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# The Role of Ultrasound in The Diagnoses of Graves' Disease

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## Abstract

***Aim:*** *To explore the use of ultrasonography and Doppler as an indispensable diagnostic modality in the evaluation and the diagnosis of Graves' disease.*
***Methods:*** *in this prospective study we examined 30 cases of gravis disease and 20 normal controls using the B-Mode sonographic criteria (thyroid size and echogenicity) and Doppler criteria (color flow mapping and spectral analysis the peak systolic velocity in the thyroidal arteries and the resistive index within the thyroid parenchymal vasculature).*
***Results:*** *when using more than one sonographic and Doppler criteria, thyroid size, echogenicity, Color flow mapping (qualitative) and spectral Doppler values as peak systolic velocity (PSV) in thyroidal arteries and thyroid parenchyma RI. As a test for diagnosis of Grave's disease. Most patients with Graves' disease showed increased thyroid volume, heterogeneous parenchyma, marked increased parenchymal vascularity and significantly increased PSV in thyroidal arteries.*
***Conclusion:*** *Ultrasonography Doppler is a cost-effective, noninvasive, portable, and safe imaging modality in the evaluation of Graves' disease,*

**Keywords:** *Thyroid, Graves' Disease, Ultrasonography, Color-Flow Doppler*

## 1. Introduction

Graves' disease (GD), as known today, is an autoimmune, diffuse, chronic disease of thyroid gland, as described by Robert Graves in 1835 [1].

Graves' disease is the most common cause of hyperthyroidism, which has an estimated prevalence in iodine sufficient areas of 20/1000 females and 2.3/1000 males [2]. It is most common in females between the ages of 20 and 50 years, but it may occur at any age. The laboratory diagnosis of Graves' disease is based on the finding of high serum thyroid hormone and undetectable serum TSH concentrations associated with circulating thyroglobulin and thyroperoxidase antibodies. TRAb is detectable in almost 90% of patients, but usually it is not needed for the diagnosis.

After the introduction of the ultrasound into clinical practice in the late sixties, thyroid ultrasonography (US) proved to be very effective in the diagnostic approach to thyroid diseases, the anatomical location of the gland being advantageous for this technique. The most widely used application of thyroid US is identification and characterization of thyroid nodules [2]. Rapid improvements in the development of US equipment have made available real-time high frequency transducers (7.5–10 MHz) with high resolution, which allow a more precise definition of the echostructure of the thyroid tissue.

In B-mode ultrasound, the normal thyroid has a peculiar echogenicity, making the gland well distinguishable from surrounding neck structures. Thyroid echogenicity is due to the gland’s follicular structure the interface between thyroid cell and colloid exhibits high acoustic impedance, causing high frequency acoustic waves to be reflected back to the probe leading to the characteristic ground glass appearance of normal thyroid (fig. 1).

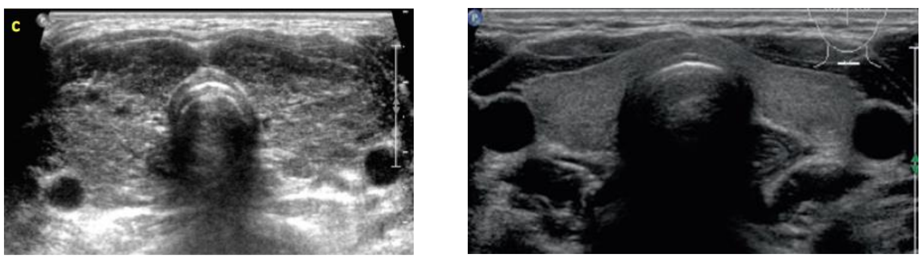

Figure1. Normal B-mode ultrasound appearance of thyroid with ground glass appearance (b) compared the enlarged heterogamous thyroid of Graves’ disease (b)

Conditions that change the normal anatomical structure of the gland as Graves’ disease cause this echo pattern to be altered (fig1). In addition, recently developed color Doppler technology allows determination of the blood flow through the gland, offering the possibility of qualitative parenchymal vascularity assessment with color flow mapping and spectral quantitative measurements, such as the peak systolic velocity of the blood flow at the level of thyroid arterial vessels (i.e. inferior thyroid artery) and thyroid parenchymal flow resistive index (R.I). Using these techniques, thyroid blood flow has been shown to be correlated with the thyroid status in patients with Graves’ disease.

In this scenario, thyroid color-flow Doppler ultrasonography (US Doppler) presents a widely available, low cost, non-invasive and radiation free method, providing initial diagnosis and follow up of patients with GD. In addition, this method is used in differential diagnosis with other causes of thyrotoxicosis in the early stage.

