World Journal of Urology (2025) 43:295
https://doi.org/10.1007/s00345-025-05680-8

RESEARCH

Multiparametric MRI lesion dimension as a significant predictor of positive surgical margins following laparoscopic radical prostatectomy for transitional zone prostate cancer

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Received: 27 December 2024 / Accepted: 28 April 2025

Abstract

Background Positive surgical margins (PSM) after laparoscopic radical prostatectomy are a critical factor influencing treatment outcomes and prognosis in prostate cancer. Optional treatment strategies (neoadjuvant therapy, surgical techniques) and intraoperative margin monitoring highlight the importance of PSM risk assessment. This study aims to evaluate the potential PSM risk in transitional zone (TZ) tumors.

Materials and methods This retrospective study included 434 patients who underwent laparoscopic radical prostatectomy after multiparametric magnetic resonance imaging at our center between 2019 and 2023.

Results The PSM rate was significantly higher in patients with TZ lesions compared to those with peripheral zone lesions (47%, $n=175$ vs. 28%, $n=226$, $p<0.01$). Lesion location in TZ (OR: 4.29, 97.5% CI: 2.60–7.23, $p<0.01$) was identified as independent risk factors for PSM. Further analysis identified largest dimension of lesions (OR: 1.27, 97.5% CI: 1.09–1.50, $p<0.01$) and the number of positive biopsy cores (OR: 1.39, 97.5% CI: 1.16–1.70, $p<0.01$) as independent risk factors for PSM in patients with TZ tumors. LASSO regression identified four significant variables (largest dimension of lesions—the most important variable, number of positive biopsy cores, prostate-specific antigen density, and International Society of Urological Pathology grade). These variables were used to construct three PSM risk prediction models, each demonstrating favorable predictive accuracy and clinical benefit.

Conclusions Certain TZ prostate cancer patients demonstrate a higher predisposition to PSM occurrence. Lesion dimension as a significant predictor of PSM for TZ patients. Separate PSM risk assessments for subgroups, like TZ prostate cancer patients, may enhance predictive accuracy and clinical utility.

Clinical trial registration China Clinical Trial Registry (ChiCTR2300075944, 2023).

Keywords MRI · Prostate cancer · Positive surgical margins · Transition zone · Lesion dimension

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Published online: 12 May 2025

Introduction

Laparoscopic radical prostatectomy (RP) is one of the leading treatment options for prostate cancer (PCa) [1, 2]. As with most tumors, positive surgical margins (PSM) have been shown to be a critical factor influencing the effectiveness of surgical treatment, adjuvant therapy decisions, and patient prognosis in PCa [3, 4]. Thus, the 16–37% incidence of PSM has consistently been a source of concern and focus [5, 6].

Recent innovations, including neoadjuvant hormone therapy, chemotherapy, and technologies for real-time margin assessment during surgery, have emerged to mitigate the incidence of PSM. The growing availability of neoadjuvant therapies, expanding surgical techniques, and enhanced intraoperative margin monitoring technologies underscore the importance of preoperative PSM risk assessment [4, 7–9].

Given the critical role of PSM risk in treatment selection and prognosis for PCa patients, numerous studies have investigated the correlation between clinical factors (such as clinical stage, biopsy pathology characteristics, and positive margin location after RP) and surgical margin status [5, 10]. The distribution of PSM across different prostate regions (apex, posterolateral, etc.) highlights the significant impact of lesion location on PSM occurrence, with certain transition zone (TZ) lesion locations potentially playing a crucial role [6, 11]. With advances in multiparametric magnetic resonance imaging (Mp-MRI), preoperative identification of most primary lesion locations has become feasible [12, 13]. Increasing evidence suggests that Mp-MRI features, such as lesion dimension and extracapsular extension, are significant predictors of PSM occurrence [14, 15]. However, the predictive performance for PSM remains suboptimal [5, 16]. We hypothesize that studying PSM occurrence in lesions across different regions and determining the impact of lesion location on PSM, followed by targeted clinical predictions for PSM in TZ tumor, may offer a more accurate and practical approach to improving preoperative PSM risk prediction.

