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ARFI elastography for differentiating malignant and benign thyroid nodules

Malign ve benign tiroid nodüllerinin ayrımında ARFI elastografi

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ABSTRACT

Aim: To examine the diagnostic performance of virtual touch tissue quantification (VTQ) mode of Acoustic Radiation Force Impulse (ARFI) elastography imaging in differentiating benign and malignant thyroid nodules.

Materials and Methods: Two hundred four solid and mostly solid nodules >5mm were prospectively evaluated with ultrasonography, VTQ mode of ARFI elastography, fine needle aspiration biopsy, and when indicated with tissue pathology. Three shear-wave velocities (SWV) measurements were done in 196 nodules. The SWV ratio for each nodule was calculated as the mean value of the SWV of the nodule divided by the mean value of the adjacent parenchyma. The diagnostic performance of SWV value and SWV-ratio were assessed by a receiver-operating characteristic (ROC) curve analysis.

Results: The mean SWV value in the normal parenchyma, in benign and malign thyroid nodules, were 2.13±0.44 m/s, 2.06±0.80 m/s, and 2.06±0.88 m/s respectively. The SWV-ratios were 0.97±0.37 for benign thyroid nodules and 1.02±0.40 for malignant thyroid nodules. There was no significant difference between benign and malign nodules in terms of mean SWV values (t=0.008) (P=0.994) or SWV-ratios (t =0.596; P=0.527). No cut-off point was found to predict malignancy. In subgroup analysis, AUCs for the SWV and SWV-ratio were significantly different-between nodules <10 mm and those ≥10 mm, but not with any other two groups (all *P*>0.05) (Table-2). The cutoff points for the differential diagnosis were 2.59 m/s for SWV and 1.0 for SWV- ratio respectively for nodules <10 mm.

Conclusion: VTQ mode of ARFI imaging does not have a good diagnostic performance for detecting malignancy and cannot contribute to reducing unnecessary thyroid biopsies.

Keywords: Thyroid, ultrasonography, elastography.

ÖZ

Amaç: *Malign ve benign tiroid nodüllerini ayırd etmede "Acoustic Radiation Force Impulse" (ARFİ) elastografinin "virtual touch tissue elastografi" (VTE) modunun tanısal performansını değerlendirmek*

Gereç ve Yöntem: *Çapı > 5 mm olan iki yüz dört adet solid ve ağırlıklı solid nodül prospektif olarak ultrasonografi, ARFI elastografinin VTQ modu, ince iğne aspirasyon biyopsisi ve endike olduğunda doku patolojisi ile değerlendirildi.*

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Yüz doksan altı nodülde üç makaslama dalgası hızı (shear wave velocity-SWV) ölçümü yapıldı. Her bir nodül için SWV oranı, nodülün SWV'sinin ortalama değerinin komşu parankimin ortalama değerine bölünmesiyle hesaplandı. SWV değeri ve SWV oranının tanısal performansı, ROC analizi ile değerlendirildi.

Bulgular: *Benign ve malign tiroid nodüllerinde normal parankimdeki ortalama SWV değeri sırasıyla 2,13±0,44 m/s, 2,06±0,80 m/s ve 2,06±0,88 m/s idi. SWV oranları benign tiroid nodülleri için 0.97±0.37 ve malign tiroid nodülleri için 1.02±0.40 idi. Ortalama SWV değerleri (t=0,008) (P=0,994) veya SWV oranları (t=0,596; P=0,527) açısından benign ve malign nodüller arasında anlamlı fark yoktu. Maligniteyi öngörmek için herhangi bir cut-off noktası bulunmadı. Alt grup analizinde, SWV ve SWV oranı için AUC'ler, <10 mm ve ≥10 mm nodüller arasında önemli ölçüde farklıydı. Bunun dışında herhangi iki grup arasında anlamlı fark saptanmadı (tümü P>0.05). SWV ve SWV oranı için en iyi cut-off noktaları, <10 mm nodüller için sırasıyla SWV için 2.59 m/s ve SWV oranı için 1.0 idi.*

