

Value of shear wave elastography in discriminating malignant and benign breast lesions

A meta-analysis

Yan Xue, PhD^a, Shuxin Yao, PhD^b, Xiaodong Li, PhD^c, Huarong Zhang, PhD^{a,*}

Abstract

The analysis was aimed to evaluate the diagnostic accuracy of shear wave elastography (SWE) for malignant breast lesions through a meta-analysis.

Related articles were searched from Pubmed, Embase, and Cochrane library. Overall sensitivity and specificity were analyzed with DerSimonian and Laird random effects model. Area under curve with corresponding 95% confidence interval (were calculated to evaluate the diagnostic accuracy of SWE. Sensitivity and publication bias were assessed as well.

A total of 25 articles including 4128 patients and 4546 breast lesions were included in the pooled analysis. In the subgroup analysis, diagnostic sensitivity and specificity of SWE in Asian population were 0.84 (0.79–0.88) and 0.87 (0.84–0.90), respectively, whereas they were 0.92 (0.86–0.96) and 0.89 (0.84–0.92) in Caucasian population. The diagnostic accuracy of SWE was a little higher for Caucasians than for Asians (0.95 vs. 0.92). The diagnostic sensitivity and specificity of virtual touch tissue quantification were 0.85 (0.77–0.91) and 0.93 (0.88–0.96), respectively. It showed a little higher value in specificity and summary ROC curve than SWE (0.93 vs. 0.87; 0.95 vs. 0.93). In addition, maximum stiffness exhibited higher detection sensitivity than that of mean stiffness (0.91 vs. 0.85).

SWE serves as an accurate diagnostic technology for discriminating between malignant and benign breast lesions.

Abbreviations: 95% CI = 95% confidence interval, ARFI = acoustic radiation force impulse, AUC = area under curve, BI-RADS = Breast Imaging Reporting and Data System, FP = false-negative, FP = false-positive, ROI = region-of-interest, SD = standard deviation, SROC = summary ROC curve, SWE = shear wave elastography, TN = true-negative, TP = true-positive, VTTI = virtual touch tissue imaging, VTTQ = virtual touch tissue quantification.

Keywords: breast cancer, diagnose, shear wave elastography

1. Introduction

Breast cancer is one of serious diseases threatening women's health. It is the major cause of death among women.^[1,2] Annually, about 1.38 million new cases and 458,000 deaths happen worldwide.^[3] Moreover, the occurrence rate of this cancer has been increasing in recent years. Early detection and diagnosis will be helpful to reduce mortality and improve prognosis. It is urgent to develop efficient detection technology for breast cancer.

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^a Department of Ultrasonography, Linyi People's Hospital, Linyi City, Shandong,

^b Department of Ultrasonography, Heze Municipal Hospital, Heze City, Shandong,

^c Department of Radiology, Linyi People's Hospital, Linyi City, Shandong, China.

* Correspondence: Huarong Zhang, Department of Ultrasonography, Linyi People's Hospital, Linyi City, Shandong Province 276000, China (e-mail: o34onb@126.com).

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Mammographic screening is a valuable tool for early detection of breast cancer.^[4] However, the increased density of breast tissue significantly reduces the diagnostic accuracy.^[5] Among other imaging methods, gray-scale ultrasonography is a valuable adjunct technique. It shows highly sensitive in distinguishing benign breast lesions from malignant ones.^[6–8] The Breast Imaging Reporting and Data System (BI-RADS) along with ultrasonography contribute to understanding the standardized terminology about ultrasonography features, assessments, and recommendations.^[9,10] Nevertheless, this technique is subjective and poorly specific.^[10–12] Ultrasound elastography emerges as an efficient tool to detect malignant solid lesions through measuring the stiffness. It exhibits 86.5% sensitivity, 89.8% specificity, and 88.3% accuracy in discriminating benign and malignant breast lesions.^[13] In the ultrasound elastography test, the performance is conducted with freehand compression. The elasticity map largely depends on the extent of tissue compression and organ's compressibility limits. Moreover, the differences in skill of the operator may result in distinct results.

