Scientific Article

Predictive Value of Multiparametric Magnetic Resonance Imaging in Risk Group Stratification of Prostate Adenocarcinoma



www.advancesradonc.org

Benjamin T Bonebrake, BSBA,^a Elsa Parr, MD,^b Linda My Huynh, MSc, PhD,^a Brendan Coutu, MD,^c Neil Hansen, MD,^d Benjamin Teply, MD,^d Charles Enke, MD,^d Chad Lagrange, MD,^d and Michael Baine, MD, PhD^{d,*}

^aUniversity of Nebraska Medical Center College of Medicine, Omaha, Nebraska; ^bMayo Clinic Department of Radiation Oncology, Rochester, Minnesota; ^cSparrow Health System, Lansing, Michigan; and ^dUniversity of Nebraska Medical Center, Omaha, Nebraska

Received 15 December 2023; accepted 26 February 2024

Purpose: The aim of this study was to further assess the clinical utility of multiparametric magnetic resonance imaging (MP-MRI) in prostate cancer (PC) staging following 2023 clinical guideline changes, both as an independent predictor of high-stage (>T3a) or high-risk PC and when combined with patient characteristics.

Methods and Materials: The present study was a retrospective review of 171 patients from 2008 to 2018 who underwent MP-MRI before radical prostatectomy at a single institution. The accuracy of clinical staging was compared between conventional staging and MP-MRI-based clinical staging. Sensitivity, specificity, positive predictive value, and negative predictive value were compared, and receiver operating characteristic curves were generated. Linear regression analyses were used to calculate concordance (C-statistic).

Results: Of the 171 patients, final pathology revealed 95 (55.6%) with T2 disease, 62 (36.3%) with T3a disease, and 14 (8.2%) with T3b disease. Compared with conventional staging, MP-MRI-based staging demonstrated significantly increased accuracy in identifying T3a disease, intermediate risk, and high/very-high-risk PC. When combined with clinical characteristics, MP-MRI-based staging improved the area under the curve from 0.753 to 0.808 (P = .0175), compared with conventional staging.

Conclusions: MP-MRI improved the identification of T3a PC, intermediate-risk PC, and high- or very-high-risk PC. Further, when combined with clinical characteristics, MP-MRI-based staging significantly improved risk stratification, compared with conventional staging. These findings represent further evidence to support the integration of MP-MRI into prostate adenocarcinoma clinical staging guidelines.

© 2024 The Author(s). Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Sources of support: This work had no specific funding. Research data are stored in an institutional repository and will be shared upon request to the corresponding author. *Corresponding author: Michael Baine, MD, PhD; Email: Prostate cancer (PC) is the most common noncutaneous cancer in men in the United States, with over 190,000 new cases every year. Although its prognosis is generally favorable, with a 5-year overall survival rate of 98%, it represents the second-greatest cause of cancer-related death in men, owing to its high prevalence.¹ Therefore, proper

https://doi.org/10.1016/j.adro.2024.101493

mbaine@unmc.edu

2452-1094/© 2024 The Author(s). Published by Elsevier Inc. on behalf of American Society for Radiation Oncology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

diagnosis, staging, and treatment of PC is a significant public health objective.

Traditionally, the evaluation of PC includes a prostate specific antigen (PSA) test, physical examination with a digital rectal examination, and a transrectal ultrasoundguided biopsy (TRUS). However, soft tissue imaging has been used with increased frequency to aid in diagnosis and staging. For example, molecular imaging of glutamate carboxypeptidase II, or prostate specific membrane antigen (PSMA), has been rapidly adopted and is considered the imaging modality of choice when it comes to PC with biochemical recurrence after radical prostatectomy.² Despite its success with biochemical recurrence and especially with nodal disease, its value has not necessarily been established in the setting of primary staging, especially in locoregional risk assessment, such as in T3a disease. PSMA-positron emission tomography (PET) cannot determine marginal invasion as well as MRI, as the dividing planes between anatomic structures are too thin for PET/computed tomography (CT), creating the need for a complementary imaging modality to help with primary diagnosis and staging beyond the ability of PSMA-PET.³

