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Bladder mucosal smoothness predicts early recovery of urinary continence after laparoscopic radical prostatectomy

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Abstract

Background To propose the bladder mucosal smoothness (BMS) grade and validate a predictive model including MRI parameters preoperatively that can evaluate the early recovery of urinary continence (UC) after laparoscopic radical prostatectomy (LRP).

Methods A retrospective analysis was conducted on 203 patients (83 patients experienced UI at the three-month follow-up) who underwent LRP in our medical center and were diagnosed with prostate cancer (PCa) from June 2016 to March 2020. Patients' clinicopathological data were collected. Prostate volume (PV), membranous urethra length (MUL), intravesical prostatic protrusion length (IPPL), and BMS grade were measured by MRI. The total sample was randomly divided into a training set ($n = 142$) and a validation set ($n = 61$). A model was developed to predict the risk of urinary incontinence (UI) at three months after LRP.

Results Age group, clinical T stage group, BMS grade group, PV group, IPPL group, and MUL group differed significantly between patients in the UI group and the UC group (all P values < 0.05). Multivariate analysis identified 3 MRI-related predictors selected for the prediction model: BMS grade (1 odds ratio [OR] 0.17, 95% CI 0.11–0.66; P value = 0.024) (2 + 3 OR 0.17, 95% CI 0.04–0.66; P value = 0.011), IPPL (> 5 mm OR 0.17, 95% CI 0.1–0.64; $P = 0.004$), and MUL (≥ 14 mm OR 6.41, 95% CI 2.72–15.09; P value < 0.001). The model achieved a highest area under the curve of 0.900 in the training set and the validation set. The sensitivity and specificity of the prediction model were 0.800 and 0.816.

Conclusion Our study confirmed that patients with lower BMS grade are associated with early recovery of urinary continence after LRP. A prediction model was developed and validated to evaluate the early recovery of urinary continence after LRP.

Clinical trial number Not applicable.

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Keywords Prostate cancer, Laparoscopic radical prostatectomy, Urinary incontinence, Prediction model, Postoperative complications

Background

Urinary incontinence (UI) is one of the most prevalent postoperative complications after radical prostatectomy (RP), and it has a considerable negative impact on the quality of life of patients. 46% of patients at 6 months after RP required absorbent pads, while 17% of patients still faced UI problems at 6 years [1]. Various factors can affect UI, including anatomic support and pelvic innervation [1]. Before performing RP, pelvic MRI can provide surgeons with a better grasp of the anatomy surrounding the prostate [2–4]. It has been demonstrated that the recovery of urinary continence after RP could be influenced by preoperative anatomic factors such as membranous urethral length (MUL) and intravesical prostatic protrusion length (IPPL) [5–9]. It is recommended to measure MUL prior to surgery using magnetic resonance imaging (MRI) in order to predict the postoperative recovery of UI [10]. Besides urethral factors, bladder factors may also be related to UI. The growth of the prostate can induce bladder outlet obstruction (BOO), causing secondary structural remodeling within the bladder wall (e.g., hypertrophy) [11]. These secondary changes may lead to detrusor overactivity (DO) based on the myogenic theory, increasing intravesical pressure and eventually resulting in UI [12–14]. Although imaging characteristics can be used by surgeons to predict postoperative UI, bladder-related imaging parameters are less frequently used in studies than urethra-related imaging parameters. The link between the bladder morphology on MRI and the recovery of continence following RP has not yet been reported. To categorize the preoperative morphology of the bladder, we proposed the bladder mucosal smoothness (BMS) grade. In order to determine the predictive value of imaging parameters and develop a prediction model for the early recovery of urinary control function, we evaluated the imaging parameters prior to LRP, including BMS grade and other clinical aspects.