Shear wave elastography (SWE), a newly developed technology, can overcome these above mentioned problems. It is performed by remotely inducing mechanical vibrations via acoustic radiation force produced by a focused ultrasound beam. The displacement induced at the focus produces shear wave that delivers information about viscoelastic properties of the tissue, thus generates the quantitative assessment to elasticity values. Till now, there were many studies investigating the clinical values of SWE in discriminating benign and malignant breast lesions; however, no consistent results were obtained.

The meta-analysis was aimed to get more accurate results about the diagnostic value of SWE in breast cancer, which contributes to the early diagnosis of breast cancer and improvement on the treatments.

2. Materials and methods

2.1. Articles retrieve

The articles were retrieved in Pubmed, Embase, and Cochrane databases. The following search terms were used to retrieve articles: “shear wave elastography,” “SWE,” “acoustic radiation force impulse,” “ARFI,” “virtual touch tissue quantification,” “VTTQ,” and “breast.” The references of retrieved articles were carefully checked for potential ones. Only the articles in English were considered.

2.2. Inclusion criteria

The studies were included if they met the following criteria: (1) the study investigated the role of SWE in the diagnosis of malignant and benign breast lesions. (2) Pathological biopsy or cytological (fine-needle aspiration) test was adopted as gold standard. (3) The data of true-positive (TP), false-positive (FP), false-negative (FN), and true-negative (TN) were provided. For the studies with overlapping data, only the study with larger sample size was included.

2.3. Information extraction

The following information was extracted by two independent authors: name of first author, sample size, number of breast lesions, number of malignant and benign breast lesions, gold

standard, SWE parameters, TP, FP, FN, and TN. The ambiguity was solved with discussion.

2.4. Statistical analysis

All the analysis was completed in Stata 12.0 (StataCorp LP, College Station, TX) software. Summary sensitivity and specificity were estimated with DerSimonian and Laird random effects model. Meanwhile, area under curve (AUC) with corresponding 95% confidence interval (CI) was calculated to evaluate the diagnostic accuracy of SWE. *P* value was adopted to evaluate the heterogeneity between studies. *P* < .05 indicated significant heterogeneity. Deek’s funnel plot was used to assess the publication bias. Subgroup analysis based on ethnicity, technology, and SWE parameters (maximum and mean stiffness) were also conducted.

3. Results

3.1. Studies selection and characteristics of included studies

The retrieved studies were selected according to inclusion criteria. The selection process was showed in Figure 1. Total of 188 studies were retrieved from databases. Then, 124 studies were excluded for combination of SWE and other technology, review studies, not SWE analysis and comparison with SWE, and other technologies. Finally, 25 studies^[14–38] were included after exclusion of studies for without available data and virtual touch tissue imaging (VTI) analysis (Table 1). The meta-analysis included 4128 patients and 4546 breast lesions. In the current meta-analysis, 18 articles were for Asian population, whereas 7 for Caucasian population. Six articles were based on virtual

