



Beyond Clinical Staging: The Combined Value of mpMRI Lesion Size and Cancer-positive Biopsy Core Rate in Predicting $\geq$ pT3 Disease

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Abstract

Objective: To investigate preoperative clinical, biopsy-related, and multiparametric magnetic resonance imaging (mpMRI)-derived factors associated with pathological stage $\geq$ pT3 after radical prostatectomy and to evaluate the discriminatory performance of significant predictors individually and in combination.

Materials and Methods: Data prospectively collected from 102 patients who underwent pre-biopsy mpMRI, transrectal ultrasound-guided prostate biopsy, and subsequent radical prostatectomy were analyzed retrospectively. Patients with radiologically detected lymph node involvement or distant metastasis were excluded. Patients were classified as having $<$ pT3 or $\geq$ pT3 disease according to final pathological findings, and preoperative clinical, biopsy-related, and mpMRI-derived parameters were compared between the two groups. Multivariable binary logistic regression was performed to identify independent predictors of $\geq$ pT3 disease. Receiver operating characteristic (ROC) curve analyses were used to evaluate the discriminatory performance of the identified predictors and derive cohort-specific thresholds.

Results: Pathological stage $\geq$ pT3 was identified in 49 patients (48.0%). Patients with $\geq$ pT3 disease had a higher cancer-positive biopsy core rate (52.28 $\pm$ 28.21% vs. 32.57 $\pm$ 17.76%; $p<0.001$) and larger MRI index lesions (median, 20.0 vs. 12.0 mm; $p<0.001$). Both variables remained independently associated with $\geq$ pT3 disease [odds ratio (OR) per 1% increase: 1.033, 95% confidence interval (CI): 1.009-1.057; $p=0.010$; OR per 1-mm increase: 1.274, 95% CI: 1.074-1.511; $p=0.005$]. The area under the curve (AUC) was 0.795 for lesion diameter, 0.703 for cancer-positive core rate, and 0.843 for the combined model. After bootstrap internal validation of the two-variable model, the optimism-corrected AUC was 0.835. ROC-derived thresholds were 17 mm and 38%, respectively. The prevalence of $\geq$ pT3 disease increased from 21.6% with neither risk factor to 47.6% with one and 91.3% with both factors (p for trend <0.001).

Conclusion: MRI index lesion diameter and the cancer-positive biopsy core rate were associated with pathological stage $\geq$ pT3. Their combined assessment may contribute to preoperative risk stratification, although external validation is required.

Keywords: Biopsy, multiparametric magnetic resonance imaging, prostate cancer, stage, tumor volume

Introduction

Prostate cancer is one of the most frequently diagnosed malignancies among men worldwide and represents a major cause of cancer-related morbidity and mortality (1). The initial diagnostic assessment is traditionally based on serum prostate-specific antigen (PSA) measurement and digital rectal examination, followed by histopathological confirmation

through prostate biopsy. In recent years, multiparametric magnetic resonance imaging (mpMRI) has become an integral component of the diagnostic pathway, improving lesion localization, guiding targeted biopsy, and contributing to risk stratification and local staging (2).

Radical prostatectomy remains one of the principal curative treatment options for patients with clinically localized prostate cancer (3). In appropriately selected patients with high-risk or

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locally advanced disease, surgery may also be performed as part of a multimodal treatment strategy that includes radiotherapy and/or systemic therapy (4). More recently, the potential role of radical prostatectomy has also been investigated in carefully selected patients with oligometastatic disease as a component of intensified multimodal management, although patient selection and the oncological benefit of this approach remain under evaluation (5).

Accurate preoperative identification of non-organ-confined disease is essential for patient counselling, surgical planning, decisions regarding nerve-sparing procedures and pelvic lymph-node dissection, and anticipation of additional postoperative treatment (4). Nevertheless, patients considered to have clinically localized disease before surgery may be found to have extraprostatic extension, seminal vesicle invasion, or pathological stage $\geq$ pT3 following radical prostatectomy. Although rectal examination, clinical stage, biopsy grade, PSA-based parameters, and mpMRI findings provide valuable staging information, no single preoperative assessment method can reliably identify all patients with occult $\geq$ pT3 disease (6).

The present study aimed to identify preoperative clinical, biopsy, and mpMRI-derived factors associated with pathological stage $\geq$ pT3 following radical prostatectomy, with particular emphasis on MRI index lesion diameter and the cancer-positive biopsy core rate. We also evaluated the discriminatory performance of these parameters individually and in combination for predicting $\geq$ pT3 disease.

