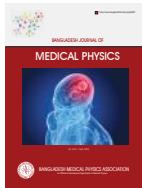




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# Evaluation of Superior Thyroid Artery Peak Systolic Velocity and Blood Flow Volume as Diagnostic Markers in Graves' Disease

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## ABSTRACT

Graves' disease (GD) accounts for the majority of hyperthyroidism cases worldwide and remains a major diagnostic challenge in settings with limited access to nuclear imaging. Although thyroid-stimulating hormone receptor antibody (TRAb) assay and thyroid scintigraphy are considered diagnostic standards, scintigraphy exposes patients to radiation, is not universally available, and is unsuitable in pregnancy. Color Doppler ultrasonography (CDU) offers a real-time, safe, and accessible alternative for assessing thyroid vascularity through Peak Systolic Velocity (PSV) and Blood Flow Volume (BFV) of the superior thyroid artery (STA). To evaluate the diagnostic accuracy of PSV and BFV of the STA measured by CDU compared with thyroid scintigraphy in TRAb-positive thyrotoxic patients and to determine optimal cut-off values for these indices. This cross-sectional study was conducted at the National Institute of Nuclear Medicine & Allied Sciences (NINMAS), Dhaka, from July 2023 to July 2024. A total of 90 TRAb-positive thyrotoxic patients (40 males, 50 females; mean age  $42.9 \pm 12.6$  years) were included. All patients underwent thyroid scintigraphy with uptake and CDU evaluation of PSV and BFV of the STA. Statistical analysis included independent t-tests and receiver operating characteristic (ROC) curve analysis to determine cut-off values, sensitivity, specificity, predictive values, and diagnostic accuracy. Thyroid scintigraphy confirmed GD in 75 patients (83.3%) and excluded it in 15 (16.7%). Mean PSV ( $78.6 \pm 12.7$  cm/s) and BFV ( $236.0 \pm 54.4$  ml/min) were significantly higher in GD compared with non-GD patients ( $p < 0.05$ ). ROC analysis identified cut-off values of 71 cm/s for PSV and 186 ml/min for BFV. PSV demonstrated sensitivity 72.0%, specificity 66.7%, positive predictive value (PPV) 91.5%, and accuracy 71.1%. BFV showed sensitivity 74.7%, specificity 53.3%, PPV 88.9%, and accuracy 71.1%. CDU-derived PSV and BFV of the STA significantly correlate with scintigraphy findings in GD. Given its non-invasiveness, accessibility, and lack of radiation hazard, CDU—particularly BFV—may serve as a reliable alternative diagnostic modality for Graves' disease.

## 1. Introduction

Thyroid scintigraphy, often combined with radioactive iodine uptake (RAIU), is considered one of the most accurate diagnostic tools for differentiating the causes of thyrotoxicosis, including Graves' disease, toxic multinodular goiter, and thyroiditis [1]. It provides functional information on thyroid tissue activity and tracer distribution, enabling distinction between hyperfunctioning and hypo-functioning conditions. However, its clinical application is limited by several factors. Availability is restricted in many healthcare settings, particularly in low- and middle-income countries where nuclear medicine facilities are concentrated in

tertiary centers. Furthermore, the procedure involves exposure to ionizing radiation, which is a significant limitation for younger patients, pregnant women, and lactating mothers [1,2]. Radioisotope use is contraindicated in specific clinical scenarios, and repeated studies are often impractical. These limitations underscore the need for alternative diagnostic methods that are both safe and widely accessible.

Color Doppler ultrasonography (CDU) has emerged as a promising, non-invasive, and widely available modality for evaluating thyroid vascularity and hemodynamics. CDU provides both qualitative and quantitative

assessments. Qualitative evaluation includes vascular patterns such as the characteristic “thyroid inferno” seen in Graves’ disease, reflecting marked hypervascularization [3]. Quantitative parameters include peak systolic velocity (PSV) and blood flow volume (BFV) in the superior and inferior thyroid arteries (4), which serve as objective markers to distinguish Graves’ disease from other causes of thyrotoxicosis.

