Original Article

ROLE OF COLOUR DOPPLER ULTRASONOGRAPHY IN DIFFERENTIATING BENIGN AND MALIGNANT THYROID NODULES

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ABSTRACT

Objective: To determine the validity of Colour Doppler Ultrasonography in differentiating benign from malignant thyroid nodules in patients attending outpatient department of Radiology of Combined Military Hospital, Rawalpindi, keeping fine needle aspiration as reference.

Study design: Validation study.

Place and duration: The Department of Radiology, Combined Military Hospital (CMH), Rawalpindi from June to December 2009.

Patients and Methods: All patients with thyroid nodules were included for diagnostic workup. Colour Doppler study was carried out recording the size and consistency of the thyroid nodule with special emphasis to vascularity pattern. US findings were noted. Ultrasound was followed by fine needle aspiration from Armed Forces institute of Pathology (AFIP), Rawalpindi. Findings on CDUS were analyzed in light of AFIP report.

Result: Among the 107 thyroid nodules studied, 6 nodules were proven to be malignant on FNA. Of these 6 malignant nodules, only 3 were picked up by Colour Doppler ultrasound. Four were wrongly labeled as malignant by the vascularity pattern shown on Colour Doppler Ultrasound. Colour Doppler ultrasound showed a sensitivity of 50%, specificity of 96%, NPV of 97%, and PPV of 42.9%.

Conclusion: The Colour Doppler characteristics of a thyroid nodule cannot be used to predict or exclude malignancy confidently. Although the future of duplex Ultrasonography is changing, FNAB is still needed to determine the nature of the nodule.

Keywords: Colour Doppler ultrasound, Fine-needle aspiration biopsy, Thyroid nodule, Vascularity.

INTRODUCTION

Thyroid nodules are not an uncommon finding encountered in our setup. Especially after the advent of improved imaging modalities, more of thyroid nodules are being detected. Ultrasonography (US) of the thyroid gland is the primary imaging investigation. Addition of CDUS may improve accuracy in distinguishing malignant thyroid nodules from benign thyroid nodules.

Majority of thyroid nodules being detected incidentally on imaging, are benign[1,2]. In general, almost 5% of the adult population has a palpable thyroid nodule[2]. Despite benign thyroid nodules being common, the possibility of cancer must always be considered.

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 biopsy (FNAB). 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[3,4]. With the advent of US with Colour Doppler flow mapping, a new sonographic feature: hemodynamics is being studied as predictor for thyroid malignancy[5].

On Colour Doppler Ultrasonography (CDUS), nodule vascularisation patterns are classified as:

Type 1: avascular

Type 2: perinodular hypervascularity

Type 3: intranodular hypervascularity[6].

In thyroid malignancy, the most common pattern of vascularity is marked intrinsic hypervascularity, defined as central flow in the tumor[7]. Addition of CDUS may improve

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Received: 26 May 2011; Accepted: 04 Nov 2011

accuracy in distinguishing malignant thyroid nodules[8].

For diagnosis of thyroid cancer, fine-needle aspiration (FNA) is an efficient tool, having a high sensitivity in picking up thyroid malignancy[9]. It has a sensitivity of 74.1% and specificity of 100%. Also it is rapid and cost effective[10,11]. Despite the advantages, it being an invasive procedure, warrants more reliable criteria to determine further management[2]. In view of the ubiquity of thyroid nodules, it is not feasible to biopsy every thyroid nodule discovered with ultrasound. Reasons for limiting thyroid biopsy, which is relatively painless and safe, include the small percentage of malignant lesions, the small number of cases of thyroid cancer in which early diagnosis may actually have an influence, the economic and social costs, the strain on radiology resources, and the patient uncertainty and anxiety incumbent on a potentially malignant diagnosis. Hence, reliable guidelines for nodules that may not require biopsy have become essential[12]. In most cases, the possibility of thyroid malignancy leads to a recommendation for partial or near-total surgical thyroidectomy[13].

In our setups, Ultrasound is limited to diagnosis of thyroid nodules. This study evaluates the role of Colour Doppler ultrasonography which will help us in formulating a predictive criterion for differentiating benign and malignant thyroid nodules during diagnostic work-up and curtail the number of needless investigations, and thus reduce health care burden.

PATIENTS AND METHODS

This validation study was carried out at Department of Radiology, CMH Rawalpindi from June 2009 to December 2009. All patients with suspected thyroid nodule, found incidentally on routine ultrasound neck examination or were incidentally detected by imaging studies performed for various reasons were included with no age and gender discrimination.

Ultrasonography was done on Toshiba Diagnostic Ultrasound Machine (APOLIO-50 MODEL 700A), using 7 MHz linear transducer with Colour and power Doppler capability. Colour Doppler study was carried out recording the size and consistency of the thyroid nodule with special emphasis on the vascularity pattern. Colour Doppler US findings were noted. Ultrasound was followed by fine needle aspiration from Armed Forces institute of Pathology (AFIP), Rawalpindi. Ultrasound diagnosis was not provided for fine needle aspiration cytology report. Findings on CDUS were analyzed in light of AFIP report.

