TITLE: A novel tool to predict functional outcomes after RARP and the value of additional surgery for incontinence

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ABSTRACT

Objectives: To develop and validate a model to predict 12-month continence status after robot assisted radical prostatectomy (RARP) from preoperative and 3-month postoperative data; this model could help in informing patients on their individualized risk of urinary incontinence (UI) after radical prostatectomy in order to choose the best treatment option.

Materials and methods: Data on 9421 patients in 25 Belgian centers were prospectively collected (2009-2016) in a compulsory regional database. The primary outcome was the prediction of continence status, using the International Consultation on Incontinence Urinary Incontinence Short Form (ICIQ-UI-SF) at 12-months after RARP. Linear regression shrinkage was used to assess the association between preoperative, 3- month post-operative characteristics, and 12-month continence status. This association was visualized using nomograms and an online tool.

Results: At 12 months the average value of ICIQ-UI questionnaire was 4.3 (SD: 4.7), 3- fold higher than the mean pre-op value (1.4). For the preoperative model, high EAU risk classification for biochemical recurrence (Est 0.606 (SE 0.165)), post-operative radiotherapy (Est 1.563 (SE 0.641)), lower preoperative EORCT QLQ-C30/QoL (Est -0.011 (SE 0.003)), higher preoperative ICIQ-UI-SF (Est 0.214 (SE 0.018)) and higher age (Est 0.058 (SE 0.009)) were associated with a higher 12-month ICIQ-UI-SF. For the 3-months model, higher preoperative ICIQ-UI-SF (Est

0.083 (SE 0.014)), higher age (Est 0.024 (SE 0.007)), lower 3-month EORCT QLQ-C30/QoL (Est -0.010 (SE 0.002)) and higher 3-month ICIQ-UI-SF (Est 0.562 (SE 0.009)) were associated with higher 12-month ICIQ-UI-SF.

Conclusions: Our models set the stage for a more accurate counselling of patients. In particular our pre-operative model assesses the risk of UI according to preoperative and early post-operative variables. Our post-operative model can identify patients who most likely would not benefit from a conservative treatment and should be counselled on continence surgery.

INTRODUCTION

Urinary incontinence (UI) represents a significant side effect for patients treated with radical prostatectomy (RP), affecting their quality of life (QoL) [1]. The overall rate of bothersome UI remains approximately 15% in contemporary series. However, for a correct evaluation of continence results after surgery, the definitions of UI, ideally, should be identical among studies, but this is not the case. Haglind et al suggest that the appropriate definition of urinary incontinence from the patient's perspective should be not pad-free and not leakage free [2]. After robot assisted RP (RARP), incontinence ranges from 4% to 30% [3]. Patient counselling is the first step to achieve the best treatment option in a specific case in a patient-centred setting. Informing patients and selecting the most suitable primary treatment according to a specific patient profile appears crucial. In an era where prospective randomized evidence supports comparable efficacy of radiotherapy (RT) and RP on cancer outcomes [4], higher risk of UI may prompt patients to opt for radiotherapy. Continence outcome depends on many factors, including patients' anatomy, preoperative patient characteristics, surgeon experience, surgical technique, continence definitions, data collection and follow-up intervals [2,4]. Pre-treatment predictive models based on large real-life datasets are essential to create realistic expectations.

It has been estimated that 3% to 6% of patients remaining incontinent after RP are willing to undergo surgery for incontinence [6–8]. However, there is no published guidance on indications for surgical treatment or on its timing. Therefore, a clear assessment of the risk of incontinence based on pre-, intra- and early post-operative characteristics, can lead to a better and earlier counselling for continence surgery.

The aim of this prognostic multivariable modelling study is twofold. First, to develop and validate a model to predict 12-month continence status after RARP from preoperative patient-level information in a real-life setting, with data extracted from a national database of centres performing RARP surgery. Second, to develop and validate a model to predict 12-month continence status from preoperative as well as 3-month postoperative patient-level information. These findings are used to create a nomogram and an online tool that can be used by the practicing clinician to assess the risk of the patient and to individualize treatment.