Sonuç: *ARFİ görüntülemenin VTQ modu, maligniteyi saptamak için iyi bir tanısal performansa sahip değildir ve gereksiz tiroid biyopsilerinin azaltılmasına katkıda bulunamaz.*

Anahtar Sözcükler: *Tiroid, ultrasonografi, elastografi.*

INTRODUCTION

Although thyroid nodules are frequent and detected in 19–67% of the population on high-resolution ultrasound (US), only 5-15% are malignant. Routine use of neck ultrasonography has resulted in an increased number of fine-needle aspiration biopsies (FNAB) and thyroidectomies. It is, therefore crucial to distinguish suspicious nodules from benign nodules to avoid unnecessary surgery (1-3). Even though several suspicious ultrasound features predicting thyroid nodule malignancy were described, the overall diagnostic performance of US is low. Its sensitivity and specificity range between 38.8 to 91.7% and 53 to 96.6% respectively (1). FNAB is the standard and most accurate tool to differentiate malignant nodules (4). However inadequate results can be observed in 10-20% of specimens in US-guided FNABs (5, 6). Moreover false negative and false positive rates are up to 5% and 5.7% respectively. New methods are required for differentiating benign and malignant nodules.

Ultrasound elastography (USE) imaging evaluates tissue stiffness and is used to assess malignancy since hard consistency on palpation is a classical feature of malignant thyroid nodules. In conventional or real-time elastography (RTE), tissue stiffness can be measured qualitatively or semi-quantitatively. It depends on the measurement of the tissue distortion by an external pressure that is produced by manual compression. Operator dependency, poor reproducibility, and qualitative results are the limitations of conventional elastography (7-8).

Virtual touch imaging (VTI) and virtual touch tissue quantification (VTQ) are two modes of acoustic radiation force-based elasticity imaging, where high-intensity short-duration acoustic pulses are utilized for mechanical excitation of the tissue. The VTI mode displays the localized tissue displacement as a gray-scale image. Localized tissue displacement generates shear waves which are perpendicular to the acoustic radiation waves. With the VTQ mode, the time to peak displacement (shear wave velocity-SWV) within a sampling box positioned on a two-dimensional B mode image (the region of interest; “ROI”) is measured and is expressed in m/s. Shear wave propagation speed is faster in stiffer tissues (4, 6, 9-11). Firmness on palpation is considered a feature of malignant thyroid nodules. It has been hypothesized that the VTQ mode of ARFI imaging may help predict which thyroid nodules are cancerous and thereby reduce the number of unnecessary biopsies and surgery (4-7, 12 -14).

We aimed to examine the diagnostic performance of VTQ mode of ARFI imaging in the evaluation of thyroid nodules and to determine a cutoff value for differentiating malignant nodules.

MATERIALS and METHODS

This prospective study was designed and conducted in accordance with the ethical guidelines of the Helsinki Declaration and approved by the institutional review board (Decision number of the ethics committee: 13-1.1/6). All patients were informed of the details and gave written informed consent. The study was performed in two referral centers: Balikesir University, Department of Radiology in Balikesir

(center 1) and Ege University Department of Radiology in Izmir (center 2). The study period was from March 2013 to April 2016.

Conventional US examination of the thyroid gland was performed in all patients by one of two radiologists with 5 and 25 years of experience in thyroid ultrasonography. Patients with at least one solid or partially cystic (less than 50% cystic component) thyroid nodule >5 mm in diameter referred for US-guided FNAB were enrolled in the study. Patients with predominantly cystic nodules, nodules with eggshell calcifications and previous interventions such as ablation or biopsy performed during the last 6 months, were excluded.

For the patients with multiple nodules, the most suspicious nodule or nodules (up to two) for malignancy on conventional US examination or the one with the largest diameter was selected for analysis.