Materials and methods

Patients

This retrospective study included 434 patients who underwent laparoscopic RP at our center between 2019 and 2023.

Inclusion criteria: (1) PCa was confirmed by primary biopsy; (2) All evaluations, including blood tests, Mp-MRI, biopsy, were performed at one center.

Exclusion criteria: (1) Diffuse or unclear MRI lesions; (2) PI-RADS score < 4 (lesions with a low likelihood of malignancy, with positive rates of 2–6% for PI-RADS 1, 4–5% for PI-RADS 2, and 19–20% for PI-RADS 3 [12, 17]); (3) Prostate-specific antigen (PSA) > 100 ng/ml (potential inaccuracies); (5)History of neoadjuvant therapy (alterations in clinical features); (6) Intraoperative margin assessments (affect the occurrence of PSM).

Mp-MRI and clinical features

All patients were imaged using the 3.0T MRI scanner with a standard spine array and 18-channel body coil. Imaging sequences were obtained as previously described [18]. MRI parameters were assessed according to the PI-RADS v2.1 guidelines [19]. The largest dimension of the lesion is the largest value among the anterior-posterior dimension, transverse dimension, and craniocaudal dimension. Lesions in the PZ were measured on the Apparent Diffusion Coefficient sequence, while those in the TZ were measured on the T2WI sequence.

A transperineal 12 + X cores biopsy (12-core system biopsy: 8 cores in the peripheral zone, 4 cores in the TZ; X-core targeted: 2–5 cores in MRI lesions) was performed using transrectal ultrasound and MRI fusion software. The pathological assessment criteria for biopsies and radical specimens were based on the Society of Urogenital Pathology and ISUP guidelines for prostate cancer [20]. The surgeries of the enrolled patients were performed by multiple surgeons.

Statistical analyses

Continuous variables were analyzed with t-tests for normal distributions and nonparametric tests for non-normal distributions. Categorical variables were evaluated using the Chi-square or Fisher's exact test. LASSO regression combined with cross-validation was employed to select variables. The random forest model was used to assess the importance of variables. Logistic regression was used to calculate regression coefficients, which were then standardized into scores and visualized as nomograms. ROC curves, calibration curves, decision curve analysis (DCA), and clinical impact curves were employed to further evaluate the nomograms. Data analysis was performed using GraphPad Prism (version 8.0.2) and R (version 4.4.0). Statistical significance was set at $p < 0.05$.

Results

Descriptive analysis of patients

The clinical characteristics of all patients are presented in Table 1.

Tumor location in the TZ is an independent risk factor for PSM

Among patients with positive surgical margins, the lesion distribution was as follows: 51.69% in the apex, 34.82% in the mid-gland, and 13.48% in the base. Notably, the apex TZ lesions had the highest proportion (29.26%). A comparison of PSM incidence across different MRI zones showed a significantly higher PSM rate in TZ lesions compared to peripheral zone (PZ) lesions (47%, $n=175$ vs. 28%, $n=226$, $p<0.01$) **(Online Resource 1).**

Univariate and multivariate logistic regression analyses revealed that TZ lesions (OR: 4.29, 97.5% CI: 2.60–7.23, $p<0.01$), largest dimension of lesion (OR: 1.14, 97.5% CI: 1.07–1.23, $p<0.01$), and the number of positive biopsy cores (OR: 1.19, 97.5% CI: 1.08–1.31, $p<0.01$) were independent risk factors for the occurrence of PSM (Table 2).

