ORIGINAL RESEARCH PAPER

Radio diagnosis

ROLE OF PEAK SYSTOLIC VELOCITY OF INFERIOR THYROID ARTERY IN DIFFERENTIATION OF GRAVES' DISEASE AND HASHIMOTOS THYROIDITIS IN THYROTOXICOSIS

KEY WORDS: Color Doppler, inferior thyroid artery (ITA), peak systolic velocity (PSV),Graves disease, hashimotos thyroiditis.

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ABSTRACT

AIM: To evaluate the role of inferior thyroid artery (ITA) peak systolic velocity (PSV) assessed by color Doppler in the differential diagnosis of thyrotoxicosis.

METHOD: Forty three patients with thyrotoxicosis were included in our study. A detailed clinical history was taken from all patients followed by physical examination and thyroid function tests and thyroid autoantibody levels. The thyroid glands were evaluated by gray scale ultrasound for volume and echotexture. Doppler ultrasonography was performed and PSV of both inferior thyroid arteries was assessed. FNAC was done in all patients to confirm the diagnoses. The patients were divided into two groups: 23 cases with Graves' disease and 20 cases with Hashimoto's thyroiditis. All patients had suppressed thyrotropin. The diagnosis was further supported by the clinical picture and follow up of the patients.

RESULTS: Peak systolic velocity of the inferior thyroid arteries were significantly higher in patients with Graves' disease than in patients with Hashimotos thyroiditis (P = 0.001). Doppler ultrasound parameters demonstrated a sensitivity of 86.9% and a specificity of 85.0% in the differential diagnosis of thyrotoxicosis.

CONCLUSION: Color Doppler assessment of inferior thyroid artery can be helpful in the differential diagnosis of thyrotoxicosis, especially when there is a contraindication or lack of availability of thyroid scintigraphy.

INTRODUCTION

Thyrotoxicosis is a hypermetabolic state resulting from elevated serum levels of thyroid hormone. Thyrotoxicosis may be caused either by hyperthyroidism in which there is excessive thyroid hormone production or it may be caused by inflammatory destruction of the thyroid with release of stored thyroid hormones. It may also be caused by ingestion of exogenous thyroid hormone. Graves' disease causes hyperthyroidism with diffuse thyroid disease while thyrotoxicosis due to destructive thyroiditis includes various subsets like lymphocytic thyroiditis, subacute thyroiditis and postpartum thyroiditis [1-4]. Differentiation between causes of thyrotoxicosis at time of diagnosis, either hyperthyroidism due to Graves' disease or destructive thyroiditis is very important as management of each case is completely different. The absence of specific signs of Graves' disease like ophthalmopathy, skin and nail changes may make it difficult to distinguish it from destructive thyroiditis, especially when the disease is mild in severity. Thyroid scintigraphy by technetium99 (Tcm99) pertechnetate or iodine 123 radioisotopes is used for this purpose. However, nuclear scan is not available everywhere and is also contraindicated in certain groups of patients like pregnant females and can also be affected by drug intake and recent iodinated contrast studies[5].FNAC can also be used to differentiate the two in majority of the patients. On ultsonography hypoechoic echopattern has been found to be characteristic of autoimmune thyroid diseases, with this echopattern found in both Graves' and Hashimoto's thyroiditis. However, it has been found that markedly increased blood flow is pathognomonic of untreated Graves' disease. Thus, Doppler ultrasound parametres may be useful in distinguishing patients with Graves' disease and Hashimoto's thyroiditis with a similar thyroid echographic pattern.

Ultrasound is an inexpensive, noninvasive and easily available method for measuring tissue vascularization and blood flow. The evaluation can be both qualitative (visual assessment of thyroid vascularity) and quantitative (measuring peak systolic, end diastolic and mean velocities in the inferior thyroid arteries). CFD ultrasonography of the thyroid gland can provide valuable information about underlying thyroid functional status and is useful in the differential diagnosis of thyrotoxicosis [6-9].

