MEDICAL SCIENCE MONITOR

HYPOTHESIS

e-ISSN 1643-3750
© Med Sci Monit, 2018; 24: 671-677
DOI: 10.12659/MSM.904703

Received: 2017.04.06
Accepted: 2017.06.09
Published: 2018.02.02

The Preciseness in Diagnosing Thyroid Malignant Nodules Using Shear-Wave Elastography

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Source of support: Departmental sources

Our study aimed to identify more accurate results about the diagnostic role of shear-wave elastography (SWE) for thyroid malignant nodules through a meta-analysis.

Potential articles were searched in PubMed, Embase, and the Cochrane Library databases. Overall sensitivity and specificity with 95% confidence intervals (CIs) was used to represent the diagnostic accuracy of SWE. Summary receiver operating characteristic (ROC) curve was constructed to illustrate the results. In addition, χ^2 and I^2 tests were performed to assess heterogeneity. A value of $p \leq 0.05$ indicated significant heterogeneity. All the analysis was conducted in Meta-DiSc version 1.4 software.

Twenty studies were included in the analysis. There were a total of 2,907 patients and 3,397 thyroid nodules included in the meta-analysis. Overall sensitivity and specificity were 0.68 (95% CI: 0.66–0.70) and 0.85 (95% CI: 0.84–0.87), respectively. The results showed the area under curve (AUC) was 0.9041, suggesting high accuracy of SWE for differentiating benign and malignant thyroid nodules.

SWE showed high accuracy in identifying thyroid malignant nodules, suggesting it could serve as a diagnostic biomarker in thyroid nodules.

MeSH Keywords: Adenocarcinoma • Adenoma, Sweat Gland • Diagnosis • Thyroiditis, Suppurative

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/904703

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Background

The incidence of thyroid nodules is approximately 19–68%, and about 5–15% of nodules are malignant [1,2]. High-resolution ultrasonographic (US) imaging is an important technique used to detect thyroid nodules [3,4]. Fine-needle aspiration (FNA) biopsy is a common way to determine whether nodules are malignant or not. The diagnostic accuracy of FNA is limited by non-diagnostic aspirates and the failure in interpretation of cytology that is brought about by the similarity in morphological signs of benign and malignant nodules [5]. In clinical settings, about 15–30% of FNA samples cannot be confirmed accurately as benign or malignant [6]. There is an urgent need to find another tool for diagnosing thyroid malignant nodules.

As a new US-based tool, elastography is used to detect tissue stiffness by measuring the degree of distortion [7–9]. The malignancy of thyroid nodules is related to nodular stiffness, especially for papillary carcinomas. While other types of thyroid cancers, such as medullary carcinoma, follicular carcinoma, and undifferentiated carcinoma show relatively soft texture [10,11]. Elastography is proposed as a crucial tool in differentiating malignant from benign thyroid nodules. However, there are several limitations for elastography: it is highly dependent on organ compressibility and it is operator dependent. Shear-wave elastography (SWE) has been presented as a novel, promising elastography technique. This technique is independent from individual operator and is more quantitative and reproducible than other techniques of elastography [12].

There have been many reports regarding the diagnostic role of SWE in discriminating malignant from benign thyroid nodules [1,13–31]. However, results have been inconsistent due to the variances in population, sample size, and reference standards. Our meta-analysis, based on previous studies aimed to obtain more accurate evaluation on the diagnostic role of SWE for identification benign and malignant thyroid nodules.

Material and Methods

Search strategy

Databases of PubMed, Embase, and the Cochrane Library were searched for potential studies using the following terms: virtual touch tissue quantification (VTQ), acoustic radiation force impulse, SWE, and thyroid. The search was restricted to studies published with the English language.

Inclusion criteria

The studies were evaluated according to the following inclusion criteria. 1) The study evaluated the diagnostic role of SWE in differentiating benign and malignant thyroid nodules. 2) The reference standard was histopathological (core biopsy) or cytological (FNA) confirmation. 3) The study provided data of true-positive (TP), false-positive (FP), true-negative (TN), and false-negative (FN) or available data to calculate these results. As for the overlapping data in more than one study, the studies with larger sample size were included.

