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Development of Machine Learning Algorithm to Predict the Risk of Incontinence After Robot-Assisted Radical Prostatectomy

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Abstract

Introduction: Predicting postoperative incontinence beforehand is crucial for intensified and personalized rehabilitation after robot-assisted radical prostatectomy. Although nomograms exist, their retrospective limitations highlight artificial intelligence (AI)'s potential. This study seeks to develop a machine learning algorithm using robot-assisted radical prostatectomy (RARP) data to predict postoperative incontinence, advancing personalized care.

Materials and Methods: In this prospective observational study, patients with localized prostate cancer undergoing RARP between April 2022 and January 2023 were assessed. Preoperative variables included age, body mass index, prostate-specific antigen (PSA) levels, digital rectal examination (DRE) results, Gleason score, International Society of Urological Pathology grade, and continence and potency questionnaires responses. Intraoperative factors, postoperative outcomes, and pathological variables were recorded. Urinary continence was evaluated using the Expanded Prostate cancer Index Composite questionnaire, and machine learning models (XGBoost, Random Forest, Logistic Regression) were explored to predict incontinence risk. The chosen model's SHAP values elucidated variables impacting predictions.

Results: A dataset of 227 patients undergoing RARP was considered for the study. Post-RARP complications were predominantly low grade, and urinary continence rates were 74.2%, 80.7%, and 91.4% at 7, 13, and 90 days after catheter removal, respectively. Employing machine learning, XGBoost proved the most effective in predicting postoperative incontinence risk. Significant variables identified by the algorithm included nerve-sparing approach, age, DRE, and total PSA. The model's threshold of 0.67 categorized patients into high or low risk, offering personalized predictions about the risk of incontinence after surgery.

Conclusions: Predicting postoperative incontinence is crucial for tailoring rehabilitation after RARP. Machine learning algorithm, particularly XGBoost, can effectively identify those variables more heavily, impacting the outcome of postoperative continence, allowing to build an AI-driven model addressing the current challenges in post-RARP rehabilitation.

Keywords: deep learning, rehabilitation, continence, artificial intelligence, surgical recovery, radical prostatectomy

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Introduction

LOCALIZED PROSTATE CANCER (PCa) has a substantial impact on health care systems, and radical prostatectomy is the treatment of choice for this malignancy.¹ This surgical procedure can, however, result in postoperative complications significantly affecting patients' quality of life (QoL).² To improve these outcomes, robotic surgery has been widely employed in this setting, leading robot-assisted radical prostatectomy (RARP) to become the most performed robotic surgery worldwide.³

Over time, various surgical techniques performed robotically were proposed to improve patients' QoL by reducing the occurrence of postoperative complications, to reduce the incidence of urinary incontinence, and to improve erectile dysfunction.⁴ In addition, many studies have emphasized the importance of continuous and intensive postoperative rehabilitation (i.e., pelvic floor muscle training [PFMT]), protocols after RARP.⁵

However, even in the setting of robotic oncologic surgery, health care systems are unable to provide adequate rehabilitation programs for all patients owing to the significant burden of disease in the general population.⁶ Therefore, it is important to predict in advance the occurrence of postoperative incontinence, to immediately plan intensified and personalized functional rehabilitation programs in those patients more probably at risk to develop it.^{7,8}

In this context, nomograms based on preoperative and intraoperative characteristics have been developed; however, these are limited by the retrospective nature of studies considered for their development.^{9,10} Today, artificial intelligence (AI) is gaining ground in health care, and in this setting, it may play a role. With constant data implementation, it is possible to build a neural network trained on large volumes of prospective data, replacing nomograms.

The aim of this study is to develop and train a machine learning algorithm capable of discriminating the postoperative incontinence risk based on patient's perioperative characteristics, starting from data obtained by a series of RARP.

