A predictive preoperative and postoperative nomogram for postoperative potency recovery after robot-assisted radical prostatectomy

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A Predictive Preoperative and Postoperative Nomogram for Postoperative Potency Recovery after Robot-Assisted Radical Prostatectomy

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Study Need and Importance: Erectile dysfunction following prostatectomy is a common complication. There are many factors associated with postoperative erectile dysfunction. No plausible methods of accurately predicting the erectile function (EF) in the preoperative period or the postoperative period currently exist. However, it is vital to know the probability of regaining sexual function for patient counseling. This study aimed to develop tools that can be used for patient counseling about their probability of regaining sexual function.

What We Found: Patients from January 1, 2008 to December 31, 2016 (development set, 6,502) were selected to develop the nomograms, and patients from January 1, 2016 to January 1, 2019 (validation set, 2,706) were used for validation. Patients in both data sets had a minimum of 12 months of followup. Starting from a set of candidate prognostic variables, the variable selection was performed by estimating the importance of predictors in a multivariable setting using survival random forests. Then Multivariable Cox regression models were fitted on the development cohort (6,502) to predict EF recovery after robot-assisted radical prostatectomy (RARP) using as prognostic factors the covariates selected. Two nomograms were drawn using the regression coefficients of the preoperative and postoperative Cox models. The discrimination ability of the preoperative model was evaluated on the development cohort using the ROC curves estimated at 3, 6, 12 and 24 months. The AUC at these time points was 0.726, 0.734, 0.754 and 0.778, respectively. The AUCs of the postoperative model at 3, 6, 12 and 24 months were 0.746, 0.756 and 0.777, and 0.801, respectively. Preoperative and postoperative predictive models were validated using a separate set of 2,706 patients. The AUCs of the preoperative model at 3, 6, 12 and 24 months were 0.789, 0.772, 0.768 and 0.778, respectively. The ROC curves of the postoperative model at 3, 6, 12 and 24 months with AUCs of 0.807, 0.797, 0.793 and 0.798, respectively. Along with age and preoperative sexual function, the nerve-sparing technique determines the potency outcomes justifying better AUC for the postoperative model vs the preoperative model.

Limitations: The limitation of the current study includes the retrospective nature of the data set from a single-center performed by a single surgeon. Also, the compliance of our patients who receive penile rehabilitation therapy may vary, which could potentially lead to a bias. The validation cohort consists of patients with higher risk (representing the current prostate cancer population in daily practice due to more active surveillance in the community) in whom the nomogram moderately overestimates the EF recovery. The limited followup of the validation set is an issue. However, the data set selected at a different time frame helps in temporal validation at different times. The tools used to evaluate EF after RARP may suffer from recall bias. However, these limitations are reflective of a real-world scenario. This study would need further external validation from other centers to confirm the performance of our nomograms.

Interpretation for Patient Care: This is a novel tool for the caregiver to predict realistic expectations of EF recovery to the patients during preoperative and immediate postoperative counseling. The proposed nomograms should be applied with caution to the population of other centers, at least until preoperative data collection and technique of RARP are standardized. Until then each high-volume center around the world should individually develop prediction models applicable to their center.

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A Predictive Preoperative and Postoperative Nomogram for Postoperative Potency Recovery after Robot-Assisted Radical Prostatectomy

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Purpose: Prediction of potency recovery following robot-assisted radical prostatectomy (RARP) is useful for better patient counseling and postoperative treatment strategies. In this study we propose a preoperative and postoperative nomogram to predict postoperative potency recovery following RARP.

Materials and Methods: Patients from development set (6,502) were selected to develop the nomograms, and patients in validation set (2,706) were used for validation. Cox regression models were fitted on the development cohort to predict potency recovery after RARP using as prognostic factors the covariates selected. Two nomograms were drawn using the regression coefficients of the preoperative and postoperative Cox models.

Results: The discrimination ability of the preoperative model was evaluated on the development cohort using the receiver operator curves estimated at 3, 6, 12 and 24 months. The AUC at these time points was 0.726, 0.734, 0.754, and 0.778, respectively. The areas under the curve of the postoperative model at 3, 6, 12 and 24 months were 0.746, 0.756 and 0.777, and 0.801, respectively. Preoperative and postoperative predictive models were validated using a separate set of 2,706 patients. The AUCs of the preoperative model at 3, 6, 12 and 24 months were 0.789, 0.772, 0.768, and 0.778, respectively. The ROC curves of the postoperative model at 3, 6, 12 and 24 months with AUCs of 0.807, 0.797, 0.793 and 0.798, respectively. Along with age and preoperative sexual function, nerve-sparing technique determines the potency outcomes justifying better AUC for postoperative model vs the preoperative model.

Conclusions: The above nomograms help us to predict with good accuracy the probability of potency recovery within 3, 6, 12 and 24 months following surgery taking into consideration preoperative and postoperative factors. This is a novel tool for the care giver to predict realistic expectation of potency outcomes to the patients, while preoperative and immediate postoperative counseling.

