Diagn Interv Radiol 2025; DOI: 10.4274/dir.2025.253311

HEAD AND NECK IMAGING

ORIGINAL ARTICLE

Vascularity assessment in Hashimoto's thyroiditis: a prospective comparative study with power Doppler and superb microvascular imaging

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Received 19 March 2025; revision requested 04 May 2025; last revision received 28 June 2025; accepted 27 July 2025.

Epub: 27.08.2025

Publication date:

DOI: 10.4274/dir.2025.253311

PURPOSE

To quantitatively evaluate the vascularity of the thyroid parenchyma in patients diagnosed with Hashimoto's thyroiditis (HT) compared with healthy controls by using vascularity index (VI) through power Doppler (PD) and color superb microvascular imaging (cSMI) and to determine a threshold VI value to effectively differentiate patients with HT and hypothyroid HT.

METHODS

This prospective cross-sectional study involved 73 patients diagnosed with HT and 66 healthy controls. The diagnosis of HT was established based on clinical and laboratory findings. The total volume of the thyroid gland was measured, and the region of interest was drawn manually by delineating the gland boundaries for VI calculation on PD and cSMI. The mean VI for both lobes of the thyroid were computed for each participant. Statistical analyses were conducted using SPSS version 29.0, with receiver operating characteristic curve analysis employed to ascertain the optimal cSMI VI cut-off values for the diagnosis of HT and for patients with hypothyroid HT.

RESULTS

The analysis revealed no significant differences in the total thyroid volume between the HT group and the control group, or between the hypothyroid and euthyroid HT subgroups. The SMI VI values were recorded at 8.85 [interquartile range (IQR): 25%–75%, 6.55–12.6] for patients with HT and 8.40 (IQR: 25%–75%, 6.70–12.8) for the control group, indicating a statistically significant increase in the HT cohort ($P < 0.001$). Additionally, the PD VI values in patients with HT were significantly higher than in the control group ($P < 0.001$). A strong positive correlation was identified between thyroid-stimulating hormone levels and cSMI VI in patients with HT (rho = 0.739, $P < 0.001$), whereas the correlation with PD VI was found to be weak (rho = 0.346, $P < 0.001$). The optimal cut-off value for SMI VI was 6.75% for the general diagnosis of HT and 8.825% for patients with hypothyroid HT.

CONCLUSION

This study indicates that the optimal threshold values of 6.75% for the diagnosis of HT and 8.825% for patients with hypothyroid HT suggest that cSMI is an effective and promising diagnostic tool for detecting alterations in thyroid vascularization. Furthermore, there is a strong concordance among radiologists regarding the VI measurements.

CLINICAL SIGNIFICANCE

The SMI technique represents a promising diagnostic tool for the detection of subtle alterations in thyroid vascularization. The higher sensitivity of cSMI in comparison to PD positions it as an innovative and effective technology for the assessment of HT, offering valuable insights into disease activity and progression.

KEYWORDS

Hashimoto's thyroiditis, power Doppler, ultrasonography, color superb microvascular imaging, vascularity index

You may cite this article as: Selçuk Can T, Özdemir S, İkizceli T, et al. Vascularity assessment in Hashimoto's thyroiditis: a prospective comparative study with power Doppler and superb microvascular imaging. *Diagn Interv Radiol.* 27 August 2025 DOI: 10.4274/dir.2025.253311 [Epub Ahead of Print].

Hashimoto's thyroiditis (HT) is an autoimmune disorder characterized by inflammation of the thyroid gland, which initially results in hyperthyroidism and subsequently progresses to hypothyroidism due to parenchymal degeneration.[1] The diagnosis of HT can be established through clinical observations, ultrasonographic findings, and the detection of circulating antithyroid autoantibodies that contribute to morphological changes.[2,3] Conventional ultrasound (US) and color Doppler imaging (CDI) typically reveal a heterogeneous echotexture characterized by lobulated contours, hypoechoic micronodules, and increased vascularity in the early stages, while diminished vascularity is observed in the chronic stages.[4,5] CDI, particularly power Doppler (PD), is essential for assessing the vascularity of the thyroid gland, which is often elevated in cases of HT. When combined with other sonographic characteristics, it enhances both the sensitivity and specificity of diagnosing diffuse thyroid pathologies, including HT. This comprehensive approach improves diagnostic accuracy in asymptomatic individuals.[6,7] However, CDI faces challenges in distinguishing genuine blood flow from motion artifacts. Superb microvascular imaging (SMI) is an advanced Doppler technique that employs adaptive algorithms to detect low-velocity blood flow while minimizing motion artifacts, thereby providing a clearer representation of true vascular perfusion. This technique can be utilized in two modalities: color SMI (cSMI) and monochrome SMI (mSMI). The cSMI modality generates color-coded Doppler signals superimposed on grayscale US images, whereas mSMI eliminates the background grayscale US data and exclusively displays the Doppler signals.[8] The vascularity index (VI), available in both PD and SMI, quantifies blood flow by calculating the ratio of colored pixels within a designated region of interest (ROI).[9,10]