Multiparametric magnetic resonance imaging (MP-MRI) provides a potential option for high-definition soft tissue imaging to aid in primary staging. MP-MRI guidance has been increasingly used in addition to TRUS to better detect potentially cancerous lesions,⁴ and MP-MRI was formally designated as preferred over CT for pelvic staging in the National Comprehensive Cancer Network (NCCN) Guidelines in 2023.⁵ MP-MRI's ability to assess the location and size of prostatic lesions affords it higher sensitivity in the detection of clinically significant cancer.^{6,7} A 2017 study by Ahmed et al,⁸ for example, demonstrated the diagnostic sensitivity of an MP-MRI guided biopsy as reaching 93% (95% CI, 88%-96%), significantly higher than that of TRUS biopsy, at 48% (95% CI, 42%-55%). With this increased sensitivity, this multicenter study estimated that routine use of MP-MRI in conjunction with TRUS could increase the detection of clinically significant PC by 18%.8

Not only does MP-MRI yield high sensitivity in the overall detection of clinically significant PC, but it also provides high specificity in diagnosing high-risk PC via detection of extracapsular extension and/or seminal vesicle involvement. According to a 2015 study by Feng and colleagues, MP-MRI is 87.2% specific for extracapsular extension of PC.9 Similarly, a 2016 meta-analysis found MP-MRI to have 88% specificity (95% CI, 85%-91%) in the detection of stage T3 disease.¹⁰ In addition to detecting these high-risk features, MP-MRI may also facilitate the detection of clinically occult features that would not otherwise be found via digital rectal examination. These include lateral and anterior extracapsular extension or seminal vesicle invasion. As curative treatment is most likely when these features are not present, the use of MP-MRI represents potential for improved clinical staging.

The NCCN guidelines have recently adopted a recommendation of soft tissue imaging as a part of additional evaluation in patients with unfavorable intermediate and higher PC, with a preference for MP-MRI over traditional CT for pelvic staging. However, owing to a lack of data validation for the use of MP-MRI for clinical decisionmaking, the American Joint Committee on Cancer (AJCC) does not currently recommend the use of MP-MRI for PC staging.¹¹ Within this context, the present study seeks to use surgical pathology as a gold standard in assessing the predictive power of MP-MRI in assessing tumor extent (T stage) and risk stratification. This will allow a direct comparison of the diagnostic accuracy of MP-MRI-based staging versus conventional clinical staging and provide further support for its utilization in primary PC staging.

Methods and Materials

Study population

The present study was approved by an institutional review board. All patients undergoing a radical prostatectomy (RP) for clinically localized prostate adenocarcinoma at our institution from 2008 to 2018 were retrospectively reviewed. Patients included in analysis underwent pretreatment MP-MRI before RP and had complete final pathologic information. Patients were excluded if they received any neoadjuvant androgen deprivation therapy or chemotherapy, as neoadjuvant systemic treatment would alter pathologic findings compared with disease characteristics at the time of MP-MRI. Patient characteristics, clinical staging, MRI findings, and final pathologic staging were reviewed via electronic medical record. Patients were systematically selected per inclusion/exclusion criteria and were representative of PC patients at our institution.

MP-MRI

All patients underwent a 1.5-3 Tesla MP-MRI at our institution as part of a standard workup before undergoing RP. Standard imaging parameters included T2 weighted, T1 weighted, diffusion weighted, and post contrast imaging in various anatomic planes. Images were viewed and processed on DynaCAD software.