The advantages of CDU are manifold: it is safe, real-time, operator-friendly, free of ionizing radiation, and can be performed during routine thyroid ultrasonography examinations. This makes CDU particularly useful for children, pregnant women, and patients requiring repeated assessments [5-7]. Among the Doppler indices, PSV has been extensively studied and shown to correlate strongly with Graves’ disease [8-10]. However, PSV is operator-dependent and influenced by technical factors such as probe angle, positioning, and respiratory variation. In contrast, BSV is less affected by these factors and provides a more stable and reproducible parameter [7,11]. Recent studies have suggested that BSV may have equal or superior sensitivity to PSV in differentiating Graves’ disease from other thyrotoxic conditions [7-8].

Several investigators have demonstrated the diagnostic reliability of CDU. Sarangi et al. [1] emphasized its dual role in qualitative and quantitative vascular assessment, while Bahn RS et al. [6] and others [12-13] reported significantly higher PSV values in Graves’ disease compared with toxic nodular goiter, with sensitivity exceeding 90% when benchmarked against scintigraphy. Likewise, Peng et al. [2], in a meta-analysis, reported that STA-PSV and BSV measurements achieved sensitivities ranging from 80% to 96%, reinforcing CDU as a valuable adjunct or alternative to scintigraphy.

Therefore, the present study aimed to evaluate the diagnostic accuracy of PSV and BSV of the superior thyroid artery (STA) measured by CDU, in comparison with thyroid scintigraphy, for the diagnosis of Graves’ disease among TRAb-positive patients. Furthermore, we sought to determine the optimal cut-off values of PSV and BSV in biochemically confirmed thyrotoxicosis.

## 2. Method and Materials

This cross-sectional observational study was conducted at the NINMAS, Dhaka, between July 2023 and July 2024. The research was carried out in compliance with the

Declaration of Helsinki (2013 revision). Ethical clearance was obtained from the Medical Research Ethics Committee (MREC) of NINMAS and all participants provided written informed consent prior to enrollment. For patients unable to provide consent independently, consent was obtained from legally authorized representatives. All clinical, imaging, and personal data were anonymized and stored in password-protected electronic files accessible only to the research team. Patient identifiers were removed during analysis to ensure confidentiality and data integrity.

### 2.1 Study Population

A total of 90 consecutive patients with biochemically confirmed thyrotoxicosis and positive TSH receptor antibody (TRAb) results were enrolled. All patients were referred to NINMAS for diagnostic evaluation of hyperthyroidism. Exclusion criteria included pregnancy, prior thyroid surgery, history of radioiodine therapy, and contraindications to Doppler ultrasonography.

### 2.2 Demographic and Clinical Data

Baseline demographic and clinical variables, including age, sex, and duration of symptoms, were recorded systematically. The study cohort included 40 males and 50 females, aged 20–75 years. Data were collected using a standardized proforma.

### 2.3 Thyroid Scintigraphy

All participants underwent thyroid scintigraphy with uptake studies, which served as the reference standard for diagnosis. Scintigraphy images were reviewed by two independent nuclear medicine specialists who categorized results as either Graves’ disease or non-Graves’ thyrotoxicosis, based on tracer distribution and uptake patterns.

### 2.4 Color Doppler Ultrasonography (CDU)

Thyroid gray-scale ultrasonography and CDU were performed using a high-frequency linear transducer (7–12 MHz). The superior thyroid artery (STA) was identified bilaterally. Doppler parameters were assessed, including, Peak Systolic Velocity (PSV, cm/s) & Blood Flow Volume (BFV, ml/min). To minimize measurement variability, the Doppler angle was maintained below 60°, and each measurement was repeated three times. The mean of the three readings was used for analysis. CDU examinations were performed by a single experienced nuclear medicine

physician to enhance consistency and reduce inter-observer variability.

## 2.5 Statistical Analysis

All data were entered into a statistical software package for analysis. Continuous variables were expressed as mean  $\pm$  standard deviation (SD). Comparisons between groups (Graves' vs. non-Graves' disease) were performed using unpaired Student's t-tests. ROC curve analysis was applied to determine the optimal cut-off values of PSV and BFV for discriminating Graves' disease from non-Graves' thyrotoxicosis. Diagnostic performance indices—including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy—were calculated. A p-value  $<0.05$  was considered statistically significant.