Materials and Methods

This prospective observational monocentric study enrolled patients diagnosed with localized PCa (cT1-3, cN0, and cM0), who underwent RARP ± pelvic lymph node dissection (PLND) between April 2022 and January 2023. RARP was performed with transperitoneal approach by a single expert surgeon (F.P.). The study was designed following the good clinical practice guidelines and all the patients signed an informed consent. Exclusion criteria were absolute contraindications to laparoscopic pelvic surgery, preoperative urinary incontinence, contraindications to pelvic floor rehabilitation, and ongoing neoadjuvant hormonal therapy.

The following preoperative variables were considered: Age, body mass index (BMI), total prostate-specific antigen (PSA) levels at diagnosis, the positivity of digital rectal examination (DRE), and primary and secondary Gleason score (GS) determined through prostate biopsy, the International Society of Urological Pathology (ISUP) at Fusion Biopsy and Standard Biopsy. In addition, all patients preoperatively completed the International Prostate Symptom Score (IPSS),

Incontinence Symptom Index (ISI), and International Index of Erectile Function questionnaires.

We assessed intraoperative variables such as blood loss, total operative time (i.e., from Veress needle insertion to surgical wound closure), and the performance of PLND during the procedure. Based on the Pasadena consensus panel,¹¹ the intrafascial, interfascial, and sub-extrafascial dissection planes are referred to as full, partial, and minimal nerve sparing (NS), respectively.

During the postoperative period, we evaluated the duration of catheterization, performance of postoperative cystography, its timing, and overall hospital stay. Postoperative complications were recorded for 90 days and classified with the modified Clavien-Dindo classification system,¹² specifying the need for hospitalization.

Pathological variables included prostate gland and tumor volume, percentage of tumor involvement in relation to the prostate, pTNM stage, GS, and the presence of positive surgical margins.

Urinary continence was assessed 7, 30, and 90 days following catheter removal using the question from the Expanded Prostate cancer Index Composite questionnaire: "How many PADS did you usually use to control urine leakage in the last 4 weeks?," modifying its last part in accordance with the specific time point. Continence was defined with the answer "zero pads" per day. ISI and IPSS questionnaires were also administered following the same timeline.

Data concerning potency recovery were not considered in this study.

Machine learning to define incontinence risk groups

The next step included building a machine learning model able to categorize each individual patient based on his risk to develop postoperative incontinence, aiming to provide a tailored rehabilitation treatment.

All the previously reported variables were evaluated together with different predictive models, to identify those more heavily impacting the postoperative continence.

Three different models were investigated:

- XGBoost, a gradient boosting machine learning algorithm: A powerful algorithm used for a variety of tasks, including classification, regression, and ranking, known for its accuracy and speed (Supplementary Data).
- Random Forest, an ensemble learning algorithm: It works by building a collection of decision trees and averaging their predictions. It is a robust algorithm, not easily prone to overfitting.
- Logistic Regression, a classification algorithm: A simple, but effective algorithm often used as a baseline for other classification algorithms.

Therefore, the areas under curve (AUC) of these models were compared through benchmark analysis to assess which found the closest relationship between perioperative variables and the occurrence of postoperative incontinence with respect to baseline.

Therefore, once the most suitable machine learning model was identified, SHAP (SHapley Additive exPlanations) values, a machine learning explainability approach used to clarify the predictions of any machine learning model, were

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assigned to all the variables depending on their impact and magnitude in the prediction of the outcome. Features with positive SHAP values impact the prediction positively, whereas those with negative values have a negative impact. The magnitude of the SHAP value indicates how strong the effect is. Open-source Python software was employed with essential libraries such as pandas, numpy, matplotlib, seaborn, sklearn, xgboost, and shap to further enhance the predictive capabilities and interpretability of the model.¹³

Results

A total of 227 consecutive patients were enrolled. Preoperative data are schematized in Table 1.

Perioperative data and postoperative complications up to 90 days are summarized in Table 2.

Overall, 67/227 (29.5%) patients underwent full NS procedure, 114/227 (50.2%) partial NS, and 46/227 (20.3%) patients minimal NS, respectively. PLND was performed in 122/140 cases. No intraoperative complication was detected.