## 2. Patient and method

30 cases with Graves' disease (3 male and 27 female) The Inclusion criteria of the cases depend on the clinical and laboratory investigation presenting in the endocrine clinics with thyrotoxicosis , Exclusion criteria included toxic nodules, multinodular goiter, history of thyroid surgery, radioiodine therapy or radiation exposure to neck. The study done in the Benghazi from 4 April 2018 to 1-January-2019. 20 adults were randomly selected as control group from patient were referred for other neck ultrasound and Doppler examinations. The inclusion criteria were absence of history of any thyroid related disease.

Sonographic and Doppler examination was performed at Al Hawari general hospital department of Radiology and Benghazi medical center department of radiology using a Hitachi and Phillips sonographic machines with a 7.5-MHz transducer supported with Color and spectral Doppler.

**B Mode Evaluation**

We evaluated the GD cases and the controls, with the B mode sonography, the gland dimension (volume) and thyroid parenchyma alterations. Although, focal lesions occurrence (nodules) is unusual in GD, whenever they are found, they should be evaluated according to their features by B mode and color Doppler

**Estimation of thyroid volume**

The thyroid gland correct volume should be obtained by maximum measures in the longitudinal (L), anteroposterior gland volume (AP) and transverse (T) axis of both lobes and isthmus (Figure 2). The volume (TV) the ellipse correction coefficient used is ($TV = L \times AP \times T \times \pi/6$) (Figure 2). The lobes and isthmus volumes are added to obtain the total thyroid volume.

The normal adult thyroid volume values 13 ± 5ml [2], with no gender distinction in the given population. According to that we divided the thyroid size into normal 10±5ml, mildly enlarged 20±5ml, and markedly enlarged 30±5ml.

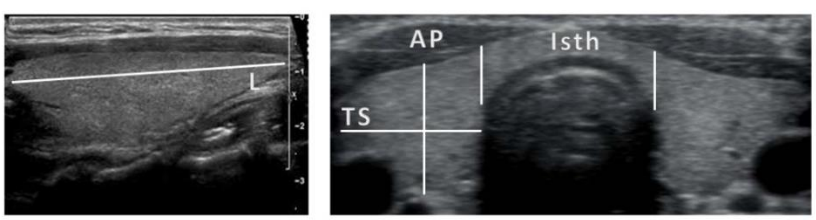


**Figure 2.**Scheme demonstrating how thyroid lobes should be measured in the longitudinal and transverse axis

**Thyroid gland echogenicity**

Normal gland has an echogenicity characteristic in ultrasound as described, easily distinguishable from different diffuse thyroid pathology by the reduction or increase in its echogenicity, micro-nodularity, nodular lymphocytic infiltration diffuse or patchy (Swiss cheese), fibrous bands. These B-Mode ultrasound features were evaluated in all of our cases of GD. And normal controls,

## 3. Color and Spectral Doppler Ultrasonography

**Color flow mapping**

Qualitative Assessment of thyroid vascularity with Color Flow Doppler Mapping (CFM) using the following criteria:

- Pattern 0 : minimal intraparenchymal blood flow
- Pattern I: presence of mild parenchymal blood flow with patchy uneven distribution (fig 3).
- Pattern II: moderate increase of color flow Doppler signal (fig 4).
- Pattern III: markedly increased color flow Doppler signal with diffuse homogeneous distribution, the so-called “thyroid inferno" (fig 5)

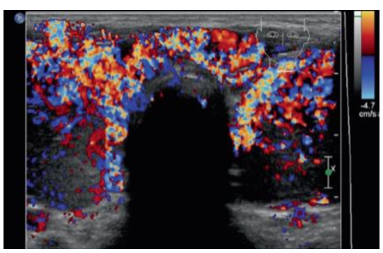

**Figure 5**

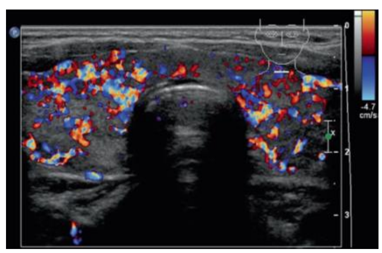

**Figure 4**

**Figure 3**

**Spectral analysis**

**Peak systolic velocity:** Thyroid arteries peak systolic velocity (PSV) measurement is done with sample volume 1-2 mm adjustment, in vessel center, the insonation angle should be $0^{\circ}$ - $60^{\circ}$ and correction angle adjusted parallel to the vessel wall (Figure 6). The PSV can be measured in the inferior or the superior thyroid arteries. There is no significant difference between the PSV in the inferior thyroid artery gland of both sides.

