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Head-to-Head Comparison of Magnetic Resonance Imaging and Micro-Ultrasound for Prostate Cancer — A Systematic Review and Meta-Analysis

Garcia Becerra, CA; Santana do Carmo, Y; Kleinfelder Molinari, V; Arias Gallardo, MI; Juarez Garcia, JE; Soltero Molinar, V; Garcia Gutierrez, CM.

Corresponding author:
Carlos Alberto Garcia Becerra

agbcarlos94@gmail.com

Author Affiliation:
Urovallarta medical center.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - The authors declare no conflicts of interest related to this systematic review and meta-analysis. No financial support, grants, or other benefits from commercial sources were received that could have influenced the study's findings. The research was conducted independently, with no involvement from pharmaceutical companies.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 8 April 2025 and was last updated on 8 April 2025.

INTRODUCTION

Review question / Objective In patients undergoing prostate cancer screening, how does micro-ultrasound image guidance compare to multiparametric MRI image guidance for prostate biopsy in terms of diagnostic accuracy (sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio, and area under the curve) based on evidence from randomized controlled trials and prospective observational studies?

Rationale Prostate cancer is the second most frequently diagnosed malignancy in men worldwide and remains a leading cause of cancer-related deaths. Timely and accurate detection is essential for optimizing treatment strategies and minimizing disease-related morbidity and mortality. Current screening methods primarily rely on prostate-specific antigen (PSA) testing and multiparametric magnetic resonance imaging (mpMRI); however, a definitive diagnosis typically requires a prostate biopsy.

mpMRI has become a widely utilized and validated imaging tool for risk assessment and biopsy guidance. Numerous prospective studies have provided substantial evidence supporting its role in prostate cancer detection, demonstrating its ability to enhance diagnostic accuracy while reducing unnecessary biopsies. Despite its advantages, mpMRI has several limitations, including high costs, variability in interpretation, reliance on contrast agents, and lengthy acquisition times.

Micro-ultrasound (micro-US) is an emerging imaging technology that offers higher resolution than conventional ultrasound, enabling real-time targeted biopsies. Compared to mpMRI, micro-US has the potential to improve diagnostic accuracy while being more accessible, cost-effective, and easier to implement in clinical practice.

This systematic review and meta-analysis aims to assess whether the diagnostic accuracy of micro-US is comparable to the well-established mpMRI in prostate cancer screening prior to confirmatory biopsy. The findings could help determine the clinical utility and feasibility of micro-US as an alternative or complementary imaging modality for prostate cancer detection.Prostate cancer is the second most common cancer in men worldwide and a leading cause of cancer-related mortality. An early and accurate detection is critical for optimizing treatment outcomes and reducing the morbidity/mortality related. Current prostate cancer screening relies on prostate-specific antigen (PSA) testing and Multi-parametric Magnetic Resonance Imaging (mpMRI), but confirmatory diagnosis typically requires a biopsy.

mpMRI has emerged as a widely used and accepted imaging modality for risk stratification and biopsy guidance, this imaging modality has been tested in several prospective studies and has accumulated a body of evidence supporting its use for prostate cancer screening, improving cancer detection while reducing unnecessary biopsies. However, mpMRI has limitations, including high costs, variable interpretation, contrast medium usage and the time of adquisition.

Micro-ultrasound (micro-US) is an emerging alternative that offers higher resolution imaging than conventional ultrasound and allows for real-time targeted biopsies. This technique has the potential to improve diagnostic accuracy while being more accessible, cost-effective, and operator-friendly compared to mpMRI.

This systematic review and Meta-Analysis attempts to evaluate whether the micro-US diagnostic test accuracy is comparable to the well stablished mpMRI for prostate cancer screening prior a confirmatory biopsy.

Condition being studied Prostate Cancer.

