Correlation between Colour Duplex and Technetium-99m Thyroid Scan in Identifying the Cause of Toxic Goitre

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Abstract: *Introduction*: Differentiation between thyroiditis induced thyrotoxicosis and Graves' disease is important for selection of proper therapy. It is often difficult to make this distinction without performing thyroid scintigraphy. Color flow Doppler sonography (CFDS) is gaining importance for the functional evaluation of the thyroid disorders. We aimed to determine the value of CFDS for the etiological diagnosis of thyrotoxicosis.

Patients and methods: Thirty patients with clinical and lab signs of hyperthyroidism (12 Graves' disease and, 18 patients with Hashimoto's thyroiditis) with 10 euthyroid controls were evaluated.Etiological diagnosis was carried out using standard methods. Conventional grey scale sonography was done, followed by CFDS. Doppler patterns of the glands were scored and peak systolic velocity (PSV) measurements were obtained from superior and inferior thyroid arteries. Results were correlated to isotope scanning which was used as a golden standard.

Results: Vascular patterns were significantly more prominent, and the mean PSV values were significantly higher in the Graves' Disease patients compared to the thyroiditis patients than controls. CFDS could differentiate the untreated Graves' Disease from the thyroiditis which had similar grey scale findings but higher vascular patterns and significantly higher PSV values, sensitivity = 96.6%, specificity= 96.6 %, and P>0.001

Conclusion: As an inexpensive, fast, and noninvasive imaging procedure, CFDS could be helpful in the initial clinical evaluation and may avoid scintigraphy in a substantial number of thyrotoxic patients.

Keywords: Thyroid scan, Thyrotoxicosis, Colour duplex, Toxic goiter.

INTRODUCTION

High resolution ultrasonography has become the first-line method in the evaluation of thyroid morphology due to its high sensitivity and ease of use [1].

Thyroid scintigraphy is the conventionally accepted method in the functional evaluation of the thyroid gland. Nowadays, color flow Doppler sonography (CFDS) also plays an important role in obtaining functional information. CFDS is a powerful technique combining the gray scale view of the conventional sonography with a color display of blood flow. This provides an evaluation of the vascular patterns of the thyroid gland, which may be an indirect measure of thyroid function. CFDS applications depend on quantitative and qualitative analyses. Peak systolic velocity (PSV) obtained from the main thyroid arteries is the parameter commonly employed for the quantitative Doppler evaluation of the thyroid gland. Measurements are usually obtained from the superior thyroidal arteries (STA) or the inferior thyroidal arteries (ITA). It is determined as the recorded Doppler wave of the point at which the highest frequency shift is observed in the images [1].

Qualitatively, various classifications of vascular patterns have been proposed, some of which overlap. Among these, the classification of Vitti *et al*. [3] for the diffuse goiter is one of the most popular ones in the literature (Table **1**). Healthy glands show either no color signals in the parenchyma or occasional intra-parenchymal spots. Blood flow limited to peripheral thyroidal arteries is normal [1].

The basic principle of CFDS depends on its ability to distinguish autoimmune hyperthyroidism (Hashimoto's thyroiditis) from other low radioiodine uptake causes of hypothyroidism. As supported by many studies, the thyroid gland's vascular signals are found to be increased in hyperthyroidism, whereas they are normal or decreased in the latter [1-3].

The aim of the study is to determine the value of CFDS in the differentiation between Graves' disease and Hashimoto's thyroiditis induced hyperthyroidism.

PATIENTS AND METHODS

Our study was approved by the ethical commitee of our hospitals and informed consent was obtained from all participants. Forty patients, 17 male and 23 females with (12 Graves' disease, 18 patients with thyroiditis, and 10 euthyroid controls) having clinical and lab signs of hyperthyroidism were referred from the period July 2013 to February 2014 to a private centre for sonographic and color flow Doppler differentiation between Graves' disease and toxic phase of Hashimoto's thyroiditis because both have the same

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clinical picture but different management and prognosis. All of the cases were newly diagnosed and did not receive therapy or any other medication that could affect thyroid vascularization.

Etiological diagnosis was carried out by measuring serum thyroid hormones, serum thyroid stimulating hormone (sTSH) levels, and auto-antibody levels. Conventional

B mode-gray scale ultrasonography, followed by CFDS was performed in all of the cases, and blood flow patterns were evaluated.

