Predicting lymph node invasion in patients treated with robot-assisted radical prostatectomy

Firas Abdollah, MD,[1] Dane E. Klett, MD,[1] Jesse D. Sammon, MD,[1] Deepansh Dalela, MD,[1] Akshay Sood, MD,[1] Linda Hsu, MD,[1] Mireya Diaz, PhD,[1] Nilesh Gupta, MD,[2] James O. Peabody, MD,[1] Quoc-Dien Trinh, MD,[3] Mani Menon, MD[1]

[1]Vattikuti Urology Institute, Center for Outcomes Research Analytics and Evaluation, Henry Ford Health System, Detroit, Michigan, USA

[2]Department of Pathology, Henry Ford Health System, Detroit, Michigan, USA

[3]Division of Urologic Surgery/Center for Surgery and Public Health, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

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Introduction: *To develop a nomogram to predict lymph node invasion (LNI) in the contemporary North American patient treated with robot-assisted radical prostatectomy (RARP).*

Materials and methods: *We included 2,007 patients treated with RARP and pelvic lymph node dissection (PLND) at a single institution between 2008 and 2012. D'Amico low risk patients underwent an obturator and hypogastric PLND, while extended PLND was reserved for intermediate/high risk patients. Logistic regression analysis tested the relationship between LNI and all available predictors. Independent predictors of LNI were used to develop a novel nomogram. Discrimination, calibration and decision-curve analysis were used to analyze the performance of our novel nomogram, and compare it to open radical prostatectomy (ORP)-based models, namely the Godoy nomogram.*

Results: *Overall, 5.3% of our patients harbored LNI. Median number of lymph nodes removed was 6.0 (interquartile range: 4-11). The most parsimonious multivariable model to predict LNI consisted of the following independent predictors: PSA value, clinical stage, and primary and secondary Gleason scores (all $p \leq 0.02$). The discrimination of our novel model was 86.2%, and its calibration was virtually optimal. Using a 2% nomogram cut off, 58% of patients would be spared PLND, while missing only 9.4% of individuals with LNI. The novel nomogram compared favorably to the Godoy nomogram, when discrimination, calibration and net-benefit were used as benchmarks.*

Conclusions: *Approximately 5% of contemporary North American patients harbor LNI at RARP. Our novel nomogram can accurately identify these patients, and this may help to improve patient selection, and avoid unnecessary PLND in the majority of patients.*

Key Words: prostate cancer, radical prostatectomy, robotics, lymph node invasion, pelvic lymph node dissection, nomogram

Introduction

Radical prostatectomy (RP) is one of the most commonly used treatment modalities for prostate cancer patients with localized disease and ≥ 10 years of life expectancy.[1-3] The importance of performing an extended pelvic lymph node dissection (PLND) during RP is a subject of continuous debate. On one hand, extended PLND is the most accurate lymph node staging procedure, outperforming any available preoperative imaging procedure.[4] In addition, extended PLND might offer survival benefit in patients with lymph node invasion (LNI).[5-7] On the other hand, extended PLND is associated with an increased risk of postoperative morbidities including lymphoceles, lymphedema, and deep venous thrombosis.[8,9]

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Address correspondence to Dr. Firas Abdollah, Vattikuti Urology Institute, Center for Outcomes Research Analytics and Evaluation, Henry Ford Health System, 2799 West Grand Boulevard, Detroit, MI 48202, USA

Given this clinical dilemma, several previous reports focused on developing preoperative tools to predict the presence of LNI at the time of surgery.[4,10] Many of these tools,[11-13] however, were based on the outcomes of limited PLND, which is hampered by its low sensitivity to detect LNI.[14,15] The few, preoperative LNI prediction tools that were based on the outcomes of extended PLND mostly originated from open RP (ORP) data and/or from non-North American patient data.[16-19] Therefore, the applicability of these prediction tools in contemporary North American patients might be limited. This stems from two main reasons: first, most contemporary North American patients are treated with robot-assisted RP (RARP), which differs in many technical aspects from ORP.[20] For example, robotic PLND samples more frequently the internal iliac nodes, which might translate into a higher LNI yield.[21] Second, there might be differences in biological characteristics and host-tumor interaction between North American versus non-North American patients.[22,23] For example, Briganti et al reported that European men have a nine-fold higher LNI risk than their North American counterparts, even after adjusting for potential confounders.[24] To address these limitations, we set to develop and internally validate the first nomogram to predict the likelihood of LNI in North American patients exclusively treated with RARP and PLND. Moreover, we compared the performance of our novel tool to the Godoy et al[18] nomogram, which represents the only available contemporary North American nomogram based on standard (not limited) PLND data.

