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Magnetic resonance imaging-guided targeted biopsy in risk classification among patients on active surveillance

A diagnostic meta-analysis

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Abstract

Background: The aim of this study was to assess the sensitivity and accuracy of magnetic resonance imaging-guided targeted biopsy (MRI-TB) in patients undergoing active surveillance (AS) procedure.

Methods: We searched databases to identify relevant studies which compared MRI-TB with systemic biopsy for diagnosing prostate cancer in patients on AS. Outcomes included sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), area under the curve (AUC) and publication bias of AS group, confirmatory biopsy group and follow-up biopsy group.

Results: Fourteen articles involving 1693 patients were included. In AS group, the sensitivity was 0.62 (95% confidence interval [CI], 0.57−0.68), specificity was 0.89 (95% CI, 0.87−0.90), NLR was 0.43 (0.31−0.60), PLR was 4.90 (3.50−6.86), DOR was 12.75 (7.22−22.51), and AUC was 0.8645. In confirmatory biopsy group, the sensitivity was 0.67 (0.59−0.74), specificity was 0.89 (0.86−0.91), NLR was 0.42 (0.27−0.65), PLR was 4.94 (3.88−6.30), DOR was 14.54 (9.60−22.02), and AUC was 0.8812. In follow-up biopsy group, the sensitivity was 0.35 (0.22−0.51), specificity was 0.88 (0.82−0.92), NLR was 0.76 (0.52−1.11), PLR was 3.06 (1.71−5.50), DOR was 4.41 (2.15−9.03), and AUC was 0.8367.

Conclusion: MRI-TB has a moderate-to-high diagnostic accuracy for diagnosing and reclassifying patients on AS with high specificity and AUC value under the SROC curve.

Abbreviations: AS = active surveillance, AUC = area under the curve, CI = confidence interval, DOR = diagnostic odds ratio, DRE = digital rectal examination, mpMRI = multiparametric magnetic resonance imaging, MRI-TB = magnetic resonance imaging-guided targeted biopsy, NLR = negative likelihood ratio, Pca = prostate cancer, PLR = positive likelihood ratio, PSA = prostate-specific antigen, RP = radical prostatectomy, SB = systematic biopsy, TURS = trans-rectal ultrasound.

Keywords: active surveillance, diagnostic meta-analysis, magnetic resonance imaging-guided targeted biopsy, systematic biopsy, trans-rectal ultrasound

1. Introduction

Prostate cancer (Pca) is the most frequent malignancy among male patients worldwide, responsible for approximately 250,000 deaths annually.[1] According to EAU Guidelines on Prostate Cancer,[2] approximately 45% of patients diagnosed with Pca using prostate-specific antigen (PSA) as a marker do not require immediate radical therapy. Active surveillance (AS) has been proven to be a safe and convenient method for long-term follow-up among low-risk patients with Pca.[2] Moreover, it has become a viable option for patients with localized low-grade and low-volume Pca, who do not require an immediate radical therapy (surgery and radiation therapy).[3] Whether a patient with Pca is an optimal candidate for undergoing AS depends on several factors, including the PSA level, magnetic resonance imaging (MRI), digital rectal examination (DRE), and, most importantly, pathological results and its corresponding Gleason score.

Pca biopsies have been performed since 1937, and trans-rectal ultrasound (TRUS) 12-core systematic biopsy (SB) remains the gold standard for Pca diagnosis.[4] A total of 10 to 12 cores are

recommended because a higher number of cores cannot significantly improve the detection rate, whereas fewer cores have a lower accuracy.[5–7] In addition, up to 40% of tumors are invisible under TRUS, making the biopsy unspecific and inaccurate.[8,9]

Over the past decade, multiparametric magnetic resonance imaging (mpMRI) has been established as an important diagnostic tool, enabling easy visualization and accurate positioning of tumors.[10] Studies have shown that mpMRI might detect, localize, and characterize Pca with volume of >0.2 ml.[11] mpMRI is also considered to be sensitive enough to detect tumors with a Gleason score of ≥7, especially for anterior tumors that can be easily overlooked with SB.[12,13] Magnetic resonance imaging-guided targeted biopsy (MRI-TB) enables the addition of the information obtained from mpMRI to TRUS images, thereby effectively combining the sensitivity of mpMRI with the availability and proficiency of TRUS. Compared with systemic biopsy, targeted biopsy is more likely to evaluate high-grade Pca with a higher diagnostic accuracy for Gleason 4 and 5 Pca, which is considered to require radical therapy rather than AS.[9,14,15] However, other studies have reported that 4% to 14% of high-grade Pca is overlooked by MRI-TB compared with those by TRUS systemic biopsy.[16]

Biopsies during AS are important to ensure that patients are eligible to undergo AS without progressing to higher grade cancer; however, the impact of MRI-TB on AS remains unclear. Therefore, we performed this meta-analysis to assess the sensitivity and accuracy of MRI-TB in patients undergoing AS procedure.

2. Materials and methods

2.1. Search strategy

Two authors (Wenbin Xue and Yu Huang) systematically searched EMBASE, Medline, and the Cochrane Central Register of Controlled Trials. All studies published till May 2017 were searched. The search terms were listed as follows: (complete search strategy: ((((fusion biopsy [Title/Abstract]) OR Targeted Biopsy[Title/Abstract]) OR Guided Biopsy)) AND active surveillance[Title/Abstract]). If eligible, the references included in the selected articles were also searched. Conference proceedings were also searched and included if they met our inclusion criteria.

2.2. Inclusion and exclusion criteria

For inclusion, studies were required to meet the following criteria: the studies should involve patients with Pca who were undergoing AS; the studies should compare MRI-TB with systemic biopsy for diagnosing Pca in patients on AS; and data from the study should be presented in 2 × 2 tables. Studies that do not involve patients on AS, noncomparable studies, and review studies were excluded.

2.3. Data extraction and quality assessment

Two authors (Wenbin Xue and Yu Huang) independently reviewed the entire text of the included studies, and extracted the data. A third author (Qiang Wei) reconciled any disagreements between the 2 authors. Data included the type of study, type of MRI score, inclusion criteria for AS, method of the targeted biopsy, period of AS, follow-up strategy, and criteria of significant Pca. The data collected from the included studies were used to construct 2 × 2 tables. Only the patients who underwent both a systemic biopsy and MRI-TB were analyzed.