Materials and Methods

Following approval by the University of Health Sciences Türkiye, Izmir City Hospital, Ethics Committee (decision no: 2024/234, date: 04.12.2024), data that had been prospectively collected from a cohort of patients who underwent preoperative imaging followed by radical prostatectomy were retrospectively reviewed. The analysis was designed to investigate the associations of clinical and mpMRI-derived parameters with final pathological T stage. A total of 102 patients were included. Eligible patients had prostate volume measured by transrectal ultrasound, underwent mpMRI before transrectal ultrasound-guided prostate biopsy, had PI-RADS scores and MRI-derived data available on lesion number and index lesion diameter, were diagnosed with prostate cancer on biopsy, and subsequently underwent radical prostatectomy. Patients with radiologically detected lymph node involvement or distant metastasis on preoperative imaging were excluded.

Patients were categorized into two groups according to the final pathological T stage reported after radical prostatectomy: those with organ-confined disease ($<$ pT3) and those with locally advanced disease ($\geq$ pT3). Demographic, clinical, biopsy-related, and mpMRI-derived characteristics were compared between the groups. The evaluated variables included age, preoperative serum PSA level, clinical T stage, biopsy ISUP grade group, cancer-positive biopsy core rate, PI-RADS category, number of MRI-detected lesions, MRI index lesion diameter, and lesion density. The cancer-positive biopsy core rate was calculated by dividing the number of cancer-positive biopsy cores by the total

number of biopsy cores obtained. Lesion density was calculated as the MRI index lesion diameter (mm) divided by the prostate volume measured by transrectal ultrasonography (mL).

Statistical Analysis

The distribution of continuous variables was assessed using the Shapiro-Wilk test and visual inspection of histograms. Normally distributed continuous variables were presented as mean $\pm$ standard deviation and compared using the independent-samples Student's t-test. Non-normally distributed variables were presented as medians and interquartile ranges (IQR) and were compared using the Mann-Whitney U test. Categorical variables were expressed as numbers and percentages and compared using the chi-square test or the Fisher-Freeman-Halton exact test, as appropriate.

A multivariable binary logistic regression analysis was performed to identify independent preoperative predictors of pathological stage $\geq$ pT3. Clinical T stage, ISUP grade group on biopsy, rate of cancer-positive biopsy cores, PI-RADS category, and MRI index lesion diameter were entered into the regression model. Results were reported as odds ratios (ORs) with 95% confidence intervals (CI). Because MRI index lesion diameter had already been incorporated into the multivariable model, lesion density was not included to avoid redundancy and potential multicollinearity.

Receiver operating characteristic (ROC) curve analyses were performed to evaluate the discriminatory ability of MRI index lesion diameter and the cancer-positive biopsy core rate for predicting pathological stage $\geq$ pT3. The area under the curve and the corresponding 95% CIs were calculated. The optimal threshold for the diameter of the MRI index lesion was determined using the maximum Youden index, whereas the threshold for the cancer-positive biopsy core rate was selected as the ROC coordinate that minimizes the absolute difference between sensitivity and specificity.

A separate binary logistic regression model with two predictors, MRI index lesion diameter and cancer-positive biopsy core rate was constructed for prediction, and its predicted probabilities were used for ROC analysis. Predicted probabilities derived from the logistic regression model incorporating both parameters were subsequently used to assess the discriminatory performance of the combined model. Internal validation of the two-variable model incorporating MRI index lesion diameter and the cancer-positive biopsy core rate was performed using bootstrap resampling. For each bootstrap sample, the model was refitted and its discriminatory performance was evaluated both in the bootstrap sample and in the original cohort. Optimism was calculated as the difference between these two AUC estimates, and the mean optimism across bootstrap samples was subtracted from the apparent AUC to obtain the optimism-corrected AUC.