Methods

Study setting and study design

For this retrospective study, we screened the medical records of prostate cancer (PCa) patients. This study included 203 PCa patients who underwent LRP at our medical center between June 2016 and March 2020. Each patient received a pelvic MRI scan before prostate biopsies. The inclusion criteria comprised: (1) pathologically confirmed PCa; (2) a pelvic MRI scan before prostate biopsy; and (3) clinicopathological data available. Exclusion criteria comprised: (1) a history of undergoing prostate surgery; (2) a history of undergoing neoadjuvant

hormonal therapy or radiation therapy; (3) an empty bladder prior to MRI; (4) a history of urinary incontinence or catheterization before surgery due to urinary retention and (5) missing follow-up data (Supplement 1).

Baseline patient characteristics were obtained, including age, pre-biopsy PSA, biopsy Gleason score, clinical staging, prostate volume (PV), and pelvic MRI images.

Assessment of urinary continence and the follow-up

Following surgery, patients received follow-up every month. The recovery of urinary continence was determined based on the following criteria [15]: Urinary control was defined as patients using no pads and having no leaking; patients requiring more than one pad per day.

MRI techniques

Preoperative MRI examinations were completed within 1 week before the biopsy. MRI was performed using a 3-Tesla superconducting scanner (Magnetom Trio, Siemens Healthcare, Erlangen, Germany/Discovery MR750, GE Healthcare, USA), and the signal was received by an abdominal phased front coil. The scan included the prostate gland and bilateral seminal vesicles. Axial, sagittal, and coronal fast spin echo T2 weighted imaging (WI) and axial T1WI were routinely performed. Sequences of T2WI/T2WIFS (fat saturation)/T1WI were reviewed for anatomic feature measurements.

Evaluation of MRI parameters

The imaging parameters on the MRI were retrospectively evaluated by two urologists with 11 and 17 years of experience. By the time of the imaging analysis, the readers were blinded by the results of urinary continence in patients.

The bladder mucosa smoothness measured by axial MRI is classified into four grades: Grade 0, the bladder mucosa is completely smooth; Grade 1, slight irregularities can be seen on the bladder mucosa; Grade 2, deep fissures can be seen in the muscular layer, less than half of the bladder wall thickness, or the presence of bladder diverticula can be seen; Grade 3, fissures exceed over half of the bladder wall thickness or progress into small muscular defects (Fig. 1).

Surgical techniques

All patients underwent extraperitoneal LRP. The pelvic fascia is cut and freed along the prostatic border to the prostatic apex before suturing the deep dorsal penile venous complex. For the patients who could preserve the neurovascular bundle (NVB) based on the preoperative