The thirty patients with hyperthyroidism performed a routine 99mTc thyroid scans with injected I.V dose of 3-5 mCi according to body weight using Philips Merredian scanner (Philips, Amesterdam, The Netherlands) in the same centre and was used as a gold standard.

The hyperthyroidism group consisted of patients with high free T3 and T4 In this group of patients, those with sTSH value less than 0.1 mIU/ mL, diffuse high tracer uptake in the thyroid scan, and positive thyroid autoantibody tests (antithyroglobulin [anti-Tg]>60U/mL, anti–thyroid peroxidase [anti-TPO]>60U/mL)] were diagnosed as Graves' Disease.

Thyroiditis was diagnosed by demonstrating the heterogeneous echogenicity of the thyroid parenchyma by ultrasonography, positivity of at least one of the thyroid auto-antibodies as described above, together with normal or increased sTSH serum levels with poor tracer uptake in the thyroid scan.

Cases with sTSH values between 0.35 and 5.5 mIU/mL, normal serum thyroid hormone levels, and negative thyroid auto-antibodies, served as controls.

B-mode and colour Doppler ultrasonography examination:

Conventional ultrasonography and CFDS were performed by using a 7–11 MHz broadband linear transducer Xario (Toshiba, Yokohama, Japan). Echogenicity of the thyroid parenchyma was graded as diffuse homogeneous or mild, moderate, or extremely heterogeneous in grey scale and the color gain was adjusted so that artifacts were prevented. The sonographic study was performed with the patient in dorsal decubitus with a cushion under the shoulders and the neck hyper-extended. In order not to underestimate the vascularization intensity, the probe was lightly positioned on the skin without any compression. A short apnea was requested from the patients during the duplex-color Doppler recordings. Color Doppler parameters were standardized and, for all studies, the same presets were used for the acquisition. The equipment was set up to ‘‘thyroid’’, configured as follows: PRF (pulse repetition frequency) 700 Hz, colour map 1, WF (wall filter) medium and flow option medium

Velocity. In addition, the gain settings (between 72 and 79) were adjusted to avoid background noise. The probe was positioned in the longitudinal and horizontal directions, with its centre at the middle third of the thyroid lobes. The isthmus vascularization was also included. For PSV measurements, the sampling volume was adjusted to 3mm at the center of the vessel. For evaluation of the superior thyroid artery (STA), the probe was positioned in the oblique sagittal plane, close to the superior thyroid pole. The inferior thyroid artery was examined in the oblique transversal plane, close to the transition between the medium and the inferior third of the thyroid. The cursor for evaluation of the inferior thyroid artery (ITA) was set close to the trachea in order to avoid artifacts coming from the common carotid artery and the internal jugular vein. The peak systolic velocity (PSV) and resistive index (RI) values in the superior and inferior thyroid arteries were obtained. The Doppler angle was corrected to values under or equal to 60°.The mean value found in the right and left lobes was used as a representative parameter. The limits of normal PSV values are generally accepted as 25–30cm/s for STA and 23–25 cm/s for ITA [4, 14].

The vascular patterns of the thyroid gland were scored for the parenchyma according to the Vitti’s classification.

Table 1: Vitti’s Classifications of Color Flow Doppler Sonography Patterns

Description	Pattern
- Blood flow limited to the peripheral thyroid arteries or to subcapsular vessels.	0
- Mildly increased color signals at the level of peripheral thyroid arteries and presence of parenchymal blood flow with patchy, uneven distribution.	I
- Clearly increased color flow Doppler signal with patchy distribution.	II
- Markedly increased color flow Doppler signals with diffuse homogeneous distribution included the ‘‘thyroid inferno’’	III

RESULTS

Laboratory data of the study groups are summarized in Table **2**. Vascular signal patterns were significantly more prominent, and the mean PSV values were significantly higher in the Graves' Disease group compared to the Thyroiditis and control (Table **3**).

Correlation analysis between CFDS parameters and thyroid function tests revealed that there is a significant correlation between free T3 and PSV values in the Graves' disease group. There was a positive correlation between intrathyroidal vascular markings in the Graves' disease and thyroiditis group. Similarly, we determined significant correlations thyroidal PSV measurements in both the Graves' disease and thyroiditis group; there was no correlation in the control group regarding these parameters.