All MP-MRI scans were interpreted by fellowshiptrained abdominal radiologists. MP-MRI staging was defined solely by review of the standard of care MRI report rendered by the radiologist, including the extent of prostate lobe involvement, extracapsular extension, and seminal vesicle involvement. All interpreting radiologists subjectively evaluated the MP-MRI scans and interpreted for local invasive features based on PI-RADS v. 2.1 criteria,¹²⁻¹⁴ and lesions that were rated a PI-RADS \geq 4 were recommended to undergo fusion biopsy. Features of seminal vesicle invasion included focal or diffuse low T2W signal, contrast enhancement within or along the seminal vesicle, restricted diffusion, obliteration of the angle between the seminal vesicle and the prostate, or direct extension of the tumor at the base of the prostate into the seminal vesicle. Features of extraprostatic extension included asymmetry or invasion of the neurovascular bundle, a bulging prostatic contour, an irregular or speculated margin/prostatic capsule, obliteration of the recto-prostatic angle, a tumor-capsule interface of > 1.0 cm, or frank breach of the capsule by tumor with invasion into adjacent structures.

T staging and risk grouping

All patients underwent a TRUS-guided prostate biopsy, physical examination performed by their managing urologist, and repeat PSA test before RP. Patients were staged and risk stratified by T stage, Gleason score (GS), and PSA as defined by the AJCC 8th edition cancer staging manual and the NCCN.¹² Clinical staging was defined using AJCC 8th edition allowable staging techniques, including clinical examination findings as reported by the managing urologist.¹³ Clinical stage and risk stratification were identified retrospectively via both conventional clinical staging and by MP-MRI findings.

Statistical analysis

All analyses were performed using SAS software version 9.4 (SAS Institute Inc, Cary, North Carolina). Patient demographics and baseline clinical characteristics were summarized by descriptive statistics, such that categorical variables were reported with n, % and continuous variables were reported with median, ranges. Univariate associations between patient characteristics and NCCN risk groups, high and very high risk,14 were assessed via regression modeling. Clinical and MRI T stages were simplified to T1, T2, T3a, T3b, and T4 to directly compare with pathologic staging. Frequencies of MP-MRI-based, clinical evaluation-based, and pathology-based T stage and NCCN risk groups were generated and compared using the McNemar test.¹⁵ The McNemar test was also used to compare sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for clinical and MRI-based staging, using pathology-based T stage as the state variable. A concordance statistic (C-statistic) was used to evaluate the fit of sensitivity and specificity in a logistic regression model.

Two multivariate models of factors predicting highrisk or very-high-risk groups were generated, one using conventional staging and the other, MP-MRI-based staging. Variables with a *P* value <.1 in the univariate analysis were included in the final models. Receiver operating characteristic (ROC) curves were generated along with the area under the curve (AUC) and compared via pairwise comparison.¹⁶ A *P* value <.05 was considered statistically significant, and 95% confidence intervals (95% CI) were reported for all odds ratios (ORs).

Results

Patient characteristics

Table 1 displays the patient characteristics of the 171 included patients. The median age at the time of diagnosis was 62 (range, 41-75). The median PSA before RP was 7.0 ng/mL (range, 1.6-76.0 ng/mL), and the median time from MP-MRI to RP was 64 days (range, 1-419 days). Thirty-seven of 171 patients (21.6%) underwent 1.5T MRI, and 115 of 171 patients (67.3%) underwent 3T MRI. MRI field strength was not specified in 19 patients (11.1%).

Final pathology demonstrated GS 6 in 2.3% (4/171) of patients, GS 7 in 70.2% (120/171) of patients, GS 8 in 7.6% (13/171) of patients, and GS 9 to 10 in 19.9% (34/171) of patients. A total of 55.6% (95/171) of patients had T2 disease, 36.3% (62/171) of patients had T3a disease, and 8.2% (14/171) of patients had T3b disease. No patients were identified as having T4 disease. Based on the NCCN's risk categorization model using PSA, GS, and clinical findings, 8.2% (14/171) of patients had low-risk disease, 59.6% (102/171) of patients had intermediate-risk disease, 25.1% (43/171) of patients had high-risk disease.