## 3. Results and Discussion

A total of 90 TRAb-positive patients with biochemical evidence of thyrotoxicosis were included in this study. The mean age of the study population was  $42.9 \pm 12.6$  years (range 20–75 years). Of these, 40 (44.4%) were male and 50 (55.6%) were female, yielding a male-to-female ratio of approximately 1:1.3. Almost half of the patients (54.4%) were younger than 40 years, while 45.6% were aged 40 years and above, indicating that Graves' disease affected a relatively younger age group. Table 1 shown this result.

**Table-1:** Age and Gender distribution of the study patients (n=90)

Variables	Frequency	Percentage (%)
Age (years)		
<40	49	54.4
$\geq 40$	41	45.6
Total	90	100.0
Mean $\pm$ SD	$42.9 \pm 12.6$	
Gender		
Male	40	44.4
Female	50	55.6
Total	90	100.0
Male: Female ratio	1: 1.3	

## 3.1 Thyroid Scintigraphy Findings

Among the 90 TRAb-positive patients, thyroid scintigraphy confirmed Graves' disease in 75 cases

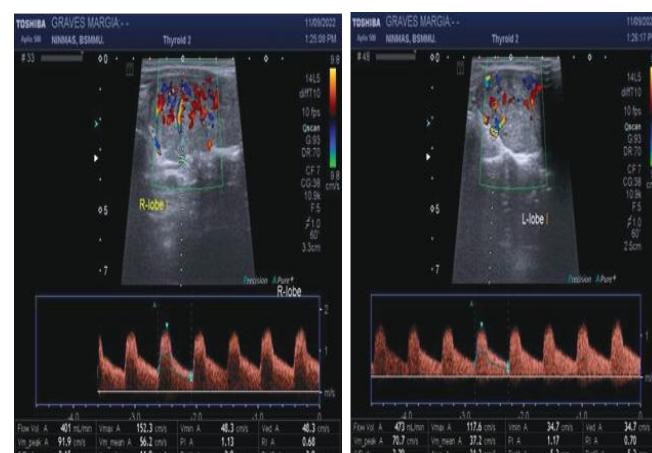
(83.3%), while 15 patients (16.7%) were diagnosed with non-Graves' thyrotoxicosis. These results highlight that, even among TRAb-positive individuals, a subset may present with alternative causes of thyrotoxicosis, emphasizing the importance of complementary diagnostic modalities. Table 2 shown this result.

**Table-2:** Thyroid scintigraphy in TRAb positive (Grave's disease) (n = 90)

Thyroid Scintigraphy	Frequency	Percentage (%)
Grave's disease	75	83.3
Non-Grave's disease	15	16.7
Total	90	100.0

## 3.2 Color Doppler Ultrasonography Findings

Quantitative Doppler analysis of the superior thyroid artery (STA) revealed that both peak systolic velocity (PSV) and blood flow volume (BFV) were significantly higher in patients with Graves' disease compared to those with non-Graves' thyrotoxicosis. The mean PSV in Graves' disease patients was  $78.55 \pm 12.71$  cm/s, whereas in non-Graves' patients it was  $64.35 \pm 22.14$  cm/s ( $p = 0.001$ ). The mean BSV in Graves' disease patients was  $236.0 \pm 54.37$  ml/min, compared to  $191.6 \pm 82.31$  ml/min in non-Graves' patients ( $p = 0.01$ ). These findings suggest a significant association between increased vascularity, as reflected by Doppler indices, and Graves' disease pathophysiology. Fig. 1 depicted the sonographic findings and Table-3 describe the PSV findings.



**Fig. 1:** Quantitative Doppler analysis of the superior thyroid artery (STA) revealed that both peak systolic velocity (PSV) and blood flow volume (BFV).