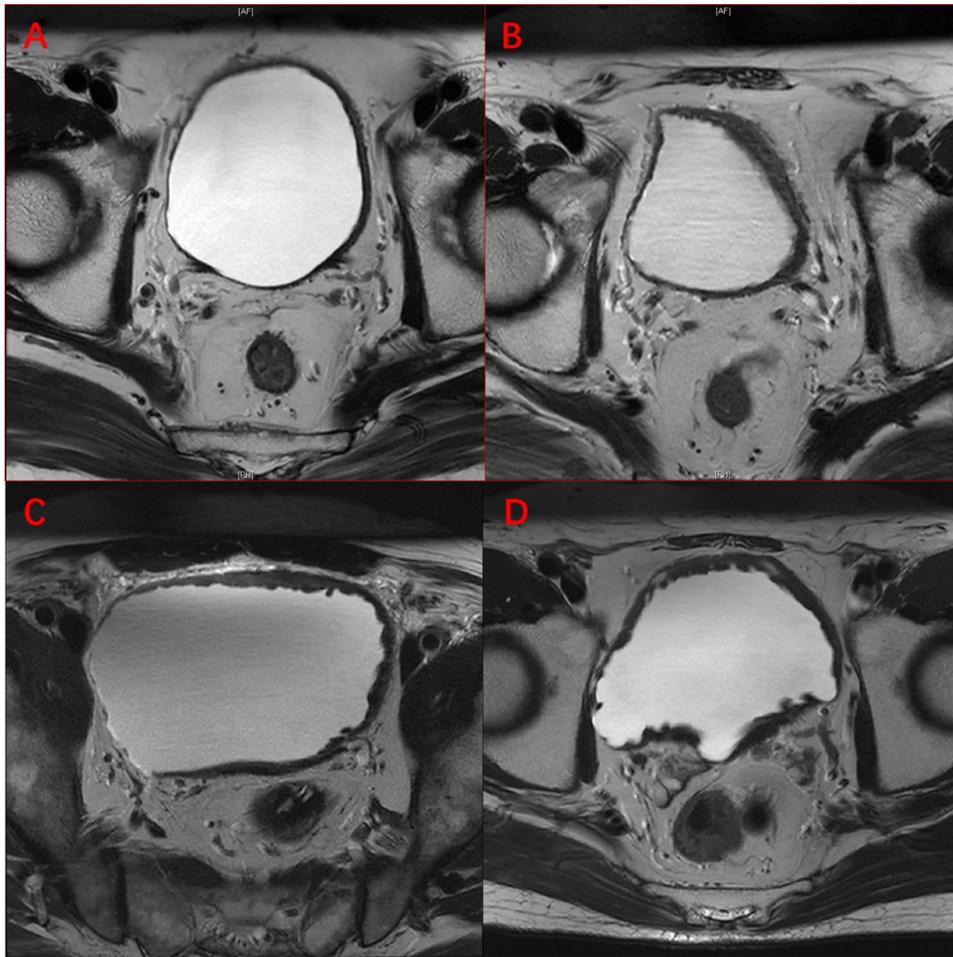


Fig. 1 Examples of BMS Grade. (A) BMS Grade 0. (B) BMS Grade (1) (C) BMS Grade (2) (D) BMS Grade (3) BMS, bladder mucosal smoothness

and intraoperative evaluation, the NVB was separated and preserved. The urethra was dissected bluntly, and the urethral membrane was preserved as much as possible.

Training and validation sets

The patients were randomly divided into a training set and a validation set by 7:3. A predictive model was developed based on the training set. Validation of the model was conducted among the validation set.

Statistical analysis

Continuous variables were expressed as median and interquartile range, and categorical variables as numbers (n) and percentages (%). The Mann-Whitney U test was utilized to evaluate the differences among the continuous variable groups, while a chi-squared test was applied to examine the differences between categorical variable groups. Multivariate logistic regression models were performed to assess the association between urinary continence recovery in patients at 3-month follow-up after LRP and selected covariates. The potential variables related to imaging features with a P value < 0.01 were

chosen. The predictive performance of the developed nomogram and associated variables was assessed using a receiver operating characteristic (ROC) curve approach. Calibration curves were also applied. Decision curve analysis (DCA) was additionally conducted to gauge the clinical value of this model. Data were analyzed using SPSS 21.0 (IBM, Armonk, NY, USA) and R software (version 3.0.1; <http://www.Rproject.org>). Results were considered statistically significant at a P value < 0.05.

Results

A total of 203 patients met the inclusion criteria and were included in this study. 120 patients (61.2%) achieved urinary continence (UC) at the three-month postoperative follow-up, while 83 patients (38.8%) experienced urinary incontinence (UI). Table 1 presents a detailed summary of patient characteristics. Age group, clinical T stage (cT) group, BMS grade group, PV group, IPPL group, and MUL group differed significantly between patients in the UI group and the UC group (P value < 0.05).

The total of 203 patients were randomly divided into a training set and a validation set by 7:3. Of the 124 patients

