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Value of three biopsy methods in prostate cancer detection: a meta-analysis and systematic review

Y.-S. DENG[1], Y.-H. HE[2], W.-W. YING[1], H.-L. LIU[1], P.-Z. LI[1], C.-Y. MA[1], Z.-S. DING[1], X. CHEN[1], J.-F. WANG[1], X.-F. ZHOU[1]

[1]Department of Urology, China-Japan Friendship Hospital, Beijing, China
[2]Department of Urology, Peking University First Hospital, Beijing, China

Abstract. – OBJECTIVE: The study aimed at investigating the value of systemic biopsy (sysPbx), magnetic resonance imaging/ultrasound fusion targeted biopsy (fusPbx) and fusPbx combined with sysPbx (comPbx) for prostate cancer (PCa) detection.

MATERIALS AND METHODS: Data from the PubMed, Cochrane, and Embase databases were searched from inception until March 23, 2020. Prospective studies comparing the detection rates of sysPbx, fusPbx and comPbx were identified. We pooled the detection rates for all PCa, clinically significant prostate cancer (csPCa), and clinically insignificant prostate cancer (cinsPCa) of fusPbx, sysPbx, and comPbx. Risk ratios (RRs) were calculated for the meta-analysis. Then, analyses were performed to identify the possible sources of heterogeneity.

RESULTS: Seventeen studies, including 18 cohorts with 3035 men, were included. No patients had previous evidence of PCa. Each patient had one or more suspicious lesions found on multiparametric magnetic resonance imaging (mpMRI) and received both fusPbx and sysPbx. The results showed that fusPbx and sysPbx did not differ significantly in detecting all PCa (RR=1.00, 95% CI: 0.95-1.05, $p>0.05$). However, fusPbx provided a higher detection rate for csPCa (RR=1.24, 95% CI: 1.14-1.34, $p<0.05$) and a lower detection rate for cinsPCa (RR=0.68, 95% CI: 0.61-0.76, $p<0.05$) than sysPbx. In addition, comPbx detected more PCa (RR=1.22, 95% CI: 1.16-1.29, $p<0.05$) and csPCa cases (RR=1.13, 95% CI: 1.05-1.21, $p<0.05$) than fusPbx.

CONCLUSIONS: In men with positive mpMRI findings, compared to sysPbx, fusPbx had significantly increased the detection rates for csPCa and decreased those for cinsPCa. The combination of fusPbx with sysPbx outperformed fusPbx in detecting both overall PCa and csPCa.

Key Words:
Magnetic resonance imaging, Targeted biopsy, Detection, Prostate cancer, Meta-analysis.

Introduction

Prostate cancer (PCa) is one of the most common cancers in men and the second leading cause of cancer-related death in the West[1]. Studies[2-4] have revealed that high-risk patients with PCa can benefit from radical prostatectomy. Therefore, accurate risk stratification is critical for PCa patients. Inaccurate risk stratification may lead to the overtreatment of clinically insignificant prostate cancer (cinsPCa) and undertreatment of clinically significant prostate cancer (csPCa) and consequently have a detrimental impact on patients' life. Besides, patients with csPCa may lose the window of curability.

Patients with increased prostate-specific antigen (PSA) and/or abnormal digital rectal examination (DRE) results are clinically suspected to have PCa. Currently, systemic biopsy (sysPbx) is regarded as the standard diagnostic method for patients with clinical suspicion of PCa. The European Association of Urology recommends 10-12 core systemic biopsy samples, including a target biopsy of suspicious lesions on multiparametric magnetic resonance imaging (mpMRI)[5]. However, due to insufficient sampling of the apical, middle, and anterior areas of the prostate, sysPbx often leads to false-negative results and an underdiagnosis of csPCa[6-8]. Some studies have shown that the false-negative rate of the initial systematic 12-core biopsy was 20-24%, and up to 40% of low-risk patients with a Gleason score

Corresponding Authors: Xiaofeng Zhou, MD; e-mail: bjzryy11188@163.com
Jianfeng Wang, MD; e-mail: zryhyy1@126.com

of 3+3 during sysPbx had higher scores on postoperative pathology[9,10]. In recent years, mpMRI has become the main imaging examination for the diagnosis of PCa due to its ability to depict the suspicious area[11]. MpMRI yields T2-weighted images, diffusion-weighted images (DWIs), and dynamic contrast-enhanced (DCE) images, which allow it to capture the PCa lesion contour easily. Magnetic resonance imaging/ultrasound fusion targeted biopsy (fusPbx) combines the advantages of MRI and ultrasound by employing fusion software to superimpose the lesion contour on mpMRI images onto live ultrasound[12,13]. Thus, a real-time targeted biopsy can be performed in the clinical environment. Some researchers have found no significant differences between fusPbx and sysPbx in overall PCa detection rates, while others have shown that fusPbx significantly increases the detection rates for csPCa[14,15]. In addition, some researchers have studied the diagnostic value of fusPbx in combination with sysPbx (comPbx), deeming that comPbx can improve the detection rates for overall PCa and csPCa[16,17].