Abbreviations and Acronyms

AUC = area under the curve
CaP = prostate cancer
CIF = cumulative incidence functions
CCI = Charlson comorbidity index
DRE = digital rectal examination
ED = erectile dysfunction
EF = erectile function
EPIC = Expanded Prostate Cancer Index Composite
GS = Gleason score
IIEF = International Index of Erectile Function
MAE = mean absolute error
NS = nerve-sparing
NVB = neurovascular bundle
PSA = prostate specific antigen
RARP = robot-assisted radical prostatectomy
ROC = receiver operator curve
RP = radical prostatectomy
SHIM = Sexual Health Inventory in Males

Key Words: nomograms, erectile dysfunction, prostatectomy

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Erectile dysfunction (ED) after radical prostatectomy (RP) for prostate cancer (CaP) is a major concern. Following robot-assisted RP (RARP), erectile function (EF) rates range between 20% and 90% at 12 months and 63 to 94% at 24 months.[1] However, the individual risk of EF recovery following surgery is affected by many preoperative and postoperative factors that determine the post-RARP EF outcomes.[2–6] With so many factors influencing the postoperative EF rates following RP, it is crucial to develop tools to improve the preoperative prediction of EF for better patient counseling and postoperative treatment strategies.

Currently, various predictive nomograms are commonly used to predict oncologic outcomes CaP. To the best of our knowledge, there are only 2 nomograms available in the current literature. However, they were developed on a small subset of patients.[7,8]

Considering the large volume of patients undergoing RARP at our center, we aimed to develop a set of simple nomograms to predict postoperative EF outcomes in candidates for RARP, which can be used in the preoperative and immediate postoperative setting by physicians during patient counseling and to assist in patient decision making.[9]

METHODS

Study Population

Data from our prospectively collected IRB database (IRB-237998-40) was used to develop nomograms to predict EF following RARP. Patients from January 1, 2008 to December 31, 2016 (6,502) were selected to develop the nomograms, and patients from January 1, 2016 to January 1, 2019 (2,706) were selected for validation. Patients in both data sets had a minimum of 12 months of followup. We excluded from our analysis patients who underwent salvage RARP, neoadjuvant androgen deprivation therapy and postoperative radiation.

Patient-reported outcomes were obtained by chart review or telephone survey of all patients at the time of analysis.

Surgical Technique

The patients underwent transperitoneal RARP with an early retrograde athermal nerve sparing (NS) technique by a single surgeon as previously described.[10] The degree of NS was assessed by the operating surgeon according to preoperative patients and tumor characteristics (ie biopsy), Gleason Score (GS), D'Amico class, multiparametric magnetic resonance imaging, PRECE (Predicting Extra-Capsular Extension in prostate cancer) and the intraoperative disease extent, based on operative cues like adhesion, desmoplasia etc. These tools were used as and when available. NS was given a score from 1 to 5 based on the scoring system previously described. These scores correspond to the percentage of NS based on anatomical landmarks.[6] The average of percentages from both sides was then grouped into 4 separate grades as follows:

- "Grade 1 (Full) NS": ≥95% of NVB preservation
- "Grade 2 (Grade 1 partial) NS": ≥75% to 94% of NVB preservation
- "Grade 3 (Grade 2 partial) NS": ≥50% to 74% of NVB preservation
- "Grade 4 (Poor) NS": <50% of NVB preservation

Covariates and Followup

Our data sets contain preoperative patient characteristics including age, clinical stage (cT stage), digital rectal examination (DRE), preoperative Sexual Health Inventory in Males (SHIM) score, preoperative American Urological Association score, modified Charlson comorbidity index (CCI), and preoperative GS. SHIM >21 was used as a cutoff for defining the preoperative normal EF. Mild ED was defined as SHIM=17–21 and ED was defined as SHIM <17.[11] A standard pelvic floor and penile rehabilitation protocol including PDE5 inhibitors and vacuum erection devices were followed by our patients postoperatively. Penile rehabilitation included regular PDE5 inhibitors after RARP, at least three times a week and the vacuum erection device was advised once a day starting 4 weeks, until recovery of sexual function.

The primary end point of EF is defined as the ability to penetrate and satisfactorily complete intercourse with or without PDE5 inhibitor usage in more than half of the attempts.[12,13]

The Clavien-Dindo grading system was used to evaluate the perioperative and postoperative complications within 30 days after surgery.[14] Regular followup data were collected prospectively every 3 months in the first year, every 6 months in the second year, and then yearly.

Statistical Analysis

Statistical analyses, reporting and interpretation of the results were conducted according to established guidelines in 6 steps.[15] A detailed description of statistical analysis is provided in the supplementary material (https://www.jurology.com). Figure 1 shows stepwise statistical analysis performed.

RESULTS

Baseline Patient Characteristics

A detailed comparison between the training and validation set is provided in table 1.

Nomogram Design

Univariate Analysis. Table 2 depicts the univariate analysis of all the candidate factors that may affect EF.

Variable selection. Figure 2, *A* and *B* depict the importance (with CIs) of preoperative and postoperative factors estimated by survival random forest. The most important and significant preoperative prognostic factors were SHIM score, age, preoperative GS, and CCI, in the order of importance. Likewise, for the postoperative prediction model, the selected prognostic factors were preoperative SHIM, NS performed, age and pT stage.

