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Micro-Ultrasound–Guided vs Multiparametric Magnetic Resonance Imaging-Targeted Biopsy in the Detection of Prostate Cancer: A Systematic Review and Meta-Analysis

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Abbreviations and Acronyms

DR = detection ratio
DRE = digital rectal examination
GG = Grade Group
mp = multiparametric
MRI = magnetic resonance imaging
PB = prostate biopsy
PCa = prostate cancer
PI-RADS™ = Prostate Imaging Reporting and Data System
PRI-MUS = prostate risk identification using micro-ultrasound
PSA = prostate specific antigen
SB = systematic biopsy
TRUS = transrectal ultrasound
US = ultrasound

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Purpose: Micro-ultrasound is a novel high resolution ultrasound technology aiming to improve prostate imaging and, consequently, the diagnostic accuracy of ultrasound-guided prostate biopsy. Micro-ultrasound–guided prostate biopsy may present comparable detection rates to the standard of care multiparametric magnetic resonance imaging-targeted prostate biopsy for the diagnosis of clinically significant prostate cancer. We aimed to compare the detection rate of micro-ultrasound vs multiparametric magnetic resonance imaging-targeted prostate biopsy for prostate cancer diagnosis.

Materials and Methods: We performed a systematic review and meta-analysis of diagnostic accuracy studies comparing micro-ultrasound–guided prostate biopsy to multiparametric magnetic resonance imaging-targeted prostate biopsy as a reference standard test (PROSPERO ID: CRD42020198326). Records were identified by searching in PubMed®, Scopus® and Cochrane Library databases, as well as in potential sources of gray literature until November 30th, 2020.

Results: We included 18 studies in the qualitative and 13 in the quantitative synthesis. In the quantitative synthesis, 1,125 participants received micro-ultrasound–guided followed by multiparametric magnetic resonance imaging-targeted and systematic prostate biopsy. Micro-ultrasound and multiparametric magnetic resonance imaging-targeted prostate biopsies displayed similar detection rates across all prostate cancer grades. The pooled detection ratio for International Society of Urological Pathology Grade Group $\geq$2 prostate cancer was 1.05 (95% CI 0.93–1.19, I^2=0%), 1.25 (95% CI 0.95–1.64, I^2=0%) for Grade Group $\geq$3 and 0.94 (95% CI 0.73–1.22, I^2=0%) for clinically insignificant (Grade Group 1) prostate cancer. The overall detection ratio for prostate cancer was 0.99 (95% CI 0.89–1.11, I^2=0%).

Conclusions: Micro-ultrasound–guided prostate biopsy provides comparable detection rates for prostate cancer diagnosis with the multiparametric magnetic resonance imaging-guided prostate biopsy. Therefore, it could be considered as an attractive alternative to multiparametric magnetic resonance imaging-targeted prostate biopsy. Nevertheless, high quality randomized trials are warranted to corroborate our findings.

Key Words: diagnostic imaging, biopsy, prostatic neoplasms, systematic reviews as topic, meta-analysis as topic

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Prostate cancer is the most common noncutaneous malignancy in males, with about 1.3 million cases globally and 360,000 deaths every year.[1] It is usually diagnosed by prostate biopsy, with more than 2 million procedures performed yearly in Europe and the U.S.[2] Prostate cancer diagnosis has traditionally been anchored on random prostate sampling by systematic transrectal ultrasound-guided 10 to 12-core prostate biopsy.[3,4] However, conventional transrectal ultrasound is not reliable in detecting prostate cancer as the majority of such tumors are isoechoic and, therefore, not visible.[5] Multiparametric magnetic resonance imaging has brought on a revolution in prostate imaging, and multiparametric magnetic resonance imaging-guided prostate biopsy of suspicious lesions is currently recommended in combination with systematic transrectal ultrasound-guided prostate biopsy for biopsy-naïve patients.[6]

Over the last few decades, various ultrasound modalities have been developed in an attempt to improve prostate imaging. Computerized TRUS,[7] shear wave elastography[8] and contrast-ultrasound dispersion imaging[9] present interesting results, but there is insufficient evidence to change the current diagnostic pathway of PCa.[10] High resolution micro-ultrasound is a novel imaging modality, developed by Exact Imaging (Toronto, Ontario, Canada), aiming to improve the diagnostic accuracy of TRUS-guided PB. Micro-ultrasound allows for better appreciation of microstructures and tissue planes, as it operates at 29 MHz, instead of 8−12 MHz with the conventional ultrasound systems, and provides resolution down to 70 μm, 300% higher than the existing platforms.[11] In accordance with the PI-RADS™ 2.1 protocol for mpMRI,[12] suspicious prostate lesions are identified in real-time via micro-ultrasound with the PRI-MUS protocol.[13]

Data suggest that micro-ultrasound−guided PB provides greater sensitivity in detecting clinically significant PCa than conventional TRUS-guided PB[14] and may even present comparable detection rates to mpMRI-targeted PB for clinically significant PCa cases.[15] In this scope, we generated a systematic review and meta-analysis aiming to assess the detection rate of micro-ultrasound−guided PB compared to mpMRI-targeted PB for clinically significant and insignificant PCa diagnosis.