As far as we know, unlike our study, few other studies have used the detection rates for comPbx versus those for fusPbx as a primary endpoint. We conducted a systematic review and meta-analysis of previous studies to evaluate the value of fusPbx, sysPbx, and comPbx to determine the most effective biopsy method for men with suspicious PCa lesions on mpMRI.

Materials and Methods

Search Strategy

PubMed, Cochrane Library, and Embase were systemically searched to identify relevant studies from inception until May 23, 2020. The relevant search terms were as follows: "prostate cancer OR prostate" AND "magnetic resonance imaging" OR "MR" OR "MRI" AND "transrectal ultrasound" OR "TRUS" OR "US" OR "ultrasonography" AND "fusion" OR "targeted" OR "registration" OR "computer". Additional relevant studies included articles suggested by the database and the cited references in the full-text articles.

Inclusion and Exclusion Criteria

Titles and abstracts were screened to identify eligible studies. The specific inclusion criteria were as follows: (1) prospective studies; (2) patients clinically suspected of having PCa without previous evidence of PCa; (3) patients with one or more suspicious lesions found on mpMRI; (4) each patient received both fusPbx and sysPbx; (5) sysPbx cores of 12±2; and (6) available detection rates or detection rates that could be calculated for overall PCa, csPCa, and cinsPCa. When more than one article was published with the same population, only the study with sufficient data was included.

Studies that met the following criteria were excluded: (1) non-prospective studies; (2) studies with unpublished data; (3) studies with unavailable fusPbx and sysPbx data; (4) non-primary research, meeting abstracts, editorials, reviews, and case reports; and (5) studies in which data could not be obtained or those with incorrect data.

Data Extraction

According to the criteria mentioned above, two reviewers screened the titles and abstracts of the published studies independently. If different opinions existed, all the authors discussed and decided whether to include the controversial study. The data extracted included first author, publication year, country, population characteristics, MRI features, and the detection rates for overall PCa, csPCa, and cinsPCa of fusPbx, sysPbx, and comPbx.

Quality Assessment and Publication Bias

The quality of the included studies was evaluated with the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2), which consists of four domains: patient selection, index test, reference standard, and flow and timing. A study was considered "low risk of bias" when all domains of bias and the first three domains for applicability concerns were judged as "low". If one or more domains were judged as "unclear risk" or "high risk of bias", the study was judged to have an overall risk of bias. The assessment was conducted by two authors, and all the authors discussed and re-evaluated the quality of the controversial study. Funnel plot analysis, Egger's test and Begg's test were performed to assess publication bias.

Statistical Analysis

Risk ratios (RRs) and 95% confidence intervals (95% CIs) were used to compare fusPbx, sysPbx, and comPbx. We used the I^2 test to assess the degree of heterogeneity (low heterogeneity: I^2 value < 25%, moderate heterogeneity: I^2 value = 25-50%, high heterogeneity: I^2 value > 50%).

When the I^2 value was > 50%, a random-effect model was used. Otherwise, a fixed-effect model was used. RRs and CIs were recalculated and compared with the previous values after eliminating the studies that may have been the source of heterogeneity. The meta-analyses were carried out with RevMan v.5.2 and STATA 12.0 software. When the p-value was less than 0.05, the difference was considered statistically significant.

Results

Literature Screening

Eventually, 1998 published studies were found in the three databases. A total of 1911 articles were excluded as irrelevant to our study by reading the titles and abstracts. After reviewing the full texts, 70 articles were excluded. Eighteen cohorts from 17 studies with 3035 men were finally included in our analysis (Figure 1).

Characteristics of the Included Studies and Quality Assessment

The 17 studies were published between 2012 and 2020, and the countries included Germany, France, America, Croatia, Brazil, China, Canada, and Australia. The sample size ranged between 20 and 582. The details of the 18 cohorts are shown in Table I[11,18-33]. The included studies varied in methodological quality, but none of them were judged to have an overall risk of bias, as we chose comPbx as the gold standard. The domains were mostly judged as having a low risk of bias (Figure 2).

FusPbx Vs. sysPbx in the Detection of all PCa

In total, we included 18 cohorts with 3035 participants. FusPbx and sysPbx detected PCa in 1364 men (44.9%) and 1366 men (45.0%), respectively (RR=1.00, 95% CI: 0.95-1.05), and there was no significant difference between these methods (p=0.45). Low heterogeneity was found among the included studies (I^2=20%, p=0.22) (Figure 3A).

FusPbx Vs. sysPbx in the Detection of csPCa

A total of 14 cohorts with 2707 participants were included. FusPbx detected significantly more csPCa cases than sysPbx (857 men *vs.* 692 men, 31.7% *vs.* 25.6%, p<0.05), with an RR of 1.24 (95% CI: 1.14-1.34). There was low heterogeneity among the studies (I^2=16%, p=0.28) (Figure 3B).