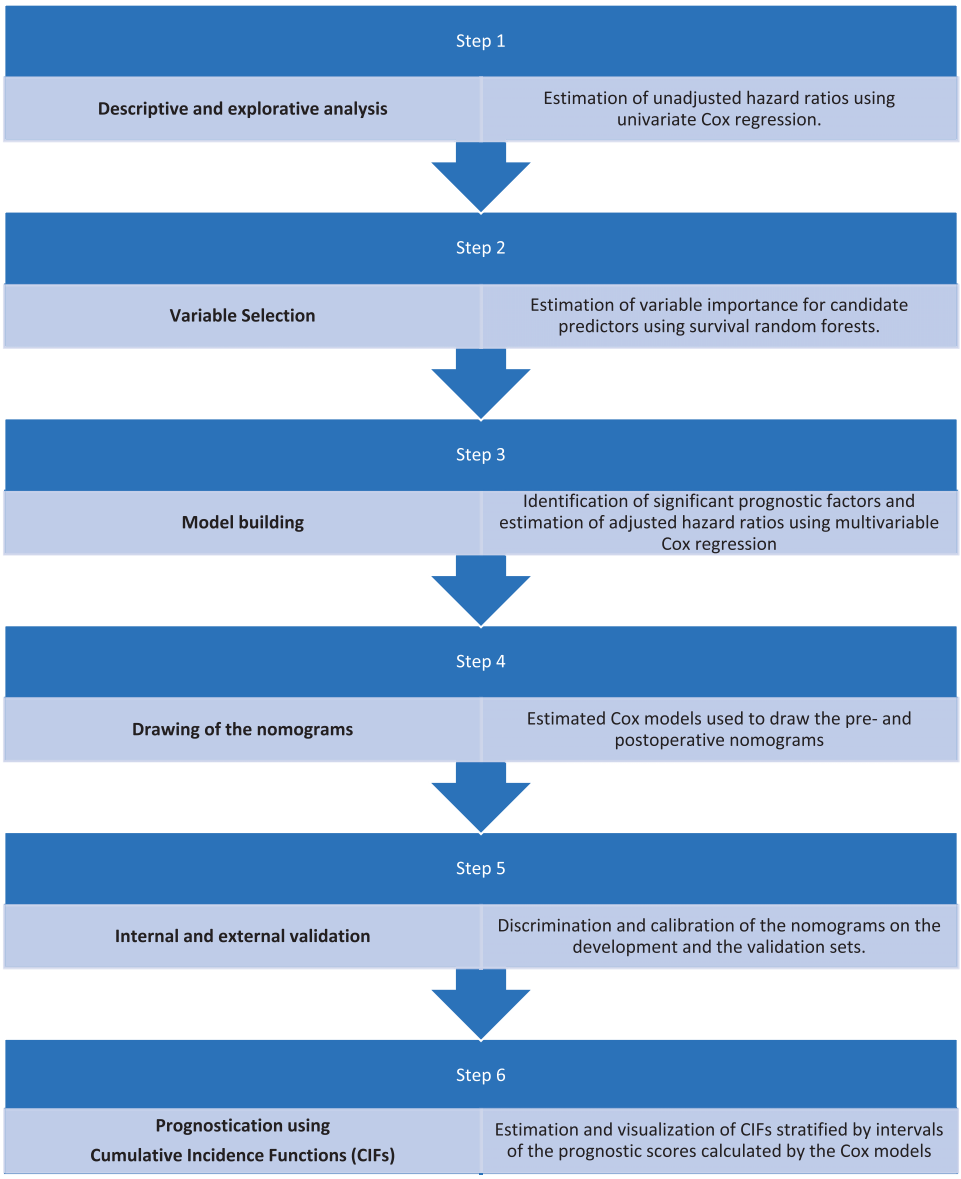

Figure 1. Stepwise description of statistical analysis.

Multivariable Prediction Models. In the preoperative Cox regression model (table 2), preoperative SHIM score (HRs estimated on the development cohort of 3.44 and 2.28 for SHIM≥ 22 and SHIM 17-21, respectively, p <0.001), age (HR=0.75 and 0.54 for age 55-65 and age >65, respectively, p <0.001), CCI (HR=0.80 for CCI >3, p <0.001) and preoperative GS (HR=0.80 and 0.52 for GS=7 and GS >7, respectively, p <0.001) were independent predictors for EF.

In the postoperative Cox regression model (table 3), preoperative SHIM (HR=2.96 and 1.95 for SHIM≥22 and SHIM 17-21, respectively, p <0.001), age (HR=0.73 and 0.51 for age 55-65 and age >65, respectively, p <0.001), grades of NS (HR=3.31, 2.38, and 1.52 for grade 1, 2 and 3, respectively, p <0.001), and postoperative pT stage (HR=0.64, 0.64, and 0.84 for pT4, pT3b and pT3a, respectively, p=0.025 and p <0.001) were independent factors for EF.

Nomograms

Starting from the estimated coefficients of the preoperative and postoperative Cox models, 2 nomograms were drawn (fig. 3, *A* and *B*). Given the values of the 4 preoperative prognostic factors for a single patient (SHIM score, age, CCI and total GS), one can graphically calculate the predicted probabilities of EF within 3, 6, 12 and 24 months after RARP. Similarly, using the values of the 4 factors in the postoperative model (preoperative SHIM score, the grade of NS, age and pT stage), one can estimate the probabilities of EF at the 4 time points.