Table 1 Baseline characteristics of patients at the follow-up of three months

	UI group (n = 83)	UC group (n = 120)	Sum (n = 203)	χ^2 value	P value
Age	70(65,76.5)	68(63,75)	69(64,75.5)	1.161	0.245
Age group				3.995	0.046
1(\geq 70)	38(45.78%)	72(60%)	110(54.19%)		
2(< 70)	45(54.22%)	48(40%)	93(45.81%)		
PSA group				2.570	0.277
1(< 10ng/ml)	32(38.55%)	56(46.67%)	88(43.35%)		
2(10 ~ 20ng/ml)	25(30.12%)	38(31.67%)	63(31.03%)		
3(> 20ng/ml)	26(31.33%)	26(21.67%)	52(25.62%)		
GS group				1.986	0.159
1(< 7)	70(84.34%)	109(90.83%)	179(88.18%)		
2(\geq 7)	13(15.66%)	11(9.17%)	24(11.82%)		
cT group				5.072	0.024
1(T1/T2)	33(39.76%)	67(55.83%)	100(49.26%)		
2(T3)	50(60.24%)	53(44.17%)	103(50.74%)		
BMS grade group				18.045	< 0.001
0	15(18.07%)	53(44.17%)	68(33.5%)		
1	46(55.42%)	54(45%)	100(49.26%)		
2/3	22(26.51%)	13(10.83%)	35(17.24%)		
PV group				5.823	0.016
1(< 40 ml)	53(63.86%)	95(79.17%)	148(72.91%)		
2(\geq 40 ml)	30(36.14%)	25(20.83%)	55(27.09%)		
IPPL group				40.975	< 0.001
1(< 5 mm)	36(43.37%)	103(85.83%)	139(68.47%)		
2(\geq 5 mm)	47(56.63%)	17(14.17%)	64(31.53%)		
MUL group				58.491	< 0.001
1(< 14 mm)	57(68.67%)	19(15.83%)	76(37.44%)		
2(\geq 14 mm)	26(31.33%)	101(84.17%)	127(62.56%)		

Note: Continuous variables were expressed as median and interquartile range, and categorical variables as numbers (n) and percentages (%). The Mann-Whitney U test was utilized to evaluate the differences among the continuous variable groups, while a chi-squared test was applied to examine the differences between categorical variable groups. UI, urinary incontinence; UC, urinary continence; PSA, prostate specific antigen; GS, Gleason Score; cT, clinical T stage; BMS, bladder mucosal smoothness; PV, prostate volume; IPPL, intravesical prostatic protrusion length; MUL, membranous urethral length

in the training set, 56 (39.5%) developed UI three months postoperatively. Of the 61 patients in the validation set, 27 (37.0%) developed UI three months postoperatively. The characteristics of the patients in the training set and the validation set are presented in Table 2. All characteristics did not show significant differences (P value > 0.05).

The prediction model was developed based on the training set. Factors (P value < 0.01) were included in the multivariate analysis. The BMS grade (categorical; 0/1/2 + 3), IPPL group (categorical; < 5 mm/ \geq 5 mm), and MUL group (categorical; < 14 mm/ \geq 14 mm) were included in the final model (Table 3).

This model was used as the basis for the novel nomogram predicting urinary control after LRP at 3 months. Figure 2 graphically depicts the multivariable effect of each variable on the effect of urinary control in the form of a nomogram. The AUC of the training set and the validation set was 0.845 (95% CI 0.779–0.910) and 0.900 (95% CI 0.822–0.979), respectively (Fig. 3A and B). The sensitivity and specificity of the prediction model were 0.800 and 0.816, respectively. The calibration ability of the model is tested in the validation set by

Hosmer-Lemeshow Goodness-of-Fit Test, with a χ^2 value of 6.106 (P value = 0.635) (Fig. 3C and D). The decision-curve analysis (Supplement 2) was developed based on the nomogram. The model exhibited a high net benefit for patients at threshold probabilities of 0–60%. Results of 12 months follow-up are presented in Supplement 3.

Discussion

Patients might face various postoperative complications after RP, including problems with bowel, sexual, or urinary function. Among urinary function issues, RP had the greatest detrimental effect on UI at 6 months postoperatively [16]. According to several studies [16, 17], the rate of UI after RP ranges from 4 to 46%. The fundamental characteristic of normal urinary control following surgery is that the urethral pressure is greater than the intravesical pressure; thus, maintaining normal urethral pressure and preventing the rise in intravesical pressure is the key to early recovery of urinary control function. Consequently, it's imperative to understand the morphology of the bladder and its surroundings of the patient prior to surgery.

