Multiparametric Prostate MR Imaging: Impact on Clinical Staging and Decision Making

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KEYWORDS

• Prostate cancer • Multiparametric MR imaging (mpMRI) • Staging

KEY POINTS

- The current paradigm for prostate cancer staging is changing with increased incorporation of multiparametric MR imaging (mpMRI) into clinical decision making.
- MpMRI has proved useful in differentiating organ-confined disease (stage $\leq$T2) from locally advanced (stage $\geq$T3) disease due to the high sensitivity and specificity for the detection of extraprostatic extension (EPE) and seminal vesicle invasion (SVI).
- Much work on mpMRI is forthcoming regarding the use of mpMRI in preoperative volumetric tumor assessment, improving biopsy targeting of transrectal ultrasound (TRUS)-negative tumors, and selection and follow-up of men on active surveillance.

INTRODUCTION

Prostate cancer is the most common noncutaneous malignancy and second leading cause of cancer-related deaths in men in the United States, with an estimated 180,890 new cases and 26,120 deaths in 2016.[1] The overall 5-year survival rate is relatively high and has increased from 83% in the 1980s to 99% from 2005 to 2011, in part due to earlier detection and earlier aggressive therapy for high-risk disease. Despite the overall high 5-year survival rate, outcomes are variable, ranging

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from near 100% survival in organ-confined disease to as low as 28% survival in more advanced stages.[2] Studies have shown that many men with low-risk disease in the United States are overtreated, resulting in significant economic impact and individual morbidity associated with aggressive therapy.[3]

In the past decade, there have been meaningful changes in the approach to the diagnosis, characterization, and management of clinically localized prostate cancer. These have become increasingly defined by more selective population screening, integration of novel diagnostic tools, and increased acceptance of active surveillance and partial ablative strategies as viable management strategies.[4] These trends have driven demand for optimized prostate imaging. The need for accurate pretherapy staging is, therefore, paramount for risk stratification with the ultimate goals of preventing overtreatment of low-risk disease in favor of active surveillance and selection of the optimal early aggressive intervention in high-risk disease. The aim of this article is to review the current and changing paradigm in prostate cancer staging with specific emphasis on the evolving role of multiparametric MR imaging (mpMRI) and how it is being integrated into clinical decision making.

OVERVIEW OF PROSTATE CANCER STAGING AND CLINICAL NOMOGRAMS

Clinical and pathologic staging is most widely performed according to the American Joint Committee on Cancer (AJCC) 2010 TNM classification system, which incorporates clinical T stage (based on digital rectal examination [DRE]) and, if available, serum prostate-specific antigen (PSA) and Gleason score.[5] *The AJCC Cancer Staging Manual*, eighth edition, recently released, incorporates several important changes to the current prostate cancer staging paradigm. Notably, the eighth edition includes the prostate prognostic group grade to histopathologic assessment, which is to be reported along with the Gleason score. Additionally, pathologic staging no longer subcategorizes pT2 due to increased emphasis placed on tumor volume over laterality, because this has been shown to have more practical and prognostic significance.[6]

Numerous clinical nomograms have been developed over the years that take into account various parameters to predict pathologic stage at radical prostatectomy.[7] One of the most widely used clinical nomograms are the Partin tables, which factor in a patient's clinical T stage, serum PSA, and Gleason score.[8,9] The Memorial Sloan Kettering nomogram includes percent positive cores from transrectal ultrasound (TRUS)-guided biopsy and the University of California, San Francisco, Cancer of the Prostate Risk Assessment scoring system also includes the patient age.[10,11]

The current paradigm for prostate cancer diagnosis centers on performing systematic 12-core TRUS-guided biopsy in men with elevated PSA or positive DRE. Aside from issues related to the morbidity of the procedure, there are several well documented limitations to this approach.[12] On one hand, undersampling can occur and has been shown to lead to false-negative biopsy results in up to 30% of cases, particularly in men with larger glands or those with anterior prostate cancers.[13] Undersampling can also lead to inaccurate risk stratification in some men. For example, a 2010 prospective study of 1565 patients showed that 47% of men classified as low-risk ($\leq$Gleason 6) who may have been potential candidates for active surveillance were actually upgraded to Gleason 7 or greater after prostatectomy.[14] Attempts to overcome undersampling errors by increasing the number of core samples by performing serial biopsies have been shown to increase the overall cancer detection rate; however, in 1 study, a majority of these cases were classified as clinically insignificant (75 of 119 cases).[15]

INTEGRATION OF MULTIPARAMETRIC MR IMAGING INTO CLINICAL ALGORITHMS AND STAGING SYSTEMS

Detection and Characterization of Prostate Cancer with Multiparametric MR Imaging

mpMRI has the potential to overcome many of the shortcomings associated with TRUS biopsy systems and has proved valuable for improving the detection of higher-grade disease (histologic Gleason score) and higher-stage disease (extraprostatic extension [EPE] and tumor volume), thereby offering a more complete clinical picture for clinical decision making. In some studies, mpMRI has been shown to increase cancer detection rates and lead to pathologic upgrading in up to 38% of cases in men with persistent clinical suspicion of prostate cancer despite prior negative biopsy.[16] A recent prospective National Institutes of Health study on 1003 men with elevated PSA or positive DRE who underwent mpMRI compared random TRUS biopsy and magnetic resonance (MR) fusion–guided biopsy. They demonstrated a 30% increase in the diagnosis of high-risk disease and a 17% decrease in the detection of low-risk disease in the targeted MR-biopsy group. For men in the series who underwent radical prostatectomy, targeted biopsy alone was the best