**Total anatomical reconstruction during robot-assisted radical prostatectomy: focus on urinary continence recovery and related complications after 1000 procedures**

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# ADVANTAGES OF TOTAL ANATOMICAL RECONSTRUCTION DURING ROBOT ASSISTED RADICAL PROSTATECTOMY: FOCUS ON URINARY CONTINENCE RECOVERY AND RELATED COMPLICATIONS AFTER 1000 PROCEDURES

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## ABSTRACT

### Objectives

- To present the functional and oncological outcomes after one-year minimum follow-up, after an experience of more than 1000 robot-assisted radical prostatectomies (RARP) with our standardized total anatomic reconstruction (TAR) technique.
- To evaluate which factor could influence the postoperative continence recovery in order to obtain a nomogram to predict the risk of post-operative incontinence.

**Materials and methods** The enrolment phase began in June 2013 and ended in May 2017. Patients were prospectively included in the study with the following inclusion criteria: (1) localized PCa (clinical stages cT1-3, cN0, cM0); (2) indication for radical prostatectomy; (3) preoperative multiparametric prostate magnetic resonance imaging. All patients underwent RARP with a TAR technique done at the end of the demolitive phase. The continence rates were assessed at 24 h, and 1, 4, 12, 24 and 48 weeks after catheter removal. Patients were defined as continent if they answered ''zero pad'' or ''one safety pad'' per day. A logistic regression model was performed to evaluate the potential impact of some pre- and intra-operative factors on the postoperative urinary continence recovery. Model discrimination was assessed using an area under (AUC) the receiver operating characteristic (ROC) curve. A nomogram to predict the risk of post-operative incontinence after RARP with TAR technique was generated based on the logistic model.

**Results** 1008 patients were enrolled in our study. At 24 h, and 1, 4, 12, 24 and 48 weeks after catheter removal, 621 (61.61%), 594 (58.93%), 803 (79.66%), 912 (90.48%), 950 (94.25%) and 956 (94.84%) patients were continent, respectively. In the logistic regression model, the variables analysed had a higher impact on continence recovery at 4 and 12 weeks. At 4 weeks, the post-operative odds of urinary continence recovery increased with the absence of diabetes (OR 2.76, 95% CI 1.41-5.41) and D'Amico low v. high risk (OR 2.01, 95% CI 1.01-3.99). At 12 weeks, increased with the absence of diabetes (OR 3.01, 95% CI 1.23-7.35), D'Amico low v. high risk (OR 4.04, 95% CI 1.56-10.47), and D'Amico intermediate v. high risk (OR 3.33, 95% CI 1.66-6.70). ROC curves were drawn and an AUC value of 61.9% (95% CI 57.49 – 66.36) at 4 weeks and 63.8% (95% CI 58.03 – 69.65) at 12 weeks were computed. Based on these parameters, two nomograms (at 4 and 12 post-operative weeks) were generated.

**Conclusion** The TAR technique confirmed excellent results in the early recovery of urinary continence. Two nomograms were created, to predict pre-operatively the post-operative odds of

urinary continence recovery at 4 and 12 weeks after RARP by integrating the presence of diabetes

and the D'Amico risk classification.

**INTRODUCTION**

Prostate cancer continues to be the most common solid organ malignancy in men in Western countries [1]. The incidence is expected to rise as the population ages and longevity increases. Over 90% of cases are organ confined at diagnosis [2], and radical prostatectomy (RP) is the gold standard among radical treatments in eligible patients. Nowadays, robot assisted RP (RARP) is the most common treatment offered in western countries [3].

The goal of surgery is to achieve complete cancer control while preserving functional outcomes in terms of urinary and sexual faculties [4], and, to date, the advantages of robotics in achieving both objectives are widely recognized [5-9]. Urinary incontinence is a particularly feared side effect of RP because it can significantly compromise patients' quality of life. The proportion of continent patients at 12 months after surgery ranges in the literature from 69% to 96% [5]. The wide range is probably due to various definitions of continence and measurement methods. A number of factors have been identified for post prostatectomy incontinence, including patient characteristics, surgeon experience, and surgical precision [10].

Concerning the surgical procedure, many authors have proposed different techniques to obtain the best early continence recovery rate [3, 11]. In 2016 our group proposed and published the Total Anatomical Reconstruction (TAR) technique during anterograde RARP [12], a ''tension-free'' anastomosis technique that aimed to restore the anterior and posterior supports to the sphincter.

The primary end-point of this study was to present the continence recovery outcomes and technique-related complications after one-year minimum follow-up, after an experience of more than 1000 RARP with our standardized TAR technique. The secondary end-points were to evaluate factors influencing the postoperative continence recovery, in order to obtain a nomogram to predict the risk of post-operative incontinence, as well as potency, quality of life and oncologic outcomes.

## MATERIALS & METHODS

### *Study design*

The enrolment phase began in June 2013 and ended in May 2017; the follow-up period was formally closed in June 2018. The study was approved by the local ethics committee of San Luigi Gonzaga Hospital in Orbassano, Italy. Patients were prospectively included in the study with the following inclusion criteria: (1) localized PCa (clinical stages cT1-3, cN0, cM0); (2) indication for radical prostatectomy; (3) preoperative multiparametric prostate magnetic resonance imaging (mp-MRI).