For clinical risk stratification, two tumor-burden risk factors were defined: MRI index lesion diameter ≥ 17 mm and cancer-positive biopsy core rate $\geq 38\%$. Patients were classified as having zero, one, or two risk factors, and the prevalence of $\geq$ pT3 disease was compared across these categories. The association between increasing risk-factor count and $\geq$ pT3 disease was evaluated

using the chi-square test and a test for linear trend. All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 102 patients were included in the study. Age and preoperative PSA data were available for 100 patients. The mean age was 66.6 ± 5.6 years, and the median preoperative PSA level was 9.39 ng/mL (IQR: 6.40 - 15.32). The median number of lesions detected on MRI was 1.5 (IQR: 1 - 2); the median index lesion diameter was 13 mm (IQR: 10 - 20); and the median cancer-positive biopsy core rate was 37.98% (IQR: 23.08 - 53.85). Biopsy ISUP grade groups 1, 2, 3, 4, and 5 were identified in 41 (40.2%), 31 (30.4%), 13 (12.7%), 12 (11.8%), and 5 (4.9%) patients, respectively. On pathological examination of radical prostatectomy specimens, ISUP grade groups 1, 2, 3, 4, and 5 were observed in 20 (19.6%), 54 (52.9%), 17 (16.7%), 4 (3.9%), and 7 (6.9%) patients, respectively. The clinical stages were cT1c in 57 (55.9%), cT2a in 13 (12.7%), cT2b in 23 (22.5%), and cT2c in 9 (8.8%) patients. Final pathological staging after radical prostatectomy revealed pT2a in 16 patients (15.7%), pT2b in 1 patient (1.0%), pT2c in 36 patients (35.3%), pT3a in 26 patients (25.5%), and pT3b in 23 patients (22.6%). Final pathological examination demonstrated $< pT3$ disease in 53 patients (52.0%) and $\geq pT3$ disease in 49 patients (48.0%).

Patients were stratified according to final pathological stage as $< pT3$ ($n=53$) and $\geq pT3$ ($n=49$). Age and preoperative PSA levels were comparable between the groups (67.19 ± 4.63 vs.

65.97 ± 6.48 years, $p=0.282$; and 8.60 (IQR: 5.60 - 14.90) vs. 9.74 (IQR: 6.72 - 17.52) ng/mL, $p=0.180$, respectively). Clinical stage distribution differed significantly between the groups ($p<0.001$); cT1c disease was more frequent in the $< pT3$ group, whereas cT2b and cT2c disease were more common among patients with $\geq pT3$ pathology. Biopsy ISUP grade group distribution was also significantly different ($p=0.022$), with higher-grade disease occurring more frequently in the $\geq pT3$ group. The cancer-positive biopsy core rate was significantly higher in patients with $\geq pT3$ disease than in those with $< pT3$ disease ($52.28 \pm 28.21\%$ vs. $32.57 \pm 17.76\%$, $p<0.001$). Similarly, PI-RADS category distribution differed significantly between the groups ($p<0.001$), with PI-RADS 5 lesions being more prevalent in the $\geq pT3$ group. Although the number of MRI-detected lesions was similar between the groups [median 1.00 (IQR: 1.00 - 2.00) vs. 2.00 (IQR: 1.00 - 2.00), ($p=0.459$), both index lesion diameter and lesion density were significantly higher in patients with $\geq pT3$ disease [20.00 (IQR: 12.50 - 29.00) vs. 12.00 (IQR: 9.00 - 13.75) mm, $p<0.001$; and 0.44 (IQR: 0.28 - 0.68) vs. 0.22 (IQR: 0.13 - 0.22), $p<0.001$, respectively]. These findings are summarized in Table 1.

In the multivariable binary logistic regression analysis, the percentage of tumor involvement in biopsy specimens and index lesion diameter on MRI were independently associated with pathological stage $\geq pT3$. Each 1-percentage-point increase in biopsy tumor involvement was associated with a 3.3% increase in the odds of $\geq pT3$ disease (OR: 1.033 , 95% CI: 1.009 - 1.057 ; $p=0.010$). Similarly, each 1-mm increase in index lesion diameter on MRI was associated with a 27.4% increase

Table 1. Comparison of demographic, clinical, biopsy, and magnetic resonance imaging characteristics between patients with pathological stage $< pT3$ and $\geq pT3$ disease

