ORIGINAL ARTICLE

ACCURACY OF COLOUR DOPPLER ULTRASONOGRAPHY IN DIFFERENTIATING BENIGN FROM MALIGNANT THYROID NODULES

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ABSTRACT

Background: The prevalence of thyroid nodular disease is commonly found in iodine deficient areas. Majority of these nodules are benign and less than 5% of thyroid nodules being malignant. High resolution Ultrasonography is primary modality of choice in diagnosis of thyroid nodules. To determine the accuracy of Color Doppler ultrasonography in diagnosis of malignant thyroid nodule conformed on Fine needle aspiration cytology.

Methods: This cross-sectional study was carried out in Department of Radiology PNS Shifa Hospital Karachi from 27th July 2012 to 26th February 2013. A total of 76 patients, having fixed palpable thyroid mass on examination, referred by clinicians for diagnostic workup were included in this study. Ultrasonography was performed using 7 MHZ linear array transducer. Thyroid nodule was assessed by grey scale sonographic features including number, size, echogenicity, margins and micro calcification. FNAC sampling was directed to the solid portion of the lesion. Cytological specimens were smeared according to the Papanicolaou technique, and were evaluated. All information was documented in the predesigned proformas.

Results: Accuracy of Color Doppler Ultrasound in detection of malignant thyroid nodule was 92.1%, with sensitivity 75%, specificity 93%, positive predictive value 37.5%, and negative predictive value 98.5%.

Conclusion: We found a comparable sensitivity and specificity to other international studies. An institutional protocol is devised to diagnose the malignant thyroid nodule as early as possible non-invasively employing Colour Doppler ultrasonography. This is helpful in early appropriate management of patients suffering from thyroid nodules.

KEY WORDS: Color Doppler ultrasonography, malignant thyroid nodule, Fine needle aspiration cytology

INTRODUCTION

Thyroid cancer is one of the most common endocrine malignancy[1]. Its incidence has been increased recently[2]. General population is commonly affected with thyroid nodule and is estimated that 5% of adult population has palpable thyroid nodules[3]. The prevalence of thyroid nodular disease is much more common in iodine deficient areas. It has been observed that 50% to 70% of subjects with thyroid nodules had no previous history of thyroid disease[4]. Fortunately majority of these nodules are benign and less than 5% of thyroid nodules being malignant[3]. Moreover, most thyroid carcinomas are of a papillary type, which usually has a good prognosis[5].

High resolution ultrasonography is primary modality of choice in diagnosis of thyroid nodules[6]. It does, not only detect presence, site, number, and sizes but clearly shows their characteristics[7], like in the Thyroid Imaging Reporting and Data System (TIRADS)[8,9,10], nodules with solidity, hypoechogenicity or marked hypoechogenicity, microlobulated or irregular margins, microcalcifications, and taller-than-wide shape are defined as suspicious malignancy. More so in comparison to FNAC, ultrasound has advantage of being non invasive and provides immediate information[3]. Several ultrasonographic characteristics have been found

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to differentiate malignant from benign nodules. These include micro calcification, irregular margins, shape and echogenicity, discontinuity of peripheral halo sign or invading adjacent structures[11].

Addition of Color Doppler Ultrasonography (CDUS) is believed to improve the diagnostic accuracy of malignant thyroid nodules[12]. On CDUS three type of vascular pattern are classified as Type 1: avascular, Type 2: perinodularhyper vascularity, Type 3: intranodularhyper vascularity. Different studies have been done and they show risk of malignancy is higher in nodules with predominately central flow than in nodules predominately avascular and perinodular flow pattern[3].

FNAC, a routine procedure increasingly performed in early detection of thyroid malignancy[13] and is most important step in preoperative diagnosis of thyroid nodule, due to its simplicity, low cost and absence of major complications. Limitation of applying ultrasound and FNAC for diagnosing thyroid nodule is that it cannot differentiate between benign and malignant follicular neoplasm[14]. Bianek-Bodzak A ,et al;[15] reported that the sensitivity and specificity of color Doppler ultrasound were 73.3% and 98.1% respectively in detecting malignant thyroid nodule as compared to FNAC.

The role of grey scale ultrasonography in evaluating the malignant thyroid nodules is well documented; however no significant work has been done on Color Doppler ultrsonography to accurately differentiate malignant from benign thyroid nodules.

The purpose of this study is to find out the accuracy of Color Doppler Ultrasonography in detection of malignant thyroid nodules compared to FNAC. If a comparable sensitivity and specificity to other international studies can be attained then an institutional protocol will be devised to diagnose noninvasively the malignant thyroid nodules, as early as possible employing Colour Doppler ultrasonography. This will be helpful in an early and appropriate management of patients suffering from thyroid nodules.