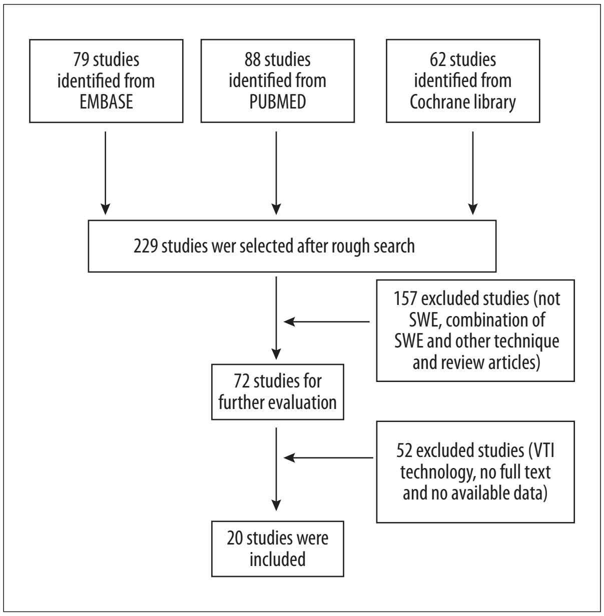

Figure 1. Flow chart for selection of studies: 20 studies were included in the meta-analysis.

Data extraction

The key information was extracted from studies, such as name of first author, year of publication, country, sample size, reference standard for the diagnosis, number of malignant and benign thyroid lesions, SWE index to distinguish benign and malignant thyroid nodules, TP, FP, FN, and TN. Data extraction was performed by two independent researchers. The inconsistent terms were confirmed with a discussion.

Statistical analysis

Pooled sensitivity and specificity with 95% confidence intervals (CIs) were adopted to test the diagnostic role of SWE in benign and malignant thyroid nodules. A summary receiver operating characteristic (ROC) curve was constructed as well. The χ^2 and I^2 tests were conducted to evaluate the heterogeneity; $p \leq 0.05$ (or $I^2 > 50\%$) indicated the presence of heterogeneity. All the statistical analyses were completed in Meta-DiSc version 1.4 software.

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Table 1. Studies characteristics.

Author	Year	Country	Patients (nodules)	Malignant/ benign	Age	SWE parameters	AUC	Cutoff	Sensitivity, %	Specificity, %
Liu BJ	2015	China	141 (141)	71/70	23–75	SWV	0.77	2.58 m/s	76.1	70.0
						SWR	0.74	1.03	85.9	50.0
Park	2015	Korea	453 (476)	379/97	15–77	EI	0.689	85.2 kPa	43.6	88.7
Liu BX	2015	China	271 (331)	101/230	18–83	EI	0.808	39.3 kPa	66.3	84.4
Kim	2013	Korea	99 (99)	21/78	25–77	EI	0.695	53 kPa	61.9	76.1
Liu BX	2014	China	49 (64)	19/45	11–71	EI	0.84	38.3 kPa	86.7	68.4
Samir	2015	America	35 (35)	11/24	23–85	EI	0.81	22.3 kPa	82.0	88.0
Hamidi	2015	Turkey	95 (95)	33/62	12–78	SWV	0.964	2.66 m/s	100.0	82.3
Xu	2014	China	375 (441)	116/325	18–75	SWV	0.86	2.87 m/sec	71.6	83.4
Zhang YF	2014	China	157 (173)	96/77	22–78	SWV	0.702	3.10 m/s	56.2	79.2
Calvete	2013	Spain	160 (157)	28/129	25–77	SWV	–	2.50 m/s	85.7	96.0
Deng	2014	China	146 (175)	56/119	18–69	SWV	0.88	2.59 m/s	80.4	84.0
Zhuo	2014	China	182 (191)	69/122	27–83	SWV	–	2.545 m/s	96.3	96.2
Sebag	2010	France	93 (146)	29/117	–	EI	0.936	65 kPa	85.2	93.9
Bojunga1	2012	Germany	138 (158)	21/137	18–83	SWV	0.69	2.57 m/s	57.0	85.0
						SWR	0.71	1.57	57.0	84.0
Hou	2012	China	77 (85)	20/65	15–70	SWV	–	2.42 m/s	80.0	89.2
Veyrieresa	2012	France	148 (297)	35/262	–	EI	0.852	66 kPa	80.0	90.5
Bhatia	2012	China	74 (62)	17/45	–	EI	0.58	28.9 kPa	47.1	86.7
						ER	0.72	2 kPa	50.0	90.5
Gu	2011	China	72 (98)	22/76	23–75	SWV	0.954	2.555 m/s	86.4	93.4
Zhang YF	2012	China	142 (173)	44/129	16–75	SWV	0.861	2.87 m/s	75.0	82.2
						SWR	0.831	1.59	63.6	88.4
Zhang FJ	2013	China	155 (155)	62/93	23–82	SWV	0.989	2.84 m/s	96.8	95.7
						SWR	0.949	1.32	91.9	81.7