		$< pT3$ (n=53)	$\geq pT3$ (n=49)	p-value
Age, years		67.19 ± 4.63	65.97 ± 6.48	0.282 ^A
Preoperative PSA, ng/mL median (IQR)		8.60 (5.60-14.90)	9.74 (6.72-17.52)	0.180 ^C
Clinical T stage	T1C	41 (77.40%)	16 (32.70%)	<0.001 ^B
	T2A	5 (9.40%)	8 (16.30%)	
	T2B	5 (9.40%)	18 (36.70%)	
	T2C	2 (3.80%)	7 (14.30%)	
Biopsy ISUP grade group	ISUP 1	27 (50.90%)	14 (28.60%)	0.022 ^B
	ISUP 2	17 (32.10%)	14 (28.60%)	
	ISUP 3	5 (9.40%)	8 (16.30%)	
	ISUP 4	4 (7.50%)	8 (16.30%)	
	ISUP 5	0 (0.00%)	5 (10.20%)	
Cancer-positive biopsy core rate, %		32.57 ± 17.76	52.28 ± 28.21	<0.001 ^A
PI-RADS category	2	0 (0.00%)	1 (2.04%)	<0.001 ^A
	3	8 (15.10%)	5 (10.20%)	
	4	36 (67.90%)	16 (32.65%)	
	5	9 (17.00%)	27 (55.11%)	
Number of MRI-detected lesions median (IQR)		2.00 (1.00-2.00)	1.00 (1.00-2.00)	0.459 ^C
MRI index lesion diameter, mm median (IQR)		12.00 (9.00-13.75)	20.00 (12.50-29.00)	<0.001 ^C
Lesion density, mm/mL median (IQR)		0.22 (0.13-0.22)	0.44 (0.28-0.68)	<0.001 ^C

IQR: Interquartile range, MRI: Magnetic resonance imaging, PSA: Prostate-specific antigen, ^C: Mann-Whitney U test, ^A: Student's t-test, ^C: Chi-square test, ^B: Fisher-Freeman-Halton exact test

in the odds of $\geq$ pT3 disease (OR: 1.274, 95% CI: 1.074-1.511; $p=0.005$). Clinical stage, biopsy ISUP grade group, and PI-RADS category were not independently associated with $\geq$ pT3 disease in the multivariable model (all $p>0.05$). Lesion density was not included in the multivariable analysis to avoid redundancy and potential multicollinearity, as MRI index lesion diameter had already been incorporated into the model. However, the markedly large standard errors observed for some ISUP grade groups and PI-RADS categories indicated sparse data and possible quasi-complete separation; therefore, the estimates for these categorical variables should be interpreted cautiously.

ROC curve analysis demonstrated that index lesion diameter on MRI had good discriminatory ability for predicting pathological stage $\geq$ pT3, with an area under the curve of 0.795 (95% CI: 0.703-0.886; $p<0.001$) (Figure 1). Based on the maximum Youden index, the optimal cut-off value was 16.5 mm, corresponding to a sensitivity of 65.3% and a specificity of 86.5%. Accordingly, an index lesion diameter of ≥ 17 mm on MRI may be considered a clinically practical threshold for identifying patients at increased risk of $\geq$ pT3 disease.

ROC curve analysis demonstrated that the proportion of cancer-positive biopsy cores had an acceptable discriminatory ability for predicting pathological stage $\geq$ pT3, with an area under the curve of 0.703 (95% CI: 0.601-0.804; $p<0.001$) (Figure 2). The ROC coordinate at which the absolute difference between sensitivity and specificity was minimized corresponded to a cut-off of 38%. At this threshold, sensitivity was 65.3% and specificity was 64.2%. Accordingly, patients with cancer involvement in $\geq 38\%$ of the sampled biopsy cores were considered to have an increased risk of pathological stage $\geq$ pT3.

A combined predictive model incorporating MRI index lesion diameter and the cancer-positive biopsy core rate demonstrated good discriminatory performance for predicting pathological

stage $\geq$ pT3, with an area under the curve of 0.843 (95% CI: 0.763-0.922; $p<0.001$) (Figure 3). The discriminatory performance of the combined model was numerically higher than that of MRI index lesion diameter alone (AUC: 0.795) and that of the cancer-positive biopsy core rate alone (AUC: 0.703), suggesting that these two tumor-burden parameters may provide complementary predictive information. Internal validation of the two-variable model using 1,000 bootstrap resamples yielded a mean optimism of 0.007, resulting in an optimism-corrected AUC of 0.835. These findings indicate that the discriminatory performance of the combined model was largely preserved after correction for optimism.