**Table-3:** Thyroid scintigraphy in TRAb positive (Grave's disease) (n=90) with Color Doppler USG

Variables	Thyroid scintigraphy in TRAb positive (Grave's disease)		p-value
	Grave's (n = 75) Mean $\pm$ SD	Non-Graves (n = 15) Mean $\pm$ SD	
PSV (cm/sec)	78.55 $\pm$ 12.71	64.35 $\pm$ 22.14	0.001*
BFV (ml/min)	236.0 $\pm$ 54.37	191.6 $\pm$ 82.31	0.010*

### 3.3 Receiver Operating Characteristic (ROC) Analysis

ROC curve analysis was performed to establish optimal cut-off values for differentiating Graves' disease from non-Graves' thyrotoxicosis. For PSV, the best cut-off was

determined to be 71 cm/s, yielding an area under the curve (AUC) of 0.720 (95% CI: 0.554–0.885, p = 0.007). At this threshold, sensitivity was 72.0%, specificity was 66.7%, PPV was 91.5%, and diagnostic accuracy was 71.1%. For BFV, the cut-off value was identified as 186 ml/min, with an AUC of 0.671 (95% CI: 0.501–0.841, p = 0.038). At this level, sensitivity was 74.7%, specificity was 53.3%, PPV was 88.9%, and diagnostic accuracy was 71.1%. These results demonstrate that both parameters have good diagnostic performance, though BFV exhibited slightly higher sensitivity, while PSV showed a higher positive predictive value and comparable overall accuracy. Figure 2 & Table 4 shown the diagnostic accuracy.

**Table 4.** Diagnostic performance of superior thyroid artery Doppler indices for Graves' disease.

Variable	AUC	SE	Cut-off Value	Sensitivity	Specificity	p-value	95% CI (Lower–Upper)
PSV (cm/s)	0.720	0.085	>71.0	72.0%	67.7%	0.007	0.554–0.885
BFV (ml/min)	0.671	0.087	>186.0	74.7%	53.3%	0.038	0.501–0.841

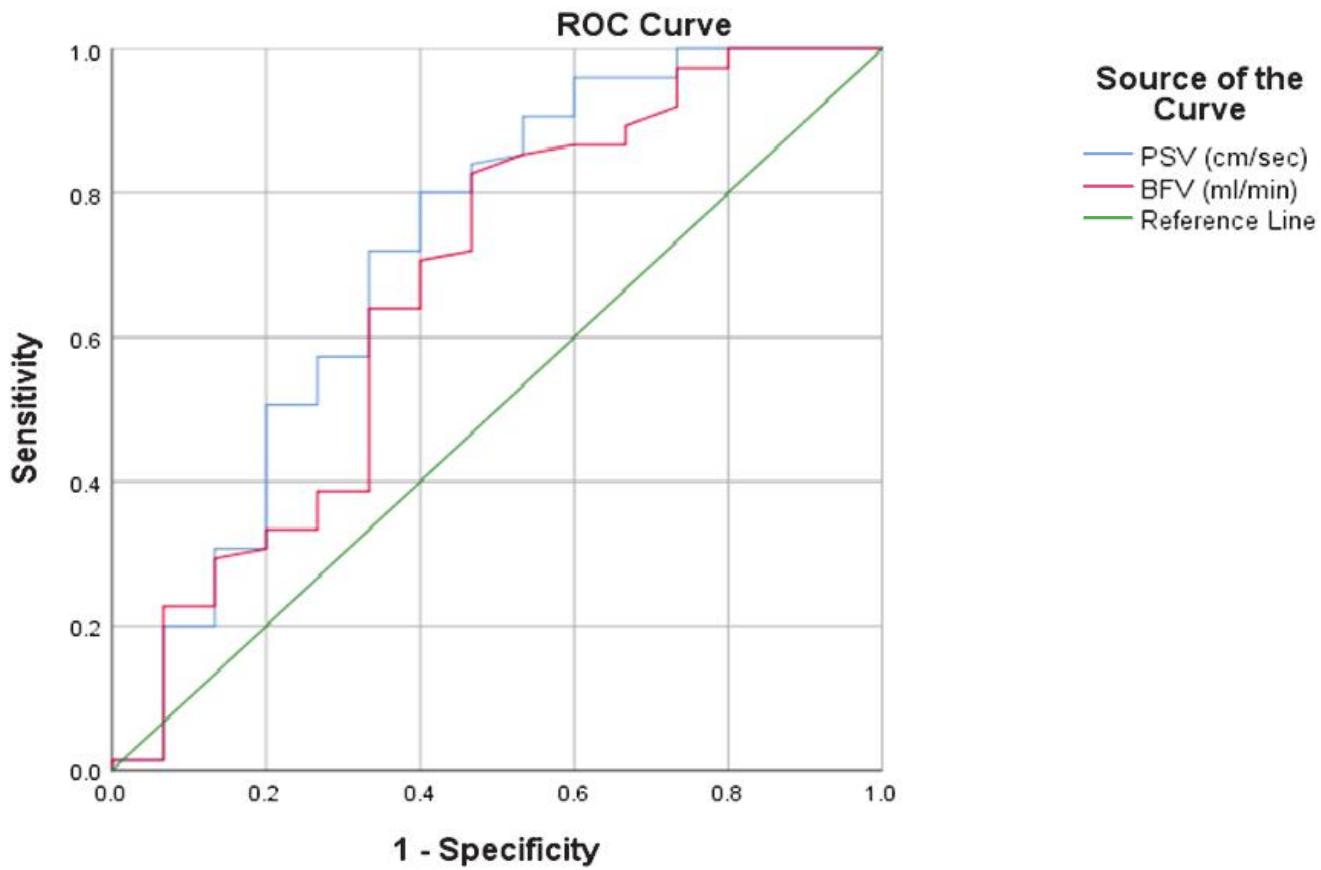
**Fig. 2.** ROC curve for diagnostic accuracy

