Int J Clin Exp Med 2019;12(8):9533-9547
www.ijcem.com /ISSN:1940-5901/IJCEM0095319

Review Article

Shear-wave elastosonography for diagnosis of prostatic cancer: a meta-analysis

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Received April 13, 2019; Accepted June 10, 2019; Epub August 15, 2019; Published August 30, 2019

Abstract: Objective: The aim of the current study was to methodically analyze the application value of shear-wave elastosonography (SWE) for diagnosis of prostatic cancer (PCa) via meta-analysis. Methods: Relevant studies concerning diagnosis of PCa using SWE, published before October 31, 2018, in China and other countries, were collected. These studies were filtered and estimated in terms of diagnostic criteria. Selected references were handled using Meta-disc 1.4, Revman 5.3, and Stata 14.0. Results: A total of 16 studies were finally included. After meta-analysis, the following values were drawn: PSNE = 0.84 [95% CI (0.76, 0.89)], PSPE = 0.85 [95% CI (0.78, 0.90)], PLR = 5.7 [95% CI (3.6, 8.9)], NLR = 0.19 [95% CI (0.12, 0.30)], DOR = 27.69 [95% CI (11.71, 65.48)], and AUC = 0.91 [95% CI (0.88, 0.93)]. Next, meta-regression was analyzed, exploring heterogeneity. The number of ROIs in per-core and levels of research were significant factors affecting heterogeneity ($p < 0.01$ and $p = 0.04$, respectively). Conclusion: SWE exhibited a favorable diagnostic value for detection of PCa. However, no clear inference could be made concerning cut-off values due to inescapable heterogeneity. In future investigations, specific recommendations regarding experimental design, especially included and excluded covariates, should be considered.

Keywords: Shear-wave elastography, biopsy, prostate cancer, meta-analysis

Background

Prostatic cancer (PCa) is a common malignant tumor of the male urinary system. Morbidity of this disease ranks fifth in overall worldwide malignancies [1]. According to relevant surveys, 1.6 million males were diagnosed PCa and 366,000 males died of PCa in 2015 (Global Burden of Disease Cancer Collaboration 2016) [2]. In 2016, a report from the American Cancer Society estimated that 26,120 American males died of PCa, becoming the second leading cause of death in American males [3]. Exploring reasons for increased incidence rates, some scholars have suggested that the increase of life expectancy of the population was a vital factor [4]. Furthermore, some researchers have suggested that change of diet-styles has led to serious obesity, increasing morbidity rates of PCa conversely [5].

The major prognostic benefit of PCa is early diagnosis and hence treatment. Traditionally, digital rectal examination (DRE), based on perceived diversities in the stiffness of normal prostatic tissues and neoplasm, has been used as the primary method for PCa. However, this method cannot judge the severity of this deadly disease [6]. Some researchers have pointed out that DRE could only detect PCa when the disease focus is found in the peripheral zone of the gland. Thus, most cases will be missed when the volume of the prostate gland ≥ 0.2 mL [7]. Furthermore, DRE may result in higher false positive rates, misleading clinicians to adopt unnecessary invasive diagnostic tests [8]. Equally important is the fact that omission diagnostic rates of DRE could be higher than 80%, as reported by Scardino PT et al. [9].

Testing the prostate-specific antigen (PSA) in serum is also a usual diagnostic method for biopsy-driven PCa. It has been established that PSA is the only generally accepted biomarker for prostate cancer. However, the threshold value of PSA is arbitrarily related with life expec-

tancy, age of the patient, and size of the prostate [10].

In current clinical application, the above two diagnostic methods are used initially for PCa. A survey showed that, in about 18% cases, PCa is suspected by DRE alone, regardless of the PSA level [7]. Another inquiry indicated that suspected DRE in patients with a PSA level < 2 ng/mL has a positive predictive value of 5-30% [11].

Definitive limitations exist in both of the above traditional methods. Therefore, finding a more reliable and non-invasive biomarker to distinguish PCa from other common prostatic diseases is crucial. The structures and morphologies of malignant and normal tissues are different, leading to discrimination of the stiffness present in the prostate. Based on results from an earlier study, the hardness of tumors was significantly higher than that of normal tissues and organs. This made it possible to use elastic stiffness as a new marker for diagnosis of prostate cancer [12].

Recently, elastosonography, a new ultrasound (US) technology, was depicted at great length by Bercoff et al. to portray tissue stiffness. This method has been used to increase accuracy of PCa diagnosis [13]. Moreover, as an innovative method, shear-wave elastosonography (SWE) can create a 2D real-time measurable image utilizing differences of tissue stiffness. This imaging technology could reduce unnecessary needle biopsies, lowering the burden of pain for patients. However, a unified conclusion concerning the diagnostic value of this innovative ultrasound imaging has yet to be determined. The European Association of Urology Guidelines pointed out that new sonographic modalities, such as elastography and contrast-enhanced US, are still under investigation [14]. Furthermore, according to results of some clinical trials, its diagnostic effects are strongly controversial. According to results portrayed by Sungmin Woo et al, the sensitivity was just 0.41 [15]. Jean-Michel Correas et al., however, showed a sensitivity of 0.96 using SWE for diagnosis of PCa [16].

In view of above facts, the present meta-analysis explored the value of SWE for diagnosis of PCa, aiming to provide reference for related follow-up studies.

Methods and materials

Literature retrieval

The current meta-analysis was performed on relevant studies published as late as October 31, 2018 in PubMed, Web of Science, Embase, China Biology Medicine Disc, Cochrane Library, Google Scholar, China National Knowledge Infrastructure (CNKI), and WANFANG databases, along with ClinicalTrials.gov. Both Chinese and English language studies were included. Search keywords included SWE and PCa and their synonyms: (shear wave elastography) OR (shear-wave elastography) OR (shear wave elastography) OR (acoustic radiation force impulse) OR (ARFI) OR (Supersonic) OR (Aixplorer) OR (virtual touch quantification) OR (VTQ) OR (virtual touch tissue imaging quantification) OR (VTIQ) AND (prostate cancer) OR (prostatic cancer) OR (prostate neoplasm) OR (prostatic neoplasm) OR (prostate tumor) OR (prostatic tumor) OR (prostate carcinoma) OR (prostatic carcinoma) OR (PCa).

Inclusion and exclusion criteria

Inclusion criteria: 1) The investigation was focused on the diagnostic accuracy of SWE for PCa; 2) All patients were diagnosed with PCa through histopathology; and 3) Related data provided a true positive, either directly or indirectly (TP), false positive (FP), true negative (TN), and false negative (FN), as well as sensitivity and specificity.