The median (interquartile range [IQR]) postoperative hospital stay was 5 (5–6) days, and median (IQR) catheterization time was 4 (4–5) days. Postoperative complications were all low grade (i.e., Clavien-Dindo I or II), but three cases, which were graded as IIIa. Specifically, these last were two patients with lymphocele, who underwent percutaneous puncture, and a suprapubic hematoma, who underwent surgical drainage.

Final pathology showed pT2 in 36.4% and pT3 in 63.5% cases (Table 3).

TABLE 1. BASELINE CHARACTERISTICS OF THE PATIENTS

| <i>Characteristics</i> | |
|---|-------------|
| Number of patients | 227 |
| Age, years, mean (SD) | 67.1 (7.0) |
| BMI, mean (SD) | 26.4 (3.4) |
| Diabetes, <i>n</i> (%) | 26 (11.4) |
| Smoke, <i>n</i> (%) | 16 (7) |
| Hypertension, <i>n</i> (%) | 110 (48.4) |
| Cardiopathy, <i>n</i> (%) | 22 (9.7) |
| PSA, ng/mL, mean (SD) | 10.0 (10.6) |
| Positive DRE, <i>n</i> (%) | 106 (46.7) |
| ECE, <i>n</i> (%) | 32 (14) |
| Biopsy GS, median (IQR) | 7 (7–8) |
| ASA score, median (IQR) | 2 (2–2) |
| IPSS (preoperative), median (IQR) | 10 (4–15) |
| IIEF-5 score (preoperative), median (IQR) | 19 (15–23) |
| ISI score (preoperative), median (IQR) | 0 (0–2) |
| D’Amico classification, <i>n</i> (%) | |
| High risk | 56 (24.7) |
| Intermediate risk | 148 (65.2) |
| Low risk | 23 (10.1) |
| Clinical stage, <i>n</i> (%) | |
| T1c | 67 (29.5) |
| T2 | 148 (65.2) |
| T3 | 12 (5.3) |

ASA = American Society of Anesthesiology; BMI = body mass index; DRE = digital rectal examination; ECE = extracapsular extension; GS = Gleason score; IIEF-5 = International Index of Erectile Function-5; IPSS = International Prostate Symptom Score; IQR = interquartile range; ISI = Incontinence Symptom Index; PSA = prostate-specific antigen; SD = standard deviation.

TABLE 2. PERIOPERATIVE VARIABLES

| <i>Perioperative data</i> | |
|--|--------------|
| Operative time, minutes, mean (SD) | 143.2 (29.9) |
| PLND, <i>n</i> (%) | 190 (83.7) |
| NS approach, <i>n</i> (%) | |
| Full NS | 67 (29.5) |
| Partial NS | 114 (50.2) |
| Minimal NS | 46 (20.3) |
| Blood losses, mL, mean (SD) | 242.7 (54.3) |
| Intraoperative complications, <i>n</i> (%) | 0 (0) |
| Catheterization time, days, mean (SD) | 4 (4–5) |
| Hospital stay, days, mean (SD) | 5 (5–6) |
| Postoperative complications, <i>n</i> (%) | 19 (8.3) |
| Fever | 3 (1.3) |
| Suprapubic hematoma | 4 (1.7) |
| Lymphocele | 3 (1.3) |
| Acute urinary retention | 4 (1.7) |
| Urine leakage | 5 (2.2) |
| Postoperative complications | 3 (1.3) |
| Clavien grade >2, <i>n</i> (%) | |

NS = nerve sparing; PLND = pelvic lymph node dissection.

Functional data are shown in Table 4.

Postoperative urinary continence was recorded in 74.2%, 80.7%, and 91.4% cases at 7, 30, and 90 days, respectively.

Machine learning model building

The plot of receiver operating characteristics curve reported in Figure 1, comparing on a benchmark analysis XGBoost, Random Forest, and Logistic Regression models, shows that the XGBoost achieved the highest AUC, followed by the Logistic Regression and Random Forest models. This suggests that the XGBoost was the best model for this task, as it was able to distinguish between positive and negative examples with the highest, even if not perfect, accuracy.