The exclusion criteria were: (1) contraindications for undergoing RARP; (2) neo-adjuvant hormone therapy; (3) anterior tumors with suspected large extracapsular extension on mp-MRI.

All patients underwent RARP performed with the transperitoneal anterograde approach [14]. Two laparoscopic and robotic surgeons performed all of the prostate apical dissections and TARs. When indicated, unilateral or bilateral neurovascular bundle preservation (nerve-sparing [NS] procedure) and extended pelvic lymph-node dissection (ePLND) were performed.

### *Surgical technique*

Total anatomic reconstruction has been previously described [12]. The most important details of the surgical technique are briefly reported below. Anteriorly, the endopelvic fascia is incised while preserving the pubo-prostatic ligaments. The visceral layer of the endopelvic fascia is sliced cranially, and the bladder neck dissection then begins with the intention to spare the anatomy of the involved structures. After the posterior Denonvillers' fascia incision, the prostate apex is anatomically dissected, and the urethra is incised at the level of the genital ridge, to preserve the maximum urethral length. After the demolitive phase, the deep venous complex is selectively sutured using a continuous 3/0 barbed suture, only in case of severe venous bleeding. The posterior reconstruction is performed in a triple layer by using a 3/0 barbed suture. The first layer involves the previously sectioned Denonvilliers' fascia and the median raphe, the second the retrotrigonal fascia and the median raphe, and the third the bladder neck (excluding the mucosa of the bladder) and the posterior aspect of the rhabdosphincter. The urethro-vesical anastomosis is performed by using two 3/0 barbed hemi-running sutures, involving the full thickness of either the bladder or the urethra. Finally, the anterior reconstruction consists of two layers of 3/0 barbed running sutures. The first layer involves the muscular fibers of the bladder and the previously dissected peri-urethral tissue, which is located between the urethra and the deep venous complex. The second involves the vesical apron and the portion of the endopelvic fascia that covers the deep venous complex while involving the pubo-prostatic ligaments. At the end of the surgery, an independent drainage is placed through a suprapubic

incision. The peritoneum is sutured using a 3/0 barbed running suture. In case of ePLND, an independent drainage is inserted through the port for the fourth robotic arm. In this way, the closure of the peritoneum causes the retropubic space not to communicate with the intraperitoneal cavity.

Concerning postoperative care, the intraperitoneal drainage was removed on postoperative day (POD) 2, and the extraperitoneal drainage on POD 3. The catheterization time was established by the first surgeon on the basis of the quality of the anastomosis. The quality was classified as: (1) "excellent", when an end-to-end anastomosis was performed; (2) "very good", when a single stitch was required to reinforce the end-to-end anastomosis; or (3) "good" (when more than a single stitch was required to reinforce the end-to-end anastomosis or in cases of more complex bladder neck reconstruction). The catheter was removed after pelvic US in POD <5 if the quality of anastomosis was rated as "excellent", in POD 5-7 in case of "very good" quality, and in POD >7 in case of "good" quality. If there was evidence of urine leakage in the drainage sac (confirmed with a creatinine measure on the drained liquid) or in case of suspected leakage at US, a retrograde and voiding cystourethrogram (RV-CU) was performed before catheter removal. A pelvic US was repeated at 4 weeks after surgery, to rule out the presence of tardive urine leakages or asymptomatic retropubic hematomas. At 12 weeks, all continent patients underwent uroflowmetry to exclude stenosis of the anastomosis. In case of Qmax <15ml/s and normal voided volume, patients underwent RV-CU and flexible cystoscopy.

### *Demographic and perioperative data*

Collected data included: (1) preoperative variables: age, serum PSA at diagnosis, BMI, American Society of Anesthesiologists (ASA) score, DRE, biopsy Gleason Score (GS), D'Amico risk stratification, prostate volume, presence of extracapsular extension (ECE) on mp-MRI; (2) intraoperative variables: estimated blood loss, skin-to-skin operative time (since the insertion of the Veress needle to the suture of surgical wounds), time to complete the anastomosis and time to complete the posterior and the anterior reconstruction, ePLND rate, number of full v. partial v. minimal NS procedures (according to the Pasadena classification [13]); (3) postoperative variables: catheterization and hospitalization time, complications; (4) and pathological variables: prostate volume, tumor volume, percentage of cancer on the whole prostate, pathologic stage (according to TNM), pathology GS, and positive surgical margin rate.

### *Functional data*

Continence evaluation: Preoperative urinary continence was assessed by validated questionnaires, namely the International Continence Society (ICS) male and the International Prostatic Symptoms Score (IPSS) with Urinary Incontinence Quality of Life Scale questionnaires.

