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Comparison of thyroid scintigraphy and ARFI-elastography in autoimmune thyroid diseases

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ABSTRACT

Aim: To compare the ARFI elastographic and scintigraphic quantitative data obtained from thyroid gland and to evaluate diagnostic value of ARFI elastographic measurements in autoimmune thyroid diseases.

Material and Method: In the study a total of 61 patients (41 women, 20 men) including 24 Graves' disease, 15 Hashimoto disease and 22 control subjects. The patients mean age was 33.9±10.9 years. Patients with thyroid nodules were not included in the study. Thyroid uptake was performed with Tc 99m pertechnetate and the elastosonography score of the thyroid gland was determined with ARFI. Findings of both disease groups were statistically compared with each other and control group

Results: For thyroid uptake test; a statistically significant difference was found between two disease ($p < 0.001$) and between each disease and control group ($p < 0.001$ for Hashimoto, $p < 0.001$ for Graves). However, for ARFI method; a statistically significant difference was not found between two disease ($p=0.336$) and between each disease and control group ($p=0.14$ for Hashimoto, $p=0.08$ for Graves).

Conclusion: Thyroid scan and thyroid uptake measurements are extremely valuable in differential diagnosis of autoimmune thyroid diseases and ARFI elastosonographic measurements don't seem to replace scintigraphic datas.

Keywords: Thyroid scintigraphy, thyroid uptake, ARFI, Graves' disease, Hashimoto's thyroiditis

INTRODUCTION

Autoimmune thyroid diseases are common in the population, thyroid scintigraphy and thyroid uptake studies are the most important diagnostic methods used in the differential diagnosis of these diseases.

Thyroid uptake studies with I-131 and I-123 have taken their place in the literature with their success in the differential diagnosis of autoimmune thyroiditis (1-6). A high degree of correlation was observed between thyroid uptake studies with Tc 99m pertechnetate and studies with radioactive iodine (7-9). Tc 99m pertechnetate is inexpensive, easily available and easily applied. Its radiation dose is low and the absence of beta (β) rays makes it more useful than radioactive iodine (9).

Ultrasonography contributes to the differential diagnosis of autoimmune thyroid diseases with additional modalities such as doppler. Elastography is one of the latest developments in ultrasound technology, which was developed in 1990-1991. It measures tissue stiffness quantitatively and qualitatively with sound waves method. Initially, the 'strain' data of the tissue were obtained by applying a certain amount of pressure. Low-strain areas given lighter values and high-strain areas given darker values in grayscale elastogram. With the contribution of computer algorithms and innovative technological developments, high quality qualitative color overlay elastograms obtained. Recently, quantitative analysis methods such as Acoustic radiation force impulse (ARFI), Shear wave elastography and Real-time elastography have been developed (10). ARFI is a new USG modality in which tissue stiffness is quantitatively measured by taking into account the velocity of sound wave propagation in the tissue (11-12).

In previous studies, it was observed that ARFI elastography scores increased in Hashimoto thyroiditis (HT) and Graves diseases (GD) compared to control groups. However, statistically, both diseases could not be differentiated from each other, in some studies, the elasticity values of GD were

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found to be higher (13-15). In some studies the elasticity values of HT were higher (16). Our purpose is to compare Tc 99m thyroid uptake values and ARFI elastography scores of patients diagnosed with HT and GD, with control groups and each other and to present the imaging findings of these diseases by both methods.

MATERIAL AND METHOD

The present prospective study was carried out with the permission of Dicle University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (Date: 26.12.2014, Decision No: 273). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this study we included subjects with HT and GD were selected from the patients who underwent a diagnosis of autoimmune thyroiditis and thyroid scintigraphy and thyroid uptake in Dicle University Medical Faculty Hospital in a two year period. The control group was selected from patients who came to the salivary gland and parathyroid scintigraphy between the same dates, but were clinically and laboratory normal in terms of thyroid diseases. After being eliminated the patients with thyroid nodüles, totally 61 subjects (41 women, 20 men) included in the study. Of which 24 Graves' disease, 15 Hashimoto disease and 22 control group. The mean age of patients was 33.9±10.9 years. The reason why they were included in the study was explained by the researcher physician and their written consent was obtained.