Factors associated with PSM in TZ patients

A comparison was made between PSM and negative surgical margins (NSM) patients within the TZ group to analyze the factors associated with PSM occurrence. The results demonstrated that PSM in TZ patients was significantly associated with clinical cT3 staging (74%, $n=23$ vs. 43%, $n=152$,

Table 1 Characteristics of the study patients

Variable	Result	
Study patients, n (%)	434	
Median age, yr (IQR)	70	(65, 75)
Median PSA, ng/ml (IQR)	12.83	(10.21, 26.49)
Median PSAD, ng/ml^2 (IQR)	0.37	(0.21, 0.68)
Clinical T stage, n (%)		
< cT3	316	(72.81)
cT3	118	(27.19)
Median number of positive cores, n (IQR)	3	(2, 6)
Biopsy ISUP grade, n (%)	2	(2, 3)
Mp-MRI characteristics		
PI-RADS score, n (%)		
4	220	(50.69)
5	214	(49.31)
Lesions Location, n (%)		
PZ	226	(52.17)
TZ	175	(40.32)
PZ+TZ	33	(7.61)
ECE detected by MRI, n (%)	112	(25.81)
SVI detected by MRI, n (%)	22	(5.07)
Median prostate volume, ml (IQR)	33.29	(24.29, 44.78)
Median largest dimension of lesion, mm (IQR)	14	(10, 18)
Median lesion volume, ml (IQR)	0.75	(0.33, 1.68)
Median lesion volume/prostate volume, % (IQR)	2.26	(1.02, 5.38)
Median TZ volume, ml (IQR)	14.38	(8.68, 22.36)
Median TZ volume/ prostate volume, % (IQR)	43.81	(34.70, 55.55)
RP pathologic characteristics		
Pathologic T stage, n (%)		
pT2	283	(65.21)
≥pT3a	151	(34.79)
ISUP grade, n (%)	3	(2, 4)
PSM, n (%)	153	(35.25)
ECE, n (%)	143	(32.95)
SVI, n (%)	59	(13.59)

IQR, interquartile; PI-RADS, Prostate Imaging Reporting and Data System; PSA, Prostate-specific antigen; PSAD, PSA density; ISUP, International Society of Urological Pathology; TZ or PZ patients, patients' index lesions of MRI in the TZ or PZ; PZ+TZ patients, patients' multiple lesions of MRI mapping lesions in the PZ and TZ; RP, Radical Prostatectomy; ECE, Extracapsular Extension; PSM, Positive Surgical Margins; SVI, Seminal Vesicle Invasion

Table 2 Univariate and multivariate logistic regression analysis of factors associated PSM in enrolled patients

Character	Univariate logistic regression analysis					Multivariate logistic regression analysis				
	OR	97.5%CI		*p*		OR	97.5%CI		*p*	
lesion location in TZ	2.44	1.63	3.66	<0.01	**	4.29	2.60	7.23	<0.01	**
Largest dimension of lesion	1.09	1.06	1.13	<0.01	**	1.14	1.07	1.23	<0.01	**
Number of positive cores	1.21	1.12	1.30	<0.01	**	1.19	1.08	1.31	<0.01	**
cT3 stage	1.85	1.20	2.85	<0.01	**	0.86	0.45	1.64	0.66	
PSA	1.05	1.03	1.07	<0.01	**	1.01	0.98	1.05	0.50	
Lesion volume	1.13	1.05	1.24	<0.01	**	0.93	0.75	1.19	0.55	
Lesion volume / prostate volume	1.06	1.02	1.09	<0.01	**	0.95	0.87	1.04	0.29	
PSA density	3.52	2.20	5.83	<0.01	**	1.83	0.69	5.01	0.23	
ISUP grade (biopsy)	1.36	1.14	1.62	<0.01	**	1.17	0.95	1.46	0.15	
TZ volume	0.99	0.98	1.00	0.27						
TZ volume / prostate volume	1.00	0.99	1.02	0.67						
Age	1.02	0.99	1.06	0.17						
Prostate volume	0.99	0.99	1.00	0.24						

