

ROLE OF DOPPLER EVALUATION OF THYROID GLAND IN DIFFERENTIATING GRAVES' DISEASE FROM OTHER THYROTOXIC STATES

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ABSTRACT

BACKGROUND

Differentiation between thyroiditis induced thyrotoxicosis and Graves' disease is needed for selection of proper therapy. It is often difficult to differentiate between them without performing thyroid scintigraphy. Colour Flow Doppler Sonography (CFDS) is gaining importance for the functional evaluation of the thyroid diseases. The purpose of the study was to determine the value of CFDS for differentiating between thyroiditis induced thyrotoxicosis and Graves' disease.

MATERIALS AND METHODS

Fifty patients with clinical and lab signs of hyperthyroidism were evaluated. Clinical history was taken, and physical examination and thyroid function tests were performed for all patients. Conventional grey scale sonography was done, followed by CFDS. Peak systolic velocity (PSV) measurements were obtained from both inferior thyroid arteries. Results were compared with Technetium 99 scanning which was used as a golden standard. The patients were divided into two groups: 32 cases with Graves' disease and 18 cases with thyroiditis based on thyroid scintigraphy. The patients had suppressed TSH levels and clinical symptoms also supported the diagnosis.

RESULTS

The Peak systolic velocity of right inferior thyroid artery was found to be elevated in patients with Graves' disease than in patients with thyroiditis ($P < 0.001$ in right inferior thyroid artery). It had a sensitivity of 90.6% and a specificity of 88.9% in differentiating the causes of thyrotoxicosis.

CONCLUSION

Peak systolic velocity is an inexpensive, fast, and noninvasive imaging procedure. Hence it will be very useful in the differential diagnosis of thyrotoxicosis, especially when thyroid scintigraphy by radioactive materials is contraindicated in special situations like pregnancy and in places where nuclear imaging is not easily accessible.

KEYWORDS

Graves', Thyroiditis, Scintigraphy.

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BACKGROUND

Thyrotoxicosis also known as toxic diffuse goitre is characterized by elevated serum levels of thyroid hormone. Graves' disease is the most common cause of hyperthyroidism. Lymphocytic thyroiditis, subacute thyroiditis and postpartum thyroiditis are different causes of thyrotoxicosis due to thyroiditis.¹⁻⁵

Ultrasound feature of Graves' disease include diffuse thyroid hypoechogenicity with diffusely increased blood

flow. Colour Flow Doppler has become the first line investigation in the evaluation of thyroid morphology due to its high sensitivity and ease of use.^{6,7} We can get a visual impression of thyroid vascularity and also measure peak systolic, end diastolic and mean velocities in the inferior thyroid arteries using CFDS.⁸⁻¹⁰

The study aims at demonstrating the efficiency of doppler study in differentiating the causes of thyrotoxicosis at time of diagnosis. The study also compares its sensitivity and specificity to technetium thyroid scintigraphy to know if thyroid doppler study can be used as an alternative study in cases of newly detected thyrotoxicosis. The basic principle of CFDS depends on its ability to distinguish between Graves' disease from thyroiditis. As supported by many studies, the Peak systolic velocity (PSV) will be increased in Graves' disease, whereas they will be normal or decreased in the latter.¹¹⁻¹³

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MATERIALS AND METHODS

The Research and Ethics committee of our hospital approved the study and written informed consent was acquired from all patients. The study population consisted of fifty patients attending Endocrinology OPD with thyrotoxicosis during the period from November 2016 to June 2017. Detailed history, clinical examination and lab investigations was done and recorded by a designated person. Patients coming under the exclusion criteria were rejected. Every third person fulfilling the study criteria was selected according to systematic random sampling to undergo ultrasound scan of the thyroid gland. Necessary details including age, lab investigations like thyroid function tests and nuclear imaging results were collected and recorded in the proforma sheet.

They then underwent gray scale imaging and Doppler imaging using ultrasound machine Voluson Pro 730 (General Electric) with high frequency linear probe (8-12 MHz). Using colour Doppler imaging, the superior and inferior thyroid arteries were studied. Blood flow in these vessels was assessed in terms of peak systolic velocity (PSV) and end diastolic velocity (EDV) which were calculated by the USG machine. The obtained values were recorded in the data collection sheet

Data Analysis

Data was entered as continual or categorical variables using software Excel. It has been expressed using bar diagrams, tables and graphs. Data analysis was done using statistical software SPSS 20. Appropriate statistical tests including t test were used. 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.