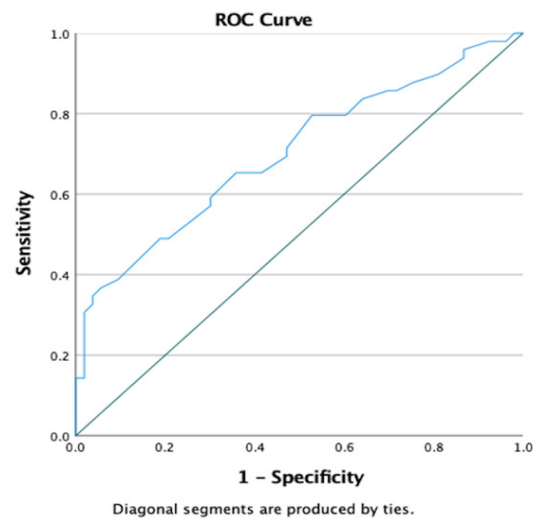


Figure 2. ROC curve of the cancer-positive biopsy core rate for predicting pathological stage $\geq$ pT3

ROC: Receiver operating characteristic

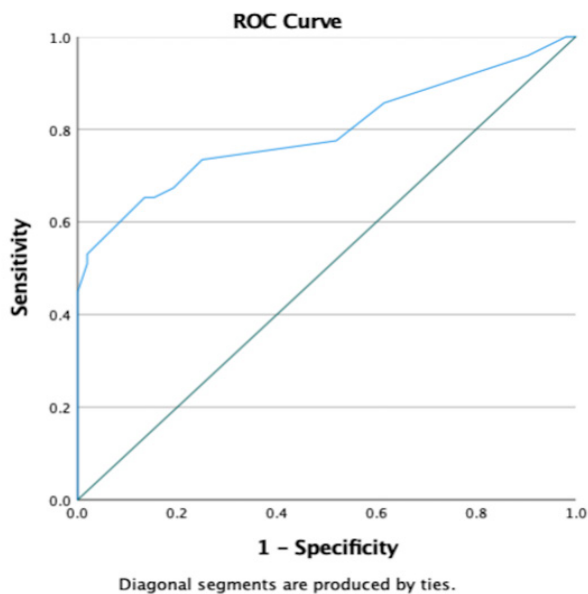


Figure 1. ROC curve of MRI index lesion diameter for predicting pathological stage $\geq$ pT3

ROC: Receiver operating characteristic, MRI: Magnetic resonance imaging

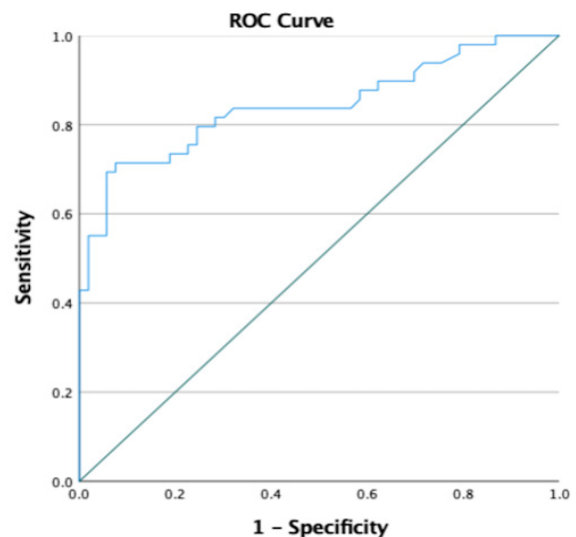


Figure 3. ROC curve of the combined model incorporating MRI index lesion diameter and the cancer-positive biopsy core rate for predicting pathological stage $\geq$ pT3

ROC: Receiver operating characteristic, MRI: Magnetic resonance imaging

When patients were stratified according to the number of tumor-burden risk factors—MRI index lesion diameter ≥ 17 mm and cancer-positive biopsy core rate $\geq 38\%$ —the prevalence of pathological stage $\geq$ pT3 increased progressively from 21.6% (8/37) among patients with no risk factors to 47.6% (20/42) among those with one risk factor and 91.3% (21/23) among those with both risk factors. The association between the number of risk factors and $\geq$ pT3 disease was statistically significant with a significant linear trend across the three risk categories ($p < 0.001$) (Table 2).

Discussion

The principal finding of the present study was that MRI index lesion diameter and the cancer-positive biopsy core rate were independently associated with pathological stage $\geq$ pT3 after radical prostatectomy. Each 1-mm increase in index lesion diameter was associated with a 27.4% increase in the odds of $\geq$ pT3 disease, whereas each 1-percentage-point increase in the cancer-positive biopsy core rate was associated with a 3.3% increase in the odds. More importantly, the model incorporating both parameters provided better discrimination than either parameter alone, reaching an AUC of 0.843. The prevalence of $\geq$ pT3 disease also increased progressively from 21.6% in patients with neither risk factor to 47.6% in those with one risk factor and 91.3% in those with both risk factors. These findings suggest that radiological and biopsy-based measures of tumor burden may provide complementary information for preoperative identification of non-organ-confined disease.