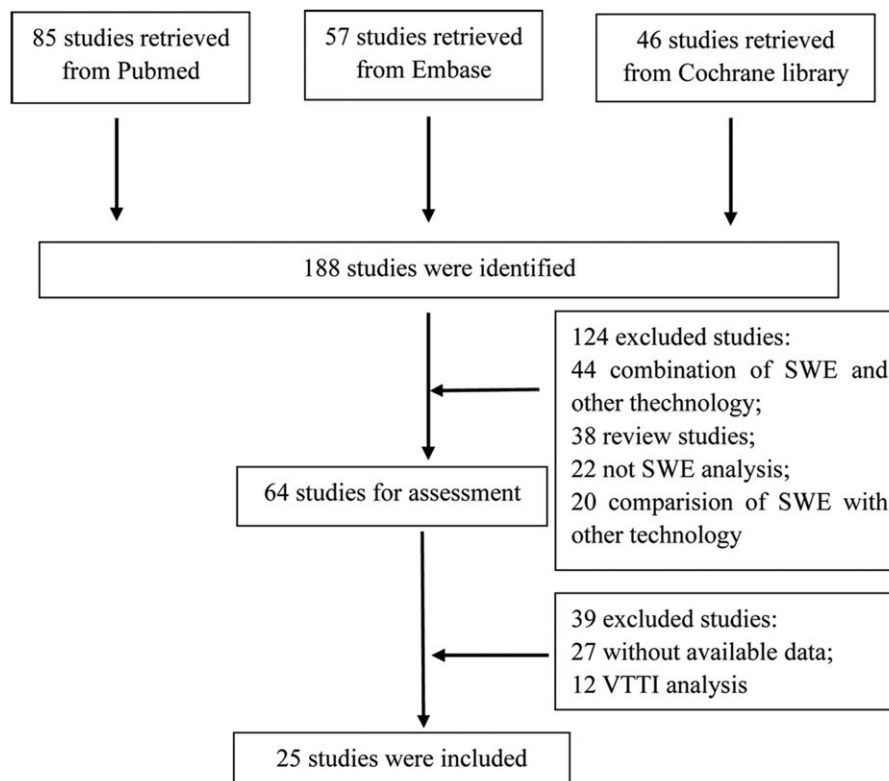


Figure 1. Flow chart of articles selection.

Table 1
Basic characteristics of included studies.

Author	Year	Country	Patients, n	Lesion, n	Benign, n	Malignant, n	Gold standard	Technology	Parameters
Lo	2015	China	81	88	57	31	Pathology	SWE	—
Xiao	2014	China	93	125	81	44	Pathology	SWE	—
Sobczak	2015	Poland	76	84	43	41	Pathology	SWE	E_{mean}
Zhang	2015	China	125	161	106	55	Pathology	SWE	E_{max}
Klotz	2014	France	142	167	65	102	Pathology	SWE	E_{max}, E_{mean}
Au	2014	Canada	112	123	79	44	Pathology	SWE	$E_{max}, E_{mean}, E_{ratio}$
Yao	2014	China	146	206	163	43	Pathology	VTTQ	SWW
Olgun	2014	Turkey	109	115	83	32	Pathology	SWE	$E_{max}, E_{mean}, E_{min}, E_{ratio}$
Zhou	2014	China	193	193	137	56	Pathology	SWE	$E_{max}, E_{mean}, E_{min}$
Bai	2012	China	108	143	102	41	Pathology	VTTQ	SWW
Jin	2012	China	95	122	66	56	Pathology	VTTQ	SWW
Meng	2011	China	86	92	65	27	Pathology	VTTQ	—
Tamaki	2013	Japan	180	182	26	156	Pathology	VTTQ	—
Tozaki	2012	Japan	158	161	70	91	Pathology	VTTQ	SWW
Evans	2010	UK	52	53	23	30	Pathology	SWE	E_{max}, E_{mean}, SD
Chang	2011	Korea	158	182	93	89	Pathology	SWE	E_{mean}
Berg	2012	England	939	939	650	289	Pathology	SWE	E_{max}
Chang	2013	Korea	129	150	79	71	Pathology	SWE	—
Gweon	2013	Korea	119	133	97	36	Pathology	SWE	SD
Lee ^{-a}	2013	Korea	139	156	120	36	Pathology	SWE	E_{max}
Lee ^{-b}	2013	Korea	134	144	77	67	Pathology	SWE	$E_{max}, E_{mean}, E_{ratio}$
Yoon ^{-a}	2013	Korea	199	222	175	47	Pathology	SWE	E_{max}
Yoon ^{-b}	2013	Korea	236	267	208	59	Pathology	SWE	$E_{max}, E_{mean}, E_{ratio}$
Youk	2013	Korea	146	163	115	48	Pathology	SWE	E_{max}
Evans	2012	UK	173	175	64	111	Pathology	SWE	E_{max}, E_{mean}

E_{max} = maximum stiffness; E_{mean} = mean stiffness; E_{min} = minimum stiffness; E_{ratio} = ratio of stiffness of the mass to the background; SD = standard deviation; SWE = shear wave elastography; SWW = shear wave velocity; VTTQ = virtual touch tissue quantification.

touch tissue quantification (VTTQ) technology and 19 based on SWE. In the articles of SWE, 13 articles adopted maximum stiffness and 10 adopted mean stiffness.