METHODS

This systematic review and meta-analysis is reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement and its extension for diagnostic test accuracy studies (PRISMA-DTA).[16] The aims and methods of our study were prespecified, registered in a protocol at PROSPERO and revised according to the peer review comments (ID: CRD42020198326). In lieu of a formal ethics committee, the principles of the Helsinki Declaration were followed

Search Strategy

We systematically searched PubMed, Cochrane Library and Scopus databases from inception to November 30, 2020 for studies comparing the detection rate of high resolution micro-ultrasound−guided vs mpMRI-targeted PB for PCa. We also conducted a targeted search of the potentially gray literature, including conference abstracts published in major urology journals, clinical trial registries (clinicaltrials.gov) and websites providing appropriate information about relevant trials (exactimaging.com). Moreover, we hand-searched the reference lists of all eligible studies and reviews. All searches were performed by 2 independent reviewers (PS, NP). The detailed search syntax and search string are presented in supplementary Appendix 1 (https://www.jurology.com).

Inclusion and Exclusion Criteria

We included prospective or retrospective diagnostic accuracy studies, that each individual underwent consecutively micro-ultrasound and mpMRI-targeted PB. On the contrary, we excluded studies comparing high resolution micro-ultrasound or mpMRI-targeted PB vs systematic PB. Additionally, we excluded case reports and single-arm studies. When multiple records with potential overlapping populations were identified, the most recent or the study reported as full text was only included.

Data Extraction and Quality Assessment

Two authors (PS, NP) screened for eligibility all identified records. Any disagreements were resolved by consensus. Data collection was performed independently in a predefined Microsoft® Excel® spreadsheet. For each included record, we retrieved information about study and participant characteristics, interventions and PCa classification according to International Society of Urological Pathology GG. Micro-ultrasound−guided PB was considered the index test and mpMRI-targeted PB the comparator test (reference standard). To ensure consistency in reviewing, we conducted a pilot test prior to data extraction.[17]

We estimated the risk of bias and applicability concerns of each study using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.[18] QUADAS-2 comprises 4 domains that include patient selection, index test, reference standard, and flow and timing. Each domain is evaluated in terms of risk of bias, while the first 3 domains are also evaluated in terms of applicability concerns.[18] Quality assessment was performed by 2 authors (NP, IM) and any discrepancies were resolved through consensus. Accordingly, we evaluated the risk of bias across studies (publication bias) via visual assessment of contour-enhanced funnel plot asymmetry and the Egger test.[19]

Grading of Evidence, Data Synthesis and Statistical Analysis

We determined the overall strength of evidence for the detection rate of clinically significant, clinically insignificant and any PCa between micro-ultrasound−guided and

mpMRI-targeted PB using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.[20] Two reviewers (PS, NP) graded risk of bias, inconsistency, indirectness, imprecision and publication bias among included trials. The detection rate was estimated as the number of participants diagnosed with the relevant GG of PCa for each outcome divided by the number of participants who underwent both micro-ultrasound–guided and mpMRI-targeted PB.[21]

We performed an inverse variance random effects meta-analysis of detection ratios. DR was estimated as the micro-ultrasound–guided PB detection rate divided by the mpMRI-targeted PB detection rate. More specifically, we synthesized DRs with the corresponding 95% CIs for the following outcomes: 1) micro-ultrasound vs mpMRI-targeted PB for clinically significant PCa (GG $\geq$2); 2) micro-ultrasound vs mpMRI-targeted PB for clinically significant PCa (GG $\geq$3); 3) micro-ultrasound vs mpMRI-targeted PB for clinically insignificant PCa (GG 1); and 4) micro-ultrasound vs mpMRI-targeted PB for any grade of PCa.

We performed a subgroup analysis based on the type of study reporting outcomes (full text article, conference abstract or multicenter registry by Exact Imaging), according to the type of MRI targeting method (cognitive or fusion), as well as based on whether the operator was blinded or unblinded to the mpMRI results at the time of micro-ultrasound–guided PB. Accordingly, we undertook a sensitivity analysis including studies at low risk of bias and with low applicability concern. A study was considered at low risk of bias and at low applicability concern when it scored low in all domains. We calculated heterogeneity with the I^2 and determined its significance with the p value of the Cochran Q test.[19] For all estimations, p values lower than 0.05 were considered statistically significant. All analyses were performed with R 3.6.3 (R Project for Statistical Computing, Vienna, Austria) using the "meta" package.