Exclusion criteria: 1) Editorials, comments, letters, and reviews; 2) Experimentation on animals; 3) Repetitive studies and research topics not meeting the requirements; 4) Lab studies; and 5) Studies that did not acquire the available two-by-two contingency table.

Data extraction

Retrieved articles were checked, independently, by two reviewers. Information concerning the surnames of the first authors, publication years, regions, and methods of research were collected. If any discrepancies existed, an additional researcher was consulted.

Literature quality evaluation

Using the quality evaluation of diagnostic accuracy studies tool (QEDAST) with Revman 5.3,

included studies were carefully evaluated [17], assessing risk of bias of the articles. Answers to the symbolic questions of each of the five sections were either "yes", "no", or "unclear" corresponding to the judgment of the risk level of bias as "low", "high", or "uncertain". If the answers to every question were "yes", the study could be at "low risk". If the answers to all questions were "no" or "unclear", the study could be judged as "high risk". If one of these answers was "no" or "unclear", the study was placed under "uncertain". Revman 5.3, special software for Cochrane collaborative network was used to output the results of QEDAST.

Statistical analyses

Pooled sensitivity (PSEN), pooled specificity (PSPE), diagnostic odds ratios (DOR), positive likelihood ratios (PLR), and negative likelihood ratios (NLR) were calculated using Stata 14.0. A summary of sensitivity and specificity levels was estimated through bivariate modeling [18, 19]. Results are graphically presented by summary receiver operating characteristic (SROC) curves with 95% confidence and prediction regions. Meta-regression analyses were used to deal with the existence of heterogeneity. Deeks' funnel plot was used for diagnostic meta-analysis, assessing publication bias of included articles. Significant asymmetry is denoted by $p < 0.10$ for the slope coefficient [20]. All statistical analyses were calculated by metandi, midan, and midas modules in Stata software. Statistical significance is indicated by $p < 0.05$. For disposition, Meta-disc 1.4 software was used to test threshold effects of this meta-analysis.

Results

Results of the literature search

An aggregate of 258 articles was first identified using the search strategy. A total of 59 articles were filtered automatically as duplicates by EndNote X8. Another 8 articles were translated and filtered manually. Approximately 167 of the remaining studies were removed because they were unrelated to the topic or were conference abstracts. Full texts of the remaining 24 studies were obtained. After evaluating the full transcripts, another 8 articles were excluded. Finally, 16 studies were determined to be eligible for the current meta-analysis (**Figure 1**).

Characteristics of eligible studies

The present meta-analysis included 16 studies (English = 8, Chinese = 8), involving a total of 1,833 patients [6, 15, 16, 21-33]. Major characteristics and basic information of included articles are listed in **Table 1**. Publication dates of the studies were from 2012 to 2018. Patients suspected of PCa from 10 studies were Easterners [15, 21, 24, 25, 27-31, 33], while the rest were Westerners [6, 16, 22, 23, 26, 32]. The Aixplorer Ultrasound System (Supersonic Imagine, France) was used in 14 articles [6, 15, 16, 22-26, 28-33], while 2 studies adopted the Siemens ACUSON S2000 US system (Siemens, Germany) with ARFI technology [21, 27]. Regarding the level of research, statistical analysis of 7 articles was per-patient [24, 25, 27-31], while 9 articles were per-core of prostate [6, 15, 16, 21-23, 26, 32, 33]. One study did not depict the age distribution [23]. Three articles did not investigate cut-off values of the SWE for diagnosis of PCa [6, 25, 28]. Three articles focused only on the peripheral zone of the prostate [16, 22, 29], while other scholars analyzed the whole gland. All studies were based pathological biopsies as the gold standard [6, 15, 21, 23-28, 30-33]. Quality of the included articles is presented in **Figure 2**, indicating that several studies had potential bias risk regarding the index test.

Accuracy of SWE in diagnosis of PCa

PSEN and PSPE of SWE [6, 15, 16, 21-33] measurements for diagnosis of PCa were 0.84 [95% CI (0.76, 0.89)] and 0.85 [95% CI (0.78, 0.90)], respectively (**Figure 3**). Higgins I^2 statistics showed substantial heterogeneity for sensitivity ($p < 0.01$, $I^2 = 93.35\%$) and specificity ($p < 0.01$, $I^2 = 97.11\%$). The PLR and NLR was 5.7 [95% CI (3.6, 8.9)] and 0.19 [95% CI (0.12, 0.30)], respectively. The DOR value was 27.69 [95% CI (11.71, 65.48)] (**Figure 4**). The area under the curve (AUC) value was 0.91 [95% CI (0.88, 0.93)] (**Figure 5**). Spearman's correlation coefficient ($r = -0.469$) indicated that there were no significant threshold effects. This suggests that the heterogeneity might have been caused by other factors. The above statistical analysis results were acceptable.

Publication bias

Deek's funnel plot was used to assess publication bias because of its lower false positive