Materials and methods

Patient population

We examined data of 2,014 prostate cancer patients treated with RARP and PLND at Henry Ford Health System, between 2008 and 2012. Of these, 7 patients were excluded because of incomplete clinical and/or pathological information. This yielded 2,007 assessable patients. The surgical procedure performed in these patients was previously described by Menon et al.[21,25] Robotic PLND was performed in all patients. The anatomical extent of the PLND, however, varied based on the clinical characteristics of each patient. Specifically, patients with D'Amico low risk prostate cancer underwent a "modified" limited PLND.[21] This consisted of tissue removal inferior to the obturator nerve and along the lateral pelvic wall in order to clear the obturator fossa. Nodal tissue from the obturator fossa to the lateral surface of the bladder was also removed. Alternatively, in patients with D'Amico intermediate/high risk prostate cancer, an anatomically extended PLND was performed. This included nodes along the external iliac, obturator, and internal iliac, as previously described.[21,25] Two dedicated uropathologists examined all PLND specimens for the presence of LNI. Specimens underwent standard 10% formalin processing, and nodes were assessed macroscopically by visual and tactile criteria. The number of positive lymph nodes, size of the largest node and their gross appearance was described for each anatomic nodal group. All soft tissue in the lymph node packet was submitted for microscopic evaluation to be assessed for non-palpable, microscopic lymph nodes. Clearing solution was not used for pelvic lymph nodes. All blocks underwent paraffin embedding, 3 µm sectioning and hematoxylin-eosin staining. Immunohistochemical staining was performed for selected cases. No patient received neoadjuvant androgen deprivation therapy.

Patient data included age at surgery (years), body mass index (kg/m^2), serum PSA level (ng/mL), clinical stage, primary/secondary biopsy Gleason score (GS), maximum percentage of tumor (MPT) on biopsy cores, D'Amico tumor risk stratification, number of removed lymph nodes (LNs), and year of surgery.

Statistical analysis

Descriptive statistics of categorical variables focused on frequencies and proportions. Medians, and interquartiles ranges (IQR) were reported for continuously coded variables. Mann–Whitney and chi square tests were used to compare the statistical significance of differences in medians and proportions, respectively.

Our analyses consisted of several steps. First, univariable and multivariable (MVA) logistic regression analysis tested the relationship between LNI and the following covariates: PSA level, clinical stage, primary and secondary biopsy Gleason grade, with or without MPT (full versus reduced model, respectively). Regression coefficients were used to develop a nomogram predicting LNI probability at RARP. Bootstrapping was performed using 200 resamples to reduce overfit bias and internally validate our model. Bootstrap corrected area under curve (AUC) was used to compare the full model (with MPT) to the reduced model (without MPT). Mantel-Haenszel test was used to determine the statistical significance of differences in AUC. A calibration plot assessed concordance between the predicted and the actual probability of LNI, thereby assessing the degree of over- or under-estimation of the novel model. Further, decision-curve analysis (DCA), as described by Vickers et al[26] was used to calculate the net-benefit of the novel models.

Second, sensitivity, specificity, and negative and positive predictive values were calculated for each

nomogram cut off from 1% to 10% (with increments of 0.5%). Third, the Godoy et al[18] nomogram was externally validated in our cohort, and its performance was compared to our novel model based on discrimination (AUC), calibration, and DCA.

Lastly, a nomogram consisting exclusively of intermediate and high risk patients was constructed using the methods noted above. Overall, 1,069 intermediate risk and 336 high risk patients were included and all low risk patients were excluded.

TABLE 1. **Descriptive characteristics of 2,007 patients undergoing robot-assisted radical prostatectomy with pelvic lymph node dissection at a single North American tertiary care institution between 2008 and 2012.**