RESULTS

Study Results and Quality Assessment

The initial literature search yielded 1,450 potentially relevant records after removal of duplicates. At the end of the process, 15 studies were included in the systematic review.[22–34] Of these, 2 were excluded from the meta-analysis, as they did not provide relevant outcomes.[33,34] Overall, 8 trials were published as full texts, 4 as conference abstracts and 3 in 1 prospective multicenter registry study provided by Exact Imaging. Regarding the latter, all centers reporting data on the detection rate of micro-ultrasound vs mpMRI-targeted PB regularly updated their registries and republished their patient series. The step-by-step selection process of studies is illustrated in supplementary Appendixes 2 and 3 (https://www.jurology.com).

Applying the QUADAS-2 tool for the included published studies, the overall methodological quality was evaluated as moderate. In particular, regarding the risk of bias, 5 trials were considered to be of low risk, 8 of moderate risk and 2 of high risk of bias. Regarding the applicability concerns, 12 trials were considered to be of low and 3 of moderate concern. The detailed assessment is available in supplementary Appendix 4 (https://www.jurology.com).

Study Characteristics

A total of 1,683 participants from 15 published trials with a mean±SD age of 65.9±8.4 years were analyzed. Ultimately, 1,391 participants underwent both micro-ultrasound–guided and mpMRI-targeted PB. In all studies, patients underwent micro-ultrasound–guided PB first, followed by mpMRI-targeted PB and by 10 or 12-core systematic TRUS-guided PB. The histological results of the exact GG after radical prostatectomy were not provided in any study. PBs were performed by a transrectal or a transperineal approach under local or general anesthesia and no complications were reported during all procedures.

Across all studies, suspicious lesions were defined as PI-RADS $\geq$3[12] and PRI-MUS $\geq$3.[13] In studies reporting the number of core samples per target, micro-ultrasound–guided PB required fewer specimens than mpMRI-targeted PB. The operators performing micro-ultrasound–guided PB received appropriate training and all mpMRIs were evaluated by a radiologist experienced in mpMRI. Moreover, all mpMRIs were performed with a strength of 1.5 or 3 Tesla with or without endorectal coil placement. Regarding the type of mpMRI-targeted PB, a cognitive approach was preferred in 9 and a fusion targeting system in 6 studies. The operator was blinded to the MRI results at the time of micro-ultrasound–guided PB in 4 studies and unblinded in 11. The characteristics of the included study records are depicted in the table.

Clinically Significant PCa Detection Rate

In the analysis of men with GG $\geq$2 PCa, we included a total of 13 studies comprising 1,125 participants receiving micro-ultrasound–guided, followed by mpMRI-targeted and systematic PB.[22–32] By adding the results of the 3 techniques, 437 patients with GG $\geq$2 PCa were identified. The micro-ultrasound–guided PB identified 341 and the mpMRI-targeted PB 327 cases (DR 1.05, 95% CI 0.93–1.19, I^2=0%, fig. 1). In the subgroup analysis based on the type of study reporting outcomes, no significant differences were observed among full texts, conference abstracts and the Exact Imaging registry (p=0.92). Similarly, no significant differences were demonstrated between studies performing a cognitive or a fusion MRI targeting method (p=0.29, supplementary Appendix 5.1, https://www.jurology.com), as well as between studies in whom the operator was blinded or unblinded to the mpMRI results at the time of micro-ultrasound–guided PB