Conventional and MP-MRI staging

Table 2 illustrates the frequency of T stage and risk group assignment as determined by conventional clinical staging versus MP-MRI-based staging. Overall, MP-MRIbased staging identified higher proportions of T stage disease and very-high-risk disease, compared with conventional clinical staging. MP-MRI upstaged clinical stage in 25.7% (44/171) of cases, 68.2% (30/44) of which were upstaged from T1-2 to T3 disease. MP-MRI identified 29 of 171 patients (17.0%) with T3a disease, compared with 5 patients (2.9%) identified by clinical staging (P < .001). MP-MRI also identified 9 of 171 patients (5.3%) with T3b disease, compared with 3 patients (1.8%) identified by clinical staging (P = .034). According to the NCCN risk group stratification, MP-MRI identified 26 of 171 patients (15.2%) with very-high-risk disease, compared with 12 patients (7.0%) identified by clinical staging (P < .001).

Table 1 Patient characteristics

	No. of patients (%)
Median age at diagnosis (range)	62 (41-75)
Median PSA (in ng/mL) at diagnosi (range)	s 7.0 (1.6-76.0)
Race	
White	156 (91.2%)
Black	12 (7.0%)
Hispanic	3 (1.8%)
Gleason score	
6	4 (2.3%)
7	120 (70.2%)
8	13 (7.6%)
9-10	34 (19.9%)
Days from MP-MRI to RP (range)	66 (1-419)
Clinical T stage	
1a	4 (2.3%)
1b	1 (0.6%)
1c	126 (73.7%)
2a	10 (5.8%)
2b	6 (3.5%)
2c	8 (4.7%)
2 (unspecified)	8 (4.7%)
3a	5 (2.9%)
3b	3 (1.8%)
MRI T stage	
1c	90 (52.6%)
2a	9 (5.3%)
2b	6 (3.5%)
2c	7 (4.1%)
2 (unspecified)	21 (12.3%)
3a	29 (17%)
3b	9 (5.3%)
Pathologic T stage	
2	95 (55.6%)
3a	62 (36.3%)
3b	14 (8.2%)
Clinical risk group	
Low	14 (8.2%)
Intermediate	102 (59.6%)
High	43 (25.1%)
Very high	12 (7%)
MRI-based risk group	
	(continued on next page

Table 1 (Continued)			
	No. of patients (%)		
Low	14 (8.2%)		
Intermediate	83 (48.5%)		
High	48 (28.1%)		
Very high	26 (15.2%)		
Pathologic risk group			
Low	4 (2.3%)		
Intermediate	72 (42.1%)		
High	43 (25.1%)		
Very high	52 (30.4%)		
<i>Abbreviations:</i> MP-MRI = mult specific antigen; RP, radical prost	iparametric MRI; PSA = prostate atectomy.		

Table 3A displays the sensitivity, specificity, PPV, and NPV of conventional versus MP-MRI-based T stages, and Table 3B displays these values for NCCN risk stratifications. In general, MP-MRI identified T3a disease with greater accuracy than conventional clinical staging. Sensitivity of MP-MRI in identification of T3a disease was 30.6%, compared with 3.2% for conventional clinical staging (P < .001). Further, MP-MRI findings of T3a disease had a higher PPV than clinical findings of T3a disease (69.7% vs 63.9%, P = .041). The C-statistic was greater for MP-MRI than for conventional clinical staging (0.607 vs 0.502, P < .001). There was no significant difference between MP-MRI and conventional clinical staging for T3b disease, although there was a trend toward greater sensitivity with MP-MRI (21.4% vs 35.7%).

Overall, MP-MRI tumor stage was concordant with final pathologic stage in 31.0% (53/171) of cases, compared

Table 2Frequency of T stage and risk group assignment by conventional clinical and MP-MRI-based staging

Parameter	Clinical	MP-MRI	P value	
T Stage				
T1	131 (76.6%)	90 (52.6%)	<.0001	
T2	32 (18.7%)	43 (25.1%)	.0076	
T3a	5 (2.9%)	29 (17.0%)	<.0001	
T3b	3 (1.8%)	9 (5.3%)	.0339	
Risk Group				
Low risk	14 (8.2%)	14 (8.2%)	1.0000	
Intermediate risk	102 (59.6%)	83 (48.5%)	<.0001	
High risk	43 (25.1%)	48 (28.1%)	.3173	
Very high risk	12 (7.0%)	26 (15.2%)	.0002	
<i>Abbreviations</i> : MP-MRI = multiparametric MRI.				