The continence rates were assessed at 24 h, and 1, 4, 12, 24 and 48 weeks after catheter removal. After surgery, all patients were instructed to undergo proper pelvic-floor rehabilitation, which started at the time of catheter removal and was performed daily with a gradual increase in training load for a period of 8 weeks. Post-operative continence was evaluated using the Expanded Prostate Cancer Index Composite (EPIC) survey question number 12: ''How many pads or adult diapers per day did you usually use to control leakage during the last 4 weeks?'' To measure continence at catheter removal and 1 week after removal, the question was modified. Patients were defined as continent if they answered ''zero pad'' or ''one safety pad'' per day. In order to evaluate the impact of incontinence on patient's quality of life, a further re-classification of continence was performed retrospectively, according to a recent paper published by Menon et al. [14]. Total continence was defined by the use of no pads or no urinary leakage within a 24-hour period, while social continence was defined by the use of $\leq 1$ pad within a 24-hour period. At week 4, week 12, week 24 and week 48 after catheter removal, all patients were reviewed with the IPSS questionnaire and Urinary Incontinence Quality of Life Scale.

Patients who were still incontinent at weeks 12 and 24 filled voiding diaries for 3-7 days. Furthermore, they were instructed to perform both the 24-h pad weight test for seven days and the standard 1-h pad test. At the week 24 they underwent urodynamics in order to establish the incontinence type. Further treatments for urinary incontinence were recorded.

For evaluation of the secondary end-point a multivariate regression model was performed. The results were used to obtain a nomogram to predict the risk of post-operative incontinence after a RARP with TAR technique.

Potency evaluation: Preoperative erectile function was evaluated by a validated questionnaire, namely the International Index of Erectile Function (IIEF)-5. For patients who underwent NS surgery, potency was defined as the ability to achieve an erection sufficient for intercourse or masturbation with or without the use of a phosphodiesterase type 5 enzyme inhibitor (score >2 at question thirty-two of the EPIC questionnaire: "How would you describe the usual quality of your erections during the last 4 weeks?"). Sexual potency was assessed at 4, 12, 24 and 48 weeks after surgery.

### *Oncologic data*

Serum PSA levels were measured at 4, 12, 24 and 48 weeks after RARP. Patients who received adjuvant therapies during the follow-up period, such as radiotherapy (RT), hormonal treatment (HT), or chemotherapy (CT), were recorded. Biochemical relapse (BCR) was denoted as (1) any

postoperative cancer treatment; or (2) PSA >0.2 ng/mL with a single repeated measurement for confirmation [15].

### *Complications and other surgical interventions*

For the purpose of the study only postoperative complications related to the TAR technique were reported. Indeed, the presence of two non-communicating spaces (the retropubic space and the intraperitoneal cavity) at the end of the surgery, drained separately, allowed us to focus on the complications related to the anastomosis and reconstruction technique. Namely, we considered the following complications: acute urinary retention and catheter removal, urine leakage, retropubic drained hematomas, and anastomosis strictures. Any further intervention after radical prostatectomy performed during follow-up were recorded. Patients who underwent surgery for incontinence were considered as incontinent for functional analysis.

### *Patient satisfaction and health status*

Questions 1 and 46 of the EPIC questionnaire ("In general, would you say your health is"; "Overall, how satisfied are you with the treatment you received for your prostate cancer?", respectively) were administered during the last follow-up visit with the aim of assessing patient satisfaction after surgical intervention and general health status as subjectively perceived by the patient.

### *Statistical Analysis*

Patient characteristics were tested using Fisher's exact test for categorical variables and the Mann-Whitney test for continuous ones. All results for continuous variables were expressed as medians (range) and the frequencies and proportions were reported as percentages.

For the evaluation of the secondary end-point a logistic regression model was performed to evaluate the potential impact of some pre and intra-operative factors on the postoperative urinary continence recovery. The results were shown in terms of Odds Ratio (OR) with their 95% Confidence Interval (95% CI). Model discrimination was assessed using an area under (AUC) the receiver operating characteristic (ROC) curve. A nomogram to predict the risk of post-operative incontinence after RARP with TAR technique was generated based on the logistic model. All the analyses were performed with SAS® Statistics Software.

**RESULTS**

One-thousand-eight patients were enrolled in our study. The mean PSA at diagnosis was 10.31 ($\pm$ 11.61) mg/dL, 280 (27.78%) patients had a positive DRE and the median GS was 7 (6-7). According to the D'Amico classification, 264 (27.33%), 537 (55.59%) and 165 (17.08%) patients had low, intermediate, and high risk respectively. The demographics variables are summarized in Table 1.

Peri-operative data are reported in Table 2. Median catheter removal was 3.5 (3-6) days, and median hospital stay was 6 (4-8) days.

**Functional outcomes**

*Continence outcomes*

The number of continent patients according to our definition, and the number of social continent patients according to Menon were reported in Fig. 1. At 24 h, and 1, 4, 12, 24 and 48 weeks after catheter removal, 621 (61.61%), 594 (58.93%), 803 (79.66%), 912 (90.48%), 950 (94.25%) and 956 (94.84%) patients were continent, respectively. The mean time to continence recovery was 4.05 ($\pm$7.36) weeks after the catheter removal.