This prospective cross-sectional study quantitatively evaluates the vascularity of the thyroid parenchyma in patients with HT and a control group by employing the VI in conjunction with PD and cSMI methodologies, thereby facilitating a comparative analysis of these techniques. Additionally, we establish a threshold VI value via cSMI to differentiate patients with HT from controls and to distinguish between hypothyroid and euthyroid cases of HT.

Main points

- This study compares power Doppler (PD) and color superb microvascular imaging (cSMI) techniques to assess thyroid parenchymal vascularity in patients with Hashimoto's thyroiditis (HT).
- The results indicate a significantly higher vascularity index (VI) in patients with HT compared with healthy controls, with cSMI demonstrating superior sensitivity over PD.
- A strong positive correlation was observed between thyroid-stimulating hormone levels and SMI VI, suggesting that SMI VI can be used to assess disease activity.
- The study highlights cSMI as a promising diagnostic tool for detecting subtle vascular changes in HT, with potential clinical applications for disease monitoring and management.

Methods

This study was approved by the Clinical Research Ethics Committee of İstanbul Haseki Training and Research Hospital (approval date: May 25, 2022; decision number: 73-2022). In this prospective cross-sectional investigation, the thyroid glands of 73 individuals diagnosed with HT and 66 healthy asymptomatic participants were comprehensively evaluated. The minimum required sample size to achieve a 95% confidence interval (CI) ($\alpha = 0.05$) and 90% power was determined to be 18 participants per group, resulting in a total of 54 participants, as calculated based on the study entitled "Vascularity Index for the Diagnosis of Autoimmune Thyroid Disease".[11]

Patients diagnosed with HT and monitored at the endocrinology outpatient clinic were included in this study (Figure 1). The diagnosis of HT was established through the detection of thyroid autoantibodies, specifically thyroid peroxidase and thyroglobulin antibodies (TgAbs), in conjunction with thyroid hormone levels, clinical manifestations, and ultrasonographic findings indicative of thyroiditis. Laboratory assessments conducted over a 1-week period were excluded from the analysis. Medical personnel who consented to participate in the investigation during their routine hospital assessments, who exhibited no indications of autoimmune disorders and exhibited normal laboratory findings, were incorporated into the control cohort.

The reference values employed in University of Health Sciences Türkiye, İstanbul Haseki Training and Research Hospital for laboratory parameters are delineated as follows: free thyroxine (T4) levels range from 0.70 to 1.74 ng/dL, thyroid-stimulating hormone (TSH) levels range from 0.35 to 4.5 mIU/L, TgAbs range from 0 to 115 IU/mL, thyroid peroxidase antibodies (TPOAbs) range from 0 to 34 IU/mL, and thyroglobulin levels range from 1.6 to 60 ng/mL. The cohort of patients diagnosed with HT was subsequently stratified into hypothyroid and euthyroid subgroups.

Ultrasonographic evaluations were performed utilizing the Canon Aplio 500 US system (Canon Medical Systems, Tokyo, Japan), equipped with a high-frequency probe (4–14 MHz). The examinations were conducted by two radiologists with 15 years (S.O.) and 10 years (T.S.C.) of relevant experience. Participants were positioned in a supine posture with their necks slightly extended. Initially, a grayscale US examination was conducted. Each thyroid lobe was assessed separately in both transverse and longitudinal planes. The