METHODS

Search strategy The search strategy will utilize a predefined Boolean string applied across the selected databases and registries. The Boolean search terms are as follows:

-(Micro-Ultrasound) AND ((MRI) OR (Magnetic Resonance Imaging)) AND (Prostate Cancer)

-(Micro-Ultrasound) AND (Multiparametric Magnetic Resonance Imaging) AND (Prostate Cancer)

-(Microultrasonography) AND ((MRI) OR (Magnetic Resonance Imaging)) AND (Prostate Cancer)

-(MicroUltrasound) AND (Multiparametric Magnetic Resonance Imaging) AND (Prostate Cancer)

-(MicroUltrasound) AND ((Magnetic Resonance Imaging) OR (MRI)) AND (Prostate Cancer)

-("Micro-Ultrasound" OR "MicroUltrasound" OR "Microultrasonography") AND ("MRI" OR "Magnetic Resonance Imaging" OR "Multiparametric MRI" OR "mpMRI") AND ("Prostate Cancer" OR "Prostatic Neoplasm" OR "Prostate Tumor")

Additionally, references from eligible studies and previous systematic reviews will be examined for potential inclusion, provided they meet the eligibility criteria.

Participant or population Patients suspected of having prostate cancer who will undergo prostate biopsy with image guidance.

Intervention
1.-Micro-ultrasound-guided biopsy
2.-Multiparametric MRI (mpMRI)-guided biopsy.

Comparator Histopathology as the reference standard, obtained from standard prostate biopsy or prostatectomy.

Study designs to be included Experimental studies (Randomized Controlled Trials) and Prospective Observational studies (Prospective Cohort studies).

Eligibility criteria Inclusion Criteria:
Peer-reviewed journal articles published in English between January 2012 (the release of the first PI-RADS guideline) and March 2025 will be included. Eligible studies must be either Experimental (Randomized Controlled Trials) or Prospective Observational Studies (Prospective Cohort Studies) with a minimum sample size of 10 patients. Studies must directly compare the diagnostic test accuracy of Micro-Ultrasound and Multiparametric Magnetic Resonance Imaging (mpMRI) as image guide for a prostate biopsy, and use a histopathology analysis as reference.

Exclusion Criteria:
The following studies will be excluded:
-Non-peer-reviewed articles (e.g., congress abstracts, brief comments, letters to the editor)

-Review articles, including Narrative Reviews and Systematic Reviews (with or without Meta-Analysis)
-Case series, retrospective cohort studies, and case-control studies
-Studies that evaluate Micro-Ultrasound or mpMRI in clinical contexts other than prostate cancer screening.

Information sources The following databases will be used for Systematic Review: Medline/PubMed, Cochrane CENTRAL and the ClinicalTrials.gov registry.

Main outcome(s)
Primary outcomes:
The primary outcomes assessed will be the necessary to elaborate a 2x2 contingency table (Prostate Cancer prevalence, True Positive, True Negative, False Positive, False Negative), and the diagnostic test accuracy results(Sensitivity, Specificity, Positive Likelihood ratio, Negative Likelihood Ratio, Diagnostic Odds Ratio, Positive Predictive Value, Negative Predictive Value, Area. Under The Curve).

Secondary Outcomes:
The secondary outcomes assessed will be the Study-level information that include Author, Year of publication, study design, follow-up, Amount of centers involved in the study, Country or countries involved in the study, Score system used for the diagnosis (PI-RADS, PRI-MUS etc.), details on diagnostic tools used for the study development, years of experience of the radiologist involved in the study, Prostate Biopsy system used and methodology. Moreover, will be assessed population-level informations, such as population mean/median age, Baseline PSA, and any other relevant data obtained during the systematic review.

Data management Following the database search, all retrieved articles will be imported into Zotero v6.0.37 (Digital Scholar, VA, USA). Duplicate records will be identified and removed before proceeding with the screening process. The remaining studies will first be assessed based on titles and abstracts, applying the predefined inclusion and exclusion criteria. Articles deemed relevant will undergo a full-text review, where the same eligibility criteria will be applied. Studies meeting the final inclusion criteria will proceed to data extraction.

To ensure accuracy and consistency, two independent investigators will extract data from the selected articles, entering relevant information into a database created in Microsoft Excel 365 (Microsoft Corporation, Redmond, WA, USA). Any discrepancies encountered during the process will be resolved through consensus among the authors. Additionally, all investigators will oversee the process independently to validate the accuracy and completeness of the extracted data.