Attention was paid to the preparation of patients for thyroid uptake study. The thyroid uptake test was performed on the 2012 model Brightview gamma camera system (Philips Medical Systems, Eindhoven, the Netherlands). The filled injectors of the patients (5 mCi Tc 99m pertechnetate) were counted for 30 seconds in anterior position at 10 cm distance with parallel hole general purpose collimator (LEGP). Empty injectors were also counted for 30 seconds after injection. In the 20th minute, 5-minute shots were taken at a distance of 10 cm with the parallel hall collimator in supine position and the neck in extension. The calculations of the thyroid uptake study were made at the Xeleris 2011 model workstation of General Electric with the thyroid uptake program. After the full injectors, empty injectors and anterior images of the patients were introduced to the device, ROIs (Region of Interest) were drawn manually around the thyroid gland. The ROI, which the device automatically draws in the neck area immediately inferior after separating both lobes, was used for background correction (**Figure 1**). Then, uptake values were obtained by using automatic calculation (via thyroid uptake formula given in the general information section), both thyroid lobes separately and total. Those with an uptake value less than 0.3% were considered to be decreased, those between 0.3% and 3.75% were considered normal, and those greater than 3.75% were considered increased (8,9).

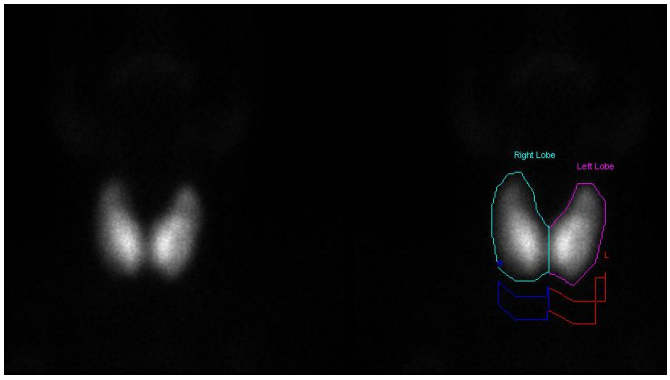

Figure 1. Drawing of both thyroid lobes and background in thyroid uptake study

ARFI imaging was performed on the same day by the experienced radiologist at Dicle University Medical Faculty Hospital Radiology Clinic. Patients with nodules in the gland were excluded by routine USG on the thyroid gland prior to ARFI imaging. The imaging procedure was performed in a supine position using the ACUSON S2000 ultrasound system (Siemens, California, US) linear probe (4–9 MHz) and a sufficient amount of ultrasound gel. Considering that it may affect the elasticity results, excessive pressure was avoided while using the probe and care was taken to ensure that the applied pressure was at a standard level in each case. SWI (shear wave velocity: tissue spread rate) was calculated in m/s by placing ROIs in the thyroid gland parenchyma. Attention was paid to keep the areas where ROI was drawn in the parenchyma. Major vascular structures within the thyroid parenchyma and soft tissues around the parenchyma were ruled out (**Figure 2**). Five AFRI values were obtained from the right thyroid lobe, five from the left lobe and one from the isthmus. Mean ARFI of thyroid gland was obtained by taking the average of these.