T stage	Clinical staging	MP-MRI staging	Difference (95% CI)	P value
Т2				
Sensitivity (%)	21.1%	30.5%	9.4% (2.5%-16.4%)	.007
Specificity (%)	84.2%	81.6%	-2.6% (-10.1%-4.6%)	.414
PPV (%)	62.5%	67.4%	4.9% (-10.2%-19.7%)	.526
NPV (%)	46.0%	48.4%	2.4% (-4.9%-9.7%)	.524
C-statistic	0.526	0.561	0.034 (-0.012-0.08)	.143
T3a				
Sensitivity (%)	3.2%	30.6%	27.4% (15.8%-39.6%)	<.001
Specificity (%)	97.2%	90.8%	-6.4% (-12.7%-1.5%)	.008
PPV (%)	40.0%	65.5%	25.5% (1.9%-45.5%)	.041
NPV (%)	63.9%	69.7%	5.9% (-1.0%-12.6%)	.093
C-statistic	0.502	0.607	0.105 (0.044-0.166)	<.001
T3b				
Sensitivity (%)	21.4%	35.7%	14.3% (-15.7%-41.4%)	.317
Specificity (%)	100.0%	97.5%	-2.5% (-6.4%-0.3%)	.055
PPV (%)	100.0%	55.6%	-44.4% (-70.3%-10.9%)	.021
NPV (%)	93.5%	94.4%	1.0% (-2.6%-4.7%)	.583
C-statistic	0.607	0.666	0.059 (-0.082-0.199)	.413

Table 3A Comparative parameters for assessing T stage by conventional clinical methods or by MP-MRI

Table 3BComparative parameters for assessing NCCN risk stratification by conventional clinical methods or by multi-
parametric MRI

Risk stratification	Clinical staging	MP-MRI staging	Difference (95% CI)	P value
Intermediate risk				
Sensitivity (%)	80.6%	76.4%	-4.2% (-10.3%-1.6%)	.083
Specificity (%)	55.6%	71.7%	16.2% (8.6%-23.5%)	<.001
PPV (%)	56.9%	66.3%	9.4% (-0.5%-19.1%)	.064
NPV (%)	79.7%	80.7%	1.0% (-5.2%-7.1%)	.757
C-statistic	0.681	0.741	0.06 (0.017-0.103)	.007
High risk				
Sensitivity (%)	25.6%	34.9%	9.3% (-4.1%-22.4%)	.157
Specificity (%)	75.0%	74.2%	-0.8% (-7.3%-5.8%)	.808
PPV (%)	25.6%	31.3%	5.7% (-7.4%-18.5%)	.398
NPV (%)	75.0%	77.2%	2.2% (-4.1%-8.6%)	.490
C-statistic	0.503	0.546	0.043 (-0.029-0.114)	.240
Very high risk				
Sensitivity (%)	19.2%	36.5%	17.3% (6.3%-28.3%)	.003
Specificity (%)	98.3%	94.1%	-4.2% (-9.6%-0.1%)	.025
PPV (%)	83.3%	73.1%	-10.3% (-28.2%-8.4%)	.283
NPV (%)	73.6%	77.2%	3.7% (-2.7%-9.9%)	.258
C-statistic	0.588	0.653	0.066 (0.011-0.121)	.019
Abbreviations: C-statistic =	concordance statistic; MP-MRI	= multiparametric MRI; NPV = n	egative predictive value; PPV = positive p	redictive value.

with 14.62% (25/171) of cases for conventional clinical staging. MP-MRI also demonstrated greater sensitivity in identifying very-high-risk PC than conventional clinical staging, at 36.5% versus 19.2% (difference: 17.3%; 95% CI, 6.3%-28.3%; P = .003). In linear regression analysis, the C-statistic was greater for MP-MRI than for clinical staging in identifying very-high-risk PC, at 0.653 versus 0.588 (difference: 0.066; 95% CI; 0.011-0.121; P = .019).