Table 2 The characteristics of patients in the training set and the validation set respectively

	Training set (n = 142)	Validation set (n = 61)	χ^2 value	P value
Urinary			0.411	0.521
Urinary continence	86(60.56%)	34(55.74%)		
Urinary incontinence	56(39.44%)	27(44.26%)		
PSA group			2.949	0.229
1(< 10ng/ml)	56(39.44%)	32(52.46%)		
2(10 ~ 20ng/ml)	47(33.10%)	16(26.23%)		
3(> 20ng/ml)	39(27.46%)	13(21.31%)		
GS group			0.010	0.920
1(< 7)	125(88.03%)	54(88.52%)		
2(\geq 7)	17(11.97%)	7(11.48%)		
cT group			0.357	0.550
1(T1/T2)	68(47.89%)	32(52.46%)		
2(T3)	74(52.11%)	29(47.54%)		
BMS grade group			2.115	0.347
0	50(35.21%)	18(29.51%)		
1	71(50.00%)	29(47.54%)		
2/3	21(14.79%)	14(22.95%)		
PV group			0.726	0.394
1(< 40 ml)	106(74.65%)	42(68.85%)		
2(\geq 40 ml)	36(25.35%)	19(31.15%)		
IPPL group			3.612	0.057
1(< 5 mm)	103(72.54%)	36(59.02%)		
2(\geq 5 mm)	39(27.46%)	25(40.98%)		
MUL group			0.003	0.959
1(< 14 mm)	53(37.32%)	23(37.70%)		
2(\geq 14 mm)	39(31.33%)	38(62.30%)		

Note: Continuous variables were expressed as median and interquartile range, and categorical variables as numbers (n) and percentages (%). The Mann-Whitney U test was utilized to evaluate the differences among the continuous variable groups, while a chi-squared test was applied to examine the differences between categorical variable groups. UI, urinary incontinence; UC, urinary continence; PSA, prostate specific antigen; GS, Gleason Score; cT, clinical T stage; BMS, bladder mucosal smoothness; PV, prostate volume; IPPL, intravesical prostatic protrusion length; MUL, membranous urethral length

Table 3 Multivariate analysis predicting urinary continence recovery of patients at 3-month follow-up after LRP in the training set

Predictors	B	SE	z	p	OR (95%CI)
BMS grade					
0	0.194	1.095	0.177	0.860	
1	-1.177	0.522	-2.256	0.024	0.31(0.11,0.86)
2+3	-1.758	0.688	-2.557	0.011	0.17(0.04,0.66)
IPPL group	-1.381	0.474	-2.915	0.004	0.25(0.1,0.64)
MUL group	1.857	0.437	4.250	0.000	6.41(2.72,15.09)

Note: BMS, bladder mucosal smoothness; IPPL, intravesical prostatic protrusion length; MUL, membranous urethral length

Surgeons nowadays can use pelvic MRI scans to better comprehend the anatomic structures of the bladder and its surroundings. The UI following LRP can be predicted by anatomical parameters. Many studies have focused on urethral factors, particularly MUL [2–4]. Besides urethra factors, bladder factors are also related to UI following

RP. The delayed recovery of urinary control function after LRP is associated with postoperative OAB syndrome [18]. Ultrasound measurements of the detrusor wall thickness and the bladder wall thickness were linked to DO and OAB syndrome, which may result in UI after prostate surgery [14, 19]. Nevertheless, compared to urethra-related MRI parameters, little research has focused on bladder-related MRI parameters.

To the best of our knowledge, our study is the first to propose bladder factors measured by MRI that were connected to the early recovery of urinary continence after LRP. We proposed the BMS grade to depict the bladder from the perspective of morphology. Our research indicated that BMS grade was an independent predicting factor in the early recovery of urinary continence after LRP. Contractile function in the bladder exists in two modalities: phasic contractions initiated by transmitters released from parasympathetic fibers to void urine and spontaneous contractions, which have a pathological role in contributing to DO [20]. Bladder outlet obstruction (BOO) could cause increased intravesical pressure during bladder voiding. A three-stage model has been hypothesized to characterize BOO-induced bladder remodeling: the phase of hypertrophy, the phase of compensation (increased detrusor contractility during the voiding phase), followed by the phase of decompensation (detrusor dysfunction, including spontaneous contractions and DO) [11]. The existence of bladder trabeculation is one of the morphological markers of bladder remodeling induced by BOO, associated with spontaneous contractions and DO [21, 22]. Involuntary detrusor contractions and DO are related to the OAB syndrome and UI, according to the myogenic theory [23]. The bladder trabeculation can eventually result in the uneven thickening of the bladder wall and the roughness of the bladder mucosa. BMS grade can depict the roughness of the bladder mucosa and represents the severity of the bladder trabeculation, therefore indicating the severity of the bladder remodeling and evaluating the dysfunction of the detrusor.