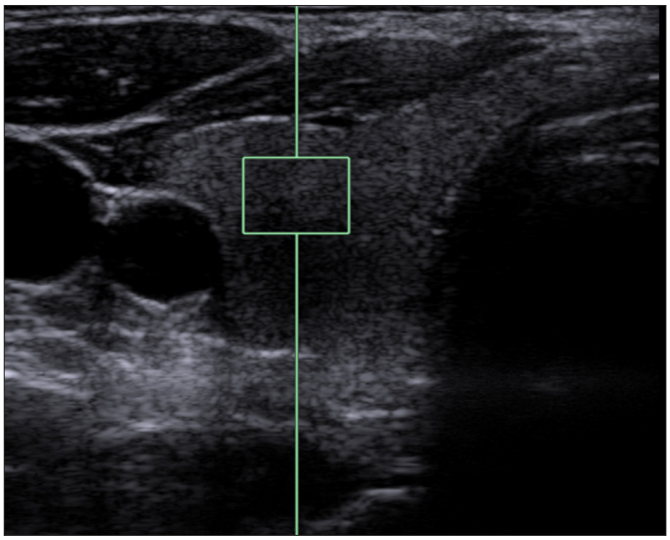

Figure 2. Obtaining ROI and ARFI values placed in thyroid parenchyma

Statistical Analysis

All statistical analyzes were done using SPSS 15.0 program. P <0.05 was considered statistically significant. The data were classified according to their numeric or nonnumeric distribution. Suitable parametric or nonparametric tests were used. Data compared using Kruskal Wallis, ANOVA and Stundient's t tests.

RESULTS

The mean age of patients between the ages of 18-65 was measured as 33.9±10.9. The mean age of GD was 34.8±11.3, and 67% of the patients were women. The mean age of HT patients was 26.5±6.6 and 75% of the patients were women. The mean age of the control group was 37.9±10.6 and 75% of the patients were women. The mean Tc 99m uptake value was 5.07±6.05% and the mean ARFI value was measured as 1.82±0.38. A statistically significant difference was found between Tc 99m Uptake values for GD and control group, HT and control group, and GD and HT; (p <0.001) (**Figure 3**).

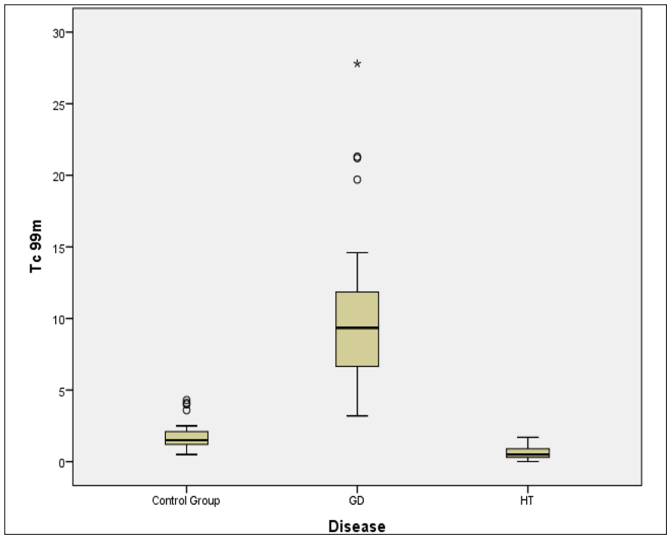

Figure 3. Tc 99m Uptake distribution of Control Group, GD and HT

The sensitivity of the thyroid uptake test performed with Tc 99m Perteknetat to predict GD and HT from each other was 100%, the sensitivity to predict GD from the control group was 95.8% and the sensitivity to predict HT from the control group was 60%.

There was no significant difference in the comparison between ARFI elastography values for GD and control group (p: 0.08), HT and control group (p: 0.14), GD and HT (p: 0.336). When the ARFI elastography values of the whole patient group were compared with the ARFI elastography values of the control group, no significant difference was observed (p: 0.09) (**Figure 4**).

A weak correlation was detected between Tc 99m pertechnetate uptake values and ARFI values (p: 0.048, r: 0.255) (**Figure 5**).

