Risk of Clinically Significant Prostate Cancer Associated With Prostate Imaging Reporting and Data System Category 3 (Equivocal) Lesions Identified on Multiparametric Prostate MRI

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OBJECTIVE. The objective of this study is to determine the frequency of clinically significant cancer (CSC) in Prostate Imaging Reporting and Data System (PI-RADS) category 3 (equivocal) lesions prospectively identified on multiparametric prostate MRI and to identify risk factors (RFs) for CSC that may aid in decision making.

MATERIALS AND METHODS. Between January 2015 and July 2016, a total of 977 consecutively seen men underwent multiparametric prostate MRI, and 342 underwent MRI–ultrasound (US) fusion targeted biopsy. A total of 474 lesions were retrospectively reviewed, and 111 were scored as PI-RADS category 3 and were visualized using a 3-T MRI scanner. Multiparametric prostate MR images were prospectively interpreted by body subspecialty radiologists trained to use PI-RADS version 2. CSC was defined as a Gleason score of at least 7 on targeted biopsy. A multivariate logistic regression model was constructed to identify the RFs associated with CSC.

RESULTS. Of the 111 PI-RADS category 3 lesions, 81 (73.0%) were benign, 11 (9.9%) were clinically insignificant (Gleason score, 6), and 19 (17.1%) were clinically significant. On multivariate analysis, three RFs were identified as significant predictors of CSC: older patient age (odds ratio [OR], 1.13; $p = 0.002$), smaller prostate volume (OR, 0.94; $p = 0.008$), and abnormal digital rectal examination (DRE) findings (OR, 3.92; $p = 0.03$). For PI-RADS category 3 lesions associated with zero, one, two, or three RFs, the risk of CSC was 4%, 16%, 62%, and 100%, respectively. PI-RADS category 3 lesions for which two or more RFs were noted (e.g., age ≥ 70 years, gland size ≤ 36 mL, or abnormal DRE findings) had a CSC detection rate of 67% with a sensitivity of 53%, a specificity of 95%, a positive predictive value of 67%, and a negative predictive value of 91%.

CONCLUSION. Incorporating clinical parameters into risk stratification algorithms may improve the ability to detect clinically significant disease among PI-RADS category 3 lesions and may aid in the decision to perform biopsy.

Keywords: MRI-ultrasound fusion targeted biopsy, PI-RADS category 3 lesions, PI-RADS version 2, prostate cancer, prostate multiparametric MRI

doi.org/10.2214/AJR.17.18516

Received May 17, 2017; accepted after revision June 25, 2017.

Based on a presentation at the Society of Abdominal Radiologists 2017 annual meeting, Hollywood, FL.

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AJR 2018; 210:347–357

0361–803X/18/2102–347

Although prostate cancer remains a leading cause of death in the United States, men with newly diagnosed prostate cancer die of other causes [1]. Determining the risk of life-threatening versus indolent prostate cancer is therefore an important goal of management. The emergence of multiparametric prostate MRI has led to improved detection of higher-grade disease with implications for active surveillance and risk stratification [2, 3].

Multiparametric prostate MRI has variable sensitivity and specificity for localizing clinically significant prostate cancer [4, 5]. In addition, variation in the performance, interpretation, and reporting of multiparametric prostate MRI examinations has been an obstacle to widespread implementation. The Prostate Imaging Reporting and Data System (PI-RADS), a structured reporting system and joint effort by several organizations, addressed these concerns by standardizing the terminology, interpretation, and content of multiparametric prostate MRI reports, developing assessment categories that outline levels of suspicion for clinically significant prostate cancer, and establishing acceptable technical parameters for data acquisition [6]. PI-RADS version 2 (PI-RADSv2) uses a Likert scale and groups lesions into five categories on the basis of the risk of clinically significant malignant disease. PI-RADS category 3 lesions are of intermediate status, with a risk of malignancy that is equivocal.

Although the PI-RADS system provides guidelines for uniform lesion character-

ization, the management of each category of PI-RADS lesion is not specified. Biopsy is generally recommended for lesions in PI-RADS categories 4 and 5. No recommendations exist for the management of PI-RADS category 3 lesions secondary to the unknown frequency of clinically significant disease in these lesions. Several investigations have been specifically aimed at evaluating lesions scored as equivocal with the use of the PI-RADS and PI-RADSv2 scoring systems or variations thereof. However, these studies have reported variable rates of prostate cancer detection, ranging from 7% to 60% for lesions scored with PI-RADS and non–PI-RADS scoring systems and from 19% to 25% for lesions scored with PI-RADSv2 [4, 7–11]. Accurately and consistently defining the risk of prostate cancer for these lesions is important for clinical decision making, particularly in light of the recent Prostate MR Imaging Study (PROMIS) trial results supporting a growing role for multiparametric MRI in the evaluation of patients with prostate cancer [4].

Given this wide range of reported cancer detection rates, we sought to determine the frequency of clinically significant cancer among PI-RADS category 3 (equivocal) lesions identified prospectively on multiparametric prostate MRI and categorized using PI-RADSv2. In addition, we sought to identify predictors of clinically significant disease that may be used to provide a more refined estimation of risk and aid in clinical decision making.

Materials and Methods

This study was approved by the institutional review board and was HIPAA compliant. A waiver of informed consent was approved by the human investigation committee at our institution.