Table 1. *Demographic, clinical and pathological characteristics of study patients in both data sets*

	Development Set		Validation Set		p Value
Median yrs age (IQR)	62	(56–67)	64	(58–69)	
No. yrs age (%):					<0.001
≤55	1,524	(23.4)	429	(16)	
56–65	2,899	(44.6)	1,100	(40.6)	
>65	2079	(32.0)	1,177	(43.5)	
Median body mass index in kg/m^2 (IQR)	27.8	(25.4–30.5)	27.9	(25.4–30.8)	0.205
No. preop GS (%):					<0.001
≤6	3,055	(47.2)	677	(25.2)	
7	2,638	(40.7)	1,402	(52.3)	
≥8	809	(12.1)	603	(22.5)	
Median modified CCI (IQR)	2	(1–2)	2	(1–3)	<0.001
Median preop PSA in ng/ml (IQR):	5.1	(4.0–7.1)	5.9	(4.6–8.6)	<0.001
≤10	5,782	(91.1)	2,249	(85.7)	
10–20	561	(9)	370	(14)	
>20	2	(0.0)	4	(0.2)	
No. D'Amico class (%):					<0.001
Low risk	2,742	(42.3)	609	(22.6)	
Intermediate risk	2,727	(42.1)	1,423	(52.9)	
High risk	1,011	(15.6)	660	(24.5)	
No. preop SHIM (%):					<0.001
No ED (SHIM ≥22)	3,052	(46.9)	1,110	(41.0)	
Mild ED (SHIM 17–21)	1,453	(22.4)	638	(23.6)	
Moderate to severe ED (SHIM ≤16)	1,997	(30.7)	958	(35.4)	
No. NS (%):					<0.001
Grade 1	3,066	(48.9)	923	(34.1)	
Grade 2	1,976	(31.6)	1,101	(40.7)	
Grade 3	691	(11.0)	536	(19.8)	
Grade 4	530	(8.5)	146	(5.4)	
No. NS based on D'Amico Class (%):					
Low risk:					<0.001
Grade 1	1,794	(67.93)	400	(14.8)	
Grade 2	642	(24.31)	183	(6.8)	
Grade 3	104	(3.94)	19	(0.7)	
Grade 4	101	(3.82)	7	(0.2)	
Intermediate risk:					<0.001
Grade 1	1,104	(42.12)	467	(17.3)	
Grade 2	984	(37.54)	651	(24.0)	
Grade 3	341	(13.01)	258	(9.5)	
Grade 4	192	(7.33)	47	(1.7)	
High risk:					<0.001
Grade 1	159	(16.24)	48	(1.7)	
Grade 2	346	(35.34)	265	(9.7)	
Grade 3	243	(24.82)	258	(9.5)	
Grade 4	231	(23.6)	89	(0.3)	
No. pathological stage (%):					<0.001
Organ confined (≤pT2c)	4,658	(71.6)	1,557	(57.5)	
Extraprostatic extension (pT3a)	1,316	(20.2)	805	(29.8)	
Seminal vesicle invasion (pT3b)	449	(6.9)	296	(10.9)	
Adjacent organ involved (pT4)	79	(1.2)	48	(1.8)	
No. pathological GS (%):					<0.001
3+3	1,855	(28.5)	373	(13.8)	
3+4	2,795	(43)	1,057	(39.1)	
4+3	1,155	(17.7)	689	(25.5)	
4+4	181	(2.7)	80	(3)	
8–10	470	(7.2)	422	(15.6)	
Deferred	46	(1)	85	(3.1)	
No. pos surgical margin (%):	1,003	(15.4)	550	(20.3)	<0.001
In organ confined (≤pT2c)	404	(8.7)	157	(10.1)	
In extraprostatic extension (pT3a)	335	(25.5)	217	(27.0)	
In seminal vesicle invasion (pT3b)	188	(41.9)	128	(43.2)	
In adjacent organ involved (pT4)	76	(96.2)	48	(100)	
Median mos followup time (IQR)	60	(37–85)	18	(11–24)	<0.001
No. potency achieved (irrespective of age, preop potency and nerve sparing)	4,029		965		<0.001
Median mos time to potency (IQR)	2.9	(1.4–8.4)	4.6	(1.4–9.1)	<0.001

Internal validation. The discrimination ability of the preoperative model was evaluated on the development cohort using the ROC curves estimated at 3, 6, 12 and 24 months. The AUC at these time points was 0.726, 0.734, 0.754 and 0.778, respectively (supplementary fig. 1, *a*, https://www.jurology.com). The calibration plot of this model showed an almost perfect agreement between observed and predicted

