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Review – Prostate Cancer

What Is the Negative Predictive Value of Multiparametric Magnetic Resonance Imaging in Excluding Prostate Cancer at Biopsy? A Systematic Review and Meta-analysis from the European Association of Urology Prostate Cancer Guidelines Panel

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Abstract

Context: It remains unclear whether patients with a suspicion of prostate cancer (PCa) and negative multiparametric magnetic resonance imaging (mpMRI) can safely obviate prostate biopsy.
Objective: To systematically review the literature assessing the negative predictive value (NPV) of mpMRI in patients with a suspicion of PCa.
Evidence acquisition: The Embase, Medline, and Cochrane databases were searched up to February 2016. Studies reporting prebiopsy mpMRI results using transrectal or transperineal biopsy as a reference standard were included. We further selected for meta-analysis studies with at least 10-core biopsies as the reference standard, mpMRI comprising at least T2-weighted and diffusion-weighted imaging, positive mpMRI defined as a Prostate Imaging Reporting Data System/Likert score of $\geq$3/5 or $\geq$4/5,

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Prostate biopsy
Risk stratification

and results reported at patient level for the detection of overall PCa or clinically significant PCa (csPCa) defined as Gleason ≥7 cancer.
Evidence synthesis: A total of 48 studies (9613 patients) were eligible for inclusion. At patient level, the median prevalence was 50.4% (interquartile range [IQR], 36.4–57.7%) for overall cancer and 32.9% (IQR, 28.1–37.2%) for csPCa. The median mpMRI NPV was 82.4% (IQR, 69.0–92.4%) for overall cancer and 88.1% (IQR, 85.7–92.3) for csPCa. NPV significantly decreased when cancer prevalence increased, for overall cancer ($r = -0.64$, $p < 0.0001$) and csPCa ($r = -0.75$, $p = 0.032$). Eight studies fulfilled the inclusion criteria for meta-analysis. Seven reported results for overall PCa. When the overall PCa prevalence increased from 30% to 60%, the combined NPV estimates decreased from 88% (95% confidence interval [95% CI], 77–99%) to 67% (95% CI, 56–79%) for a cut-off score of 3/5. Only one study selected for meta-analysis reported results for Gleason ≥7 cancers, with a positive biopsy rate of 29.3%. The corresponding NPV for a cut-off score of ≥3/5 was 87.9%.
Conclusions: The NPV of mpMRI varied greatly depending on study design, cancer prevalence, and definitions of positive mpMRI and csPCa. As cancer prevalence was highly variable among series, risk stratification of patients should be the initial step before considering prebiopsy mpMRI and defining those in whom biopsy may be omitted when the mpMRI is negative.
Patient summary: This systematic review examined if multiparametric magnetic resonance imaging (MRI) scan can be used to reliably predict the absence of prostate cancer in patients suspected of having prostate cancer, thereby avoiding a prostate biopsy. The results suggest that whilst it is a promising tool, it is not accurate enough to replace prostate biopsy in such patients, mainly because its accuracy is variable and influenced by the prostate cancer risk. However, its performance can be enhanced if there were more accurate ways of determining the risk of having prostate cancer. When such tools are available, it should be possible to use an MRI scan to avoid biopsy in patients at a low risk of prostate cancer.

1. Introduction

A correlation with radical prostatectomy specimens has demonstrated that multiparametric magnetic resonance imaging (mpMRI) has excellent sensitivity in detecting prostate cancer (PCa) with a Gleason score of ≥7 [1–3]. As a result, prostate mpMRI is increasingly used in patients with a suspicion of PCa to localise abnormal areas before biopsy. A large body of literature has shown that targeted biopsies of suspicious lesions seen on mpMRI (TBx) improved the detection of clinically significant PCa (csPCa), at least in the repeat biopsy setting [4–6]. As a result, it is now recommended that an mpMRI is performed before repeat biopsy to allow TBx of suspicious lesions in addition to standard biopsies [7].

Some authors have recently suggested that, besides improving csPCa detection, mpMRI could also be used as a triage test so that patients with negative mpMRI findings could obviate biopsy. Such a strategy remains highly controversial [8] and depends upon the negative predictive value (NPV) of mpMRI. Therefore, the European Association of Urology Prostate Cancer Guidelines Panel undertook this systematic review and meta-analysis to assess the NPV of mpMRI in patients with a suspicion of PCa and, thus, its potential role in eliminating unnecessary prostate biopsy.

2. Evidence acquisition

2.1. Objective

Our primary aim was to systematically evaluate the performance of negative prebiopsy prostate mpMRI in predicting a negative biopsy result for overall PCa and csPCa in biopsy-naïve men and in men with previously negative biopsies. A further objective was to explore and define factors that may contribute to relevant thresholds in order to provide guidance for future studies.

2.2. Data acquisition and search strategy

The review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement [9]. The review protocol was published in PROSPERO database (http://www.crd.york.ac.uk/PROSPERO; registration number CRD42015021929). Databases searched included the Embase and OVID Medline databases, the Cochrane database of systematic reviews, and the Cochrane Central Register for Clinical Trials, covering from January 1, 2000 to February 13, 2016. Systematic or standard prostate biopsies were used as reference standards, with positive or negative cases of PCa being determined by histopathological examination. The detailed search strategy is presented in Supplement 1.

2.3. Inclusion and exclusion criteria

Included studies focused on men who were assessed for suspected PCa by mpMRI before undergoing prostate biopsy. Studies enrolling both biopsy-naïve men and men who had undergone previous negative biopsies were included. Prebiopsy prostate mpMRI was considered the index test and comprised T2-weighted imaging (T2WI) and at least one functional imaging technique (diffusion-weighted imaging [DWI], dynamic contrast-enhanced imaging [DCEI], or magnetic resonance spectroscopic imaging [MRSI]). For inclusion, studies had to report on

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