We performed a retrospective review of all consecutively seen men (mean age, 65 years; range, 41–85 years) who underwent prostate MRI at a single academic center between January 2015 and July 2016. Inclusion criteria for the study were having MRI performed using a 3-T scanner, followed by MR-US fusion targeted biopsy, and having a lesion scored as PI-RADS category 3 with the use of PI-RADSv2. Exclusion criteria were not undergoing targeted biopsy, having a study performed either on a 1.5-T scanner or at an outside facility, and having a lesion scored as PI-RADS category 2, 4, or 5. All patients were treatment naive. A total of five patients with PI-RADS category 3 lesions underwent scanning performed using a 1.5-T scanner to reduce artifact from orthopedic hardware or hip prostheses. Figure 1 provides details about the inclusion and exclusion criteria used in the present study.

Demographic, clinical, MRI, and pathologic data were collected for each patient with a PI-RADS category 3 lesion. Demographic data included age and race. Clinical data included prostate specific antigen (PSA) and digital rectal examination (DRE) results (normal vs abnormal findings). The referring urologist performed DRE, and abnormal examination results were reported as areas of localized or generalized firmness, induration, irregularity, or nodularity suggestive of a cT2 lesion. MRI data included total prostate volume, lesion volume, lesion location, and PI-RADSv2 score. Pathologic data included the Gleason score. For the purpose of analysis, PI-RADS category 3 lesions were divided into three categories on the basis of targeted biopsy results: benign, clinically insignificant disease (defined by a Gleason score ≤ 6 or lower), and clinically significant cancer (CSC) (defined by a Gleason score ≥ 7).

All studies were prospectively interpreted by board-certified body subspecialty radiologists at a single academic institution in the course of routine clinical work. A total of nine attending radiologists with 1–32 years of experience (median, 6 years) participated in examination interpretation. Studies were reviewed on dedicated diagnostic monitors with the use of PACS software (Synapse, Fuji Film). Source dynamic contrast-enhanced images without postprocessing were used for interpretation. Lesions were scored using the PI-RADSv2 scoring system, and all radiologists were trained in the use of the PI-RADSv2 system before evaluating examinations.

Multiparametric prostate MRI scans were performed using a 3-T scanner (Verio, Siemens Healthcare) with a 32-channel body coil. No endorectal coils were used. Given the extended period chosen for the study, the exact protocols were not constant across all cases; however, all scans included axial, sagittal, and coronal T2-weighted sequences, axial T1-weighted sequences with fat saturation, axial DW images with an extrapolated b value of 1600, and axial T1-weighted dynamic contrast-enhanced sequences with fat saturation and a temporal resolution of 6 seconds, as recommended by PI-RADSv2. Gadobutrol IV contrast medium (0.1 mmol/kg of body weight; Gadovist, Bayer HealthCare) was used.

Target lesions were contoured by radiologists using dedicated imaging software (Profuse, Eigen). Targeted lesion biopsy was performed by one of two urologists with a median of 21.5 years of experience (range, 6–37 years), with use of MRI fusion with a transrectal ultrasound–guided biopsy system (Artemis, Eigen). A mean of five biopsy core specimens were obtained from each targeted lesion. After targeted biopsy, each patient underwent 12-core systematic biopsy. Systematic biopsy was performed using a template map that was generated by the fusion software.

Gleason scoring was determined in a subspecialty sign-out at the same academic center by one of two genitourinary pathologists with a median of 19 years of experience (range, 11.5–26.5 years). Modified Gleason grading was performed using 2014 International Society of Urologic Pathology guidelines [12].

Demographic and clinical data were reviewed and initially were compared using the *t* test, for continuous variables, and the Fisher exact test, for categoric variables. A multivariate logistic regression model was then constructed to identify risk factors (RFs) associated with clinically significant prostate cancer. Factors were chosen based on inclusion criteria for which $p < 0.15$ on univariate analysis, and the multivariate model was created using forward selection. Collinearity was assessed using variance inflation factors with interaction terms to adjust for collinear factors. Statistical analysis was performed using SAS software (version 9.4, SAS Institute).

Results

Frequency of Clinically Significant Cancer

Characteristics of the patients with PI-RADS category 3 lesions selected for analysis are summarized in Table 1. MRI-US fusion targeted biopsy revealed that 81 of these 111 lesions were benign (72.9%), 11 were clinically insignificant (9.9%), and 19 harbored CSC (17.1%). Of the 19 lesions with CSC, 14 had a Gleason score of 3 + 4, three had a Gleason score of 4 + 3, and two had a Gleason score of 4 + 4. No PI-RADS category 3 lesion was associated with a Gleason score of 9 or 10. Of the 81 benign lesions, one had inflammatory changes on pathologic analysis, and the remaining 80 lesions had benign prostatic tissue on pathologic analysis. Representative images of PI-RADS category 3 lesions for which pathologic results of targeted biopsy denoted benign status and CSC can be seen in Figures 2 and 3, respectively. In addition, representative images for transition zone lesions with benign status and CSC are shown in Figures 4 and 5, respectively.

Of the 111 lesions evaluated, 51 were in prostates with only one targeted lesion (the index PI-RADS category 3 lesion), 37 were in glands with two lesions (i.e., other PI-RADS lesions), 19 were in glands with three lesions,

TABLE 1: Clinical and Demographic Characteristics of Patients With 111 Prostate Imaging Reporting and Data System Category 3 Lesions Selected for Analysis

Characteristic	Value
Age (y)	
Median	63
Range	46–82
PSA level (ng/mL)	
Median	5.9
Range	1.0–50.0
PSA density (ng/mL^2)	0.12
Lesion volume (mL)	
Median	0.15
Range	0.01–11.1
Prostate volume (mL)	
Median	49.8
Range	15.6–145.0
Abnormal DRE finding	40 (36)
Peripheral zone location of lesion	93 (84)

Note—Except where otherwise indicated, data are number (%) of lesions. PSA = prostate specific antigen, DRE = digital rectal examination.