MATERIAL AND METHODS

Data and participants

In October 2009, a total of 25 centres (academic, public non-academic, and private hospitals) performing RARP in Belgium, registered at the Belgian Cancer Registry and the National Institute for Health and Disability Insurance, submitted clinical, pathological, and follow-up data for consecutive patients undergoing robotic prostatectomy. Data registration was mandatory to receive reimbursement for the use of robotic disposables during RARP. The data were electronically encoded in a prospective manner. The data gathering was continued for 6 years and was closed on February 29, 2016 [9].

The Belgian Cancer Registry was responsible for storing the data [9] and all analyses were performed at their premises via a connection to a secured server.

Outcome

Our interest was to predict scores for the International Consultation on Incontinence Urinary Incontinence Short Form (ICIQ-UI-SF) at 12 months after RARP.

To predict urinary status, we used the ICIQ-UI-SF. This questionnaire consists of four questions of which three generate scores of 0-5, 0-6, and 0-10 points, respectively. This produces a total score ranging from 0 to 21 points with a higher score indicating a greater severity of UI. The fourth question evaluates the UI status on a 7-point scale [10,11]. The questionnaires were administered by the treating team to the patients, who completed them at baseline, 1-month, 3-month, 12-month and 24-month after prostate surgery.

Predictors

Multiple candidate predictors for UI were considered based on literature reviews, clinical evidence and expert opinion within the confines of data availability from the RARP project [12–18]. For the first objective, preoperatively available candidate predictors included patient age, previous urological condition, hormonal therapy (HT), RT, EAU prostate cancer risk classification for biochemical recurrence (BCR) [19] preoperative European Organization for Research and Treatment for Cancer Quality of Life Questionnaire global health status / QoL score (EORTC QLQ-

C30/QoL), and preoperative ICIQ-UI-SF. Previous urological conditions or treatments included any condition or treatment that could influence urinary tract function (e.g. TURP, urethral stricture, urinary stones, recurrent urinary tract infection) before RARP. For the second research objective, following additional postoperative candidate predictors were included: nerve sparing surgery (NS), lymphadenectomy (LND), intraoperative complications, postoperative morbidity, resection margin, 3-months EORTC QLQ-C30/QoL, and 3-month ICIQ-UI-SF. In addition, we included information on RALP surgery volume. For each patient it was known whether the surgery took place in a hospital with an average yearly volume of <50, 50-100 or >100. Age, EORTC QLQ-C30/QoL and ICIQ-UI-SF were evaluated as continuous variables. Intraoperative complications included: bleeding, intestinal perforation, rectal injury, bladder injury, ureteral injury, nerve injury, conversion to open surgery. Post-operative morbidity included: bleeding, urinary leakage, prolonged lymphorrhea, ureteral obstruction, nerve injury/neuropraxia, compartment syndrome, rhabdomyolysis, oliguria/anuria, reintervention, deep venous thrombosis. In EORTC QLQ-C30/QoL, a larger value reflects a better functional outcome. The study sample size (see results section) largely exceeded the suggested requirement of at least 10 events per candidate variable for model building and at least 100 events for model validation [20].

Statistical analysis

First, descriptive data for urinary incontinence were attained. Means and standard deviations are reported for the ICIQ-UI-SF over time (pre-operative, and at 1, 3, 6 and 12 months postoperative). Candidate categorical predictor variables were cross-tabulated with 12-month ICIQ-UI-SF, i.e. the primary outcome. Continuous predictors were reorganized into quantiles for this descriptive analysis only. This provided information on linearity of the effect.

Second, model building and evaluation was performed identically for the two research questions. Our approach was conducted and is reported in line with the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) statement [20]. The data were non-randomly split by the first and second half of registration dates into a development and validation data set to allow for non-random variation in these sets. [20]. We conducted complete case

analysis. As a prediction selector strategy we opted for Least Absolute Shrinkage and Selection Operator (LASSO) [21] in conjunction with data partitioning to simultaneously process development and validation data and conduct cross validation. Optimal combination of model parameters was based on Mallows' CP, with a value close to the number of predictors indicating a relatively unbiased model in estimating the true regression coefficients and predicting future responses. Regular multivariable linear regression analyses were conducted to obtain parameter estimates with confidence intervals for the predictors suggested by LASSO regression.

Calibration plots were used to compare predicted 12-month ICIQ-UI-SF with actual ICIQ-UI-SF. We applied the training data equation and parameter estimates to the validation data. We then constructed a classic nomogram for each research objective, accompanied by online prediction tools.