SWE – shear wave elastography; SWV – shear wave velocity; SWR – shear wave velocity ratio; EI – elasticity indices; ER – elasticity ratio; AUC – area under curve.

Results

Studies selection

In the primary selection, 229 studies were identified from Embase, PubMed, and the Cochrane Library. Then 157 studies were excluded for the following: no SWE, combination of SWE and other technique, and review articles. In the further evaluation, 52 studies were excluded for virtual touch tissue imaging (VTI) technology, no full text, and no available data. After exclusions, 20 studies were included for meta-analysis [1,13–32]. The study selection process is shown in Figure 1.

Studies characteristics

The studies were from China, Korea, America, Turkey, Spain, Germany, and France. The number of patients in the meta-analysis was 2,907 and number of thyroid nodules was 3,397. The age of patients ranged from 11 to 85 years. As for SWE, the parameters were shear-wave velocity (SWV), shear-wave velocity ratio (SWR), elasticity indices (EI), and elasticity ratio (ER). Sensitivity, specificity, area under curve (AUC), and cut-off value are listed in Table 1.

Differentiation of benign and malignant thyroid nodules

As shown in Figure 1, the lowest value for sensitivity was 0.44, while the maximum value was 1.00. After the overall

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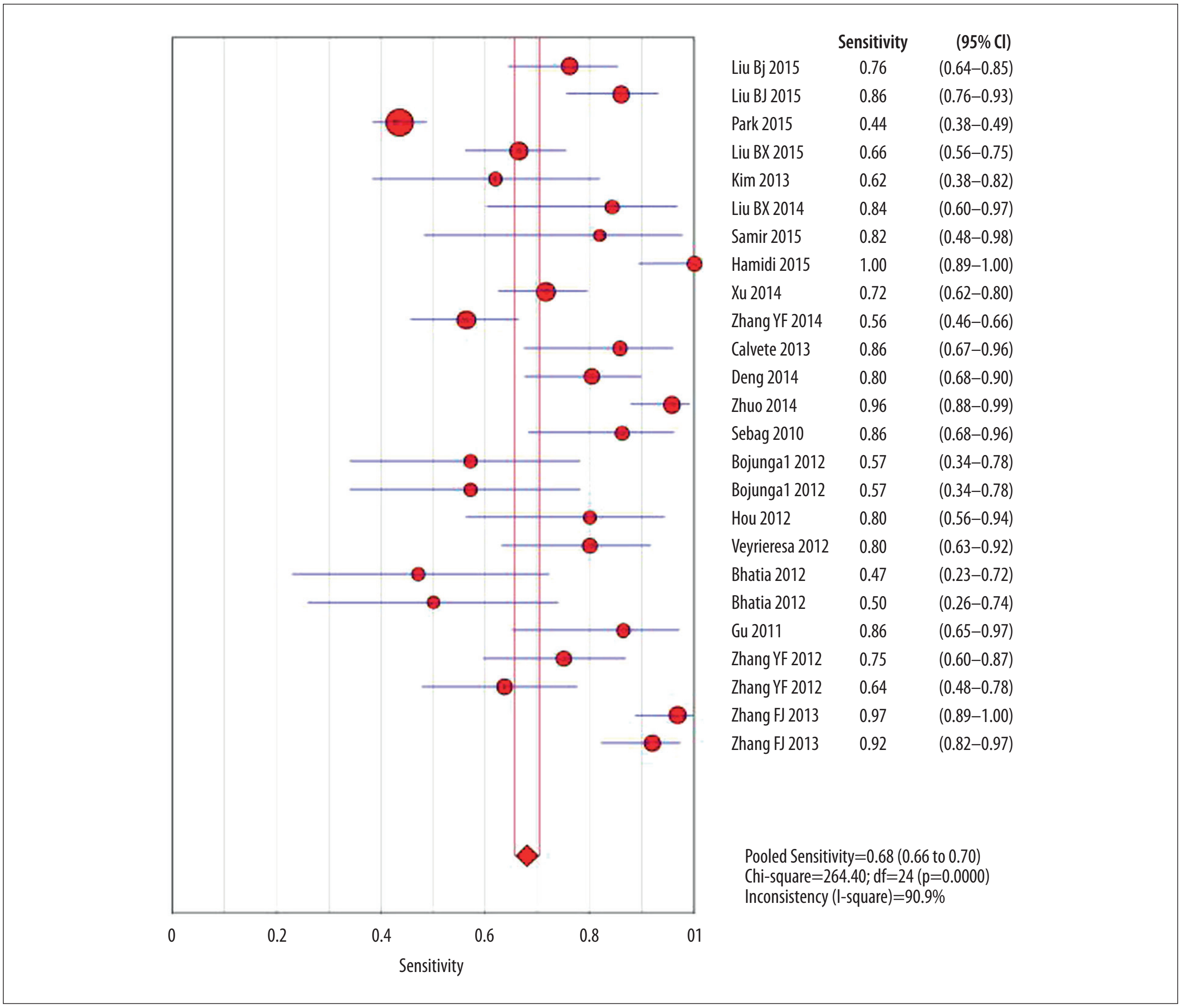

Figure 2. Overall sensitivity of studies was 0.68 (0.66–0.70).

analysis, we found that SWE showed sensitivity of 0.68 (95% CI: 0.66–0.70) (Figure 2). The specificity of SWE in diagnosing malignant thyroid nodules was 0.85 (95% CI: 0.84–0.87) (Figure 3). SROC analysis showed AUC was 0.9041, suggesting high accuracy of SWE for differentiating benign and malignant thyroid nodules (Figure 4).

Discussion

Commonly, malignant tissues are stiffer than benign ones. In recent years, studies have tried to apply ultrasound elastography to distinguish malignant from benign nodules in many organs; breast, prostate, and thyroid [8,32,33]. SWE uses focused pulses of ultrasound to stimulate tissues [29]. Based on the signals, the results about elasticity of the tissue are output in real-time. If possible, the elasticity is even evaluated both quantitatively and qualitatively. In the quantitative analysis, the elasticity is expressed by color. In the latter analysis, elasticity of certain region is expressed by kPa [34,35].