Patients who were still incontinent at 12 and 24 weeks after surgery filled the 24h pad test. The mean pad weight after the test was 257 g and 156 g respectively. At 24 weeks, 58 (5.75%) patients were incontinent, 57 with low or mild incontinence, whilst one had severe incontinence, according to the International Continence Society. All the patients underwent urodynamics, which resulted in 3 cases of urge urinary incontinence and in 55 cases of a stress urinary incontinence. During the first year of follow-up, 10 (0.99%) patients underwent surgical treatment for incontinence. Nine patients with a low or mild incontinence underwent a trans-obturatory sling application; one patient with severe incontinence required the application of an artificial urinary sphincter. In all the cases, after surgery for incontinence, patients were continent.

The results of a logistic regression model at different catheter removal time points are reported in Figure 2. The analysed variables had a higher impact on continence recovery at 4 and 12 weeks. At 4 weeks, the post-operative odds of urinary continence recovery increased with the absence of diabetes (OR 2.76, 95% CI 1.41-5.41) and D'Amico low v. high risk (OR 2.01, 95% CI 1.01-3.99). At 12 weeks, increased with the absence of diabetes (OR 3.01, 95% CI 1.23-7.35), D'Amico low v. high risk (OR 4.04, 95% CI 1.56-10.47), and D'Amico intermediate v. high risk (OR 3.33, 95% CI 1.66-6.70). ROC curves were drawn and an AUC value of 61.9% (95% CI 57.49-66.36) at 4 weeks and 63.8% (95% CI 58.03-69.65) at 12 weeks were computed (Fig. 3a-b). The best cut-off values

were 40 at 4 weeks and 60 at 12 weeks. Based on these parameters, two nomograms (at 4 and 12 post-operative weeks) were generated (Fig. 4a-b).

*Potency outcomes*

Eighteen (2.56%) patients reported an andrological drop out and were excluded from the analysis on potency recovery. Considering only patient who underwent a bilateral full NS procedure, the potency recovery rate was 24.82%, 38.20%, 58.10%, 67.74%, and 74.90% at 1, 3, 6, and 12 months, respectively. The mean time for potency recovery was 3.32 ($\pm$3.16) months after the surgery.

## Pathological findings and oncological outcomes

Pathological findings are reported in Table 3. 22.87% apical positive surgical margins were recorded. During the follow-up period, 78 (8.32%) patients experienced a BCR. The mean time to recurrence was 10.2 ($\pm$11,82) months after the surgery. One-hundred-twenty-seven (13.86%) patients underwent RT, 89 (70.08%) adjuvant and 38 (29.92%) salvage RT; 95 (10.57%) patients underwent post-operative HT.

## Complications and other surgical interventions

An acute urinary retention was recorded in 37 patients, all of them treated with corticosteroids and re-catheterization for a total of 5 days.

Urine leak was diagnosed in 25 cases, leading to catheter maintenance or to re-catheterization. The catheter was maintained for a minimum of 7 days, after which patients underwent pelvic US and cystography to schedule its removal. In one case the leakage was accompanied by fever.

Symptomatic and/or large retropubic hematomas ($\geq$10 cm) were recorded in 22 cases. All of them were treated with a small suprapubic incision and surgical drainage within 24 hours to prevent the accumulation of blood in an enclosed space and therefore damage to the anastomosis due to an increased tension. In two cases, a blood transfusion was necessary. In three cases the hematoma was accompanied by fever.

Finally, 5 stenosis of the anastomosis were diagnosed within six months from the surgery. Four patients with a sub-stenosis were treated with a urethral dilatation under direct vision during a flexible cystoscopy, whilst one patient underwent a laser urethral incision, without stenosis relapse during the follow-up.

## Quality of life outcomes

At one year follow-up 96% of patients were "completely satisfied" or "satisfied" after the surgery for prostate cancer, and 98% of patients rated their own health status as "excellent", "very good", or "good".

**DISCUSSION**

Our results of more than 1000 RARP with TAR at one-year minimum follow-up confirmed the preliminarily published data on continence rates [12], and the excellent safety profile of the technique.

The impact of urinary incontinence after radical prostatectomy on patient's quality of life has driven the development of more refined surgical techniques [16]. It is well known that the preservation of a pelvic normal anatomy is of utmost importance to maintain a good postoperative urinary continence [17], together with the application of some reconstructive techniques which could influence early postoperative continence recovery [18].