In addition, we also confirmed that MUL and IPPL were independent risk factors for UI at 3 months after LRP. Our prediction model also included these two factors. Previous studies [6, 24] have confirmed that a shorter preoperative MUL is an independent risk factor for UI after prostatectomy, consistent with the results of our study. The choice of UI treatment may be further guided by the preoperative MUL assessed by MRI. According to Oza P [24], patients with a MUL < 12 mm had a higher risk of eventually having surgery for UI, whereas those with a MUL > 17 mm were more likely to receive non-invasive treatments. Preserving MUL and functional urethral length to the greatest extent during surgery can significantly improve postoperative urinary

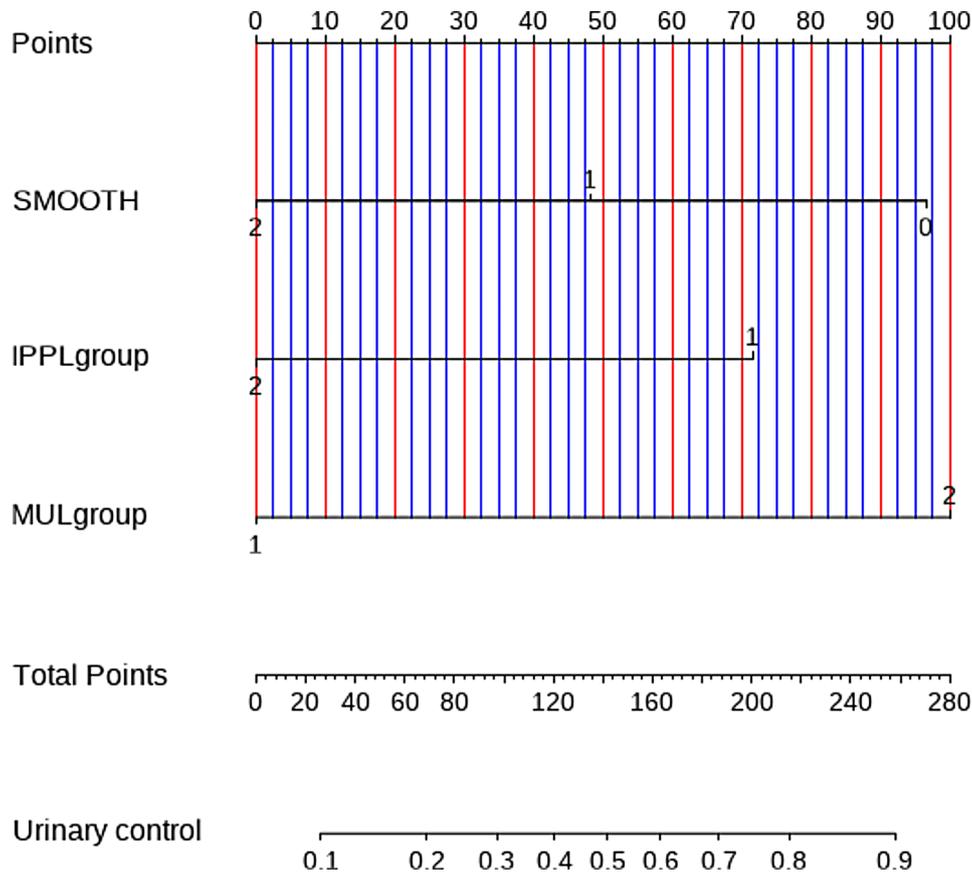


Fig. 2 The nomogram prediction model for predicting urinary control after LRP at 3 months. IPPL, intravesical prostatic protrusion length; MUL, membranous urethral length