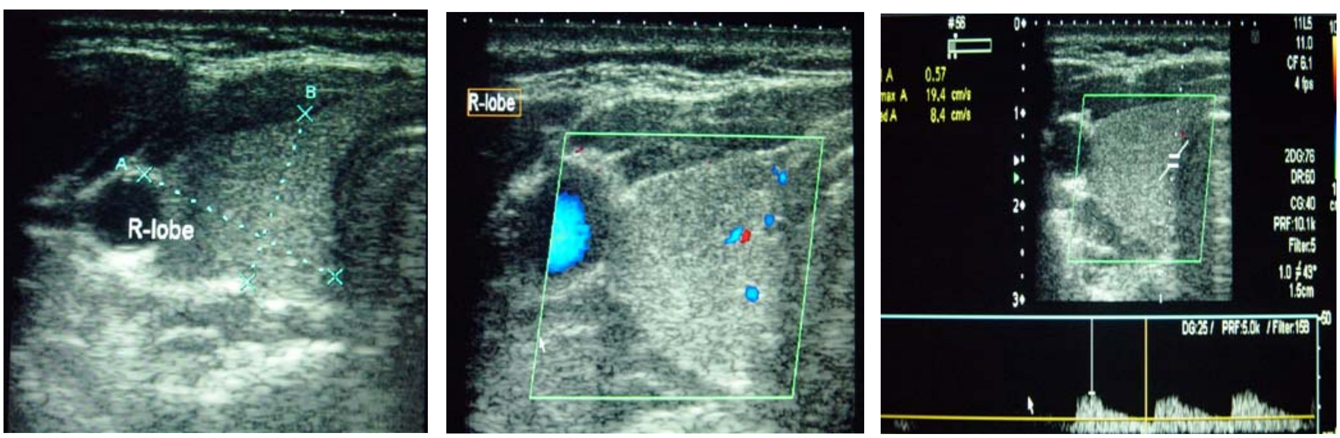
Parenchymal echo patterns differed significantly when the Graves' disease group was compared with the control group and the thyroiditis group. Similarly, the difference in parenchymal echo patterns was significant between the control and thyroiditis groups. A positive correlation was determined between parenchymal echo patterns and some Doppler parameters in the Graves' disease group. Thus, increasing echo correlated with increasing thyroidal PSV values as well as more prominent intrathyroidal CFDS patterns. When correlated to thyroid scan, colour doppler sonography showed sensitivity = 96.6% and specificity 96.6%, and P>0.001.

Table 2: Summary of the Laboratory Results of the Study Groups

	Number of Cases	sTSH mIU/L	Free T3 Ngm/ml	Anti Thyroglobulin U/ml
Graves' disease	12	0.05 +/- 0.08	18 +/-5	500 +/- 150
thyroiditis	18	5.50 +/- 2	4 +/- 1	225 +/- 100
Control	10	1.50 +/- 0.5	6 +/- 2	20 +/- 10

Table 3: Summary of the Doppler Findings in the Study Groups

	Number of Cases	Color Doppler Flow Pattern				Mean PSV (cm/sec)
		0	I	II	III	
Graves' disease	12			5	7	75 +/- 25
Thyroiditis	18		2	13	3	40 +/- 20
Diffuse goiter	10	8	2			25 +/- 15



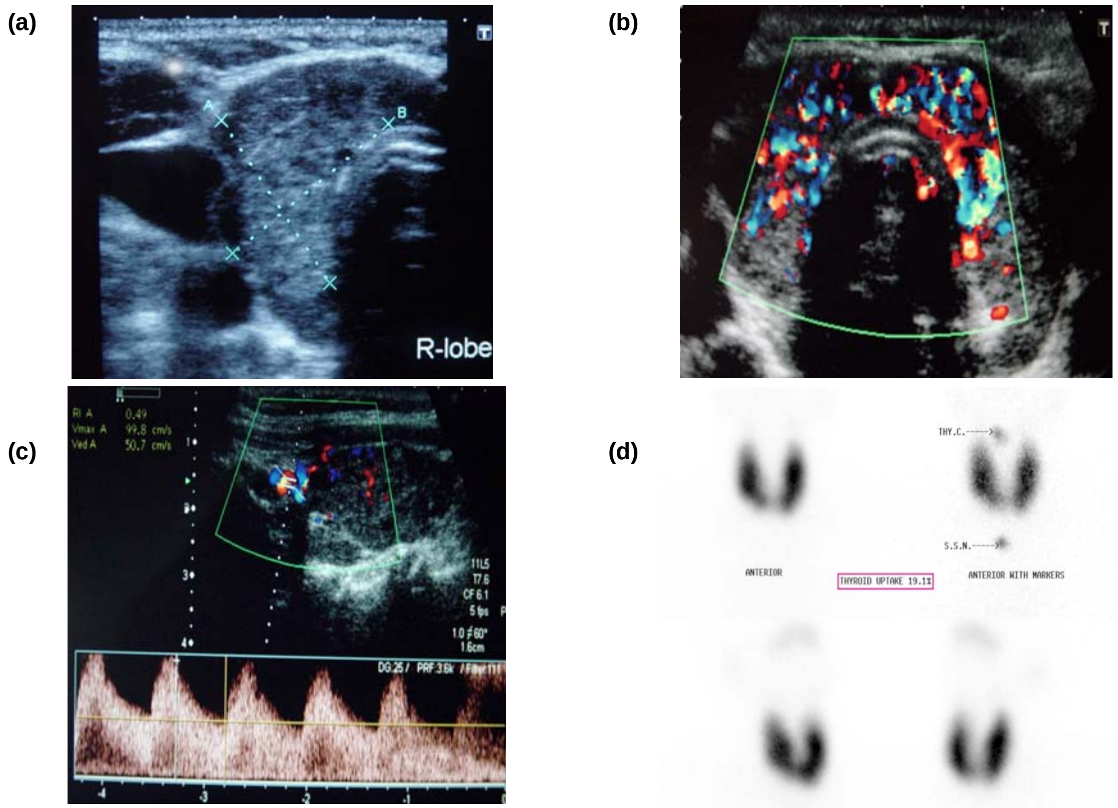
(a) (b) (C)