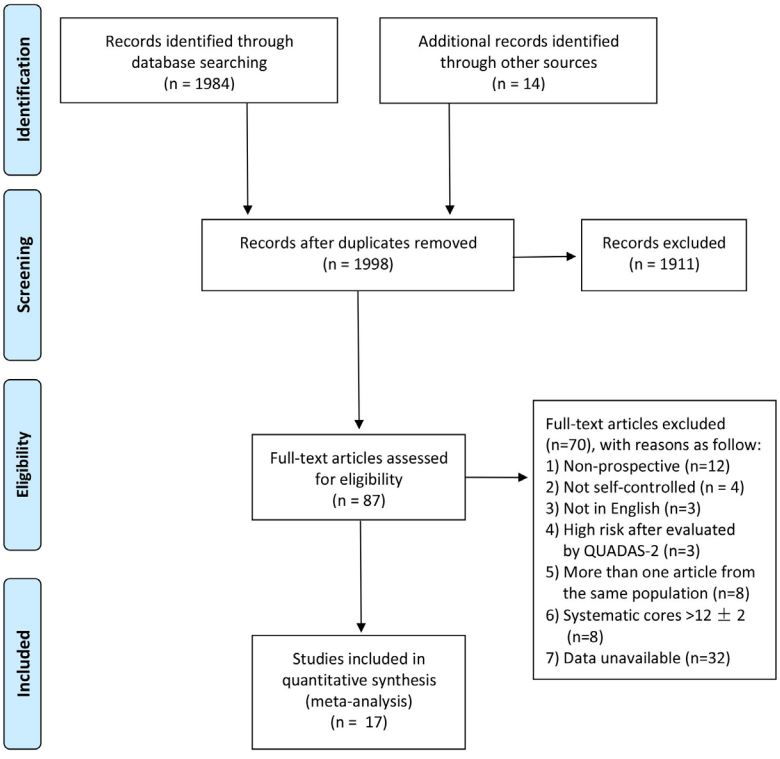

Figure 1. Flow diagram showing the outcome of the study selection process.

Table I. Summary data of the included studies in the review.

Study	Year	Sample size	Country	Biopsy history (n)	Age, yr	PSA, ng/ml	Prostate volume, ml	MRI Strength, T	MRI scoring system	fusPbx		sysPbx	
										Route	Fusion platform	Route	sysPbx first
Borkowetz[18]	2015	263	German	Biopsy naive (68), prior negative biopsy (195)	66 (47-83)	8.3 (0.39-86.57)	50 (12-220)	3	PI-RADS	TP	BioJet	TR	No
Cool[19]	2016	38	Canada	Biopsy naive	59.4 ± 7.7	6.0 ± 3.5	38 ± 18	3	PI-RADS v2	TR	Artemis	TR	No
de Gorski[20]	2015	232	France	Biopsy naive	64 ± 6.4	6.5 ± 1.8	47 ± 24.3	1.5	Likert	TR	UroStation	TR	Yes
Delongchamps[21]	2016	108	France	Biopsy naive	65 (42-77)	7.2 (3.6-23.63)	46 (19-150)	1.5;3	PI-RADS	TR	UroStation	TR	Yes
Fiard[22]	2013	20	France	Biopsy naive (13); prior negative biopsy (17)	64 (61-67)	6.3 (5.2-8.8)	46 (31-59)	3	PI-RADS	TR	UroStation	TR	Yes
Filson(C1)[23]	2016	272	America	Biopsy naive	64.4 (58.5-69.4)	5.8 (4.4-8.1)	45.0 (33.0-61.5)	3	PI-RADS	TR	Artemis	TR	No
Filson(C2)[23]	2016	265	America	Prior negative biopsy (324)	65.7 (59.3-70.2)	7.6 (5.0-11.5)	57.7 (39.8-83.5)	3	PI-RADS	TR	Artemis	TR	No
Junker[24]	2015	50	Austria	partially	63.7 ± 7.9	7.6 ± 4.2	49.2 ± 21.9	3	PI-RADS	TR	Logiq	TR	No
Kulič[25]	2020	63	Croatia	Prior negative biopsy	67 (57-84)	10.7 (4.86-64)	NM	3	PI-RADS	TR	NM	TR	No
Lian[26]	2017	101	China	Prior negative biopsy	68.9 ± 8.1	10.8 ± 6.1	42.1 ± 15.3	3	PI-RADS v2	TP	RVS	TP	No
Mariotti[27]	2017	100	Brazil	Biopsy naive (78); prior negative biopsy (22)	62.5 (35-86)	5.3 (0.2-36.0)	NM	3	Likert	TR	MyLab; Smartfusion; Logiq	TR	Yes
Mendhiratta[28]	2015	382	America	Biopsy naive	64.5 ± 8.4 (36-64)	6.8 ± 0.3	44	3	Likert	TR	Artemis	TR	No

Table Continued

Table I *(Continued)*. Summary data of the included studies in the review.

