The Diagnostic Value of Sonoelastography in the Differentiation of Benign and Malignant Thyroid Nodules: Comparison of Nodule/Strap Muscle and Nodule/Normal Parenchyma Strain Value Ratios

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Purpose

Sonoelastography is a newly developed dynamic imaging technique that displays tissue elasticity by measuring the degree of distortion under the application of an external force. Tissue stiffness is determined quantitatively and an index known as "strain ratio" is defined. Two indexes called parenchyma-to-nodule strain ratio (PNSR) and muscle-to-nodule strain ratio (MNSR) are defined (1-7) in the literature.

The aim of this study is to investigate the diagnostic value of sonoelastography and MNSR in the differential diagnosis of benign and malignant thyroid nodules and to see whether there is any difference between MNSR and PNSR in the diagnosis.
Methods and Materials

Patients

This prospective study was approved by the institutional ethics committee and informed consent was obtained from all patients. Between November 2011 and April 2012, 209 consecutive patients with thyroid nodules referred for ultrasound-guided fine-needle aspiration (FNAB) were examined through ultrasonography (US), color Doppler ultrasound (CDU), and sonoelastography before FNAB. Patients with nodules larger than 40 mm, purely cystic nodules, less than 50% solid component containing nodules, and shell-calcified nodules that could cause color-coding problems were not included in the study. A total of 103 patients were excluded from the study due to unreliable and inadequate histopathological examination results (51 patients had non diagnostic and 39 had atypia of undetermined significance) and failure of elastography examination (seven were too fat and six had nodules too deep). Finally, 106 patients (88 female and 18 male, mean age 48 ± 12 years; range 19-79 years) with definite pathological results were evaluated.

Conventional Thyroid Ultrasound Imaging and Sonoelastography (Imaging and Analysis)

Both conventional US imaging and sonoelastography were performed before FNAB with 12-MHz linear probe on an Aplio XG ultrasound machine (Toshiba Medical Systems, Otawara, Japan) by a radiologist specializing in thyroid US and sonoelastography.

The presence or absence of hypoechogenicity, microcalcification, poorly defined margins, an anteroposterior/transverse (A/T) diameter ratio of one or greater, and type three Doppler color flow pattern of the thyroid nodules was determined in the conventional US examination.

Sonoelastographic measurements were performed immediately after conventional US imaging. The elastogram was displayed over the B-mode image in a color scale that ranged from red- which indicated components with the greatest elastic strain (i.e., softest components)-to blue, which indicated components with no strain (i.e., hardest components). According to the classification proposed by Asteria et al. (8), the visualization patterns were classified into four types. Strain ratio measurements (PNSR and MNSR) were obtained from appropriate relaxation waves, which had a sinusoidal shape in the waveform scale.

All patients underwent FNAB after conventional US imaging and sonoelastography evaluation by a radiologist specializing in thyroid FNAB.

Statistical analysis
All statistical analyses were performed using the SPSS packet program (version 15.0, SPSS). For the statistical analysis, quantitative variables were compared using Student $t$ test and qualitative variables were compared using the chi-square test. To determine the best cutoff point for the strain ratios, the receiver operating characteristic analysis (ROC) was used. The agreement between the two strain ratio methods was assessed using the weighted # test statistic. The quantitative data were presented as mean (± SD). A $p$ value less than 0.05 indicated a statistical significance with a 95% confidence level.
Results

A total of 106 thyroid nodules in 106 patients were examined in this prospective study. The mean age of the examined patients (88 female and 18 male) was 48 ± 12 years (range, 19-79 years). The examined nodules had a mean size of 21.2 ±8.1 mm (range 10.1-40 mm). Histopathologic examination indicated 83 benign nodules and 23 malignant nodules.

Conventional ultrasound imaging

The sonographic patterns indicating malignancy included nodule hypoechogenicity (sensitivity, 56.5%; specificity, 84.3%; \( p=0.0001 \)), microcalcification (sensitivity, 47.8%; specificity, 85.2%; \( p=0.001 \)), poorly defined margins (sensitivity, 60.9%; specificity, 92.8%; \( p=0.0001 \)), an A/T diameter ratio of one or greater (sensitivity, 56.5%; specificity, 79.6%; \( p=0.0001 \)), and type three Doppler color flow pattern (sensitivity, 30.4%; specificity, 82.8%; \( p=0.003 \)).