Previous studies have shown that integrating clinicopathological parameters with mpMRI findings improves the detection and risk stratification of clinically significant prostate cancer compared with either approach alone (7). Nevertheless, accurate identification of extraprostatic disease before surgery remains challenging. In the present study, clinical T stage, biopsy ISUP grade group, and PI-RADS category differed significantly between patients with $<$ pT3 and $\geq$ pT3 disease. In particular, cT2b–cT2c disease, higher biopsy grade groups, and PI-RADS 5 lesions were more frequent among patients with $\geq$ pT3 pathology. However, these categorical variables did not retain statistical significance in the multivariable model. This finding should not be interpreted as indicating that clinical stage, grade group, or PI-RADS category is clinically unimportant. Rather, their predictive information may partially overlap with the quantitative tumor-burden parameters included in the model. For example, lesion size contributes to PI-RADS categorization, and higher-volume tumors are more likely to be associated with extensive biopsy involvement. Moreover, the small number of patients in certain ISUP and PI-RADS categories resulted in large standard errors and possible quasi-complete separation, thereby limiting the reliability of their adjusted estimates.

Previous evidence indicates that models integrating MRI with clinicopathological variables generally provide better staging performance than the use of individual variables alone, although their accuracy remains imperfect (8).

MRI index lesion diameter was the strongest individual discriminator in our analysis, with an AUC of 0.795. The ≥ 17 -mm threshold demonstrated relatively high specificity of 86.5%, although its sensitivity was moderate at 65.3%. This pattern suggests that a lesion diameter above this threshold may identify a subgroup with a high probability of locally advanced pathology, whereas a lesion below this threshold cannot reliably exclude microscopic extraprostatic extension. Previous studies have similarly reported associations between MRI-derived tumor size or volume and adverse pathological features (9,10). Sugano et al. (11) showed that MRI-derived index tumor volume independently predicted extraprostatic extension, lymph-node invasion, and seminal vesicle invasion. Danacioglu et al. (12) also found that lesions larger than 10 mm were independently associated with extraprostatic extension and positive surgical margins. Our findings are further supported by Baboudjian et al. (13), who reported that a maximum lesion diameter of ≥ 15 mm on mpMRI was associated with a significantly higher rate of pathological upstaging to $\geq$ pT3a compared with lesions < 15 mm (46.5% vs. 35.0%; $p = 0.006$). In their multivariable analysis, a lesion diameter of ≥ 15 mm was also independently associated with adverse pathology, defined as a composite of $\geq$ pT3a disease, lymph node involvement, and/or ISUP grade group ≥ 3 (OR: 1.65, 95% CI: 1.14–2.39; $p = 0.01$). These findings are consistent with our observation that increasing MRI index lesion diameter is associated with a greater likelihood of pathological stage $\geq$ pT3. However, because pathological T stage was not evaluated as an isolated outcome in their adjusted model, direct comparison of the independent predictive estimates should be made cautiously (13). A meta-analysis evaluating quantitative mpMRI parameters reported pooled sensitivity and specificity values of 62% and 75%, respectively, for tumor size in predicting extraprostatic extension and emphasized that optimal thresholds varied considerably among studies (10). The 17-mm threshold observed in our cohort should therefore be considered a cohort-specific risk threshold rather than a universally applicable anatomical boundary.

The cancer-positive biopsy core rate was also independently associated with $\geq$ pT3 disease, although its individual discriminatory performance was more modest than that of MRI index lesion diameter. This variable provides an easily obtainable estimate of the extent of cancer detected across the sampled prostate rather than the percentage of tumor involvement within an individual core. Previous studies have consistently demonstrated that the proportion of cancer-positive cores is associated with pathological stage, tumor volume, seminal vesicle invasion, lymph-node involvement, and other adverse

Table 2. Distribution of pathological stage $\geq$ pT3 according to the number of tumor-burden risk factors

Number of risk factors	$<$ pT3, n	$\geq$ pT3, n	Prevalence of $\geq$ pT3, %	p-value
0	29	8	21.6%	< 0.001
1	22	20	47.6%	
2	2	21	91.3%	

pathological outcomes. Winkler et al. (14) reported that the percentage of positive biopsy cores improved the prediction of pathological stage, while Valette et al. (15) demonstrated a progressive increase in extraprostatic disease with each 10% increase in the positive-core category. These observations are consistent with our finding that the cancer-positive biopsy core rate remained independently associated with $\geq$ pT3 disease after adjustment for imaging and clinical variables.