control function recovery [25]. The results of this study also suggest that IPPL is an independent risk factor that influences early postoperative UI. Prostate protrusion into the bladder poses challenges in LRP surgery, which has a negative impact on surgery steps such as bladder neck disconnection and bladder urethral anastomosis, increasing the risk of perioperative complications. Preoperative MRI measurement of IPPL allows for a quantitative assessment of the prostate protrusion into the bladder. Patients with preoperative IPPL ≥ 5 mm have delayed postoperative recovery of urinary control function [7].

There are still some limitations to our study. Firstly, this study is a retrospective, single-center analysis. It was difficult to avoid the biases. Secondly, we did not take the experience of surgeons into account. The reliability of the study could be impacted by patients receiving LRP from different surgeons at various times. The recovery of postoperative urinary control function may vary depending on the experience of the surgeon. Danny Trieu reported that patients who underwent RP performed by a surgeon with an annual surgical case load of >50 cases per year can expect better urinary continence recovery results [26].

Thirdly, postoperative UI often manifests as mixed UI, encompassing stress UI and urgent UI [27]. It has been suggested that stress UI may contribute to the development of urgent UI [28, 29]. Urine leakage into the urethra may activate urethral afferents, consequently enhancing detrusor instability. The underlying mechanism remains speculative due to the lack of Overactive Bladder Symptom Score (OABSS) data in our current analysis. We acknowledge that this limitation restricts a more comprehensive exploration of the precise relationship between postoperative UI and bladder-related factors involved in our study. This data gap represents a critical avenue for future research, and we aim to explore this in subsequent studies. Besides, not all participants in our study had the information necessary for urodynamic evaluation. Some participants refused to undergo urodynamics tests because they were invasive. Hence, it was challenging to further investigate the preoperative BMS grade's role in predicting LRP patients' early postoperative urinary control function recovery. Besides, our model is based on LRP patients. Before our model is applied to patients undergoing robot-assisted radical prostatectomy, it still needs to be validated. A prospective study including patients