Study	Year	Sample size	Country	Biopsy history (n)	Age, yr	PSA, ng/ml	Prostate volume, ml	MRI Strength, T	MRI scoring system	fusPbx		sysPbx	
										Route	Fusion platform	Route	sysPbx first
Puech[29]	2013	95	France	Biopsy naive or prior negative biopsy	65 (49-76)	10.05 ± 8.8	52 ± 24	1.5	Likert	TR	MyLab	TR	No
Salami[30]	2015	140	America	Prior negative biopsy	NM	NM	NM	3	Likert	TR	UroNav	TR	No
Siddiqui[11]	2013	582	America	Biopsy naive (262), prior negative biopsy (320)	61.3 ± 8.4	9.9 ± 13.1	56.4 ± 31.2	3	Low, moderate, high	TR	UroNav	TR	No
Vourganti[31]	2012	195	America	Prior negative biopsy	62 (37-80)	9.13 (0.3-103)	56 (16-187)	3	Low, moderate, high	TR	NM	TR	Yes
Wysock[32]	2014	67	America	Biopsy naive	65 (56-70)	5.1 (3.4-6.9)	40.5 (29.25-61)	3	5 point scale	TR	Artemis	TR	No
Zhang[33]	2015	62	China	Biopsy naive	68.38 ± 6.57	10.21 ± 5.57	34.05 ± 9.86	3	PI-RAD	TP	RVS	TP	No

Notes: NM, not mentioned; PCa, prostate cancer; PSA, prostate-specific antigen; MRI, magnetic resonance imaging; TR, transrectal; TP, transperineal; fusPbx, magnetic resonance imaging/ultrasound fusion targeted biopsy; sysPbx, systemic biopsy.

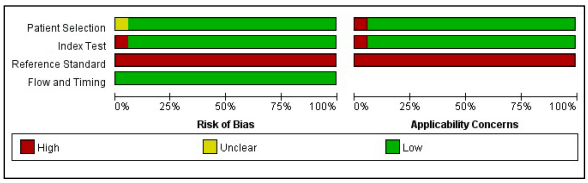

Figure 2. Risk of bias assessment using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2).

FusPbx Vs. sysPbx in the Detection of cinsPCa

The same 14 cohorts above were included in this analysis. FusPbx detected significantly fewer cinsPCa cases than sysPbx (387 men *vs.* 568 men, 14.3% *vs.* 21.0%, $p<0.05$), with an RR of 0.68 (95% CI: 0.61-0.76). The heterogeneity test showed moderate heterogeneity ($I^2 = 42\%$, $p=0.05$) (Figure 3C).

ComPbx Vs. fusPbx in the Detection of all PCa

In total, 17 cohorts with 2968 participants were included in this analysis. ComPbx detected significantly more PCa cases than fusPbx (1635 men *vs.* 1337 men, 55.1% *vs.* 45.0%, $p<0.05$), with an RR of 1.22 (95% CI: 1.16-1.29). No heterogeneity was found in the analysis ($I^2=0\%$, $p=1.00$) (Figure 4A).

ComPbx Vs. fusPbx in the Detection of csPCa

A total of 14 cohorts with 2660 men were included in this analysis. ComPbx detected significantly more csPCa cases than fusPbx (954 men *vs.* 845 men, 35.9% *vs.* 31.8%, $p<0.05$), with an RR of 1.13 (95% CI: 1.05-1.21). No heterogeneity was found in the analysis ($I^2=0\%$, $p=1.00$) (Figure 4B).

Galbraith Plot

In the comparison of overall PCa detection rates for fusPbx and sysPbx, the Galbraith plot showed that the study by Borkowetz et al[18] was the main source of heterogeneity (**Supplementary File 1A**). A new meta-analysis was performed after excluding the study, and we found no heterogeneity among the remaining studies ($I^2=0\%$, $p=0.48$). However, the detection rate was still not statistically significant (RR=0.98, 95% CI: 0.93-1.04, p>0.05) (**Supplementary File 2A**).

In the comparison of the cinsPCa detection rates between fusPbx and sysPbx, the Galbraith plot showed that the studies from Borkowetz et al[18], Siddiqui et al[11], and Salami et al[30] were the main sources of heterogeneity (**Supplementary File 1B**). A meta-analysis was performed again after excluding those three studies, and we found no heterogeneity among the remaining studies ($I^2=0\%$, $p=0.95$), but fusPbx still detected significantly fewer cinsPCa cases than sysPbx (RR=0.59, 95% CI: 0.50-0.69, $p<0.05$) (**Supplementary File 2B**).

In the comparison of the csPCa detection rates between fusPbx and sysPbx, the Galbraith plot did not find any sources of heterogeneity from the included studies (**Supplementary File 1C**). No heterogeneity was found in the following comparisons: comPbx versus fusPbx in overall PCa detection and comPbx versus fusPbx in csPCa detection.

Meta-Regression Analysis and Subgroup Analysis

In the comparison of overall PCa detection rates between fusPbx and sysPbx, biopsy history and Route of fusPbx are the reasons for heterogeneity ($p=0.029$ and 0.015, respectively), while the other factors (publication year, sample size, age, PSA, prostate volume, Route of sysPbx, and whether sysPbx was performed first) might not be sources of heterogeneity (Table II). Subgroup analysis showed that fusPbx had a lower detection rate for overall PCa than sysPbx in biopsy-naive patients (RR=0.913, 95% CI: 0.844-0.988, $p<0.05$) and a higher detection rate for overall PCa in patients who underwent transperineal fusPbx (TP-fusPbx) (RR=1.252, 95% CI: 1.048-1.495, $p<0.05$) (**Supplementary File 3**).

In the comparison of the csPCa detection rates between fusPbx and sysPbx, biopsy history, age, and PSA were the reasons for heterogeneity ($p=0.021$, 0.045, and 0.048, respectively), while the other factors were not sources of heterogeneity (Table III). Subgroup analysis showed that in the subgroup of ≤100 samples and the subgroup in which sysPbx was performed first, fusPbx and sysPbx did not differ significantly in detecting csPCa (RR=1.183, 95% CI: 0.995-1.408, p>0.05; RR=1.094, 95% CI: 0.940-1.274, $p>0.05$, respectively) (**Supplementary File 4**).