3.2. Summary sensitivity and specificity analysis

The diagnostic sensitivity and specificity of SWE were analyzed and the results were showed in Figures 2 and 3. The analysis

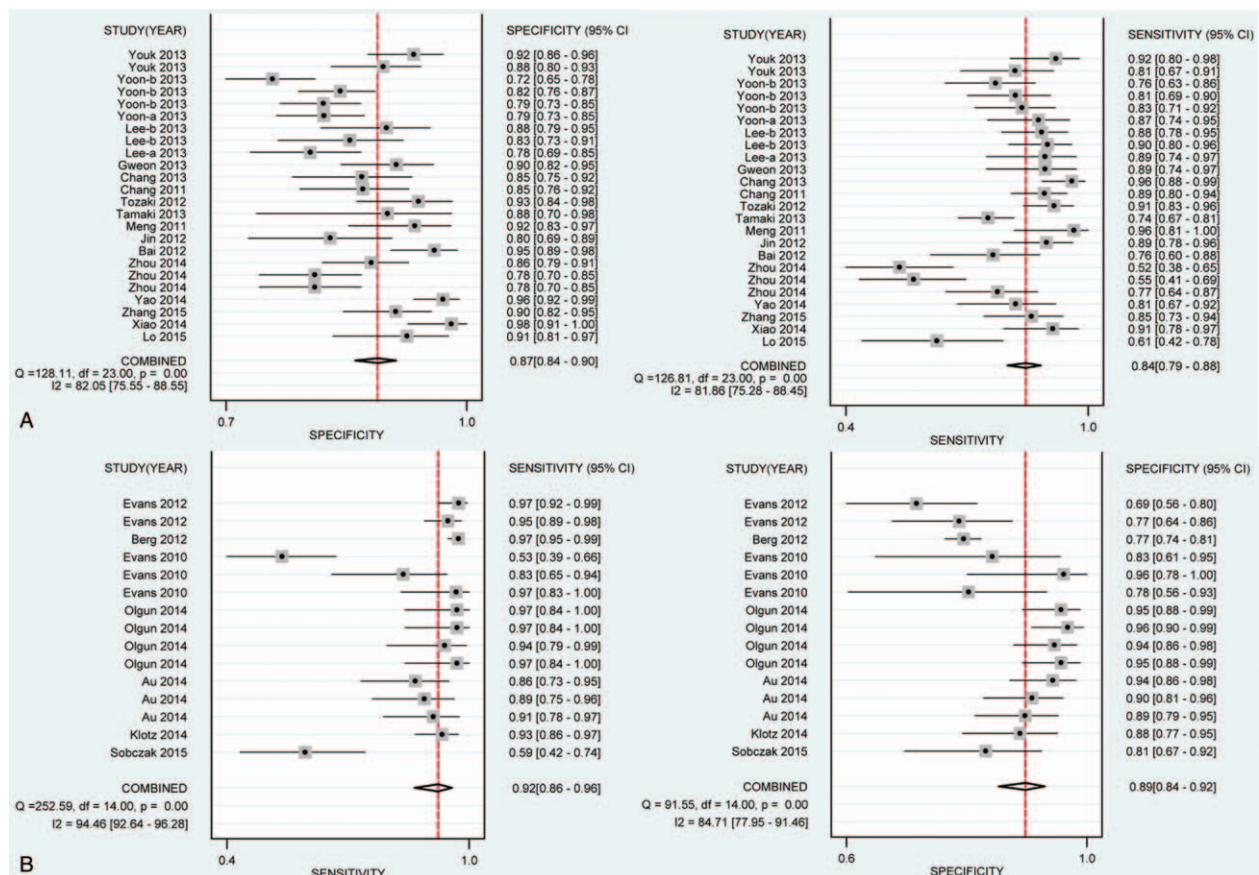


Figure 2. Role of SWE in discriminating breast malignant lesions from benign lesions in subgroup analysis of ethnicity. A, Sensitivity and specificity results based on Asian population. B, Sensitivity and specificity results based on Caucasian population.