TABLE 2: Comparison of Clinical and Demographic Characteristics of Patients With Prostate Imaging Reporting and Data System Category 3 Lesions With Benign Status or Insignificant Disease Versus Clinically Significant Disease

Characteristic	Benign or Clinically Insignificant Lesions[a] (n = 92)	Clinically Significant Lesions[b] (n = 19)	p
Median age (y)	63	70	0.02[c]
Median PSA level (ng/mL)	6.1	5.9	0.19
PSA density (ng/mL^2)	0.17	0.12	0.13
Median lesion volume (mL)	0.17	0.12	0.13
Median prostate volume (mL)	56	36	0.01[c]
Abnormal DRE finding	18 (20)	8 (42)	0.07[c]
Peripheral zone location of lesion	79 (86)	14 (74)	0.16

Note—Except where otherwise indicated, data are number (%) of lesions. PSA = prostate specific antigen, DRE = digital rectal examination.
[a]Clinically insignificant disease was defined by a Gleason score of 6 or less.
[b]Clinically significant disease was defined by a Gleason score of at least 7.
[c]Statistically significant.

and four were in glands with four lesions. Of the glands with only a single targeted PI-RADS category 3 lesion, 5.9% (3/51) were found to have a higher Gleason score on the basis of pathologic findings for the targeted lesion than on pathologic findings for standard biopsy specimens obtained anywhere else in the gland. Of the glands with more than one targeted lesion, 33.3% (20/60) had a higher Gleason score on the basis of pathologic findings for a different targeted lesion within the same prostate.

A total of 8.1% (9/111) of targeted PI-RADS category 3 lesions had a higher Gleason score than did standard biopsy specimens obtained anywhere in the gland, 35.1% (39/111) had a higher Gleason score on the basis of pathologic findings for standard biopsy specimens from elsewhere in the gland, and 57.7% (64/111) had equivalent pathologic findings for targeted biopsy and standard biopsy specimens. None of the PI-RADS category 3 lesions with a higher Gleason score on the basis of pathologic findings from targeted biopsy compared with standard biopsy (9/111) had a higher Gleason score for a different non–PI-RADS category 3 target lesion (in glands with more than one lesion).

Predictors of Clinically Significant Cancer and Risk Stratification

In comparison with lesions found to be benign or clinically insignificant, lesions that harbored CSC were associated with a significantly older median patient age (p = 0.02) and a smaller median prostate size (p = 0.01), and they also showed a trend toward a higher frequency of abnormal DRE findings (p = 0.07) on univariate analysis (Table 2).

No statistically significant associations existed between the identification of clinically significant disease on biopsy and the median PSA level (p = 0.19), median PSA density (PSA level [ng/mL]/gland volume [mL]) (p = 0.13), or median lesion volume (p = 0.13). In all, 93 of 111 lesions (84%) were located in the peripheral zone, but no statistically significant difference between benign or clinically insignificant lesions and clinically significant lesions existed on the basis of peripheral zone location (p = 0.16).

Multivariate logistic regression identified three significant RFs associated with a higher likelihood of CSC: older patient age (median, 70 years; odds ratio [OR], 1.13; p = 0.002), smaller prostate volume (median, 36 mL; OR, 0.94; p = 0.008), and clinically abnormal DRE results (OR, 3.92; p = 0.03). The CSC detection rate (defined as the proportion of lesions with clinically significant disease) for each RF and combination of RFs is shown in Table 3. The cancer detection rate based on the number of risk factors present per lesion, as well as the corresponding sensitivity, specificity, positive predictive value, and negative predictive value, was then determined (Table 4). Using a criterion of two or more risk factors, we found a CSC detection rate of 67% (with 10 of the 19 lesions with CSC identified), corresponding to a sensitivity of 53%, a specificity of 95%, a positive predictive value of 67%, and a negative predictive value of 91%.

Discussion

In our series of PI-RADS category 3 lesions, malignancy with a Gleason score of at least 6 was found in approximately one of four lesions scored as PI-RADS category 3, and approximately one of six lesions harbored CSC. MRI-US fusion targeted biopsy of the index PI-RADS category 3 lesion resulted in identification of the highest Gleason score in 8% of cases, compared with the highest Gleason score identified on standard biopsy or for other targeted lesions within the same gland. We identified three clinical parameters (age ≥ 70 years, an abnormal DRE finding, and gland size ≤ 36 mL) that predicted CSC among PI-RADS category 3 lesions. In addition, we found that PI-RADS category 3 lesions for which two or more of these risk factors were noted had a rate of CSC of 67%, and incorporating these two factors with a PI-RADS category 3 finding was associated with a high specificity and negative predictive value. These results suggest that the use of clinical parameters in risk stratification algorithms may improve the rate of detection of CSC and aid in the decision to biopsy or monitor PI-RADS category 3 lesions. Of importance, our study

TABLE 3: Cancer Detection Rate Associated With Each Risk Factor Identified on Multivariate Analysis to Be Associated with Clinically Significant Disease on Targeted MRI-Ultrasound Fusion Biopsy of Prostate Imaging Reporting and Data System Category 3 Lesions

Risk Factor(s)[a]	No. of Lesions		Cancer Detection Rate (%)
	Total (*n* = 111)	With Clinically Significant Prostate Cancer (*n* = 19)	
None	53	2	4
Patient age ≥ 70 y	8	1	13
Gland volume ≤ 36 mL	20	5	25
Abnormal DRE	15	1	7
Patient age ≥ 70 y and gland volume ≤ 36 mL	4	3	75
Patient age ≥ 70 y and abnormal DRE finding	8	4	50
Abnormal DRE finding and gland volume ≤ 36 mL	1	1	100
Patient age ≥ 70 y, abnormal DRE finding, and gland volume ≤ 36 mL	2	2	100

Note—DRE = digital rectal examination.
[a]Risk factors for clinically significant disease included age 70 years or older, abnormal findings of DRE, and gland size of 36 mL or less.

is one of the first to present data exclusively based on the PI-RADSv2 scoring system.