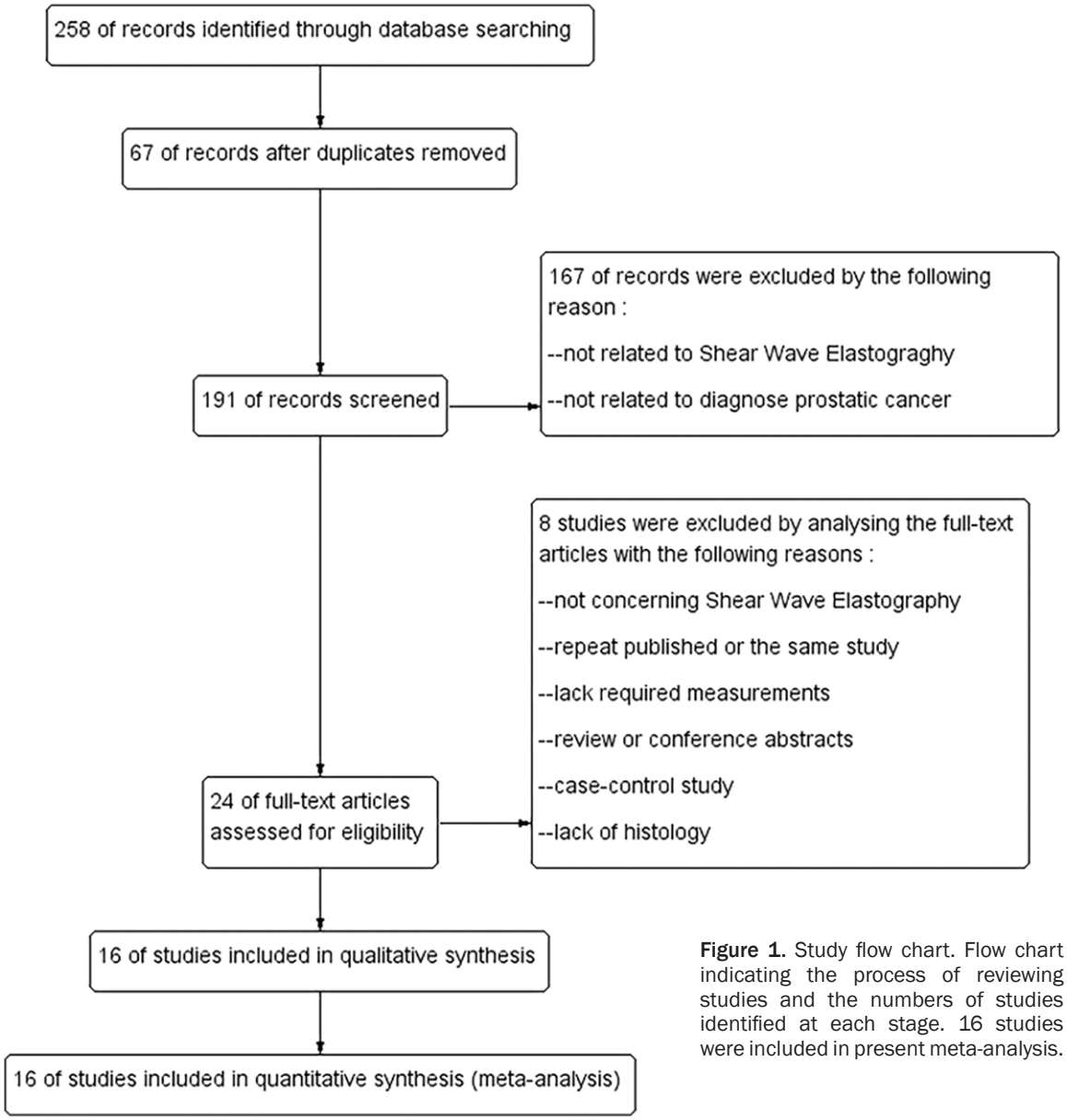

Figure 1. Study flow chart. Flow chart indicating the process of reviewing studies and the numbers of studies identified at each stage. 16 studies were included in present meta-analysis.

rates, compared to Egger's and Begg's funnel plots [34]. The *p*-value was 0.179 (P > 0.05), indicating that the publication bias was not because of statistical analysis (**Figure 6**).

Heterogeneity detection

In view of the strong heterogeneity of studies included in merger statistics, meta-regression was adopted. Some clinically relevant variables of investigation were analyzed, including the Ultrasound System (Supersonic or Siemens), level of research (per-person or per-core), localization of research (peripheral zone or whole gland), race of chosen patients (Westerners or Easterners), average age of patient samples (age < 60 or age ≥ 60), and the concrete method for measurement of SWE (number of ROIs in per-core). Results of regression analysis are exhibited in **Table 2**. Of these covariates, it was found that only the variable of the ROI of placement had significant statistical significance for sensitivity ($p < 0.01$). The study chose two placements as the ROI showed low sensitivity, 0.43 [95% (0.06, 0.80)] [15]. However, the others selected one placement as the ROI, with higher summary sensitivity i.e., 0.85 [95% (0.80, 0.91)] [6, 16, 21-33]. According to summary specificity, just the level of research sh-

Table 1. Characteristics of included studies

First Author	Date of publication	Country	US System	Number of Patients	Age (Years)	Cutoff value	Number of PCa Patient	Total Cores of Prostatic Biopsy	Total Cores of PCa	Level of Research	Race of patients	Localization of Research	Number of ROIs in Per-core
Zheng X	2012	China	Siemens	107	66.7 ± 12.9	2.5 m/s	-	209	57	Per Core	China	Whole gland	1
Sarfraz Ahmad	2013	UK	Supersonic	50	69.0 ± 6.2	-	33	626	424	Per Core	UK	Whole gland	1
Richard G. Barr	2014	US	Supersonic	53	53-79, 64.2*	37 KPa	11	318	26	Per Core	US	Peripheral zone	1
Jean-Michel Correas	2014	France	Supersonic	184	65.1 ± 7.6	35 KPa	68	1040	129	Per Core	France	Peripheral zone	1
Sungmin Woo	2014	Korea	Supersonic	87	66.0 ± 9.0	43.9 KPa	26	1058	79	Per Core	Korea	Whole gland	2
Katharina Boehm	2015	Germany	Supersonic	28	-	50 KPa	-	322	141	Per Core	Germany	Whole gland	1
Zhang M	2015	China	Supersonic	489	70.2 ± 12.7	28.5 KPa	221	-	-	Per Person	China	Whole gland	1
Yang Houmeng	2015	China	Supersonic	60	49-82, 65.3*	-	19	-	-	Per Person	China	Whole gland	1
Markus Porsch	2016	Germany	Supersonic	10	61.5 ± 6.3	50 KPa	-	120	58	Per Core	Germany	Whole gland	1
Gong Jijun	2016	China	Siemens	71	36 ± 11	2.94 m/s	42	-	-	Per Person	China	Whole gland	1
Yang Ye	2017	China	Supersonic	76	51.6-84.2, 68.5*	-	32	-	-	Per Person	China	Whole gland	1
Sun Ting	2017	China	Supersonic	64	71.0 ± 1.6	41 KPa	49	-	-	Per Person	China	Peripheral zone	1
Bai Qifeng	2017	China	Supersonic	92	74. 21 ± 4. 98	48.1 KPa	42	-	-	Per Person	China	Whole gland	1
Ding Xinhua	2017	China	Supersonic	127	69.62 ± 7.43	42.35 KPa	37	-	-	Per Person	China	Whole gland	1
Cheng Wei	2018	UK	Supersonic	212	67.6 ± 5.4	82.6 KPa	-	2544	405	Per Core	UK	Whole gland	1
Fang Yi	2018	China	Supersonic	123	67.38 ± 7.59	39.85 KPa	-	774	224	Per Core	China	Whole gland	1

Note. US: ultrasound; PCa: prostate cancer; -: the study was not mentioned; *: these studies just showed the range of age and mean of age.