A threshold of 38% for the cancer-positive biopsy core rate yielded a sensitivity of 65.3% and a specificity of 64.2%. This value was selected as a clinically balanced threshold rather than as the threshold producing the absolute maximum Youden index, and therefore should not be interpreted as a definitive biological cut-off. Previous studies have proposed varying thresholds for biopsy core positivity. A core positivity rate of 76% was reported to predict extraprostatic extension with a sensitivity of 65% and a specificity of 87.1%, while a dominant-side positive core rate of $\geq 55\%$ was found to provide useful discrimination for non-organ-confined disease (16,17). In a multicenter study of 698 patients with biopsy ISUP grade group 2 disease, Baboudjian et al. (13) found that a positive-core rate of $\geq 25\%$ was associated with pathological upstaging in univariable analysis, with $\geq$ pT3a disease occurring in 41.4% versus 30.5% among patients with lower cancer-positive biopsy core rates ($p=0.006$). However, the cancer-positive biopsy core rate was not independently associated with the composite endpoint of adverse pathology after multivariable adjustment (OR: 1.08, 95% CI: 0.76-1.52; $p=0.7$) (13). These variations likely reflect differences in patient selection, biopsy protocols, pathological endpoints, and methods used for threshold determination. In this context, the 38% threshold identified in our cohort provides a sensitivity-specificity-balanced estimate specifically for $\geq$ pT3 disease and may be particularly useful when combined with MRI index lesion diameter. Nevertheless, the positive-core rate may be affected by the total number of cores obtained, the distribution between systematic and targeted sampling, the lesion location, and the biopsy technique. Its routine availability, simple calculation, and absence of additional cost support its potential role in preoperative risk assessment, although external validation of the proposed threshold is required.

The most clinically relevant aspect of this study was the improvement observed when MRI index lesion diameter and the rate of cancer-positive biopsy cores were combined. The AUC of the combined model was numerically higher than the AUCs of MRI index lesion diameter alone and the cancer-positive biopsy core rate alone. Similarly, Ahmed et al. (18) reported that a model combining mpMRI-derived index lesion size and capsular contact length with biopsy-based tumor-burden parameters provided good discrimination for side-specific extracapsular extension, with an internally validated AUC of 0.83. This supports the concept that these variables represent related but non-identical dimensions of tumor burden: MRI lesion diameter reflects the radiologically visible dominant tumor focus, whereas the rate of cancer-positive biopsy cores reflects the distribution and extent of cancer captured histologically across biopsy specimens. The marked stepwise increase in $\geq$ pT3 prevalence according to the number of risk factors further supports their complementary value. The discrimination of the combined model also compares

favorably with the pooled AUC of approximately 0.80 reported for validated MRI-inclusive models predicting extraprostatic extension. However, a formal paired comparison of the ROC curves was not performed. Therefore, the statistical superiority of the combined model over either individual parameter cannot be claimed. Importantly, the proposed thresholds of 17 mm for MRI index lesion diameter and 38% for the cancer-positive biopsy core rate were derived from the present cohort and should therefore be considered cohort-specific, rather than universally applicable, cut-off values. Before these thresholds can be incorporated into routine clinical decision-making, their reproducibility and clinical utility should be confirmed in larger, independent, preferably multicenter cohorts.

The performance of our combined model should also be considered in the context of established preoperative nomograms. Traditional tools such as the Partin tables and the Memorial Sloan Kettering Cancer Center nomogram, as well as more recent MRI-inclusive models, integrate multiple clinicopathological variables to estimate the probability of extraprostatic disease. For contextual reference, a recent meta-analysis reported AUCs ranging from approximately 0.72 to 0.80 for validated traditional and MRI-inclusive models predicting extraprostatic extension (8). Similarly, Martini et al. (19) developed an mpMRI-based side-specific nomogram incorporating PSA, biopsy grade, core involvement, and MRI findings and reported an internally validated AUC of 0.82 for extracapsular extension. In the present study, bootstrap internal validation of the two-variable model yielded an optimism-corrected AUC of 0.835, indicating that its discriminatory performance was largely preserved. Nevertheless, this value should not be interpreted as evidence of equivalent or superior performance compared with established nomograms because the respective models differ in patient populations, predictors, pathological endpoints, and validation strategies, and were not evaluated within the same cohort. Accordingly, MRI index lesion diameter and the cancer-positive biopsy core rate should be regarded as potentially complementary parameters rather than replacements for established prediction tools. Direct head-to-head comparison and assessment of their incremental predictive value within validated nomograms will require larger independent cohorts and appropriate external validation.