One of the main goals of this study was to determine the risk of clinically significant prostate cancer in PI-RADS category 3 lesions with the use of PI-RADSv2, so that more appropriate clinical decisions can be made regarding patient management. Our study achieved this goal and identified specific clinical and demographic characteristics that better define the underlying risk and aid in decision making. Before this study was conducted, our institutional policy was to biopsy all PI-RADS category 3 lesions; however, our findings could be valuable in determining the necessity of biopsy for a PI-RADS category 3 lesion in the future, especially if there are patient factors that make biopsy unfavorable. For example, a clinician may choose to be more aggressive in managing a patient with a PI-RADS category 3 lesion who has two or more of our identified RFs versus one with no RFs.

There has been significant variability in the reported estimates of prostate cancer associated with equivocal lesions. For instance, Pokorny et al. [8] classified 33 lesions as equivocal on the basis of PI-RADS, version 1 (PI-RADSv1), in a series of 250 men and found that 45% (15/33) of equivocal lesions had histologically confirmed prostatic adenocarcinoma with a Gleason score of at least 6, and 15% (5/33) had disease with a Gleason score of at least 7. Similarly, also using PI-RADSv1, Thompson et al. [7] reported a 26% (15/57) detection rate of prostatic adenocarcinoma in their series of 150 biopsied equivocal lesions. In contrast, Liddell et al. [9] reported a cancer detection rate of only 7% (6/92) in their series of 92 equivocal lesions in 118 men, with use of a modified PI-RADS scoring system. The recently published PROMIS trial reported a malignancy detection rate of 60% (98/163) among lesions classified as equivocal, also with the use of a validated (non–PI-RADS) consensus scoring system, in a series of 576 lesions [4]. Finally, using PI-RADSv2, Mehralivand et al. [10] reported a cancer detection rate of 25% (33/133), and Tan et al. [11] reported a rate of 19% (6/31), both of which approximate our findings.

On multivariate analysis, we identified three clinical parameters that, on the basis of prior studies, are known risk factors for clinically significant prostate cancer. Advanced age has long been associated with a higher risk of prostate adenocarcinoma. DRE findings have recently been shown to independently predict the risk of significant prostate cancer and improve the accuracy of risk assessment with the use of multivariate risk calculators [13]. In addition, despite being a subjective test, DRE findings are still used in the seventh edition of the American Joint Committee on Cancer staging guidelines for prostate cancer, on the basis of their continued prognostic importance. Smaller gland size has also been associated with a higher risk of significant prostate cancer and has similarly

TABLE 4: Prostate Imaging Reporting and Data System Category 3 Lesions With Risk Factors for Clinically Significant Disease and Associated Values

No. of Risk Factors[a]	No. of Lesions		Cancer Detection Rate (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	Total (*n* = 111)	With Clinically Significant Prostate Cancer (*n* = 19)					
0	53	2	4	11	45	4	71
1	43	7	16	37	61	16	82
2	13	8	62	42	95	62	89
3	2	2	100	11	100	100	84
≥ 2	15	10	67	53	95	67	91

Note—PPV, positive predictive value, NPV = negative predictive value.
[a]Risk factors for clinically significant disease included age 70 years or older, abnormal findings of digital rectal examination, and gland size of 36 mL or less.

been found to be an independent predictor of CSC in risk assessment models [14]. More recently, Radtke et al. [15] determined the clinical parameters of more than 1100 men who underwent multiparametric prostate MRI followed by MR-US fusion biopsy between 2012 and 2015. They then performed multivariate regression to identify predictors of CSC for use in the development of combined risk models that incorporate clinical and imaging findings. They found that a higher PSA level (OR, 2.08), a smaller gland size (OR, 0.81), abnormal DRE results (cT2 [or higher] lesion; OR, 4.09), and advanced age (OR, 1.09) were independently associated with CSC in models using PI-RADSv1 findings. Of interest, abnormal DRE findings (cT2 [or higher] lesion) were associated with the highest OR in the study by Radtke and colleagues as well as in our study.

In addition, previous studies have shown a correlation of higher PSA density and larger lesion volume with an increased risk of clinically significant cancer [16–18]. These studies did not specifically analyze the subset of PI-RADS category 3 lesions. In our study that exclusively evaluated PI-RADS category 3 lesions, we did not find a similar association between PSA density or lesion volume and the risk of clinically significant disease, although both variables showed a trend toward significance. The lack of significance is likely attributable to the smaller sample size, or it may be related to an interactive effect with prostate volume. It is also possible that lesions with a higher PSA density, lesion size, or both more commonly present as lesions categorized as PI-RADS category 4 or 5 and therefore may not be truly correlated with PI-RADS category 3 lesions. Further studies from other institutions would be useful to corroborate or refute this finding.

Our study has several strengths and limitations. The main strengths of our study include prospective scoring of PI-RADS lesions in routine practice, evaluation by radiologists trained in the use of PI-RADSv2 at a high-volume center, and a large number of patients. One of the main limitations is the use of multiple readers, and prospective scoring introduces interobserver variability of lesion identification and classification. However, when strictly adhering to PI-RADSv2, classification is particularly problematic when findings are equivocal. According to the PI-RADS lexicon, these lesions "include all others that do not qualify as 2, 4, or 5," [6] which leaves room for interpretation. A recent publication by Greer et al. [19] evaluated the accuracy and agreement of readers using PI-RADSv2 and showed a mean agreement of 74% between readers for assignment of PI-RADS category. An additional study evaluating interobserver agreement by Muller et al. [20] also showed moderate agreement between readers using PI-RADSv2. Finally, although the use of multiple readers inherently introduces variability, it also is a strength of our study in that it reflects the results that may be realistically achieved in real prospective clinical work at a large academic center.