Focusing on the reconstruction phase, with the evolution of the surgical techniques many authors combined an anterior with a posterior reconstruction, demonstrating improvements in functional outcomes [19]. Nevertheless, the results of some randomized controlled trials showed opposite results. On one side, some authors like Sammon et al. [20] and Menon et al. [21] found no differences in terms of early or late continence recovery when adding anterior and posterior reconstruction to conventional anastomosis; on the other side, authors like Koliakos et al. [22] and Hurtes et al. [23] found better and earlier continence recovery applying reconstructive techniques. More recently, two total vesico-urethral anastomosis reconstruction techniques were described. The first one was published in 2008 by Tewari et al [24] and was composed by a reattachment of the arcus tendineus to the lateral aspect of the bladder neck and a refixation of the puboprostatic ligaments to the anterior aspect of the anastomosis. The second one, the TAR technique, was published by our group in 2016 [12]. Both techniques showed an early recovery of urinary continence. According to these results, in a recent meta-analysis investigating the comparison of total v. non-total reconstruction techniques in recovery of continence, Wu et al. demonstrated the superiority of total reconstruction techniques in terms of shorter recovery of continence after radical prostatectomy at every time point [25]. Concerning early recovery of continence, the outcomes were statistically in favor of the total reconstruction techniques at 1 week (OR 2.76, 95% CI 1.58-4.84, $p < 0.001$), 2 weeks (OR 2.57, 95% CI 1.74-3.80, $p < 0.001$), 4 weeks (OR 2.61, 95% CI 1.56-4.38, $p < 0.001$), and 12 weeks (OR 4.33, 95% CI 2.01-9.33, $p < 0.001$) after surgery.

In 2010, the introduction of robotic surgery favored the development of a new approach to performing an RARP, the so-called "Retzius-sparing" or "posterior approach" prostatectomy [26]. The technique consisted of performing the prostatectomy through a posterior plane going directly through the Douglas space and avoiding any dissection of the anterior compartment, demonstrating excellent results in terms of continence and potency recovery. Once the posterior approach was

introduced, one randomized comparative study with the standard anterior approach was made. Dalela et al. compared the short-term urinary continence rates of patients with low and intermediate-risk localised prostate cancer, randomized to receive either posterior (n=60) or anterior (n=60) RARP [27]. The urinary continence (defined as 0 pads/one security pad per day) at one week, 4, 8, and 12 weeks after catheter removal was reached by 71%, 83%, 88%, and 95% of men undergoing the posterior approach v. 48%, 67%, 72%, and 86% undergoing the anterior approach, respectively (p = 0.02).

Even if the RCT provided a high evidence to support early return to continence with posterior RARP, those functional results must be weighted against some caveats [28]. First is the higher rate of positive surgical margins (25% v. 13% for posterior v. anterior RARP), with a not significant p-value mostly due to the small sample size and considering that the primary outcome was continence. Second is the selection of patients with low or favorable intermediate risk disease. Third is the steep learning curve.

In this scenario, the TAR technique can be considered an excellent compromise between an anterograde prostatectomy with a partial reconstruction and a posterior prostatectomy, allowing the achievement of an excellent early recovery of continence with a negligible rate of related complications and a satisfactory positive margins rate, as demonstrated in a consecutive series of patients with any risk PCa. The early recovery of continence reported (90.48% at 12 weeks) was possible because of the standardized technique based on two cornerstones which allowed for tension-free anastomosis: the anatomical dissection of the prostatic apex; and the protection of the anastomosis by reconstructing three posterior layers and two anterior layers. Moreover, three other aspects derived from the surgical technique are to be highlighted. First was the short catheterization time (median of 3.5 days). Second was the low rate of related complications to the technique. Both of them derived from the meticulous tension-free urethro-vesical anastomosis and reconstruction of the peri-urethral structures. Third was the relatively low rate of apical margins (22.87%), which confirmed the safety of a meticulous apical dissection.

Regarding continence outcomes of our study more deeply, we developed two preoperative nomograms predicting urinary continence recovery after RARP with TAR including three significant variables: age, D'Amico risk classification and presence of diabetes. At 1 week, patients without diabetes and with a D'Amico risk low or intermediate were significantly more continent. At 4 weeks, absence of diabetes was still important, while the D'Amico score became insignificant, though at the limits. On the contrary, age <66 years old was now significant. At 12 weeks, absence of diabetes, D'Amico risk low or intermediate and age <66 years old were significant in order to

recover continence. At 24 and 48 months, only a D'Amico risk low or intermediate remained significant. In order to know the nomograms reliability, ROC curves were performed. As we expected, the nomogram at 4 weeks was less performing than the 12 weeks one, because the D'Amico score at 4 weeks was less significant. However, the AUC was good in both cases (61.9% at 4 weeks and 63.8% at 12 weeks). The absence of any variable directly related to the surgical approach (e.g., the grade of NS) was probably due to the precise standardization of the TAR technique from the beginning of the study, which led to reach a plateau phase early in the learning curve of the first surgeon. Moreover, it permits administration of the nomogram before the surgery, to predict which patients will not recover continence after surgery, making this tool a useful adjunct for pre-operative counselling.

Concerning the literature, as reported by a recent systematic review by O'Callaghan et al., seven nomograms on the prediction of urinary incontinence in patients who had undergone radical prostatectomy were externally validated [29]. Among them, only two tools were reported to have a c-index >70% (e.g., good accuracy). Matsushita et al. studied 2849 patients who underwent robot-assisted or open radical prostatectomy. Authors reported an AUC value of 72.9% and 70.9% at 6 and 12 months, respectively, for the prediction of social continence [30]. The second study was conducted by Jeong et al., including 1168 men treated with robot-assisted or open radical prostatectomy. The accuracy for the prediction of continence was reported as 71.1% [31]. In both studies, the cohort was split to achieve an external validation of the model. A more recent model was published by Tienza et al. in 2018, including age, prior prostate surgery, membranous urethral length and urethral wall thickness as risk factors for urinary incontinence after radical prostatectomy in 746 men. The predictive accuracy and the AUC value of the model were 78.7% and 71.7%, respectively. The main limitation of the study was the non-systematic surgical approach [32].

