Section: Radiodiagnosis

Original Research Article

ROLE OF SUPERIOR THYROID ARTERY DOPPLER IN DIFFERENTIATING GRAVES DISEASE AND THYROIDITIS

T. Ramya[1], N. Suriyaprakash[2], S. Usha[3]

[1]Assistant Professor, Department of Radiodiagnosis, Government Tiruvarur Medical College, Tamil Nadu, India.
[2]Assistant Professor, Department of Radiodiagnosis, Government Medical College, Tiruppur, Tamil Nadu, India.
[3]Senior Resident, Department of Radiodiagnosis, Stanley Medical College, Chennai, India.

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Corresponding Author:
Dr. N. Suriyaprakash,
Email: cbesuriya@gmail.com

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Abstract

Background: Thyrotoxicosis, characterized by increased thyroid hormone levels, includes conditions like hyperthyroidism, which results from an overactive thyroid gland. Distinguishing between hyperthyroidism and thyrotoxicosis without hyperfunction is critical for appropriate treatment. Graves' disease and destructive thyroiditis share clinical features, necessitating precise diagnostic methods. **Materials and Methods:** A cross-sectional study was conducted in South India from August 2022 to August 2023. A total of 56 newly diagnosed thyrotoxic patients were included. Thyroid ultrasound, including Color Doppler, was performed to assess peak systolic velocity (PSV) and resistive indices (RI) in the superior thyroid artery (STA). The study aimed to determine cut-off values for PSV and RI to differentiate between Graves' disease and thyroiditis. **Result:** Of the 56 participants, 9 (16.1%) had Graves' disease, and 47 (83.9%) had thyroiditis. Mean PSV values were significantly higher in Graves' disease (66.00 ± 11.38) compared to thyroiditis (29.15 ± 11.51), with statistical significance ($p < 0.05$). Mean RI values were also significantly different, with Graves' disease at 0.77 ± 0.06 and thyroiditis at 0.66 ± 0.11 ($p < 0.05$). Moreover, thyroid volumes and end diastolic velocity (EDV) showed significant differences between the two groups ($p < 0.05$). The Receiver Operating Characteristic (ROC) curve analysis indicated that a PSV cut-off value of 49.4 cm/s had a sensitivity of 100% and a specificity of 95.74% for diagnosing Graves' disease. For RI, the cut-off value was 0.68, with a sensitivity of 100% and a specificity of 91.7%. These findings suggest that both PSV and RI are effective diagnostic indicators for distinguishing Graves' disease from thyroiditis. **Conclusion:** Results showed that mean PSV and RI in Graves' disease significantly exceeded those in thyroiditis. Cut-off values of PSV > 49.4 cm/s and RI > 0.68 demonstrated high sensitivity and specificity in diagnosing Graves' disease. These parameters can serve as valuable tools for distinguishing between these two conditions, offering a cost-effective and widely available alternative to more expensive diagnostic methods.

INTRODUCTION

The metabolic implications of increased thyroid hormone levels are the hallmarks of thyrotoxicosis. The terms "thyrotoxicosis" and "hyperthyroidism" are not interchangeable. A particular subclass of thyrotoxic diseases known as hyperthyoidism is brought on by the overactive thyroid gland.[1] The most frequent causes of hyperthyroidism are toxic multinodular goitre, toxic adenoma, and Graves' disease. On the other hand, thyrotoxicosis without actual hyperfunctioning of the gland can also result from thyroid gland inflammation (destructive thyroiditis) with release of stored thyroid hormones or excessive exogenous thyroid hormone preparation consumption (thyrotoxicosis factitia).[2]

Diffuse thyroid illness and thyrotoxicosis can both be caused by Graves' disease and destructive thyroiditis.[3] It is crucial to distinguish between these two illnesses because their treatment plans and prognoses are entirely different. Antithyroid medications, radioiodine therapy, and thyroidectomies are a few of the treatment options for Graves' disease.[4] On the other hand, nonsteroidal anti-inflammatory medications (NSAIDs) and blockers are typically used in the conservative management of destructive thyroiditis. Goitre, ophthalmopathy, and dermopathy make up the

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traditional Graves' disease triad. But without these results, it might be very difficult clinically to distinguish between destructive thyroiditis and Graves' illness.[5]