Baseline characteristics of included studies

References	Study Period	Compared Techniques	Population	No. Pts	Mean±SD Age (yrs)	Mean±SD PSA (ng/dl)	No. Abnormal DRE	Mean±SD Prostate Vol (ml)	No. Pts Undergoing Micro-US +mpMRI Biopsy	Cores/Micro-US Target	Cores/mpMRI Target
Abouassaly et al[22]	01/18—08/18	Micro-US vs mpMRI vs SB	Suspicion of PCa	67	65±7.4	5.9±3.4	7	37.5±19.3	19	Mean±SD 2.3±0.7	Mean±SD 2.9±0.4
Cornud et al[33]	02/19—07/19	Micro-US vs mpMRI	Suspicion of PCa+at least 1 mpMRI lesion (PI-RADS ≥3)	118	66±13	11±19	16	53±26	118	Mean±SD 5±2	Mean±SD 5±2
Eure et al[23]	12/16—12/16	Micro-US vs mpMRI vs SB vs conventional transrectal US	Men with PCa in active surveillance protocol	9	65.6±4.4	6±1.1	9	38.8±8.2	9	2—3	2—3
Klotz et al[24]	Not available	Micro-US vs mpMRI vs SB	Suspicion of PCa	77	Not available	Not available	Not available	Not available	77	Not available	Not available
Lopez et al[25]	Not available	Micro-US vs mpMRI vs SB	Elevated PSA or abnormal DRE	51	Not available	Not available	Not available	Not available	51	Not available	Not available
Luger, as reported by Klotz et al[24]	Not available	Micro-US vs mpMRI vs SB	Suspicion of PCa	62	Not available	Not available	Not available	Not available	62	Not available	Not available
Lughezzani et al[26]	10/17—09/19	Micro-US vs mpMRI vs SB	Suspicion of PCa+at least 1 mpMRI lesion (PI-RADS ≥3)	320	64.7±8.2	7.5±3.5	72	48.3±29.6	320	Mean±SD 4.3±2.2	Mean±SD 4.3±2.2
Martel et al[34]	05/18—03/19	Micro-US vs mpMRI vs SB	Biopsy-naïve pts, pts with previous neg biopsy or on active surveillance, or pts undergoing PCa stratification	148	66.3±8.2	7.3±4.3	Not available	Not available	148	Not available	Not available
Pereira-Arias et al[27]	02/17—01/18	Micro-US vs mpMRI vs SB	Elevated PSA or abnormal DRE	96	67±5.5	7.5±5.6	Not available	56±16.3	79	2	2
Perez[28]	Not available	Micro-US vs mpMRI vs SB	Suspicion of PCa+available mpMRI	55	Not available	15.3±9	Not available	Not available	55	Not available	Not available
Claros et al[29]	02/17—09/18	Micro-US vs mpMRI vs SB	Suspicion of PCa+at least 1 mpMRI lesion (PI-RADS ≥3)	269	67.5±7.4	7.8±3.5	Not available	49.5±21.5	47	Mean±SD 3±1.5	Mean±SD 3±1.5
Shore, as reported by Klotz et al[24]	Not available	Micro-US vs mpMRI vs SB	Suspicion of PCa	14	Not available	Not available	Not available	Not available	14	Not available	Not available
Rodríguez-Socarrás et al[30]	02/18—09/19	Micro-US vs mpMRI vs SB	Elevated PSA or suspicious DRE or PI-RADS ≥3 in mpMRI	194	62±7.4	6.5±3.3	31	58.1±33.3	194	Mean±SD 2±1.5	Mean±SD 2.3±2.2
Staerman[31]	11/17—04/19	Micro-US vs mpMRI vs SB	Men with PCa in active surveillance protocol	44	Not available	Not available	Not available	Not available	39	Not available	Not available
Wiemer et al[32]	02/18—12/18	Micro-US vs mpMRI vs SB	Suspicion of PCa	159	69.5±7.4	8.2±4.2	42	54.5±17	159	2-3	2-3

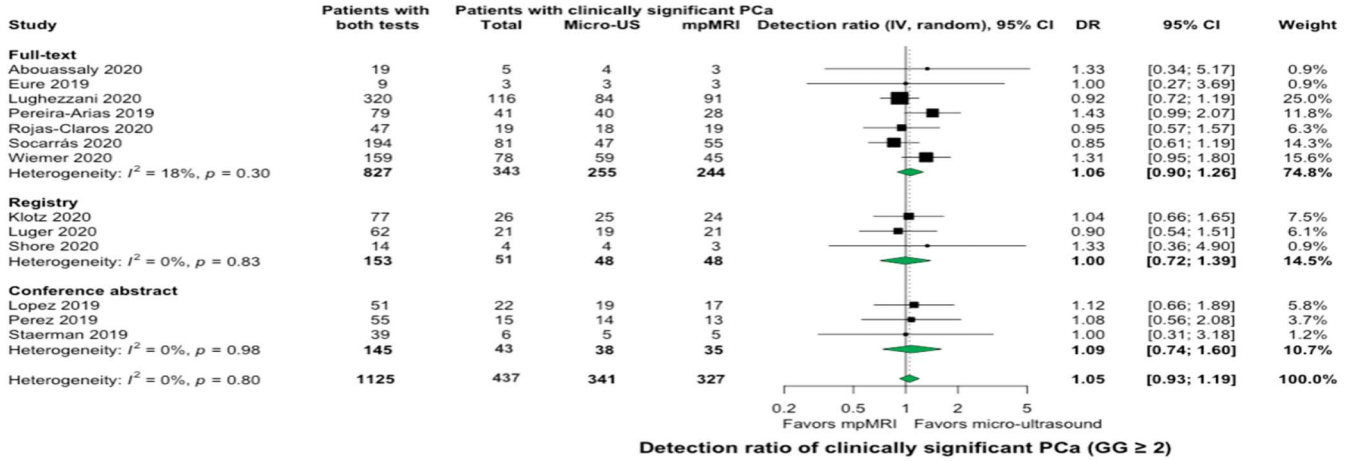

Figure 1. Forest plot of detection rate of micro-ultrasound vs mpMRI-targeted prostate biopsy for clinically significant PCa (GG ≥2). Studies were grouped by type of reported outcomes. *IV*, inverse variance.

