

The role of shear wave elastography in the diagnosis of chronic autoimmune thyroiditis

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Abstract

Aims: The aim of this study is to assess the applicability of shear wave elastography (SWE) in the diagnosis of chronic autoimmune thyroiditis (CAT) patients. **Material and methods:** The study group consisted of 50 patients with first-diagnosed CAT and 40 control subjects (CS). In all patients with CAT and CS, sonoelastographic measurements were made in both thyroid lobes. Optimal cut-off values were chosen to maximize the sum of sensitivity and specificity. Positive predictive value (PPV), negative predictive value (NPV), and accuracy values were also calculated. **Results:** Quantitative elastographic analysis evaluated by SWE in CAT patients (2.56 ± 0.30 m/s) was significantly higher compared with CS (1.63 ± 0.12 m/s) ($p < 0.001$). The optimal cut-off value was 2.42 m/s. SWE had 77% sensitivity, 71% specificity, 92% PPV, 81% NPV, and 87% accuracy for the presence of CAT. **Conclusions:** Our data indicate that SWE correctly defines the elasticity of thyroid parenchyma, and this technique may assist in the diagnosis and treatment monitoring of CAT.

Keywords: shear wave elastography, ultrasonography, chronic autoimmune thyroiditis,

Introduction

Due to the impact of environmental factors, the incidence of chronic thyroiditis and thyroid cancer has increased markedly. In industrial populations, chronic autoimmune (Hashimoto's) thyroiditis (CAT) is characterized by variable degrees of lymphocytic inflammatory infiltration and fibrosis of thyroid tissue [1]. CAT is a severe, diffuse thyroid pathology, presenting with hypothyroidism, increased antithyroid autoantibodies, and diffusely decreased echogenicity of the thyroid parenchyma on conventional ultrasonography (US). Primarily, CAT can be diagnosed with thyroid functional tests and elevated antithyroid autoantibodies. Clinically it is silent

and typically is not characterized by painful thyroid enlargement or biochemical signs of inflammation. Though elevated antithyroid autoantibodies are highly indicative of CAT, these do not exclude the diagnosis of other types of thyroiditis [2] and correct diagnosis may be difficult in some cases without biopsy. US examination is a non-invasive and commonly used imaging modality for CAT diagnosis [3]. However, it reveals limited findings such as heterogeneous-decreased echogenicity, lobulated contour, and hyperemia on color Doppler US at initial phase of the disease. As a consequence of the pathology, thyroid parenchyma becomes stiff compared with the healthy thyroid tissue due to progression of fibrosis and this finding can be evaluated by elastography [4,5].

Strain elastography is a US based dynamic tool to evaluate tissue elasticity by measuring the degree of distortion under the application of an external force. The system allows the instant evaluation of tissue elasticity and, as in color Doppler imaging, it superimposes the information in color on the grayscale images. However, being a qualitative imaging technology it can not reveal quantitative data. Thus, elastography with freehand compression has several limitations being highly dependent on the

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compressibility limits or on the extent of tissue compression; also it is an operator dependent technique [5].

Recently, a new elastography method has been developed that uses tracking of shear-wave propagation through tissue to obtain the elastic modulus [6]. In this technology, the target tissue generates small (1-10 μm) localized displacements when it is mechanically “pushed” by short-time acoustic radiation force transmitted from the probe. The displacement of the target tissue generates the “shear wave” which is detected by sonographic detection pulses. This shear-wave elastography (SWE) is operator-independent, reproducible and point quantification capability [7]. SWE is proportional to the square root of tissue elasticity as a quantitative technique that allows local elasticity estimation of tissues [8].

Acoustic Radiation Force Impulse (ARFI) quantification is a type of SWE [9,10]. ARFI quantification estimates the elasticity of the US wave by Virtual Touch Tissue Quantification (VTQ) technique. VTQ application is used to create local tissue displacements using lateral shear wave propagation of US beam in SWE. VTQ generates objective and reproducible numeric data. In this mode, numeric values –meters per second- (m/s) of SWE were depicted from ROI evaluation area [11].

The aim of the present study was to evaluate the diagnostic value of SWE by ARFI in CAT patients by creating a cut-off value for diagnosis.

