ORIGINAL ARTICLE

CORRELATION OF COLOR DOPPLER SONOGRAPHY AND PERIPHERAL THYROID HORMONE LEVELS IN THYROTOXICOSIS

Gozde Arslan,[1] Inci Kizildag Yirgin[2]

[1] Erzincan University, Mengucek Gazi Training-Research Hospital, Radiology Department, Turkey
[2] Batman State Hospital, Radiology Department, Turkey

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ABSTRACT

PURPOSE: Aim of this study was to evaluate the correlation between the gray-scale &Color Doppler Ultrasonography (CDUS) findings and thyroid hormone values in patients with thyrotoxicosis due to thyroiditis and to question their applicability in daily practices. **METHODS:** The CDUS parameters like peak systolic and end diastolic velocities of superior thyroid artery and resistive index values were compared with thyroid d hormone levels in 60 patients with known thyroiditis. Forty-two healthy cases were also studies as control. **RESULTS:** Intergroup comparison did not show any significant difference in the CDUS parameters like peak systolic and end diastolic velocities (PSV and EDV) of superior thyroid artery (STA) but a significant correlation was found for the resistive index value (RI) of the superior thyroid artery ($p< 0.05$). In patients with thyroiditis, positive correlation was found between free T3, free T4 and CDUS parameters ($p<0.05$). **CONCLUSION:** Color Doppler ultrasonography parameters has good correlation with serum thyroiod hormone level in patients with thyrotoxicosis caused by thyroiditis. sonographic analysis lacks this diagnostci accuracy.

Introduction

Hyperthyroidism is defined as a condition in which thyroid gland produces excessive thyroid hormone resulting in thyrotoxicosis.Thyrotoxicosis is the clinical status secondary to raised circulating thyroid hormones. Thyroiditis is an inflammatory condition of thyroid gland resulting from autoimmune, viral, medication and radiation effects with raised thyroid hormone due to release of stored hormones from damages thyroid follicles. Each factor requires a different way of treatment. The thyroid dysfunction is biochemically evaluated with TSH (Thyroid Stimulating Hormone), f (free) T3 and f (free) T4 values in the blood. We expect the f T3, f T4 values to increase in the cases with thyrotoxicosis. Radio-nuclide thyroid scan showing reduced thyroid uptake with low serum TSH is the diagnsotic criterai for thyroiditis. Although sonography is not the primary tool for diagnosing thyroiditis, but it might be helpful if evaluated along with the biochemical tests. The degree of destruction within the gland is evaluated by the sonographic examination. A normal healthy thyroid gland has a homogenous echo structure and a higher echogenicity than the peripheral muscle groups.[1] Among the sonographic findings of thyroiditis are mostly the diffuse hypoechoic appearance, fibrous echogenic layers and hypoechoic micronodules The vascular structure of the gland can be evaluated through the Color Doppler Ultrasonography (CDUS) analysis. The thyroid gland is fed by the superior and inferior thyroid arteries in both of the lobes. The superior thyroid artery (STA) is the branch of the external carotid artery, whereas the inferior thyroid

Correspondence : Dr. Gozde Arslan
Basibuyuk mahallesi, Emek caddesi,
Narcity C1-26, Maltepe, Istanbul, Turkey.
Ph: 90 555 688 08 96
E-mail: gunesgozde@gmail.com

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artery (ITA) is the largest branch of the thyrocervical trunk. The variation in vascular flow of the thyroid gland may give us an idea about the degree of inflammation of the gland with respect to several subjects.[2] Our objective in this study was to find out a relationship between the thyroid hormone values and ultrasound findings using gray-scale and color doppler ultrasonography parameters in patients with thyroditis.

Material and Method

This was a prospective and ethically approved study conducted in Department of Radiology, Erzincan University between 2013 and 2014. Sixty patients with known thyrotoxicosis (raised fT3, fT4 and low TSH) secodnary to thyroiditis were included and 42 controls having no thyroid ailment were also studied. In thyroiditis group 42/60 were female and 18/60 were male, with no systemic ailment apart from hyperthyroidism. In control group 25/42 were female and 17/42 were male with statu-euthyroid in terms of sonography and thyroid hormone levels. Sonographic analysis was performed by a radiologist (with 7 years experience who was blind to patients) by using the Voluson 730 PRO device with a SP6-12 wide band linear ultrasound transducer. A day before the sonographic analysis, serum free thyroxine (f T4), free tri-iodothyronine (f T3),and thyrotropin (TSH) values were assessed. The reference ranges taken as the basis for this measurement in our hospital were determined as 0.89-1.76 ng/dl for f T4, 2.3-4.2 pg/ml for f T3 and 0.55- 4.78 mIU/ml for TSH. The cases whose TSH, f T3 and f T4 values were measured and who were regarded as clinically having thyrotoxicosis were sent to the sonographic examination/analysis. These patients were analysed by gray-scale CDUS. During the sonographic analysis, cases were divided into 3 grades by means of a subjective method we used in our clinic in accordance with the parenchymal echoic structure of the thyroid gland. (Tab. 1, Fig. 1a, 1b).