The aim of the study is to evaluate the efficiency of Doppler ultrasound in differentiation of causes of thyrotoxicosis at time of diagnosis, either hyperthyroidism due to Graves' disease or destructive thyroiditis with confirmation of diagnoses made by FNAC supported by clinical and lab findings.

MATERIALS AND METHODS:

A prospective observational study involving individuals with thyrotoxicoses was carried out in a tertiary care hospital from August 2018 to March 2019. Institutional Ethics Committee clearance was obtained. Informed consent was taken from all individuals prior to performing the study. All of them underwent thyroid hormone analysis for routine evaluation earlier. All the subjects underwent detailed clinical evaluation including history taking, resting pulse rate, neck examination, etc., prior to ultrasonography. FNAC was also performed under ultrasound guidance to help in the diagnoses of Graves or Hashimotos thyroiditis. Any subjects with incidentally found thyroid nodule were excluded from the study to exclude possibility of toxic nodule. Any patient with history of thyroid surgery, radioiodine therapy or radiation exposure to neck were also excluded.

Graves' disease was diagnosed on the basis of clinical parameters (marked weight loss, adrenergic symptoms, goiter, skin and nail changes, eye signs) and confirmed with FNAC. Thyroiditis was diagnosed on the basis of presence of insignificant symptoms (no or minimal weight loss, occasional palpitations, absent eye signs with or without goiter) or later development of hypothyroidism and confirmed with FNAC.

Doppler ultrasonography of the subjects was performed after making them to take adequate rest. The subjects were made to lie in supine position with neck extended upon increasing pillow height. The study was conducted using the GE LOGIQ P5 ultrasound system and a linear array probe with frequency range of 6-12 MHz was used. Greyscale ultrasound was performed first to assess thyroid echopattern, as well as to measure thyroid volume. Thyroid volume was calculated as the sum of the volumes of both thyroid lobes; the volume of the isthmus was excluded. The volume was calculated as anteroposterior (AP) dimension x transverse dimension x longitudinal dimension x 0.50 as is measured for any ellipse.

Then, the inferior thyroid artery was found just posterior to the inferior pole of the thyroid gland and spectral Doppler pattern was taken and the values such as the peak systolic velocity (PSV), the end diastolic velocity (EDV), the mean velocity were calculated for the bilateral inferior thyroid arteries. The parameters used for Doppler assessment were pulse repetition frequency (PRF) of 2.7 kHz, the frequency of 7.2 MHz, the wall filter of 76 Hz with Doppler angle <60 degrees.

The observations were tabulated using Microsoft Excel 2010 worksheet. The mean values of all parameters were calculated. The Mann-Whitney U test was used to compare the values between both genders and the values of the parameters in the bilateral thyroid arteries. Student's t test was used as a test of significance at 5% level. Screening test evaluation was carried out with positive/negative outcomes, sensitivity, specificity, positive and negative predictive values and likelihood ratios for positive and negative tests were calculated with the concomitant 95%CIs. Receiver operating characteristic (ROC) analysis of the results was done to determine the appropriate cut-off value of peak systolic velocity to differentiate Graves' disease from thyroiditis.

RESULTS

All patients who participated in this study had suppressed TSH level (0.3-0.006 IU/L) with normal or high free T4 and T3 levels. FNAC was done for all patients as the gold standard test to differentiate Graves' disease and thyroiditis. Supported by the clinical data, 23 patients were found to have Graves' disease and 20 patients were diagnosed as destructive thyroiditis. Difference in age between both groups (P = 0.565) was found to be insignificant.