(p=0.45, supplementary Appendix 6.1, https://www.jurology.com). This effect was also evident in the sensitivity analysis of the 5 cohort studies with good methodological quality (DR 1.08, 95% CI 0.87–1.35, I^2=43%, supplementary Appendix 7.1, https://www.jurology.com). Additionally, funnel plot inspection and Egger statistical testing did not indicate any important publication bias among the trials included in our quantitative synthesis (p=0.67, supplementary Appendix 8, https://www.jurology.com).

Regarding patients with GG ≥3 PCa, a total of 5 cohort studies with 546 individuals receiving micro-ultrasound–guided followed by mpMRI-targeted and systematic PB provided relevant data.[22,23,26,31,32] Ultimately, 122 cases of GG ≥3 PCa were reported by adding the results of the 3 techniques. The micro-ultrasound–guided PB identified 99, while the mpMRI-targeted PB 79 patients (DR 1.25, 95% CI 0.95–1.64, I^2=0%, fig. 2). No significant difference was calculated between the 4 full texts and the conference abstract (p=0.77), as well as between studies with cognitive or fusion MRI targeting method (p=0.69, supplementary Appendix 5.2, https://www.jurology.com) and studies in whom the operator was blinded or unblinded to the mpMRI results at the time of micro-ultrasound–guided PB (p=0.7, supplementary Appendix 6.2, https://www.jurology.com). Three studies with good methodological quality reported the cases of GG ≥3 PCa. No significant difference was demonstrated between micro-ultrasound–guided PB and mpMRI-targeted PB (DR 1.27, 95% CI 0.96–1.68, I^2=0%, supplementary Appendix 7.2, https://www.jurology.com).

Clinically Insignificant and Overall PCa Detection Rate

A total of 9 cohort studies with 893 patients undergoing consecutively micro-ultrasound–guided, mpMRI-targeted and systematic PB reported cases of clinically insignificant PCa (GG 1).[22,23,25,26,28–32] The total number of men with clinically insignificant PCa was 158, of which 95 were identified after micro-ultrasound–guided PB and 102 after mpMRI-

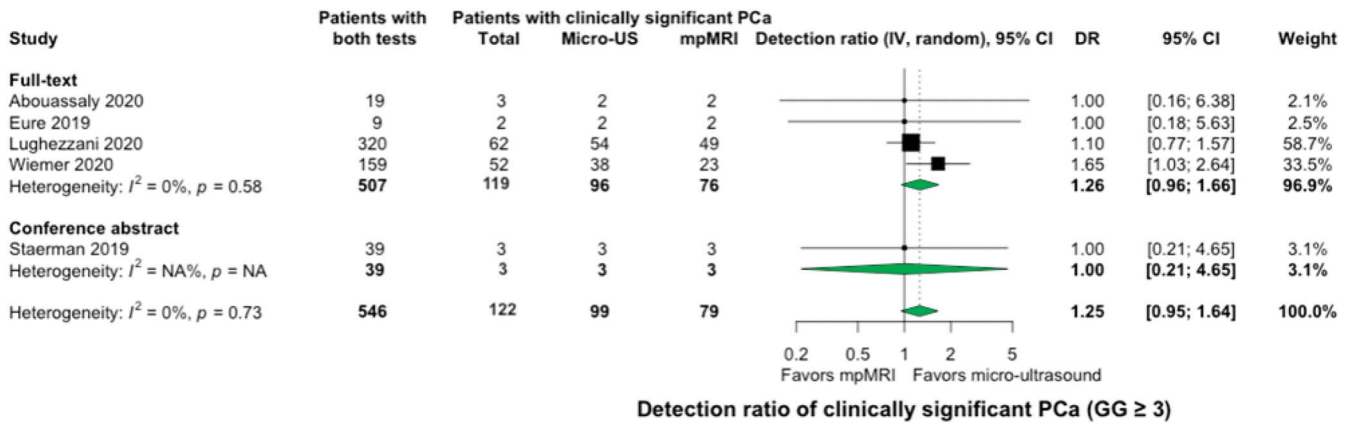

Figure 2. Forest plot of detection rate of micro-ultrasound vs mpMRI-targeted prostate biopsy for clinically significant PCa (GG ≥3). Studies were grouped by type of reported outcomes. *IV*, inverse variance. *NA*, not available.