The gold-standard diagnostic to distinguish between these two conditions is thyroid scintigraphy using technetium 99 (Tc-99m) pertechnetate or iodine-123 radioisotope. Nuclear imaging is nevertheless expensive and not recommended for use when pregnant or nursing.[6] According to a recent meta-analysis of PSV-STA's usefulness in separating Graves' illness from destructive thyroiditis, the test has an 86% sensitivity and 93% specificity in this area.[2] The diagnostic accuracy of these methods has been compared to findings from nuclear scans such radioactive iodine uptake or Tc-99m pertechnetate in previous research analyzing the function of color Doppler flow parameters in the diagnosis of thyrotoxicosis.[3,4]

Thyrotropin (thyroid stimulating hormone [TSH]) receptor antibody levels can also be measured because they are directly linked to the diagnosis of Graves' illness. However, in environments with little resources, these techniques are not generally used.[1]

The evaluation of thyroid problems can benefit greatly from the use of high-resolution ultrasonography as a diagnostic tool. It is the most used non-invasive, low-cost radiographic approach for the diagnosis of thyroid disorders. Blood flow and tissue vascularization can be assessed using Color Doppler sonography.[2]

Both qualitative (visual examination of thyroid vascularity) and quantitative (peak systolic velocity [PSV] of superior and inferior thyroid arteries) assessment are included in the evaluation.3 Autoimmune thyroiditis is characterized by thyroid hypoechogenicity, and thyroiditis and Graves' disease share this echographic pattern. When comparing the thyroid blood flow in thyroiditis and Graves' disease, Doppler ultrasound can be utilized to distinguish between these disorders.[1,2,5,6] As a result, it can offer important details on the functional health of the thyroid underneath. The benefit of ultrasound is that it can reveal thyroid nodules that were previously unidentified and may have been cancerous.[6,7]

We intended to conduct this study to produce cut-offs that might be more effectively used in our population because earlier studies had been conducted in many ethnic populations and had offered various cut-offs with differing sensitivity and specificity. This study looked into how to distinguish between Graves' illness and thyroiditis using PSV of the superior thyroid artery (STA), also known as PSV-STA.

Aim and Objectives:

The aim of the study is to assess the Peak Systolic Velocity (PSV) and Resistive Indices (RI) of superior thyroid artery in differentiating Graves' disease and thyroiditis. The objective of the study is to evaluate the differences in Peak Systolic Velocity (PSV) and Resistive Indices (RI) of superior thyroid artery in Graves' disease and thyroiditis. The secondary objective is to determine a cut off value for Peak Systolic Velocity (PSV) and Resistive Indices (RI) of superior thyroid artery in differentiating Graves' disease and thyroiditis.

MATERIALS AND METHODS

A cross sectional study was conducted in a tertiary care hospital in South India over a period of one year from August 2022 to August 2023. Ethical permission to conduct the study was obtained from Institutional Ethical Committee. 56 newly diagnosed thyrotoxic patients without medications for hyperthyroidism were included in the study. Patients with toxic nodular goitre, multinodular goitre, drug induced thyrotoxicosis and previous history of thyroid surgery were excluded. Written informed consent was obtained from all the participants.

A radiologist who was blinded to the patients' initial diagnoses undertook extensive ultrasound examination of the thyroid gland on each patient. By using a 5 to 12 MHz linear high frequency transducer in a high end ultrasound machine, the thyroid gland was examined using both grayscale B mode imaging and Color Doppler. On a gray scale, thyroid metrics such gland echogenicity and volume were assessed. The echo pattern of a healthy thyroid gland was uniform on a medium-gray scale and was more echogenic than the muscles around it. When the echo density was lower than or equivalent to the muscles of the prethyroid state, the thyroid was considered to have hypoechoic echogenicity.

After measuring both lobes' maximum longitudinal (L), anteroposterior (AP), and transverse (T) axes, the thyroid gland's volume was calculated using the ellipsoid formula (V = L AP T /6). The gland's total volume was calculated by adding the volumes of the two lobes. The same basic operating parameters (PRF 700 Hz and WF 50 Hz, velocity scale 5.0 cm/s, Gain 65%) were used in each case to achieve Color Doppler sonography. By having an opposing flow direction from the nearby CCA in transverse scanning, the STA can be distinguished just medial to the CCA at the top pole of the thyroid gland.

Doppler testing was done at the location where the STA crosses the upper pole of the thyroid gland (just before the artery enters the thyroid parenchyma). After accurate angle correction, PSV-STA was measured on each side. The Doppler angle was maintained at or below 60 degrees, and the angle correction cursor was parallel to the flow direction. PSV was estimated within the axis of a straight stretch of vessel with the sampling volume set to 3 mm at the vessel's center. The average of the PSV for the right and left STA was referred to as mean PSV-STA. Similar calculations were made for each artery's end diastolic velocity (EDV), pulsatility index (PI), and resistive index (RI). Additionally, PSV and EDV of CCA were computed.