Materials and methods

This prospective nonrandomized study was performed in accordance with the ethical guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of University. All of the participants were informed of the research and gave their written informed consent. From August 2012 to November 2014, 50 consecutive patients diagnosed with CAT (42 male and 8 female) were included. Forty consecutive subjects with no thyroid pathology (23 male and 17 female) were selected from the normal population as the control group. The diagnosis of CAT was confirmed by histopathologic examination obtained by fine needle aspiration (FNA) or biopsy. The patients were first evaluated by endocrinologists. Patients with suspected CAT pathology (clinical examination and specific markers) were referred for US-elastography examination and FNA biopsy. Exclusion criteria were prior thyroid surgery or fine needle biopsy in the previous 6 months for possible alterations in the parenchyma, the presence of nodule, calcification, or cystic lesions over 5 mm in thyroid lobes.

All patients underwent a conventional US examination of the thyroid gland, including color Doppler US,

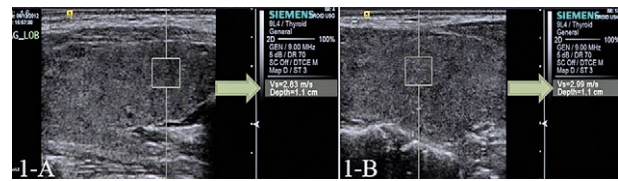


Fig 1. A) 47 year-old woman with CAT. Diffuse heterogeneous parenchyma and increased velocities of SWE with 2.83 m/s; B) SWE sonoelastographic evaluation of a 50 year-old male CAT patient. Measurements of ROI area shows as 2.99 m/s.

followed by real-time SWE imaging. An Acuson S3000 diagnostic US system (Siemens Medical Solutions, 2013, Erlangen, Germany) was used for SWE imaging with ARFI technique using 4-9 MHz broadband frequency 9L4 linear probe. The technique was performed with the patient in a supine decubitus position on the examination couch and the neck in hyperextension, eased by positioning of a pillow behind the neck. The examinations were conducted by two radiologists with more than 3 years of experience in elastography (S.A., A.O.), who were blinded to the cytology. The probe was placed on the gel gently and, slight compression was maintained during the SWE study. Ten successful measurements per patient were performed, with the ROI (5x6 mm) placed in five different points in per thyroid lobe. While the velocities were obtained, the patients held their breath to avoid respiratory movement artifacts. The average SWE examination time was 6 ± 3 minutes (range 3-9 minutes). The measurement values revealed as meter/second (m/s) from ROI area depending on the VTQ calculation (fig 1).

Serum assays were performed at the same day by a classical method. Assessment of hormone concentration was performed using Hitachi Cobas e601 chemiluminescent analyser and included measurement of serum thyroid stimulating hormone (TSH) and free thyroxine (FT4). Thyroid autoantibody concentrations of antithyroid peroxidase antibody (TPO-Ab) and antithyroglobulin antibody (Tg-Ab) were assessed by radioimmunological method using commercially available kits and scintillation gamma counter (LKB Wallac CliniGamma 1272, USA).

The US, SWE, and FNA biopsy results were collected by the statistical coordinator of the study (A.C.Y.) and the values were prospectively entered into a computer database.

Statistical analysis

Statistical analysis was performed with SPSS version 17.0 software (SPSS Inc, Chicago, IL). From the collected variable numeric ARFI measurements of CAT patients and control groups, descriptive statistics were calculated. Reliability of the ten successful measurements per patient was analyzed by intraclass correlation coefficient (ICC).

Normality of distribution of the variables was analyzed using the Shapiro-Wilk test, and the Levene test was used to assess the homogeneity of variances in the groups. Parametric test assumptions were not available; thus comparison between the group of patients with CAT and the control group were performed with the Mann-Whitney U test. P values smaller than 0.05 were considered statistically significant. Diagnostic performance of ARFI elastography was assessed using the receiver operating characteristic curve (ROC) that was constructed from sensitivity and specificity values due to a reference line. Optimal cut-off value was chosen to maximize the sum of sensitivity and specificity. Positive predictive value (PPV), negative predictive value (NPV), and accuracy values were also calculated.

Results

A total of 90 thyroid US-SWE examinations were performed successfully (50 patients and 40 healthy control group subjects).

Conventional US revealed diffuse hypoechogenicity and heterogeneous parenchyma in all CAT patients. The mean SWE value was 2.564 ± 0.30 m/s in CAT patients (range 2.098- 3.164 m/s) (fig 1-2) and in the control group 1.630 ± 0.12 m/s (range 1.322-1.838). The mean SWE velocity result and serum assays of CAT patients were significantly higher than the mean value of the normal control group ($p < 0.001$) (table I). ICC for right and left lobe were 0.968 ($p < 0.001$) and 0.963 ($p < 0.001$) respectively.