The standard of a reference method for the final diagnosis of a benign or malignant thyroid nodule was histology results or benign cytology with at least 6 months follow-up US. FNAB was done after thyroid USE on the same day. Indications for referral to surgery were compressive symptoms, nondiagnostic or indeterminate results in 2 FNABs, malignancy or suspicious malignancy on FNAB, or the preferences of the patients. Cytological and/or postsurgical histopathological results were obtained within the study period.

The one-to-one matching of histopathological diagnoses with the corresponding nodules on US examinations was performed according to distinctive features such as laterality and dimension.

Nodules were established as benign when the nodule cytology was benign and did not show more than 20% increase in size during follow-up for at least 6 months or histological analysis of the surgical specimen was benign. Patients with suspicious or malign cytology were included if thyroidectomy was performed and the diagnosis of malignancy was confirmed with histological evaluation of the specimen. Patients with nondiagnostic biopsy results were referred to re-aspiration after a 3-months waiting period and were included in the study if a final diagnosis could be achieved during the study period. Nine patients with indeterminate or non-diagnostic cytology result by FNAB without repeated FNAB, and 9 patients with suspicious or malignant cytology by FNAB without histopathologic confirmation and 14 patients with benign cytology by FNAB but without follow up, 6 patients without FNAB results, 1 patients with repeated biopsy but nondiagnostic results, 2 patient with repeated biopsy but unavailable biopsy results, 3 patients with less than 3 SWV measurements and 3 patients who had history of thyroid surgery were excluded.

Conventional Ultrasound

US was performed with Acuson S2000 equipment (Siemens AG, Erlangen, Germany) and a 4-9 MHz multifrequency linear probe was used in all examinations. The thyroid nodules were evaluated for number, location, size, absence of halo, echogenicity, margin smooth or poorly marginated); calcifications (absent, macro calcification or micro calcifications), shape (taller than wide or not), and the presence of any cystic component was investigated. The largest diameter of the nodule was accepted as the nodule size. To investigate whether the nodule size has any effect on the diagnostic performance of VTQ, the nodules were divided into three subgroups according to their sizes as Group 1: Nodules <10 mm; Group 2: Nodules sized 10–15 mm; Group 3: Nodules ≥ 15 mm. Echogenicity was defined as hyper-, iso- or hypoechoic, compared with normal parenchyma or marked hypoechoic when the nodule was as hypoechoic as the nearby strap muscles. In heterogeneous nodules, the nodule was classified according to the lower echogenicity.

Nodules with a well-defined smooth margin were accepted as benign. Nodules with micro lobulated or spiculated borders were accepted as poorly marginated and malignant. Micro calcifications were defined as punctate hyperechoic foci < 1 mm without acoustic shadowing and ring-down artifact. In nodules with micro and macro calcifications, micro calcifications were accepted for the final decision.

ARFI Imaging:

After evaluating the nodules with the conventional US, ARFI-imaging (Virtual-Touch™-Tissue-Quantification, Siemens-ACUSON-S2000) was obtained by the same operator using the same probe. USE evaluation was performed in the longitudinal plane (to exclude the carotid arteries) with the transducer perpendicular to the neck with minimal scanning pressure. SWVs within a Region-of-Interest (ROI) cursor with a fixed dimension of 6×5 mm positioned on conventional ultrasound images were measured. The patients were asked not to breathe and swallow for a few seconds. Measurement after

deep inspiration was avoided. Three successful measurements in the solid portions of the target nodule were obtained. The mean SWV of each nodule was noted. Cystic areas and macro calcifications were not included in the ROI. After the nodule examination, three consecutive measurements in healthy thyroid tissue surrounding the target nodule were performed. When the target nodule was surrounded by multiple nodules and the other lobe at the same depth had a knobby appearance, the ROI was placed at any normal tissue. The SWV ratio for each nodule was calculated as the mean value of the SWV of nodule divided by the mean value of the adjacent parenchyma. The nodules with a VTQ value exceeding the threshold of the software (displayed as X.XX m/s) were excluded from the study.