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RESULTS

Of the 56 participants, 47 participants (83.9%) were females and 9 participants (16.1%) were males. The mean age of the study participants was 36.34 ± 12.33 years of age. 16 participants (28.6%) were from 41 to 50 years of age, 16 participants (28.6%) were from 21 to 30 years of age, 13 participants (23.2%) were from 31 to 40 years of age, 6 participants (10.7%) were from 51 to 60 years of age, 4 participants (7.1%) were from 11 to 20 years of age, 1 participant (1.8%) was from 61 to 70 years of age. [Table 1]

Of the 56 patients, 9 participants (16.1%) had Graves disease and 47 participants (83.9%) had thyroiditis. [Figure 1]

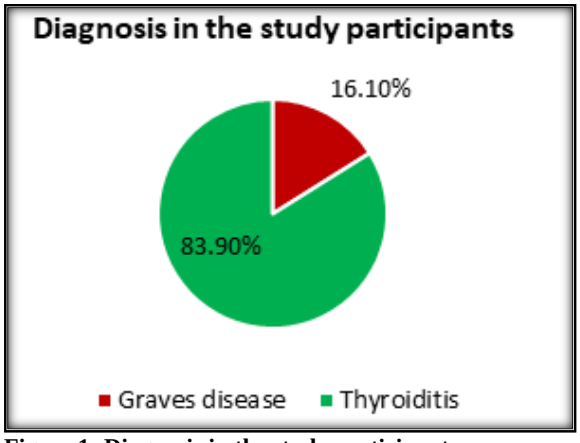

Figure 1: Diagnosis in the study participants

The mean PSV values in Graves disease was 66.00 ± 11.38 and in thyroiditis was 29.15 ± 11.51 which was statistically significant by independent t test. ($p < 0.05$) The mean RI values in Graves disease was 0.77 ± 0.06 and in thyroiditis was 0.66 ± 0.11 which was statistically significant by independent t test. ($p < 0.05$) The mean right thyroid volume (cc) values in Graves disease was 13.65 ± 4.80 and in thyroiditis was 6.41 ± 2.22 which was statistically significant by independent t test. ($p < 0.05$) The mean left thyroid volume (cc) values in Graves disease was 13.36 ± 5.40 and in thyroiditis was 6.53 ± 3.11 which was statistically significant by independent t test. ($p < 0.05$) The mean EDV values in Graves disease was 12.69 ± 4.79 and in thyroiditis was 9.19 ± 3.78 which was statistically significant by independent t test. ($p < 0.05$) [Table 2].

The Receiver Operating Characteristic (ROC) curve analysis of PSV values for Graves disease showed cut-off threshold value as 49.4 (95% C.I = 48.5-55.6), with a sensitivity of 100%, and a specificity of 95.74%. The area under the curve (AUC) was 0.991 (95% C.I = 0.919-1.000) with a statistically significant p value ($p < 0.001$). [Table 3 & Figure 2]

The Receiver Operating Characteristic (ROC) curve analysis of RI values for Graves disease showed cut-off threshold value as 0.68 (95% C.I = 0.64-0.7), with a sensitivity of 100%, and a specificity of 91.7%. The area under the curve (AUC) was 0.804 (95% C.I = 0.676-0.898) with a statistically significant p value ($p < 0.001$). [Table 3 & Figure 3]