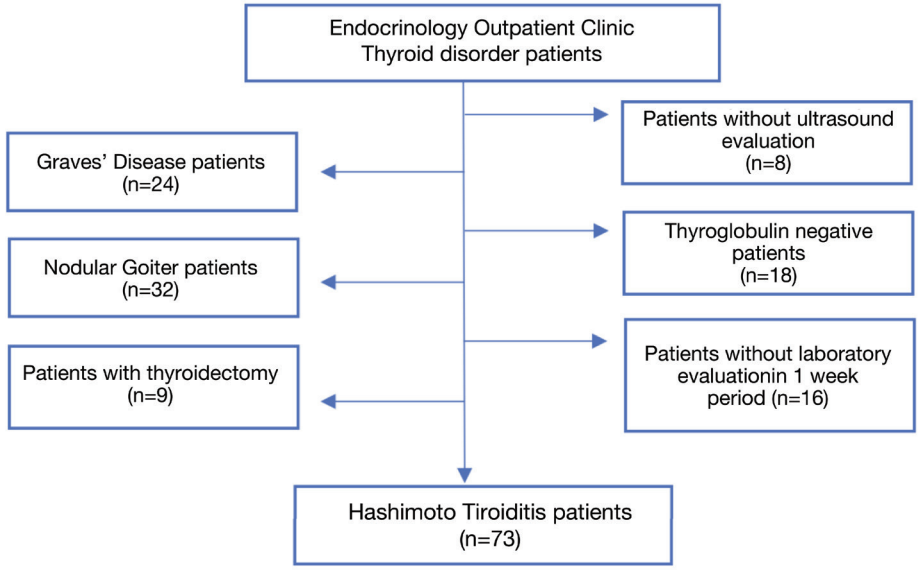

Figure 1. Flow diagram of the study.

dimensions of the thyroid gland were measured across three planes for each lobe, and the thyroid volume for each lobe was calculated using the following formula: length × width × depth × 0.52. The total thyroid volume was determined by summing the volumes of both lobes while excluding the volume of the isthmus from the calculation. Furthermore, the structure and echogenicity of the thyroid parenchyma were evaluated in detail.

Following the grayscale examination, vascular imaging was performed in the longitudinal plane for both lobes using PD and cSMI techniques. The pulse repetition frequency was calibrated within a range of 150–80 Hz. During the PD and cSMI evaluations, participants were instructed to refrain from swallowing and to hold their breath for a duration of 5 seconds. After capturing the relevant images, the boundaries of the thyroid gland were manually delineated, and a ROI was established (Figure 2). The VI was calculated by quantifying the colored pixels using the device's algorithm and expressing this quantity as a proportion of the total pixel count within the ROI. This procedure was conducted independently three times for each lobe, and the mean of the three measurements was computed. To determine the overall thyroid VI, the average of the measurements from both lobes was calculated. All values were derived by averaging the VI results obtained from both radiologists.

Statistical analysis

The statistical analysis was conducted utilizing SPSS version 29.0. Categorical variables were represented as counts and percentages, and numerical variables were expressed as means ± standard deviations or medians with interquartile ranges (IQR), depending on the distribution characteristics of the data. To compare independent numerical variables between two distinct groups, either Student's t-test or the Mann–Whitney U test was employed, based on the normality assumption of the data distribution. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cut-off value for the cSMI VI in distinguishing patients with HT from healthy controls, as well as in distinguishing hypothyroid from euthyroid HT. The data were stratified according to the threshold values established by the Youden index and the area under the curve (AUC) metrics. Subsequently, measures of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio, and negative likelihood ratio were calculated. The study also assessed the concordance of findings among each radiologist, which was evaluated using the intraclass correlation coefficient (ICC). The interpretation of Kappa values was categorized as follows: 0.81–1.00 (very good), 0.61–0.80 (good), 0.41–0.60 (moderate), 0.21–0.40 (fair), and <0.20 (poor).

Results

In the current study, a cohort of 73 patients diagnosed with HT, aged between 11 and 78 years, was designated as the case group. A control group consisting of 66 healthy individuals, aged from 19 to 72 years, was also established. The median age of the 66 healthy controls, which included 43 women and 23 men, was determined to be 33 years (IQR: 25%–75%, 25.3–44). In contrast, the mean age of the 73 individuals in the HT group, comprising 63 women and 10 men, was calculated to be 38.8 ± 14.1 years. Statistical analysis revealed that the age differences between the control group and the case group were not statistically significant ($P = 0.187$, Mann–Whitney U test). Within the case group, the mean age of the 35 patients with hypothyroidism was recorded as 38.7 ± 12.8 years, whereas the mean age of the 38 patients with euthyroidism was 38.9 ± 15.3 years. The statistical evaluation indicated no significant age difference between the patients with hypothyroidism and those with euthyroidism within the HT cohort ($P = 0.950$, Student's t-test).