The descriptive findings and model building and validation strategy for this paper were generated using SAS software. The nomogram and online tool were constructed in R [22] and R Shiny [23].

RESULTS

Patient characteristics

There were 9421 patients from 25 centres diagnosed with PCa and treated with RARP. Full set of outcomes and candidate predictors was available for 5193 (55.1%) patients. Preoperative, 1-month, 3-month, 12-month and 24-month ICIQ-UI-SF were recorded for 9364, 8841, 8509, 8030 and 7219 patients, respectively. There was about a five-fold increase between the average preoperative ICIQ-UI-SF score (1.4 (SD 3.3)) and the 1-month ICIQ-UI-SF (9.4 (SD 5.7)) (Table 1). This score steadily decreased at 3 (6.4 (SD 5.3)), 12 (4.3 (SD 4.7)) and 24 (3.8 (SD 4.4)) months. Mean age at surgery was 63.7 (SD 6.7). 4.1% of patients were aged 75 and older. About 21% of patients had a previous urological condition, which resulted in a higher 12-month ICIQ-UI-SF compared to patients without (4.67 (SD 5.03) versus 4.32 (SD 4.69), $P=0.031$). Very few patients had received HT (0.7%) or radiotherapy (0.7%). Nevertheless, these showed statistically significantly higher 12-month ICIQ-UI-SF compared to patients without HT ((6.24 (SD 4.72) versus 4.38 (SD 4.76), $P=0.023$) or radiotherapy (6.61 (SD 5.46) versus 4.38 (SD 4.75), $P=0.004$)). Patients with high

EAU risk (4.76 (SD 4.90)) also showed higher 12-month ICIQ-UI-SF compared to patients with intermediate (4.32 (SD 4.78)) or low (4.12 (SD 4.53)) EAU risk and the overall difference was statistically significant ($P<0.001$). Patients for whom non-NS surgery or a lymphadenectomy were performed also had higher 12-month ICIQ-UI-SF versus NS ((4.89 (SD 4.94) versus 4.22 (SD 4.69), $P=0.003$) or no lymphadenectomy ((4.68 (SD 4.94) versus 4.25 (SD 4.66), $P=0.002$) patients. Last, surgery volume was not statistically significantly associated with ICIQ-UI-SF.

Model development

For the preoperative model, a full set of outcomes and candidate predictors was available for 6295 (66.8%) patients. The training and validation datasets for the preoperative model included 3123 and 3172 patients, respectively. For the postoperative model, a full set of outcomes and candidate predictors was available for 5193 (55.1%) patients. The training and validation datasets for the preoperative model included 2582 and 2611 patients, respectively. Candidate predictors and 12-month ICIQ-UI-SF of the preoperative and postoperative regression model subsets were clinically comparable to the full data set.

The most parsimonious preoperative prediction model suggested by LASSO regression included EAU risk classification for BCR, radiotherapy, preoperative EORCT QLQ-C30/QoL, preoperative ICIQ-UI-SF and patient age as contributive predictors of 12-month ICIQ-UI-SF (Figure 1 panel A). EAU risk classification and preoperative EORCT QLQ-C30/QoL were no longer suggested by the postoperative LASSO model, which proposed intraoperative complications, 3-month EORCT QLQ-C30/QoL and 3-month ICIQ-UI-SF next to preoperative ICIQ-UI-SF and patient age (Figure 1 panel C). The preoperative Mallow's CP value equalled 8.46, which was high relative to the number of included predictors. In the postoperative LASSO model, Mallow's CP value equalled 5.15, which suggested good model fit.

Nomogram and online tool

Estimates, standard errors and P values for the subsequent preoperative and postoperative regular multivariable linear regression models are displayed in Table 2. For the preoperative model, high EAU risk classification for BCR (Est 0.606 (SE 0.165), $P<0.001$), post-operative radiotherapy (Est 1.563 (SE 0.641), $P<0.015$), lower preoperative EORCT QLQ-C30/QoL (Est -0.011 (SE 0.003), $P<0.001$), higher