The plot reported in Figure 2 shows the average SHAP values for different features, whereas Figure 3 provides a useful overview of the magnitude of different variables in the dataset, from the most to the least impacting the “immediate continence” outcome.

TABLE 3. PATHOLOGIC VARIABLES

| <i>Pathological data</i> | |
|------------------------------------|-------------|
| Positive margins, <i>n</i> (%) | 48 (21.1) |
| Prostate volume, mL, mean (SD) | 45.1 (22.3) |
| Tumor volume, mL, mean (SD) | 5.2 (6.1) |
| % Tumor, mean (SD) | 13.2 (12.8) |
| Pathological T stage, <i>n</i> (%) | |
| pT2 | 89 (39.2) |
| pT3 | 138 (60.8) |
| Pathological N stage, <i>n</i> (%) | |
| pN0 | 183 (80.6) |
| pN1 | 7 (3.0) |
| Pathological GS, <i>n</i> (%) | |
| 6 | 5 (2.2) |
| 7 | 181 (79.7) |
| 8 | 17 (7.5) |
| 9 | 24 (10.6) |

TABLE 4. FUNCTIONAL OUTCOMES AND RELATIVE QUESTIONNAIRES

| <i>Functional outcomes</i> | |
|--|------------|
| Postoperative continence, <i>n</i> (%) | |
| 1 week | 170 (74.9) |
| 1 month | 185 (81.5) |
| 3 months | 209 (92.0) |
| Postoperative IPSS, median (IQR) | |
| 1 week | 8 (4–10) |
| 1 month | 7 (4–12) |
| 3 months | 7 (3–10) |
| Postoperative ISI score, median (IQR) | |
| 1 week | 4 (2–4) |
| 1 month | 2 (2–4) |
| 3 months | 1 (0–2) |

The feature NS approach, age, DRE, and total PSA had the highest average SHAP values, with consequent significant impact on the predictions and classification. In contrast, the features ISUP at FB and GS had small average SHAP values, with a small impact on predictions. It is important to note that the SHAP values are just average values: the actual SHAP value for a given instance may be different, depending on the values of the other features.

The plots reported in Figure 4 describe the SHAP force plot prediction for a continent or incontinent patient at catheter removal.

The model, based on the current dataset, considered the threshold value of 0.5. If the value detected was lower than 0.5, the model assigned the patient to the higher risk category to develop incontinence. If the value, on the contrary, was

higher than 0.5, the patient was classified in the low-risk category. Plot “a” shows the characteristics of a continent patient; indeed, the value assigned by the model to him is 1.18, higher than the threshold value of 0.5. Contrarily, in plot “b,” the patient results to be incontinent, being the value assigned by the model lower than the threshold value (0.08).

Discussion

To date, the development of cutting-edge technology for the treatment of PCa brought a significant improvement in functional outcomes, with robotic surgery undoubtedly playing a key role.¹⁴ Nevertheless, a significant percentage of patients still reports postoperative functional issues following RARP (i.e., 20%–65% urine incontinence and 20%–90% erectile dysfunction at 1 year).^{15,16}

In this scenario, a postoperative protocol based on PFMT is a key component of the rehabilitation process and has a substantial influence on patients’ QoL.^{17,18} When started immediately after surgery, if followed consistently and methodically, and if adjusted based on clinical results, these rehabilitation protocols have proven their ability to quicken and enhance the recovery of both sexual potency and urinary continence.^{19,20}

However, the application of such protocols for post-RARP rehabilitation in routine clinical practice may be difficult. The high prevalence of RARP, which in fact accounts for more than 70% of all surgical procedures in high-volume uro-oncological centers, represents one of the main issues.²¹

Owing to the high number of PCa surgeries, intensive rehabilitation is challenging in the public health system. Hospital departments struggle with multidisciplinary rehabilitation, making manual data interpretation for protocol adherence and