Characteristic	Overall (%) (n = 2,007, 100%)	pN0 (%) (n = 1,901; 94.7%)	pN1 (%) (n = 106; 5.3%)	p value
Age, year				0.1
Mean (median)	60.4 (61)	60.4 (61)	61.6 (62)	
IQR	55-66	55-66	56-68	
BMI, kg/m^2				0.4
Mean (median)	28.3 (28)	28.3 (28)	28.6 (28)	
Range	25-30.2	25-31	26-30	
PSA, ng/mL				< 0.001
Mean (median)	6.3 (5.1)	6.1 (5)	9.8 (7.2)	
IQR	4-7.1	4-6.9	5-12.9	
MPT on biopsy				< 0.001
Mean (median)	41.3 (40)	40.2 (35)	62 (70)	
IQR	10-70	10-68	30-90	
Clinical stage (%)				< 0.001
T1c	1555 (77.5)	1500 (78.9)	55 (51.9)	
T2a-b	364 (18.1)	332 (17.5)	32 (30.2)	
≥ T2c	88 (4.4)	69 (3.6)	19 (17.9)	
Primary GS (%)				< 0.001
3	1506 (75)	1480 (77.9)	26 (24.5)	
4	479 (23.9)	409 (21.5)	70 (66)	
5	22 (1.1)	12 (0.6)	10 (9.4)	
Secondary GS (%)				< 0.001
3	1009 (50.3)	979 (51.5)	30 (28.3)	
4	912 (45.4)	863 (45.4)	49 (46.2)	
5	86 (4.3)	59 (3.1)	27 (25.5)	
D'Amico risk stratification				< 0.001
Low risk	602 (30.0)	600 (31.6)	2 (1.9)	
Intermediate risk	1069 (53.3)	1027 (54.0)	42 (39.6)	
High risk	336 (16.7)	274 (14.4)	62 (58.5)	
Number of removed nodes				<0.001
Mean (median)	7.6 (6.0)	7.3 (6.0)	13.4 (12.0)	
IQR	4.0-11.0	4.0-11.0	8.8-18.0	
Year of surgery				0.3
2008	499 (24.9)	478 (25.1)	21 (19.8)	
2009	470 (23.4)	444 (23.4)	26 (24.5)	
2010	456 (22.7)	425 (22.4)	31 (29.2)	
2011	447 (22.3)	423 (22.3)	24 (22.6)	
2012	135 (6.7)	131 (6.9)	4 (3.8)	

IQR = interquartile range; BMI = body mass index; PSA = prostate-specific antigen; MPT = maximum percentage of tumor; GS = Gleason score

All statistical analyses were performed using R statistical package (R Foundation for Statistical Computing, Vienna, Austria). All probability tests were two-sided, with significance level set at $p < 0.05$.

Results

Descriptive characteristics of 2,007 patients are reported in Table 1. Median age and PSA level were 60.4 years (IQR: 55.0-66.0), and 6.3 ng/mL (IQR: 4.0-7.1), respectively. The majority of patients harbored clinical T1c disease (77.5%), a primary GS of 3 (75%), a secondary GS of 3 (50%) and an intermediate risk prostate cancer (53.3%). Overall, 106 (5.3%) patients had pathologically confirmed LNI. Patients with LNI had a significantly higher PSA level (median: 7.2 ng/mL versus 5 ng/ml), clinical stage (≥ T2c: 17.9% versus 3.6%), primary GS (grade 5: 9.4% versus 0.6%), secondary GS (grade 5:25.5% versus 3.1%), and MPT (median: 70% versus 35%) compared to patients without LNI (all $p < 0.001$).

At multivariable analysis, PSA level (odds ratio [OR]: 1.07), clinical stage ≥ T2c (OR: 1.95), primary GS (grade 4 OR: 6.80, grade 5 OR: 20.68), secondary GS (grade 4 OR: 2.25, grade 5 OR: 3.96), and MPT (OR: 1.01) were all independent predictors of LNI (all $p < 0.04$, Table 2). The discrimination (AUC) of this full model was 86.6% versus 86.2% for the reduced model ($p = 0.1$). The latter did not include MPT, and was used to develop a novel nomogram, Figure 1a. The calibration of this nomogram was very favorable, Figure 1b.

The performance characteristics of the nomogram-derived cut offs from 1%-10% are shown in Table 3. In our cohort, 1,106 (55.1%) of our patients had a nomogram-calculated probability of less than 2% and could have been spared an extended PLND, at the cost of missing 10 patients with LNI (9.4% of all patients with histologically confirmed LNI).

In our cohort, the discrimination of the Godoy nomogram was 70.3%, and its calibration characteristics were unfavorable, Figure 2. In DCA, the net-benefits of the full and reduced models were overlapping, and both were superior to the Godoy nomogram up to a threshold probability of 60%, where all model net-benefits become equal, Figure 3.

Finally, the intermediate/high-risk nomogram had 80.0% discrimination and very favorable calibration, Figure 4.