METHODS

This cross-sectional study was carried out in the department of radiology, PNS Shifa hospital Karachi from 27th July 2012 to 26th February 2013. A total of 76 patients, having fixed palpable thyroid mass on examination, referred by clinicians for diagnostic workup were included in this study. The cases were selected by non probability consecutive sampling. We included all patients, of both genders, 18- 60 years old, having palpable thyroid mass on examination and having solitary or multinodular thyroid nodules with size more than 1cm confirmed on ultrasound.

Patients already diagnosed for thyroid disease, or having history of previous thyroid surgery and those who refused to sign informed consent were excluded from the study.

Patients fulfilling the above mentioned inclusion criteria having solitary or multinodular palpable fixed thyroid mass and size more than 1cm confirmed on ultrasound were included in this study. Consultant radiologists having 10 years' experience in standard maneuve carried out the ultrasonographic examination of thyroid. Ultrasonography was performed using 7 MHZ linear array transducer. Thyroid nodule was assessed by grey scale sonographic features including number, size, echogenicity, margins and microcalcification. In patients with multiple thyroid nodules, only largest nodule was evaluated. Color Doppler study was performed after grey scale sonography with special emphasis on assessing the pattern of vascularity. Based on Color Doppler Ultrasound, vascularity nodule was classified as benign or malignant followed by Ultrasound guided FNAC in radiology department. Risk and benefit of FNAC was explained and informed consent was taken from the patients for FNAC procedure and inclusion in this study. FNAC sampling was directed to the solid portion of the lesion. Cytological specimens were smeared according to the Papanicolaou technique and evaluated by experienced cytopathologists.

Adequate cytological material was classified as benign or malignant thyroid nodule on the following bases;

- **Benign thyroid nodule on Color Doppler Ultrasonography:** It was labeled benign when type 1 (avascular i.e. no flow) & type 2 (perinodular flow i.e. presence of vascularity around at least 25% circumference of a nodule) patterns of vascularity was obtained on Color Doppler Ultrasound scan.

- **Malignant thyroid nodule on Color Doppler Ultrasonography:** It was labeled malignant when type 3 pattern of vascularity (marked intrinsic hyper vascularity i.e. flow in central part of tumor is greater than that surrounding parenchyma) was found on Color Doppler Ultrasound scan.

- **Benign thyroid nodule on Fine Needle Aspiration Cytology:** Thyroid nodule was labeled benign when on FNAC benign looking cells having no oncocytic cytology and nuclear atypia were observed.

- **Malignant thyroid nodule on Fine Needle Aspiration Cytology:** Thyroid nodule was labeled malignant when on FNAC malignant cells having oncocytic cytology, mitotic activity and cellular atypia.

FNAC findings of each patient were collected and findings were compared with colour Doppler

ultrasonography. All informations were documented over predesigned proformas.

Statistical software packages (SPSS 14.0) was used for data analysis.

Mean and standard deviation were calculated for quantitative variables (i.e. age and duration of symptoms).While, frequency and percentages were calculated for qualitative variables (i.e. gender, accuracy, benign/ malignant nodule as per CDUS and FNAC).

Effect modifiers like age and gender were controlled through stratification of age, gender and duration of symptoms to determine effect on outcomes. Chi-square test was applied and P value equal to or less than 0.05 is considered significant.

RESULTS

A total of 76 patients representing 68.4% females and 31.6% males, having fixed palpable thyroid were included. The average age of the patients was 36.12±9.19 years (95%CI: 34.02 to 38.22) with a median duration disease as 10 months (IQR= 23). Solitary nodule was observed in 11(14.5%) cases and 65(85.5%) cases were multi nodular.

Rate of malignant and benign thyroid nodule confirmed by FNAC was 5.3% (4 cases) and 94.7% (74 cases) respectively, while with Color Doppler Ultrasound 10.5% (8 cases) were diagnosed as malignant and 89.5% (68) as benign cases.

Sensitivity, specificity, positive and negative predictive value as well as accuracy of Color Doppler Ultrasound in detection of malignant thyroid nodule was 75%, 93%, 37.5%, 98.5% and 92.1% respectively.

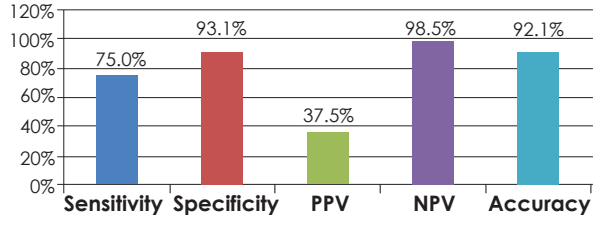

Figure 1: Accuracy of Color Doppler Ultrasonography in Diagnosis of Malignant Thyroid Nodule Conformed On Fine Needle Aspiration Cytology

Effective modifiers were controlled by stratification of age, gender, duration of disease and nodular solitary. Outcomes of color Doppler ultrasound are specified in table 1.