We categorized our results into 3 groups as the patients in different studies had different AS periods: confirmatory biopsy group 6 to 12 months after the initial biopsy; the follow-up biopsy group after the confirmatory biopsy; and AS group containing data from both groups mentioned before and data from studies lacking distinguishing confirmatory and follow-up biopsies.

The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) scoring system was used to assess the quality in terms of the risk of bias and applicability among the included studies. The 2 authors separately performed the assessment, and any discrepancies were solved by discussion with a third author (Ping Tan).

2.4. Data synthesis and analysis

Data from the included studies were entered into 2 × 2 tables to assess sensitivity and specificity. For each group, sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), area under the curve (AUC), and 95% confidence interval (CI) were calculated, reflecting the accuracy of MRI-TB in AS. For each result, $I^2 \geq$ 50% was considered to be a significant heterogeneity. Random effects models were used for results with significant heterogeneity, otherwise fixed effects models were used. Review manager (version 5.3), STATA (version 12.0), and Meta-disc were used to perform this meta-analysis. An MRI score was assessed before MRI-TB. When the MRI score suggested that a site was not likely to be Pca, MRI-TB would not be performed at the site. In this case, the patients could be viewed as Pca negative.

Meta-regression was performed to identify the source of heterogeneity. Deek's funnel plots were chosen to test the publication bias. A threshold of $P < .05$ was considered significant.

All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

3. Results

3.1. Evidence synthesis
3.1.1. Literature search and study selection. In total, 311 nonduplicated publications were searched, 60 of which were selected based on their abstracts, and the remaining 251 articles were excluded. In addition, 46 articles were excluded after screening the entire text because they only mentioned MRI without biopsy (n=8), did not mention AS (n=11), were irrelevant to our meta-analysis (n=13), lacked comparison (n=1), or lacked sufficient data (n=13). Finally, 14 articles were included, covering 1693 patients (Fig. 1).[3,16–28]

3.2. Study characteristics

General information of the included patients is presented in Table 1. The median age ranged from 60.2 to 70 years old, and the median PSA ranged from 4.2 to 7.0 ng/mL. The ratio of significant Pca in the AS group ranged from 16.22% to 51.43%; however, in the confirmatory biopsy and follow-up biopsy groups, the ratio of significant Pca ranged from 22.22% to 58.54% and 24.27% to 46.67%, respectively.

General information of the included studies is presented in Table 2. Table 3 presents information pertaining to the AS protocol. Seven of the included studies were retrospective studies and 6 were prospective studies. Most studies used a 5-point
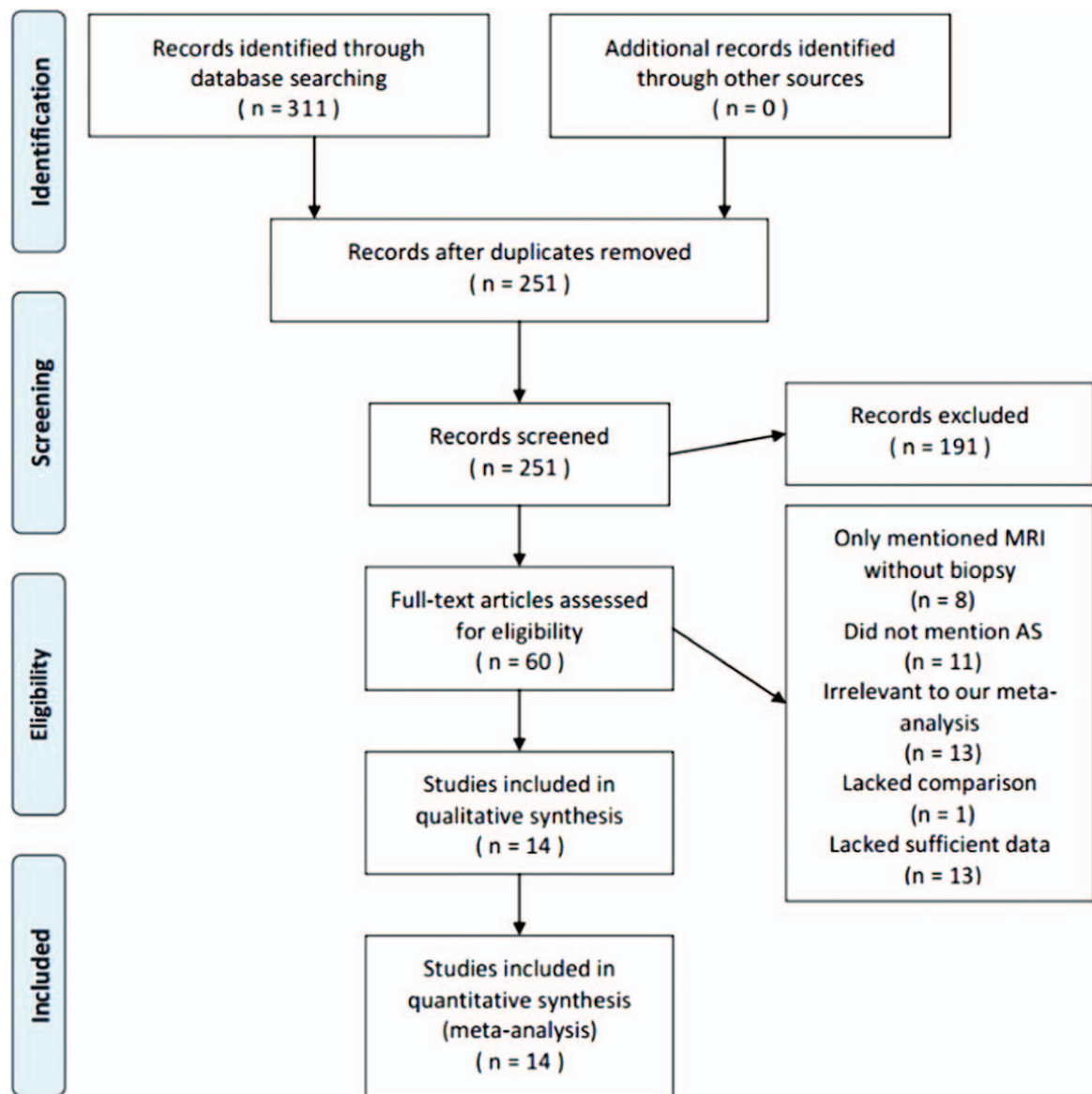
Figure 1. PRISMA flow diagram of the search process for eligible studies.

scoring system for Pca detection with mpMRI, including PIRADS (6 articles), Likert scale (2 articles), UCLA scoring system (1 article), and a standardized 5-point scale (2 articles); 2 studies used a 3-point grading system. The inclusion criteria for AS also varied among the analyzed studies, including Johns Hopkins AS criteria, Epstein histological criteria, PRIAS criteria, and the University of Toronto AS protocol. Two studies used visual estimation targeted biopsy in some patients, and 1 study used this method in all their patients. One study used Magnetic resonance guided biopsy, whereas the rest of the studies used MRI/US fusion-guided biopsy to identify the suspicious area. Two included studies had no clear inclusion criteria, whereas other studies all had clear inclusion criteria.