The McNemar test was applied to compare diagnostic performance of peak systolic velocity with the technetium scan for discriminating between Grave's disease and thyroiditis. 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 levels (0.08-0.005 IU/L). Thyroid scanning by Tcm99 was done for all patients as the gold standard test for differentiation between Graves' disease and thyroiditis. Based on the thyroid scan, thirty-two patients had Graves' disease and eighteen patients had thyroiditis. Among the total of 50 subjects, twenty-three subjects (46%) came under the age group of 30-45 years; fifteen subjects belonged to 16-30 years & twelve of the subjects were above 45 years.

Thyroid scanning by Tcm99 was done for all patients as the gold standard test for differentiation between Graves' disease and thyroiditis. Among the 50 patients studied, 32 patients (64%) showed increased uptake in Technetium scan suggestive of Graves' disease. 18 patients (36%)

showed normal or decreased uptake suggestive of thyroiditis. The peak systolic velocity in right inferior thyroid artery ranged from 15.8 to 67.8 cm/s with a mean PSV of 39.64 cm/s and standard deviation of 14.5. The peak systolic velocity in left inferior thyroid artery ranged from 15 to 67.2 cm/s with a mean of 39.54 and standard deviation of 14.35. The End Diastolic Velocity (EDV) in right inferior thyroid artery ranged between 6.7 to 20.3 with a mean of 15.21 and SD of 4.22. The EDV in left inferior thyroid artery ranged between 7.2 to 20.3 with mean of 15.19 and SD of 4.23. The mean inferior thyroid artery EDV in Graves' disease was 18.18 with SD of 1.27. The mean EDV in thyroiditis was 9.94 and SD was 1.59. The p value obtained was <0.001 which shows that there is significant difference between EDV values of Graves' disease and thyroiditis. Thyroid blood flow, as assessed by colour flow imaging and Doppler spectral analysis of the inferior thyroid arteries, was significantly higher in patients with Graves' disease than in patients with thyroiditis. End diastolic velocity was also significantly higher in Graves' patients than in patients with thyroiditis.

Receiver Operating Characteristic curve was plotted using the values of Peak systolic velocity. The area under the curve (AUC) was 0.976 that signifies that this is an excellent test. From the ROC, the reliable cut off for differentiating Graves' disease from thyroiditis was 36.1 cm/s. 29 out of 32 patients diagnosed as Graves' disease by Tcm99 scan, had an inferior thyroid artery flow velocity greater than 36.1 cm/s. Diagnosis of Graves' disease in the remaining three patients was established by increased uptake on the thyroid scan and clinical findings that favour Graves' disease. Sixteen out of 18 patients with Hashimoto thyroiditis, had an inferior thyroid artery flow less than 36.1 cm/s and low Tcm 99 uptake. Two patients were diagnosed as thyroiditis due to low Tcm99 uptake and by its clinical picture and follow up of patient.

The Kappa value was 0.913 which shows that there is strong agreement between the Tc99 scan and PSV values of ITA (Table 1). The McNemar test result was significant which indicates that the two diagnostic tests (technetium scan and colour Doppler) are not significantly different with respect to sensitivity. CFD showed a sensitivity of 90.6% and a specificity of 88.9%, positive predictive value of 90.6%, negative predictive value of 88.9% and a diagnostic accuracy of 90 % in the differential diagnosis of thyrotoxicosis compared to thyroid scanning by Tcm99 pertechnetate (Table 2).

The sensitivity of Colour Doppler Flow Study was 90.6%. There was no significant difference between the sensitivity of Colour Doppler Flow Study and Technetium scan in differentiating Graves' disease from Thyroiditis.