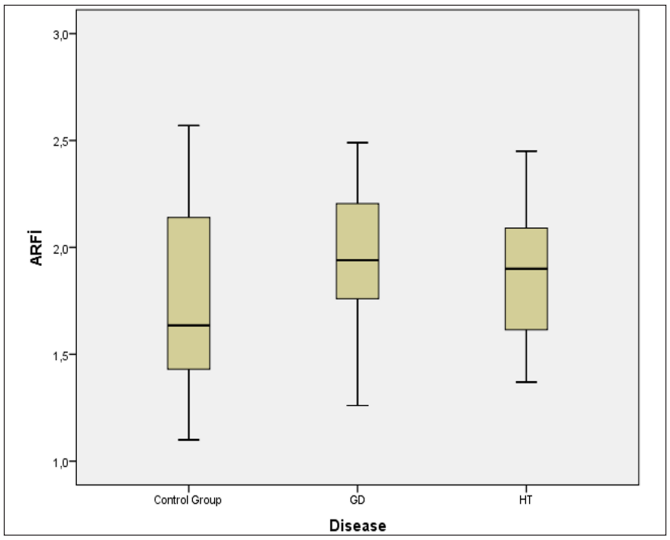

Figure 4. The distribution of ARFI values of Control Group, GD and HT

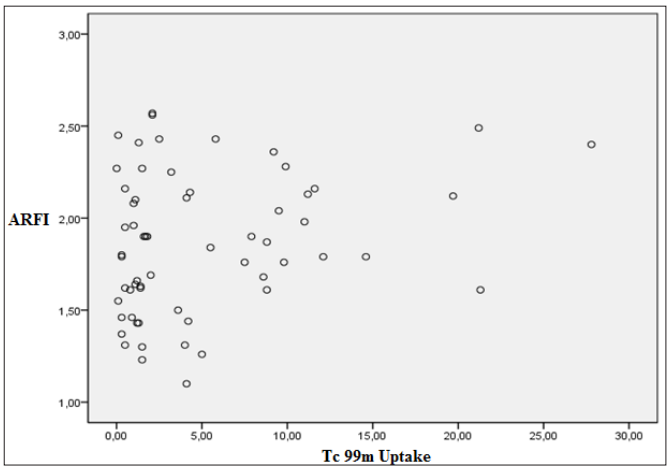

Figure 5. Correlation Between Tc 99m Pertechnetate Uptake Value and ARFI Elastography Values

DISCUSSION

In the differential diagnosis of autoimmune thyroid diseases, thyroid uptake test and thyroid scintigraphy are very valuable diagnostic methods used in the routine. RAIU test is one of the most important methods used in routine using I-131 and I-123 in the differential diagnosis of thyrotoxicosis. The fact that Tc 99m Perteknetat is inexpensive, easily available and easily applied, its radiation dose is low, and the absence of β rays makes it more attractive than radioactive iodine (9). In the thyroid uptake study conducted by Sostre et al. (7) using a group of 123 patients, using Tc 99m Pertechnetate and I-131, the uptake values of Tc 99m Pertechnetate correlated with I-131 at a rate of 89%. As a result of the study of Ramos et al. (17), group of 47 euthyroid patients; stated that Tc 99m Pertechnetate is the most suitable option for thyroid scintigraphy and thyroid uptake study due to its low radiation dose, ease of application and cheapness.

The sensitivity and specificity of the Tc 99m Uptake test they studied in 15 pediatric patients diagnosed with Duck and Sty's (18) GD were higher than 90%. In the study where Zuhur et al (19) compared Color Doppler USG, Tc 99m Uptake and TRAb values in 150 GD, 79 silent thyroiditis patients and 71 euthyroid patients; The separation sensitivity and specificity of these three groups of the Tc 99m Uptake test were found to be 90.7% and 89.9%, respectively. As stated in these studies, the success of the Tc 99m Thyroid Uptake test in GD has taken its place in the literature. Similarly, in our study, the sensitivity of this test to GD and HT from each other was 100%, and the sensitivity to differentiate Graves patients from control group was 95.8%.

Thyroid scintigraphy and Thyroid Uptake studies in HT vary according to the stage of the disease. In the early period of the disease, that is, when the atrophy does not start in the thyroid parenchyma, uptake studies are followed within normal limits. In the late period, atrophy begins and the cell reserve begins to decrease and the follicles are replaced by fibrotic tissues (20). During this period, uptake values begin to decrease. The sensitivity of our study to differentiate HT and control group was 60%. HT cases with uptake values within normal limits may be due to early stage of disease.

In the literature, although GD and HT can be seen at any age, it has been reported that it occurs most frequently between the ages of 20-40 and is observed 3-8 times more in women than in men (21-25). Similar to the literature in our study; the mean age of GD patients is 34.8±11.3, 67% of the patients are women, while the mean age of HT patients is 26.5±6.6, 75% of the patients are women.