3.3. Quality assessment

Most (12/14) of the included studies contained specific inclusion criteria, and SB was performed together with MRI-TB without

knowledge of either results. All included studies also had specific standards for the diagnosis of significant Pca. Moreover, all included patients were initially diagnosed via prostate biopsy; therefore, the case–control design was avoided. Consequently, all included studies had a low or unclear risk of bias and applicability concerns (Fig. 2). Thus, no article was excluded after quality assessment. Because 2 studies had no specific inclusion criteria, the risk of bias and applicability concerns of the patient selection were unclear.

3.4. Threshold effect

Threshold effect is an essential factor to be assessed because different sensitivities and specificities for different research conditions led to a different threshold effect and DOR. In AS group, the Spearman correlation coefficient was 0.081, and P value was .782. When patients were divided into 2 groups (confirmatory biopsy and follow-up biopsy), the Spearman

Table 1

General information of included patients.

First author	Patients who met AS criteria				Patients with confirmatory sessions				Patients with follow-up sessions				Age, median (range)	PSA, median (range)
	Total	Pca promoted	Pca without promotion	Ratio of promoted Pca, %	Total	Pca promoted	Pca without promotion	Ratio of promoted Pca, %	Total	Pca promoted	Pca without promotion	Ratio of promoted Pca, %		
Annerleim et al 2015[16]	210	51	159	24.29	152	34	118	22.37	58	17	41	29.31	61.4 (40–79)	5.2 (0.2–23.3)
Nabeel et al 2014[17]	35	10	25	28.57	NR	NR	NR	—	35	10	25	28.57	61.6 (45–77)	5.16 (0.2–20)
Arnout et al 2017[18]	56	19	37	33.93	39	12	27	30.77	26	7	19	26.92	65 (60–70)	7.0 (5.2–9.6)
Caroline et al 2014[19]	30	14	16	46.67	NR	NR	NR	—	30	14	16	46.67	65.7 (62.1–70.1)	6.5 (5.99–6.93)
François et al 2014[20]	41	24	17	58.54	41	24	17	58.54	NR	NR	NR	—	63.5 (59.5–69.5)	5.3 (4.4–6.9)
Hamidreza et al 2015[21]	111	28	93	16.22	NR	NR	NR	—	NR	NR	NR	—	62.9 (58.2–67.6)	6.1 (4.4–8.1)
Jim C. Hu et al 2014[22]	113	26	87	23.01	113	26	87	23.01	NR	NR	NR	—	63 (58–68)	4.2 (2.6–6.3)
J.P. Radtke et al 2016[23]	149	47	102	31.54	149	47	102	31.54	NR	NR	NR	—	66 (61–75)	6.1 (4.7–8.0)
M. Minhaj et al 2015[3]	94	25	69	26.60	94	25	69	26.60	NR	NR	NR	—	60.2 (NR)	4.8 (NR)
Michael R. Da Rosa et al 2015[24]	73	16	57	21.92	NR	NR	NR	—	NR	NR	NR	—	64.8 (41–79)	5.0 (1.1–17.6)
Pedro et al 2016[25]	135	58	77	42.96	NR	NR	NR	—	NR	NR	NR	—	NR	NR
Rodrigo R. et al 2017[26]	105	54	51	51.43	105	54	51	51.42	NR	NR	NR	—	63 (57–68)	5.2 (3.8–7.4)
Ting Martin et al 2017[27]	157	37	120	23.57	54	12	42	22.22	103	25	78	24.27	70 (66–74)	5.4 (3.2–7.4)
Xiaosong et al 2015[28]	139	53	86	38.13	NR	NR	NR	—	NR	NR	NR	—	66 (58–74)	5.4 (1.1–9.7)

AS = active surveillance, Pca = prostate cancer, PSA = prostate-specific antigen.

Table 2

General information of included studies.

Study	Type of study	MRI score	TB in MRI	TB way	TB opportunity		SB scores	START	Endorectal MRI coil
					Confirmatory	Follow-up			
Annerleim et al 2015[16]	Retrospective	Suspicion score (low, moderate, or high)	Each lesion identified	MRI/US fusion-guided	Yes	Yes	12	Unclear	Yes
Nabeel et al 2014[17]	Retrospective	Not mentioned	Increase in mpMRI suspicion level, lesion diameter, number of visualized lesions	MRI/US fusion-guided		Yes	12	Unclear	Unclear
Arnout et al 2017[18]	Prospective	PIRADS	All suspicious lesions	MRI/US fusion-guided	Yes	Yes	8–12	Yes	Unclear
Caroline et al 2014[19]	Prospective	PIRADS	Every CSR	Magnetic resonance guided biopsy		Yes	10	Unclear	YES
François et al 2014[20]	Retrospective	Likert-like standardized score	Score ≥ 3	Visual registration or MRI-US image fusion <10 mm lesions	Yes		12	Unclear	No
Hamidreza et al 2015[21]	Retrospective	PIRADS	PIRADS score <3 were considered negative	Cognitively or mpMRI-ultrasonography fusion targeting			8–12	Unclear	No
Jim C. Hu et al 2014[22]	Prospectively	UCLA scoring system	Image grade 2 or greater	MRI/US fusion-guided	Yes		12	Yes	No
J.P. Radtke et al 2016[23]	Prospective	PIRADS	All suspicious lesions	MRI/US fusion-guided	Yes		Unclear	Unclear	No
M. Minhaj et al 2015[3]	Retrospective	NIH scale (3 grades)	Lesions were identified	MRI/US fusion-guided	Yes		12	Unclear	YES
Michael R. Da Rosa et al 2015[24]	Prospective	Likert scale	All identifiable MRI targets (≥ 3)	MRI/US fusion-guided			12	Yes	No
Pedro et al 2016[25]	Unclear	Likert scale	Score ≥ 3	MRI-target biopsy (not clear)			14	Yes	Unclear
Rodrigo R. et al 2017[26]	Prospective	PIRADS	Grade ≥ 2 scores	Visual estimation TRUS-Bx	Yes		12	Yes	No
Ting Martin et al 2017[27]	Retrospective	PIRADS	Score ≥ 3	MRI/US fusion-guided	Yes	Yes	12	Yes	Unclear
Xiaosong et al 2015[28]	Retrospective	MRI suspicion scores (mss) 5 score system	Score ≥ 2	MRI/US fusion-guided			Unclear	Unclear	Unclear