Comparing volume of the thyroid gland between both groups revealed significantly larger volume in Graves' patients (mean thyroid volume=18.2 +/-4.2 ml) than in patients with thyroiditis (mean thyroid volume= 9.6+/-5.0 ml) with p value = 0.028 (Table 1). On Doppler assessment it was found that values like PSV, EDV and mean velocity was significantly higher in patients with Graves disease than in patients with destructive thyroiditis (P =0.001 in the right inferior thyroid artery and P = 0.001 in the left inferior thyroid artery). 20 out of 23 patients diagnosed as Graves' had an inferior thyroid artery peak systolic velocity greater than 40 cm/s. 17 out of 20 patients with destructive thyroiditis had an inferior thyroid artery PSV less than 40 cm/s. ROC analysis of the results showed that cut-off value of 40-cm/s peak systolic velocity was significant enough to differentiate between Graves' disease and thyroiditis with area under curve 0.910. PSV with cut off of 40 cm/s showed a sensitivity of 86.9% and a specificity of 85.0%, positive predictive value of 87, negative predictive value of 85 and a diagnostic accuracy of 86 in the differential diagnosis of thyrotoxicosis with FNAC supported by clinical data as gold standard (Table2).

Table 1: Various parametres in two groups of patients psv= peak systolic velocity

Parameter	Graves	Hashimotos	P value
Mean age(years)	29.5 +/-7.6	31.2+/-8.1	0.622
Thyroid volume(ml)	18.2+/-4.2	9.6+/-5.0	0.15
Rt PSV	62.3+/-21	23.2+/-8.0	0.001
Lt PSV	58.6+/-19	22.4+/-8	0.001
Mean PSV	60.4+/-20	22.8+/-8	0.001

Table 2: Sensitivity and specificity of PSV values in inferior thyroid artery

Parameter	Estimate	Lower-upper 95% CI
Sensitivity	86.9%	69.7-92.0
Specificity	85.0%	65.4-94.0
Positive predictive value	87%	71.0-91.2
Negative predictive value	85%	62.8-93.5
Diagnostic accuracy	86%	68.0-93.7

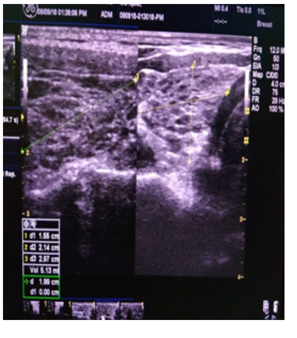
CI= confidence interval

DISCUSSION

Clinical manifestations of thyrotoxicosis in cases of thyroiditis and early or mild Graves' disease may be difficult to differentiate. Although persistence of symptoms and signs in Graves' disease can distinguish it from thyroiditis, it is very important to diagnose the disease early for the proper management. Isotope uptake scan of the thyroid is one of the definitive diagnostic tools, especially when there is clinical confusion between the two conditions. However, limited availability, high cost and contraindications to a radioisotope scan during pregnancy and lactation may restrict its application. Although radioactive iodine is often useful in the diagnosis and treatment of thyrotoxicosis, such tests cannot be performed in many patients because of recent use of iodinated contrast for other diagnostic studies, such as computed tomography (CT) scanning which interfere with the accuracy of radioactive iodine tests. In their study, Phillips et al[13] found that 45% of patients with newly diagnosed thyrotoxicosis had received iodinated contrast within 2 week before endocrinology evaluation; 43% had received iodine for CT and the other 2% for angiography. Alternatively, FNAC can be used as problem solving tool to differentiate the two. However, FNAC of thyroid is invasive with inherent associated complications although minor in nature. In this study, FNAC was used as the definitive investigation to differentiate the two types of thyrotoxicosis supported by clinical findings. PSV in inferior thyroid arteries was evaluated by color Doppler as a parameter to differentiate the types of thyrotoxicosis and compare its sensitivity and specificity to FNAC. Peak systolic, end diastolic and mean velocities of inferior thyroid artery in patients with Graves' disease were significantly higher than patients with thyroiditis[14]. Doppler ultrasonography in our study showed a sensitivity of 86.9% with specificity of 85.0%. These results are comparable to the results of a study carried out by Kurita et al[15] on 75 patients with thyrotoxicosis, which demonstrated that Doppler had a sensitivity of 84% and specificity of 90% in the differential diagnosis of thyrotoxicosis. Hari Kumar et al[16] in 2009 studied 65 patients with thyrotoxicosis and found significantly higher blood flow in inferior thyroid arteries in Graves' than in destructive thyrotoxicosis. He also depicted that color Doppler ultrasonography had a sensitivity of 96% and a specificity of 95% in the differential diagnosis of thyrotoxicosis. Other forms of estimation of thyroid blood flow assessment, like thyroid blood flow area, vascularization index and high-resolution power Doppler, have been used by investigators to provide better differentiation[17-19]. A cut-off value of 40 cm/s was considered as significant in differentiating between Graves' diseases and Hashimotos thyroiditis based on a review of relevant literature[16,20-23]. This cut-off was also in agreement with the results obtained from our study. The different values for sensitivity and specificity obtained from ROC curve justifies this decision.