In the near future, the intra-operative use of bioengineering materials aimed at neuro-regeneration to improve urinary continence recovery may allow us to start treating post-operative incontinence "during surgery", while also implementing the results of future nomograms [33-35].

The strengths of the study are the large series considered in a limited period of time, the use of a standardized and reproducible surgical technique that permitted the obtaining of successful results on post-operative continence from the beginning of the study, and the meticulous study of the post-operative incontinence with a clear description of the type and treatment of incontinence type.

Nevertheless, the study is not free of limitations. First of all is the lack of randomization, even if it was performed in a prospective fashion and was based on a consecutive series of patients.

Moreover, the study lacks a comparison with other techniques to compare functional outcomes. The

predictive models created were based on a population from a single tertiary hospital treated by a single experienced surgeon, which thus may limit their widespread use, even if it permitted standardization of the procedure. For the same reasons, our nomogram requires external validation in a multicentre study to verify its applicability in a general context and to consider it for routine clinical implementation.

In conclusion, the TAR technique confirmed excellent results in the early recovery of urinary continence, as well as a low catheterization time, and a low rate of related complications, even if at a short-term follow-up, the oncologic results were not affected. Two nomograms were created, to predict pre-operatively the post-operative odds of urinary continence recovery at 4 and 12 weeks after RARP by integrating the presence of diabetes and the D'Amico risk classification.

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**FIGURE LEGENDS**

**Fig. 1.** Post-operative continence recovery rate according to our definition and the Menon definition.

**Fig. 2.** Logistic regression models were performed to evaluate the potential impact of perioperative factors on the postoperative urinary continence recovery; results were showed as OR and relative 95% CI. OR of the main variables (dots) with their 95% CI (horizontal bars) are shown at 1 week (a), 4 weeks (b), 12 weeks (c), 24 weeks (d) and 48 weeks (e). BCR = biochemical recurrence; CI = confidence interval; ECE = extracapsular extension; HT = hormonal therapy; NS = nerve sparing; OR = odds ratio; pT = pathologic stage T; RT = radiotherapy.

**Fig. 3**. ROC curves of the two models at 4 (a) and 12 (b) weeks were performed. The blue line represents the relationship between 1-Specificity (x axis) and Sensitivity (y axis). The AUC shows the reliability of the model. The bisector represents an AUC of 50%. AUC = Area Under the Curve; ROC = Receiver Operating Characteristic.

**Fig. 4**. Nomograms at 4 (a) and 12 (b) weeks were performed. The total score is calculated by summing the partial scores.