Such grading was also performed in the previous studies in a similar way.[3] From each grade, 20 patients were selected. The sonographic characteristics of echotexture included fine, coarse, and micronodulative patterns.

Grade 1	Grade 2	Grade 3
Normoechoic gland with focal- minimal heterogenous areas with small pseudo-nodules.	Mild hypoechoic gland with echogen septations and pseudo-nodules. Normal and destroyed parencyhma together.	Very hypoechoic gland with thick and echogen septations and marked pseudo-nodules. Completely destroyed gland.

Table 1: The Grading of the Cases with Thyroiditis During the Grayscale Sonographic Analysis

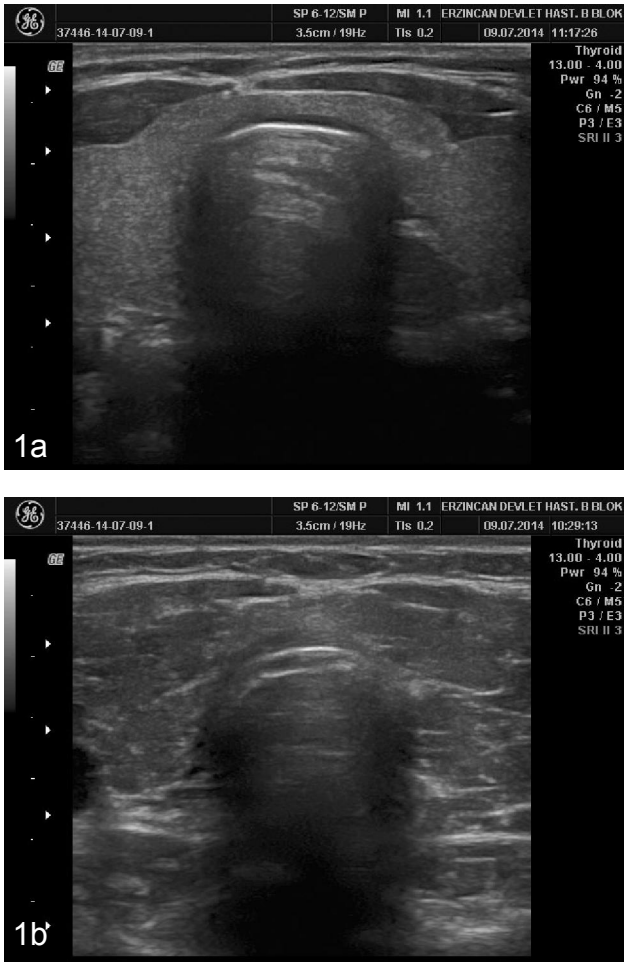

Figure 1a: Eutyhroid patient with homogenous thyroid gland **(b):** Patient with grade 3 thyroiditis (hypoechoic gland with marked echogen septations)

The cases that had nodules and that were using antithyroid drugs were not incorporated in the study on account of the fact that they could affect the thyroid vascularization. After the cases had been

graded on the gray-scale, the blood flow was evaluated through CDUS. The PRF (pulse repetition frequency)values of the device were adjusted to a maximum level so as not to cause an aliasing in the neighbouring vascular structures. The Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV) and RI (Resistive index) values of STA and ITA were measured from the proximal intrathyroid segments with a sampling volume of 0.7 mm. In the course of the measurements, the angle was adjusted to 30-40°. (Fig. 2a, 2b)