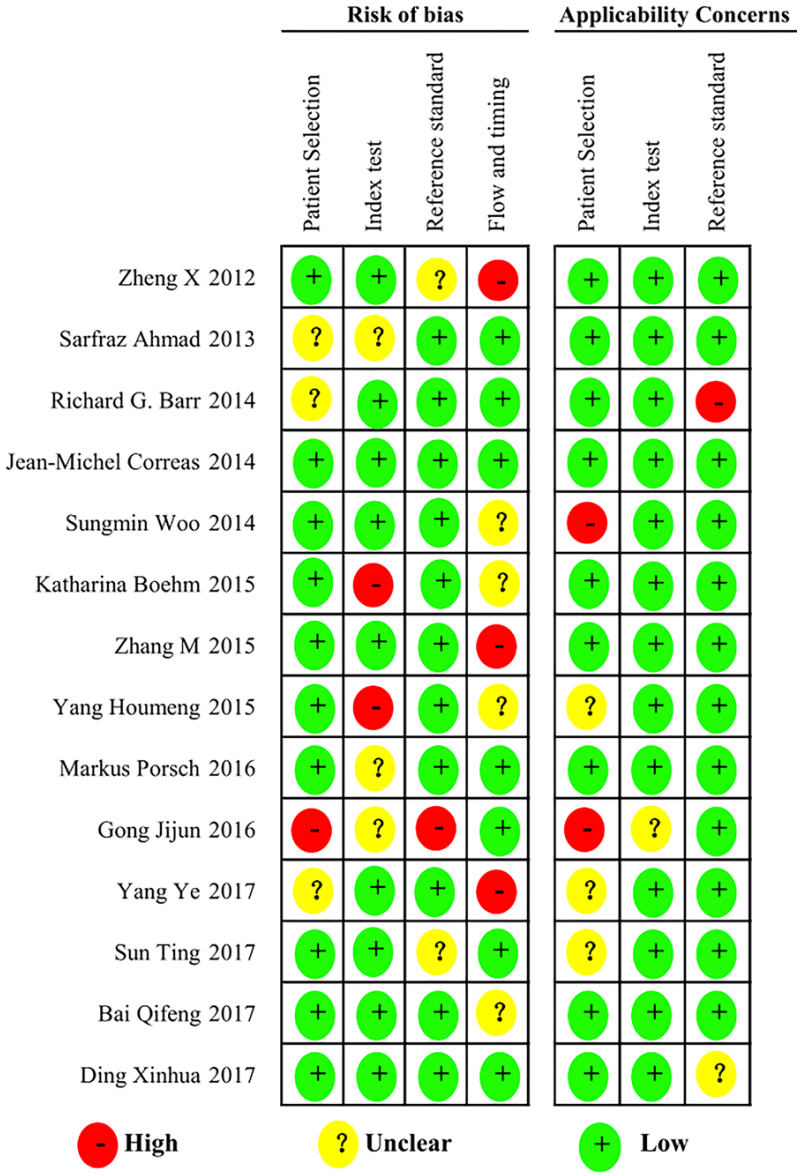

Figure 2. Bias risk of included studies (QUADAS 2 criteria). Judgments of review authors about each domain for each included study.

owed insignificant statistical significance (p = 0.04). The summary specificity of subgroup for statistics based on per person was 0.83 [95% (0.72, 0.94)] [24, 25, 27-31]. Another subgroup that analyzed data based on per-core in the prostate gland was 0.86 [95% (0.79, 0.94)] [6, 15, 16, 21-23, 26, 32, 33]. Differences of specificity were not obvious after comparing the two subgroups of data.

Sensitivity analysis

Adopting the method of omitting one study at a time, sensitivity analysis results are shown in **Table 3**. It should be noted that no studies influenced PSEN and PSPE. Excluding the included articles one by one, Higgins I^2 also did not change significantly.

Fagan plot analysis

Fagan plot analysis demonstrated that SWE could offer some useful information for detection of PCa, with an 85% probability of correct diagnosis following the "positive" measurement and lowering the probability of disease to 16% following the "negative" measurement when the pre-test probability was 50% (**Figure 7B**). When the pretest probability was 25% and 75%, the positive posttest probability was 65% and 94% and the negative posttest probability was 6% and 36%, respectively (**Figure 7C**).

Discussion

In the current study, the diagnostic value of SWE for detection of PCa was assessed and analyzed via meta-analysis. PSEN and PSPE levels for the 16 included studies were 0.84 [95% CI (0.76, 0.89)] and 0.85 [95% CI (0.78, 0.90)], respectively. This outcome was an important development, compared with the existing established ultrasound technology. In routine screening programs using transrectal ultrasound (US), some scholars have found that the actual rate of detection of PCa in hypoechoic areas was only 15%-57% [35]. The negative rate for diagnosis of PCa by the US assisted puncture was 66%-77% [36]. Real-time elastography, at its initial stage of development, has a sensitivity and specificity for diagnosis of PCa of 0.72 [95% CI (0.70, 0.74)] and 0.76 [95% CI (0.74, 0.78)], respectively, as shown in the meta-analysis by Zhang et al. [37]. Although it is not possible to draw reliable conclusions by