Table 2. *Univariate analysis of all factors considered in nomogram development*

Covariate	Unadjusted HR with CI	p Value (Wald test)
Age (yrs):		
≤55	Reference	
56–65	0.60 (0.56–0.65)	<0.001
>65	0.31 (0.28–0.34)	<0.001
Body mass index (kg/m^2)	0.98 (0.97–0.99)	<0.001
Preop SHIM:		
Moderate to severe ED (SHIM≤16)	Reference	
Mild ED (SHIM 17–21)	2.63 (2.38–2.91)	<0.001
No erectile dysfunction ED (SHIM ≥22)	4.23 (3.87–4.61)	<0.001
Modified CCI:		
0	Reference	
1–2	0.56 (0.49–0.62)	<0.001
3–4	0.26 (0.23–0.30)	<0.001
>4	0.19 (0.12–0.29)	<0.001
PSA (ng/dl):		
<10	Reference	
10–20	0.78 (0.69–0.88)	<0.001
>20	1.79 (0.45–7.18)	0.409
D'Amico Class:		
1	Reference	
2	0.78 (0.73–0.84)	<0.001
3	0.49 (0.45–0.55)	<0.001
Pos DRE findings:		
Not performed	Reference	
1—Lt base	1.39 (0.52–3.75)	0.516
2—Lt mid gland	1.35 (0.50–3.68)	0.559
3—L apex	1.60 (0.59–4.35)	0.358
4—Rt base	1.20 (0.45–3.24)	0.715
5—Rt mid gland	1.73 (0.64–4.70)	0.280
6—Rt apex	1.57 (0.63–4.44)	0.377
Neg	1.66 (0.63–4.45)	0.625
Total preop GS:		
6	Reference	
7	0.79 (0.74–0.84)	<0.001
>7	0.44 (0.39–0.50)	<0.001
Clinical T stage:		
Organ confined (≤cT2c)	Reference	
Extraprostatic extension (cT3a)	0.51 (0.32–0.80)	0.004
Seminal vesicle invasion (cT3b)	0.40 (0.05–2.85)	0.362
Adjacent organ involved (cT4)	0.26 (0.04–1.85)	0.179
History of previous abdominal surgery	0.84 (0.78–0.89)	<0.001
History of recreational drug use	0.40 (0.19–0.84)	0.016
History of smoking:		
No	Reference	
Former smoker	0.78 (0.70–0.83)	<0.001
Current smoker	0.88 (0.78–0.99)	<0.001
History of alcohol use:		
No	Reference	
Rare	0.99 (0.89–1.13)	0.997
Social	1.13 (1.05–1.22)	0.001
Daily/abuse	1.09 (1.01–1.19)	0.028
Clavien-Dindo score:		
Up to 2	Reference	
More than 2	0.65 (0.49–0.87)	0.004
NS:		
Grade 4	Reference	
Grade 3	2.02 (1.62–2.53)	<0.001
Grade 2	3.93 (3.22–4.78)	<0.001
Grade 1	6.66 (5.49–8.07)	<0.001
Pathological GS:		
6	Reference	
7	0.78 (0.73–0.83)	<0.001
>7	0.39 (0.34–0.45)	<0.001
Pathological pos surgical margin	0.80 (0.73–0.87)	<0.001
Pathological T stage:		
Organ confined (≤pT2c)	Reference	
Extraprostatic extension (pT3a)	0.64 (0.59–0.69)	<0.001
Seminal vesicle invasion (pT3b)	0.42 (0.36–0.49)	<0.001
Adjacent organ involved (pT4)	0.39 (0.27–0.57)	<0.001

probabilities of EF, with mean absolute error (MAE) of 0.024, 0.014, 0.007 and 0.014 at the 4 time points (supplementary fig. 2, *a*, https://www.jurology.com). The AUCs of the postoperative model at 3, 6, 12 and 24 months were 0.746, 0.756 and 0.777, and 0.801, respectively (supplementary fig. 1, *b*, https://www.jurology.com). This model showed an almost perfect calibration, with MAE of 0.027, 0.022, 0.007 and 0.015 at the 4 time points (supplementary fig. 2, *b*, https://www.jurology.com). Finally, supplementary figure 3, *a* and *e* (https://www.jurology.com) show the CIFs for different levels of the preoperative and postoperative prognostic index; they depict the predictive ability of the preoperative model and postoperative model in the development data set. Patients with very high scores (192 < prognostic index ≤ 240) showed the highest probabilities of attaining EF compared with the other patients. Supplementary figure 3, *c* and *g* (https://www.jurology.com) show CIFs for individual prognostic factors for preoperative and postoperative models, respectively.

Validation on a Separate Data Set

Preoperative and postoperative predictive models were separately validated using a validation set. The AUCs of the preoperative model at 3, 6, 12 and 24 months were 0.789, 0.772, 0.768, and 0.778, respectively (supplementary fig. 1, *c*, https://www.jurology.com). The calibration plots at 3, 6, 12 and 24 months showed a moderate overestimation of EF probabilities, with MAE of 0.132, 0.116, 0.127, and 0.135, respectively (supplementary fig. 2, *c*, https://www.jurology.com). Supplementary figure 1, *d* (https://www.jurology.com) shows the ROC curves of the postoperative model at 3, 6, 12 and 24 months with AUCs of 0.807, 0.797, 0.793 and 0.798, respectively. A moderate overestimation was depicted by the calibration plots, with MAE of 0.118, 0.124, 0.143 and 0.14 at 3, 6, 12 and 24 months (supplementary fig. 2, *d*, https://www.jurology.com). Supplementary figure 3, *b* and *f* show the CIFs estimated in the validation set at different levels of the prognostic index calculated using the preoperative and postoperative models, respectively. Supplementary figure 3, *d* and *h* (https://www.jurology.com) depict CIFs for the individual prognostic factors used in the preoperative and postoperative models, respectively.