Another limitation of the present study is the use of different imaging protocols over the course of many years. Presumably, lesion conspicuity may differ depending on differences in specific examination settings. To attempt to control for this, we analyzed a subset of lesions identified using the same 3-T MRI scanner. Although there were mild discrepancies in protocols and image acquisition parameters, all sequences recommended by the PI-RADSv2 lexicon were obtained in all scans. This study can be expanded in the future to analyze and compare results obtained from various scanners, which would closely resemble routine clinical practice, where multiple scanners and even vendors coexist.

Additional limitations include exclusion of multiparametric MRI performed using a 1.5-T scanner, lack of endorectal coil utilization, and possible selection bias resulting from the retrospective nature of the study and the small number of patients who did not undergo MRI-US fusion biopsy. These factors may limit the generalizability of our results to centers using 1.5-T scanners and endorectal coils. The possibility of inaccurate targeting via MR-US fusion biopsy is another consideration because fusion biopsy may be less accurate for small lesions [21]. Histologic contamination of PI-RADS category 3 lesions by systematic biopsy is another less likely but plausible confounding factor. Furthermore, on the basis of our definition of CSC, any lesion with a Gleason malignancy score of 6, even with extraprostatic extension or volume greater than 0.5 mL, would have been classified as nonsignificant. Therefore, our estimation of clinically significant disease may be lower. Finally, peripheral zone PI-RADS category 3 lesions are the dominant lesions in our cohort, whereas indeterminate lesions are expected to be found more often in the transition zone.

In conclusion, PI-RADS category 3 lesions continue to present a major problem for the interpreting radiologist, treating clinician, and, most importantly, the patient. Although PI-RADSv2 currently represents the most up-to-date information on how to acquire, interpret, and report results of multiparametric prostate MRI, the categorization and management of PI-RADS category 3 lesions remains inexact and challenging. The incorporation of pre-MRI clinical parameters into risk stratification models may therefore be useful in selecting patients for biopsy or close follow-up. Additional research, ideally involving a larger sample size and multiple institutions, is needed to validate these findings and may lead to more refined risk estimates. Further modifications of PI-RADS and more granular estimates of risk will likely emerge as research continues, experience accrues, and technology evolves.

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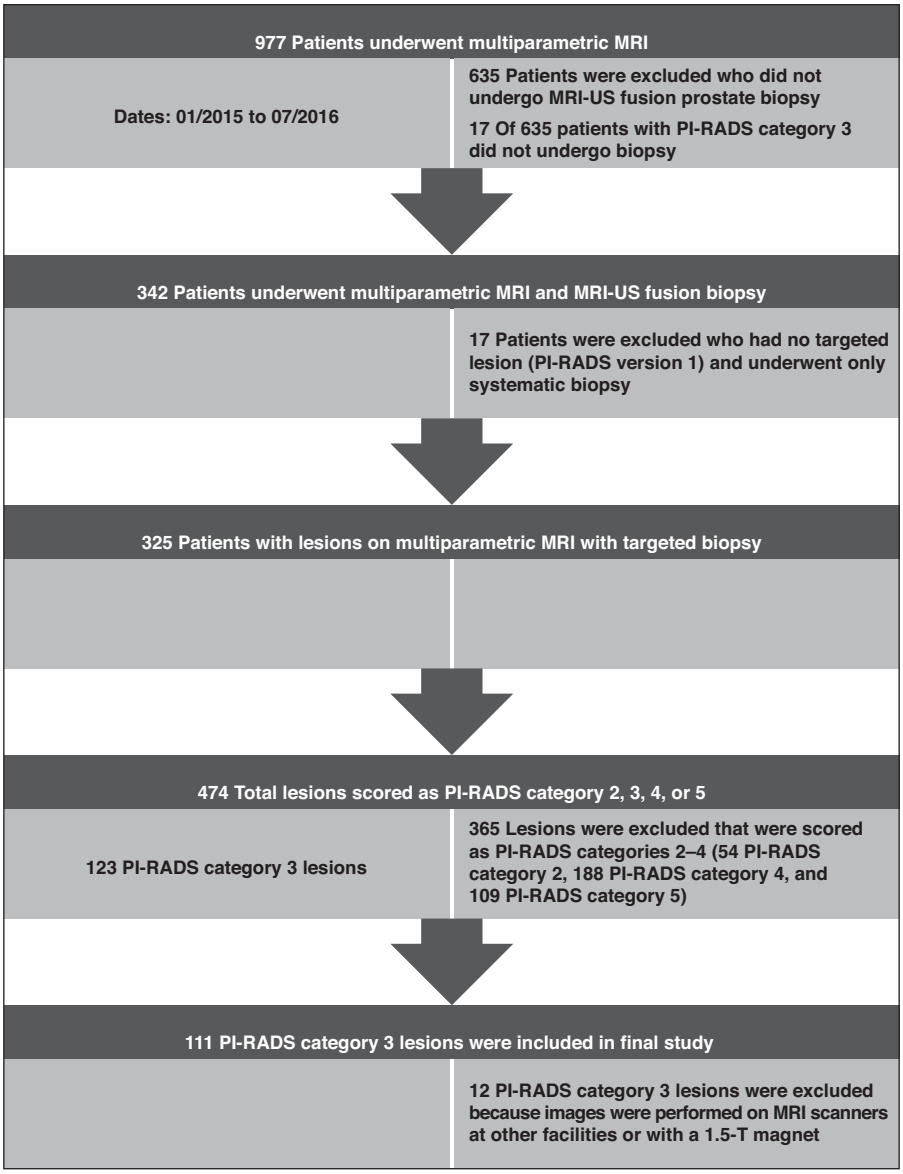

Fig. 1—Diagram with inclusion and exclusion criteria used for study population. US = ultrasound, PI-RADS = Prostate Imaging Reporting and Data System.