PSV	Tc99				Kappa	p Value
	Increased		Normal / Decreased			
	N	%	N	%		
>36.1	29	90.6	2	11.1	.913	1.000
<36.1	3	9.3	16	88.9		
Total	32	100	18	100		
Table 1. Comparison of Tc99 Scan Uptake with Right Inferior Thyroid Artery PSV Cut Off Value						

Parameters	Estimate
Sensitivity	90.6
Specificity	88.9
Positive Predictive Value	90.6
Negative Predictive Value	88.9
Diagnostic Accuracy	90

Table 2. Statistical Indices for Colour Flow Doppler Study in Differentiating Graves' Disease from Thyroiditis Compared to Gold Standard

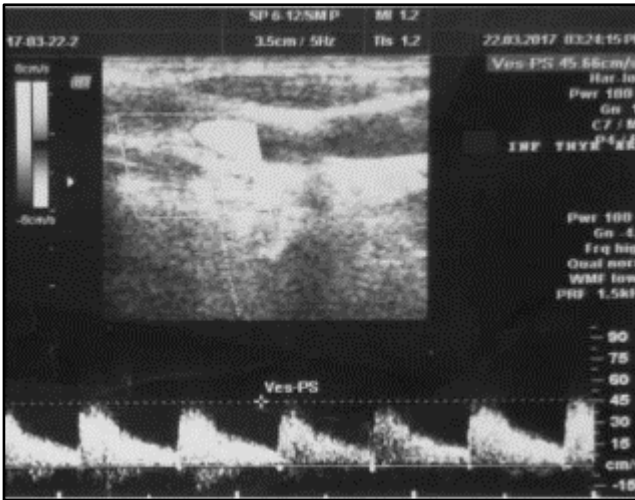


Figure 1. Ultrasound Measurement of PSV of Right ITA in a Patient with Graves' Disease

PSV of inferior thyroid artery in this patient is 45 cm/s and was later confirmed as having Graves' disease with Tc99 scan.

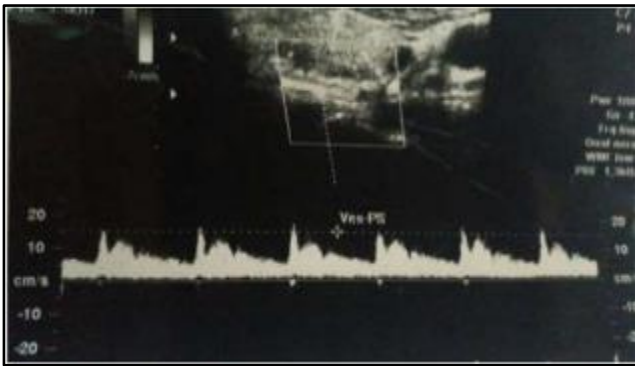


Figure 2. Ultrasound Measurement of PSV of Right ITA in a Patient with Thyroiditis

PSV of right inferior thyroid artery is 15 cm/s, which later confirmed as having thyroiditis with Tc99 scan.

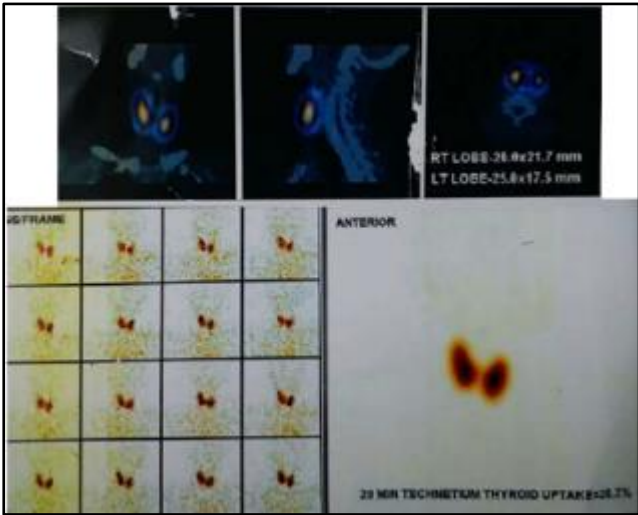


Figure 3. Tc99 Scan of a Patient with Graves' Disease

Diffuse increased uptake is seen.