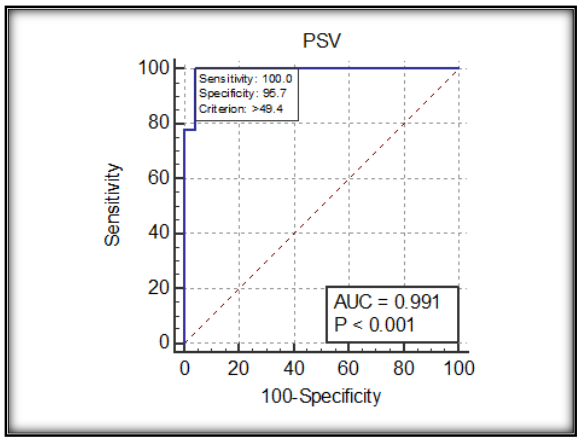

Figure 2. ROC curve for PSV for Graves disease

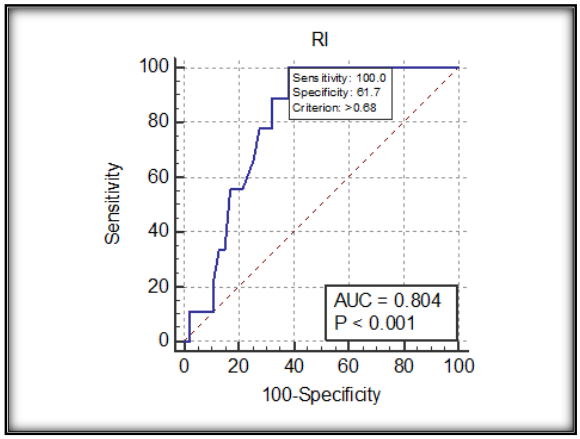

Figure 3: ROC curve for RI for Graves disease

Table 1: Sociodemographic details of the study participants

Sociodemographic details		Frequency	Percentage
Age group (in years)	11 to 20	4	7.1
	21 to 30	16	28.6
	31 to 40	13	23.2
	41 to 50	16	28.6
	51 to 60	6	10.7
	61 to 70	1	1.8
Gender	Male	9	16.1
	Female	47	83.9

Table 2: Mean Color doppler values in Graves disease and Thyroiditis

	Graves disease	Thyroiditis	Independent t test value	P value
PSV	66.00 ± 11.38	29.15 ± 11.51	8.81	< 0.001*
RI	0.77 ± 0.06	0.66 ± 0.11	2.91	0.005*

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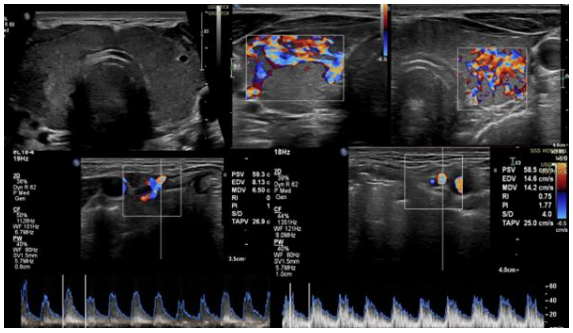
Thyroid volume (cc) Right	13.65 ± 4.80	6.41 ± 2.22	3.85	< 0.001*
Thyroid volume (cc) Left	13.36 ± 5.40	6.53 ± 3.11	2.414	0.01*
EDV	12.69 ± 4.79	9.19 ± 3.78	2.42	0.01*

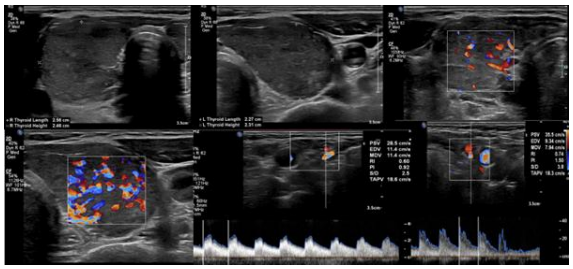
*- statistically significant by independent t test

Table 3: ROC curve values of PSV and RI for Graves disease

	Cut off for Graves disease (at 95% CI)	AUC (95% CI)	Youden index	Sensitivity % (95% CI)	Specificity % (95% CI)	+LR	-LR
PSV	> 49.4 (48.5-55.6)	0.991 (0.919-1.000)	0.957	100.00 (66.4-100.0)	95.74 (85.5-99.5)	23.50	0.00
RI	> 0.68 (0.64 - 0.7)	0.804 (0.676-0.898)	0.6170	100.00 (66.4-100.0)	61.70 (46.4-75.5)	2.61	0.18



Case 1: Graves Disease



Case 2 - Thyroiditis

DISCUSSION

In our study of the 56 patients, 9 participants (16.1%) had Graves' disease and 47 participants (83.9%) had thyroiditis. The mean PSV values in Graves disease was 66.00 ± 11.38 and in thyroiditis was 29.15 ± 11.51 which was statistically significant by independent t test. ($p < 0.05$) The mean RI values in Graves disease was 0.77 ± 0.06 and in thyroiditis was 0.66 ± 0.11 which was statistically significant by independent t test. ($p < 0.05$)