OR, Odds Ratio; CI, Confidence Interval; PSA, Prostate-Specific Antigen; TZ, Transitional Zone; ISUP: International Society of Urological Pathology; **: $p<0.01$

$p<0.01$), MRI-detected extracapsular extension (ECE) (81%, $n=21$ vs. 43%, $n=154$, $p<0.01$), higher PSA levels (16.87 vs. 9.97 ng/ml, $p<0.01$), greater largest dimension of lesion (18 vs. 11 mm, $p<0.01$), lesion volume (1.28 vs. 0.50 ml, $p<0.01$), lesion volume/ prostate volume (3.73% vs. 1.33%, $p<0.01$), PSA density (0.54 vs. 0.25 ng/ml², $p<0.01$), ISUP (biopsy) grade (3 vs. 2, $p<0.01$), and the number of positive biopsy cores (4 vs. 3, $p<0.01$) (Fig. 1).

In contrast, no significant association was found with age, prostate volume, transition zone volume, TZ volume percentage, or MRI-detected seminal vesicle invasion (SVI) ($p>0.05$) (Online Resource 2).

Univariate and multivariate logistic regression analyses revealed that largest dimension of lesion (OR: 1.27, 97.5% CI: 1.09–1.50, $p<0.01$), and the number of positive biopsy cores (OR: 1.39, 97.5% CI: 1.16–1.70, $p<0.01$) were independent risk factors for the occurrence of PSM in TZ patients. Due to the clear direct association between cT3 and MRI-detected ECE, only cT3 was included in the multivariable analysis (Online Resource 3).

Construction and validation of PSM risk prediction model in TZ patients

Due to the differences between univariate and multivariate analysis results, correlation analysis was used to verify multicollinearity among factors (Online Resource 4). LASSO regression and cross-validation were used to select variables (AUC: 0.86, 95%CI: 0.80–0.91, Online Resource 5–6). From the factors mentioned earlier, four significant variables were identified, and their importance was ranked using a random forest model: largest dimension of lesion (Mean Decrease Gini value: 33); PSA density (Mean Decrease Gini value: 27); Number of positive biopsy cores (Mean Decrease Gini value: 19); ISUP (biopsy) grade (Mean Decrease Gini value: 7) (Online Resource 7).

Subsequently, a Nomogram Model 1 was constructed using the four significant variables. Given that largest dimension of lesion had the highest importance among all variables, a simplified model (Nomogram Model 2) was developed based solely on it. Additionally, considering the variability in systematic biopsy templates and the decreasing recommendation for systematic biopsy in the future, the widespread use of the variable "number of positive biopsy cores" may be limited. Therefore, a three-variable model (Nomogram Model 3) was constructed using the remaining three variables: largest dimension of lesion, PSA density, and ISUP (biopsy) grade (Fig. 2).

The calibration curves comparing the three models (based on the Brier score, where a lower value indicates less difference between predicted probability and actual outcome) are shown in Fig. 2d.

The comparison of the models' ROC curves is shown in Fig. 2e. Nomogram Model 1 (AUC: 0.86, 95% CI: 0.81–0.92, cut-off: 0.50, sensitivity: 0.75, specificity: 0.87) outperformed Nomogram Model 3 (AUC: 0.83, 95% CI: 0.77–0.89, cut-off: 0.58, sensitivity: 0.70, specificity: 0.89), which in turn outperformed Nomogram Model 2 (AUC: 0.78, 95% CI: 0.70–0.85, cut-off: 0.55, sensitivity: 0.60, specificity: 0.85).

Additionally, the clinical impact and decision curves demonstrate that all models effectively identify almost all high-risk patients who ultimately develop PSM, providing substantial clinical benefits (Online Resource 8).