The differences in thyroid function assessments between the HT group and the control cohort were found to be statistically significant. Median TSH concentration was 3.90 mIU/L (IQR: 25%–75%, 1.73–6.33) in the HT group and 2.55 mIU/L (IQR: 25%–75%, 1.59–3.33) in the control group. In the HT group, median TSH concentration was 6.39 mIU/L (IQR: 25%–75%, 5.23–10.1) in the hypothyroid subgroup and 2.07 ± 1.08 mIU/L in the euthyroid subgroup. This showed that TSH levels were significantly elevated in the patients with HT compared with the control group, and were also significantly higher in the hypothyroid subgroup compared with the euthyroid subgroup ($P < 0.001$, Mann–Whitney U test). Median T4 levels were 11.6 ng/L (IQR: 25%–75%, 10.7–12.7) in the euthyroid group and 10.9 ng/L (IQR: 25%–75%, 9.14–11.6) in the hypothyroid group, showing notable reduction in the latter subgroup compared with the former ($P < 0.001$, Mann–

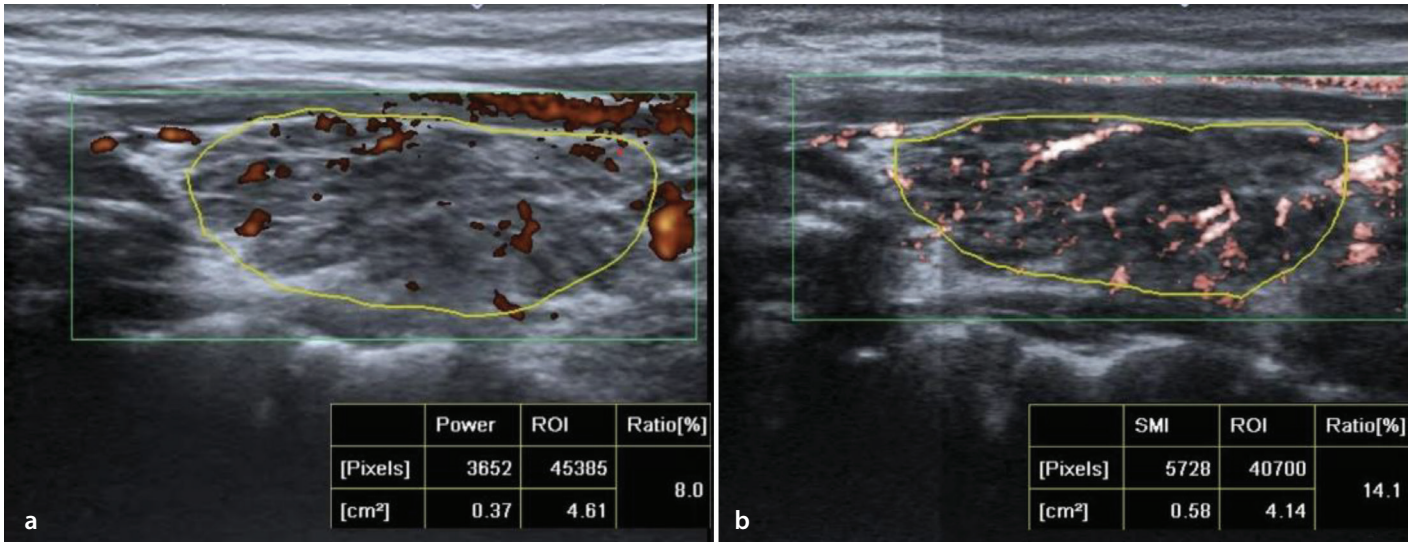

Figure 2. Quantitative vascularity index values were determined by manually tracing the contours of the thyroid gland structure in **(a)** power Doppler and **(b)** color superb microvascular imaging mode. The measurements were performed in the longitudinal planes of the right lobe. ROI, region of interest; SMI, superb microvascular imaging

Whitney U test). However, no statistically significant difference was observed in T3 levels.

There was no statistically significant difference observed between the HT group and the control group, or between the hypothyroid and euthyroid HT groups, regarding the volume of both thyroid lobes and the total thyroid volume, as determined using the Mann–Whitney U test (Table 1).

The SMI VI values for the right and left thyroid lobes in the control cohort were measured at 3.75% (IQR: 25%–75%, 2.82–5.16) and 3.97% ± 1.34%, respectively. In contrast, the HT cohort exhibited SMI VI values of 8.85% (IQR: 25%–75%, 6.55–12.6) for the right lobe and 8.40% (IQR: 25%–75%, 6.70–12.8) for the left lobe. Importantly, the SMI VI values for both lobes demonstrated a statistically significant increase in the HT cohort ($P < 0.001$, Mann–Whitney U test).

In the HT cohort, the SMI VI values for the right lobe were measured at 14.0% ± 4.53% for the hypothyroid subgroup and 6.77% ± 2.08% for the euthyroid subgroup. A statistically significant difference was observed, favoring the hypothyroid cohort ($P < 0.001$, Student's t-test). Regarding the left lobe, the median SMI VI value of 12.8% (IQR: 25%–75%, 10.8–14.1) in the hypothyroid cohort was significantly higher than the 6.78% (IQR: 25%–75%, 5.11–7.75) in the euthyroid cohort ($P < 0.001$, Mann–Whitney U test) (Table 2).