(a) grey scale B mode ultrasound showing homogeneous texture of the gland **(b)** color doppler image showing normal intra thyroid vascularity (grade 0) **(c)** pulsed doppler of the ITA showing normal PSV (19 cm/sec) and RI (0.57).

Case 1: 38 yrs female with mild diffuse goiter, normal T3, TSH serving as a control.

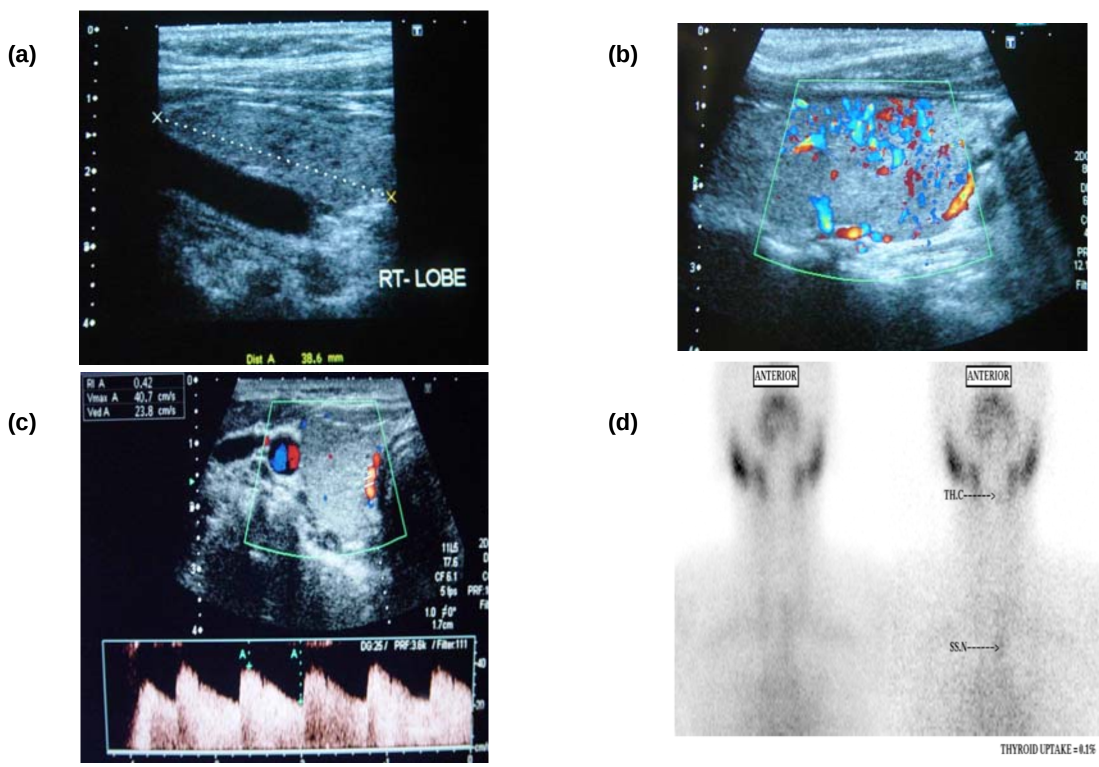
DISCUSSION

The characteristic grey scale ultrasonographic and CFDS findings of Graves' disease patients in our study are generally in accord with the literature [2,6,12]. In one of the Doppler studies, Vitti *et al*. [3] have evaluated CFDS patterns and PSV values of treated and untreated Graves' disease and thyroiditis patients.