Multivariate modeling with patient characteristics

In multivariate modeling, both conventional staging and MP-MRI-based staging were significantly and independently associated with very-high-risk or high-risk stage on final pathology (conventional staging: OR, 7.343; 95% CI, 2.716-19.849; P < .0001 vs MRI staging: OR, 11.035; 95% CI, 4.617-26.375; P < .0001) (Supplementary Table 1). ROC curve analysis yielded an AUC of 0.753 for conventional staging (95% CI, 0.679-0.828; P < .0001) and 0.808 for MP-MRI-based staging (95% CI, 0.741-0.874; P < .0001). Pairwise comparison of the ROC curves is displayed in Fig. 1, illustrating a significant difference of 0.0544 (95% CI, 0.009-0.0993; P = .0175).

Discussion

The present study is a retrospective review directly comparing the diagnostic accuracy of conventional staging versus MP-MRI-based staging. Not only did MP-MRI significantly improve identification of patients with T3a disease and very-high-risk or high-risk PC, but it also resulted in accurate upstaging in over 25% of patients. The present findings represent an opportunity to integrate MP-MRIbased staging with patient characteristics to further facilitate clinical decision-making and personalized treatment.

First, the present study showed that the use of MP-MRI-based staging yielded high specificity, NPV, and PPV in identifying high- and very-high-risk PC. This is in contrast with Ahmed et al,⁸ who found similar PPVs and NPVs ranging from 50% to 70% and 70% to 90%, respectively, but low specificity (<50%) and high sensitivity (>90%). However, our results align well with those of a 2014 study by Billing and colleagues, who found the sensitivity for detection of T3a disease to be approximately 30%, compared with a 93.3% specificity.¹⁷ In this regard, the high specificity suits the purpose of MP-MRI-based staging for the identification of high-risk or very-high-risk disease: A positive result rules in the presence of high-risk disease characteristics, while a negative result is not necessarily useful for ruling out these characteristics.

Second, the use of MP-MRI-based staging resulted in the accurate upstaging of over 25% of patients. Among these 44 patients, 30 (68.2%) were upstaged from stage T2 or below to stage T3. This increase in stage holds considerable clinical significance, as it warrants the consideration of more aggressive treatment options that may not be indicated for locally limited disease. In this regard, treatment recommendations regarding external beam radiation therapy and its fractionation, the addition of a brachytherapy

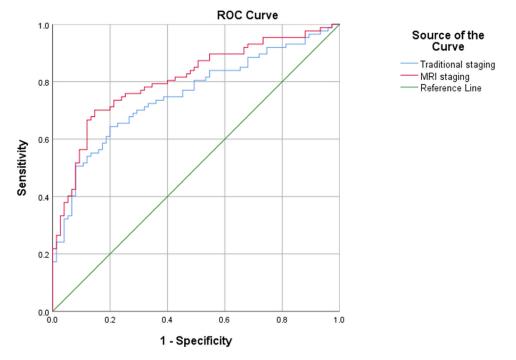


Figure 1 Receiver operating characteristic curve of conventional staging versus multiparametric magnetic resonance imaging—based staging in predicting high- or very high-risk disease (P = .0175).

boost, addition and duration of androgen deprivation therapy, and prophylactic irradiation of lymph nodes are all subject to change when the stage is increased to T3. These findings are consistent with those of several other studies demonstrating significant upstaging following MP-MRI. In a 2020 study by Bakavicius and colleagues, the use of MP-MRI resulted in 29% of patients being upstaged. Even further, patients who were upstaged were at a 2.1 times increased risk of biochemical recurrence following RP, and metastasis-free survival and ten-year cancer free survival were also significantly reduced.¹⁸ As cancer upstaging is associated with a substantially higher risk of recurrence and inferior rates of oncologic control, the use of MP-MRI-based staging is a critical tool for preemptive risk stratification and clinical decision making.