TABLE 2. **Univariable and multivariable logistic regression analyses predicting the presence of lymph node invasion in 2,007 patients treated with robot-assisted radical prostatectomy and pelvic lymph node dissection at a single North American tertiary care institution between 2008 and 2012.**

Covariates	Univariate analysis		Multivariate analysis			
			Full model		Reduced model	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Preoperative PSA level, ng/mL	1.1 (1.07-1.13)	< 0.001	1.07 (1.03-1.1)	< 0.001	1.07 (1.04-1.11)	< 0.001
Clinical stage						
T1	[REF]	-	[REF]	-	[REF]	-
T2a-b	2.63 (1.67-4.13)	< 0.001	1.18 (0.71-1.95)	0.5	1.25 (0.76-2.06)	0.3
≥ T2c	7.51 (4.23-13.34)	< 0.001	1.95 (1.06-3.96)	0.04	2.3 (1.15-4.6)	0.02
Primary GS						
3	[REF]	-	[REF]	-	[REF]	-
4	9.74 (6.13-15.48)	< 0.001	6.80 (4.03-11.48)	< 0.001	7.33 (4.37-12.28)	< 0.001
5	47.44 (18.82-119.56)	< 0.001	20.68 (7.38-57.93)	< 0.001	24.02 (8.76-65.87)	< 0.001
Secondary GS						
3	[REF]	-	[REF]	-	[REF]	-
4	1.85 (1.17-2.95)	< 0.001	2.25 (1.35-3.74)	0.002	2.27 (1.37-3.73)	0.001
5	14.93 (8.34-26.74)	0.009	3.96 (2.09-7.52)	< 0.001	4.1 (2.16-7.78)	< 0.001
MPT on biopsy	1.02 (1.02-1.03)	< 0.001	1.01 (1.00-1.02)	0.006	---	---

CI = confidence interval; PSA = prostate-specific antigen; GS = Gleason score; MPT = maximum tumor percentage

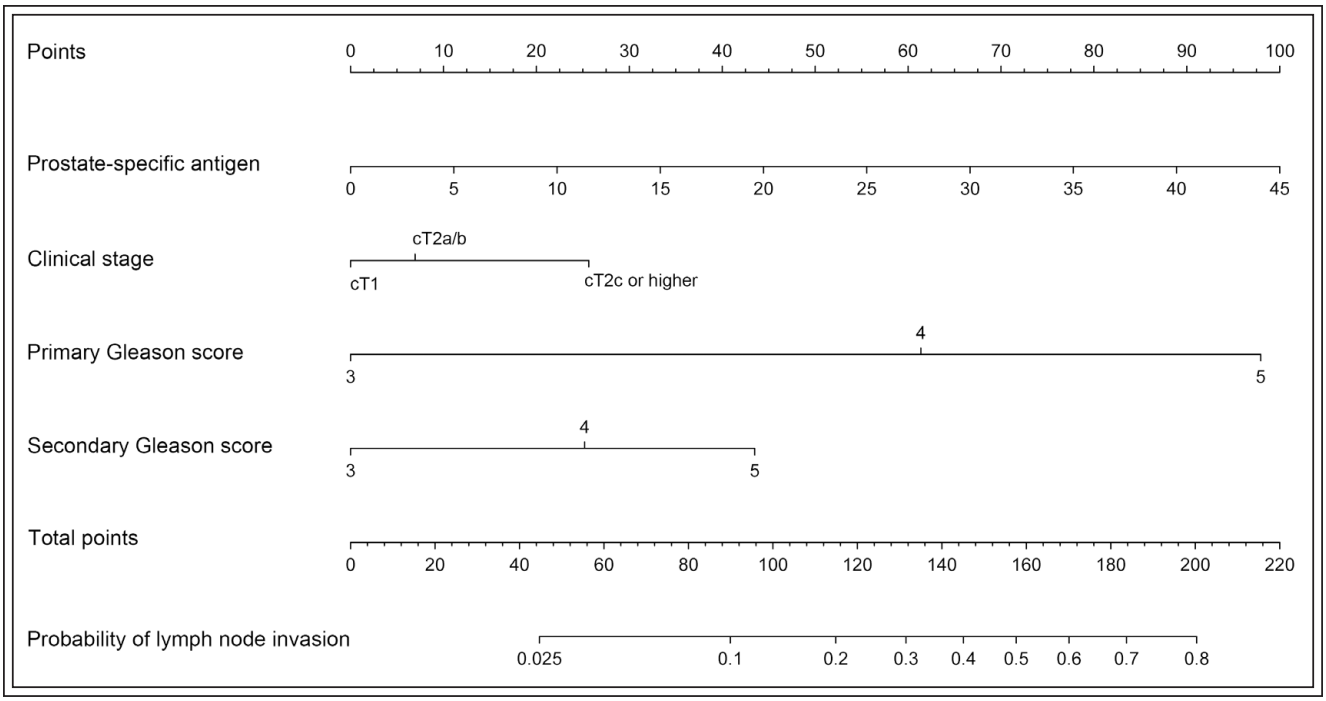

Figure 1a. Nomogram predicting the probability of lymph node invasion (LNI) in patients undergoing robot-assisted radical prostatectomy with pelvic lymph node dissection based on preoperative serum prostate-specific antigen (PSA) level, clinical stage, primary Gleason score and secondary Gleason score.
Instructions: The patient's preoperative PSA is marked on the PSA axis. From this point, a line is drawn straight upward to the point axis to determine how many points are contributed by his PSA towards the probability of LNI. This step is repeated for each additional variable. Points from all the predictors are summed, plotted on the "total points" axis, and a perpendicular drawn from this point downwards to determine the final probability of LNI in the patient.