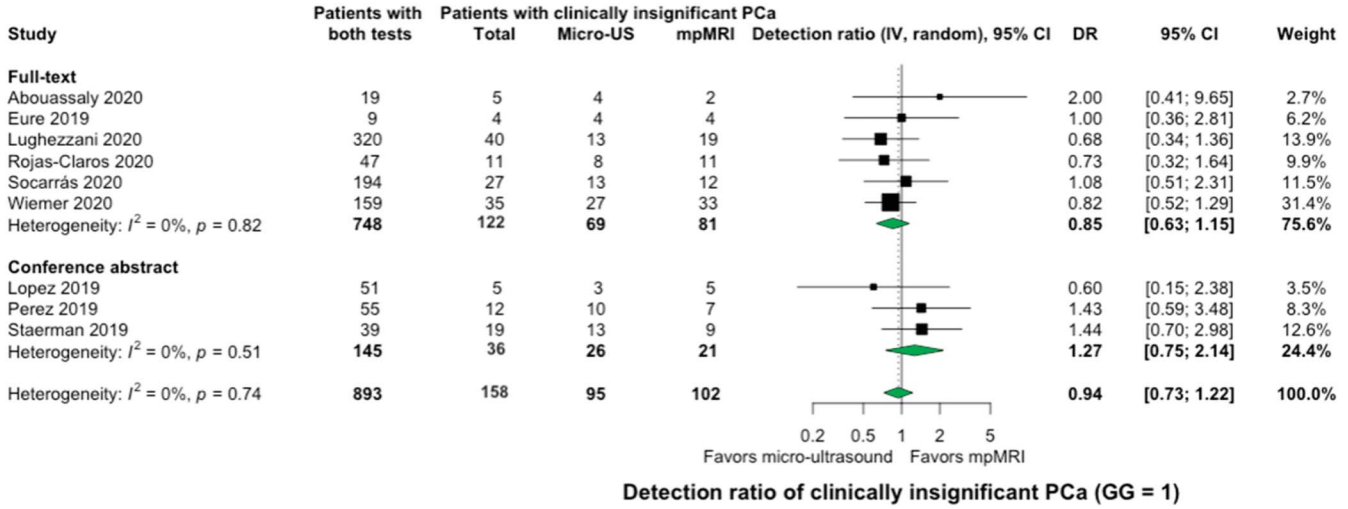

Figure 3. Forest plot of detection rate of micro-ultrasound vs mpMRI-targeted prostate biopsy for clinically insignificant PCa (GG 1). Studies were grouped by type of reported outcomes. *IV,* inverse variance.

targeted PB (DR 0.94, 95% CI 0.73–1.22, I^2=0%, fig. 3). Regarding the type of reported outcomes, a nonsignificant difference was estimated between the 6 full texts and the 3 conference abstracts (p=0.19). Accordingly, no significant difference was calculated between studies performing mpMRI-targeted PB with cognitive or fusion method (p=0.42, supplementary Appendix 5.3, https://www.jurology.com), as well as between studies in whom the operator was blinded or unblinded to the mpMRI findings at the time of micro-ultrasound–guided PB (p=0.28, supplementary Appendix 6.3, https://www.jurology.com). Similar results were observed in the sensitivity analysis of the 4 studies with good methodological quality (DR 0.84, 95% CI 0.61–1.17, I^2=0%, supplementary Appendix 7.3, https://www.jurology.com).

The same 9 cohort studies reported the total cases of PCa diagnosed through micro-ultrasound–guided, mpMRI-targeted and systematic PB.[22,23,25,26,28–32] From the 503 individuals with positive biopsy, 348 were diagnosed by micro-ultrasound–guided PB and 353 by mpMRI-targeted PB (DR 0.99, 95% CI 0.89–1.11, I^2=0%, fig. 4). Nonstatistically significant differences were observed in the subgroup analysis based on the type of study reporting outcomes (p=0.28). Furthermore, no significant differences were estimated between mpMRI-targeted PB that were performed with a cognitive or fusion method (p=0.76, supplementary Appendix 5.4, https://www.jurology.com), as well as between studies in whom the operator was blinded or unblinded to the mpMRI findings at the time of micro-ultrasound–guided PB

