

THE ROLE OF MRI IN PROSTATE CANCER MANAGEMENT: A SCOPING REVIEW OF THE EVOLVING LANDSCAPE

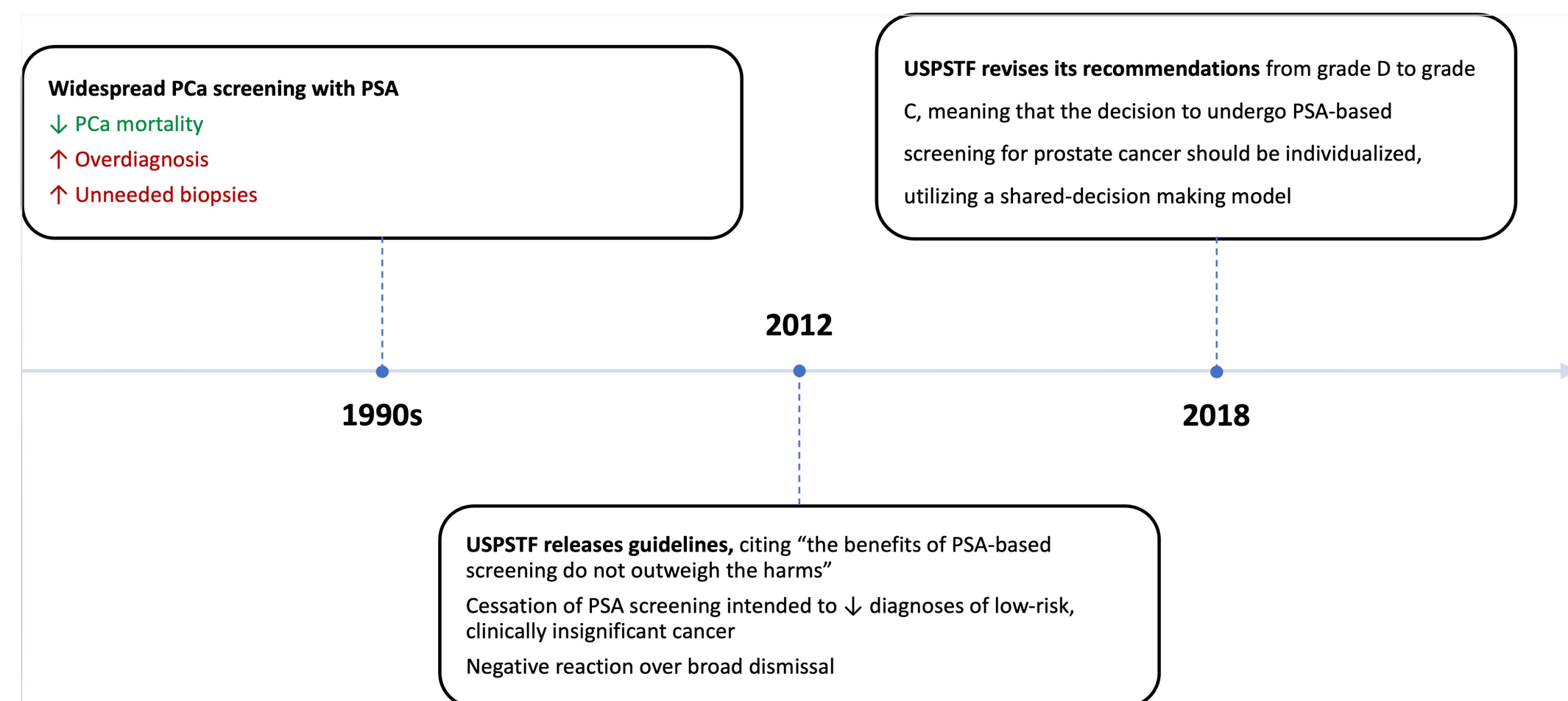


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Background

- Prostate cancer (PCa) is the 2nd most common cancer in the United States and a prominent cause of death globally
- Pathological examination of tissue samples is considered the foundation of PCa diagnosis, guides treatment, and predicts prognosis
- In recent decades, the approach to screening, diagnosis, and management has undergone rapid progression
- Magnetic resonance imaging (MRI) as a diagnostic and treatment planning tool in PCa has grown significantly and is now considered an important asset in the management of PCa.
- Currently, MRI is used in various capacities, such as risk stratification, determining need to undergo biopsy, performing targeted biopsies of suspicious lesions, response to treatment, and active surveillance.
- Despite the increasing use of MRI as a fundamental tool in PCa management, there remains significant debate surrounding its optimal utilization
- The purpose of this review is to examine the existing literature on the use of MRI for the diagnosis and management of PCa, its current applications, and to investigate its potential as a screening modality.



Methods

- The PubMed database was searched using the following keywords: mpMRI, prostate cancer, image-guided biopsy, screening, PSA, clinically significant, prostate cancer screening, cost-effectiveness, in January of 2023.
- Articles were selected based on study population size, journal prestige, and representation in the overall literature.
- To evaluate utility for screening, we referenced the principles of screening domains outlined by Dobrow et al. These domains include the disease/condition, the test/intervention, and the program/system.