Third, combining MP-MRI with clinical characteristics illustrated improved predictive capability, compared with using conventional staging alone. The use of MP-MRI in the present study improved the AUC from 0.753 to 0.808, thus significantly facilitating the identification of highand very-high-risk PC. These results are similar to those of Rayn and colleagues, who published a large single-institution study of 532 PC patients in 2018. In their study, the use of MP-MRI was incorporated into clinical nomograms, the inclusion of which significantly increased the AUC by 0.1 for organ confined disease, 0.1 for extracapsular extension, and 0.09 for seminal vesicle invasion.¹⁹ This further suggests that adding MRI-based information to clinical nomograms significantly improves the detection of T2, T3a, and T3b PC. Despite demonstrating significant improvement in clinical staging when using MP-MRI over conventional clinical staging, the absolute rate of concordance with final pathology for MP-MRI is still just 31%. While this is significantly greater than that for conventional clinical staging, this demonstrates that there is still plenty of room for improvement. This low concordance rate is unsurprising, as our patient population was clinically restaged to exclude any imaging in order to evaluate the impact of MP-MRI on clinical staging. Opportunities for further improvement could be found using AI and other computer-aided imaging models to help improve radiologists' ability to more accurately stage PC.

While this study demonstrates the added value of MP-MRI to accurately stage patients with PC, it is not without limitation. This study represents a single-institution retrospective analysis and may be limited by sample size and influenced by the bias of practice patterns. The low incidence of both clinically identified and pathologically staged T3a and T3b disease reflects an institutional pattern of referring T3 patients for consideration of definitive external beam radiation therapy. Furthermore, interobserver variation between radiologists could not be assessed, as MRI reports were generated without a confirmatory or contradicting evaluation by a second radiologist. While PI-RADS v. 2.1 (2019, ACR) outlines a standardized approach,¹⁴ improved nomenclature standardization, template reporting, and more quantitative interpretation criteria may facilitate the elimination of interradiologist variability. Within this context, analysis between Tesla 1 and Tesla 3.5 imaging was unable to be assessed, owing to underpowering. Additionally, as this study spans a decade, improved clinical staging and MP-MRI assessment may bias the results. Finally, it is important to acknowledge the financial burden to both patients and the health care system associated with the implementation of MRI for all PC patients.

Overall, while past studies have shown MP-MRI to improve the likelihood of finding clinically relevant PC, the present study is a direct comparison of conventional versus MP-MRI-based staging methods. Utilization of MP-MRI significantly improved staging and risk stratification, especially in locoregional disease, as demonstrated by the significant upstaging of patients, particularly from T2 to T3 disease. As the addition of MP-MRI significantly improved the detection of extracapsular extension, seminal vesicle invasion, and high- or very-high-risk disease, the use of MP-MRI-based staging would also result in a change in treatment recommendation. The improved accuracy associated with MP-MRI in staging and risk stratification further supports the recent inclusion of soft tissue imaging in the initial evaluation of unfavorable intermediate and higher primary PC per the NCCN guidelines. Given these findings, this study argues for the further use of MP-MRI in the clinical staging of PC, including the adoption of MP-MRI in the risk stratification and staging work up in the AJCC guidelines, as well as utilization in lower risk PC per the NCCN guidelines, given the greater than 25% rate of upstaging achieved using MP-MRI in this study. Further investigation of the ability of MP-MRI to accurately assess disease extent is warranted, including a focus on the variation of sensitivity and specificity of MP-MRI between studies.

Conclusion

The present study demonstrates the value of MP-MRI in accurately identifying T3a disease and improving risk stratification for patients with high- or very-high-risk PC, compared with conventional clinical staging without imaging. The addition of MP-MRI not only resulted in the accurate upstaging of over 25% of patients, but also significantly enhanced the predictive capability when combined with patient characteristics. Overall, these findings represent an opportunity to further integrate MP-MRI into clinical staging guidelines to better facilitate clinical decision-making and personalized treatment.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.adro.2024. 101493.