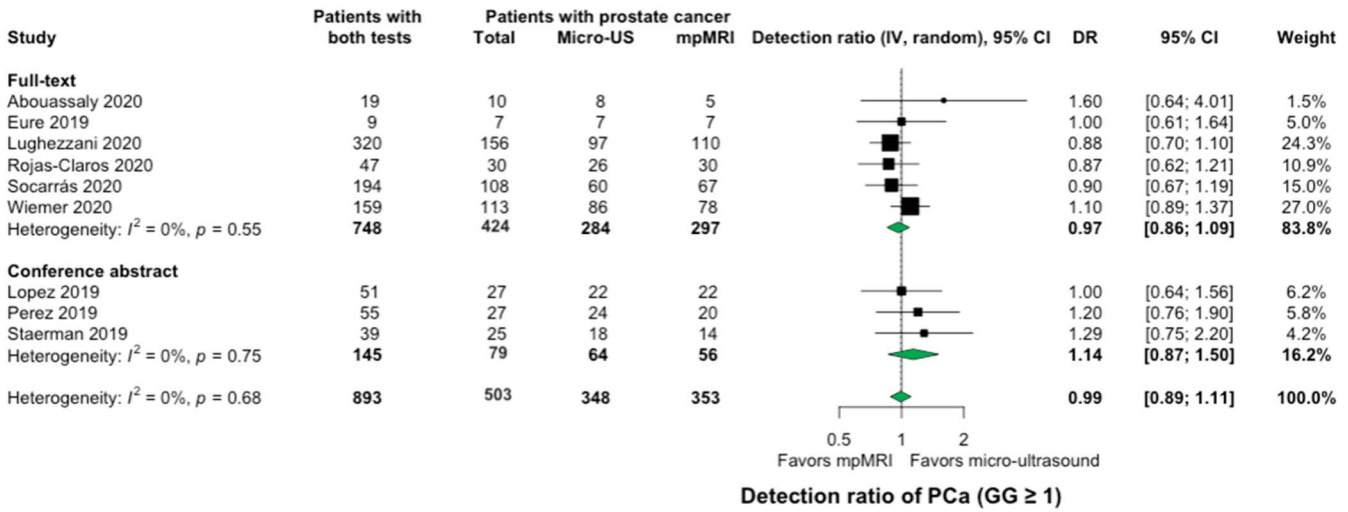

Figure 4. Forest plot of detection rate of micro-ultrasound vs mpMRI-targeted prostate biopsy for any grade of PCa. Studies were grouped by type of reported outcomes. *IV,* inverse variance.

($p=0.56$, supplementary Appendix 6.4, https://www.jurology.com). These results were also demonstrated in the sensitivity analysis based on studies with good methodological quality (DR 0.97, 95% CI 0.85−1.11, $I^2=0\%$, supplementary Appendix 7.4, https://www.jurology.com).

Grading of Evidence

Although the importance of our findings was deemed critical, the overall strength of evidence was considered low for all outcomes between the reviewers. The fact that the operators performing micro-ultrasound−guided PB were not familiar with this novel technique might have reduced the detection rate of micro-ultrasound in PCa diagnosis. On the other hand, the observational design of all studies, the unclear or high risk of bias of some trials and the fact that about half of the included records were published as conference abstracts or registries downgraded the quality of evidence. The detailed grading is summarized in supplementary Appendix 9 (https://www.jurology.com).

DISCUSSION

This systematic review and meta-analysis suggests that micro-ultrasound−guided PB should be considered as an alternative diagnostic modality to mpMRI-targeted PB. Based on our findings, the detection rate of clinically significant and insignificant PCa, as well as the overall detection rate of PCa were similar between micro-ultrasound−guided and mpMRI-targeted PB. Of interest, these findings were consistent in the subgroup and sensitivity analyses. In particular, including only studies that underwent the peer review process or studies at low risk of bias and at low applicability concern, we demonstrated that micro-ultrasound−guided PB and mpMRI-targeted PB display similar detection rates. Similarly, neither the MRI targeting method (cognitive or fusion approach) nor the status of the operator at the time of micro-ultrasound−guided PB (blinded or unblinded to the mpMRI results) affected the DR of the 2 diagnostic modalities.

The addition of mpMRI-targeted to systematic TRUS-guided PB has led to an improvement in the diagnosis of clinically significant PCa.[35,36] Still, patients should undergo both types of PB,[6] as MRI-targeted PB may miss some clinically significant PCa cases.[37,38] In particular, it has been demonstrated that 16% to 35% of all lesions harboring clinically significant PCa remain undetected or underestimated by mpMRI.[39,40] Moreover, apart from the apparent drawbacks of cost and accessibility compared to TRUS-guided PB,[41] MRI-targeted PB presents also limited inter-reader and intraoperator reproducibility even among experienced radiologists.[42] Another limitation of mpMRI-guided PB is that the accurate interpretation of prostate mpMRI findings requires a high level of expertise and training.[43] Similarly, mpMRI-guided PB, either with cognitive or fusion approach, is usually performed via a TRUS probe, and thus is prone to cross-modality registration errors.[44]