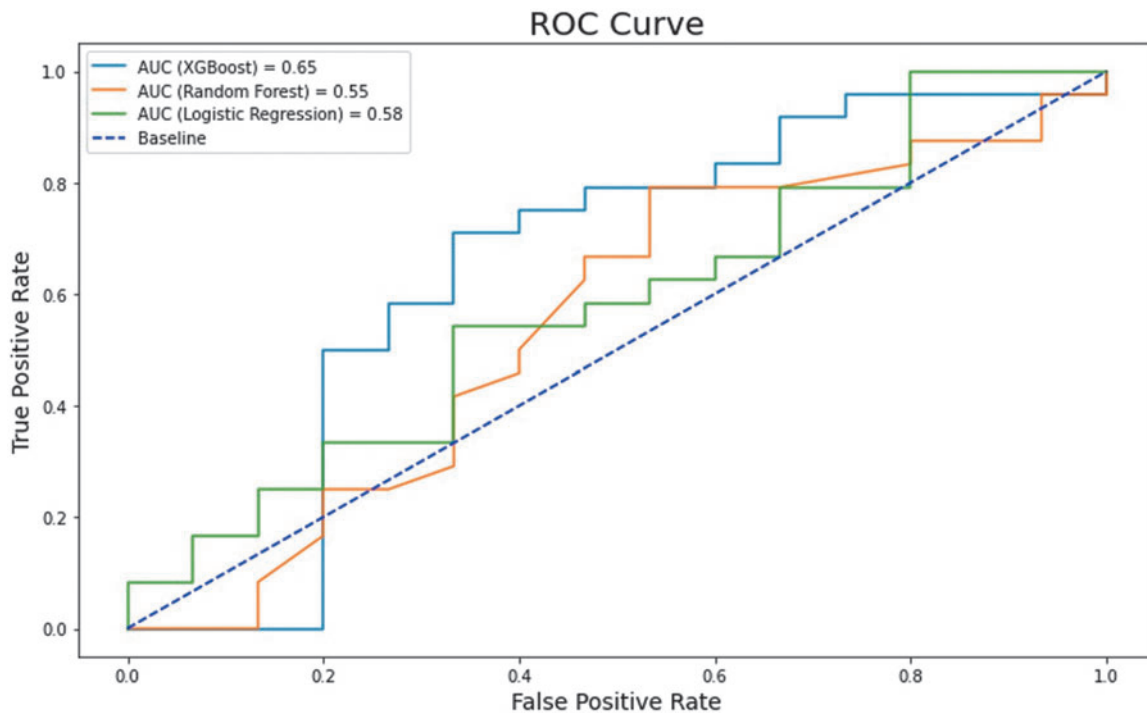


FIG. 1. ROC curves of machine learning models compared to baseline model. ROC=receiver operating characteristics curve.