To date, two different SWE modes are most commonly used, acoustic radiation force impulse (ARFI) technique [36] and supersonic shear imaging (SSI) [37]. During ARFI imaging, tissues in the region of interest (ROI) are mechanically excited via short-duration acoustic pulses to generate small localized tissue displacements. There are two kinds of imaging methods for ARFI: VTQ and VTI, which detect lesion stiffness quantitatively and qualitatively, respectively. The SWV increases with the stiffness, greater SWV corresponding to much stiffer tissue [38,39]. Thus, SWV is regarded as a measurement of the intrinsic and reproducible property of tissues [40]. Improved diagnostic accuracy has been reported in ARFI compared to conventional US and elasticity imaging (EI) [25,41,42]. Several studies have described its application in kidney and liver diseases [43–46].

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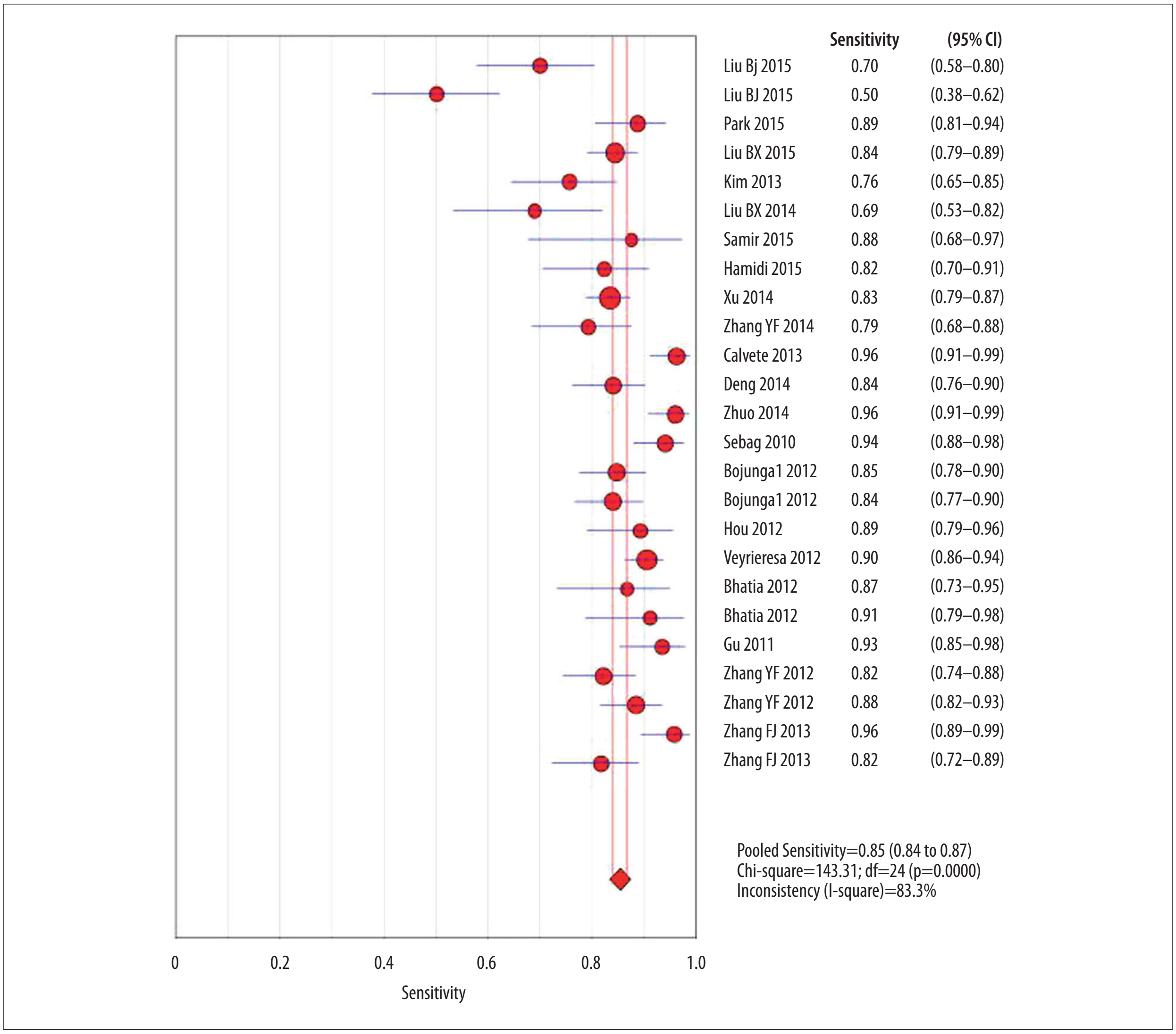

Figure 3. Overall specificity of studies was 0.85 (0.84–0.87).