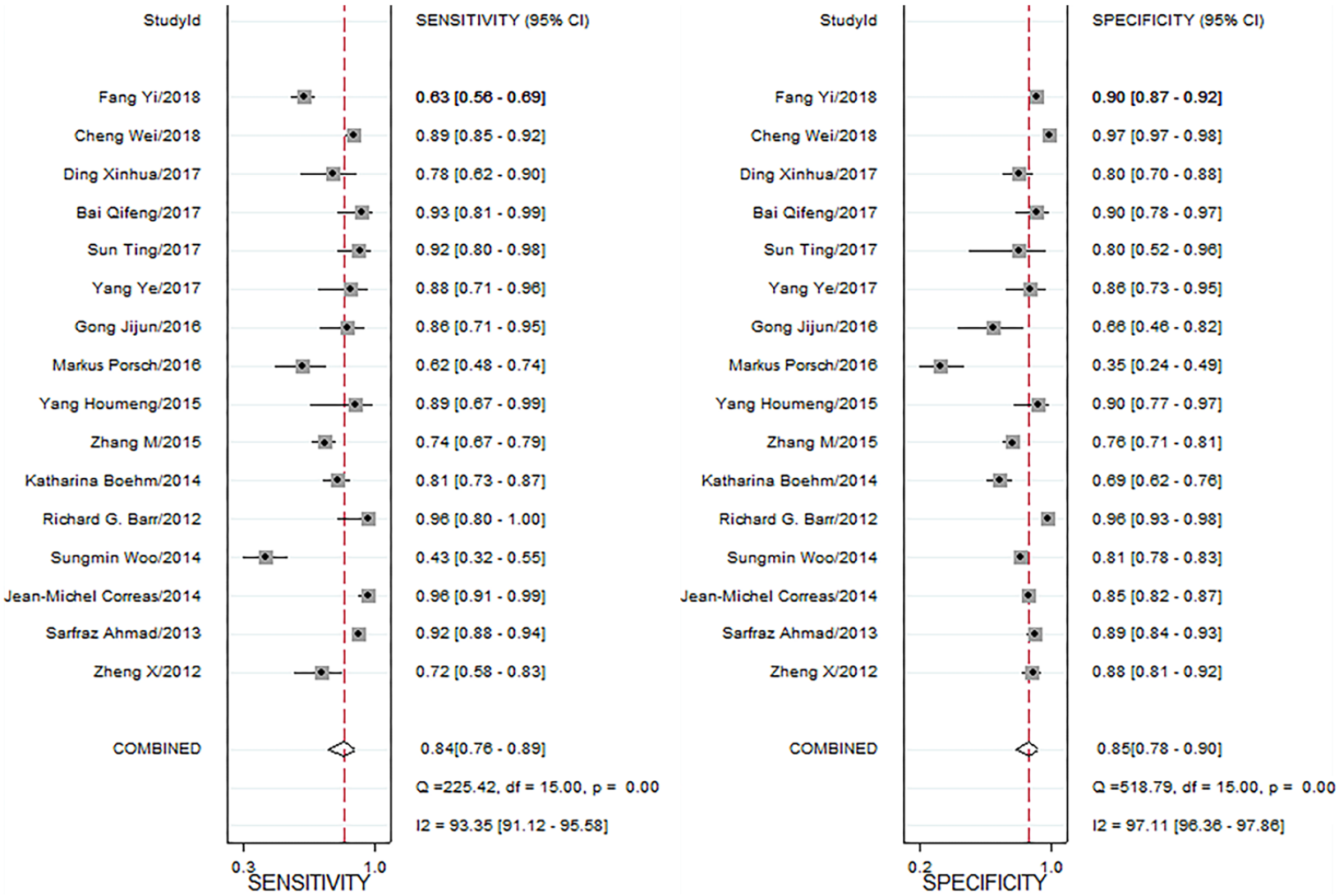

Figure 3. Forest plot of sensitivity and specificity for diagnostic PCa. Horizontal lines illustrate 95% confidence intervals of the individual studies.

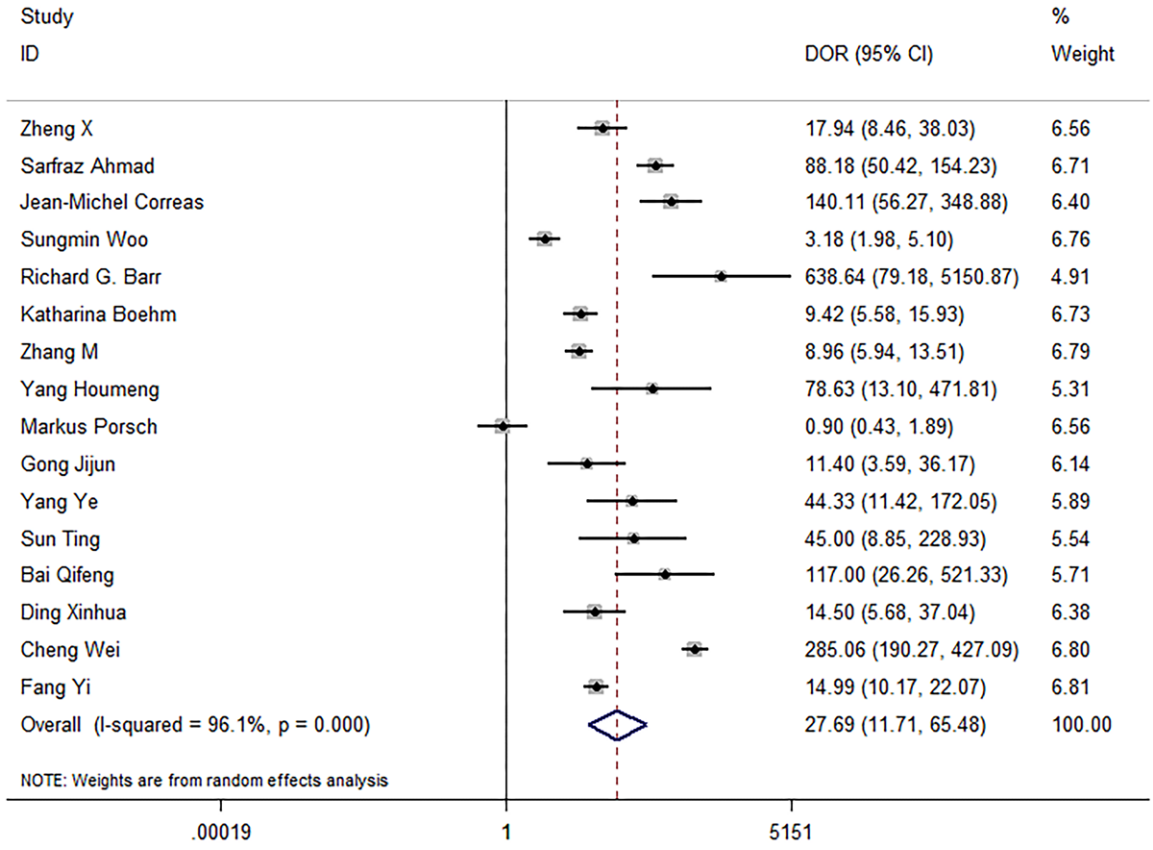

Figure 4. Diagnostic odds ratios (DOR) for diagnosis of PCa. Horizontal lines illustrate 95% confidence intervals of the individual studies.

indirectly comparing the results of these meta-analyses, it can be inferred that sensitivity levels increased significantly without meaningfully reducing specificity.

Compared with an earlier meta-analysis, the current study obtained some new results [38]. On one level, a larger number of relevant studies were incorporated, compared to the earlier report (16 vs. 8). This suggests that results were more stable. On another level, according to meta-regression analysis, not only the number of ROIs was shown to have a significant impact on sensitivity, but also the level of analysis produced an obvious significance on pooled specificity. Additionally, Fagan plot analysis was employed to explore clinical utilities of SWE.

Multiparametric magnetic resonance imaging (mp MRI) is another common non-invasive imaging method in which some scholars have measured sensitivity and specificity for diagnosis of PCa as 0.89 [95% CI (0.86, 0.92)] and 0.73 [95% CI (0.60, 0.83)], respectively using meta-analysis [39]. In addition, positron emission tomography/computed tomography (PET/CT) is a novel technology, helpful in research concerning diagnosis of PCa. The meta-analysis of Ouyang Q et al. estimated that sensitivity and specificity were 0.767 [95% CI (0.714, 0.813)] and 0.804 [95% CI (0.746, 0.851)], respectively [40]. Comparing the two techniques mentioned above, the diagnostic value of SWE is roughly comparable. Furthermore, SWE neither exhibits a disadvantage of high expense nor an exposure to harmful radiations like PET/CT.