MRI = magnetic resonance imaging, TB = targeted biopsy, SB = systematic biopsy, START = Standards of Reporting for MRI Targeted Biopsy Studies, mpMRI = multiparametric magnetic resonance imaging, CSR = cancer-suspicious regions, PIRADS = Prostate Imaging Reporting And Data System.

Table 3

Information regarding the active surveillance protocol.

Study	AS including criteria	Follow-up strategy	Significant Pca
Annerleim et al 2015[16]s	John Hopkins University criteria (Clinical Stage t1c, Gleason grade ≤ 6, PSA density ≤ 0.15, tumor involving ≤ 2 cores, ≤ 50% any core)	Underwent subsequent SB and TB until Gleason score progression.	Gleason grade ≥ 3+4
Nabeel et al 2014[17]	Johns Hopkins AS criteria (PSA density ≤ 0.15, ≤ 2 positive cores, ≤ 50% tumor in any core, Gleason score ≤ 6, and stage t1c)	Not mentioned	Gleason score ≥ 7
Arnout et al 2017[18]	As the only exclusion criterion was the presence of high-grade (Gleason score ≥3+4) Pca	PRIAS PROTOCAL	High-grade Pca (GS ≥3+4)
Caroline et al 2014[19]	Clinical stage ≤ Ta, PSA <10 ng/mL, ≤2 positive cores, Gleason grade ≤ 6, PSA density ≤ 0.2	After initial diagnosis: MRI and mpMRI 2nd month, MRGB 3rd month; mpMRI and MRGB at 12 mo of follow-up	(a) Cancers with GS 4 or 5 (b) multifocality ≥ 3
François et al 2014[20]	Clinical stage ≤t2a, serum PSA < 10 ng/mL, ≤2 positive cores, no Gleason pattern 4 or 5, <5mm of any core	Confirmatory biopsy at least a 3-mo interval from the initial biopsy	Gleason 4 or 5, 3 or more positive SB cores. Any positive core ≥ 5mm
Hamidreza et al 2015[21]	Unclear	PSA every 3–6 mo, DRE every 6 mo, confirmatory biopsy 6–12 mo, subsequent biopsies every 1–4 y	Any Gleason score pattern 4 cancer
Jim C. Hu et al 2014[22]	Epstein criteria (Gleason score ≤ 6, ≤ 2 positive, ≤ 50% tumors in any core)	Not mentioned	Beyond Epstein histological criteria
J.P. Radtke et al 2016[23]	PRIAS criteria (clinical stage T1c or T2, GS ≤ 6, involving ≤2 cores, PSA < 10 ng/mL, PSA density ≤ 0.2)	Restratification biopsy was performed after 2 y of AS.	Beyond PIRADS criteria
M. Minhaj et al 2015[3]	Johns Hopkins AS criteria (PSA density ≤ 0.15, ≤ 2 positive cores, ≤ 50% tumor in any core, 98 Gleason score ≤ 6, and stage t1c)	Not mentioned	Beyond criteria of ≤ 50% tumor in any core, Gleason score ≤ 6
Michael R. Da Rosa et al 2015[24]	Toronto protocol: Gleason ≤ 6, PSA ≤ 10 ng/mL; patients ≥ 70 y: PSA ≤ 15 ng/mL, Gleason ≤ 3 +4	Schedule of the University of Toronto AS protocol	Upgrading of GS since last biopsy occurred
Pedro et al 2016[25]	Gleason score 6, PSA ≤ 20,and clinical tumor stage ≤ T2a.	Imaging at least 3 mo after diagnostic biopsy or every 2 or 3 y	Gleason grade ≥ 3+4
Rodrigo R. et al 2017[26]	Clinical stage t1c–t2a, Gleason score ≤ 6, PSA ≤ 10 ng/mL, positive cores ≤ 3, biopsy cores < 50% involvement.	mpMRI ≥ 6 wk after initial biopsy, MRI-TB 90 d after initial mpMRI	Gleason ≥ 7, ≥ 3 fragments positive, > 50% tumor in any core
Ting Martin et al 2017[27]	Epstein criteria (stage t1c, PSA density < 0.15, Gleason score ≤ 6, positive cores ≤ 2, ≤ 50% tumor in any core)	Semiannual PSA measurement, a clinical examination, annual biopsy in most men	Gleason grade ≥ 7
Xiaosong et al 2015[28]	Unclear	Not mentioned	Gleason grade ≥ 7

AS = active surveillance, Pca = prostate cancer, SB = systemic biopsy, TB = targeted biopsy, PIRADS = Prostate Imaging Reporting And Data System, MRI = magnetic resonance imaging, mpMRI = multiparametric magnetic resonance imaging, PSA = prostate-specific antigen, DRE = digital rectal examination.

correlation coefficient of the former was 0.659 and P value was .076. Meanwhile, the Spearman correlation coefficient of the latter was 0.100 and the P value was .873. No threshold effect was observed for any group.

3.5. Diagnostic accuracy

AS group: This group comprised 1448 patients. Heterogeneity was observed for sensitivity ($I^2 = 77.7\%$, $P = .0000$), specificity ($I^2 = 77.6\%$, $P = .0000$), PLR ($I^2 = 61.2\%$, $P = .0014$), NLR ($I^2 = 84.2\%$, $P = .0000$), and DOR ($I^2 = 60.4\%$, $P = .0018$). The pooled sensitivity and specificity were 0.62 (95% CI, 0.57−0.68) and 0.89 (95% CI, 0.87−0.90), respectively. The pooled NLR for all studies combined was 0.43 (0.31−0.60), and the pooled PLR was 4.90 (3.50−6.86). The pooled DOR was 12.75 (7.22−22.51), and the AUC under SROC curve was 0.8645 (Fig. 3).