Figure 2. Receiver operating characteristic (ROC) curves for superior thyroid artery Doppler indices in the diagnosis of Graves' disease, using thyroid scintigraphy as the reference standard. The blue curve represents peak systolic velocity (PSV, cm/s) and the red curve represents blood flow volume (BFV, ml/min). ROC analysis demonstrated

significant diagnostic performance for both indices. PSV showed an AUC of 0.720 (95% CI: 0.554–0.885;  $p = 0.007$ ) with a cut-off value  $>71.0$  cm/s, yielding 72.0% sensitivity and 67.7% specificity. BSV showed an AUC of 0.671 (95% CI: 0.501–0.841;  $p = 0.038$ ) with a cut-off value  $>186.0$  ml/min, yielding 74.7% sensitivity and 53.3% specificity.

**Table 5.** Diagnostic performance of PSV and BSV in differentiating Graves' disease from non-Graves' thyrotoxicosis (reference standard: thyroid scintigraphy)

Parameter	Cut-off	TP	FP	FN	TN	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
PSV (cm/s)	$>71$	54	5	21	10	72.0	66.7	91.5	32.3	71.1
BSV (ml/min)	$>186$	56	7	19	8	74.7	53.3	88.9	29.6	71.1

Diagnostic performance analysis using thyroid scintigraphy as the reference standard is presented in Table 5. For PSV  $>71$  cm/s, 54 true positives, 21 false negatives, 5 false positives, and 10 true negatives were observed. This corresponded to a sensitivity of 72.0%, specificity of 66.7%, positive predictive value (PPV) of 91.5%, negative predictive value (NPV) of 32.3%, and over-all diagnostic accuracy of 71.1%. For BSV  $>186$  ml/min, 56 true positives, 19 false negatives, 7 false positives, and 8 true negatives were recorded, yielding a sensitivity of 74.7%, specificity of 53.3%, PPV of 88.9%, NPV of 29.6%, and an accuracy of 71.1%. While PSV demonstrated superior specificity and PPV, BSV provided higher sensitivity, indicating their complementary roles in the non-invasive diagnosis of Graves' disease.