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preoperative ICIQ-UI-SF (Est 0.214 (SE 0.018), $P < 0.001$) and higher patient age (Est 0.058 (SE 0.009), $P < 0.001$) were associated with a statistically significant higher 12-month ICIQ-UI-SF. In the postoperative model, in addition to higher preoperative ICIQ-UI-SF (Est 0.083 (SE 0.014), $P < 0.001$) and higher patient age (Est 0.024 (SE 0.007), $P < 0.001$), lower 3-month EORCT QLQ-C30/QoL (Est -0.010 (SE 0.002), $P < 0.001$) and higher 3-month ICIQ-UI-SF (Est 0.562 (SE 0.009), $P < 0.001$) were associated with a statistically significant higher 12-month ICIQ-UI-SF. The direction and magnitude of these estimates were similar to the estimates proposed by LASSO regression, except for intraoperative complications, which in the postoperative model was no longer significantly associated with 12-month ICIQ-UI-SF. R^2 equalled 4% and 43% in the preoperative and postoperative models, respectively. For both models the calibration plot showed a satisfactory configuration between the actual and predicted 12-month ICIQ-UI-SF (Figure 1 panels B and D). It should however be noted that in both models, with higher actual 12-month ICIQ-UI-SF, the estimated 12-month ICIQ-UI-SF slightly underestimated the actual 12-month ICIQ-UI-SF.

The estimates from the multivariable linear regression model were used to create the nomograms (Figures 2 and 3) and online tools, which are available at

<https://universityhospitalsleuven.shinyapps.io/Preoperative-Nomogram-To-Predict-12-Month-ICIQ-UI-SF/>

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DISCUSSION

UI after RP represents a significant burden over patient's QoL and psychological well-being, with roughly 9% reporting UI as a moderate-big problem at 24 months, regardless of oncologic and sexual outcomes [24,25]. Since cancer survival rates range between 87% to 92%, even in locally advanced disease, and different treatment options and a multimodal approach exist, QoL outcomes deserve major consideration in the decision making process [26,27].

The presence of a predictive tool for continence status is crucial to help the clinician in counselling upfront patients for the appropriate treatment. Since continence is clearly multifactorial, the development of an accurate and useful predictive model proves to be challenging and requires a large real-life dataset. Predictive factors encompass not only anatomical and surgical aspects, but also patient's and disease characteristics [17].

In the first part of our study we assessed incontinence status at 12-months according to pre-operative factors, in a large prospectively collected real-life multicentre dataset.

At 12 months average ICIQ score was 4.3 (SD: 4.7). This value is 3- fold higher than the mean pre-op ICIQ (1.4). Thus an "ideal continence" defined in some previous studies as the same preoperative ICIQ, has not been reached [28]. One can argue that a difference between pre and post-operative average ICIQ scores of 2.9 is not clinically relevant. However, Nystrom and colleagues, in their study on continence treatment results in women, demonstrated that the minimum reduction in overall score that could be detected is 2.5. Therefore, a difference in the overall score, to be considered clinically relevant, should exceed 2.5 [29].

It should be underlined an ICIQ value between 4 and 5 means having a small amount of urine loss, maximum 3 times per week, but not being disturbed at all from this condition which can be considered an overall satisfactory outcome. Our results are in line with previous studies reporting a UI incidence at 12-months ranging from 8% to 11% [3].

Previous studies suggested that advanced age, increasing BMI, medical comorbidities, history of TURP, RT, HT, LUTS, decreased mid urethral length (MUL),

LND, non-NS surgery, may be risk factors for UI [17]. Our predictive model showed that high EAU risk of BCR, lower preoperative EORCT QLQ-C30/QoL, higher preoperative ICIQ-UI-SF and higher patient age predict higher ICIQ-SF scores at 12-months. However, our preoperative model has a high Mallows' CP value and quite low R^2 (4%). It should be noticed that incontinence is multifactorial and, due to the availability of data of our dataset, some important variables are missing.

Among available tools to predict UI, the accuracy is in general poor and only two models were externally validated and reported to have a c-indices >70% [4,5,13,15, 17, 28].

Matshushita et al showed that Age, BMI, ASA score, and MUL were predictors of continence at 6 and 12-months. However, in contrast to our population, patients included were completely continent before surgery and did not receive any adjuvant treatment. Moreover, the prediction of social continence was based on a patient's or surgeon's reported, non-validated, 5 point scale [12].

Jeong and colleagues predicted continence at 12-months in a cohort of patients completely continent before surgery and not having had RT. They showed that age, MUL and type of surgery significantly predict continence. Also in this study continence was assessed with non-validated tools [16].