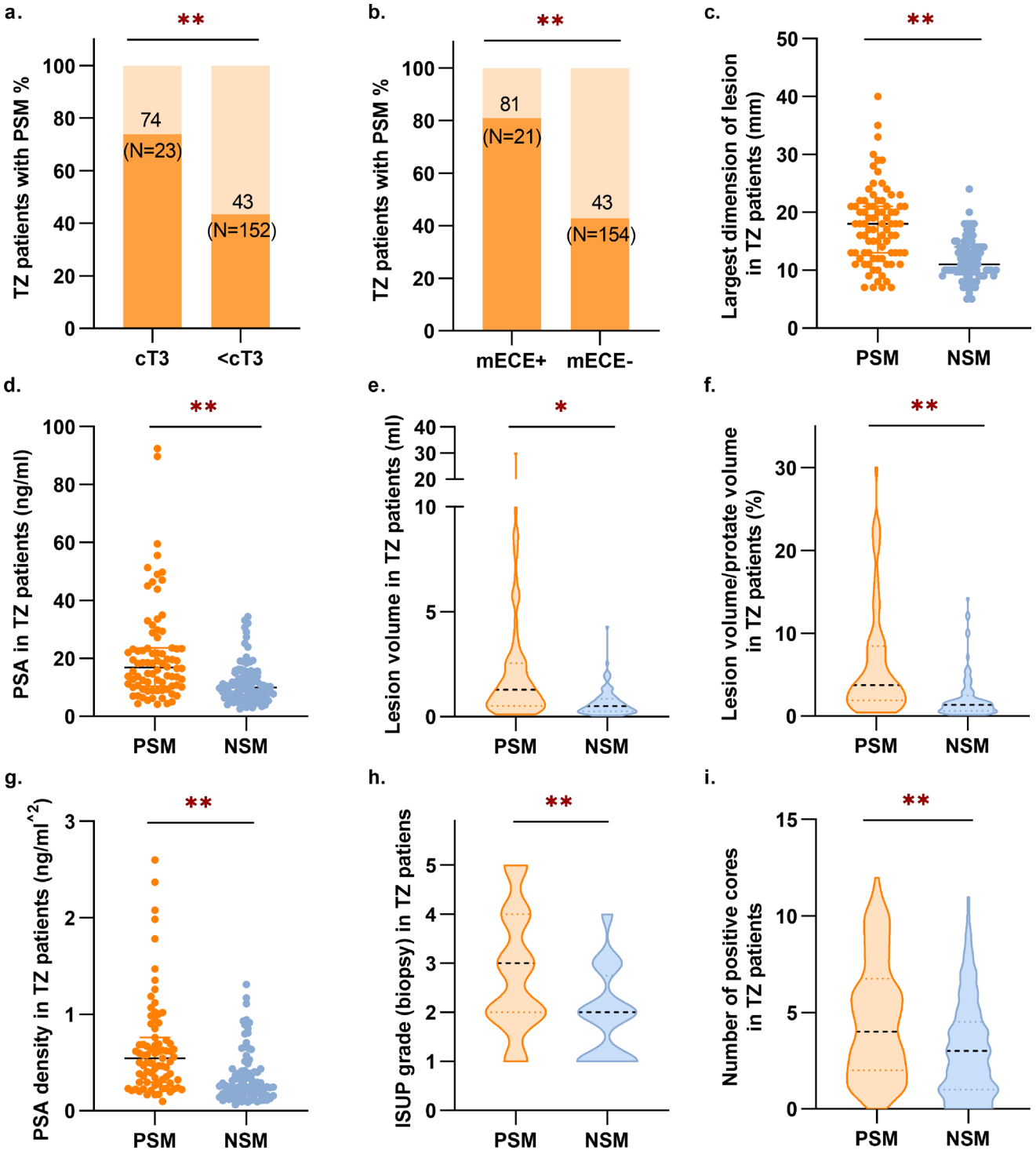

Fig. 1 Factors associated with PSM in TZ patients. cT3 (**a**) and mECE+ (**b**) patients had a higher incidence of PSM. Compared to NSM patients, PSM patients exhibited greater largest dimension of lesion (**c**), PSA levels (**d**), lesion volume (**e**), lesion volume/ prostate volume (**f**), PSA density (**g**), ISUP (biopsy) grade (**h**), and a greater number of positive biopsy cores (**i**). (PSM: Positive Surgical Margins; NSM: Negative Surgical Margins; mECE+: MRI-detected ECE; mECE-: no MRI-detected ECE; *: $p<0.05$, **: $p<0.01$)