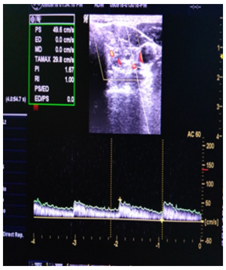
Referring to our study and similar other studies[24-30], inferior thyroid artery PSV values can be considered to be one of the initial investigations that can help in the differentiation of Graves' from Hashimoto's thyroiditis. Color Doppler is a cheap, simple, cost effective and easily available technique with no exposure to ionizing radiation [31-35]. Inferior thyroid artery PSV value is a useful parameter in the differential diagnosis of thyrotoxicosis. It is an acceptable alternative to radioisotope scans, especially when there is a contraindication to nuclear imaging of the thyroid. We recommend measurement of PSV in inferior thyroid arteries by Doppler as an essential part of initial investigations of thyrotoxicosis.

Figures:

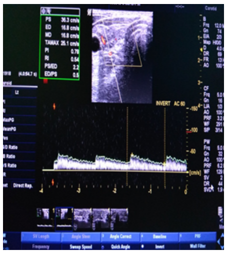


(1a)

(1b)



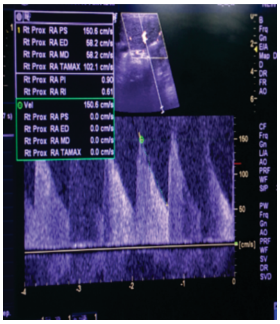
(1c)



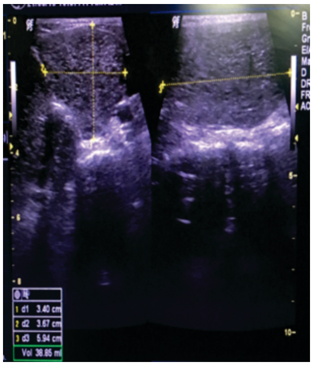
(1d)

Figure 1a and 1b showing volume of left and right lobe of thyroid in a patient with Hashimotos as 5.13 and 4.82 ml respectively.

Figure 1c and 1d showing PSV in right and left ITA in same patient with values of 49.5 and 36.3 cm/s respectively.



(2a)



(2b)

Figure 2a showing markedly increased flow in ITA in a patient with Graves disease with PSV of 150 cm/s.

Figure 2b showing increased thyroid volume in same patient with volume of 38 ml in single lobe of thyroid.

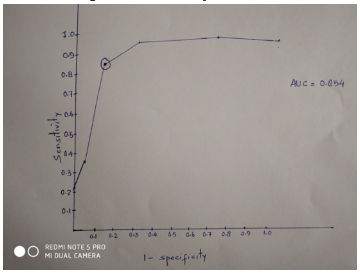


Figure 3: ROC curve showing the most appropriate cut off value of PSV of 40 cm/s with AUC =O.854

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