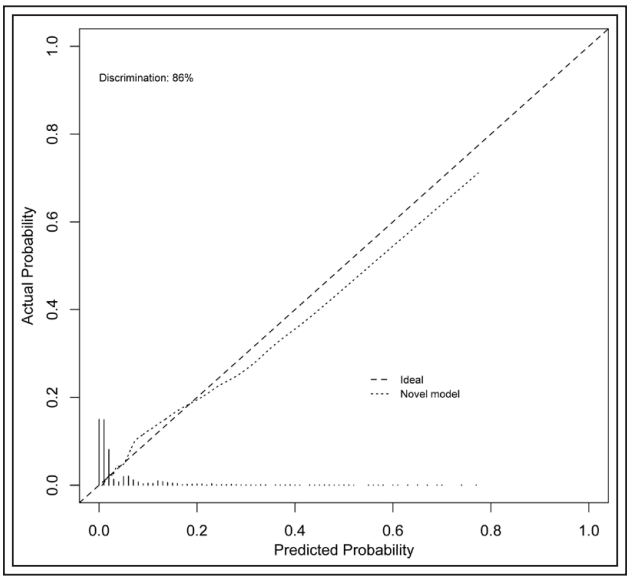

Figure 1b. Nomogram calibration plot. The broken line indicates location of the ideal nomogram, in which predicted and actual probabilities are identical. Dotted line indicates the performance of our novel nomogram.

Discussion

The role of PLND as a staging procedure in patients with prostate cancer has been widely established.[4] In addition, several reports indicate PLND might also have a therapeutic impact in these individuals.[5-7] However, surgeons may be reluctant to perform an anatomically extended PLND during surgery, because it is time consuming and may lead to higher postoperative morbidity.[8,9] This holds true in the current RARP-era, where less patients are treated with PLND.[27,28] For these reasons, many previous reports have focused on the development of preoperative tools to identify ideal candidates for PLND.[10,11,16-19] Since these data originated mostly from non-North American patients undergoing ORP with limited PLND, the validity and generalizability of these models to contemporary North American patients frequently treated with RARP may be suboptimal. To address this issue, we set to develop a new LNI-predicting nomogram, based on contemporary North American RARP patients, and we compared its performance to a previously published

TABLE 3. **Nomogram derived cut offs probabilities and their performance in discriminating between patients with and without histopathologically confirmed lymph node invasion.**