Traditionally in HT and GD, the gland is said to have diffused somewhat diffusely and acquired a tire consistency. ARFI-elastography evaluates tissue stiffness quantitatively and current studies in this field are ongoing. In a study by Sporea et al. (13) ARFI values of thyroid gland were evaluated in a group of 136 patients. Of these, 44 are healthy, 48 are GD, 37 are HT, 4 are diffuse goiter and 1 are amiodarone-related thyroiditis. In this study, it was reported that ARFI values were higher in GD and HT compared to the healty population and that they could predict these two groups statistically from the healthy population. In another study by Sporea et al. (14) of 74 people, 23 of them were normal, 29 of them were GD and 22 of them were HT. ARFI values of GD and HT were higher than the control group. Rahatlı et al. (15) in a study where they evaluated Shear wave elastography with 30 HT patients, 22 GD patients and 30 healthy patients; Shear wawe velocite values have been reported to be higher in GD and HT compared to the healthy population. Although not statistically significant, in our study, ARFI values of GD and HT were slightly higher than the control group. The probable reason that these differences could not be confirmed statistically may be the low number of cases in our patients and control group (Graves: 24, Hashimoto: 15, control: 22). If we could increase the number of cases in our patients and control group to over 30; we could possibly detect statistically significant differences for these comparisons in our study as well. However, due to the limited working time, we could not reach the desired numbers.

In the same studies of Sporea et al. (13) and Rahatlı et al. (15); reported that ARFI and Shear wave velocite values of the thyroid gland are slightly higher in GD than HT, but GD and HT were not statistically differentiated. Although not statistically significant in our study, ARFI values of GD was slightly higher than the HT. However, in the elastography study of Wee et al. (16) with a group of 34 patients, including 15 GD, 3 HT, 1 diffuse goiter patient and 15 control groups; the elasticity of the gland was found to be higher in HT than in GD. The fact that the number of Hashimotos in the work of Wee et al. was limited to only 3 cases may have caused this difference.

In the literature, current studies with Shear Wave Elastography and Real-Time Elastography; in HT and GD, the elasticity values were increased as compared to the healthy patients (26-32).

In study by Sporea et al (13); the mean ARFI value for GD was 2.62±0.58, and the mean ARFI value for HT was 2.34±0.61 and the mean ARFI value was 1.98±0.37 for the control group. In addition, both convex and linear USG probes were used in their studies and in their comparison; stated that the use of convex or linear USG probes did not change ARFI values in all three patient groups. In study by Fukuhara et al. (26) using a linear probe; the mean ARFI value for HT was 2.56±0.57 and 1.59±0.41 for the control group. In our study, we used a linear USG probe and found the mean ARFI value of 1.96±0.32 for GD, 1.87±0.31 for HT, and 1.75±0.46 for the control group. It is noteworthy that the mean ARFI values of all patient groups in these two studies were higher than in our study. Although we all worked with the same device, the different results cause of the application differences during the measurements. One of these application differences is the pressure difference applied to the probe while ARFI measurements are made. While we were making ARFI measurements, we applied as little pressure on the probe as we thought it might affect the stiffness of the tissue. However, in the other two studies, the pressure applied to the probe during the measurements was not specified, and a possible high pressure that they may have applied may result in higher results in the measurements. In addition, unlike our other study, measurements were not taken from isthmus in the other two studies. The measurements we take from istmus may have reduced our measurement averages.

In our study; we found a weak correlation between Tc 99m Pertechnetate uptake value and ARFI scores. We have not encountered any previous study in the literature on this subject. However, the number of patients in the HT group of this correlation (15); We attributed it to less than the GD (24) and control groups (22). Because, in the Tc 99m uptake test, the results of Graves patients were found higher than the control group, while the results of HT patients were lower than the control group. However, in our ARFI measurements, both the Graves group and the Hashimoto group were higher than the control group. If the HT group in our study was slightly higher in number, it would affect our correlation analysis negatively and perhaps we would not find the weak correlation we obtained.

CONCLUSION

In the differential diagnosis of autoimmune thyroid diseases; Thyroid scintigraphy and thyroid uptake data with Tc 99m Pertechnetate are very valuable. The role of ARFI elastography in the differential diagnosis of autoimmune thyroid diseases seems to be limited for now, more studies are needed to evaluate the contribution of this method.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Dicle University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (Date: 26.12.2014, Decision No: 273).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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