According to our model, high EAU risk of BCR is one predictor of high ICIQ-SF. This finding can be a proxy of "less conservative surgery" and more extended LND. In our population the majority of patients is affected by high-intermediate risk disease. This could have led to a more aggressive surgical approach with higher probability of subsequent urinary incontinence. This is underscribed by the fact that intraoperative complications also predict a higher ICIQ-SF score. Seikkula et al showed that a super extended LND is associated with delayed continence recovery compared to eLND [31]. This observation might possibly be explained by an increased damage of nerve fibres innervating the pelvic floor muscles. On the contrary, Van der Poel et al. demonstrated that eLND was not associated with delayed continence recovery after RARP [32]. However, the extent of LND in this group of patients was not clearly described.

In the second part of our study we aimed to create a predictive tool to define which patient should be counselled for early continence surgery. This model showed acceptable Mallows' CP and R^2 (43%) values.

Higher ICIQ-SF scores at 12 months scores have been observed when including intra- and early post-operative variables in the model. In particular together with higher pre-operative ICIQ-UI-SF and higher patient age, intraoperative complications, lower 3-months EORTC QLQ-C30/QoL, and higher 3-month ICIQ-SF predicted higher 12 months ICIQ-SF scores.

Our results show an important added value of including 3-months values of ICIQ-SF and EORTC QLQ30/QoL to baseline values. Previous results demonstrated a pre-existing 7% of incontinence complaints and 20% of LUTS at baseline in men undergoing treatment for prostate cancer [33]. This is a pre-existing impairment in QoL before surgery, together with the already demonstrated psychological aspect connected with pCa [25]. Including these questionnaires in an early post-operative setting can give the clinician a better understanding of the patient's current and even future status.

This study has several strengths. To the best of our knowledge it is the first tool to predict continence status, based on a large group of patients treated only with RARP, in a real-life multi-centre regional setting. Secondly, data were prospectively collected in a compulsory database. Thirdly, data included complete pre- and post-operative assessment of UI and QoL based on validated questionnaires. Fourth, building and validation of the model was conducted according to the TRIPOD statement in order to improve the transparency of the reporting of our predictive model. Finally, our second nomogram represents a completely new tool to inform patients, at an early stage, about the possibility of an additional surgery for incontinence or, on the other hand, about the importance of enduring with a strict pelvic floor muscle training protocol.

Our study is not devoid of limitations. Firstly, some important variables known as predictors or involved in continence status after RP are missing, which may explain the relatively low R^2 of our preoperative model. This is mainly due to the retrospective nature of the study and to the intrinsic characteristics of the database.

Secondly, a single dataset has been used for development and validation of the model. Although a non-random splitting of the data is an acceptable design for evaluating model performance, external validation still has to be performed. Due to the privacy regulation of the cancer registry, another highly well-established predictor of functional outcomes is missed: the surgeon. This could represent a limitation since, in some cases, an individual surgeon's outcomes may be much better, or worse, than the nomogram prediction.

However, our results did not show any association with ICIQ-UI-SF, when including surgery volume (namely <50, 50-100 or >100 cases per year).

Finally, one criticism toward our model could be that the use of a continuous outcome score to predict continence status after RARP may not be “user-friendly” to the patient. A specific ICIQ cut-off for males has never been reported, thus we could not define a precise value suggesting a conservative approach or indicating the need of surgical correction. However, although a specific cut-off does not exist, the physician could consider clinically relevant a difference in the overall score, of more than 2.5 [29] This value, together with patient will, could help in the counselling towards conservative or interventional treatment.

Conclusions:

Our model focuses on the importance of pre-, peri- and early post-operative variables to predict functional outcomes. We identified, developed and internally validated, a novel tool to predict continence status after RARP. Our model has a dual role. It may help, in a preoperative setting, in better counsel patients about their risk of UI. On the other hand, in a postoperative setting, patients can be informed already, at 3-months, on the probability of an additional surgery for incontinence. This can help in selecting those patients who can't benefit from conservative approaches and help to opt for faster recovery with surgery. Moreover, our model highlights the idea that validated questionnaires have to be included in any predictive model dealing with patients' return to normal activities.

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Conflicts of Interest

WE and SJ are senior research fellows of the FWO Flanders.