Therefore, there is certainly space for more sophisticated ultrasound modalities that overcome the limitations of the mpMRI-guided PB and provide improved imaging and accuracy in PCa detection. Advances in imaging technologies have led to the development of the first 29 MHz micro-ultrasound system.[45] The ExactVu™ platform is a fast and urologist-friendly imaging modality that provides easier lesion targeting than mpMRI-targeted PB.[13,46] Moreover, micro-ultrasound follows the standardized schemes of conventional TRUS and is more sensitive in detecting clinically significant PCa than conventional TRUS.[14] Nonetheless, it should be stressed that the diagnostic accuracy of micro-ultrasound is limited by large prostate volume and specific tumor location, such as the transitional zone, while the accuracy of mpMRI is independent to these factors.[47]

According to a recent meta-analysis of 7 studies containing 769 patients, micro-ultrasound displays a sensitivity, specificity, diagnostic odds ratio and area under the summary ROC curve of 0.91, 0.49, 10 and 0.82, respectively.[48] Of interest, a study published as a conference abstract pooled data from 5 sites and included a total of 274 men undergoing consecutively micro-ultrasound−guided and mpMRI-targeted PB.[15] The authors concluded that micro-ultrasound−guided PB presents higher sensitivity and negative predictive value, similar positive predictive value and lower specificity than mpMRI-targeted PB. Still, a relevant prospective, multicenter registry, micro-ultrasound−guided PB presented similar specificity to mpMRI-targeted PD.[24] However, these data were not comparative, and thus the authors could not demonstrate the superiority of one diagnostic modality over the other.

Strengths and Limitations

In an attempt to overcome these biases and compare the 2 diagnostic modalities, we undertook a meta-analysis of DRs. In particular, we performed, to our knowledge, the first meta-analysis that compared the detection rate of micro-ultrasound−guided PB vs mpMRI-targeted PB for the the diagnosis of clinically significant, clinically insignificant and any PCa grade. Of interest, we validated the robustness of our findings by undertaking multiple subgroup and sensitivity analyses, which demonstrated that our results displayed minimal within and between-study variation. Still, it was beyond the scope of the present study to assess the sensitivity, specificity and

predictive value of the 2 diagnostic modalities. Similarly, given that systematic TRUS-guided PB is currently recommended to all patients undergoing PB,[6,36] we did not aim to compare the detection rate of micro-ultrasound–guided PB vs systematic TRUS-guided PB.

It should be stressed that the nonrandomized design of all included studies, as well as the low quality of most of the included studies downgraded the strength of available evidence, highlighting the need for randomized trials. Similarly, the relatively small number of included studies may also limit the generalizability of our findings. In particular, some of the included studies were not published as peer-reviewed, full text articles, while others raised performance bias concerns, as the operators were unblinded to the mpMRI findings at the time of the micro-ultrasound–guided PB. Furthermore, in most studies, data were collected retrospectively. Interestingly, given that broad eligibility criteria were applied across the included studies, our results may vary among different subgroups of patients undergoing PB. In particular, the included studies enrolled men with clinical suspicion of PCa, men on active surveillance protocols, PB-naïve individuals or patients with previous negative PB. Nevertheless, the absence of adequate relevant data did not allow us to conduct further predefined analyses.

Future Perspectives

It should be stressed that, although high resolution micro-ultrasound may constitute a step forward in the detection and localization of clinically significant PCa, further large-scale studies are necessary to validate the robustness of our findings. Most centers using the micro-ultrasound are expected to update their published patient series and the results of other centers conducting similar trials are anticipated with great interest. Furthermore, additional studies with blinded operators at the time of micro-ultrasound–guided PB or with advanced sophisticated fusion technologies for mpMRI-targeted PB may provide higher level of evidence regarding the absolute added value of each pathway compared to conventional systematic TRUS-guided PB. Moreover, studies aiming to determine the learning curve of micro-ultrasound and the interobserver agreement in the PRI-MUS score are also needed. Hence, it should be noted that due to the current lack of randomized controlled trials comparing micro-ultrasound to mpMRI in PCa diagnosis, high quality randomized trials are needed to evaluate the diagnostic accuracy of both pathways in clinically significant and insignificant PCa.

CONCLUSIONS

Our findings indicate that micro-ultrasound–guided PB displays similar detection rates for clinically significant and insignificant PCa to mpMRI-targeted PB. Due to its high sensitivity and negative predictive value as well as its ability to implement systematic PB with real-time targeting of suspicious lesions, micro-ultrasound may be an attractive diagnostic alternative to multiparametric MRI-targeted biopsy for the detection of PCa. Still, head-to-head randomized trials comparing micro-ultrasound–guided to mpMRI-targeted PB are warranted to corroborate our findings and to establish micro-ultrasound in the diagnostic algorithm of PCa.

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