The PD VI metrics for the right and left lobes in patients diagnosed with HT were measured at 6.15% (IQR: 25%–75%, 3.65–8.05) and 6.30% (IQR: 25%–75%, 4.10–7.75), respectively. These values were found to be statistically significantly elevated when compared with the mean values of the corresponding lobes in the control cohort, which were 3.28% ± 1.35% and 3.35% ± 1.32%, respectively ($P < 0.001$, Mann–Whitney U test). Furthermore, the PD VI measurements obtained from the right and left lobes of the patients with hypothyroid HT were 7.35% (IQR: 25%–75%, 5.35–11) and 7.30 (IQR: 25%–75%, 5–8.50), respectively. These measurements were found to be significantly greater than those observed in the patients with euthyroid HT, which were 5.22% (IQR: 25%–75%, 3.26–6.86) and 4.80% (IQR: 25%–75%, 3.65–6.64), respectively, with statistical significance ($P = 0.002$, $P = 0.003$; Mann–Whitney U test) (Table 3).

When interobserver agreement was evaluated in VI values, the ICC value for cSMI was 0.994 [F (179,72) = 57.2, $P < 0.001$, 95% CI: 0.990–0.996] for the right lobe and 0.995 [F (214,72) = 57.7, $P < 0.001$, 95% CI: 0.992–0.997] for the left lobe. For PD VI, the ICC value was 0.995 [F (210,72) = 33.7, $P < 0.001$, 95% CI: 0.990–0.997] for the right lobe and 0.997 [F (405,72) = 21.9, $P < 0.001$, 95% CI: 0.994–0.998] for the left lobe. This shows a high level of agreement between the two radiologists regarding the SMI and PD VI measurements.

The results of the Spearman correlation analysis performed on a cohort of individuals diagnosed with HT revealed a moderate positive correlation between the right SMI VI and right PD VI (rho = 0.613, $P < 0.001$). Additionally, a similar moderate positive correlation was found between the left SMI VI and left PD VI (rho = 0.607, $P < 0.001$).

The results of the Spearman correlation analysis conducted on the control group revealed a strong positive correlation between right SMI VI and right PD VI (rho = 0.727, $P < 0.001$). Additionally, a robust positive correlation was identified between left SMI VI and left PD VI (rho = 0.825, $P < 0.001$).

When the correlation between TSH values and VI values was assessed in patients with HT, a strong positive correlation was found between TSH and SMI VI (rho = 0.739, $P < 0.001$). In contrast, a weak correlation was noted between TSH and PD VI values (rho = 0.346, $P < 0.001$).

The correlation between SMI VI and the antibodies, anti-TG and anti-TPO, was found to be weak, with Spearman's rho values of 0.296 and 0.303, respectively. Similarly, the correlation between PD VI and these antibodies was also weak, with Spearman's rho values of 0.304 and 0.217.

The correlation between SMI and PD VI values and thyroid volumes in patients with

Table 1. Thyroid gland volumes of Hashimoto's thyroiditis and control groups

Group	Right thyroid volume (mm^3) Median (IQR: 25%–75%)	Left thyroid volume (mm^3) Median (IQR: 25%–75%)	Total thyroid volume (mm^3)
Hashimoto's thyroiditis	43.6 (29.9–61.9)	43.7 (28.4–57.6)	88.8 (61.5–116)
Control	41.7 (31.8–51.3)	36.2 (30–48.4)	76.7 (60.5–94.8)
P value	0.464	0.280	0.440
Hashimoto's thyroiditis (euthyroid)	39.7 (27.2–64.8)	37.4 (26.7–56.7)	71.7 (58.2–116)
Hashimoto's thyroiditis (hypothyroid)	48.1 (35.4–60.9)	47.0 (29.8–57.3)	93.3 (64.2–115)
P value	0.359	0.365	0.353

IQR, interquartile range.