Nomogram calculated probability of LNI (threshold, %)	Patients in whom PLND is not recommended according to the threshold (below threshold)	Patients below threshold without histological LNI**	Patients below threshold with histological LNI#	Patients in whom PLND is recommended according to the threshold (above thresfold)
> 1	554 (27.6)	552 (29.0)	2 (1.9)	1453 (72.4)
> 1.5	699 (34.8)	696 (36.6)	3 (2.8)	1308 (65.2)
> 2	1106 (55.1)	1096 (57.7)	10 (9.4)	901 (44.9)
> 2.5	1333 (66.4)	1316 (69.2)	17 (16.0)	674 (33.6)
> 3	1406 (70.1)	1387 (73.0)	19 (17.9)	601 (29.9)
> 3.5	1438 (71.6)	1419 (74.6)	19 (17.9)	569 (28.4)
> 4	1455 (72.5)	1436 (75.5)	19 (17.9)	552 (27.5)
> 4.5	1469 (73.2)	1449 (76.2)	20 (18.9)	538 (26.8)
> 5	1482 (73.8)	1460 (76.8)	22 (20.8)	525 (26.2)
> 5.5	1508 (75.1)	1484 (78.1)	24 (22.6)	499 (24.9)
> 6	1555 (77.5)	1530 (80.5)	25 (23.6)	452 (22.5)
> 6.5	1591 (79.3)	1563 (82.2)	28 (26.4)	416 (20.7)
> 7	1631 (81.3)	1601 (84.2)	30 (28.3)	376 (18.7)
> 7.5	1665 (83.0)	1635 (86.0)	30 (28.3)	342 (17.0)
> 8	1676 (83.5)	1644 (86.5)	32 (30.2)	331 (16.5)
> 8.5	1691 (84.3)	1656 (87.1)	35 (33.0)	316 (15.7)
> 9	1702 (84.8)	1665 (87.6)	37 (34.9)	305 (15.2)
> 9.5	1709 (85.2)	1669 (87.8)	40 (37.7)	298 (14.8)
> 10	1714 (85.4)	1674 (88.1)	40 (37.7)	293 (14.6)
Nomogram calculated probability of LNI (threshold, %)	**Patients above threshold without histological LNI^**	**Patients above threshold with histological LNI$**	**Positive predictive value**	**Negative predictive value**
> 1	1349 (71.0)	104 (98.1)	7.2	99.6
> 1.5	1205 (63.4)	103 (97.2)	7.9	99.6
> 2	805 (42.3)	96 (90.6)	10.7	99.1
> 2.5	585 (30.8)	89 (84.0)	13.2	98.7
> 3	514 (27.0)	87 (82.1)	14.5	98.6
> 3.5	482 (25.4)	87 (82.1)	15.3	98.7
> 4	465 (24.5)	87 (82.1)	15.8	98.7
> 4.5	452 (23.8)	86 (81.1)	16.0	98.6
> 5	441 (23.2)	84 (79.2)	16.0	98.5
> 5.5	417 (21.9)	82 (77.4)	16.4	98.4
> 6	371 (19.5)	81 (76.4)	17.9	98.4
> 6.5	338 (17.8)	78 (73.6)	18.8	98.2
> 7	300 (15.8)	76 (71.7)	20.2	98.2
> 7.5	266 (14.0)	76 (71.7)	22.2	98.2
> 8	257 (13.5)	74 (69.8)	22.4	98.1
> 8.5	245 (12.9)	71 (67.0)	22.5	97.9
> 9	236 (12.4)	69 (65.1)	22.6	97.8
> 9.5	232 (12.2)	66 (62.3)	22.1	97.7
> 10	227 (11.9)	66 (62.3)	22.5	97.7

LNI = lymph node invasion; PLND = pelvic lymph node dissection; **percentage is indicative of specificity; #percentage is indicative of 1-senstivity; ^percentage is indicative of 1-specificity; $percentage is indicative of sensitivity

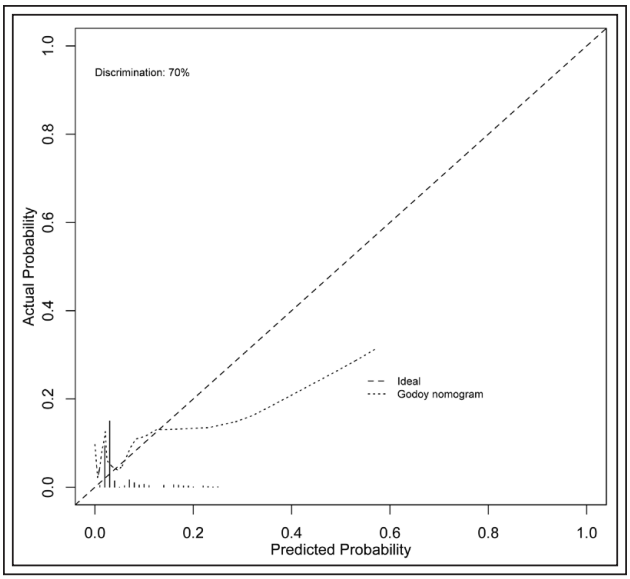

Figure 2. Godoy's nomogram calibration plot. The broken line indicates location of the ideal nomogram, in which predicted and actual probabilities are identical. Dotted line indicates the performance of Godoy nomogram in external validation setting.

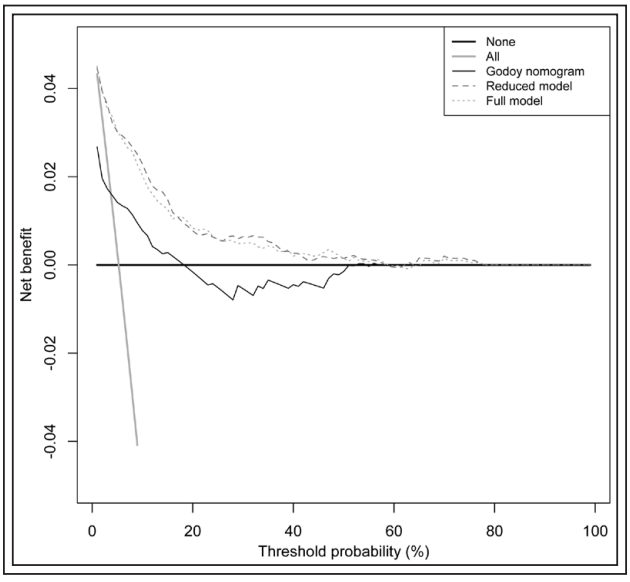

Figure 3. Decision-curve analysis demonstrating the net-benefit associated with the use of the novel nomogram with and without the use of maximum percentage of tumor on biopsy (green line, full model versus red line, reduced model, respectively), compared to the Godoy nomogram (black line). Net-benefit can be estimated as the proportion of all patients who have lymph node invasion and are recommended for lymph node dissection, if no patients with negative lymph nodes were treated.