Computer package SPSS version 10 was used for computation and data analysis. Descriptive statistics were used to describe the data i.e. Mean and SD for quantitative variable while frequency and percentages for qualitative variables. Sensitivity, specificity, positive predictive, negative predictive values and accuracy were calculated for CDUS taking FNA as gold standard.

RESULTS

A total of 107 patients were included in the study. There were 20 (17.8%) males and 87 (82.2%) females.

The age statistics of patients under study are shown in table 5. Year wise age distribution is shown in figure 1. The age of the patients ranged from 10 yrs to 80 yrs with mean age of 39 yrs. Peak incidence of disease was observed during the 3rd decade.

Seven patients were diagnosed to have malignant thyroid nodule on Colour Doppler ultrasound in which 4 did not show malignant changes on FNAB.

Colour Doppler ultrasound was unable to pick up 3 cases of malignant thyroid nodules.

Statistical analysis of our study revealed the following: Colour Doppler ultrasound showed a sensitivity of 50%, specificity of 96%, NPV of 97%, and PPV of 42.9% with an accuracy of 93.4%.

DISCUSSION

Thyroid nodules are ubiquitous in Pakistan. Presently thyroid related problems/ goitre is a common cause of referrals to hospital

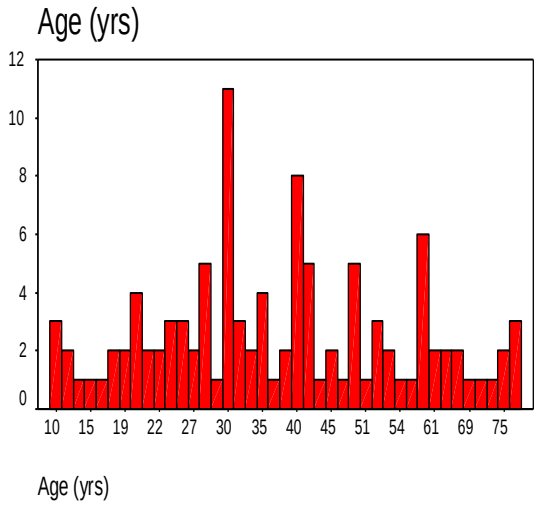

Figure 1: Year wise age distribution

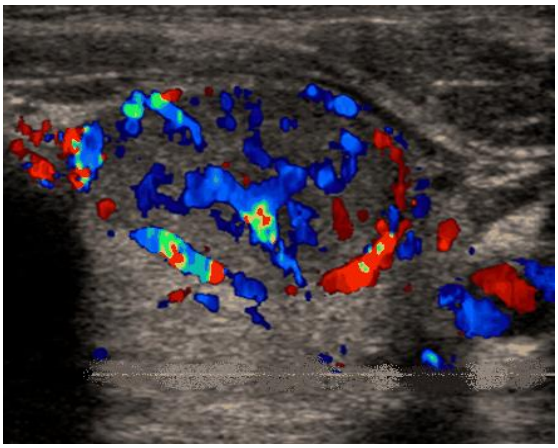

Figure 2: Transverse image of a solid thyroid nodule with addition of Colour Doppler mode showing marked internal vascularity.

and hospital admission in surgical departments. Currently thyroidectomies contribute significantly to the surgical scenario of our hospitals.

Thyroid nodule is defined as a discrete swelling within an otherwise apparently normal gland. FNAB is considered to be the gold standard for diagnosing thyroid malignancy within these thyroid nodules which may later on be substantiated by histopathological report of the excisional surgical specimen. Although FNAB is relatively safe it is still associated with patient discomfort. In addition FNAB examinations may lead to false negative results due to inadequate or inappropriate thyroid tissue sampling. Therefore, there is a need to develop a simple, reliable and non-invasive technique in order to assess the thyroid nodules.

Sonography depicts the internal structure of the thyroid gland and the regional anatomy and pathology without using ionizing radiation or iodine containing contrast medium[14]. The procedure is safe and is less costly than any other imaging procedure. The patient remains comfortable during the test, which takes only a few minutes, does not require discontinuation of any medication, or preparation of the patient. Doppler ultrasonography being a non-invasive, inexpensive and repeatable modality can be used as a valuable tool during the diagnosis and follow up of patients with thyroid nodules.

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, parotid gland, ovary, kidney, prostate tumors, as well as in the differential diagnosis of lymph nodes enlargement.

Our study showed that patients harbouring thyroid nodules were mainly females (82%). This is very much in accordance with international studies, which favour female predilection for the disease. The overall percentage of malignancy in our series is lower (5.8%) than previously reported, but similar to that recently observed by Cappelli et al[16] (4.6%) and Lin et al[17] (3.6%). This suggests that we have not missed very many malignant nodules.

Many studies have investigated whether the ultrasonographic characteristics of thyroid nodules are useful indicators of histological malignancy. There is almost unanimous agreement that the presence of microcalcifications within a nodule is associated with thyroid cancer[18,19].