Table 2. Comparison of SMI VI values across groups

Group	SMI VI % (R) Radiologist 1	SMI VI % (R) Radiologist 2	SMI VI % (R)	SMI VI % (L) Radiologist 1	SMI VI % (L) Radiologist 2	SMI VI % (L)
Control	3.99 ± 1.5	3.91 ± 1.34	3.75 (2.82–5.16)	4.16 ± 1.54	3.79 ± 1.16	3.97 ± 1.34
Hashimoto's thyroiditis	8.80 (6.80–12.3)	9.00 (6.50–13.0)	8.85 (6.55–12.6)	8.30 (6.90–12.6)	8.60 (6.60–13.1)	8.40 (6.70–12.8)
P value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
*Mann–Whitney U Test						
Hashimoto's thyroiditis (hypothyroid)	13.9 ± 4.47	14.2 ± 4.64	14.0 ± 4.53	12.6 (10.4–14.2)	13.1 (11.3–14.1)	12.8 (10.8–14.1)
Hashimoto's thyroiditis (euthyroid)	6.71 ± 2.14	6.84 ± 2.06	6.77 ± 2.08	7 (4.95–7.68)	6.75 (5.23–7.95)	6.78 (5.11–7.75)
P value	<0.001**	<0.001**	<0.001**	<0.001*	<0.001*	<0.001*

*Mann–Whitney U Test; **Student's t-test (Welch's t). SMI, superb microvascular imaging; VI, vascularity index.

Table 3. Comparison of PD VI values across groups

Group	PD VI % (R) Radiologist 1	PD VI % (R) Radiologist 2	PD VI % (R)	PD VI % (L) Radiologist 1	PD VI % (L) Radiologist 2	PD VI % (L)
Control	3.29 ± 1.48	3.28 ± 1.25	3.28 ± 1.35	3.30 ± 1.50	3.41 ± 1.17	3.35 ± 1.32
Hashimoto's thyroiditis	6.20 (3.60–8.20)	6.30 (3.80–8.10)	6.15 (3.65–8.05)	6.20 (4–7.80)	6.30 (4.10–7.80)	6.30 (4.10–7.75)
P value	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
*Mann–Whitney U Test						
Hashimoto's thyroiditis (hypothyroid)	7.10 (5.25–10.5)	7.30 (5.50–11.1)	7.35 (5.35–11)	7.20 (5–8.40)	7.40 (5–8.50)	7.30 (5–8.50)
Hashimoto's thyroiditis (euthyroid)	5.25 (3.20–6.68)	5.25 (3.30–7.05)	5.22 (3.26–6.86)	5.29 ± 2.35	5 (3.65–6.83)	4.80 (3.65–6.64)
P value	0.002*	0.003*	0.002*	0.004*	0.003*	0.003*

*Mann–Whitney U Test. PD, power Doppler; VI, vascularity index.

HT was found to be weak, with Spearman's rho values of 0.254 and 0.268, respectively.

The AUC value, derived from the ROC curve, was calculated to differentiate patients diagnosed with HT based on varying threshold SMI VI values. The AUC was found to be 0.933, leading to the establishment of the threshold SMI VI value at 6.75%.

In alignment with the varying threshold values of the SMI VI, the AUC value derived from the ROC curve developed to differentiate between patients with hypothyroidism and those diagnosed with HT was determined to be 0.959. As a result, the SMI VI threshold value was established at 8.825%. The findings from the diagnostic value assessment conducted in accordance with these threshold values are presented in Table 4.

The AUC value, derived from the ROC curve constructed using varying threshold values of PD VI to distinguish patients diagnosed with HT was found to be 0.838. In contrast, the AUC for differentiating patients with hypothyroid HT from those with euthyroid HT was determined to be 0.714. However, the Youden's indexes for these analyses were 0–0.0455 and 0.311–0.353, respectively, indicating a low diagnostic performance.

Discussion

HT is recognized as the most prevalent autoimmune disorder affecting the thyroid gland, with an annual incidence rate ranging from 2 to 498 cases per 100,000 individuals.[12,13] The progression of this condition typically begins with a phase of hyperthyroidism, which is subsequently followed by hypothyroidism due to the degeneration of thyroid tissue.[14] US is a widely utilized imaging modality for the diagnostic evaluation and ongoing monitoring of HT.[3] In the assessment of vascular characteristics, SMI represents an innovative ultrasonographic technique that facilitates the detection of low-velocity blood flow.

In this study, we examined the vascular characteristics of the thyroid gland in patients diagnosed with HT utilizing both SMI and PD modalities. Our findings revealed that patients with HT exhibited significantly elevated VI values when compared with the control group. Additionally, in the HT cohort, the hypothyroid subgroup demonstrated higher VI values than the euthyroid subgroup. However, the diagnostic efficacy of PD for differentiating HT cases based on its VI threshold was found to be suboptimal. In contrast, the SMI method produced more favorable results, with a threshold VI of 6.75% for the detection of HT and 8.825% for the identification of hypothyroid HT.