In total, 747 patients from 8 studies were analyzed at the stage of the confirmatory biopsy. Significant heterogeneity was

observed in sensitivity ($I^2 = 77.3\%$; $P = .0001$), specificity ($I^2 = 66.6\%$; $P = .0038$), and NLR ($I^2 = 78\%$; $P = .0000$), but not for DOR ($I^2 = 47.2\%$; $P = .0661$) or PLR ($I^2 = 50.0\%$; $P = .0513$). The pooled sensitivity and specificity for the 8 combined studies were 0.67 (0.59−0.74) and 0.89 (0.86−0.91), respectively. The pooled PLR was 4.94 (3.88−6.30) and the pooled NLR was 0.42 (0.27−0.65). In addition, the pooled diagnosis odds ratio was 14.54 (9.60−22.02). In addition, the AUC under the SROC curve was 0.8812 (Fig. 4).

In 5 studies involving 252 patients, the biopsy was performed during the follow-up stage. Significant heterogeneity was observed in sensitivity ($I^2 = 69.1\%$; $P = .0116$), specificity ($I^2 = 56.8\%$; $P = .0550$), and NLR ($I^2 = 55.5\%$; $P = .0615$), but not for DOR ($I^2 = 25.0\%$, $P = .2549$) or PLR ($I^2 = 5.3\%$, $P = .3765$). The pooled sensitivity and specificity were 0.35 (0.22−0.51) and 0.88 (0.82−0.92), respectively. The pooled positive LR and negative LR were 3.06 (1.71−5.50) and 0.76 (0.52−1.11), respectively. Moreover, the pooled DOR was

Figure 2. Quality assessment of included studies.

4.41 (2.15–9.03), and the AUC under the SROC curve was 0.8367 (Fig. 5).

3.6. Publication bias

Figure 6 shows the Deek's funnel plot of the AS group and confirmatory biopsy group. The statistical nonsignificance of the Deek's test in both groups of the Egger test ($P = .244$ in AS group and $P = .103$ in confirmatory biopsy subgroup) indicates the presence of a low likelihood of publication bias.

4. Discussion

It is widely accepted that a certain proportion of patients with Pca are overtreated.[16] In addition, AS is one of the methods to avoid this situation as it enables patients with low-risk Pca to be closely

monitored before their condition becomes potentially life-threatening.[2] Patient selection and the follow-up rate are the most crucial issues concerning AS. Patients on AS should be limited to those with organ-confined low-risk cancer. Follow-up during AS helps to maintain patients under surveillance and, consequently, to initiate active treatment once Pca progression is identified[29]; however, consistent criteria are yet to be established for determining the inclusion requirements for AS and the endpoint of the AS procedure for initiating radical therapy.[30,31] Repeated biopsy, repeated PSA level assay, and digital rectum examination were the standard procedures performed during follow-up.

Systemic TRUS biopsy has become a regular and the most practical method for diagnosing Pca, as well as managing the repeated biopsies during AS.[24] However, infective complications, increased erectile dysfunction, and pain caused by the
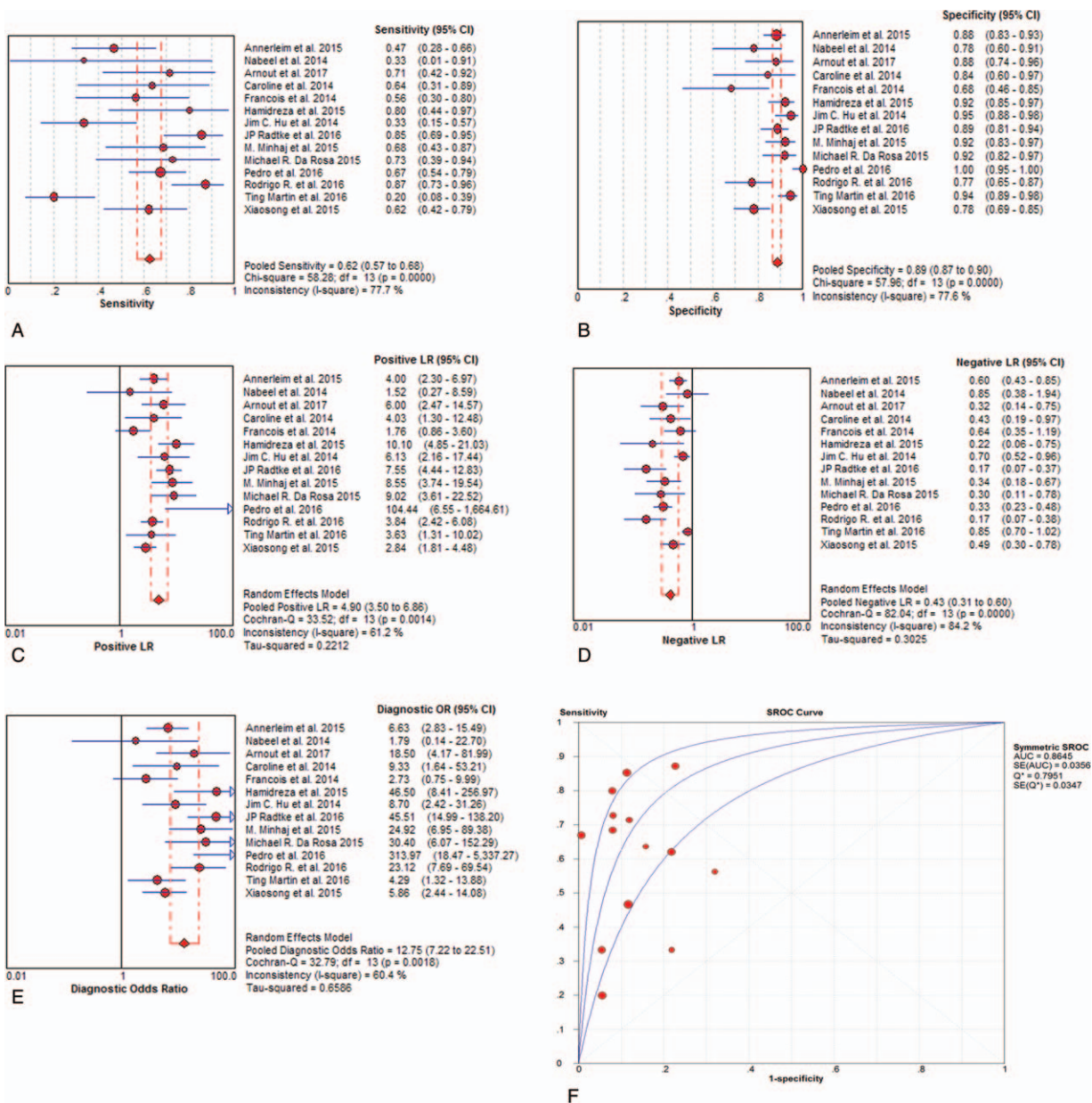
Figure 3. Diagnostic accuracy for AS group: (A) sensitive, (B) specificity, (C) PLR, (D) NLR, (E) DOR, and (F) AUC. PLR = positive likelihood ratio; NLR = negative likelihood ratio; DOR = diagnostic odds ratio; AUC = area under the curve.