In the comparisons of the cinsPCa detection rates between fusPbx and sysPbx, the overall PCa detection rates between comPbx and fusPbx, and the csPCa detection rates between comPbx and fusPbx, none of the factors were sources of heterogeneity, (**Supplementary File 5**).

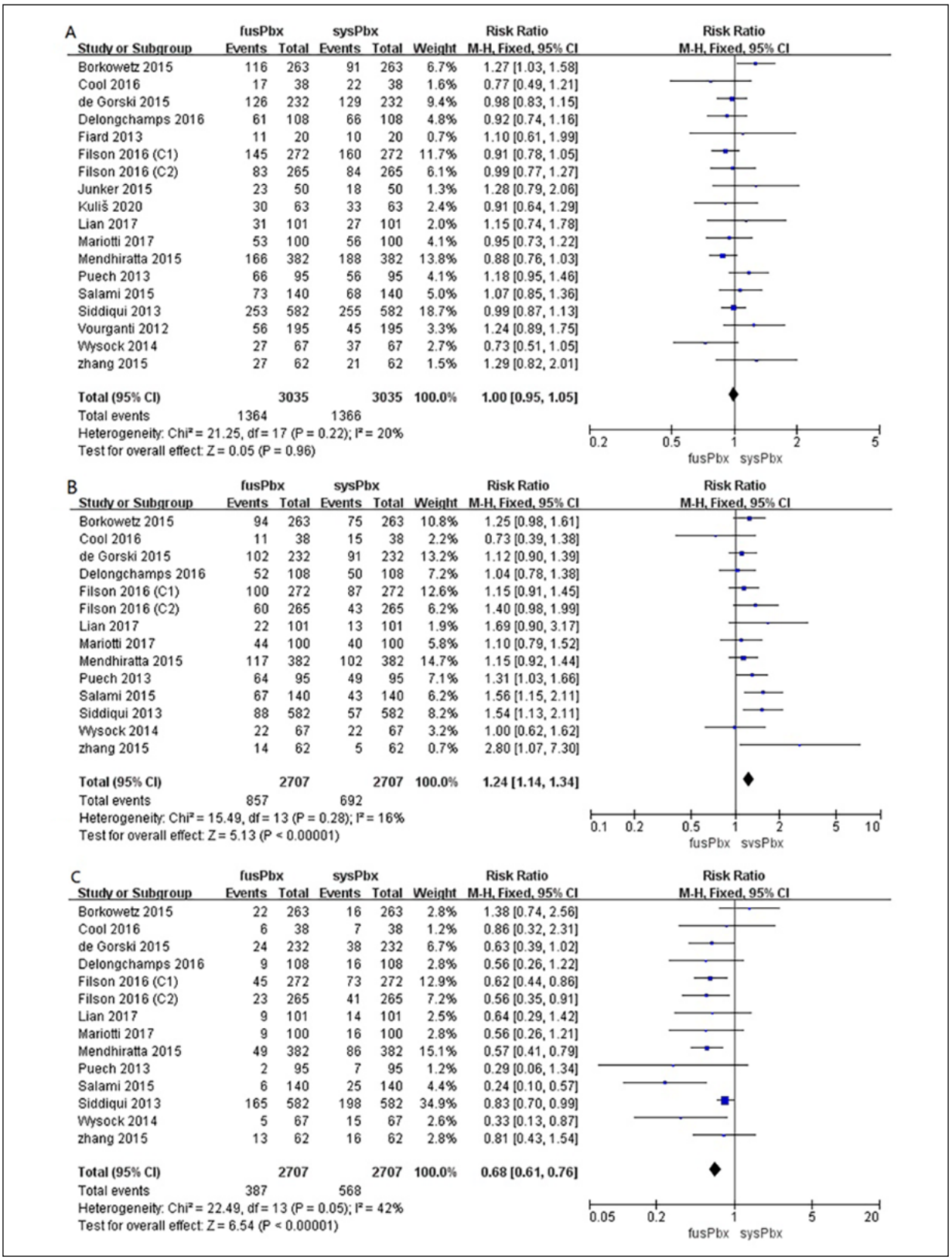

Figure 3. Forest plot of the RR for the detection rates comparing fusPbx and sysPbx. **A,** Overall PCa. **B,** csPCa. **C,** cinsPCa. PCa, prostate cancer; csPCa, clinically significant prostate cancer; cinsPCa, clinically insignificant prostate cancer; fusPbx, magnetic resonance imaging/ultrasound fusion targeted biopsy; sysPbx, systemic biopsy.