Few studies have utilized the SMI technique in the context of HT, meaning our investigation makes a significant contribution to this specialized field.[15,16] Bayramoglu et al.[15] identified a VI cut-off value of 10.58% with an AUC of 0.794, which yielded a sensitivity of 67.1% and a specificity of 90% for diagnosing HT in a pediatric cohort consisting of 70 patients with HT and 30 controls. The reported sensitivity was 67.1%, specificity was 90%, PPV was 94%, NPV was 54%, and the overall diagnostic accuracy was determined to be 74%. In the present study, comparable sensitivity and specificity metrics were obtained for the SMI VI threshold of 6.75%, which was established alongside a superior AUC value. In addition to SMI VI, we additionally established a threshold value for PD VI. Nevertheless, our findings indicated that the threshold values derived from the ROC analysis displayed suboptimal diagnostic efficacy, as evidenced by exceedingly low Youden indices; consequently, these values were deemed insufficient for the differentiation of patients with HT from healthy controls, akin to SMI VI. Bayramoglu et al.[15] categorized patients based on the extent of glandular involvement as assessed by gray-scale US and noted a statistically significant difference in VI values between the two patient cohorts with HT. However, while they suggested that this finding was related to the degree of glandular involvement, they did not specify a cut-off value. In a larger cohort of pediatric patients with HT, Durmaz et al.[17] reported a cut-off value of 6.00% for the average VI across all thyroid glands, achieving a sensitivity of 86.3% and a specificity of 82.2% for HT diagnosis, thereby indicating substantial diagnostic accuracy. Additionally, they established distinct cut-off values for various measurement planes: 6.350% for the VI of the right and left thyroid lobes in

Table 4. Diagnostic performance of cSMI VI

Group (cut-off value)	Sensitivity % (GA)	Specificity % (GA)	PPV % (GA)	NPV % (GA)	PLR (GA)	NLR (GA)	Accuracy % (GA)
Hashimoto's thyroiditis vs. Control (6.75)	75%, 34 (63, 86–84, 68)	100% (94, 56–100)	100%	78%, 57 (71, 06–84, 56)	–	0.25 (0.17–0.37)	87%, 05 (80, 31–92, 14)
Hypothyroid vs. Euthyroid (8.825)	34%, 29 (19, 13–52, 21)	100% (90, 75–100)	100%	62%, 3 (56, 53–67, 73)	–	0, 66 (0, 52–0, 84)	68%, 49 (56, 56–78, 87)

cSMI, color superb microvascular imaging; VI, vascularity index; GA, gray-scale area; PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio.

the longitudinal plane, 6.225% for the mean VI in the longitudinal plane, and 6.350% for the VI in the transverse plane. The threshold value identified in our research closely resembles that reported by Durmaz et al.[17] A significant factor contributing to the variability in VI values observed in both previous studies and our own may be the average age of the participants, which could influence VI values due to age-related changes in thyroid vascularization. Furthermore, Bayramoglu et al.[15] systematically excluded individuals with fibrotic thyroid glands, echogenic septa, and pronounced pseudonodular characteristics in their investigation. These factors have the potential to affect VI measurements, possibly leading to divergent cut-off values. Moreover, as noted by Durmaz et al.[17], the identification of varying cut-off values across different imaging planes may suggest that the measurement methodologies employed could contribute to the discrepancies observed in cut-off values. Such findings underscore the necessity for age-specific considerations in the assessment of thyroid vascularization using the VI, particularly when comparing results from different studies involving diverse populations.

In the present study, it was observed that the volumes of the thyroid gland were significantly elevated in patients diagnosed with HT, particularly within the hypothyroid subgroup, when compared with the euthyroid cohort. However, these findings did not achieve statistical significance. Similarly, the research conducted by Bayramoglu et al.[15] and Durmaz et al.[17] reported increased thyroid gland volumes in patients with HT relative to the control group. In the early stages of the pathology, an enlargement of the glandular structure may be noted, which can be attributed to increased vascularization. This enhancement in vascularity occurs as a result of the immunological response and the inflammatory processes taking place within the glandular tissue.[18]