The aim of this study was to stress the importance of Doppler ultrasound to assess the differentiation of benign from malignant thyroid nodules in patients with thyroid nodules[8]. This is also mentioned in many international studies. Varverakis et al concluded that reports published in the

literature to date have shown that all patients with thyroid nodules should be studied in the first stage of their illness and in follow-up by using Doppler techniques. With new ultrasound software, one can obtain a better and more complete vascular study of the thyroid gland. Resistance and pulsatility indices, diameter of inferior thyroid artery and its flow velocity are parameters prone to pathologic and morphologic changes[20-24].

In our study, one of these parameters: types of vascularity was noted which others have also described[25]. A number of studies done with Colour-flow Doppler (CFD) sonography have disclosed intense vascularization of malignant thyroid nodules, as this method might be able to provide important reference data to enable differentiation between benign and malignant nodular pathology. Many studies confirmed the clinical use of this technique in the diagnosis of benign from malignant thyroid nodules[26,27].

Nodule vascularisation patterns were classified as: Type 1: avascular, Type 2: perinodular hypervascularity, Type 3: intranodular hypervascularity[28]. In thyroid malignancy, the most common pattern of vascularity is marked intrinsic hypervascularity, defined as central flow in the tumor[7].

Varverakis et al suggested that the absence of vascularization correlates with the size of the nodules, but not with their benign or malignant feature which also supports findings of the study[15]. Moreover, Shiamamoto et al found that the detection of Colour signals inside the thyroid nodule depends on its size but not on its histologic features[29].

Most studies evaluating the role of Colour Doppler sonography for the prediction of malignancy have limited the study population to nodules that are cold on radionuclide scans (i.e., nodules that do not take up a radioisotope)[30]. Several small series of cold nodules suggest that internal flow in a cold nodule is indicative of malignancy.[7,11,12] In a larger study of more than 100 patients with cold nodules, a hypervascular pattern alone was not a statistically significant finding for the prediction of malignancy[9]. In our study, scintigraphy was not performed routinely, and nodules were assessed only for size and sonographic and Doppler characteristics before biopsy.

Our study shows that although the degree of vascularity as determined by Colour Doppler imaging differs in malignant and benign nodules, the role of Colour Doppler sonography in the evaluation and treatment of thyroid nodules is limited. Characteristics revealed by ultrasonography — such as hypoechogenicity, microcalcifications, irregular margins, increased nodular flow visualized by Doppler, and, especially, the evidence of invasion or regional lymphadenopathy — are associated with an increased risk of cancer; however, sonographic findings cannot reliably distinguish between benign and cancerous lesions on the basis of the sonographic appearance (cystic versus solid), Colour Doppler characteristics, or both[31,32]. More than 50% of the hypervascular solid nodules (those with Colour type 3) in our series were benign. In addition, 50% of the nonhypervascular solid nodules were malignant. These results confirm those of others. One large study that included 30 cases of papillary cancer found no significant difference in the Colour flow patterns of benign versus malignant nodules[9]. In another smaller series that included 7 malignancies, when Colour Doppler sonography was used in conjunction with gray scale sonography, it aided in the differentiation of neoplastic lesions from colloid nodules but was not sensitive enough to distinguish benign from malignant neoplasms[14]. Another large series, which compared Colour Doppler with power Doppler sonography, included more than 300 cold nodules (including 20 papillary cancers) and had results similar to ours, with a hypervascular Colour Doppler pattern common in, but not diagnostic of papillary cancer[13]. Argalia et al pointed out that the measurement of Peak Velocity and Resistance Index may be useful in the characterization of solid nodules and the selection of patients to undertake FNA[33].

The fact that we found a tendency for Colour Doppler characteristics to differ in malignant compared with benign nodules suggests one type of patient in which Doppler sonography might be useful: the patient with a large number of thyroid nodules who might otherwise be subjected to multiple FNAs. In such a patient, the presence of type 3 Colour vascularity in a solid nodule could direct the choice of the lesion to sample. Colour Doppler sonography was helpful in delineating nodules in otherwise inhomogeneous glands[34].

There are certain limitations to our study. Firstly, we had to perform FNAC, which is cumbersome to patients. Secondly also it is an expensive examination. Small sample size is another limitation to our study. The safety of Doppler ultrasound remains a concern. In particular the use of pulsed Doppler involves the use of higher intensities compared to diagnostic ultrasound, and may cause significant tissue heating and other thermal effects. These thermal effects depend on the presence of a tissue/air interface and may therefore not be clinically significant in thyroid ultrasound examinations. Lastly, facility of Doppler ultrasound is not present in majority of Pakistani medical facilities.

To summarize, not many studies have been conducted in this regard in our country and our study suggests further investigation into the assessment of thyroid nodules.

CONCLUSION

The Colour Doppler characteristics of a thyroid nodule cannot be used to predict or exclude malignancy confidently. FNAB is still needed to determine the nature of the nodule. Though the future of duplex ultrasonography is changing, FNAB is still the gold standard by which other modern methods are measured.

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