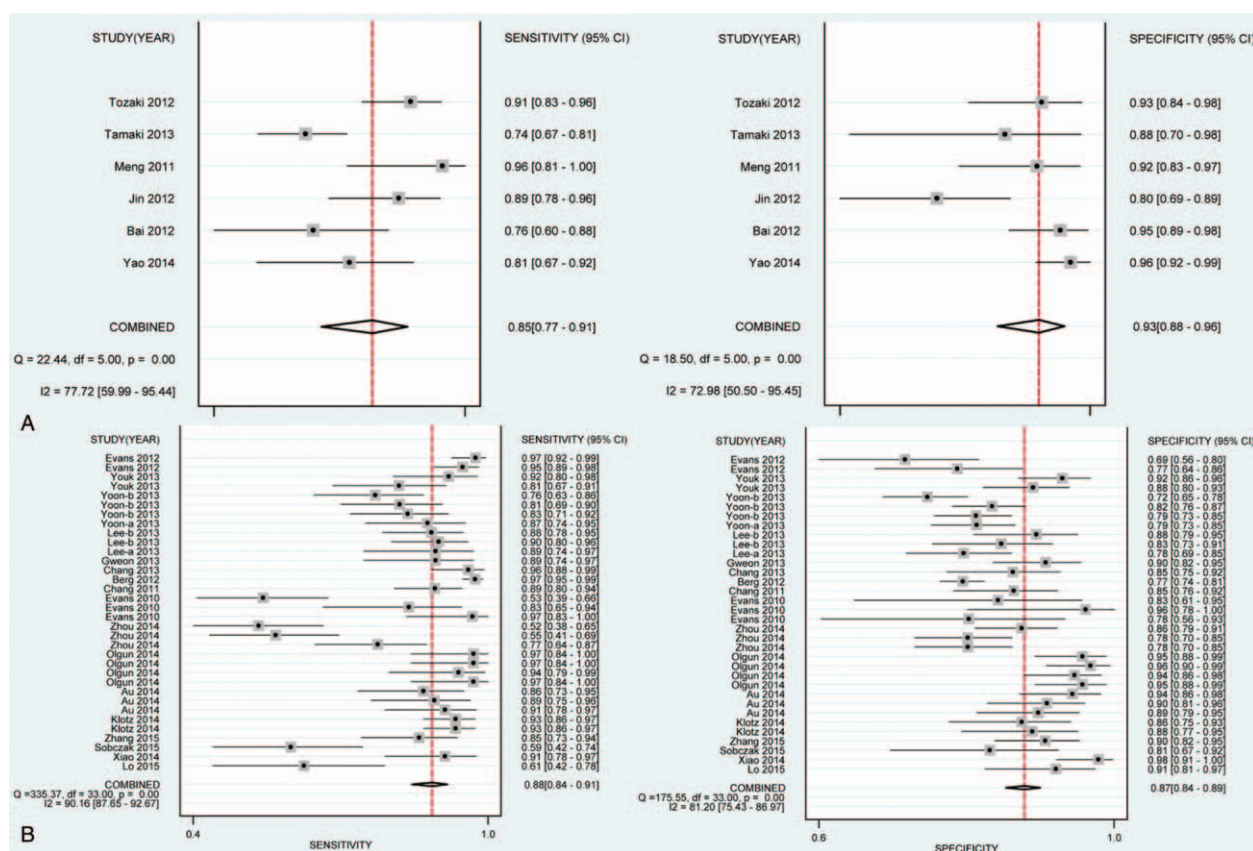


Figure 3. Role of SWE in discriminating breast malignant lesions from benign lesions in subgroup analysis of technology. A, Sensitivity and specificity results based on VTTQ. B, Sensitivity and specificity results based on SWE.