Reference Standard:

All thyroid FNABs were performed under US guidance by a radiologist using a 21-G or 25-G needle attached to a 10-mL syringe. Smears were air-dried for Giemsa staining in center 1, and fixed in 90% ethanol for Papanicolaou or hematoxylin-eosin stains in center 2. All cytological and histopathological examinations were made by an experienced cytologist and a pathologist. Four cytological diagnostic categories were used: malignant, suspicious of malignancy, benign or insufficient material. Histological diagnoses were based on World Health Organization criteria valid in the study period.

Statistical analysis:

The statistical analysis was performed with SPSS v. 25.0 (SPSS Inc., Chicago, IL, USA) for Windows. Continuous variables from the study groups were reported as mean ± standard deviation. A descriptive analysis of all variables was performed by determining the frequency distribution. The characteristic parameters of the quantitative variables (mean, standard deviation, and range) were calculated and differences were considered statistically significant if $P<.05$. The mean nodule diameter, SWV, and SWV-ratio of benign and malign nodules were compared with independent sample t-test. Chi-square test was used in the evaluation of categorical data. The diagnostic performance of SWV and SWV-ratio, in differentiating benign from malignant nodules were evaluated by receiver-operating characteristic curve (ROC) analysis. Separate ROC analyses were performed and areas under the receiver-operating characteristic curves (AUC) were calculated with subgroups of nodules with different sizes.

RESULTS

One-hundred-seventy-six patients (34 men and 142 women) with 204 nodules were included in the study. The final diagnosis was benign in 173 nodules either by histology or FNAB and sonographic follow-up. Among the malignant nodules, there were 27 papillary carcinomas (7 of them were follicular variants of papillary carcinoma), 2 medullary carcinomas, and 2 follicular carcinomas. The patient's age ranged from 16 to 84 years (mean±SD= 51.2±12.5 yrs.). No significant difference was found between the ages of patients with benign (51.9±12.6 yrs.) or malign nodules (48±11.8 yrs.).

Thirty (14.7 %) patients had a single nodule and 174 (85.3%) patients had multiple nodules. Ninety-nine of the 204 nodules were located in the right lobe; 90 nodules in the left lobe and 15 nodules in the isthmus of the thyroid gland.

The mean nodule size (mean±SD (range)) was 21.11±9.28 mm. It was similar in benign (21.39±8.85 -range 5.5-56.5 mm) and malignant (19.55±11.45 mm -range 6-52 mm) nodules.

Basic characteristics of the 204 nodules on grayscale ultrasonography and mean SWV and SWV-ratios of benign and malignant nodules are given in Table-1. The risk of malignancy was not associated with the number of nodules, nodule position, or shape (taller-than-wide) ($P>0.05$). Absence of cystic component, presence of micro calcifications, absence of halo, poorly-defined margin, hypo echogenicity and marked hypo echogenicity showed significant association with malignancy ($P<.001$). Among the different features of the US, pure solid echo structure was the most sensitive (87.1%) and had the highest negative predictive value (NPV) (94, 87%). However, having an irregular margin was the most specific (91.33%) feature with the highest positive predictive value (PPV) (51, 61%).

Virtual Touch Tissue Quantification Analysis

The SWV value was shown as X.XX m/s in 8 nodules. They were counted as unsuccessful measurements and were not included in the statistical analysis. Three appropriate measurements were done in the remaining 196 nodules. In 9 patients (12 nodules) with multinodular goiter, nodules occupied the entire gland and a measurement from the normal parenchyma was not possible.

The mean SWV value in the normal parenchyma, in benign and malign thyroid nodules, were 2.13±0.44 m/s, 2.06±0.80 m/s and 2.06±0.88 m/s respectively, and the difference between benign

and malign nodules was not significant (t=0.008) (*P*=0.994) (Figures. 1-4).

The nodule to adjacent parenchyma SWV-ratio were 0.97±0.37 for benign thyroid nodules and 1.02±0.40 for malignant thyroid nodules respectively and the difference was not statistically significant (t =0.596; *P*=0.527).