Durmaz et al.[17] elucidated a positive relationship between VI values and the concentrations of TSH, TgAbs, and TPOAbs. However, these associations were characterized by a lack of strength. Additionally, Bayramoglu et al.[15] identified a significant fair positive correlation between the VI derived from SMI and serum TgAb concentrations, indicating that the VI exhibits an upward trend suggestive of enhanced vascularity within the thyroid gland. Furthermore, they observed a significant moderate positive correlation between the VI and TPOAb levels, which, being a more robust correlation compared with TgAb levels, implies that TPOAb concentrations are more closely associated with increased vascularity in the thyroid gland. A positive and statistically significant correlation between autoantibody concentrations and VI values suggests that the VI measurement of the thyroid gland may be associated with the extent of inflammation and could provide insights regarding disease activity. However, our investigation revealed a significant yet weak correlation between the SMI and PD VIs alongside the autoantibodies. The levels of serum antibodies may serve as indicators of the severity of thyroid gland inflammation in patients diagnosed with HT.[19] While TgAbs may be responsible for the early immune response, TPOAbs are associated with thyroid damage, representing a later immune response.[20] The significant yet modest correlation observed in our investigation, along with findings from other research, may be attributed to the variability inherent in the different stages of HT present within the studied patient cohorts. Bayramoglu et al.[15] found a statistically significant moderate correlation between VI values and serum TSH levels in their study, whereas Durmaz et al.[17] reported a statistically significant weak positive correlation. Significant correlations between TSH levels and thyroid blood flow have been documented in studies utilizing CDI techniques.[21-23] In contrast to previous studies that reported a weaker correlation, our study found a highly positive correlation between serum TSH levels and VI values (rho = 0.739, $P < 0.001$).

Given that the utilization of SMI within the framework of the adult HT demographic has not been explored or documented in the prevailing scholarly literature, we synthesized the conclusions drawn from our analysis in this particular context. The reproducibility of SMI VI and PD VI measurements executed by two separate operators was scrutinized, resulting in an interobserver concordance that can be described as almost perfect. The diagnostic performance of the cSMI VI in differentiating patients with HT from asymptomatic controls exhibited a substantial degree of precision, thereby offering significant contributions to the scholarly discourse, as the threshold VI value we established through SMI for individuals with HT is anticipated to enhance clinical management, particularly in the detection of aberrant blood flow while ensuring tissue uniformity.

Our investigation is subject to several limitations. The primary limitation is that the identification of HT was conducted through clinical evaluation rather than histopathological examination. Due to the absence of biopsy specimens, we were unable to assess and interpret the histopathological alterations and the extent of inflammation within the thyroid tissue. Additionally, a majority of the participants enrolled in the study were receiving pharmacological treatment, and the duration of the disease and the disease stage were not documented. A statistically significant disparity was observed in the TSH values between the hypothyroid and euthyroid cohorts within the HT population. Despite the majority of individuals in the HT group undergoing therapeutic interventions, the pronounced variation in TSH levels among these patients substantiates the hypothesis that the administered drug dosage was inadequate for those receiving treatment. Nevertheless, the absence of documentation regarding the treatment status, as well as the absence of the transient hyperthyroid phase of the patients, constitutes a notable limitation of this investigation. Moreover, a deficiency of information pertaining to autoantibody titers within the control group impedes the comprehensive exclusion of subclinical autoimmune thyroid pathology. In addition, our measurements of PD and VI were conducted within a single plane (longitudinal). Bayramoglu et al.[15] employed a single-plane (transverse) methodology for VI measurement similar to our approach; however, unlike our methodology, which involved calculating the mean of three measurements derived from the same segment (middle), they averaged three measurements taken from the upper, middle, and lower sections of the gland. While this may represent a limitation, Durmaz et al.[17] found no statistically significant variation in VI measurements across different planes, suggesting that a single measurement obtained from one plane can be utilized with a high degree of reliability. This finding reduces the need for multiple measurements and simplifies the process in clinical settings. Additional limitations inherent to our investigation include, first, the predominance of the female demographic within our cohort, which precluded the opportunity for subgroup analysis. While the predominance of female patients is anticipated in cases of HT, this gender disproportion remains a significant limitation. Second, the vascular characteristics associated with various manifestations of HT, encompassing both atrophic and goitrogenic variants, were not assessed, and consequently, no subgroup analysis was conducted in this regard.

In conclusion, our study highlights the significant elevation of SMI VI values in

patients with HT, particularly among those with hypothyroidism, in comparison to healthy controls. The identified optimal threshold values of 6.75% for the diagnosis of HT and 8.825% for hypothyroid HT suggest that SMI may serve as a promising diagnostic tool for detecting subtle alterations in thyroid vascularization. The enhanced sensitivity of SMI in relation to PD technology positions it as an innovative and effective method for the assessment of HT, providing valuable insights into disease activity and progression. Future research, particularly studies that incorporate histopathological data and multi-plane measurements, in addition to the therapeutic condition of patients, is essential to further refine the diagnostic capabilities of SMI and to explore its clinical applications.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

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