#### 3.4 Correlation of PSV and BSV

A strong positive correlation was observed between PSV and BSV values across the study population, underscoring their ability to reflect the hypervascular state characteristic of Graves' disease. Notably, BSV appeared to be the more robust parameter, given its relatively lower dependence on operator skill and respiratory variability. Thyroid scintigraphy confirmed Graves' disease in 83.3% of TRAb-positive patients, while Color Doppler ultrasonography revealed significant elevations in both PSV and BSV in these cases. ROC curve analysis identified optimal cut-off values of PSV  $>71$  cm/s and BSV  $>186$  ml/min, each demonstrating reliable diagnostic performance with an overall accuracy of 71.1%. PSV yielded a particularly high positive predictive value (91.5%) (Table 6), whereas BSV offered slightly superior sensitivity (74.7%). Collectively, these findings highlight the clinical utility of both Doppler parameters, with BSV

emerging as the more consistent diagnostic marker for Graves' disease.

**Table 6:** Results of diagnostic performance test (PSV)

Statistic	Value	95% CI
Sensitivity	72.000%	60.437% to 81.759%
Specificity	66.667%	38.380% to 88.176%
Positive Predictive Value	91.525%	83.890% to 95.726%
Negative Predictive Value	32.258%	22.242% to 44.219%
Accuracy	71.111%	60.601% to 80.184%

#### 4. Discussion

The present study evaluated the diagnostic performance of (CDU) parameters—specifically (PSV) and (BSV) of the superior thyroid artery (STA)—in differentiating Graves' disease from non-Graves' thyrotoxicosis among TRAb-positive patients. Our findings demonstrated significantly higher PSV and BSV values in patients with Graves' disease compared to those with other causes of thyrotoxicosis. The study also determined optimal cut-off values of PSV ( $>71$  cm/s) and BSV ( $>186$  ml/min) with diagnostic accuracies of 71.1%, highlighting the potential of CDU as a non-invasive, reliable, and radiation-free diagnostic alternative to thyroid scintigraphy. Thyroid scintigraphy, often considered the gold standard for differentiating thyrotoxicosis etiologies, confirmed Graves' disease in 83.3% of our TRAb-positive patients. This underscores the fact that, although TRAb assays have excellent sensitivity and specificity (1), a subset of patients may yield discordant results, necessitating additional confirmatory testing. Scintigraphy, however, is

associated with radiation exposure, limited accessibility, and contraindications in pregnancy and lactation, which reduce its universal applicability (2,14,16). In contrast, CDU offers a safe and repeatable technique that can complement or, in some cases, replace scintigraphy.

Our study aligns with earlier reports that have highlighted the role of CDU in assessing thyroid vascularity. The hallmark CDU finding in Graves' disease is the so-called "thyroid inferno," characterized by intense parenchymal vascularity on color flow mapping (3,14,15). While qualitative patterns are helpful, quantitative Doppler indices such as PSV and BFV provide objective measurements that improve diagnostic accuracy.

We observed that PSV values were significantly elevated in Graves' disease compared to non-Graves' thyrotoxicosis. This finding corroborates the work of Zuhur et al. (4), who demonstrated that PSV of the inferior thyroid artery had a sensitivity of 93.7% and specificity of 83.3% when RAIU was used as the reference standard. Similarly, several studies [1,14,16] emphasized that PSV reflects the hemodynamic changes associated with thyroid hyperactivity. However, as highlighted in our study, PSV is susceptible to operator dependency and respiratory variability, which may limit its reproducibility.

BFV, on the other hand, demonstrated slightly higher sensitivity (74.7%) compared to PSV (72.0%) in our population, despite its lower specificity. Importantly, BFV is considered less dependent on angle correction and respiratory movements, making it a more stable parameter for longitudinal follow-up. Peng et al. [2] & other studies [6, 8,10], confirmed the high diagnostic value of STA-BFV, reporting sensitivity of 96.8% and specificity of 94.4%. Although our cut-off values and accuracy rates were somewhat lower, this discrepancy may be attributed to differences in study design, patient demographics, and iodine intake status, which is known to influence thyroid hemodynamics.