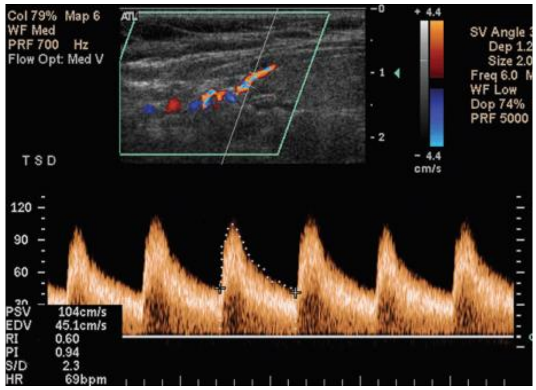


**Figure 6.** Duplex-colour Doppler of the superior thyroid artery with the probe positioned in the oblique sagittal Flow Parameter Measured the Peak Systolic Velocity (PSV) and (RI).

**Thyroid parenchymal Flow Resistive Index RI:** The arterial flow resistive index RI. is reflecting the intraparenchymal flow resistance in the thyroid, we estimated RI. Either in the thyroidal arteries or in the intraparenchymal thyroid arterioles with the smallest sample volume 1-2mm. it was calculated using the software built in the used ultrasound equipment.

## 4. Results

Fifty subjects were included in this study. Thirty (60%) subjects were diagnosed with Grave's disease by clinical examination and laboratory tests, while 20 (40%) were not having the disease.
Thirty four of the subjects were females (68%), and 16 (32%) subjects were males.
The mean age of all the subjects was 39.40 years. With SD 13 years, there was no significant (P> 0.05) differences between the patients and the normal subjects regarding their mean ages (37.73 years, 41.90 years respectively).
After performing ultrasonography and Doppler study of thyroid gland for all the subjects, 93.3% of the GD. patients showed enlarged thyroid gland size, and all normal subjects had a normal gland size. Increased vascularity was obvious among the vast majority of the GD. patients 96.7%, while it was recognized among only 10% of the normal subjects. Heterogeneous echo-pattern was seen only among 56.7% of the GD. patients. High PSV were seen among 83.3% of GD. Cases and high RI 23.3% of the patients respectively figure 7.

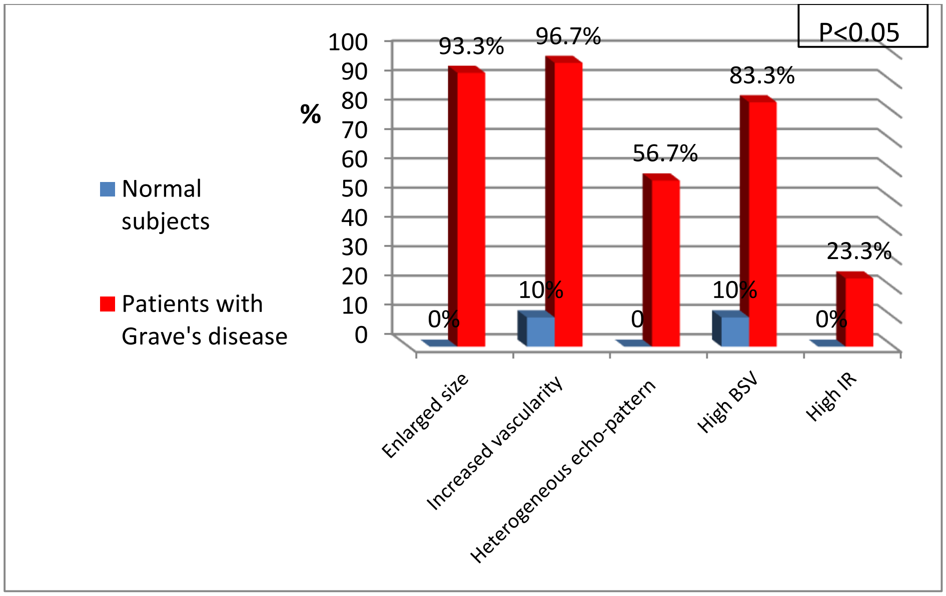


**Figure 7.** Distribution of the subjects according to the result of ultasonography and Doppler study of thyroid gland**.**

- The size is significantly higher in patients with Graves' disease than in normal subjects (X2= 42.42 , P = 0.000). The sensitivity of increased size only as a test for diagnosis of Grave's disease is 93.33 % (95% CI 77.93%- 99.18%), its specificity is 100% (95% CI 83.16%- 100%)

- Heterogeneity is significantly (P=0.000) more among subjects with Graves's disease (table 2). The sensitivity of the heterogeneity as a test for diagnosis of Grave's disease is 56.67% (95% CI 37.43%- 74.54%), its specificity is 100% (95% - CI 83.16%- 100 %), figures 8&9.