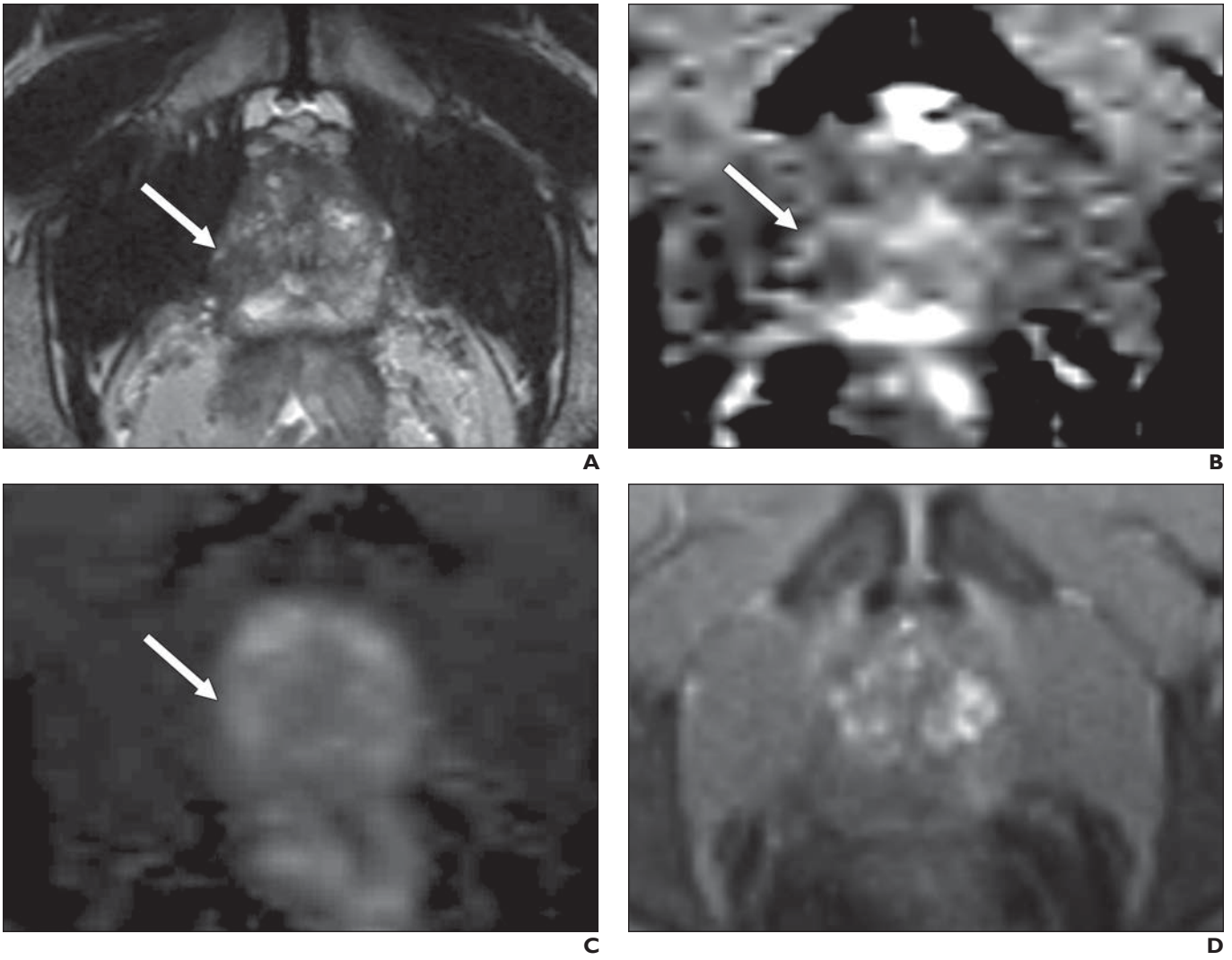

Fig. 2—61-year-old man with concern for prostate cancer, prostate specific antigen level of 4.9 ng/mL, and benign pathologic finding on standard transrectal ultrasound–guided biopsy who was found to have representative Prostate Imaging Reporting and Data System category 3 lesion in peripheral zone with benign status after targeted biopsy.
A–D, Lesion (size, 1 cm) (*arrow*, **A–C**) identified in right posterolateral apex of peripheral zone appears moderately homogeneous and hypointense on T2-weighted MR image (**A**), moderately hypointense on apparent diffusion coefficient map (**B**), and mildly hyperintense on high-b-value DW image (**C**) but shows no focal enhancement on early phase dynamic contrast-enhanced MR image (**D**).