focused on the subgroup analysis based on ethnicity, technology, and SWE parameters (Table 2). In the analysis of ethnicity, the detection sensitivity and specificity of SWE in Asian population were 0.84 (0.79–0.88) and 0.87 (0.84–0.90), respectively. Summary ROC curve showed the AUC was 0.92 (0.90–0.94) (Fig. 4). As for Caucasian population, SWE showed a little higher detection sensitivity (0.92) and specificity (0.89). The corresponding AUC was 0.95 (0.93–0.97). In the analysis of technology, the detection sensitivity and specificity of VTTQ were 0.85 (0.77–0.91) and 0.93 (0.88–0.96), respectively. SROC showed AUC was 0.95 (0.93–0.97). Meanwhile, the detection sensitivity and specificity of SWE were 0.88 (0.84–0.91) and 0.87

(0.84–0.89), respectively. The AUC was 0.93 (0.90–0.95). In addition, we investigated the diagnostic role of SWE parameters (maximum and mean stiffness). As shown in Figure 3, maximum stiffness exhibited higher detection sensitivity than that of mean stiffness (0.91 vs. 0.85).

3.3. Sensitivity and publication bias analysis

Sensitivity analysis was performed by deleting one study each time to observe the changes of results. The analysis indicated that the results were stable. Moreover, no publication bias was found in the meta-analysis (VTTQ: $P = .216$; SWE: $P = .08$) (Fig. 5).

Table 2

Subgroup analysis of meta-analysis.

Subgroup	Sensitivity (95% CI)	P_h	Specificity (95% CI)	P_h
Ethnicity				
Asian	0.84 (0.79–0.88)	.00	0.87 (0.84–0.90)	.00
Caucasian	0.92 (0.86–0.96)	.00	0.89 (0.84–0.92)	.00
Technology				
SWE	0.88 (0.84–0.91)	.00	0.87 (0.84–0.89)	.00
VTTQ	0.85 (0.77–0.91)	.00	0.93 (0.88–0.96)	.00
SWE parameters				
E_{max}	0.91 (0.87–0.94)	.00	0.84 (0.80–0.87)	.00
E_{mean}	0.85 (0.71–0.93)	.00	0.84 (0.79–0.88)	.01

CI = confidence interval; E_{max} = maximum stiffness; E_{mean} = mean stiffness; SWE = shear wave elastography; VTTQ = virtual touch tissue quantification.

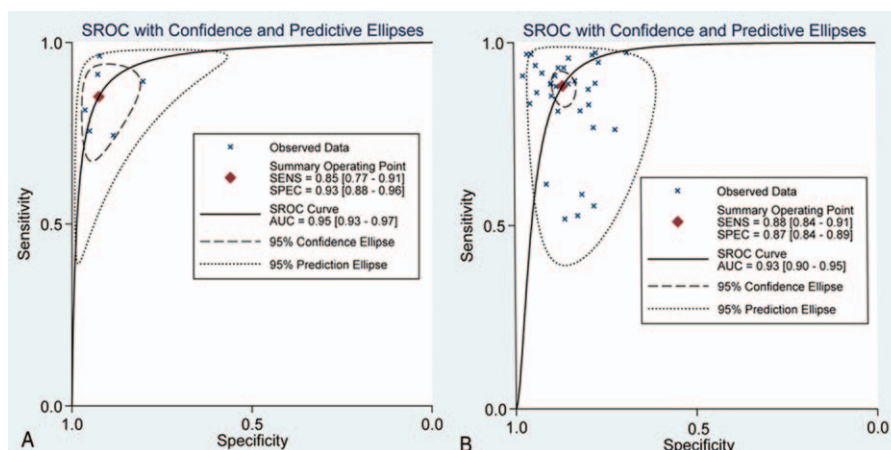


Figure 4. SROC analysis in subgroup analysis of technology. A, SROC results of VTTQ. B, SROC results of SWE.