The optimal cut-off value for CAT prediction was 2.42 m/s (77% sensitivity, 71% specificity, 92% PPV, 81% NPV, and 87% accuracy). Area under the curve was 0.849. The 95% confidence interval was 0.741 to 0.958.

Discussions

In the recent years, elastography has been introduced into clinical practice enabling the determination of tissue elasticity using ultrasound devices. Preliminary studies have been performed as a qualitative method real-time elastography in thyroid gland. Usefulness of this method in thyroiditis and differentiating benign - malignant nodules has been widely described. Studies concerning about thyroid nodules concluded that most of the benign nodules were significantly softer comparing with malignant nodules and SWE imaging had a good diagnostic quality with high sensitivity and specificity in evaluating this pathology [5,12-16]. Thyroiditis was another major scope of the real-time elastography. First studies emphasized that, SWE correctly defines the elasticity changes in thyroiditis. Although SWE may provide some useful information in differentiating thyroiditis from the multinodular goiter, it gives misleading results in the differential diagnosis of thyroiditis and thyroid cancer [17-19]. Ruchala et al emphasized that, CAT was associated with only a minimal increase in the stiffness of the thyroid parenchyma, and that remains unchanged during therapy. Thus, SWE had a restricted value for diagnosing the types of thyroiditis and the required clinical assistance [17]. Magri et al concluded that the presence of CAT does not affect the ability of SWE to correctly define the elasticity of thyroid nodules [18]. In the study of Friedrich-Rust et al the median velocity of SWE was 1.98 m/s in the healthy thyroid gland, a value very similar to our results (1.63 ± 0.13) [14]. According to the other related articles published in the literature, the SWE velocity in thyroid tissue ranged between 0.5 and 4.9 m/s with the highest values reported for malignant nodules ranging

Table I. Mean Age, SWE values and Serum assays of Patients and Control Group.

| | Control Mean \pm Standard deviation Median (min-max) | Patients Mean \pm Standard deviation Median (min-max) | p |
|--------------------|---|--|------------------|
| Age (years) | 30.800 ± 6.467 31 (20-46) | 45.320 ± 17.843 47 (12-72) | <0.001 |
| SWE (m/s) | 1.630 ± 0.118 1.657 (1.322-1.838) | 2.564 ± 0.299 2.487 (2.098-3.164) | <0.001 |
| FT4 (ng/dL) | 1.12 ± 0.6 1.2 (0.8-1.4) | 1.72 ± 0.8 1.8 (1.4-2.8) | <0.001 |
| TSH (μ IU/mL) | 2.5 ± 1.2 2.8 (1-4.5) | 0.13 ± 0.1 0.1 (0.001-0.2) | <0.001 |
| TPO-Ab (IU/mL) | 0.4 ± 0.8 0.4 (0.01-3) | 263 ± 48 310 (50-560) | <0.001 |
| Tg-Ab (IU/mL) | 0.2 ± 0.6 0.3 (0.01-1.6) | 220 ± 33 255 (155-280) | <0.001 |

FT4: Free thyroxine; TSH:Thyroid-stimulating hormone; TPO-Ab: Antithyroid peroxidase antibody; Tg-Ab:Antithyroglobulin antibody

from 2.09 to 4.9 m/s. The cut-off point was found to be 2.75 m/s for SWE for distinguishing between malignant and benign thyroid nodules [13,15,16,19-21].

In a recently published study by Sporea et al acoustic radiation force impulse-imaging was used for the evaluation of 37 patients with CAT pathologies [22]. Median values in healthy subjects were calculated significantly lower (2 ± 0.40 m/s) than in CAT patients (2.43 ± 0.58 m/s). They found an optimal cut-off value of 2.36 m/s for diffuse thyroid pathology with a relatively lower sensitivity (62.5% versus 77%). In comparison to this research, we calculated a little higher cut-off value (2.42 m/s) with similar sensitivity and specificity rates. However, the values obtained by Sporea et al could be affected from their heterogeneous patient groups which include Basedow-Graves or diffuse thyroid goiter patients.

There were some limitations in the present study that need to be addressed. First, the research had a relatively small group. Secondly, the main objective of this study was to show the SWE quantitative evaluation of CAT patients. Hence, detailed description of elastographic image variation for each of the particular conditions was not included.

Conclusions

In clinical practice, SWE may assist in the diagnosis of CAT patients. SWE could be used easily after performing routine US examination of thyroid gland. For predicting the presence of autoimmune diffuse thyroid pathology with high sensitivity, the cut-off value should be selected as 2.42 m/s or more in SWE imaging. Further investigations are required to compare these findings with various thyroid pathologies.

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Conflict of interest: none

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