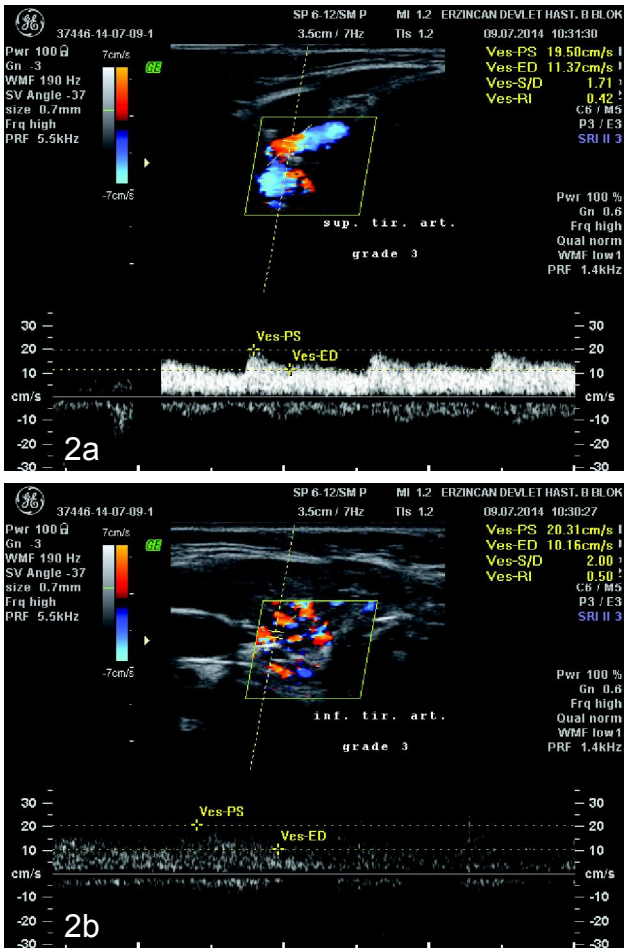

Figure 2a: The CDUS analysis of the Inferior Thyroid Artery of the case with Grade 3 thyroiditis. (PSV: 20 cm/s, EDV: 10 cm/s)
2b: The CDUS analysis of the Superior Thyroid Artery of the case with Grade 3 thyroiditis. (PSV: 19 cm/s, EDV: 11 cm/s)

In our study, the serum hormone values, sonographic grades, flow rates and RI values of the cases with thyrotoxicosis were primarily compared among themselves. Afterwards, the STA and ITA, PSV, EDV and RI values of the volunteer group comprising our hospital staff who were normal in terms of laboratory and sonography analyses were measured and compared with the case group with thyroiditis. The Kolmogorov–Smirnov test was used to test the normality of data distribution. The Kruskal–Wallis test was used to compare the continuous variables for more than two groups. Pearson correlation and Student T-test methods were used for correlative purposes.

Results

The values of the control group and the thyroiditis group were compared by means of the Student-T test. The mean/average flow rates of STA PSV and EDV were calculated. In the same way, the mean/average flow rates of ITA PSV and EDV were calculated, as well. Both groups were compared both in the control group and the hyperthyroidism group.
No significant difference was observed between the average PSV, EDV values of STA and ITA in the control group and also in the thyroiditis group. The control and the thyroiditis groups were compared within and between themselves (Tab. 2). Interestingly, there was a significant difference only for STA RI values between the control and hyperthyroidism

t-test for Equality of Means		Sig. (2-tailed)	Mean Difference	Std. Error Difference
Inf PSV	Equal variances assumed	0,717	-0,53762	1,47843
	Equal variances not assumed	0,709	-0,53762	1,43604
Inf EDV	Equal variances assumed	0,384	0,685881	0,783898
	Equal variances not assumed	0,367	0,685881	0,757327
Inf RI	Equal variances assumed	0,380	-0,06307	0,07152
	Equal variances not assumed	0,370	-0,06307	0,07008
Sup PSV	Equal variances assumed	0,766	-0,39533	1,32510
	Equal variances not assumed	0,763	-0,39533	1,30867
Sup EDV	Equal variances assumed	0,308	0,79936	0,77990
	Equal variances not assumed	0,293	0,79936	0,75608
Sup RI	Equal variances assumed	0,037	-0,14338	0,06771
	Equal variances not assumed	0,017	-0,14338	0,05875

Table 2: Independent samples test. Significant difference of STA RI value between control and thyroiditis groups.

groups. (p= 0,037) (Tab. 2). The mean values of each grade were calculated. By means of Kolmogorov-Smirnov and Shapiro- Wilk methods and no significant difference was determined between the 3 grades by means of the biochemical and CDUS values.

In the thyroiditis group, a positive correlation was foud among f T3, f T4 values and ITA and STA peak systolic and end diastolic velocity values. No significant correlation was observed between the TSH and CDUS values. A positive correlation was seen between Superior PSV-EDV and Inferior PSV-EDV.