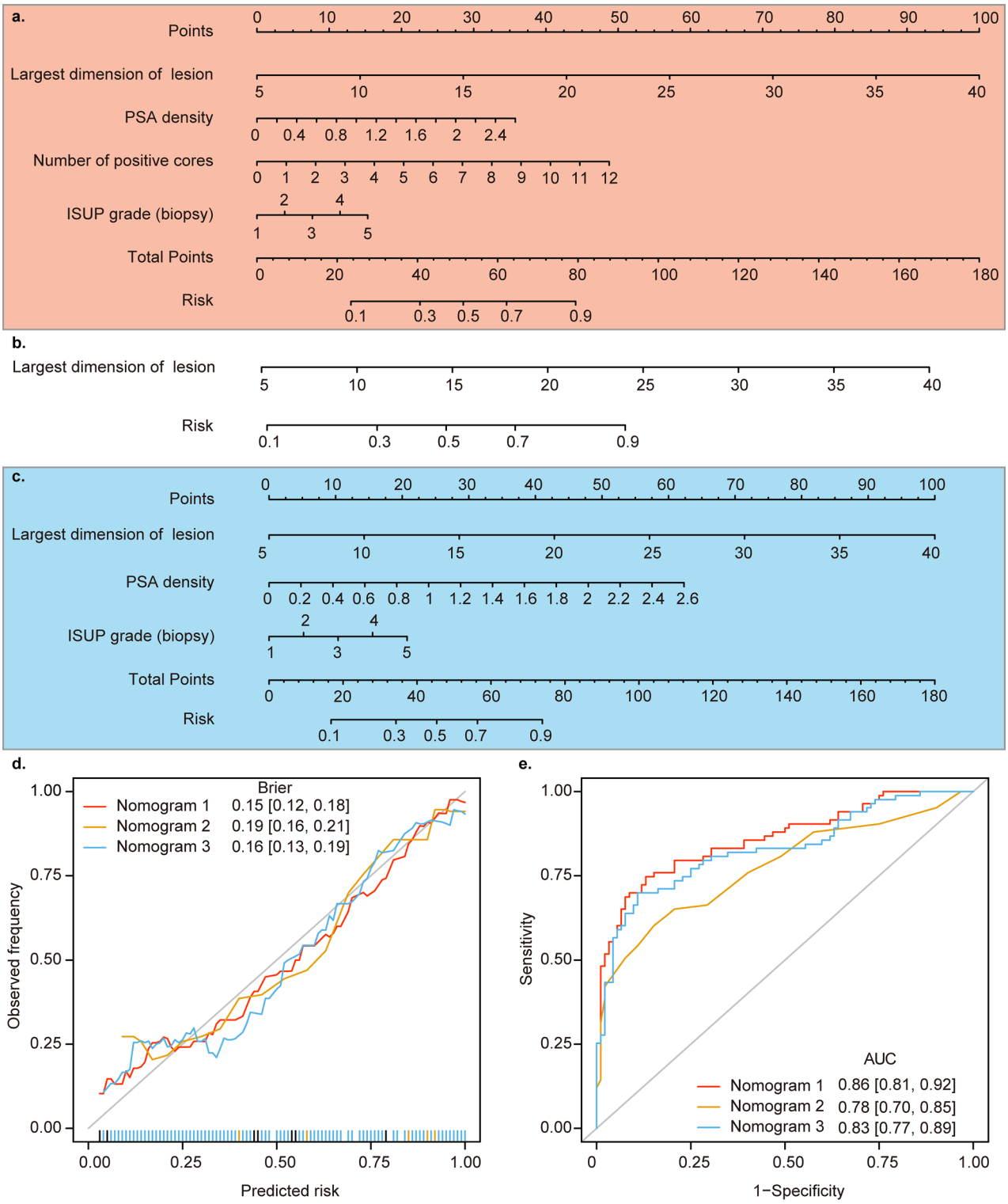

Fig. 2 Construction and validation of PSM risk prediction model in TZ patients. (**a**) Nomogram Model 1 (**b**) Nomogram Model 2 (**c**) Nomogram Model 3 (**d**) Calibration curves for the three models. (**e**) ROC curves for the three models

Discussion

PSM after laparoscopic RP are a critical factor influencing treatment outcomes and prognosis in PCa. Optional treatment strategies (neoadjuvant therapy, surgical techniques) and intraoperative margin monitoring highlight the importance of PSM risk assessment [4, 9]. However, the predictive performance for PSM remains limited [5, 16]. The distribution of PSM across different prostate regions highlights the significant impact of lesion location on PSM occurrence [6, 11, 21].

In this study, TZ lesions were identified as an independent risk factor for PSM. Further analysis of PSM risk factors in patients with TZ lesions revealed that largest dimension of lesion and the number of positive biopsy cores were independent predictors of PSM. Based on LASSO regression, random forest model analysis, and Nomogram modeling, as well as considering clinical applicability, we developed three Nomogram models to predict the preoperative risk of PSM in TZ patients. Despite slight differences in predictive performance and applicable conditions, all three models demonstrated strong efficacy and clinical benefit. Overall, we confirmed the impact of tumor location on PSM risk and showed that region-specific PSM prediction could potentially improve clinical prediction accuracy.

In our study, the overall incidence of PSM was 35.25%, which, although within the reported range of 20–37%, is slightly higher compared to some studies [3, 6]. This may be due to our exclusion of patients with a PI-RADS < 4. Patients with PI-RADS < 4 generally have lower malignancy levels and a lower incidence of PSM compared