DISCUSSION

Traditional preoperative EF risk criteria predict EF as low, intermediate, or high risk of ED and this may not be easily understood by patients in their preoperative counseling.[16–18] Previously, Cozzi et al proposed a postoperative nomogram that quantified EF recovery by the probability of having a sexual

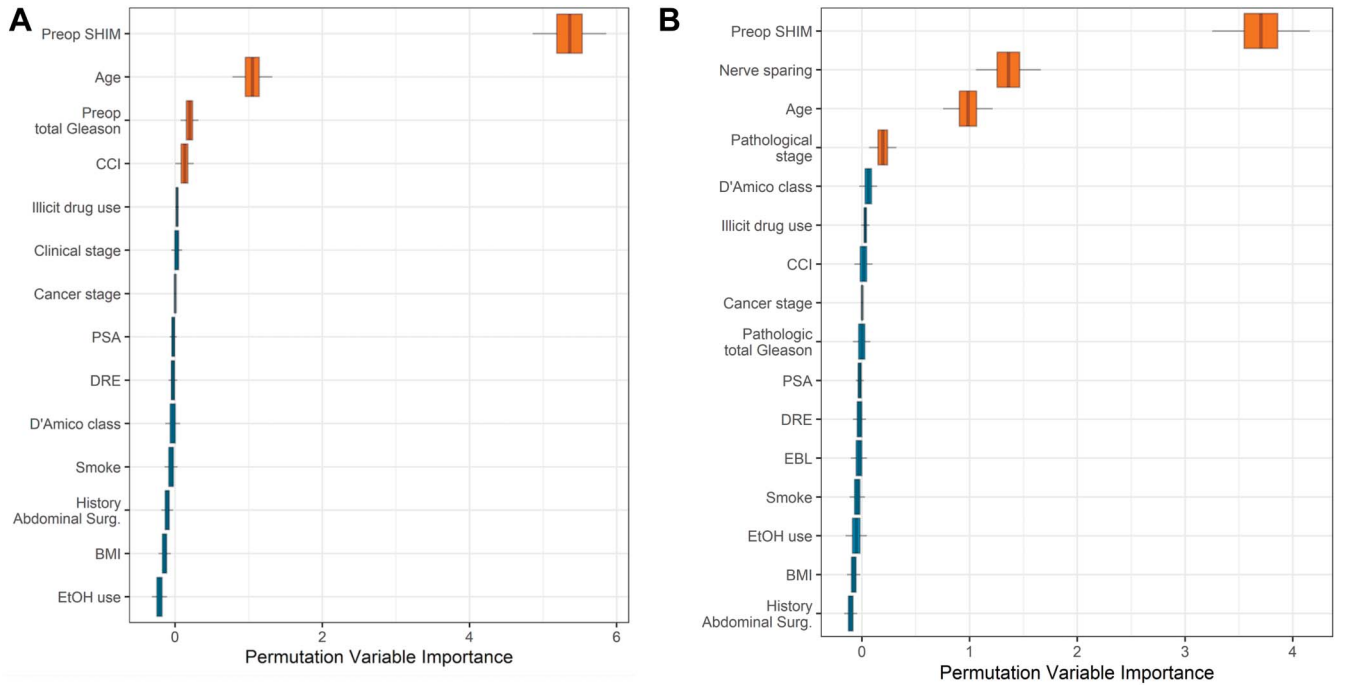

Figure 2 *A*, variable importance with confidence intervals estimated using survival random forest in preoperative setting. *B*, variable importance with CIs estimated using survival random forest in postoperative setting. *EBL*, estimated blood loss. *BMI*, body mass index. *EtOH*, alcohol.

EF score >25%, 50%, or 75% at 1 year.[8] Mulhall also proposed a set of 3 nomograms to predict the probability of International Index Erectile Function (IIEF) score ≤10 at 24 months and the probability of IIEF score ≥24 at 24 months postoperatively. The first nomogram is used preoperatively, the second in the immediate postoperative period and the third at 12 months post-surgery.

In the present study, we propose 2 nomograms; one can be used preoperatively and one in the immediate postoperative setting to predict the probability within EF at 3, 6, 12 and 24 months following

Table 3. *Preoperative and postoperative multivariable Cox regression models estimated on development set*

	Preop Model		Postop Model	
Covariate	HR with CI	p Value (Wald test)	HR with CI	p Value (Wald test)
Age (yrs):				
≤55	Reference		Reference	
56–65	0.75 (0.70–0.81)	<0.001	0.73 (0.68–0.79)	<0.001
>65	0.54 (0.49–0.59)	<0.001	0.51 (0.47–0.56)	<0.001
Preop SHIM:				
Moderate to severe ED (SHIM ≤16)	Reference		Reference	
Mild ED (SHIM 17–21)	2.28 (2.06–2.53)	<0.001	1.95 (1.76–2.17)	<0.001
No erectile dysfunction ED (SHIM ≥22)	3.44 (3.14–3.77)	<0.001	2.96 (2.70–3.25)	<0.001
Modified CCI:				
0–2	Reference			
>3	0.80 (0.72–0.88)	<0.001		
Total preop GS:				
6	Reference			
7	0.80 (0.75–0.86)	<0.001		
>7	0.52 (0.46–0.58)	<0.001		
NS:				
Grade 4			Reference	
Grade 3			1.52 (1.21–1.91)	<0.001
Grade 2			2.38 (1.95–2.92)	<0.001
Grade 1			3.31 (2.70–4.05)	<0.001
Pathological T stage:				
Organ confined (≤pT2c)			Reference	
Extraprostatic extension (pT3a)			0.84 (0.77–0.92)	<0.001
Seminal vesicle invasion (pT3b)			0.64 (0.55–0.76)	<0.001
Adjacent organ involved (pT4)			0.64 (0.44–0.95)	0.025