- PSV is significantly higher in patients with Graves' disease than in normal subjects (X2= 25.98, P = 0.000). The sensitivity of increased PSV only as a test for diagnosis of Grave's disease is 83.33 % (95% CI 65.28%- 94.36%), its specificity is 90% (95% CI 68.30%- 98.77%)

- Vascularity grade III is significantly (P=0.000) more among subjects with Graves's disease (table1). The sensitivity of increased vascularity as a test for diagnosis of Grave's disease is 96.67 % (95% CI 82.78%- 99.92%), its specificity is 90% (95% - CI 68.30%- 98.77%), figures 8&9.

- RI is significantly higher in patients with Graves' disease than in normal subjects (X2= 5.42, P = 0.02).

The sensitivity of increased RI only as a test for diagnosis of Grave's disease is only 23.33%.

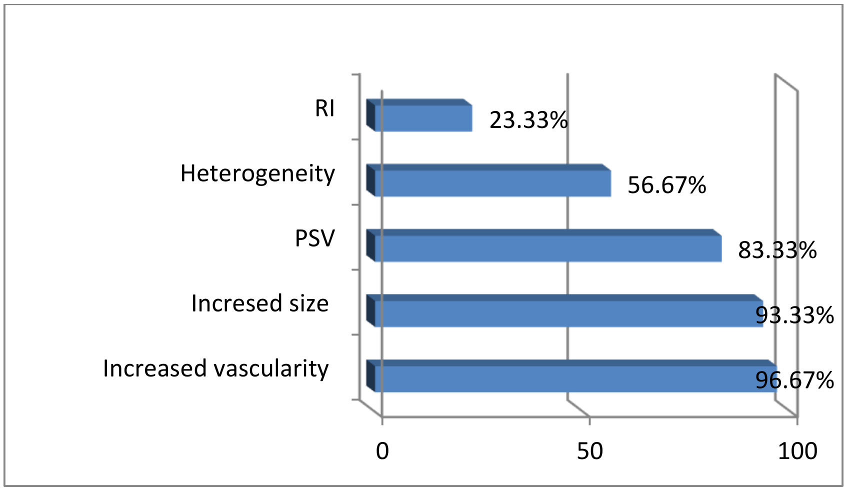


**Figure 8.** Distribution of the criteria according to the level of their sensitivity in diagnosis of Grave's disease

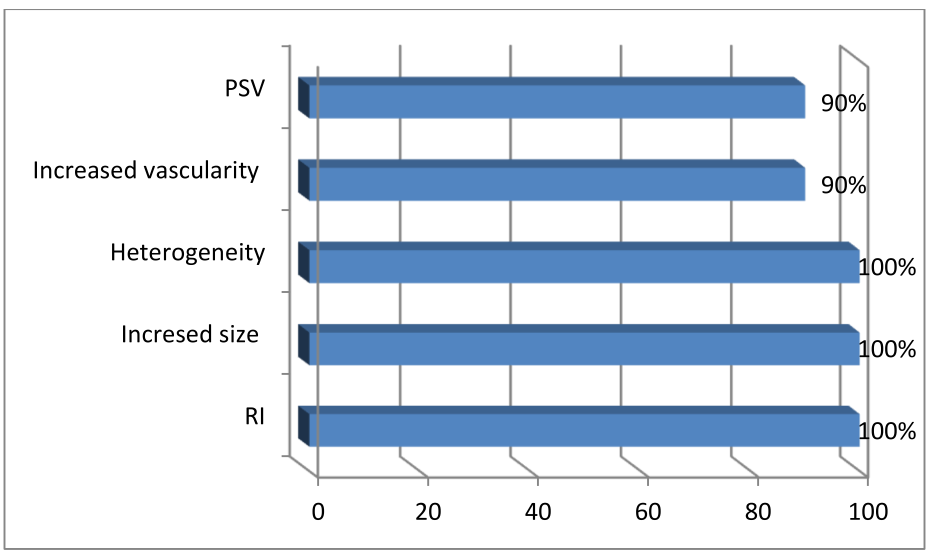


**Figure 9**. Distribution of the criteria according to the level of their specificity in diagnosis of Grave's disease.

Table 1 shows that the vascularity grade III is significantly (P=0.000) more among subjects with Graves's disease.