to those with PI-RADS 4 or 5 scores [11]. For this reason, excluding these patients is unlikely to have any significant impact on other aspects of PSM research. The primary reason for excluding patients with PI-RADS < 4 was to ensure accurate correspondence between MRI lesions and actual tumor characteristics [12].

The higher PSM rate in TZ lesions compared to PZ is an important finding, even though it is not a new observation [22]. Li et al. found that PSM rates in patients with TZ and mixed-origin tumors were significantly higher than in those with PZ tumors ($p < 0.01$). Furthermore, studies have indicated that the rate of missed ECE is significantly higher in TZ lesions compared to PZ lesions [23]. Multiple studies have shown that ECE is a significant, and even independent, risk factor for PSM [5, 14]. The higher rate of missed ECE in TZ lesions may contribute to the increased PSM observed in these patients.

Previous research on PSM has mainly focused on analyzing all patients collectively to identify risk factors and develop methods to predict PSM risk. Despite identifying numerous risk factors, the final predictive performance has often been unsatisfactory [5, 16]. Few studies have considered whether PSM differs across tumor locations, particularly by separately analyzing PZ and TZ lesions. However, distinctions between PZ and TZ tumors are increasingly recognized in recent studies [24]. In our research, we focused on patients with the TZ lesions and developed a predictive model for PSM risk to enhance prediction accuracy and practical applicability. Our model includes four variables: largest dimension of lesion (represents tumor size as assessed by MRI); PSA density (reflects tumor progression at the clinical); Number of positive biopsy cores (indicates tumor size at the biopsy level); ISUP grade (represents tumor heterogeneity at the biopsy pathology level).