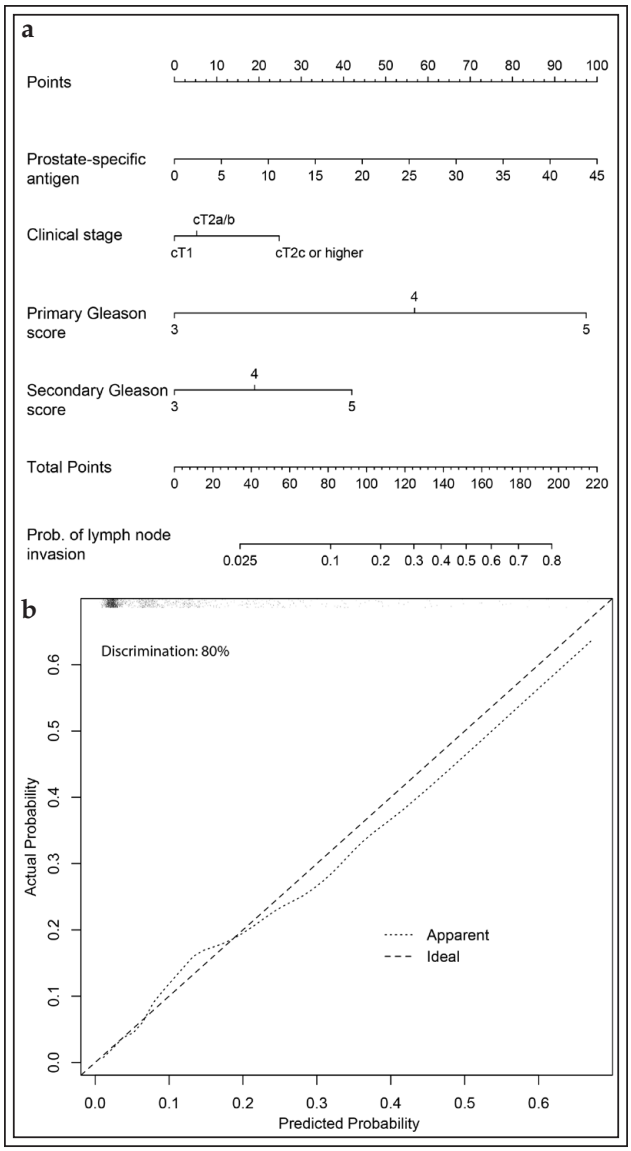

Figure 4. a) Nomogram calibration plot. The broken line indicates location of the ideal nomogram, in which predicted and actual probabilities are identical. Dotted line indicates the performance of this nomogram and includes only intermediate and high risk patients. **b)** Nomogram predicting the probability of lymph node invasion in intermediate and high risk patients undergoing robot-assisted radical prostatectomy with pelvic lymph node dissection based on preoperative serum PSA level, clinical stage, primary and secondary Gleason scores.

model: the Godoy nomogram.[18] We chose to compare our PLND nomogram to the Godoy nomogram for one very important reason: the data used to formulate the Godoy nomogram was based on contemporary North American patients, and as such, is considered

to be most similar to our North American patient population. The Briganti nomogram was not selected for comparison as it is based entirely on European patients. European patients have significantly different tumor characteristics and lymph node invasion rates.[24] In addition, stage and grade migration affected North American and European populations to different extents and significant differences may exist between these two populations.[29]

Several important findings of our study deserve mention. First, we found that 5% of our patients had LNI. This rate was virtually the same as a previous report,[18] which focused on North American patients treated mainly with ORP and standard (not limited) PLND. The number of nodes removed in our cohort, however, was lower than the ORP series (median: 6 nodes versus 11 nodes). This might seem contradictory to the well-established knowledge that a higher LN count is associated with more accurate nodal staging.[3,14,30] This apparent paradox may be due to several reasons. For example, it is possible that internal iliac nodes are better sampled with RARP as compared to ORP, which may translate into more accurate LN staging, despite a lower LN count.[21] Likewise, differences in pathological handling of the PLND specimen can artificially alter LN count, without affecting LN staging accuracy. Regardless of the exact cause of this paradox, our LNI rate was comparable to that reported by high-quality ORP[18] and RARP[31] data, implying that our PLND was adequate and that our LNI rate was not compromised by omitting extended PLND in low risk prostate cancer patients.