Similar to our study, Sarangi et al reported that people with Graves disease had a mean PSV-STA that was considerably higher than people with thyroiditis.1According to Uchida et al., patients with destructive thyroiditis (28 ± 12.84 cm/sec) had considerably lower PSV-STA than those with Graves disease (78.48 ± 36.28 cm/sec).[8] Similar findings were reported by Karakas et al,[9] Zhao et al,[10] Chen et al,[11] Kim et al,[12] Hiraiwa et al,[13] Sundaram et al14 PSV-STA was discovered by Sarangi et al. to favorably correlate with FT3, FT4, and thyroid volume in patients with Graves' illness.[1] PSV-STA was found to significantly positively correlate with thyroid hormones and volume in untreated Graves' disease patients, according to Hiraiwa et al.[13] Uchida et al. reported conflicting findings, finding that PSV-STA positively linked with FT3 alone, but not FT4 or thyroid volume. There is a positive link between these two characteristics, according to certain studies.[13]

In our study the optimum cut off value for mean STA-PSC was 49.4 (95% CI = 48.5 to 55.6) cm/s. In our study the optimum cut off value for mean RI was 0.68 (95% CI = 0.64 to 0.7). Zhao et al. observed that a mean STA-PSV of 50.5 cm/s was effective in separating Graves' disease from thyroiditis, with 81.04% sensitivity and 96.08% specificity.10 According to Sarangi et al., the ideal cut-off value for mean STA-PSV was 54.3 cm/s, which had an 82.9% sensitivity and 86.2% specificity. A mean PSV-STA value greater than 84.92 cm/s was 100% specific for Graves' illness, according to Sarangi et al.[1]

Another study by Chen et al. found that the best cut-off for mean PSV-STA in detecting Graves' illness in the Chinese population was 45.25 cm/s (80.4% sensitive and 81.4% specific).[11] The diagnostic cut-offs for PSV-STA for separating Graves' illness from thyroiditis were 45 and 43 cm/s in two earlier studies from the Japanese population.[8,13] This variation in cutoffs can be the result of racial or ethnic variances. In a prospective cohort research conducted in India, Sundarram et al. found that mean PSV-STA was statistically higher in Graves' disease (54.09 ± 4.67 cm/s) than thyroiditis (28.92 ± 4.39 cm/s) in 120 newly diagnosed thyrotoxicosis patients (54 with Graves' disease and 66 with thyroiditis).[14] They did not, however, establish a cut-off value for the mean PSV-STA to distinguish between thyroiditis and Graves' disease.

A meta-analysis on the effectiveness of PSV-STA in separating Graves' disease from thyroiditis has been written by Peng et al. The authors came to the conclusion that PSV-STA was a relevant indicator after including 11 research in their study. They demonstrated that PSV-STA could discriminate between destructive thyroiditis and Graves' disease with a pooled sensitivity of 0.86 (95% confidence interval [CI]: 0.80-0.90) and a pooled specificity of 0.93 (95% CI: 0.86-0.97).2 In their cohort of patients, Sarangi et al. observed that PSV-STA greater than greater than 84.93 cm/s was 100% specific for the diagnosis of Graves' disease.[1] Karakas et al.'s conclusion that a value of more than 87 cm/s was 100% specific for the diagnosis of Graves' disease is consistent with our findings.[9]

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Additionally, we have demonstrated that mean PSV-STA and mean RI both considerably improved on the capacity to distinguish between the two circumstances. According to Uchida et al. and Zhao et al., who have similar findings to ours, STA-PSV is a substantially superior parameter than FT3/FT4 ratio for the differential diagnosis of thyrotoxicosis.[8,10]

According to a meta-analysis that summarized the diagnostic efficacy of TRAb, the third-generation TRAb assays' pooled sensitivity and specificity values are 98.3 and 99.2%, respectively. Patients who are TRAb positive are more likely to have Graves' disease than those who are TRAb negative by a factor of 1,367 to 3,420.[15]

Although highly helpful, TRAb tests are expensive and not frequently accessible. Nuclear imaging is expensive and not advised during pregnancy or lactation, despite being the gold-standard test. Color Doppler ultrasound is a more accessible, available, and affordable diagnostic technology than the previous two ones.

CONCLUSION

The mean PSV-STA and mean RI in Graves' disease is significantly higher than thyroiditis. In our cohort, mean STA-PSV >49.4 cm/s and mean RI > 0.68 had a good sensitivity and specificity in diagnosing Graves' disease and, hence, serve as good diagnostic tool in differentiation between these two conditions.

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