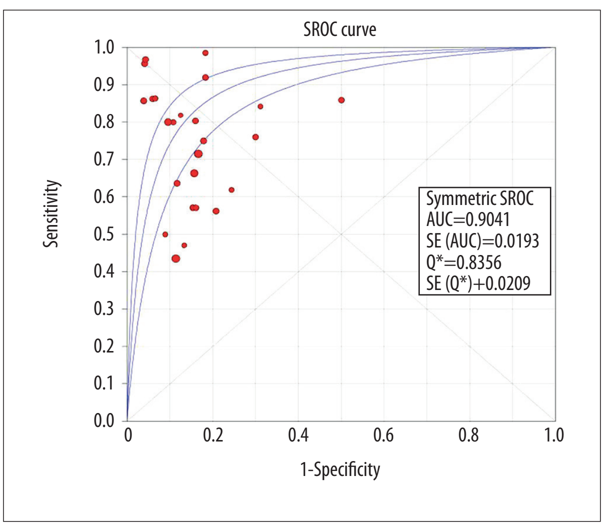

Figure 4. SROC analysis: AUC of SWE was 0.9041.

In recent years, extensive studies about the diagnostic role of SWE in thyroid nodules have been conducted. Bojunga1 et al. concluded that SWE showed no priority in diagnosing malignancy of thyroid in comparison with real-time elastography (RTE) [26]. One study based on a Chinese population also obtained results with low accuracy [21]. Bhatia et al. concluded that the precious results could not confirm the role of SWE in identifying thyroid malignancy [29]. A retrospective study by Park et al. reported that EI was an independent diagnostic biomarker with 43.6% sensitivity and 88.7% specificity, while the diagnostic accuracy was relatively lower, represented by AUC (0.689) [14]. Samir et al. concluded that SWE showed priority in diagnosis of malignant thyroid nodules compared to conventional US [18]. One study conducted in Turkey obtained satisfying outcome. The sensitivity, specificity, and AUC were 100.0%, 82.3%, and 0.964, respectively [19]. Our results based on these studies concluded that the diagnostic sensitivity, specificity,

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and AUC were 0.68 (0.66–0.70), 0.85 (0.84–0.87), and 0.9041, respectively. These results reflected high diagnostic accuracy of SWE in thyroid malignant nodules. These result confirmed the results from a previous meta-analysis by Zhang et al. [47] that also reported that SWE had high sensitivity and specificity in evaluating thyroid nodules. In addition, a similar conclusion was drawn by Lin et al. in their meta-analysis on this topic [48]. However, the included studies of these aforementioned meta-analyses were smaller than our current study, suggesting that our results might be more reliable.

Overall, our meta-analysis uncovered high accuracy of SWE in diagnosing malignant thyroid nodules. These results are encouraging; however, the diagnostic sensitivity of SWE was relatively low. Further studies could adopt the combination of SWE with other techniques to improve sensitivity. Our analysis was based on 2,907 patients and 3,397 nodules and involved countries of China, Korea, America, Turkey, Spain, Germany, and France, and as such, the results were considered reliable and accurate. However, our study did not analyze the effects of ethnicity and index through a subgroup analysis, which, if done, might have illustrated the potential effects of these factors on function mechanism of SWE.

Conclusions

SWE showed high diagnostic accuracy in identifying thyroid malignancy. We hope the results of our meta-analysis will contribute to the early diagnosis and improved treatments of patients with thyroid cancer.

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