Second, based on our reduced MVA model, we developed a novel nomogram to preoperatively predict LNI. This nomogram showed very favorable discrimination (86%) and calibration characteristics. Based on our analyses, MPT on biopsy was an independent predictor of LNI. This variable did not, however, improve the overall accuracy of the MVA model. In light of these observations, and the fact that MPT is not always available in clinical practice, we opted to exclude this variable from our nomogram. Similar results were observed by Kim et al who found that MPT did not improve the rate of LNI prediction in Asian patients.[19]

Third, when examining the performance characteristics of nomogram generated cut offs, we found that the use of 2% as the cut off to perform PLND would allow avoidance of PLND in about 58% of patients at the cost of missing only 9% of patients with LNI. This trade-off was recommended by the National Comprehensive Cancer Network guidelines, when deciding the necessity of performing a PLND.[1,32] It might not, however, be acceptable to all physicians, who may want to choose their own cut off based on their patient's clinical characteristics and preferences. In such a case, our findings, Table 3 may be of a great value in addressing the performance characteristics of the selected cut off.

In the final part of our analyses, we compared the performance of our novel nomogram to the Godoy et al nomogram. We chose the Godoy nomogram because it represents the only available contemporary LNI-prediction nomogram based on data originating from North American patients treated mainly with ORP and standard (not limited) PLND. In our cohort, we found that the predictive accuracy of the Godoy nomogram was significantly lower than our novel nomogram. This denotes that nomograms based on ORP data might not be applicable to patients undergoing RARP. It must be mentioned, however, that the performance of the Godoy nomogram was tested in an external validation setting, and compared to the performance of our novel nomogram, which was tested in internal validation setting. This may artificially favor the performance of our novel nomogram. This issue warrants further investigation in future studies, where ideally both nomograms should be compared head-to-head in an external validation setting.

Taken together, our novel nomogram represents the first LNI-prediction model to date based exclusively on North American RARP patient data. The performance of this model was very favorable and superior to previous models based mainly on ORP data. In clinical practice, the use of this tool may be helpful in selecting optimal candidates for PLND.

Our study is not devoid of limitations. First, because variations across data sets can affect the accuracy of any predictive model, the internal validation results obtained in this report should be validated in an external setting, ideally in multi-institutional and prospective cohorts. Therefore, prior to suggesting its use in the everyday clinical practice, a formal external validation of our novel nomogram is warranted. Second, in our study the anatomical extent of PLND was not equal for all patients, and it varied based on tumor characteristics. In this context, most low risk patients did not receive an anatomically extended PLND, which may have compromised their LNI detection accuracy. Given the very low risk of LNI in these patients, however, it might be argued that the number of patients with undetected LNI is minimal. Indeed, our overall LNI rate was identical to previous reports, which originated from high quality PLND data.[18,31] This implies that the overall extent of PLND in our cohort was adequate. It should also

be noted that our rate of PLND in low risk patients is consistent with current trends.[28] Third, the median number of LN removed was 6. This is consistent with the number of LN removed in other RARP series as well as other U.S. RARP data.[28,31] More importantly, it should be noted that our overall rate of LNI is nearly identical to previous reports.[18,31] This implies that the overall extent of PLND in our cohort was probably adequate. Potential explanations for the relatively low number of LN removed include changes in surgical technique, surgeon preference, how LN are sent for pathologic review (i.e. in packets versus en bloc), and/or how LN are counted by pathologists at the time of review. Regardless of cause, this limitation should be considered when interpreting our results. Fourth, a pathological review of all specimens was not performed. This limitation is shared with virtually all-previous observational data focusing on a similar endpoint. Since we focused on a relatively contemporary period (2008-2012) during which there were no substantial changes in the pathological protocols used to examine RP and PLND specimens, the impact of this limitation on our cohort is considered minimal.

Conclusions

We report the first, internally validated nomogram to predict LNI in a contemporary North American patient treated with RARP and PLND. This model is based on routinely available clinical and pathological characteristics, which include PSA value, clinical stage, and Gleason grade on biopsy. The accuracy of the novel model was high (AUC: 86%), and it outperformed previous model based on ORP data. Using a 2% nomogram cut off can spare PLND in the majority of patients, while missing only a minority of patients with LNI. □

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