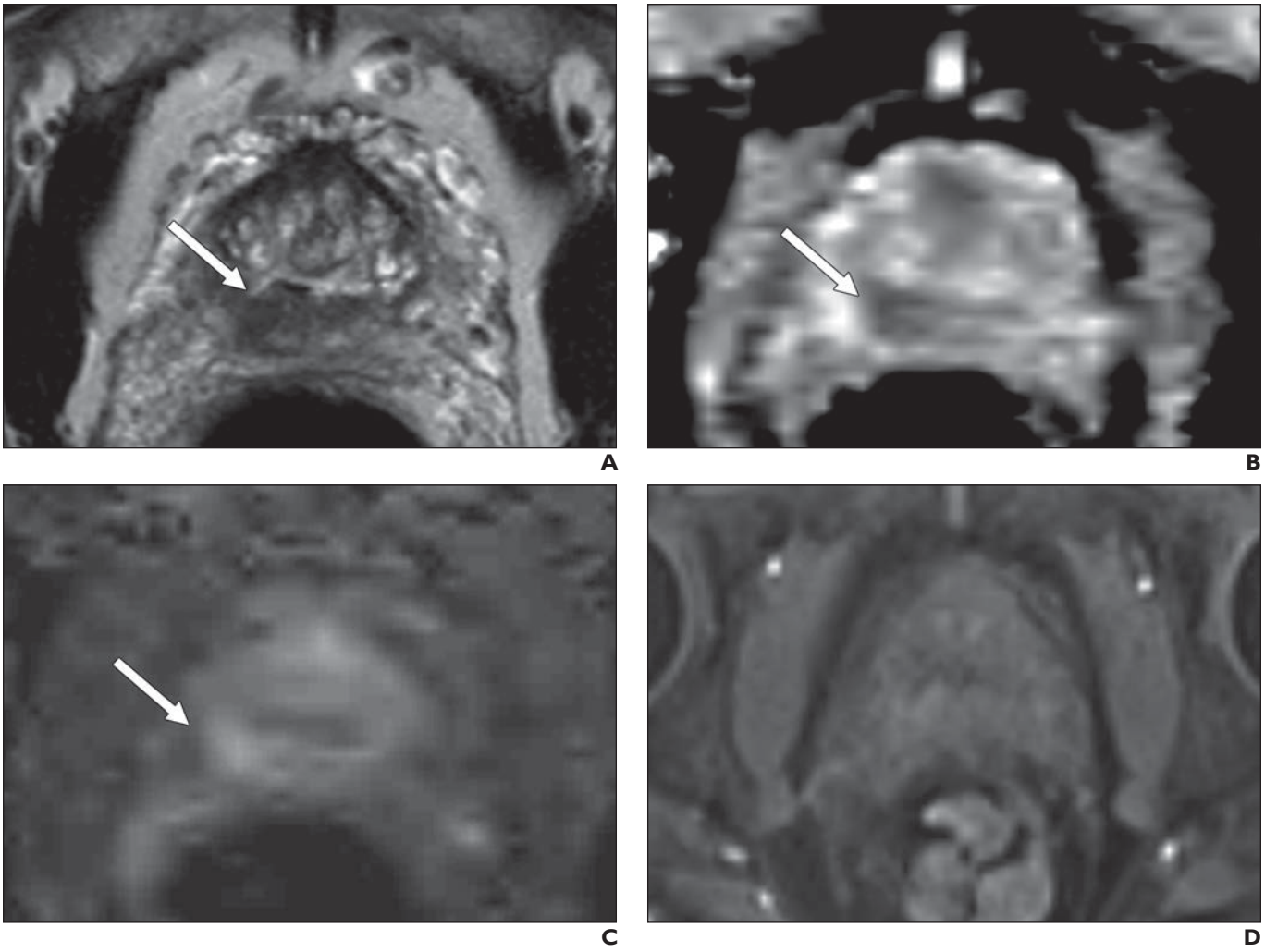

Fig. 3—71-year-old man with prostate cancer, prostate specific antigen level of 7.1 ng/mL, and disease with Gleason score of 3 + 4 on standard transrectal ultrasound–guided biopsy who had representative Prostate Imaging Reporting and Data System category 3 lesion in peripheral zone with clinically significant cancer (Gleason score, 3 + 4) noted as pathologic finding after targeted biopsy.
A–**D,** Lesion (size, 1 cm) (*arrow*, **A**–**C**) in right medial posterior base of peripheral zone is moderately homogeneous and hypointense on T2-weighted MR image (**A**), moderately hypointense on apparent diffusion coefficient map (**B**), and mildly hyperintense on high-b-value DW image (**C**) but shows no focal enhancement on early phase dynamic contrast-enhanced MR image (**D**).