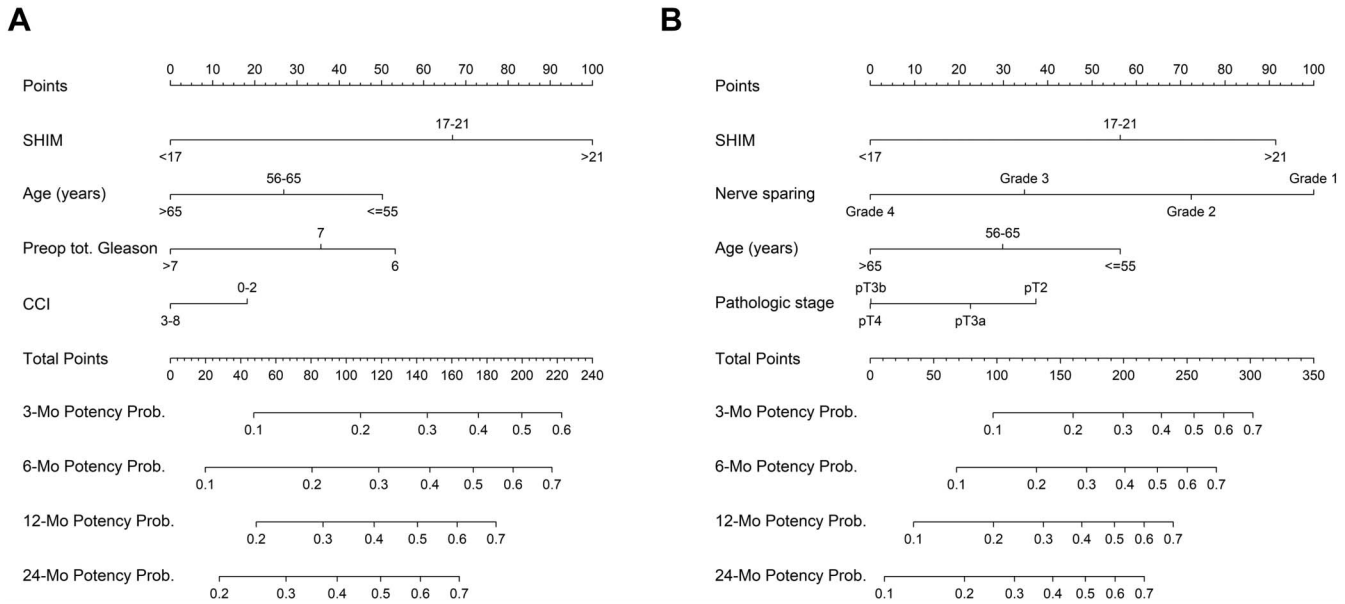

Figure 3. *A*, preoperative nomogram to predict potency at 3, 6, 12 and 24 months following prostatectomy. *B*, postoperative nomogram to predict potency at 3, 6, 12 and 24 months following prostatectomy.

surgery. Our nomograms were constructed using the largest sample size of patients treated with RARP available to date. The preoperative model focused on available variables namely age; SHIM score, GS and CCI, which were selected based on variable importance estimated by survival random forests and then incorporated in a Cox regression model. The most important factors predicting EF outcomes following RARP were preoperative EF followed by age.

The nomogram proposed by Mulhall et al used baseline IIEF, age, and comorbidities.[7] However, the oncologic parameters of the disease were not considered. In comparison, we used the SHIM score and the advantage of using this variable is that it is a validated, easy-to-use questionnaire, and similar to the traditional IIEF in measuring EF.[11,19] Furthermore, our nomogram gives an idea about the probability of EF within 3, 6, 12 and 24 months at the time of preoperative counseling. On internal validation, our model had a very small MAE at different time points, which indicates a satisfactory calibration. Also, the AUCs for the 24-month probability was higher than 12, 6 and 3 months, thus indicating that this nomogram has moderately better ability when predicting EF within 24 months, probably because of the time for neuronal recuperation following surgery.

In the postoperative model, the NS status along with the preoperative SHIM score, age, and pT stage contributed to the prediction of EF. Interestingly, in the postoperative model, the pT stage replaced the preoperative GS. Ideal patients, less than 55 years with SHIM score >21, full NS, pathological stage <pT2, and no comorbidities have a predicted EF of 0.65 within 3 months, 0.7 within 6 months, and more than 0.7 within 12 and 24 months respectively. Furthermore, our nomogram can be useful in providing the patients with the predicted trend within 3, 6, 12 and 24 months, while one waits for his EF. The postoperative model is also well-calibrated and has higher AUCs for 3, 6, 12 and 24 months and EF prediction (0.746, 0.756, 0.777 and 0.801, respectively) compared to their preoperative counterpart (0.726, 0.734, 0.754 and 0.778, respectively), indicating the moderately better predictive ability of the postoperative nomogram compared to the preoperative nomograms. In a clinical setting, one would like to be able to predict the probability of EF outcomes both preoperatively and postoperatively.