Another notable finding was that lesion density was significantly higher in patients with $\geq$ pT3 disease. In the present study, lesion density was calculated as the MRI index lesion diameter divided by prostate volume measured by transrectal ultrasonography, thereby expressing lesion size relative to overall gland size. This approach may better reflect the proportional radiological tumor burden than absolute lesion diameter alone. Emerging studies have similarly evaluated lesion-size-to-prostate-volume parameters and reported associations with clinically significant prostate cancer detection (20). Nevertheless, lesion density has not been uniformly defined in the literature, as some studies use lesion length relative to prostate volume, whereas others use lesion volume divided by prostate volume (20,21). Because the lesion-density variable in our study shared its numerator with the index lesion diameter, it was not included in the multivariable model to avoid redundancy and potential multicollinearity. Its association with $\geq$ pT3 disease should therefore be considered exploratory and requires validation in studies specifically

designed to compare absolute and prostate-adjusted lesion measurements.

From a clinical perspective, improved recognition of occult $\geq$ pT3 disease may contribute to more realistic preoperative counselling and surgical planning. Patients with both an MRI index lesion diameter ≥ 17 mm and a cancer-positive core rate $\geq 38\%$ had a particularly high prevalence of $\geq$ pT3 pathology. Awareness of this risk may influence discussions concerning the likelihood of non-organ-confined disease, the feasibility and extent of nerve-sparing, resection margins, lymph-node assessment, and the possible need for postoperative multimodal management. Nevertheless, the proposed parameters should complement rather than replace established clinical nomograms, direct MRI signs of extraprostatic extension, pathological grade, PSA-based measures, or multidisciplinary assessment. Current guidelines support radical prostatectomy in selected cN0 patients with locally advanced disease as part of a multimodal strategy, further emphasizing the importance of accurately characterizing local disease extent before surgery (22).

Study Limitations

This study has several limitations. Its single-center design and relatively small sample size may limit generalizability, while sparse data in some clinical-stage, PI-RADS, and ISUP grade-group categories may have resulted in unstable regression estimates. The proposed cut-off values and combined model were developed and evaluated in the same cohort without external validation, and should therefore be considered cohort-specific. The proposed model was not directly compared with established clinical or MRI-inclusive nomograms within the same cohort. Interobserver variability in mpMRI interpretation and lesion measurement was not assessed. In addition, lesion density, which was calculated using MRI-derived lesion diameter and TRUS-measured prostate volume, was excluded from multivariable analysis because of its close relationship with lesion diameter. The cancer-positive biopsy core rate may also be influenced by biopsy technique and the number of systematic and targeted cores obtained. Only patients undergoing radical prostatectomy were included, and long-term oncological outcomes were not evaluated. Larger multicenter studies are needed to validate these findings.

Conclusion

MRI index lesion diameter and the cancer-positive biopsy core rate were associated with pathological stage $\geq$ pT3 after radical prostatectomy. The combined evaluation of these parameters showed a numerically higher discriminatory performance than either parameter alone, while the prevalence of $\geq$ pT3 disease increased with the number of risk factors present. These findings suggest that radiological and biopsy-derived parameters may contribute to preoperative risk assessment; however, validation in larger multicenter cohorts is needed.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Türkiye, İzmir City Hospital Ethics Committee (decision no: 2024/234, date: 04.12.2024).

Informed Consent: Data that had been prospectively collected from a cohort of patients who underwent preoperative imaging followed by radical prostatectomy were retrospectively reviewed.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: A.E., M.Ç., E.H., B.K., M.B.N., M.M., Y.C., D.B., T.D., S.Ç., Concept: A.E., D.B., T.D., S.Ç., Design: A.E., E.H., Y.C., T.D., S.Ç., Data Collection or Processing: A.E., M.Ç., E.H., B.K., M.B.N., M.M., Y.C., D.B., S.Ç., Analysis or Interpretation: A.E., M.Ç., E.H., B.K., M.B.N., Y.C., D.B., T.D., S.Ç., Literature Search: A.E., M.Ç., B.K., M.M., Y.C., T.D., S.Ç., Writing: A.E., M.Ç., D.B., S.Ç.

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