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Table 1. Descriptive statistics for 12-month ICIQ-UI-SF and candidate predictors for 9421 patients diagnosed with prostate cancer and treated with robotic-assisted laparoscopic prostatectomy

Parameter	Parameter statistic, n (%) for categorical variables; mean (SD) for continuous variables	12-month ICIQ-UI-SF, mean (SD)	p value ^a
Urinary incontinence (outcome)			
ICIQ-UI-SF, mean (SD)			
Preoperative	1.4 (3.3)		
1 month postoperative	9.4 (5.7)		
3 month postoperative	6.4 (5.3)	--	--
12 month postoperative	4.3 (4.7)		
24 month postoperative	3.8 (4.4)		
Surgery volume			
<50 / year	1160 (22.3)	4.48 (4.98)	
50-100 / year	3118 (30.1)	4.28 (4.70)	0.0650
>100 / year	915 (17.6)	4.68 (4.68)	
Preoperative predictors			
Previous Urological Condition, n (%)			
Yes	1092 (21.0)	4.67 (5.03)	0.031
No	4101 (79.0)	4.32 (4.69)	
Hormonal therapy, n (%)			
Yes	34 (0.7)	6.24 (4.72)	0.023
No	5159 (99.3)	4.38 (4.76)	
Radiotherapy, n (%)			
Yes	38 (0.7)	6.61 (5.46)	0.004
No	5155 (99.3)	4.38 (4.75)	
EAU risk classification, n (%)			
High	1454 (28.0)	4.76 (4.90)	
Intermediate	2476 (47.7)	4.32 (4.78)	0.001
Low	1263 (24.3)	4.12 (4.53)	
Preoperative EORCT QLQ-C30/QoL, mean (SD)	74.0 (22.4)	--	
Q1 (38.0, 18.8)	1091 (21.0)	5.10 (5.13)	
Q2 (63.3, 4.4)	1256 (24.2)	4.62 (4.87)	
Q3 (83.0, 0.5)	1624 (31.3)	4.40 (4.54)	<0.001
Q4 (97.6, 4.0)	1222 (23.5)	3.53 (4.45)	
Preoperative ICIQ-UI-SF, mean (SD)	1.4 (3.3)	--	
Patient age, mean (SD)	63.7 (6.7)	--	
Q1 (54.4, 3.2)	1223 (23.6)	3.97 (4.49)	
Q2 (61.7, 1.7)	1519 (29.3)	4.02 (4.52)	
Q3 (66.5, 1.1)	1203 (23.2)	4.68 (4.97)	<0.001
Q4 (72.0, 2.6)	1248 (24.0)	4.99 (5.01)	
Postoperative predictors			
Nerve sparing, n (%)			
Yes	3864 (74.4)	4.22 (4.69)	0.003
No	1329 (25.6)	4.89 (4.94)	
Lymphadenectomy, n (%)			

Parameter	Parameter statistic, n (%) for categorical variables; mean (SD) for continuous variables	12-month ICIQ-UI-SF, mean (SD)	p value ^a
Yes	1742 (33.5)	4.68 (4.94)	0.002
No	3451 (66.5)	4.25 (4.66)	
Resection margin, n (%)			0.741
Negative	3868 (74.5)	4.41 (4.73)	
Positive	1325 (25.5)	4.36 (4.85)	
Intraoperative complications, n (%)			0.061
Yes	158 (3.0)	5.03 (4.59)	
No	5035 (97.0)	4.32 (4.69)	
Postoperative morbidity, n (%)			0.129
Yes	228 (4.4)	4.86 (5.26)	
No	4965 (95.6)	4.37 (4.74)	
3-month EORCT QLQ-C30/QoL, mean (SD)	70.4 (23.6)	--	--
Q1 (36.4, 20.5)	1224 (23.57)	6.02 (5.56)	<0.001
Q2 (69.0, 4.2)	1441 (27.75)	5.21 (4.89)	
Q3 (83.0, 0.06)	1618 (31.16)	3.47 (3.97)	
Q4 (97.2, 4.2)	910 (17.52)	2.56 (3.52)	
3-month ICIQ-UI-SF, mean (SD)	6.4 (5.3)	--	--
Q1 (0.1, 0.3)	1277 (24.59)	1.09 (2.58)	<0.001
Q2 (3.9, 0.9)	1241 (23.90)	2.72 (3.06)	
Q3 (7.3, 1.1)	1281 (24.67)	4.55 (3.60)	
Q4 (13.6, 3.0)	1394 (26.84)	8.77 (5.15)	

EORCT QLQ-C30 QoL = European Organization for Research and Treatment for Cancer Quality of Life Questionnaire; ICIQ-UI-SF = International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form; EAU = European Association of Urology

^a Student's t-test and one-way anova were used to compare two groups and three groups, respectively.