Quality assessment / Risk of bias analysis For the risk of bias and quality assessment, the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool will be used to evaluate potential bias in the included studies. This assessment will take place during the data extraction phase of the systematic review. Two reviewers will independently conduct the evaluation, and any disagreements will be resolved through consensus among all four reviewers, with an additional author serving as a tiebreaker if needed.

Strategy of data synthesis The minimum number of studies required for data synthesis will be three. From each included study, the prevalence, true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN) will be extracted. These raw data will be used to construct 2×2 contingency tables, which will allow for the estimation of sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR).

The extracted data will be logarithmically transformed and analyzed using a bivariate model, following the Reitsma et al. approach, to pool sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio and area under the curve estimates. The summary results will be visually presented using a summary Receiver Operating Characteristic (sROC) curve, forest plots, and meta-regression analyses to explore the comparison between both diagnostic tools. A subgroup analysis may be conducted using univariate models to evaluate the diagnostic accuracy of each imaging modality individually.

To assess heterogeneity, the I^2 statistic will be used, incorporating the Zhou & Dendukuri approach and Holling's approach to account for variability in diagnostic accuracy studies. If significant heterogeneity ($I^2 > 50\%$) is detected, univariate meta-regression models will be performed to explore potential sources of variation. Study-level and patient-level covariates will be examined as potential effect modifiers. These covariates will be selected post hoc based on the findings of the systematic review, considering variables that may influence diagnostic performance.

A funnel plot analysis and Egger's test will be conducted to assess the potential presence of publication bias in the studies included in the systematic review. The funnel plot will be used to visually examine the symmetry of studies based on sample size and estimated effect, helping to identify any potential biases related to study size. Subsequently, Egger's regression analysis will be employed to statistically evaluate the asymmetry of the funnel plot. In the case of detecting significant bias, additional analytical methods, such as sensitivity analysis, will be considered. A p-value of ≤ 0.05 will be considered statistically significant. All analyses will be performed in performed in RStudio 2024.12.0+467 (RStudio Team, Boston, MA, USA), using the 'Metafor' (v4.8-0), 'Meta' (v8.0-2) and 'Mada' (v0.5.11) packages. Rstudio Software.

Subgroup analysis A subgroup analysis will not be considered for this meta-analysis.

Sensitivity analysis A leave-one-out analysis will be performed as part of the sensitivity analysis to evaluate the stability and robustness of the meta-analysis results, particularly if substantial bias is detected through funnel plot assessment or Egger's test. This approach involves systematically excluding each study one at a time to assess its influence on the overall pooled estimates. If omitting a specific study results in a substantial shift in the findings, it will indicate that the study may disproportionately impact the conclusions. This process will help assess the reliability and consistency of the meta-analysis outcomes.

Language restriction English.

Country(ies) involved México and Brasil.

Keywords Ultrasonography, Multiparametric Magnetic Resonance Imaging, mp-MRI, Prostatic Neoplasms, Prostate Cancer, Diagnosis.

Dissemination plans The dissemination plan include congress abstracts, and published peer review articles.

Contributions of each author

Author 1 - Carlos Alberto Garcia Becerra - Conception, design, and drafting of the protocol manuscript, moreover, critical revision of the manuscript for important intellectual content.
Email: agbcarlos94@gmail.com
Author 2 - Yuri Santana do Carmo - Conception, design, and drafting of the protocol manuscript, moreover, critical revision of the manuscript for important intellectual content.
Email: yscmedicina@gmail.com
Author 3 - Victor Kleinfelder Molinari - Conception, design, and drafting of the protocol manuscript, moreover, critical revision of the manuscript for important intellectual content.
Email: vkmolinari@hotmail.com
Author 4 - Maria Isabel Arias Gallardo - critical revision of the manuscript for important intellectual content.
Email: ariasgallardomariaisabel@gmail.com
Author 5 - Jesus Eduardo Juarez Garcia - critical revision of the manuscript for important intellectual content.
Email: jejuarezgarcia@gmail.com
Author 6 - Veronica Soltero Molinar - critical revision of the manuscript for important intellectual content.
Email: verosoltero97@gmail.com
Author 7 - Carlos Martin Garcia-Gutierrez - critical revision of the manuscript for important intellectual content.
Email: drcgarcia@hotmail.com