The 16 studies included in this meta-analysis exhibited some differences. For example, the cut-off values of these studies were unstable. Articles using the US equipment produced by Siemens adopted shear wave velocity (SWV) as the index. Results were 2.5 m/s [21] and 2.94 m/s [27]. Eleven articles used the mean elasticity value (E_{mean}) as the cut-off value index using the Aixplorer Ultrasound System (Supersonic Imagine, France), with results ranging be-

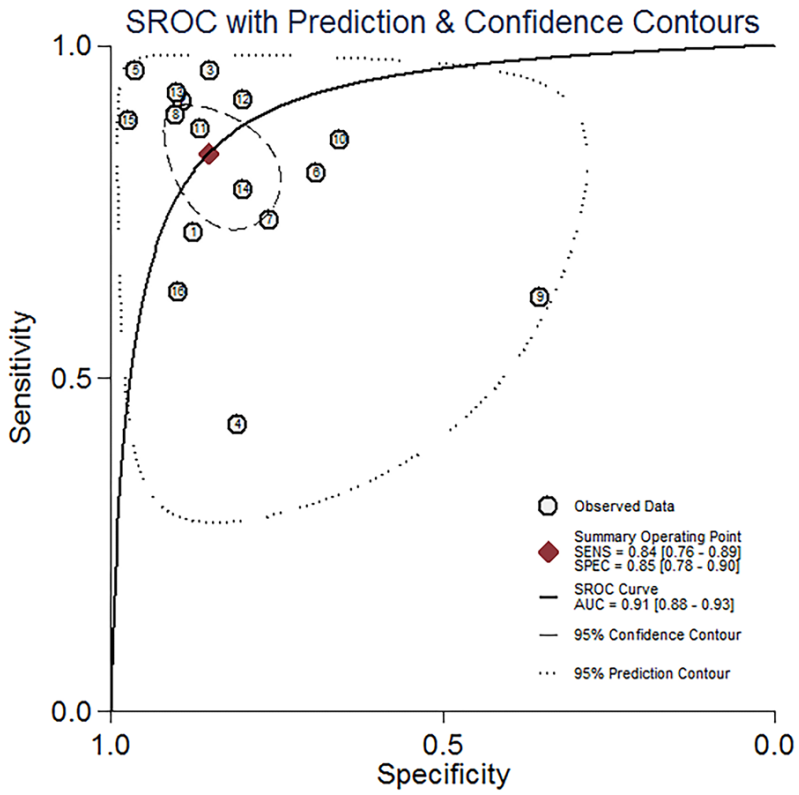

Figure 5. Receiver operating characteristic curve (ROC). SENS: sensitivity; SPEC: specificity; SROC: summary receiver operating characteristic curve; AUC: area under the SROC curve.

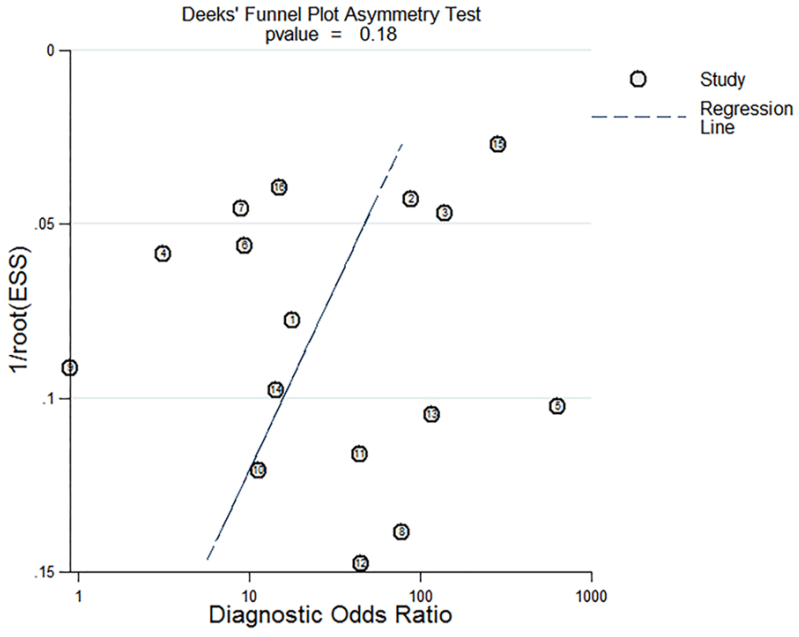

Figure 6. Publication bias of included studies. No significant publication bias was found in the present meta-analysis. Each circle represents an eligible study. ESS: effective sample size.

tween 28.5 KPa to 82.6 KPa [15, 16, 22-24, 26, 29-33]. Thus, it is recommended that further investigations concerning SWE for detection of PCa should be carried out.

In the current meta-analysis, existing covariates were analyzed. Thus, the preliminary combination of sensitivity, specificity, and other indicators using bivariate mixed effects models of the random effects model was the preferred choice [41]. Afterward, meta-regression was selected, attempting to deal with the high heterogeneity due to several potential causes. It was considered that the concrete method for measurement of SWE viz. and the number of ROIs in per-core had a significant impact on sensitivity. The measurement method of SWE used by Sungmin Woo et al. was different from the other 15 articles included. The sensitivity was lower than theirs [15]. Due to a conception that the specimen of the puncture biopsy is a strip, the value of SWE measured was the mean of the two ROIs. As the stiffness of normal gland tissues is less than a malignant mass [38, 42], it was inevitable that the average measurement value of the mixture from tumor tissues and normal tissues would be lower, resulting in reduced sensitivity.

