differential diagnosis of lymph nodes enlargement. Color flow Doppler ultrasonography is widely available and is more

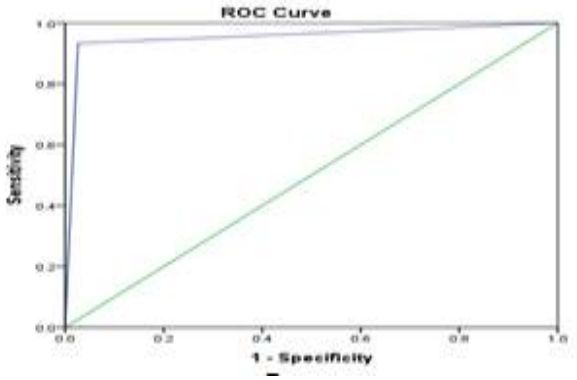

Figure: ROC curve of colour doppler.

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[16,17].

Our study showed that patients harbouring thyroid nodules were mainly females (79.23%). This is very much in accordance with many studies, which favor female predilection for the disease[18,19].

In our study most of the patients were 31 to 50 years of age and the mean age was found to be 40.75 ± 9.77 years. This is in accordance with a study done by Algin, et al[19].

In this study, we found 82 (63.08%) cases had microcalcification and 48 (36.92%) had coarse calcification. Micro calcification is one of the most specific features of thyroid malignancy with a specificity of 71.0%-98.8%[20-23]. In histopathology, micro-calcification is thought to represent psammoma bodies, which are 10–100 μm round laminar crystalline calcific deposits. Psammoma bodies are a typical finding in papillary carcinoma[24].

Malignant nodules are typically hypo-echoic when compared with normal thyroid parenchyma; however, nearly 50% of benign nodules also have this appearance. In our study we found a total of 32 (24.62%) hypo-echoic nodules. The hypoechogenicity of thyroid nodule is not a reliable sign of malignancy since the specificity and PPV are low[20,25,26]. Some studies have observed that marked hypoechogenicity was highly specific for diagnosing malignant nodules, but with low sensitivity.

In our study sensitivity of color flow Doppler ultrasonography in detection of malignant thyroid nodule was 96.9%, The sensitivity of color flow Doppler ultrasonography investigation is affected by the technical parameters as settings of a wall filter, nodule depth, and pulse repetition frequency (PRF)[11,27]. Individual variations of tissue attenuation, patient movement and lack of cooperation, motions as swallowing or breathing and pulsations of adjacent arterial structures may affect Doppler ultrasound investigation[11,27]. Over-pressing thyroid tissue may also prevent detecting vascularity[28]. An operator must consider these points and use an appropriate technique. We assume that in our study the technical issues mentioned were controlled by having ultrasound performed by the single experienced sonologist.

In our study rate of malignant solitary thyroid nodule was 11.5% cases and benign 88.5% cases confirmed by FNAC while color Doppler ultrasound diagnosed 13.7% malignant and 86.9% benign. This suggests that we have not missed very many malignant nodules. This is in contrast to the studies done by Cappelli et al[21] (4.6%) and Lin et al[13] (3.6%).

CONCLUSION

Color flow Doppler was found to be a useful diagnostic modality in the management of thyroid nodules, although the primary means should be FNA Biopsy.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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