Sonoelastography

According to the four-point scoring system, 44 of the 83 benign nodules (53%) had a score of one or two while 22 of the 23 malignant nodules (95.6%) had a score of three or four with a sensitivity of 95.6%, specificity 50.6%, a PPV of 35%, and a NPV of 97.6% (area under the ROC curve (AUC), 0.79; \( p<0.001 \)) (Figure 1).

The mean PNSR and mean MNSR for the benign nodules were 1.70 ± 0.75 and 1.15 ± 0.47 (Figure 2), respectively and the mean PNSR and mean MNSR for the malignant nodules were 5.16 ± 1.18 and 3.36 ± 0.82 (Figure 3), respectively. The PNSR and MNSR values were significantly higher in the malignant compared with the benign nodules (\( p<0.001 \)) (Figure 4). The best cutoff point for PNSR was 3.14 in the differentiation of benign and malignant thyroid nodules (AUC, 0.98; \( p<0.001 \)) (Figure 1). Using this cutoff point, the sensitivity, specificity, PPV, and NPV were 95.6%, 93.4%, 81.5%, and 98.7%, respectively. The best cutoff point was 1.85 for the MNSR (AUC, 0.99; \( p<0.001 \)) (Figure 1). Using this cutoff point, the sensitivity, specificity, PPV, and NPV were 95.6%, 92.8%, 78.6%, and 98.7%, respectively. The # value for PNSR and MNSR methods was 0.87, which indicated an almost perfect agreement between PNSR and MNSR in differentiating between benign and malignant nodules (\( p<0.001 \)).
**Fig. 1:** Comparison of the receiver-operating characteristics curves of different methods on sonoelastography in differentiating malignant from benign lesions. The area under the ROC curve (AUC) for the four-point system, PNSR and MNSR were 0.79, 0.98 and 0.99, respectively.

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Fig. 2: Images of a 35-year-old man who underwent routine checkup. a. Transverse US image of the left thyroid nodule shows ovoid shape, isoechogenicity, smooth margin, hypoechoic halo, and blood flow pattern II at color Doppler ultrasound (b). The nodule had a score of one (benign) on the four-point scoring system. c. MNSR yielded a value of 1.10 and PNSR yielded a value of 1.09 (d), suggesting the benign nature of this nodule. This thyroid nodule was diagnosed as follicular adenoma at cytologic evaluation after surgery.

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Fig. 3: Images of a 57-year-old woman who underwent routine checkup. a. Transverse US image of left thyroid nodule shows an irregular shape, hypoechogenicity, poorly defined margins, and blood flow pattern III at color Doppler ultrasound (b). The nodule had a score of four (malignant) on the four-point scoring system. c. MNSR yielded a value of 4.19 and PNSR yielded a value of 6.80 (d), suggesting malignancy. This thyroid nodule was diagnosed as papillary thyroid carcinoma at cytologic evaluation after surgery.

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Fig. 4: Box plot shows a comparison of the PNSR and MNSR of 83 benign and 23 malignant thyroid nodules. The mean PNSR and MNSR values were significantly higher in the malignant compared with the benign nodules (p

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Conclusion

Sonoelastography can detect the difference between the hardness of different tissues and it can reflect the different hardness characteristics of benign and malignant lesions, providing a new approach for the differentiation of benign and malignant thyroid nodules. The strain ratio is a quantitative index that can provide accurate information about thyroid nodules (1-7). The PNSR is calculated by the mean strain of the normal thyroid parenchyma at the same depth of the nodule by dividing the mean strain within the thyroid nodule (1-5). However, it can be deceiving to use this index in patients with nodules covering all of the thyroid gland without leaving any normal parenchyma and abnormal thyroid tissue (i.e., thyroiditis). It can be beneficial to use an adjacent muscle to the thyroid as a reference instead of the normal thyroid parenchyma in such patients. In this method, MNSR is calculated by the mean strain of the adjacent muscle to the thyroid by dividing the mean strain of the thyroid nodule (6, 7). We did not find any study in the literature where these two indexes were used together and compared.

Sonoelastography has a high diagnostic value in the differentiation of benign and malignant thyroid nodules. We found that the best cutoff point for MNSR is 1.85 and 3.14 for PNSR in the differentiation of benign and malignant thyroid nodules. There was an almost perfect agreement between PNSR and MNSR in the differentiation of benign and malignant thyroid nodules. Therefore, we think that MNSR could safely be used in situations where PNSR could not be used.