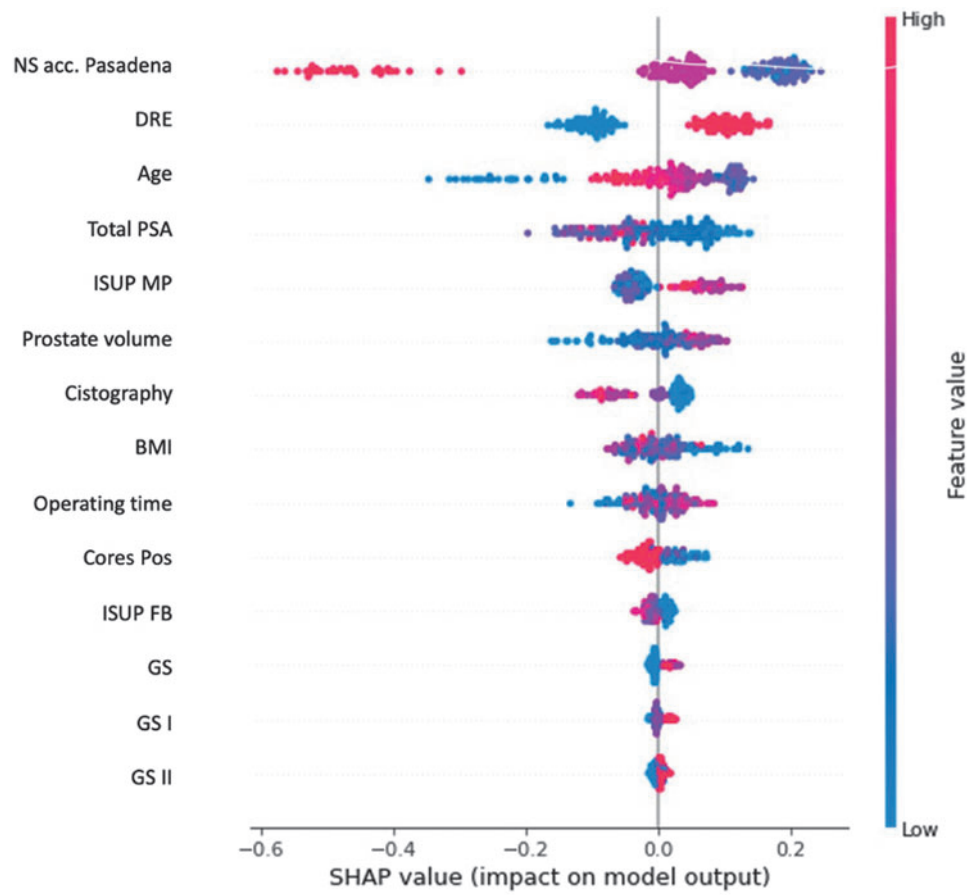


FIG. 2. SHAP values of perioperative variables. The y-axis of the plot shows the feature names, and the x-axis shows the average SHAP values. The color of the points represents the value of the feature, ranging from low to high. SHAP= SHapley Additive exPlanations.

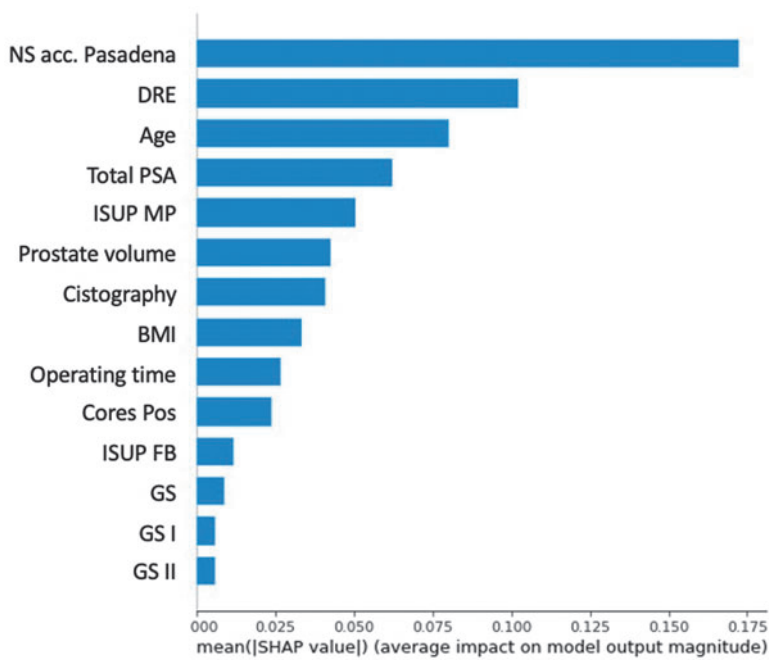


FIG. 3. SHAP value and average impact on XGBoost model.