Additionally, the level of analysis was a significant element in the meta-analysis. It may have produced an obvious significance in pooled specificity. The calculation from the level of per-person was slightly less th-an the level of per-core (0.83 vs. 0.86, p = 0.04). Using per-core criteria to determine the diagnostic value showed a

Table 2. Results of meta-regression analysis about the SWE in diagnosis application of PCa

Covariate and Subgroup		Number of included studies	Sensitivity (95% CI)	*P*	Specificity (95% CI)	*P*
US System	Supersonic	14	0.84 (0.77, 0.91)	0.87	0.86 (0.80, 0.92)	0.99
	Siemens	2	0.80 (0.58, 1.00)		0.80 (0.57, 1.00)	
Level of Research	Per Person	7	0.87 (0.78, 0.95)	0.27	0.83 (0.72, 0.94)	0.04
	Per Core	9	0.81 (0.72, 0.91)		0.86 (0.79, 0.94)	
Localization of Research	Peripheral zone	4	0.90 (0.81, 0.99)	0.72	0.90 (0.82, 0.99)	0.54
	Whole gland	12	0.81 (0.73, 0.89)		0.83 (0.75, 0.91)	
Race of patients	Westerners	6	0.89 (0.81, 0.96)	0.42	0.86 (0.77, 0.95)	0.12
	Easterners	10	0.79 (0.70, 0.89)		0.85 (0.77, 0.93)	
Average Age of Patient Samples	< 60	1	0.86 (0.62, 1.00)	0.75	0.66 (0.22, 1.00)	0.23
	≥ 60	14	0.84 (0.77, 0.91)		0.87 (0.81, 0.93)	
No. of ROIs in Per-core	1	15	0.85 (0.80, 0.91)	< 0.01	0.81 (0.52, 1.00)	0.72
	2	1	0.43 (0.06, 0.80)		0.85 (0.79, 0.92)	

Note. CI: confidence interval; US: ultrasound.

strong correlation between SWE images and puncture biopsy tissues. Extensive research work is necessary to improve the diagnosis value of SWE-guided targeted prostate puncture related to areas involved in prostatic cancer.

Considering the US System, localization of research, and the race of patients, *p*-values showed no significant differences in these covariates in meta-regression. However, these factors may still have led to heterogeneity in the present article. Pertaining to the US System subgroup using Aixplorer Ultrasound System from Supersonic, sensitivity and specificity levels were higher than the subgroup using the Siemens ACUSON S2000 US system (0.84 vs. 0.80, p = 0.87; 0.86 vs. 0.80, p = 0.99). However, the summary estimate for the latter US System was pointless because it was mentioned only in two articles [21, 27]. Park et al. considered that the different techniques and vendors would use different shear wave frequencies. Thus, the US system is a potential confounder [43]. Therefore, further prospective studies with larger and wider samples are necessary to investigate this issue.

Moreover, due to differences between Easterners and Westerners, dietary structure, and gene construction, incidence of prostate cancer in Westerners is slightly higher than that in Easterners [44]. Variety in elastic measurements are based on the structure of the organization [45]. Thus, it was speculated that the race of included patients could also be a factor. In this analysis, the summary sensitivity showed no obvious differences (0.89 vs. 0.79, p = 0.42). Statistical differences in elasticity of prostates between different races has never been reported in large sample studies. Thus, it requires further clinical analysis.

The 16 included studies were also divided into two subgroups, according to research done on peripheral zone only or the whole prostatic gland. Differences showed no statistical significance. Studies pointed out that the peripheral zone had a harder stiffness than the transition zone [46]. However, limited data impeded further analysis and discussion. Furthermore, a considerable portion of the studies did not provide the specific anatomical location of the prostate puncture point and the size of the prostate. Fortunately, the position of tumors mainly originated from the peripheral zone. Thus, detection of PCa from the prostatic periphery may seem to be a decent point for improving accuracy [47].

Analysis was done using the age of included patients. It is worth mentioning that all but one study performed on younger age groups (No. of patients: 71, mean age of cohort: 36 ± 11). The specificity of this subgroup was low (0.66 vs. 0.87, p = 0.23) [27]. A higher incidence of benign prostatic hyperplasia in the elderly has been generally accepted by comparing the characteristics of prostates in old and young patients. However, the report considered that

Table 3. Sensitivity analysis using the method of eliminating articles one by one

Delete article	Sensitivity (95% CI)	I^2 (95% CI), %	*P*	Specificity (95% CI)	I^2 (95% CI), %	*P*	AUC (95% CI)
Zheng X	0.85 (0.76, 0.90)	93.79 (91.68, 95.50)	< 0.01	0.85 (0.77, 0.91)	97.31 (96.60, 98.01)	< 0.01	0.91 (0.89, 0.94)
Sarfraz Ahmad	0.83 (0.75, 0.89)	92.28 (89.49, 95.08)	< 0.01	0.85 (0.77, 0.90)	97.26 (96.54, 97.98)	< 0.01	0.91 (0.88, 0.93)
Jean-Michel Correas	0.82 (0.74, 0.88)	92.90 (90.38, 95.41)	< 0.01	0.85 (0.71, 0.91)	97.37 (96.69, 98.06)	< 0.01	0.90 (0.88, 0.93)
Sungmin Woo	0.85 (0.79, 0.90)	91.16 (87.82, 94.49)	< 0.01	0.85 (0.78, 0.91)	97.06 (96.27, 97.85)	< 0.01	0.92 (0.89, 0.94)
Richard G. Barr	0.83 (0.75, 0.88)	93.43 (91.16, 95.70)	< 0.01	0.84 (0.76, 0.89)	97.06 (96.27, 97.85)	< 0.01	0.90 (0.87, 0.92)
Katharina Boehm	0.84 (0.76, 0.90)	93.72 (91.58, 95.86)	< 0.01	0.86 (0.79, 0.91)	97.12 (96.35, 97.89)	< 0.01	0.92 (0.89, 0.94)
Zhang M	0.84 (0.76, 0.90)	93.59 (91.39, 95.79)	< 0.01	0.86 (0.78, 0.91)	97.22 (96.49, 97.96)	< 0.01	0.92 (0.89, 0.94)
Yang Houmeng	0.83 (0.75, 0.89)	93.68 (91.52, 95.84)	< 0.01	0.85 (0.77, 0.90)	97.27 (96.55, 97.99)	< 0.01	0.91 (0.88, 0.93)
Markus Porsch	0.85 (0.77, 0.90)	93.63 (91.45, 95.81)	< 0.01	0.87 (0.82, 0.91)	96.46 (95.46, 97.47)	< 0.01	0.93 (0.90, 0.95)
Gong Jijun	0.84 (0.75, 0.90)	93.80 (91.69, 95.90)	< 0.01	0.86 (0.79, 0.91)	97.29 (96.58, 98.00)	< 0.01	0.92 (0.89, 0.94)
Yang Ye	0.84 (0.75, 0.89)	93.71 (91.57, 95.86)	< 0.01	0.85 (0.77, 0.91)	97.29 (96.58, 98.00)	< 0.01	0.91 (0.88, 0.93)
Sun Ting	0.83 (0.75, 0.89)	93.55 (91.33, 95.76)	< 0.01	0.85 (0.78, 0.91)	97.26 (96.54, 97.98)	< 0.01	0.91 (0.88, 0.93)
Bai Qifeng	0.83 (0.75, 0.89)	93.53 (91.30, 95.75)	< 0.01	0.85 (0.77, 0.90)	97.25 (96.53, 97.98)	< 0.01	0.91 (0.88, 0.93)
Ding Xinhua	0.84 (0.76, 0.90)	93.86 (91.79, 95.94)	< 0.01	0.85 (0.78, 0.91)	97.33 (96.63, 98.03)	< 0.01	0.92 (0.89, 0.94)
Cheng Wei	0.84 (0.75, 0.90)	93.33 (91.01, 95.64)	< 0.01	0.83 (0.76, 0.89)	94.47 (92.65, 96.28)	< 0.01	0.93 (0.87, 0.93)
Fang Yi	0.85 (0.77, 0.90)	92.52 (89.84, 95.21)	< 0.01	0.85 (0.77, 0.90)	97.22 (96.43, 97.93)	< 0.01	0.92 (0.89, 0.94)