With ROC curve analyses the area under the curve (AUC) was 0.532 (95 % CI: 0.415-0.648, *p*<0.001) for SWV-ratio and 0.482 (95 % CI: 0.366-0.599, *p*<0.001) for mean SWV values. In both of the analysis, AUC values were close to 0.5 and no cut-off point was found to predict malignancy.

In subgroup analysis, AUCs for the SWV and SWV ratio were significantly different–between nodules <10 mm and those ≥10 mm, but not with any other two groups (all *P*>0.05) (Table-2). The cutoff points for the differential diagnosis were 2.59m/s for SWV and 1.0 for SWV ratio for nodules <10 mm. The sensitivity, specificity, accuracy, PPV, and NPV for SWV were 71%, 90%, 0.600%, 83.3%, 81.8% respectively, and were 86%, 80%, 0.628%, 66.7%, and 87,5%, respectively, for SWV-ratio for nodules <10mm.

Table-1. Basic characteristics of the sonogragraphic and elastography features of the 204 thyroid nodules.

	Frequency, N, %	**Benign Nodules** (n=173), %	**Malignant Nodules** (n=31), %	***P** value**
Position				0.412
Right	*99 (48.5)*	81 (81.8)	18 (18.2)	
Left	*90 (44.1)*	78 (86.7)	12 (13.3)	
Isthmus	*15 (7.4)*	14 (93.3)	1 (6.7)	
Nodule size				0.133
Mean±SD		21.39±11.45	19.55±8.85	
Max		56.5	52	
Min.		5.5	6	
Number of the nodules				0.058
Single	*30 (17.7)*	22 (12.7)	8 (25.8)	
Multiple	*174 (85.3)*	151 (87.3)	23 (74.2)	
Echostructure				0.002*
Solid	126 (61.8)	99 (57.2)	27 (87.1)	
Mixed solid and cystic	78 (38.2)	74 (42.8)	4 (12.9)	
Echogenity				0.001*
Isoechoic, hyperechoic	122 (59.8)	115 (66.5)	7 (22.6)	
Hypoechoic	49 (24)	38 (22.0)	11 (35.5)	
Marked hypoechoic	33 (16.2)	20 (11.6)	13 (41.9)	
Anteroposterior/Transvers diameter				0.122
Anteroposterior<Transvers diameter	*181 (88.7)*	156 (90.2)	25 (80.6)	
Anteroposterior≥Transvers diameter	*23 (11.3)*	17 (9.8)	6 (19.3)	
Calcifications				0.001*
None	139 (68.1)	126 (73.4)	12 (38.7)	
Micro calcifications	39 (18.6)	25 (14.4)	14 (45.2)	
Isolated macro calcifications	27 (13.2)	22 (12.7)	5 (16.1)	

**p*-value indicates comparison between benign and malignant nodules.

ŧData in parenthesis indicate percentages.

Table-2. Subgroup analysis for the diagnostic performance of SWV and SWV ratio in differentiating benign from malignant thyroid nodules.

	AUC (%95 CI)	
Nodules	SWV	SWV-ratio
<10mm	0.800* (95% CI : 0.575, 1.000)	0.814** (95% CI : 0.603, 1.000)
10-15mm	0.545 (95% CI :0.315, 776)	0.550 (95% CI :0.308, 792)
≥15mm	0.345 (95% CI :0.213, 477)	0.418 (95% CI :0.273, 563

*Compared with AUC of SWV in nodules ≥10mm, p<0.05

**Compared with AUC of SWV-ratio in nodules ≥ 10mm, p<0.05

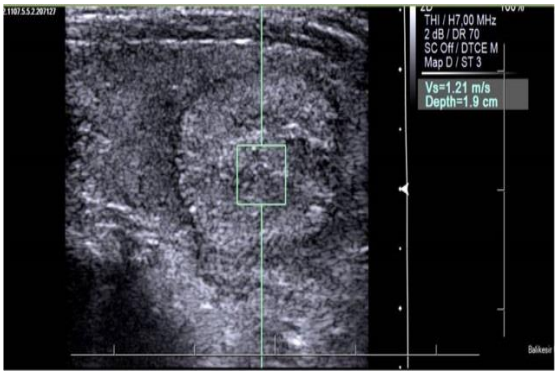

Figure-1. VTQ image from an entirely solid benign nodule. The nodule is isoechoic with smooth margins and a halo. The SWV is 1.21m/s; mean SWV was 1.43 m/s.