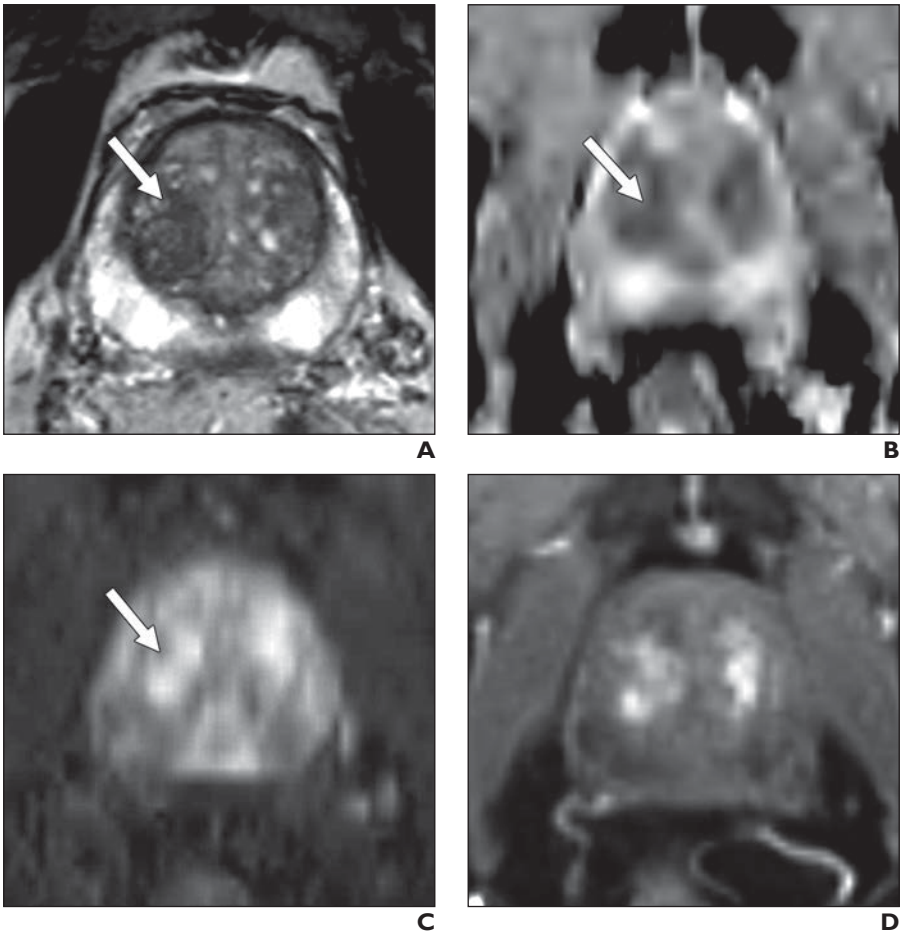

Fig. 4—63-year-old man with concern for prostate cancer, prostate specific antigen level of 10.8 ng/mL, and benign pathologic finding on standard transrectal ultrasound–guided biopsy who was found to have representative Prostate Imaging Reporting and Data System category 3 lesion in transition zone with benign pathologic finding after targeted biopsy.
A–**D,** Lesion (size, 1 cm) (*arrow*, **A**–**C**) in right posterior transition zone shows heterogeneous T2 signal intensity with obscured medial margin on T2-weighted MR image (**A**), is focally mild to moderately hypointense on apparent diffusion coefficient map (**B**), is mildly hyperintense on high-b-value DW image (**C**), and shows no focal enhancement on early phase dynamic contrast-enhanced MR image (**D**).

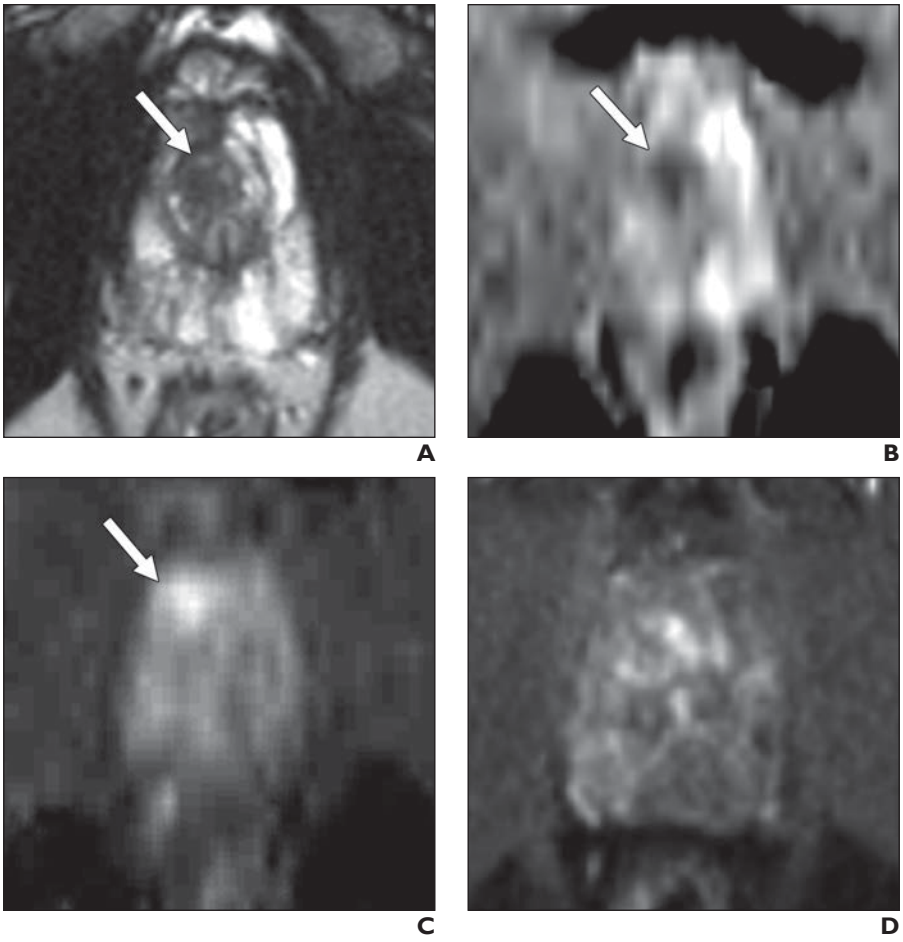

Fig. 5—54-year-old man with concern for prostate cancer, prostate specific antigen level of 5.7 ng/mL, and disease of Gleason score 4 + 3 on standard biopsy who was found to have representative Prostate Imaging Reporting and Data System (PI-RADS) category 3 lesion in transition zone with clinically significant cancer (Gleason score, 4 + 3) noted as pathologic finding after targeted biopsy.
A–**D**, Lesion (size, 0.6 cm) (*arrow*, **A**–**C**) in right anterior transition zone in apex of gland shows heterogeneous T2 signal intensity with obscured margin on T2-weighted MR image (**A**), is focally markedly hypointense on apparent diffusion coefficient (ADC) map (**B**), is focally markedly hyperintense on high-b-value DW image (**C**), and shows no focal enhancement on early phase dynamic contrast-enhanced MR image (**D**). This lesion was classified as PI-RADS category 3 on basis of appearance on T2-weighted MR image and was not upgraded to PI-RADS category 5 despite marked hypointensity on ADC map and hyperintensity on DW image because of size less than 1.5 cm.

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