When validating the nomograms on a separate data set, the calibration plots showed a moderate overestimation of the probability of EF in both nomograms and the preoperative and postoperative nomograms had acceptable AUCs, close to the AUCs estimated from internal validation. CIF graphs provided in supplementary figure 3 (https://www.jurology.com) show the prediction of the nomograms at different timepoints and for different values of the prognostic index. Higher scores showed an association with a shorter time and a higher probability of EF. This was also true when individual prognostic factors were considered separately.

In summary, the main advantage of our nomograms is that they were built on a large, single surgeon, homogeneous data set, validated on a separate dissimilar data set. Our ability to predict EF outcomes at different time points adds value to

Table 4. *Comparison between the existing nomograms to predict potency following prostatectomy*

	Mulhall et al	Cozzi et al	Current nomogram
No. pts	328	643	Development set (6,502) Validation set (2,706)
Type of procedure	RP	RARP	RARP
No. nomograms	3	1	2
Baseline sexual potency measured	IIEF	EPIC (Questions 8-12)	SHIM score
Time of use	Nomograms to be used in 1. Preop period 2. Early postop period 3. 12 mos following surgery		Nomograms to be used in 1. Preop period 2. Immediate postop
End points	Predicts the probability of IIEF EFD- $\leq$10 at 24 mos and IIEF EFD score $\geq$24 at 24 mos	Predicts the probability of sexual potency at 12 mos as probability of score $>$ 25, 50 or 75 on questions 8-12 of the EPIC questionnaire	Predicts the probability of potency as potency is defined as the ability to penetrate and satisfactorily complete intercourse with or without PDE5 inhibitor usage in more than half the attempts at 3, 6, 12 and 24 mos following surgery
Internal validation	Calibration plot Concordance index 1. Preop period—0.76 2. Early post period—0.78 3. 12 mos following surgery —0.87	Calibration plot Concordance index —0.75 (95% CI: 0.71—0.79).	Calibration plot with MAE Preop nomogram—MAE of 0.024, 0.014, 0.007 and 0.014 at 3, 6, 12 and 24 mos Postop nomogram—MAE of 0.027, 0.022, 0.007 and 0.015 at 3, 6, 12 and 24 mos
External validation	Not performed	Not performed	External validation using a different data set shows acceptable calibration and AUC on ROC curves. (fig. 3, *c* and *d*, and fig. *4*, *c* and *d*)
Comments	Potency measured at 24 mos following RP Single validation used Oncologic parameters not considered	Linear functions were used to exclude missing values Potency measure at 12 mos following RARP Single validation used NS status not considered	Cases with missing values were excluded by listwise deletion Potency measured at different time points after surgery Multiple validation tools used on a large database Used both oncologic and validated NS grading system

IIEF-EFD, IIEF-Erectile Function Domain.

our nomogram, unlike the previously reported nomograms which provide the EF data at either 12 or 24 months after surgery. This time-wise prediction could be used to counsel patients at various time frames during followup and help the patient to understand a realistic timeline of improvement of sexual function. Also, in our nomogram, we used the SHIM score in the preoperative setting and the ability to penetrate and sustain an erection as a practical end point. Traditional IIEF-15 and EPIC questionnaires are long and cumbersome to administer and currently most of the literature uses SHIM score in the preoperative setting and postoperative erection suitable for intercourse in the postoperative setting to categorize patients with ED post-RARP.[13] We developed two nomograms, one to be used in the preoperative period and one in the immediate postoperative period. As recommended by Royston et al, we used several statistical tools for internal and external validation; CIF curves at different levels of the prognostic index and different levels of the single prognostic factors, hazard ratios across risk groups, ROC curves and AUCs, calibration plots[20] while the other 2 used only calibration plots in their validation.[7,8] Finally, our nomogram is simple to use and easy to comprehend. A summary of the comparison between the published nomogram is detailed in table 4.

The limitation of the current study includes the retrospective nature of the data set from a single-center performed by a single surgeon. Also, the compliance of our patients who receive penile rehabilitation therapy may vary, which could potentially lead to a bias. The validation cohort consists of patients with higher risk (representing the current CaP population in daily practice due to more active surveillance in the community) in whom the nomogram moderately overestimates the EF recovery. The limited followup of the validation set is an issue. However, the data set selected at a different time frame helps in temporal validation at different times. The tools used to evaluate EF after RARP may suffer from recall bias. However, these limitations are reflective of a real-world scenario. This study would need further external validation from other centers to confirm the performance of our nomograms.

CONCLUSIONS

The NS technique and preoperative SHIM score seem to have the most influence on postoperative EF. The proposed nomograms are sufficiently accurate in predicting the EF within 3, 6, 12 and 24 months. This is a novel tool for the caregiver to predict realistic

expectations of EF recovery to the patients during preoperative and immediate postoperative counseling. The proposed nomograms should be applied with caution to the population of other centers, at least until preoperative data collection and technique of RARP are standardized. Until then each high volume center around the world should individually develop prediction models applicable to their center.

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