Fig. 1



Fig. 2

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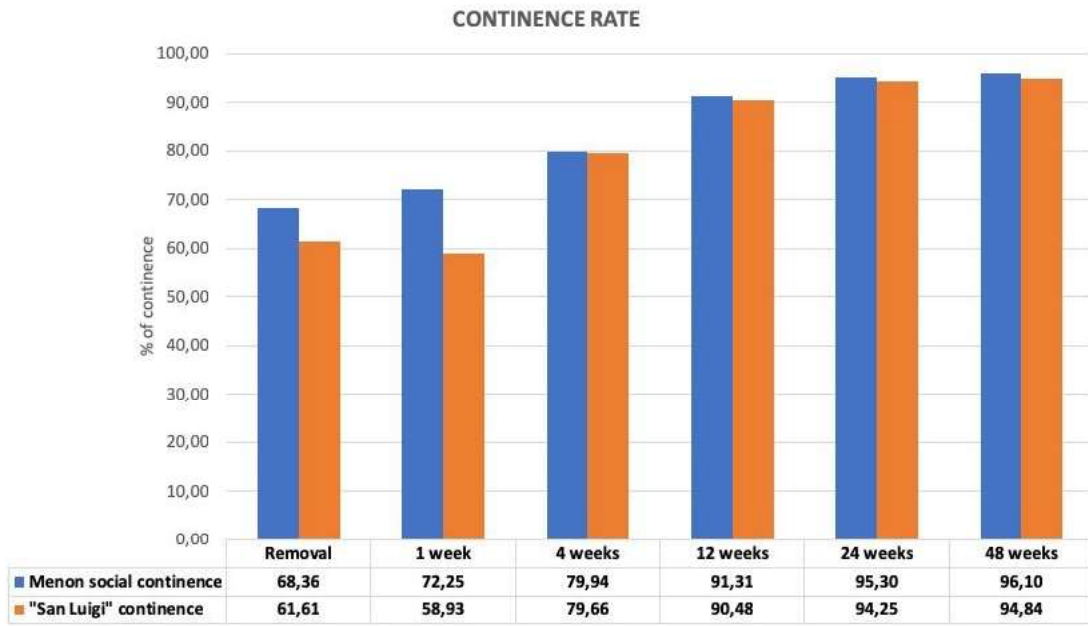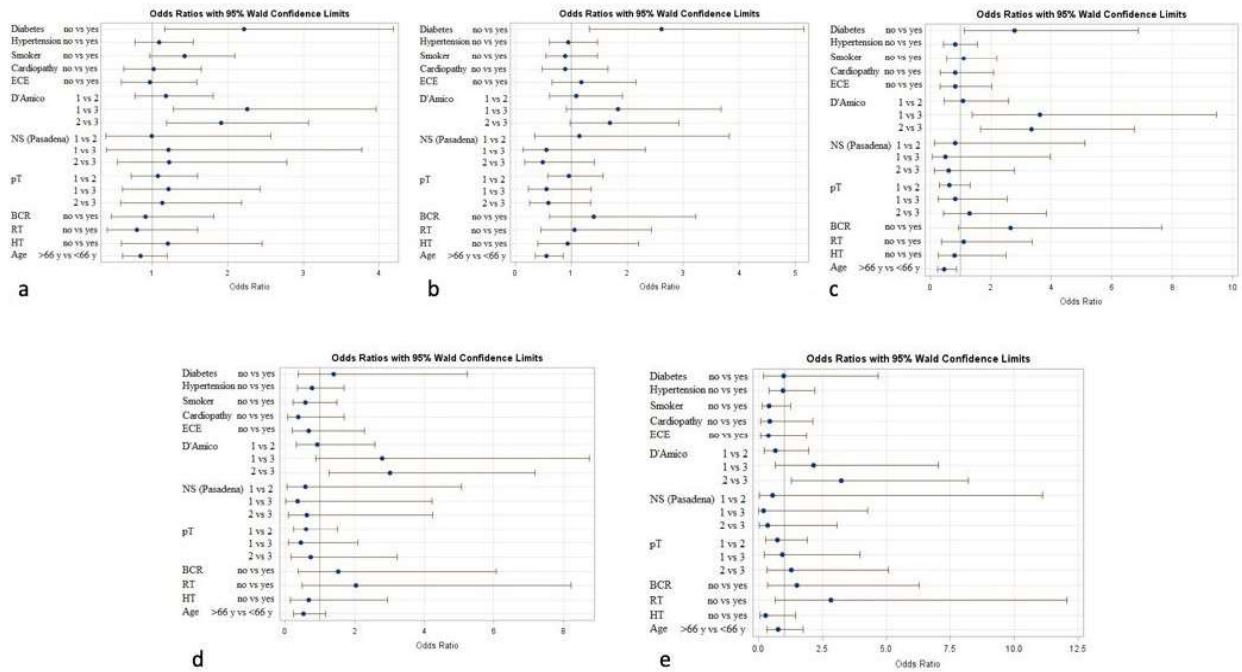44
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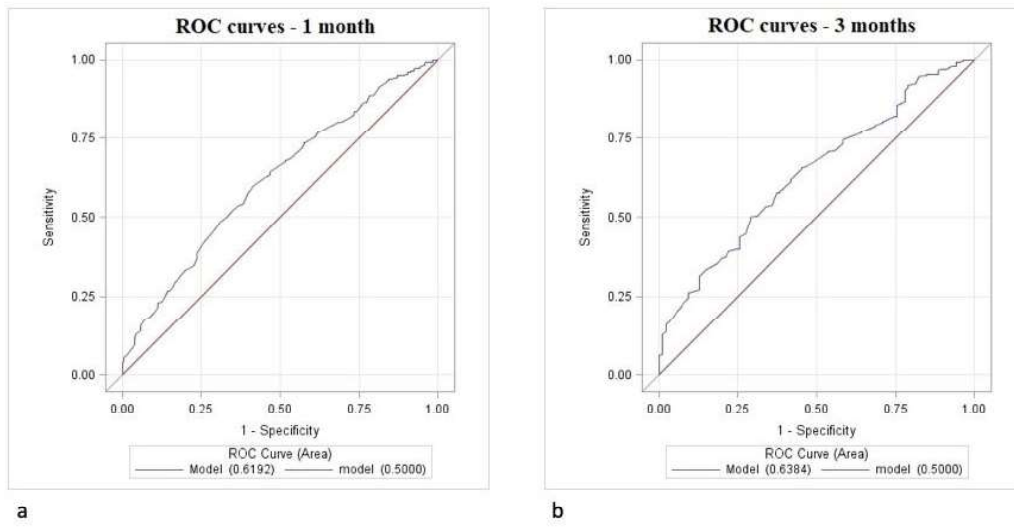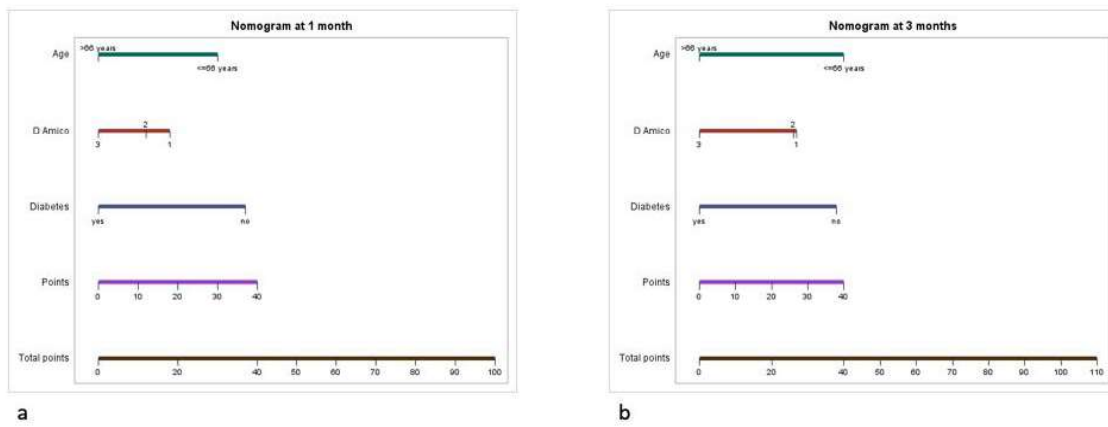54
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Fig. 3