Review/Results

Prostate Imaging Reporting and Data System (PI-RADS)

- Assigns a score to the MRI based on the presence and characteristics of any suspicious lesions and the overall quality of the imaging., ranging from 1 → 5
- Improves the detection of clinically significant prostate cancer with the average sensitivity of MRI for identifying index lesions demonstrated to be 91% (Greer et al., 2016).
- When MRI exhibits low-risk features (PI-RADS < 2), supplementary clinical data to facilitate informed decision-making processes must be utilized
 - NPV of negative MRI has been shown to be 90% in patients with a PSAD less than 0.15 ng/ml/cc, and 94% in patients with a PSAD less than 0.10 ng/ml/cc (Oishi et al., 2019)
 - Suspicious findings on DRE are associated with a significantly increased relative risk of 1.7 (95% confidence interval [CI] 1.6%-1.8%) and absolute risk of 9.3 (95% [CI] 7.9%-10%) of csPCA among patients with elevated PSA (≥ 3 ng/mL) (Halpern et al., 2018).

Biopsy Naïve

- Both the AUA and the EAU recommend MRI prior to biopsy in patients with elevated PSA.
- A hybrid approach that incorporates both MRI-targeted and systematic biopsy in biopsy-naïve individuals has demonstrated superior detection of high-grade cancer (Biurlin et al., 2016).
- The GÖTEBORG-2 trial was a large, population-based randomized screening trial of 38,775 men which evaluated the impact of omitting systematic biopsy for all men with an elevated PSA level (≥3 ng per milliliter) and instead, performing targeted biopsy of only MRI-positive lesions.
- Marked a 54% reduction in the detection of clinically insignificant cancers, but 19% fewer clinically significant (csPCA) cancers compared to the reference group (Hugosson et al., 2022).
- Clinically significant cancers missed in the experimental group had a Gleason score of 3+4, with 60% managed via active surveillance and 40% via radical treatment.
- However, the population-based STHLM3-MRI trial showed that the experimental arm (MRI-guided targeted biopsy and standard biopsy) was noninferior in detecting clinically significant cancers as compared to the standard arm (systemic biopsy) (21% vs 18%) and demonstrated a lower incidence of clinically insignificant cancers (4% vs 12%) (Eklund et al., 2021).

Previously Negative Biopsy

- The utilization of prebiopsy MRI in conjunction with MRI-targeted biopsy results in the detection of a greater number of cancers compared to systematic biopsy alone (Mendhiratta et al., 2015).
- The AUA and EAU guidelines endorse the administration of MRI prior to biopsy.
- Notably, a previously negative systemic biopsy is associated with a very low prostate cancer-specific mortality, comparable to the mortality observed after re-biopsy (Kawa et al., 2022).

Staging and Therapeutic Approach

- Utilized in the staging assessment as a means of determining the presence or absence of significant disease, by making discriminations between organ confined cancers and those with extracapsular dissemination and seminal vesicle involvement, identifying the overall extension of high-grade lesions
- While MRI has shown to be highly specific, its sensitivity has remained poor (Rooij et al., 2016).
- Advancements in imaging technology, such as the integration of whole-body MRI and PET-MRI utilizing the prostate-specific membrane antigen (68Ga-PSMA) have demonstrated considerable potential in this realm (Evangelista et al., 2021).

As a Screening Modality

- Both the AUA and the EAU guidelines do not endorse the use of MRI as a sole approach in population-based prostate cancer screening.
- Likely due to a multitude of factors, including cost considerations, variations in the quality and interpretation of MRI results by different radiologists, the possibility of MRI missing higher-grade cancers, and the availability of alternative risk stratification tools such as risk calculators, free/total prostate-specific antigen (PSA) measurements, biomarkers, and digital rectal examination

Cost

- Cost affects the accessibility and feasibility
- A cross-European study from 2009 found that PCa was the fourth most costly cancer, accounting for 7% of total cancer costs, or \$9.14 billion (Luengo-Fernandez et al., 2013).
- Prior to updated PSA guidelines and use of risk stratification tools, as high as 1 in 7 men who underwent PSA screening had an elevated PSA, nearly 85% of those men received biopsies (Martin et al., 2018).
- Quadrennial PSA-based prostate cancer screening, utilizing STHLM3-MRI trial data, incorporating MRI and a combined biopsy approach.
- Decrease in lifetime PCa-related fatalities with an additional cost-effectiveness ratio of US\$53,736 per QALY gained, compared to no screening (Hao et al., 2022).
- Reduction of approximately 50% in both lifetime biopsies and overdiagnosis.
- Cost-effectiveness analysis published in *European Urology*, using PROMIS trial data, also found MRI screening before biopsy to be cost-effective.
- The use MRI prior to biopsy, detects more CS cancers per dollar spent than a strategy using systemic biopsy, with a cost-effectiveness ratio of \$9,049 per QALY gained (Faria et al., 2018).

Limitations

- The use of MRI-targeted prostate biopsy may result in the reassignment of Gleason Grade without a complete understanding of its clinical significance.
- Few studies have followed patients for long enough to track disease specific outcomes.

Conclusions

- MRI has a wide scope of applications in the management of PCa
- Significant benefit of using MRI for PCa screening as it allows for increased detection of CS cancers while avoiding the detection and subsequent over-treatment for indolent cancers.
- MRI-based screening and targeted biopsies has been shown to be cost-effective and could potentially result in significant savings on the healthcare system.
- More studies are needed to better understand the long-term benefits of implementing MRI in the diagnosis and management of prostate cancer, as well as investigating its utility as a sole approach in population-based screening