Note. CI: confidence interval.

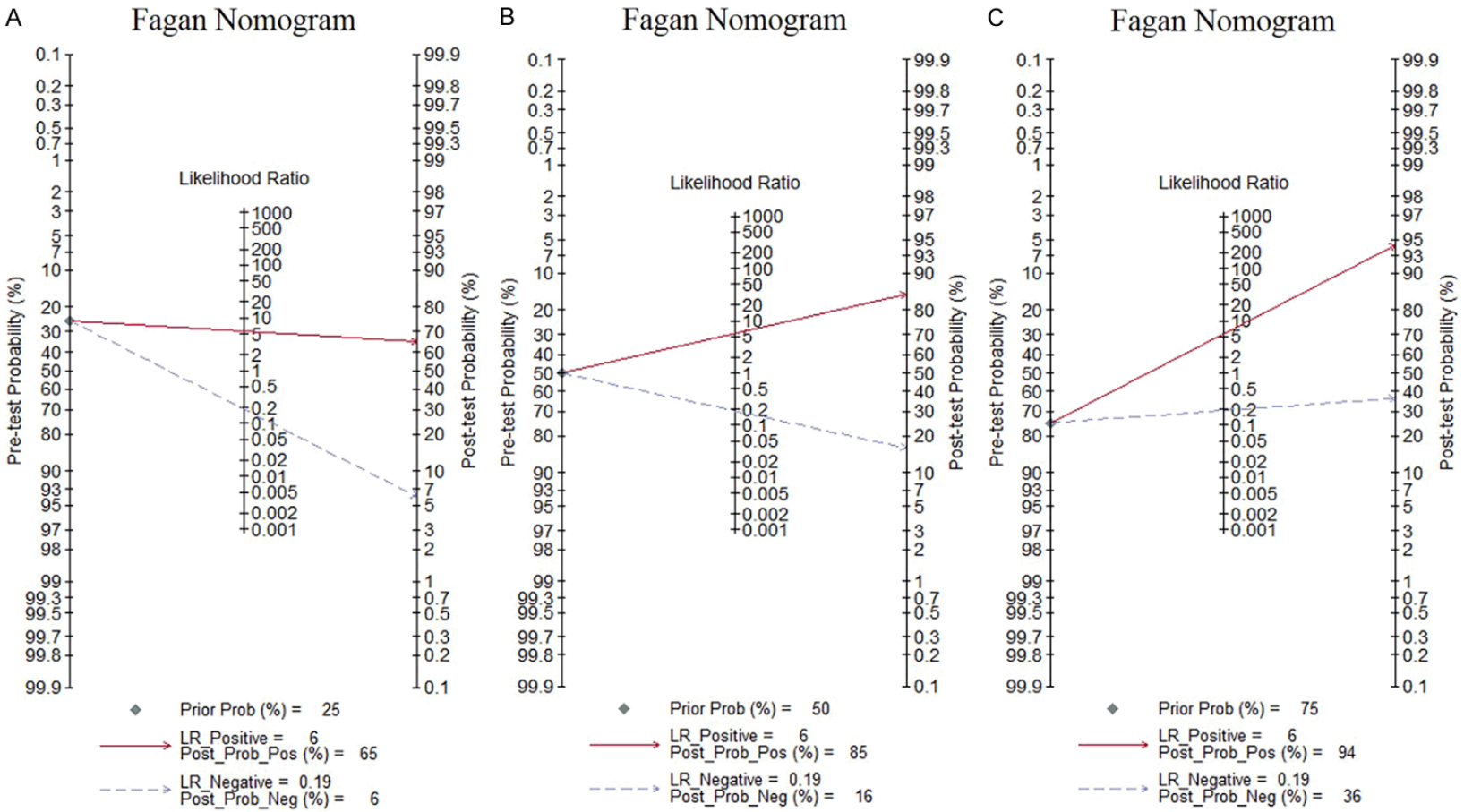

Figure 7. Fagan plot analysis for SWE in detection of PCa. A. Pre-test probability at 25%; B. Pre-test probability at 50%; C. Pre-test probability at 75%. Fagan plot is composed of the left vertical axis representing the pre-test probability, the middle vertical axis representing the likelihood ratio, and the right vertical axis representing the post-test probability.

prostatic hyperplasia showed no obvious increases in the measurement of stiffness [48]. To explore causes, it was suspected that the quality of the studies was a vital reason. The author depicted a rough experimental design and never explained sonographers and pathologists at a technical level. This led to instability of results.

To explore the clinical practical application of SWE, Fagan plot analysis was adopted. Results indicated that SWE could have the potential to identify PCa. When the pre-test probability was 50%, the probability of correct diagnosis for PCa was 85% following a "positive" measurement. PCa was diagnosed in only 16% of patients following a "negative" measurement.

The current meta-analysis had some limitations. First, certain included writings may have increased the risk of bias due to subpar clinical features. Second, included studies were too limited because of the exclusion of unpublished and ongoing investigations. Third, in the study by Ahmad S, the sensitivity and specificity of the men suspected of PCa was PSA > 20 μm/L, much better than those patients with PSA < 20 μm/L [6]. Regrettably, these articles cannot offer accurate quantitative value. Therefore, this study had no way of perfecting meta-regression using PSA levels.

In conclusion, SWE exhibited favorable diagnostic value for detection of PCa with 0.84 [95% CI (0.76, 0.89)] in PSEN and 0.85 [95% CI (0.78, 0.90)] in PSPE. However, no clear inference can be made concerning cut-off values due to inescapable heterogeneity.

Disclosure of conflict of interest

None.

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