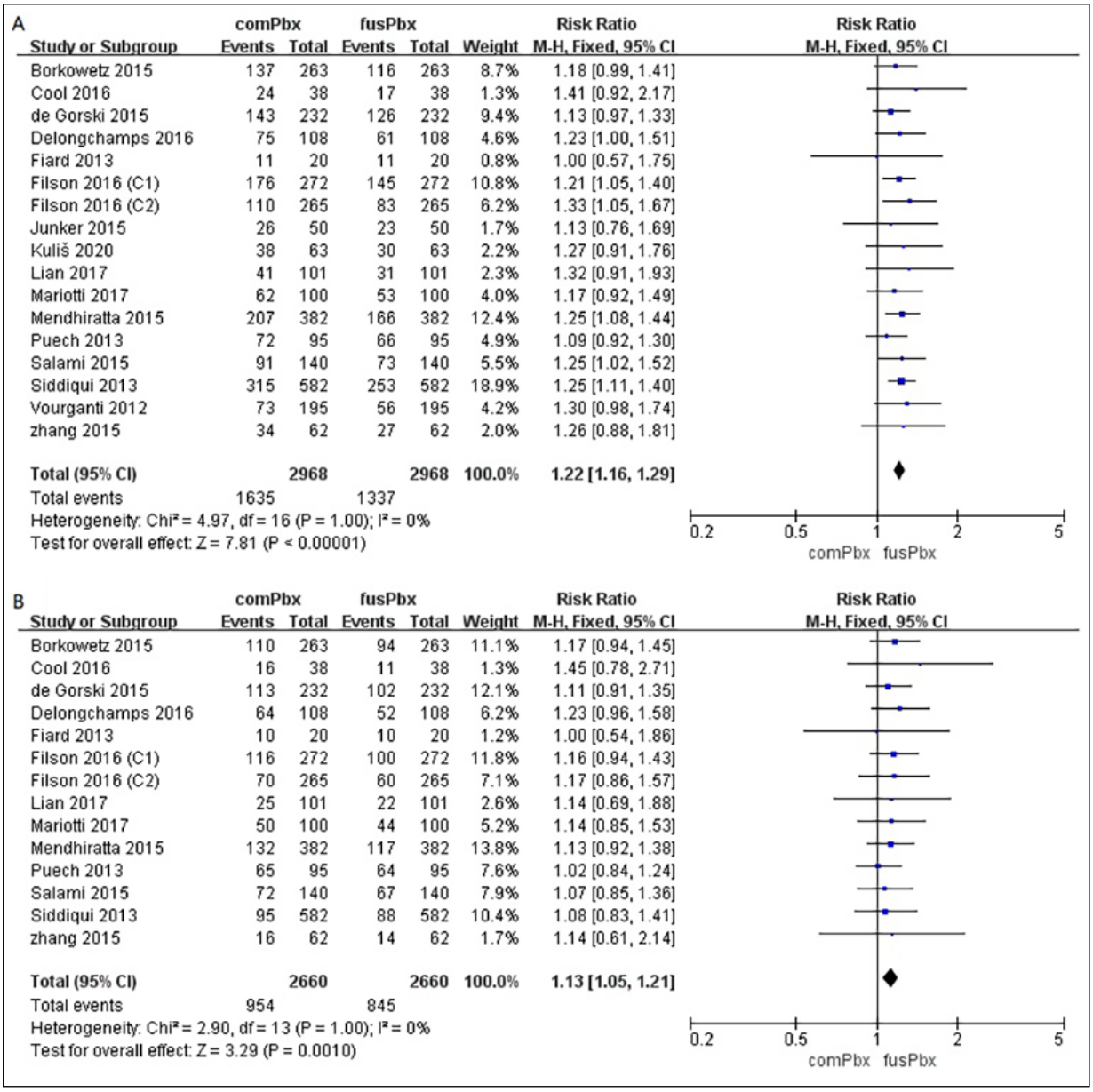

Figure 4. Forest plot of the RR for the detection rates comparing comPbx and fusPbx. **A,** Overall PCa. **B,** csPCa. PCa, prostate cancer; csPCa, clinically significant prostate cancer; fusPbx, magnetic resonance imaging/ultrasound fusion targeted biopsy; comPbx, fusPbx combined with systemic biopsy.

Publication Bias

All the funnel plots (Figure 5) were symmetrical. No publication bias was found among those comparisons, and the values of Begg's test and Egger's test are shown in Table IV.

Discussion

SysPbx is the standard method for the diagnosis of PCa, and the extended 12-core scheme is a commonly suggested approach[34]. However, up to 50% of PCa detected by sysPbx might be cinsPCa, resulting in overdiagnosis and overtreatment. In addition, sysPbx was more likely to miss aggressive diseases than fusPbx or comPbx, leading to a risk of undertreatment[35]. The optimal biopsy method for patients with suspected PCa lesions on MRI is still controversial[36,37]. With the development of mpMRI, the detection and localization of PCa have been improved. Less suspicious lesions on mpMRI were associated with

Table II. Meta-regression analysis for overall PCa detection rates comparing fusPbx and sysPbx.

Heterogeneity factor	Coefficient	SE	*t*	*p*
Publication year	-0.1053886	0.067276	-1.57	0.137
Sample size	-0.0089984	0.0783074	-0.11	0.910
Biopsy history	0.0900084	0.0374094	2.41	0.029
Patient age (year)	0.0912272	0.0528665	1.73	0.104
PSA(ng/ml)	0.081103	0.0565079	1.44	0.170
Prostate volume(ml)	0.0274181	0.0458071	0.60	0.558
Route of fusPbx	0.2589475	0.0948324	2.73	0.015
Route of sysPbx	0.2032035	0.1676565	1.21	0.243
SysPbx first	-0.0095122	0.077733	-0.12	0.904

Notes: PCa, prostate cancer; PSA, prostate-specific antigen; fusPbx, magnetic resonance imaging/ultrasound fusion targeted biopsy; sysPbx, systemic biopsy.