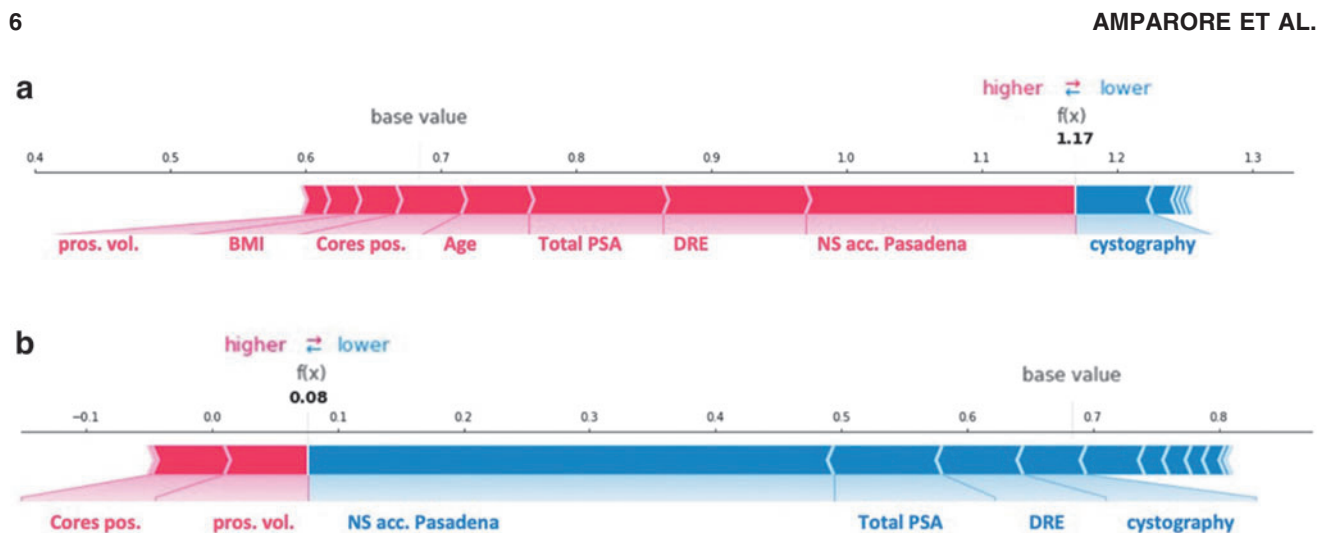


FIG. 4. Plots of SHAP force to predict risk of continence or incontinence. (a) Patient assigned to low-risk class; (b) patient assigned to high-risk class.

efficiency assessment difficult.²² To address these issues, we explored machine learning methodologies to classify patients based on postoperative incontinence risk, incorporating perioperative characteristics.^{23,24} Our goal was to develop a tool for automatic, personalized PFMT protocols using preoperative, intraoperative, and early postoperative data. This approach aims to tailor the rehabilitation process, automatically modifying the plan based on continence outcomes at intermediate steps, offering potential solutions to current rehabilitation challenges.

In fact, classic protocols are “rigid,” based exclusively on progressive schemes taking into account only the incontinence degree, ignoring his perioperative characteristics.²⁵ By including the patient-related characteristics (e.g., BMI, age, smoking habits) in the pre-PFMT evaluation, it is possible to profile the patient and create a rehabilitation program that is customized and flexible.²⁶

In addition, this machine learning algorithm can be integrated into developing digital platforms for telerehabilitation programs, contributing to make the whole process more automatized and physician independent.^{27,28}

To date, the increased time and clinical resources needed for reviewing biometric data and patient-reported outcomes in telemedicine protocols have raised the overall number of medical visits, even when conducted remotely.²² This is linked to the widespread use of digital health interventions, which initially require specialized personnel for data monitoring. However, integrating technology to streamline clinical workflows, interpret data, and communicate promptly with patients is crucial for success.²⁹

Considering this, implementing machine learning algorithms for real-time tracking of symptoms, physiological metrics, and patient outcomes, with automated alerts to clinicians or program adjustments, can be a viable strategy. This approach addresses the current challenge of the substantial work burden associated with digital data monitoring and interpretation.

Looking at our machine learning algorithm development, some interesting findings have to be discussed. First of all, we identified the most suitable model to predict the risk of incontinence in the current cohort of patients. This model,

called XGBoost, can assign specific weights (referred to as SHAP values) to individual variables. These weights help balance the impact of all other factors that might influence the risk of postoperative incontinence. In simpler terms, XGBoost considers various factors and assigns importance to each one, ensuring a comprehensive assessment of the risk of incontinence after surgery.