systemic TRUS biopsy might lead to low compliance of patients with Pca during the AS protocol.[32–35] In addition, a blinded and randomized procedure cannot help to focus on specific lesions and some tumors might be overlooked.[16] Compared with the radical specimens, the Pca detection rate of TRUS biopsy ranges from 40% to 68%,[4,25,36–42] whereas the cancer risk misclassification is 23% to 60%.[3,20] Some studies have also reported that approximately 20% to 30% patients on AS can be reclassified, and most reclassifications were explained by undersampling instead of tumor progression.[43,44] Nontumor-oriented biopsies could also cause an imprecise resampling of cancerous areas during the AS procedure.

mpMRI comprises T2-weighted, diffusion-weighted, and contrast-enhanced dynamic imaging widely used for Pca detection, staging, and monitoring.[44] In addition, mpMRI

allows better visibility of the prostate anatomy and can identify potentially malignant lesions.[45] Recently, mpMRI and MRI-TBs have been used for monitoring patients on AS. Moreover, an accurate and precise coregistration of MRI and ultrasound enables biopsy-targeted lesions to be identified via MRI.[24] The mpMRI and MRI-TB results are in agreement with the radical prostatectomy (RP) Gleason score; in particular, the detection rate for clinically significant Pca is superior.[46–48] Moreover, MRI-TB can reduce unnecessary cores from normal or insignificant Pca tissue.[9] Therefore, compared with a systemic biopsy, MRI-TB exhibits higher detection rate for high-risk Pca and a relatively lower detection rate for low-risk Pca.[27]

For the AS group, according to the criteria used by Guo,[49] PLR of >10 or NLR of <0.1 indicates high diagnostic accuracy. Our PLR (4.9) and NLR (0.43) for AS patients indicated
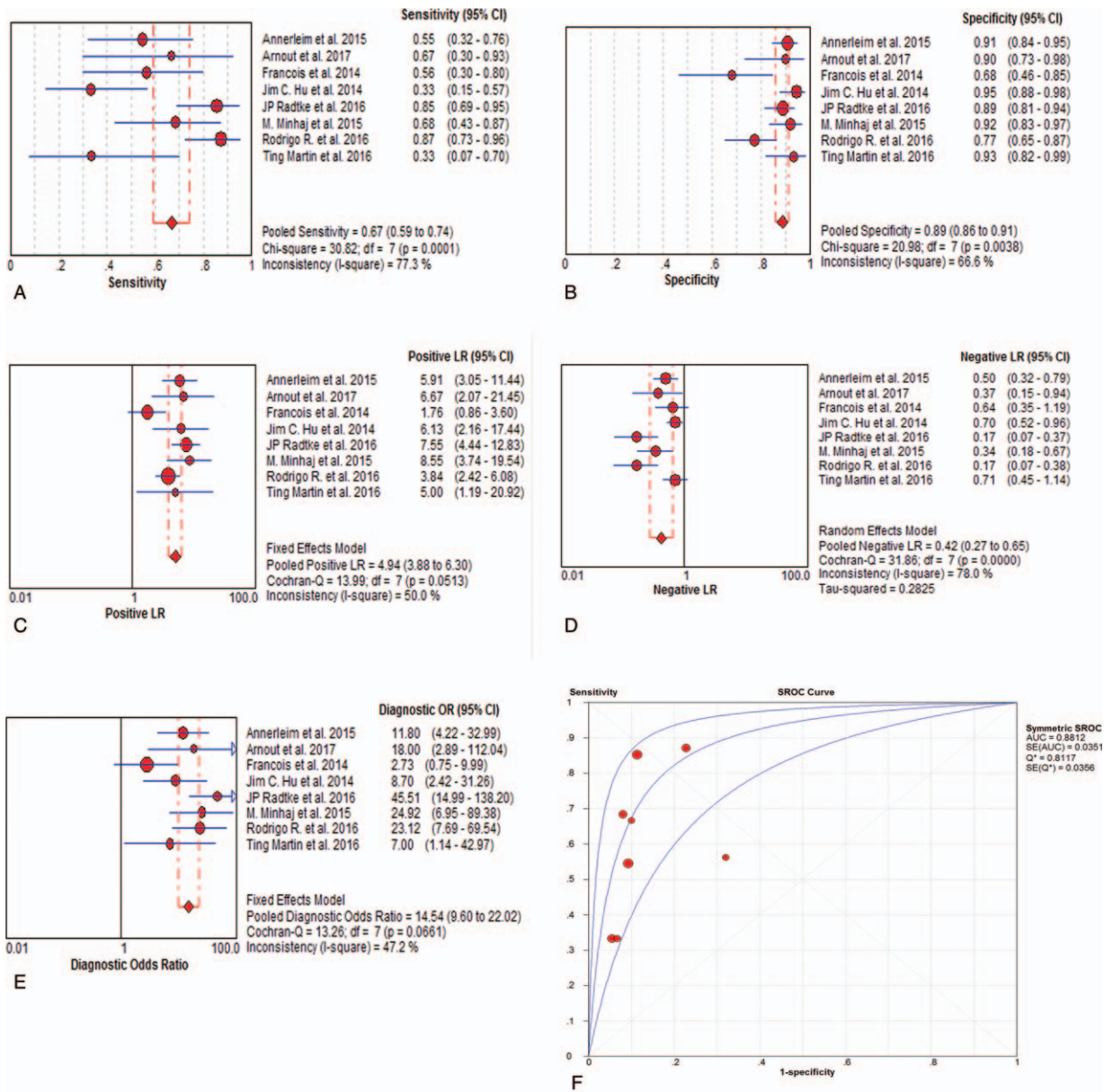
Figure 4. Diagnostic accuracy for confirmatory biopsy group: (A) sensitive, (B) specificity, (C) PLR, (D) NLR, (E) DOR, and (F) AUC. PLR=positive likelihood ratio; NLR=negative likelihood ratio; DOR=diagnostic odds ratio; AUC=area under the curve.