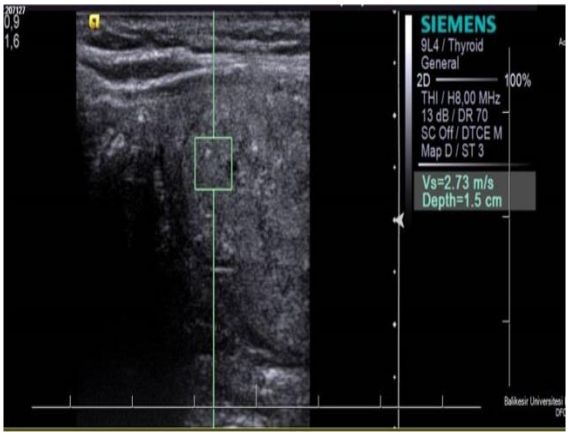

Figure-2. VTQ image of a 65-year-old woman with a benign nodule. The nodule is isoechoic with smooth margins and a halo. The SWV is 2.73 m/s; mean SWV was 2.75m/s.

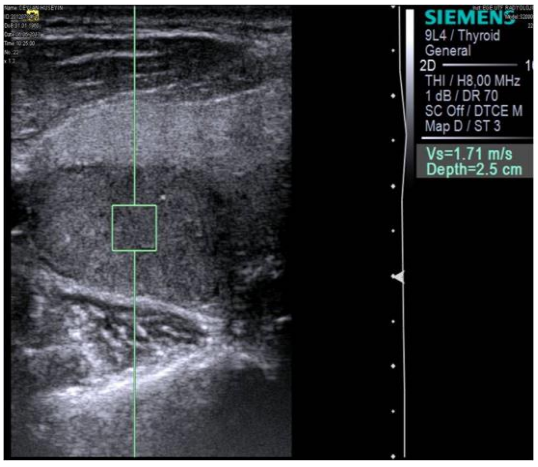

Figure-3. VTQ image in a 53-year-old man. The ROI is placed within a hypoechoic thyroid nodule in the right thyroid lobe measuring a velocity of 1.71 m/s; the mean SWV was 1.69 m/s. Histology revealed follicular carcinoma.

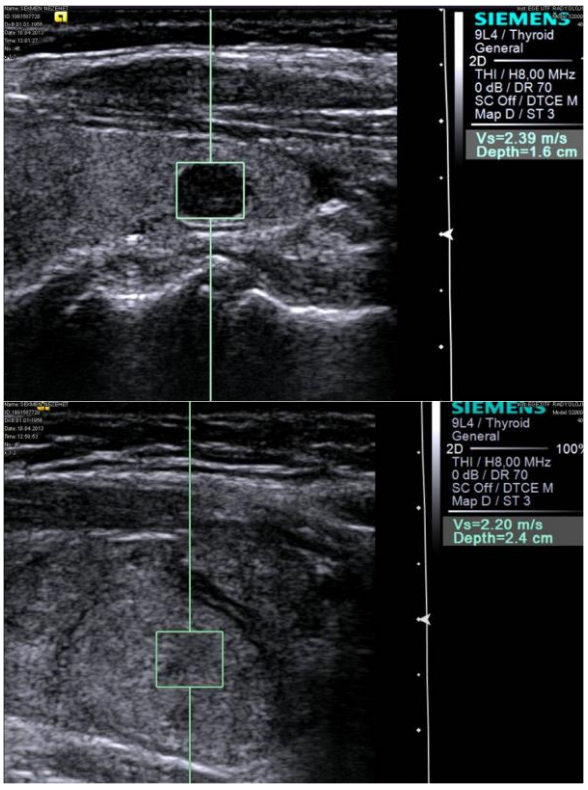

Figure-4. Virtual touch quantification images of a 57-year-old woman with papillary carcinoma in both thyroid lobes. The SWV value was 2.39m/s when the region of interest was placed within the marked hypoechoic nodule in the right lobe (a), and 2.20 m/s when the region of interest was placed within the isoechoic nodule in the left lobe (b).