References

- 1. American Cancer Society. Key Statistics for Prostate Cancer: Prostate Cancer Facts. Available at: www.cancer.org/cancer/prostate-can cer/about/key-statistics.html. Accessed April 1, 2024.
- Calais J, Ceci F, Eiber M, et al. 18F-fluciclovine PET-CT and 68Ga-PSMA-11 PET-CT in patients with early biochemical recurrence after prostatectomy: A prospective, single-centre, single-arm, comparative imaging trial. *Lancet Oncol.* 2019;20:1286-1294. Published correction appears in *Lancet Oncol.* 2020;21:e304.
- Mottaghy FM, Heinzel A, Verburg FA. Molecular imaging using PSMA PET/CT versus multiparametric MRI for initial staging of prostate cancer: Comparing apples with oranges? *Eur J Nucl Med Mol Imaging*. 2016;43:1397-1399.
- Turkbey B, Brown AM, Sankineni S, Wood BJ, Pinto PA, Choyke PL. Multiparametric prostate magnetic resonance imaging in the evaluation of prostate cancer. *CA Cancer J Clin.* 2016;66:326-336.
- National Comprehensive Cancer Network. Prostate Cancer (Version 4.2023). Available at: https://www.nccn.org/professionals/physi cian_gls/pdf/prostate.pdf. Accessed September 20, 2023.
- Ahdoot M, Wilbur AR, Reese SE, et al. MRI-targeted, systematic, and combined biopsy for prostate cancer diagnosis. N Engl J Med. 2020;382:917-928.
- Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med. 2018;378:1767-1777.

- Ahmed HU, El-Shater Bosaily A, Brown LC, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): A paired validating confirmatory study. *Lancet*. 2017;389:815-822.
- Feng TS, Sharif-Afshar AR, Wu J, et al. Multiparametric MRI improves accuracy of clinical nomograms for predicting extracapsular extension of prostate cancer. *Urology*. 2015;86:332-337.
- de Rooij M, Hamoen EH, Witjes JA, Barentsz JO, Rovers MM. Accuracy of magnetic resonance imaging for local staging of prostate cancer: A diagnostic meta-analysis. *Eur Urol.* 2016;70: 233-245.
- 11. Amin MB, Greene FL, Edge SB, et al. The eighth edition AJCC cancer staging manual: Continuing to build a bridge from a populationbased to a more "personalized" approach to cancer staging. *CA Cancer J Clin.* 2017;67:93-99.
- Mohler JL, Antonarakis ES, Armstrong AJ, et al. Prostate cancer, version 2.2019, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2019;17:479-505.
- Amin MB, Edge SB, Greene FL, et al. AJCC Cancer Staging Manual. 8th ed. Springer; 2017.
- 14. Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS prostate imaging - reporting and data system: 2015, version 2. *Eur Urol*. 2016;69: 16-40.
- Kim S, Lee W. Does McNemar's test compare the sensitivities and specificities of two diagnostic tests? *Stat Methods Med Res.* 2017;26: 142-154.
- DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: A nonparametric approach. *Biometrics*. 1988;44:837-845.
- Rayn KN, Bloom JB, Gold SA, et al. Added value of multiparametric magnetic resonance imaging to clinical nomograms for predicting adverse pathology in prostate cancer. J Urol. 2018;200:1041-1047.
- Bakavicius A, Drevinsakaite M, Daniunaite K, et al. The impact of prostate cancer upgrading and upstaging on biochemical recurrence and cancer-specific survival. *Medicina*. 2020;56:61.
- **19.** Billing A, Buchner A, Stief C, Roosen A. Preoperative mp-MRI of the prostate provides little information about staging of prostate carcinoma in daily clinical practice. *World J Urol.* 2015;33:923-928.