Largest dimension of lesion is the most critical variable for predicting PSM risk. A univariate Nomogram model (Model 2) using lesion length as the variable achieved an AUC of 0.78. Several studies have shown that largest dimension of lesion correlates significantly with ECE, SVI, and T stage, making it a valuable and reproducible quantitative marker for predicting tumor characteristics [25]. It is well established that higher clinical T stage correlates with increased PSM risk, a relationship confirmed by multiple studies, including ours. However, due to the known limitations in the sensitivity of current clinical T staging assessments, lesion length might be more valuable for inclusion in predictive models [26]. We did not use variables like tumor volume or tumor volume ratio because they may be influenced by other confounding factors. For example, tumor volume is calculated as the product of length, width, height, and a constant (0.52), introducing potential variability beyond the primary long axis. Moreover, largest dimension of lesion also partially reflects the irregularity of tumor shape, which generally correlates with greater malignancy and aggressiveness.

Hyeon et al. demonstrated that when the number of positive cores exceeds three, the risk of PSM significantly increases, making it a useful predictor for PSM risk [27]. However, in terms of diagnosing clinically significant prostate cancer, systematic biopsies introduce a greater needle burden, and they are no longer strongly recommended by guidelines for routine use [1]. This limits the applicability of the positive biopsy core count as a variable. Therefore, we excluded this variable in developing Nomogram Model 3, which achieved an AUC of 0.83 (95% CI: 0.77–0.89)—a result superior to most PSM prediction models for general patient populations.

PSA density has long been an important indicator for diagnosing prostate cancer and assessing tumor progression. Multiple studies have identified PSA density as an independent risk factor for postoperative PSM [14, 28]. Unlike PSA alone, PSA density accounts for both PSA levels and prostate volume, which may explain why PSA

density was included in our model while PSA itself was not. In many predictive models for prostate pathology and prognosis, ISUP (biopsy) grade is considered a significant factor [28, 29]. However, the potential discrepancies between the ISUP grade from biopsy and the postoperative ISUP grade reduce its relative importance as a model variable, resulting in its lower weight in our model [30].

This study has several limitations. First, the findings primarily apply to patients with PI-RADS > 3 lesions detected by MP-MRI and may not be generalizable to those with negative MP-MRI or PI-RADS 3 findings. Second, this is a single-center retrospective study lacking multi-center, large-sample data to validate the findings across diverse clinical settings. Variability in surgical approach, learning curves, and surgeon proficiency within a single institution may introduce confounding factors. While surgical technique may influence PSM risk, this study focuses on objective risk indicators inherent to the lesion. Surgeons can incorporate assessments of their own skills and treatment approaches, such as nerve preservation, alongside these objective indicators to develop personalized PSM risk management strategies. Third, as a high-volume referral center, our inpatient population is shaped by PSA screening practices at affiliated lower-tier hospitals, potentially leading to variability in patient composition.

Conclusion

This study found that certain TZ prostate cancer patients demonstrate a higher predisposition to PSM occurrence. Multiparametric MRI lesion diameter as a significant predictor of PSM following laparoscopic radical prostatectomy for TZ patients. Conducting a focused analysis on TZ lesions and developing a PSM risk prediction model for these patients can help improve the predictive accuracy and practical application of PSM models.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00345-025-05680-8.

Acknowledgements This work was supported by the National Natural Science Foundation of China (Grant No. 32200533) and the Gusu Health Personnel Training Project of Suzhou City (No. GSWS2019033).

Author contributions Xin Chen, Yanzhong Chen, and Chengbo Qian contributed equally to this work. X.C., Y.C. and C.Q.: Conceptualization, Methodology, Formal analysis, Writing – Original Draft, Visualization. C.W.: Methodology, Software. Y.L.: Conceptualization, Writing – Review & Editing, Funding acquisition. Y.H., J.H., and X.W.: Data Curation, Supervision, Resources, Project administration, Writing – Review & Editing, Funding acquisition. All authors reviewed and approved the final manuscript.

Data availability The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request.

Competing interests The authors declare no competing interests.

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