Table: 1 Outcome of Color Doppler Ultrasonography in Diagnosis of Malignant Thyroid Nodule with respect to age groups

Variables	Cutoff	n	TP	FP	TN	TN	P-Values
	≤36	45	0	2	1	42	0.99
Age Groups	>36	31	3	3	0	25	0.004

* True positive ** False positive *** False negative **** True negative.

Sensitivity, specificity, positive and negative predictive value as well as accuracy of Color Doppler Ultrasound in detection of malignant thyroid nodule was 75%, 93%, 37.5%, 98.5% and 92.1% respectively.

DISCUSSION

With the advent of improved imaging modalities, thyroid nodules are not encountered as uncommon findings in our setup. Ultrasonography (US) of the thyroid gland is the primary imaging investigation and addition of colour Doppler ultrasonography may improve accuracy in distinguishing malignant thyroid nodules from benign thyroid nodules.

Majority of thyroid nodules detected incidentally on imaging are benign[16]. Many sonographic features including size, shape, location, echogenicity, outline, presence of a halo and microcalcifications are evaluated for differentiation between benign and malignant thyroid nodules[17,18]. Ultrasonography (US) being the primary imaging investigation, is easily tolerated by patients and is cheaper and faster to perform than other methods. Additionally, it provides the ability to perform ultrasonographically guided fine-needle aspiration cytology (FNAC). Many thyroid diseases are presented clinically with one or more nodules. Palpable thyroid nodules occur in 4 to 7% of population, but nodules found incidentally on sonography suggest a prevalence of 13-67%[19]. The nodular shape has also been studed as marker of malignancy. Noduler width on a transverse scan corresponds to the natural growth planes. Malignant tumors grow centrifugally and show expansion perpendicular to the natural growth plane.[20,21,22].

In present study, the average age of the patients were 36.12±9.19 years concurrent to Khan et al[23] representing 68.4% female and 31.6% male.

In this study solitary nodule was observed in 11(14.5%) and multi nodular cases observed were

65(85.5%). However in Yunus and Ahmed[11] study 66 patients were evaluated, out of 66 patients fifty nine (89.4%) patients had single thyroid nodule while the remaining 7 (10.6%) patients had multiple solid nodules. Our study showed that patients harboring thyroid nodules were mainly females (68.4%). This is very much in accordance with international studies, which favor female predilection for the disease.
In this study rate of malignant thyroid nodule was 5.3% and benign 94.7% confirmed by FNAC and Color Doppler. The overall percentage of malignancy in our series is lower (5.3%) than previously reported, but similar to that recently observed by Cappelli et al[4] (4.6%) and Lin et al[24] (3.6%).

Many studies have investigated whether the ultrasonographic characteristics of thyroid nodules are useful indicators of histological malignancy. Overall, these investigations suggest few ultrasonographic features that are significantly more frequent in malignant than in benign thyroid nodules. There is almost unanimous agreement that the presence of microcalcifications within a nodule is associated with thyroid cancer[25,26].

In our study its specificity is 93.1%, which correlates with other studies where it is stated as 85.8% to 95%[27] and positive predictive value is 37.5% in current study which is also in agreement with other studies. Microcalcifications are found in 24% to 59% of all primary thyroid carcinomas[27] most commonly in papillary thyroid carcinomas but their occurrence has been described in follicular and anaplastic thyroid carcinomas as well as benign conditions, such as follicular adenomas and Hashimoto's thyroiditis. In contrast to microcalcifications, coarse and peripheral calcifications are commonly present in multinodular goiter[6].

However, there is almost unanimous agreement that the presence of micro calcifications within a nodule is associated with thyroid cancer among rest of the ultrasonic features intrinsic micro calcifications is the strongest criterion predicting malignancy[4]

Color Doppler Ultrasonography is widely available 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 FNAC and surgery[29].

Researchers from Nagoya University (Japan) 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[29]

CONCLUSION

We found sensitivity and specificity comparable to other international studies. An institutional protocol is devised to diagnose the malignant thyroid nodule as early as possible non-invasively employing Color Doppler Ultrasonography. This would signify aid in the management of patients with thyroid nodules.

The Color Doppler characteristics of a thyroid nodule are good indicators of the benign and malignant nature of thyroid nodules and it helps in screening out cases needing immediate further histopathological confirmation. Though the future of duplex Ultrasonography is changing, FNAC is still the gold standard by which other modern methods are measured.

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