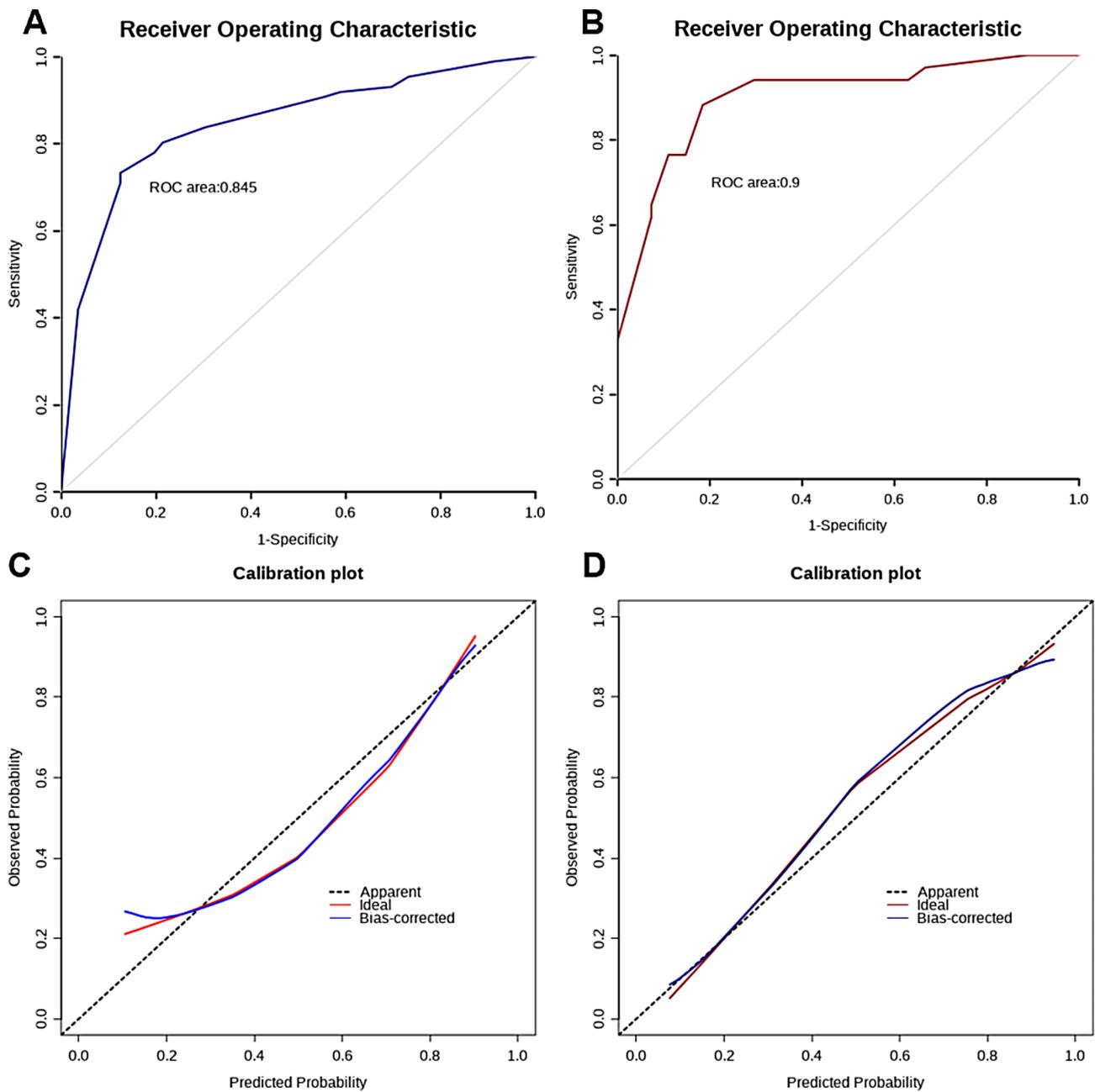


Fig. 3 The predictive performance of novel model in the training set and the validation set. **(A)** Illustrates the ROC curve for the prediction model within the training set. **(B)** Illustrates the ROC curve for the prediction model within the validation set. **(C)** Depicts the calibration curve of the prediction model within the training set. **(D)** Depicts the calibration curve within the prediction model within the validation set. ROC, Receiver Operating Characteristic

with urodynamics data will be the direction of our future work.

In conclusion, the present study demonstrates that our prediction model based on preoperative MRI parameters exhibits efficacy in predicting early recovery of urinary continence after LRP.

Conclusions

Our study proposed BMS grade and confirmed that patients with a lower BMS grade are associated with an early recovery of urinary continence after LRP. Moreover, we developed and validated a predictive model in the form of a nomogram to predict the risk of UI after LRP at 3 months, including three independent risk factors, MUL, IPPL, and BMS grade.

Abbreviations

BMS	Bladder mucosal smoothness
UC	Urinary continence
LRP	Laparoscopic radical prostatectomy
UI	Urinary incontinence
PCa	Prostate cancer
PV	Prostate volume
MUL	Membranous urethra length
IPPL	Intravesical prostatic protrusion length
OR	Odds ratio
RP	Radical prostatectomy
DO	Detrusor overactivity
WI	Weighted imaging
ROC	Receiver operating characteristic
DCA	Decision curve analysis
CT	Clinical T stage

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None.

Author contributions

LY participated in data analysis and wrote the majority of the manuscript. YY developed the project, analyzed the data and participated in manuscript editing. HC participated in data analysis. SD collected data. JY collected data. GW collected data. YH collected data. FZ developed project, and edited manuscript. SZ developed project, and edited manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Consent for publication

Not applicable.

Human ethics and consent to participate declarations

This study has received ethics approval from Peking University Third Hospital Ethics Committee (M2023503). The study was performed in accordance with the Declaration of Helsinki. Informed consent to participate was obtained from all of the participants in the study.

Competing interests

The authors declare no competing interests.

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