The variables more impacting the outcome of immediate continence, as reported in the example of Figure 4, for both patients were the NS approach according to Pasadena, the total PSA, and the DRE. However, looking at the values of these variables (that were also the ones that more clearly distinguished the population of continent from the one of incontinent patients at SHAP values graph; Fig. 2), this evidence seems to find correspondence from a clinical perspective. In fact, in plot “a,” the patient underwent a full NS RARP, and had a PSA 4 ng/mL (not high value) and a negative DRE. This suggests that the patient could be affected by a not highly aggressive or extended disease, reflecting in a more conservative surgical approach that can justify a precocious recovery of urinary continence.

Conversely, in plot “b,” the patient underwent minimal NS RARP according to Pasadena and had a PSA >10 ng/mL and a positive DRE. All these factors are suggestive for a more aggressive or extended tumor that make necessary a wider resection of periprostatic tissues for oncologic reasons, impacting more heavily on anatomical structures responsible for postoperative urinary continence recovery.

Considering all these factors, the result is a predictive model capable of classifying a patient as potentially continent or incontinent based on their characteristics. It specifies which factors are more likely to impact the risk of incontinence and the weight of those favoring continence recovery. Although built on a cohort with defined urinary continence outcomes, the model can prospectively be applied to new patients with unknown outcomes. The study cohort served as the machine learning training set, necessitating validation on a new patient cohort.

Furthermore, the analysis focused on immediate postoperative continence outcomes (i.e., catheter removal), but it can be extended to different time points in a telerehabilitation

program where continence recovery is assessed. At each time point evaluation, the algorithm's variables may be adjusted, considering previous continence outcomes, allowing the model to adapt and refine itself with the accumulating information over time.

This can match the final goal of the machine learning model implementation in a futuristic rehabilitation program: To be strictly tailored on patients' features during his continence recovery journey.³⁰ However, it is important to acknowledge the limitations of our study. First, the sample size was limited, which may affect the general application of our findings. Furthermore, the follow-up period of 90 days was relatively short and may not be sufficient to draw definitive conclusions. Moreover, the surgical outcomes reported may not be applicable to low-volume RARP centers, although detailed descriptions of the operative technique were extensively provided for replication purposes.

Moreover, XGBoost is a good machine learning model that can assign the patient to a certain risk category, but, like all machine learning and AI models, it is necessary to employ big data (i.e., a higher number of instances), since increasing the sample size (i.e., study population) may increase the AUC value.

We are still in a developmental stage of the project, and further studies will be needed to improve both the platform and the machine learning model to achieve a tool that can truly help the clinician in daily practice.

Conclusions

In conclusion, it is crucial to predict postoperative incontinence accurately to customize rehabilitation plans after RARP. In this context, machine learning methods, particularly XGBoost, show promise in efficiently pinpointing essential factors, like the NS approach, age, DRE, and total PSA, specifically for this study. The setup of this algorithm, which can evaluate the risk of postoperative incontinence for each patient based on these identified variables, can find great application in clinical practice and health care optimization.

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Supplementary Material

Supplementary Data

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Abbreviations Used

AI = artificial intelligence
 ASA = American Society of Anaesthesiology
 AUC = area under curve
 BMI = body mass index
 DRE = digital rectal examination
 ECE = extracapsular extension
 GS = Gleason score
 IIEF-5 = International Index of Erectile Function-5
 IPSS = International prostate Symptom Score
 IQR = interquartile range
 ISI = Incontinence Symptom Index
 ISUP = International Society of Urological Pathology
 NS = nerve sparing
 PCa = prostate cancer
 PFMT = pelvic floor muscle training
 PLND = pelvic lymph node dissection
 PSA = prostate-specific antigen
 QoL = quality of life
 RARP = robot-assisted radical prostatectomy
 ROC = receiver operating characteristics curve
 SD = standard deviation
 SHAP = SHapley Additive exPlanations