4. Discussion

SWE is a highly reproducible technology.^[39] It determines the propagation velocity of shear waves within the tissues to quantify the stiffness in kPa or m/s.^[29,40] Many tissue elasticity characters can be determined within the region-of-interest (ROI), including maximum (E_{max}), mean (E_{mean}) and minimum (E_{min}) stiffness, standard deviation (SD), and ratio of stiffness of the mass to the background (E_{ratio}). Qualitative SWE pattern classification is also reported to show good diagnostic performances.^[30,32] E_{max} and E_{mean} refers to the general stiffness of the mass, whereas E_{ratio} represents the relative stiffness of the mass to the fat tissue, the elasticity value of which is 3 kPa.^[28] SD and pattern classification illustrate the internal heterogeneity of the mass,^[32] as the malignant masses are almost histologically heterogeneous. The quantitative measurements of SWE have been recognized as more objective information about the breast mass.^[39,40]

Among the included studies, the application value of SWE in discriminating malignant and benign breast lesions was controversial. In the study of Zhou et al,^[22] 193 women with 193 breast lesions were included to analyze the diagnostic performance of SWE, E_{max} , E_{mean} , and E_{min} were adopted to represent tissue stiffness. However, the diagnostic sensitivity (0.52, 0.55 and 0.77) and specificity (0.86, 0.78, and 0.78) of these three parameters were all low compared with other studies. Meanwhile, Youk et al^[37] reported high detection sensitivity (0.92) and specificity (0.92) of SWE, in which E_{max} represent tissue elasticity.

Evans et al (2012)^[38] found that the detection sensitivity of SWE was 0.97 (0.92–0.99), whereas specificity was only 0.69 (0.56–0.80). On the contrary, Evans et al (2010)^[28] reported 0.53 detection sensitivity and 0.83 detection specificity. The variances in results might be attributed to the differences in characters of patients, ethnicity or SWE parameters.

Subgroup analysis based on ethnicity, technology and SWE parameters was performed in our analysis. The diagnostic sensitivity, specificity and AUC of SWE in Caucasian population were all higher than in Asian population. As we all known, acoustic radiation force impulse (ARFI) includes VTTI and VTTQ. The result of VTTI is characterized by elastographic image, whereas the result of VTTQ is measured by SWV (m/s). Soft tissue shows slow SWV, compared with hard tissue.^[41] VTTQ has been used for diagnosis in thyroid, prostate, pancreas, liver, and breast.^[42–46] In our study, subgroup analysis according to technology (VTTQ and SWE) was conducted. VTTQ showed higher detection specificity and accuracy than SWE. In terms of SWE parameters, the diagnostic performance of E_{max} was better than E_{mean} .

The meta-analysis was based on 4128 patients and 4546 breast lesions. The results were reliable and stable. However, some defects must be pointed out. The number of articles based on Caucasian population was much less than that of Asian population. The accuracy of results on Caucasian population might be affected. In addition, significant heterogeneity exhibited between the included studies. The heterogeneity might be caused

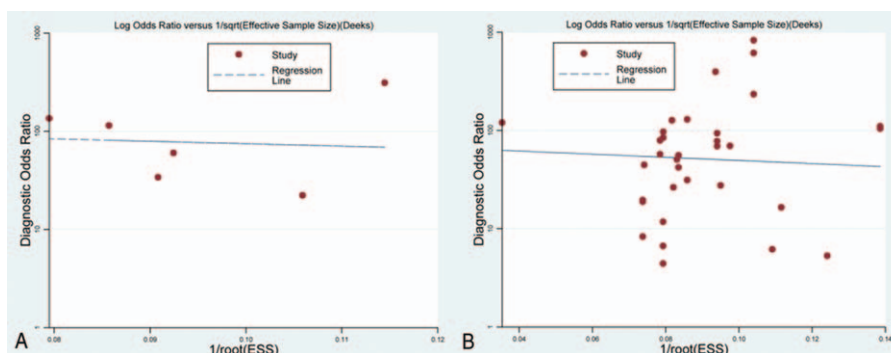


Figure 5. Deek's funnel plot in subgroup analysis of technology. A, Funnel plot of VTTQ. B, Funnel plot of SWE.

by the patients' number, basic feature of patients, and experiments methods, and so on.

Our meta-analysis demonstrates that SWE is an accurate and reliable diagnostic tool in discriminating malignant and benign breast lesions. With wide application, SWE may significantly improve the early diagnostic of breast cancer.

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