(a) Grey scale B mode ultrasound showing heterogeneous texture of the gland with coarseness. **(b)** color doppler image showing increased intra thyroid vascularity (grade III). **(c)** pulsed doppler of the ITA showing high PSV (99 cm/sec) and low RI (0.49). **(d)** thyroid scan showing typical features of Graves' disease with uptake = 19 %.

Case 2: 34 yrs female Graves' disease with high free T3, low TSH and increased anti thyrogloblin antibodies.



(a) grey scale B mode ultrasound showing inhomogeneous texture of the gland with fine coarseness. **(b)** color doppler image showing increased intra thyroid vascularity (grade II). **(c)** pulsed doppler of the ITA showing high PSV (40 cm/sec) and low RI (0.42). **(d)** thyroid scan showing typical features of thyroiditis with uptake = 0.1 %.

Case 3: 45 yrs male, thyroiditis with increased T3, high TSH and increased anti thyroglobulin.

They have discovered clear relationships between patients' functional status and CFDS parameters. They found pattern III vascular signals (''thyroid inferno''), previously described by Ralls *et al*. [9], in the majority of the untreated Graves' disease patients (Table **1**). Similar findings were reported by Bogazzi *et al*. in untreated Graves' disease patients [8].

Most of our untreated Graves' disease patients corresponded to pattern III, but not II of Vitti's classification (Table **1**). CFDS could generally differentiate the untreated Graves' disease patients from diffuse goiter, but more importantly from the patients with thyroiditis (who have similar grey scale ultrasonographic findings) (Table **3**).

However, we have observed a few overlaps of CFDS patterns between Graves' disease and thyroiditis patients that are also supported by the literature [3,8]. Our findings suggest that, although what is described as thyroid inferno is seen in some of the untreated cases, it is neither pathognomonic nor specific for untreated Graves' disease and could also be seen in thyroiditis.

PSV measurements, obtained from both STA and ITA vessels, were also significantly higher in Graves' disease patients when compared with the other diffuse groups. This parameter could help to differentiate the overlapping Doppler patterns observed in the Graves' disease and thyroiditis groups [3,8,13]. PSV measurement seems to be more useful than evaluation of CFDS patterns in the differential diagnosis of autoimmune thyroid disorders. Contrary to our findings, PSV values of thyroiditis patients with hyperthyroidism have been found to be significantly higher than their euthyroid counterpart in some of the literature [5,8]; however, they were still lower than those of untreated Graves' disease patients, which we also found [7]. In accordance with our findings, Vitti *et al*. [3] could not determine any correlations between sTSH levels and Doppler parameters in the thyroiditis group. In a recent paper, Schulz *et al*. [11] have reported the results of 89 patients with Hashimoto's thyroiditis. They observed Vitti pattern III in six of the cases, and pattern II in 11 of their patients. Increased signal intensity was explained as a part of ongoing autoimmune process but not by serum sTSH levels. They found strong positive correlations between Doppler patterns and PSV values and serum thyroid autoantibody levels. However, most of their cases were under treatment, and any possible effect of the therapy on vascular signals has to be taken into account. Regarding intrathyroidal signals, Bogazzi *et al*. [8] have made PSV measurements from intrathyroidal arteries in untreated Graves' disease cases, and reported mean values of 65cm/s. This value was 75cm/s in our group. Our Hashimoto's thyroiditis patients' values were also higher than this group (40 cm/s vs. 35 cm/s). These differences may result from variations in measurement methods or devices used [10, 15].

Our results are in coordinance with Donkol *et al* [16] and Sekulic *et al* [17], both showed good correlation between color duplex sonography and Tc 99m thyroid scan in differentiating Graves' disease from thyroiditis.

CONCLUSION

CFDS 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 strikingly in differentiation of Graves' disease, nontoxic diffuse goiter, and Hashimoto's thyroiditis.. Finally, CFDS could avoid scintigraphy in a substantial number of thyrotoxic patients during the routine clinical work-up.

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