Table 2. Multivariable linear regression analyses assessing the postoperative prediction of the 12-month ICIQ-UI-SF score among patients diagnosed with prostate cancer and treated with robotic-assisted laparoscopic prostatectomy

	xxx Preoperative model		xxx Postoperative model	
	Est (SE)	P-value	Est (SE)	P-value
Preoperative predictors				
EAU risk classification, n (%)				
High	0.606 (0.165)	<0.001	--	
Intermediate	0.057 (0.148)	0.6976		
Low	Reference category			
Radiotherapy				
Yes	1.563 (0.641)	0.015	--	
No	Reference category			
Preoperative EORCT QLQ-C30/QoL	-0.011 (0.003)	<0.001	--	
Preoperative ICIQ-UI-SF	0.214 (0.018)	<0.001	0.083 (0.014)	<0.001
Patient age	0.058 (0.009)	<0.001	0.024 (0.007)	<0.001
Postoperative predictors				
3-month EORCT QLQ-PR25			-0.010 (0.002)	<0.001
3-month ICIQ-UI-SF			0.562 (0.009)	<0.001

Confidence Interval (CI) 95%

EORCT EORCT QLQ-C30/QoL: European Organization for Research and Treatment for Cancer Quality of Life Questionnaire of Prostate Cancer. ICIQ-UI-SF: International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form. EAU: European Association of Urology

Figure 1. LASSO regression plots and regular multivariable linear regression calibration plots for the training and validation data sets. The LASSO regression plots show the change in the regression coefficients at each step. The coloured vertical line represents the selected preoperative (panel A) and postoperative (panel C) model. The calibration plots compare the estimated 12-month ICIQ-UI-SF with the actual 12-month ICIQ-UI-SF for the preoperative (panel B) and postoperative model (panel D).

Figure 2. Nomogram for the preoperative prediction of the 12-month ICIQ-UI-SF score among patients diagnosed with prostate cancer and treated with robotic-assisted laparoscopic prostatectomy. Instructions: Locate the patient's values for age, EAU risk classification, preoperative EORTC QLQ-C30/QoL and preoperative ICIQ-UI-SF on the corresponding axes. Draw a straight line up to the Points axis for each value to determine the number of points for that value. Calculate the sum of the values on the Points axis and locate this sum score on the Total Points axis. Draw a straight line down to find the patient's predicted ICIQ-UI-SF score at 12 months. Alternatively, the online tool may be used via

<https://universityhospitalsleuven.shinyapps.io/Preoperative-Nomogram-To-Predict-12-Month-ICIQ-UI-SF/>

EORTC QLQ-C30/QoL = European Organization for Research and Treatment for Cancer Quality of Life Questionnaire of Prostate Cancer; ICIQ-UI-SF = International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form; EAU = European Association of Urology.

Figure 3. Nomogram for the postoperative prediction of the 12-month ICIQ-UI-SF score among patients diagnosed with prostate cancer and treated with robotic-assisted laparoscopic prostatectomy. Instructions: Locate the patient's values for age, 3-month EORCT QLQ-C30/QoL, intraoperative complications, preoperative ICIQ-UI-SF and 3-month ICIQ-UI-SF on the corresponding axes. Draw a straight line up to the Points axis for each value to determine the number of points for that value. Calculate the sum of the values on the Points axis and locate this sum score on the Total Points axis. Draw a straight line down to find the patient's predicted ICIQ-UI-SF score at 12 months. Alternatively, the online tool may be used via

<https://universityhospitalsleuven.shinyapps.io/Postoperative-Nomogram-To-Predict-12-Month-ICIQ-UI-SF/>

EORCT QLQ-C30/QoL = European Organization for Research and Treatment for Cancer Quality of Life Questionnaire of Prostate Cancer; ICIQ-UI-SF = International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form.