Fig. 4

| Table 1. | |
|---|---|
| **Number of patients** | 1008 |
| **Age, years; mean (SD)** | 64.84 (6.76) |
| **BMI; mean (SD)** | 26.47 (3.11) |
| **Diabetes; number (%)** | 71 (7.04) |
| **Smoke; number (%)** | 268 (26.59) |
| **Hypertension; number (%)** | 443 (43.95) |
| **Cardiopathy; number (%)** | 138 (13.69) |
| **PSA, ng/ml; mean (SD)** | 10.31 (11.61) |
| **Positive DRE; number (%)** | 280 (27.78) |
| **Prostate volume (TRUS), ml; mean (SD)** | 49.47 (21.74) |
| **Biopsy GS; median (IQR)** | 7 (6-7) |
| **ASA score; median (IQR)** | 2 (2-2) |
| **IPSS score (pre-operatively); median (IQR)** | 7 (5-11) |
| **IIEF-5 score (pre-operatively); median (IQR)** | 18 (15-21) |
| **D'Amico classification; number (%)** | |
| • **Low-risk PCa** | 264 (27.33) |
| • **Intermediate-risk PCa** | 537 (55.59) |
| • **High-risk PCa** | 165 (17.08) |

Table 1. Preoperative variables. ASA score = American Society of Anesthesiologist score; BMI = body max index; DRE = digital rectal exploration; GS = Gleason score; IIEF = International Index of Erectile Function; IPSS = International Prostate Symptoms Score; IQR = interquartile range; PSA = prostate specific antigen; SD = standard deviation; TRUS = transrectal ulltrasound.

| Table 2. | |
|---|---|
| **Operative time, min; mean (SD)** | 117.28 (26.05) |
| **Lymphadenectomy; number (%)** | 583 (57.8) |
| **Nerve sparing approach; number (%)** | |
| • **Full NS** | 102 (10.12) |
| • **Partial NS** | 408 (40.48) |
| • **Minimal NS/not performed** | 498 (49.4) |
| **Blood losses, ml; mean (SD)** | 250.75 (64.44) |
| **Catheterization time, days; median (IQR)** | 3.5 (3-6) |
| **Hospital stay, days; median (IQR)** | 6 (4-8) |
| **Transfusions; number (%)** | 18 (1.78) |
| **TAR-related post-operative complications; number (%)** | |
| • **Acute urinary retention** | 37 (3.67) |
| • **Urine leak** | 25 (2.48) |
| • **Retropubic drained hematomas** | 22 (2.18) |
| • **Stenosis of anastomosis** | 5 (0.49) |

Table 2. Perioperative variables. IQR = interquartile range; NS = nerve sparing; SD = standard deviation.

| Table 3. | |
|---|---|
| **Positive margins; number (%)**<br>• **Total**<br><br>• **pT2**<br>• **pT3**<br>• **pT4**<br><br>• **Apical**<br>• **Equatorial**<br>• **Basal** | 241 (23.91)<br><br>90/549 (16.58)<br>151/458 (32.97)<br>1/1 (100)<br><br>75/328 (22.87)<br>97/400 (24.25)<br>64/280 (22.86) |
| **Prostate volume, ml; mean (SD)** | 44.16 (12.14) |
| **Tumor volume, ml; mean (SD)** | 24.20 (2.06) |
| **% tumor; mean (SD)** | 15.78 (5.51) |
| **Stage; number (%)**<br>• **pT2**<br>• **pT3**<br>• **pT4** | 549 (54.46)<br>458 (45.44)<br>1 (0.1) |
| **Pathology GS; number (%)**<br>• **≤6**<br>• **7 (3+4)**<br>• **7 (4+3)**<br>• **8-10** | 97 (9.66)<br>452 (44.89)<br>310 (30.75)<br>148 (14.7) |

Table 3. Histopathological data. GS = Gleason Score; pT = pathologic stage T; SD = standard deviation.