Table III. Meta-regression analysis for csPCa detection rates comparing fusPbx and sysPbx.

Heterogeneity factor	Coefficient	SE	*t*	*p*
Publication year	-0.1008576	0.093297	-1.08	0.301
Sample size	0.03931	0.1109198	0.35	0.729
Biopsy history	0.1516582	0.0572955	2.65	0.021
Patient age (year)	0.1532366	0.0685676	2.23	0.045
PSA(ng/ml)	0.1550283	0.0702688	2.21	0.048
prostate volume(ml)	0.1000505	0.0581539	1.72	0.111
Route of fusPbx	0.1247449	0.1351495	0.92	0.374
Route of sysPbx	0.4880355	0.2727657	1.79	0.099
SysPbx first	-0.1561669	0.0931273	-1.68	0.119

Notes: csPCa, clinically significant prostate cancer; PSA, prostate-specific antigen; fusPbx, magnetic resonance imaging/ultrasound fusion targeted biopsy; sysPbx, systemic biopsy.

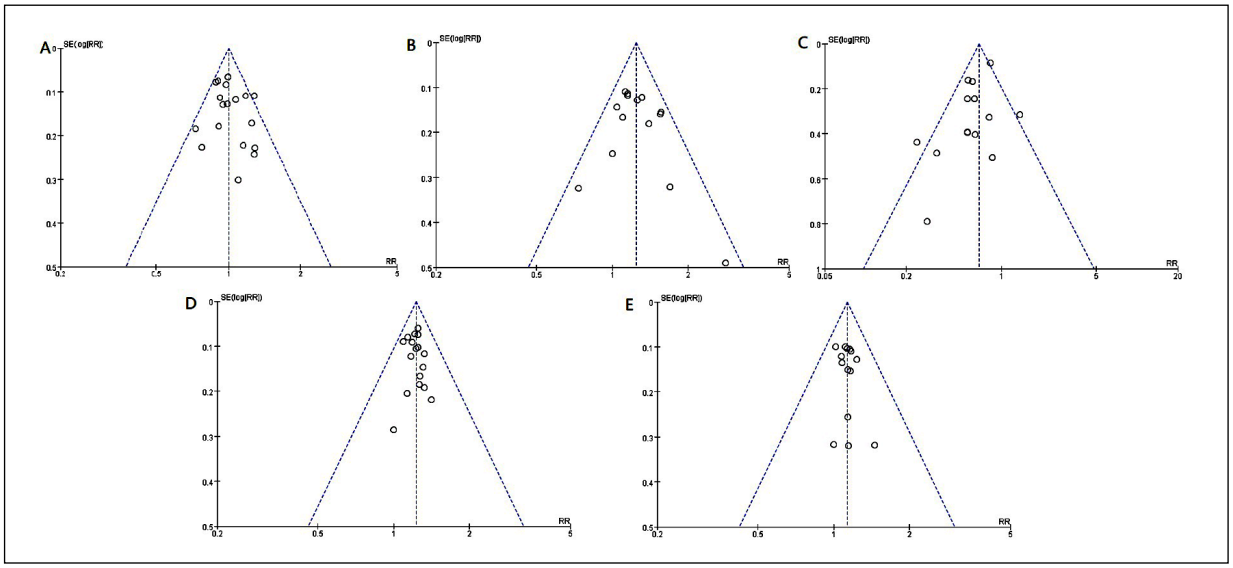

Figure 5. Funnel plot of five comparisons. **A,** Overall PCa detection rates of fusPbx versus sysPbx. **B,** csPCa detection rates of fusPbx versus sysPbx. **C,** cinsPCa detection rates of fusPbx versus sysPbx. **D,** Overall PCa detection rates of comPbx versus fusPbx. **E,** csPCa detection rates of comPbx versus fusPbx. PCa, prostate cancer; csPCa, clinically significant prostate cancer; cinsPCa, clinically insignificant prostate cancer; fusPbx, magnetic resonance imaging/ultrasound fusion targeted biopsy; sysPbx, systemic biopsy; comPbx, fusPbx combined with systemic biopsy.

Table IV. *p* value of the Begg's test and Egger's test.

Comparion	PCa	Begg's *p* value	Egger's *p* value
FusPbx vs sysPbx	Overall PCa	0.705	0.329
	csPCa	0.381	0.396
	cinsPCa	0.443	0.069
ComPbx vs fusPbx	overall PCa	0.837	0.677
	csPCa	0.324	0.366

Notes: PCa, prostate cancer; csPCa, clinically significant prostate cancer; cinsPCa, clinically insignificant prostate cancer; fusPbx, magnetic resonance imaging/ultrasound fusion targeted biopsy; sysPbx, systemic biopsy; comPbx, fusPbx combined with systemic biopsy.

cinsPCa or negative prostate biopsies[38]. Siddiqui et al[39] reported that mpMRI may identify only csPCa without overdiagnosing cinsPCa. MpMRI can accurately identify the lesion areas that can be used as targets, and image fusion technology makes real-time target biopsy more convenient. FusPbx can be performed in the clinical environment rather than the MRI suite, which requires dedicated MRI-compatible hardware[19]. Moreover, fusPbx can accurately detect the true pathological grade of patients and reduce the possibility of misdiagnosing cinsPCa. Thus, the incidences of both overtreatment and undertreatment would be reduced due to the reduction in diagnostic uncertainty[28,40,41].