moderate accuracy (PLR of 2−5 and NLR of 0.2−0.5 indicate moderate accuracy) in the use of MRI-TB for diagnosing and reclassifying patients on AS. Although our DOR (12.75) was >1, it could not reach the limit of moderate accuracy (DOR > 25), indicating a relatively low accuracy. Although the sensitivity was relatively low (0.62), the specificity was high (0.89) and the AUC value under the SROC curve was 0.86, indicating a relatively high diagnostic accuracy as the value was between 0.8 and 0.9.[50] Notably, with both high specificity and AUC value, it can be concluded that patients without reclassification diagnosed by MRI-TB are less likely to have high-risk Pca and should continue AS.

The results in the confirmatory biopsy group were similar to those of the AS group as the sensitivity (0.67), PLR (4.94), NLR (0.42), and slightly higher specificity (0.89), DOR (14.54), and

AUC value under the SROC (0.88) indicated a moderate-to-high diagnostic accuracy. In the follow-up biopsy group, the results were not so promising, with poor sensitivity (0.35) and DOR (4.41), low-accuracy NLR (0.76), moderate-accuracy PLR (3.06), high-accuracy AUC value under the SROC (0.84) and specificity (0.88), indicating a moderate accuracy for a significant Pca diagnosis.

In all, 3 groups were analyzed in our study. Some results presented statistical heterogeneity with $I^2 > 50\%$. All these results used a random effects model. Although the threshold effect was first considered, none of the results exhibited the threshold effect. We performed a meta-regression for the AS group to identify the source of heterogeneity. The type of study (prospective or retrospective), MRI score of the target patients being biopsied (all suspect areas with MRI score ≥2 or ≥3), type
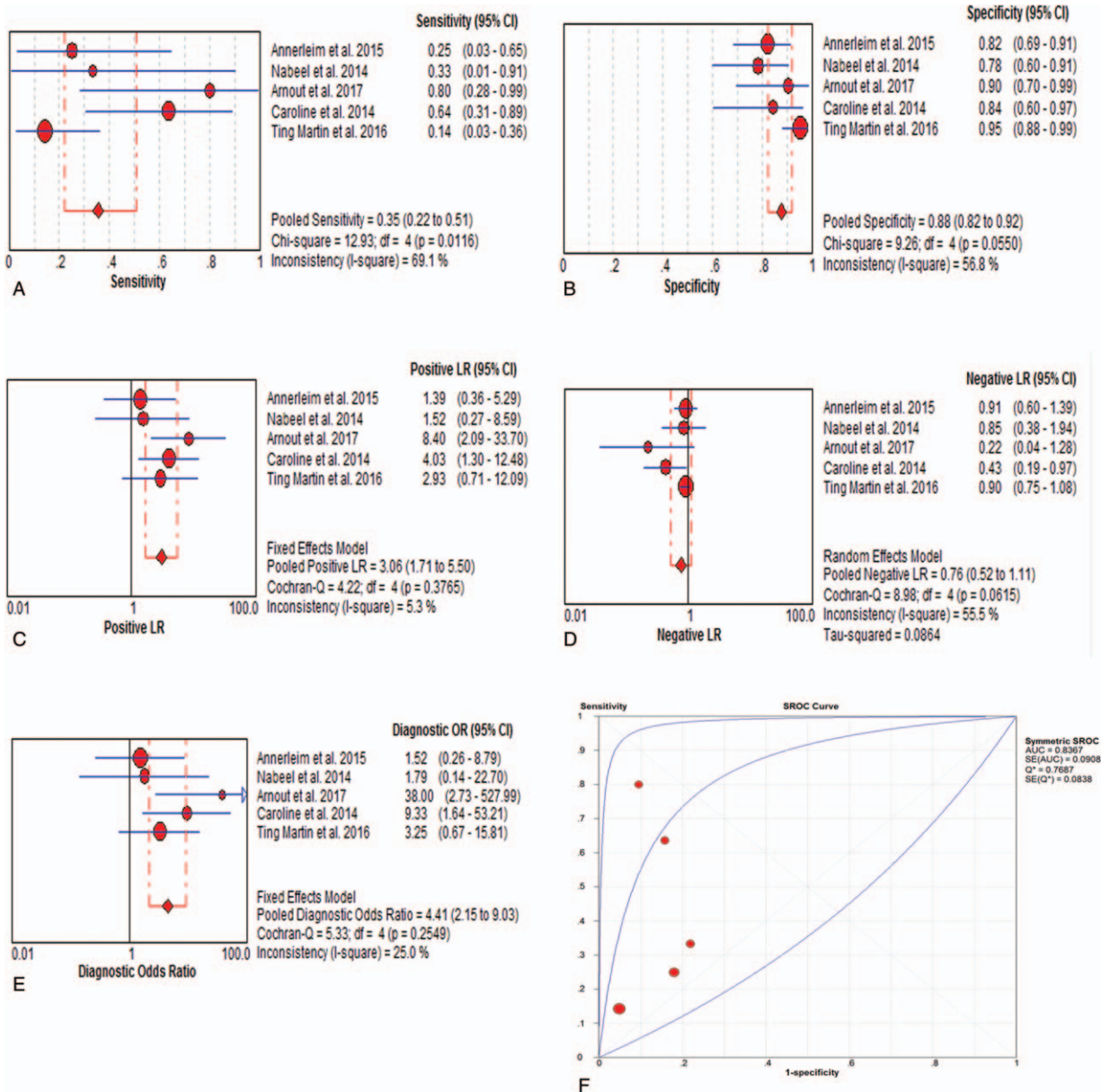
Figure 5. Diagnostic accuracy for follow-up group: (A) sensitive, (B) specificity, (C) PLR, (D) NLR, (E) DOR, and (F) AUC. PLR = positive likelihood ratio; NLR = negative likelihood ratio; DOR = diagnostic odds ratio; AUC = area under the curve.

of targeted biopsy (MRI–ultrasound fusion biopsy or visual estimated biopsy), accordance with Standards of Reporting for MRI Targeted Biopsy Studies guidelines or not, MRI with an endorectal coil or not were analyzed; however, none of these factors could be considered as the source of heterogeneity (see Table, Supplemental Content, http://links.lww.com/MD/D57, which illustrates the meta-regression of AS group).