Table 1 .Distribution of the study subjects according to clinical &lab. Diagnosis and vascularity grading.

| Type of echopattern | Grave's disease | | Total | $X^2$ | P-Value |
|---|---|---|---|---|---|
| | No | Yes | | | |
| Homogenous | 20 (100%) | 13 (43.3%) | 33(66%) | 17.172 | 0.000 |
| Micro nodular ecopattern | 0 (0%) | 8(26.7%) | 8 (16%) | | |
| Heterogeneous | 0 (0%) | 9 (30%) | 9 (18%) | | |
| Total | 20 (100%) | 30 (100%) | 50 (100%) | | |

Table 2 shows that the heterogeneous and micro nodular echo pattern is significantly (P=0.000) more among subjects with Graves's disease.

Table 2.Distribution of the study subjects according to clinical &lab. Diagnosis and the ecopattern type.

| Vascularity grade | Grave's disease | | Total | $X^2$ | P-Value |
|---|---|---|---|---|---|
| | No | Yes | | | |
| I | 5 (25%) | 1 (3.3%) | 6 (12%) | 26.06 | 0.000 |
| II | 13 (65%) | 4 (13.3%) | 17 (34%) | | |
| III | 2 (10%) | 25 (83.3%) | 26 (54%) | | |
| Total | 20(100%) | 30 (100%) | 50 (100%) | | |

## 5. Discussion

In our study B mode ultrasound evaluation. Thyroid gland dimension (volume) and diffuse thyroid parenchymal alterations representing the two major sonographic diagnostic features in GD. If compared to the normal thyroid with high sensitivity and specificity, on the other hand these two features loss this advantage if compared to the other thyroid autoimmune disease as Hashimotos thyroiditis. As in both pathological entities thyroid gland is enlarged with diffuse parenchymal heterogenecity.

In Graves'disease, there is a diffuse increase of thyroid parenchymal vascularization, known as "thyroid inferno" (Figure 5), a term first used to describe this phenomenon by Ralls et al. publication, in 1988[5]. Thyroid hypervascularization can also occur in thyroiditis, but at a lesser level

[5]. In our study more than 96% of GD. Thyroid Showed hypervascularity adding a major sonographic color Doppler feature in the diagnosis of GD. That also differentiate thyroid of GD. Not only from normal thyroid but also from other autoimmune thyroiditis.

The quantitative Doppler evaluation, the peak systolic velocity (PSV) in the inferior thyroidal artery (ITA) or superior thyroidal artery (STA). The normal PSV values obtained was 24.80 cm/s and 25.85 cm/s in the superior thyroid arteries and 20.92 cm/s and 21.50 cm/s in the inferior thyroid arteries [7]. In our study, the mean PSV in the thyroid arteries in GD thyroid was 73.8 cm/s. Compared to 23.5 cm/s. in normal thyroid In our experience, a cut off 50.0 cm/s velocity is considered to GD diagnosis measurement in the inferior thyroid arteries , The sensitivity of increased PSV only as a test for diagnosis of Grave's disease is 83.33 % and its specificity is 90%.

Donkol et al. [6] considered the systolic peak velocity 40.0 cm/s in the inferior thyroid artery and higher is suggestive of GD, Therefore, the high PSV in GD. correlates with increased cardiac output due to hyperdynamic status secondary to thyrotoxicosis. There is significant increases in systolic BP (blood pressure), PR (pulse rate) and CCV (common carotid artery velocity) on both sides in GD. patients.

Finally the quantitative Doppler value R.I. which represents the change in thyroid tissue peripheral vascular resistance, in our study it was showing a limited value in differentiation thyroid of GD. From the normal thyroid, as it was showing an increased RI. In 23% of cases of GD.

## 6. Conclusion

Thyroid gland imaging assessment in GD should be multifactorial, considering B-mode, color Doppler and spectral Doppler features these will increase the diagnostic accuracy of GD. The ultrasound and Doppler diagnostic criteria is the glandular volume increase, heterogeneity and parenchyma hypoechogenicity, diffuse increase in parenchymal vascularity and thyroid arteries increase peak systolic velocity

The B-Mode ultrasound and Doppler are very important for diagnosis of GD and follow up in order to assist the physician during therapy.

Thus, US Doppler is an excellent alternative to radioisotopes exams, with similar accuracy and without contraindication

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