DISCUSSION

In this study absence of cystic component and halo, the presence of micro calcifications, hypo-marked hypo echogenicity and poorly defined margins were associated with malignancy with varying sensitivities, specificities, NPVs, and PPVs, but none of them had both high sensitivity and high PPV. Among the assessed categories a pure solid composition (87.1%), absence of a halo (74.19%), and hypo-marked hypo echogenicity (77.42%) had the highest sensitivity with a fairly low PPV. The chance of being malignant was only 21.43% in a pure solid nodule, 23.71% in nodules without a halo, and 29.27% within hypo–marked hypo echogenic nodules. Poorly defined margin was the feature with the highest PPV (51.61%); however, it was not sensitive enough to diagnose malignancy.

In contrast to earlier reports, this current study does not confirm the usefulness of shear-wave-

based ARFI imaging in distinguishing benign and malignant nodules. The mean SWVs of benign and malignant thyroid nodules and nodule-free parenchyma were similar. The difference between the mean SWV -ratios of benign and malignant thyroid nodules compared with the adjacent thyroid tissue was not statistically significant. VTQ mode of SWE did not achieve enough diagnostic performance in distinguishing malignant and benign nodules.

In previous studies the diagnostic performance of ARFI imaging shows significant heterogeneity for sensitivity (57% to 100 %), specificity (62% to 96%), PPV (37.5% to 100%) and NPV (59.2% to 97.8%) (4-7, 13, 15). One reason for this heterogeneity can be the relatively small sample size of the series since small series (less than 50 patients) have low statistical power for calculating the real diagnostic performance (16). Even when these studies were excluded; heterogeneity in the sensitivity and specificity persisted. A meta-analysis by Zhan et al showed that with an increasing number of thyroid nodules investigated, the sensitivity and specificity of ARFI imaging might decrease as with RTE imaging (9). The potential bias risk associated with patient selection and reference standard may be another reason for different diagnostic performances. Most of the studies do not reflect the normal population because of enrolling patients who were referred for surgery and had pathological confirmation of their nodules with histology. The high malignancy rate in these studies might have affected the results (6, 7, 12-15, 17-19). The preferred method for suspicious thyroid nodules is cytological examination after US-guided FNAB and managing according to cytology and US features. However, false-positive and false-negative results of cytological examination also might have affected the results of the studies.

The results of the studies comparing the diagnostic performance of conventional US with and without ARFI imaging show discrepancy. One study showed that sensitivity, PPV, and NPV increase with combining SWE with B-mode US (20). However, they used a few sonographic features (hypo echogenicity, micro calcifications, and intranodular vascularity) as predictors of malignancy. It is known that the risk of malignancy increases with an increasing number of suspicious US features (2, 3, 21, 22). In another study, the diagnostic performances of US and VTQ mode of ARFI imaging added US were similar. The authors concluded that if the radiologist received adequate training for ARFI imaging and US is combined with VTQ and virtual touch tissue imaging (VTI) modes of ARFI imaging, PPV, and specificity of US significantly improved (12).

Xu et al showed superior overall diagnostic performance of ARFI imaging to conventional US but VTQ mode of ARFI was not useful for nodules in men, in single nodules and for nodules sized 5-10 mm (14). In concordance with their results, Zhang et al reported an association between the diagnostic value of VTQ and nodule size. It was relatively high for nodules > 20 mm and inadequate for nodules ≤ 10 mm in diameter (15). But in a recent study, Zhang et al suggested that adding ARFI imaging for nodules smaller than 10 mm improves the number of correctly diagnosed nodules significantly compared to conventional US (19). With our study, ARFI was diagnostic in distinguishing benign and malignant nodules less than 10mm, but the diagnostic value was insufficient in larger nodules.