Our study also highlights the complementary nature of PSV and BFV. While PSV demonstrated a high positive predictive value (91.5%), suggesting its strength in ruling in Graves' disease, BFV exhibited better sensitivity, making it useful for screening and identifying cases that might otherwise be missed. Hence, incorporating both indices into clinical practice may enhance diagnostic confidence.

The implications of our findings are clinically significant. CDU, by combining qualitative and quantitative

assessment, provides an immediate, non-invasive diagnostic tool that can be used even in resource-limited settings. In pregnancy, where scintigraphy is contraindicated, CDU becomes invaluable. Furthermore, its radiation-free nature allows for repeated evaluations, making it ideal for monitoring disease activity, treatment response, and remission in Graves' disease.

Our study underscores the complementary roles of PSV and BFV in the diagnostic evaluation of Graves' disease. PSV demonstrated a high positive predictive value (91.5%), highlighting its strength in ruling in Graves' disease with high diagnostic certainty. Conversely, BFV exhibited superior sensitivity, making it particularly useful for screening and detecting cases that might otherwise be missed. Incorporating both indices into clinical practice may therefore enhance diagnostic confidence and improve overall accuracy.

The clinical implications of these findings are substantial. CDU, by combining qualitative vascular assessment with quantitative Doppler indices, offers an immediate, non-invasive diagnostic tool that is well suited to both advanced and resource-limited settings. In pregnancy, where radionuclide scintigraphy is contraindicated, CDU provides a safe and effective alternative. Moreover, the absence of ionizing radiation allows for repeated evaluations, making CDU an ideal modality for monitoring disease activity, treatment response, and remission in patients with Graves' disease.

Our results align with global evidence supporting CDU as a reliable tool in the differential diagnosis of thyrotoxicosis. Peng et al. [2] first described the characteristic "thyroid inferno" pattern in Graves' disease, which has since been consistently validated as a hallmark of this condition. More recent investigations have emphasized quantitative assessment, with PSV and BFV emerging as robust diagnostic markers [4–6, 17–18]. For example, Ralls et al. [19] demonstrated that Doppler sonography could accurately distinguish Graves' disease from thyroiditis by identifying markedly increased vascularity in the former. Donkol et al. (17) reported significantly higher PSV in the superior thyroid artery among patients with Graves' disease compared to toxic multi-nodular goiter, with diagnostic accuracy exceeding 85%. Similarly, Hiraiwa et al. [13] confirmed that PSV correlated strongly with disease activity and therapeutic response, further supporting its role as a dynamic biomarker in clinical practice.

## Strengths and Limitations

The strengths of our study include the prospective design, use of both scintigraphy and TRAb assays as reference standards, and quantitative evaluation of Doppler parameters. By focusing on TRAb-positive patients, we ensured biochemical confirmation of thyrotoxicosis, thus improving the reliability of our analysis.

However, several limitations must be acknowledged. First, the sample size was relatively modest ( $n = 90$ ), which may limit the generalizability of the cut-off values to broader populations. Second, intra- and inter-observer variability in Doppler measurements were not assessed, although efforts were made to standardize techniques. Third, iodine intake, which can influence thyroid vascularity, was not systematically evaluated in our cohort. Additionally, we did not stratify patients by disease severity or duration, which might influence vascular parameters. Future studies incorporating larger, multicentric cohorts with standardized Doppler protocols are warranted to refine diagnostic thresholds and validate reproducibility.

## 5. Conclusions

Color Doppler ultrasonography (CDU) of the superior thyroid artery provides reliable diagnostic utility in differentiating Graves' disease from non-Graves' thyrotoxicosis among TRAb-positive patients. Elevated peak systolic velocity (PSV) and blood flow volume (BFV) reflect thyroid hypervascularity, with PSV  $>71$  cm/s offering high positive predictive value and BSV  $>186$  ml/min demonstrating superior sensitivity. CDU is non-invasive, radiation-free, widely accessible, and cost-effective, making it particularly valuable in pregnancy and resource-limited settings. Incorporating CDU into routine thyroid evaluation may reduce dependence on scintigraphy, improve patient safety, and enable earlier, more accurate diagnosis and management of Graves' disease.

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