Guo[49] has performed a meta-analysis assessing the diagnostic accuracy of MRI on disease reclassification among candidates on AS, with sensitivity of 0.69, specificity of 0.78, PLR of 3.1, NLR of 0.4, DOR of 8, and AUC of 0.79. In contrast, we found that MRI-TB exhibited a superior diagnostic accuracy in all aspects compared with the use of MRI alone for detecting reclassification among patients on AS. Another meta-analysis conducted by Schoots[9] found that the diagnostic accuracy of MRI-TB was

superior to that of TRUS-SB for significant Pca detection. Moreover, the patients of that study consisted of previous negative TRUS-SB patients and initial biopsy patients.[9] Our study mainly focuses on patients after the initial biopsy and who have undergone the AS procedure as this stage is also very important in Pca management.

Our study has 2 main limitations: first, inclusion and follow-up strategies differed among the included studies; moreover, the targeted biopsy strategy and MRI score also differed. This may explain the relatively higher heterogeneity without the threshold effect. The second limitation is regarding the gold standard of Pca diagnosis and grading. We choose SB as the gold standard because this is the most recognized and widely used method in AS. However, as previously mentioned, many limitations are associated with SB, and thus, it has disadvantages as a gold
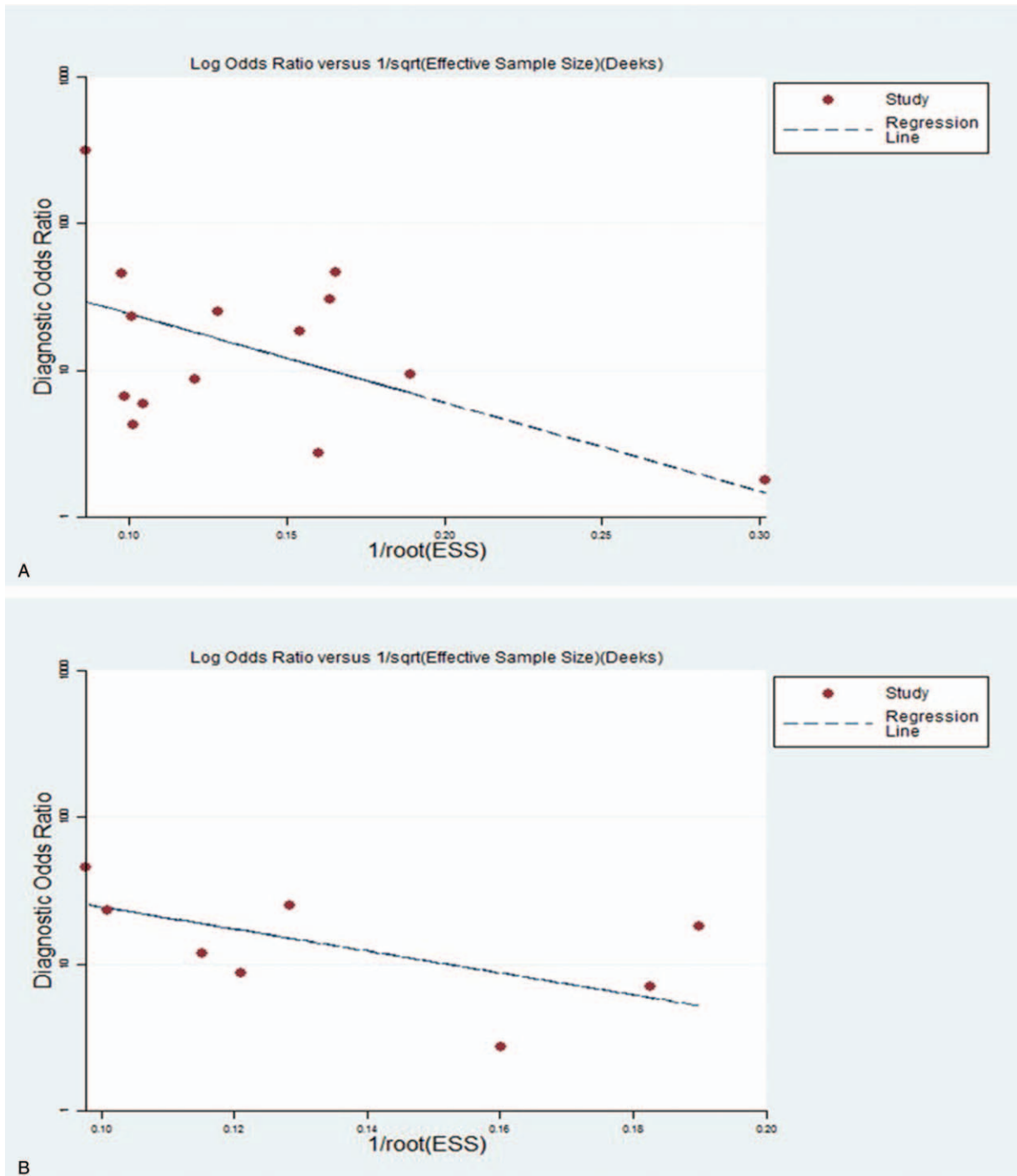
Figure 6. Publication bias: (A) AS group and (B) confirmatory biopsy group.

standard. An RP specimen is the most precise method to assess the condition of Pca patients; however, few patients in AS are willing to undergo radical therapy without significant Pca detected by a confirmatory or follow-up biopsy.

Overall, this study aimed to assess the diagnostic accuracy of MRI-TB in the AS procedure. In total, data of 1693 patients obtained from 14 articles were included. The high specificity and AUC value under the sROC curve demonstrated the potential value of MRI-TB in the AS procedure as negative results indicate

that tumors are less likely to proceed. However, the relative sensitivity suggested that the combination of other examinations (PSA level and density) should be used to make decisions that will benefit patients the most.

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