Discussion

Thyrotoxicois caused by thyroiditis is evaluated along with the laboratory tests and the sonographic findings for its diagnosis.[4] The thyroid parenchymal echo-genicity in cases with thyroiditis may include different findings according to the phase of the infla-mmatory process, like increased or decreased parenchymal echogenicity, micronodular appearance and echogenic layers. In our study, we divided the cases with thyroiditis into 3 grades (depending on the manifestation of the disease sonographically) through the gray-scale sonographic analysis in the similar way as Kim et al. had previously performed.[5] The subjectivity of the grading method applied here may be a limitation, however, we think that a total of 3 grades minimize the risk of intra- and inter-observer differences.

We performed the measurements on the cases we had mentioned in the method section and compared them among themselves. Apart from this, we compared the CDUS values in the cases with thyroiditis with those who were sonographically and biochemically normal.

The mean PSV values in the thyroiditis group were: PSV STA: 17,0787 cm/s, ITA PSV: 18,3067 cm/s; the mean PSV values in the control group were: PSV STA: 16,6833 cm/s, ITA PSV: 17,7690 cm/s.

We could not find any significant difference among different grades of the cases with thyroiditis with regard to CDUS and biochemical values, which suggests that the biochemical and CDUS values of a for example; sonographically grade 3 case (with micronodular appearance involving intensive echogenic layers) may differ due to the cause of thyroiditis or according to the active-chronic phase of disease. For example, in De Quervain's thyroiditis; there may be an increase in the thyroid values in the early stages resulting from the destruction of the gland and releasing of hormones into the circulation and a decrease in the hormone levels in the later stages resulting from depletion of the gland. The biochemical values will differ in different phases.But the gray scale sonography grade 3 apperance (as we defined) of the gland will persist even if the disease returns to a silent phase.

In the study conducted by Bogazzi et al.the argument that the gland vascularization did not significantly increase despite the elevated TSH values which rose secondarily to the gland destruction was put forward with respect to the cases with Hashimoto's thyroidits.[6] Similar to their study, we also have not determined any increase in the blood flow of some cases with sonographically extremely heterogenous gland.

Consequently, we cannot state that a case has an active or chronic thyroiditis by depending on the gray-scale sonographic imaging. We simply come to understand to what extent the thyroid gland has been destroyed.

One of the reasonable outcomes in our study was the significant correlation between the CDUS values and f T3 and f T4 values. As the CDUS values increase, so do the f T3 and f T4 values, which shows us that whatever the underlying cause may be, there will be an increase in the flow rates of both the Superior and Inferior Thyroid Arteries in the cases with thyroiditis. There may be a connection between the increased blood flow rate and more hormone secretion of the gland. Boggazzi et al.[6] found the mean intrathyroidal PSV values to be 15 ± 3 cm/s in the untreated hyperthyroid patients with Basedow Graves' disease (BGD),while this value was 5.6 ± 1.4 cm/s in those with hypothyroid Hashimoto's thyroiditis, 4.3 ± 0.9cm/s in those with euthyroid Hashimoto's thyroiditis, and 4 ± 0.8 and 4.2 ± 1.1 cm/s, respectively,in those with thyrotoxic thyroiditis (toxicosis due to destructive process of thyroid gland). Separately, in another similar study conducted previously, only the Superior Thyroidal Arterial PSV

were measured, which is in concordance with our study.[7] In the light of this result, we can say that the case has hyperthyroidism by measuring the flow rates without obtaining the blood hormone values yet, In addition, the CDUS values of the cases with hyperthyroidism can lead us the way during their post treatment check-ups.[8] The fact that there was a significant difference in only the STA RI value between the control and hyperthyroidism groups and that there was no significant difference in the ITA RI and other CDUS measurement values are the interesting consequences of this study. Here, our limitation may be the number of our cases. Once the number of the cases increase, there may be significant differences showing up.

In conclusion, we can gain more insight about the way the thyroid gland functions by performing the gray-scale and color Doppler ultrasonographic examination of an easily accessible superficial organ like the thyroid. We are of the opinion that we need to take maximum advantage of such methods of analysis and in order to be able to provide this, we require to carry out further studies regarding this subject.

Conflict of Interest

There are no financial or other relations that could lead to a conflict of interest.

Ethical Statement

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.[5] Informed consent was obtained from all patients for being included in the study.

Additional informed consent was obtained from all patients for which identifying information is included in this article.

This article does not contain any studies with human or animal subjects performed by the any of the authors.

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