In this study no cut-off value was found for SWV predicting malignancy. The cut-off value for the SWV ranged from 2.01 m/s to 3.74 m/s in previous studies and there is not an agreement on a single value (4-7, 9, 16, 18, 19, 23-26). One factor for this variety may be the technical limitations of ARFI imaging. If the measurement is not reliable due to motion or breathing or the SWV is beyond 0-9 m/s, it is displayed as ‘‘X.XX m/s’’ on the screen. No consensus has been reached on the value of X.XX m/s. The numbers of the nodules with invalid measurements and whether they were included in the mean value calculation are not clear in all studies (9, 11, 12, 15, 19, 24). In some studies it is allocated to be 0 m/s, 8.4 m/s or 9 m/s with 0 m/s corresponding to cystic portion and 8.4 m/s or 9 m/s corresponding to solid portion. (4, 6, 9, 14, 15, 18, 25-30). These nodules were discarded in some previous studies as in our study (13, 17, 19, 27, 31-32). If the nodules with invalid measurements were included in our study and recorded as “9 m/s”, the mean SWV value of malign nodules could have been significantly higher than the benign nodules. Measurement differences’ such as the position of the ROI and the number of measurements may affect the mean value of the nodules and might be another reason for the variety of cut-off values of SWV. Generally, in large nodules, the ROI was moved randomly in the solid portion of the nodules. Less often

measurements were made without movement of the probe (11, 14). The number of measurements made in different studies ranged from 2 to 10 (4, 5). The wide range of cut of values of SWV also shows the overlaps of the stiffness of benign and malignant nodules.

The value of SWV-ratio in the differential diagnosis of thyroid nodules was evaluated in a few studies (4, 15, 25). Although different best cut-off (Youden cut-off) points were found; high diagnostic accuracy was reported for SWV-ratio. Our results were not concordant with theirs. In a study by Zhang et al, the diagnostic performance of SWV and SWV-ratio were compared between 3 groups of nodules which were classified according to their sizes as nodules ≤10 mm, 11-20 mm, and >20 mm. The specificity and PPV of SWV-ratio were higher than SWV in nodules larger than 10 mm but lesser in smaller nodules (15). With our study, a cut-off value for SWV for predicting malignancy could be calculated for only nodules <10 mm in size, and a sub analysis for sensitivity and specificity in terms of nodule size was not applicable. The better diagnostic performance with nodules < 10 mm can be secondary to patient selection bias. FNAB was performed for a nodule < 10 mm, if the nodule was highly suspicious for malignancy on B-mod images and the rate of malignancy among these nodules was 70%.

This study has some limitations. Although USE could only be used as an adjunctive method to US and could not be used as an independent test for the diagnosis of thyroid nodules, we did not compare the accuracy of USE added grayscale US to grayscale US. The malignancy rate was higher than the normal population in our study because we did not include the coalescent nodules and nodules having more than 25% cystic component. Most of these nodules have a high probability of being benign. In this study we could not investigate whether there was a significant difference in VTQ measurements of different types of malignant nodules. Since 27 of malignant nodules were papillary carcinoma, 2 were follicular, and 2 were medullary carcinoma. There are also technical limitations for the VTQ mode of ARFI imaging. The sampling ROI for VTQ is 6x5 mm and cannot be altered and is only suitable for nodules ≥5 mm in diameter. The presence of macro calcifications in the nodule and the values exceeding the upper detection limit of 9cm/s are also limitations of SWE. The lack of evaluation of inter and intra observer variability is a limitation of our study.

CONCLUSION

Our results indicated that ARFI imaging or any B-mode US feature does not have good diagnostic performance to detect malignancy in a thyroid nodule. We believe more prospective studies in a large series and screening populations are needed to evaluate the diagnostic accuracy of VTQ mode of ARFI imaging and combined different features of conventional US should be investigated.

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