In our study, there was no significant difference in overall PCa detection rates between fusPbx and sysPbx. However, the subgroup analysis found that fusPbx detected fewer PCa cases in biopsy-naive patients than sysPbx. In addition, fusPbx and sysPbx did not significantly differ in overall PCa detection rates of patients who received at least one negative previous biopsy. Vourganti et al[31] reported that fusPbx detected PCa in 34-37% of patients with previously negative sysPbx, of whom one-third had a Gleason score ≥ 7. Therefore, more large-sample research is needed to show significant differences among these methods. In the subgroup analysis, fusPbx significantly detected more PCa cases than sysPbx in patients who underwent transperineal fusPbx (TP-fusPbx). Nonetheless, fusPbx was not superior to sysPbx in detecting PCa in patients who underwent transrectal fusPbx (TR-fusPbx). It has been suggested that the most missed anatomic sites of PCa are the apical, dorsolateral, and anterior prostatic segments, which are easy to puncture in the transperineal pathway[42]. Thus, it can be concluded that the transperineal approach helps to improve the overall detection rates of PCa. Compared to transrectal approaches, the transperineal approach has a lower infection risk, and its infection-related hospitalization rate is negligible[43,44]. However, transperineal biopsy typically requires patient sedation and adequate local anaesthesia in the perineal area or general anaesthesia, which impose restrictions on its widespread use.

When compared with sysPbx, fusPbx had a significantly increased detection rate for csPCa and significantly reduced detection rate for cinsPCa. However, in the subgroup with ≤ 100 samples, fusPbx did not outperform sysPbx in detecting csPCa, so sample size might be crucial to show the superiority of fusPbx. In the three cohorts that underwent sysPbx first, fusPbx and sysPbx did not significantly differ in detecting csPCa. Some studies[18,45] have suggested that performing sysPbx first may lead to bleeding and oedema of the prostate tissue, which then affect the target of fusPbx and decrease the detection rate. However, performing fusPbx first will also reduce the csPCa detection rate of sysPbx since the tissue of the clinically significant area has been removed.

Compared with sysPbx, fusPbx can not only significantly increase the detection rates for csPCa but also reduce the number of biopsy cores needed. Some studies have noted that 12-core sysPbx may be replaced by fusPbx, especially for diseases with prostate imaging reporting and data system (PIRADS) scores of 4 and 5 detected by mpMRI[46,47]. It has been reported that omitting fusPbx can reduce the number of csPCa cases that can be detected by combined biopsies by nearly 25% in MRI-positive patients[10]. However, fusPbx also has drawbacks. Due to some differences in the definition of csPCa in the included studies that performed fusPbx, there is an urgent need for a new unified standard to define csPCa in clinical practice[34]. In our research, we found that compared to fusPbx, comPbx significantly increased

the detection rates of overall PCa and csPCa. Ahdoot et al[48] performed comPbx in 2103 patients with lesions on mpMRI, and they found that performing fusPbx or sysPbx alone led to missed diagnoses of PCa patients with an International Society of Urological Pathology (ISUP) grade ≥ 2. The number of patients who underwent comPbx and were upgraded to grade 3 or higher after radical prostatectomy was significantly reduced (3.5%) compared with that of patients who underwent fusPbx (8.7%) or sysPbx (16.8%) alone. Meta-analysis has indicated that both fusPbx and sysPbx may omit csPCa and that comPbx is better in detecting csPCa than fusPbx or sysPbx alone[49]. Adding fusPbx to sysPbx also helps to reduce the detection of cinsPCa[10,16]. In summary, comPbx is a more reasonable choice for patients with one or more suspected PCa lesions on mpMRI.

Our study also has some limitations. First, although no publication bias was found in our study, we only searched three databases and included only English published literature. Second, there are some differences in the image fusion platforms as well as in the definition of csPCa, and the impact of these factors on the results is still unclear. Third, we lack a recognized scoring system for suspected PCa lesions on mpMRI, so the criteria for each study are not entirely consistent.

Conclusions

We comprehensively analysed the current high-level clinical studies that evaluated fusPbx and sysPbx or both to determine the most effective biopsy method for men with positive mpMRI. To our knowledge, few studies have used the detection rates for comPbx versus those for fusPbx as a primary endpoint. We found that fusPbx had no significant advantage over sysPbx in overall PCa detection rates but could significantly increase the detection rates for csPCa and decrease those for cinsPCa. Compared with fusPbx, comPbx can significantly increase the detection rates for overall PCa and csPCa. Therefore, we believe that comPbx is a more advantageous biopsy method for patients with suspected PCa lesions on mpMRI.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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