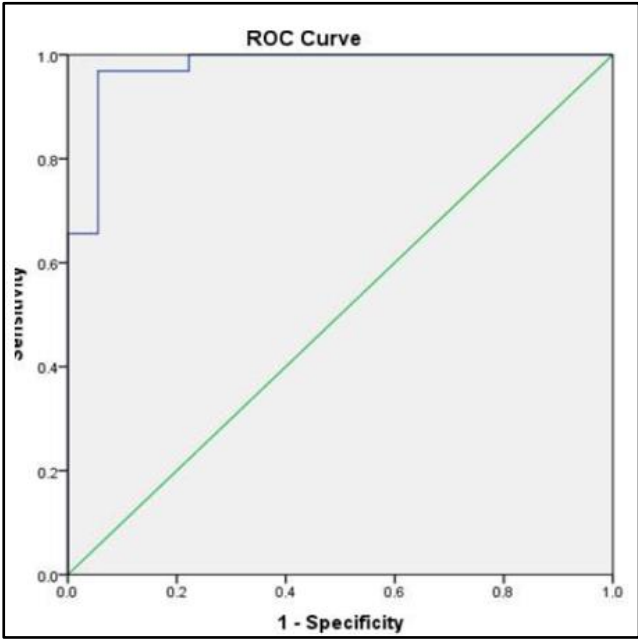


Figure 4. ROC Curve

DISCUSSION

It is difficult to differentiate the signs and symptoms of thyrotoxicosis in cases of thyroiditis and early or mild Graves' disease. But for proper management of the patients, it depends on the correct diagnosis. In such condition, Isotope uptake scan of the thyroid is one of the definitive diagnostic tools. But there are many disadvantages like limited availability, high cost and contraindications to a radioisotope scan during pregnancy and lactation that can limit its application. In our study, Tcm99 pertechnetate was used as the definitive radiological investigation to differentiate the two types of thyrotoxicosis. Peak systolic velocity of right inferior thyroid artery evaluated by colour Doppler was used as a parameter to differentiate the types of thyrotoxicosis. Its sensitivity and specificity were then compared to Tcm99 thyroid uptake. Peak systolic velocities of inferior thyroid

artery in patients with Graves' disease were significantly higher than patients with thyroiditis.¹⁴

In our study, CFD ultrasonography yielded a sensitivity of 90.6% with specificity of 88.9%. These results were comparable to the results of the study conducted by Kurita et al¹⁵ which was performed on 75 patients with thyrotoxicosis, where the outcome demonstrated that CFD ultrasonography had a sensitivity of 84% and specificity of 90% in the differential diagnosis of thyrotoxicosis. On the other hand, Hari Kumar et al¹⁶ in 2009, studied 65 patients with thyrotoxicosis, where he found significantly higher blood flow in inferior thyroid arteries in Graves' disease than in destructive thyrotoxicosis. The study also demonstrated that CFD ultrasonography had a sensitivity of 95.9% and a specificity of 95% in the differential diagnosis of thyrotoxicosis. Donkol et al¹⁷ studied 26 patients with thyrotoxicosis. They found that CFD ultrasonography had a sensitivity of 88.9% and specificity of 87.5% in the differential diagnosis of thyrotoxicosis. Ghany et al¹⁸ studied thirty patients with thyrotoxicosis and found that colour flow Doppler study could differentiate untreated Graves' disease from thyroiditis with a sensitivity of 96.6% and specificity of 96.6%.

There are other methods for evaluating thyroid blood flow, like thyroid blood flow area, vascularization index and high-resolution power Doppler, which can be used to provide better differentiation.

Based on ROC curve of different values of sensitivity and specificity from our own data, a cut-off value of 36.1 cm/s was considered in differentiation between Graves' disease from thyroiditis. Results from a review of relevant literatures also helped in determining the cut off value.¹⁹⁻²³

Based on this study and similar various studies, Colour Doppler ultrasonography of the thyroid gland can be of great help as an initial investigation in the differentiation of Graves' disease and Hashimoto's thyroiditis. Colour Doppler is also cheap with no risk of ionizing radiation exposure.

CONCLUSION

Colour Flow Doppler Study could provide important information about the functional state of the thyroid gland and could be used in all endocrinology departments as a part of clinical evaluation of thyrotoxic patients. It can help in differentiation of Graves' disease, nontoxic diffuse goiter, and Hashimoto's thyroiditis. Colour Flow Doppler Sonography could avoid scintigraphy in a substantial number of thyrotoxic patients during the routine clinical work-up. It is an acceptable alternative to radioisotope scans, especially when there is contraindication to nuclear imaging of the thyroid. We recommend measurement of thyroid blood flow by Doppler as an essential part of initial investigations of thyrotoxicosis.

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