Postoperative Non-Surgical Interventions to Improve Urinary Continence After Robot-Assisted Radical Prostatectomy: A Systematic Review

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Abstract

Background  The occurrence of postoperative urinary incontinence (UI) remains a problem for patients undergoing robot-assisted radical prostatectomy (RARP). Non-surgical interventions (NSI) in addition to intraoperative techniques and patient behavioral changes have been proposed to improve urinary continence (UC) recovery after RARP. However, to date, the real clinical impact of postoperative NSI remains not well characterized.

Materials and Methods  We performed a Systematic Review in April 2021, using Allied and Complementary Medicine (AMED), Embase, and MEDLINE according to the PRISMA recommendations and using the Population, Intervention, Comparator and Outcome (PICO) criteria. Primary outcome of interest was the impact of NSI on UC recovery rate and time to achieve UC after RARP. Secondary outcomes of interest were the assessment of patient adherence to NSI, risk factors associated with UI, and correlation between postoperative NSI and sexual activity recovery.

Results  A total of 2758 articles were screened, and 8 full texts including 1146 patients were identified (3 randomized controlled trials, 3 prospective single-arm trials, and 2 retrospective series). Postoperative NSI of interest included pelvic floor muscle training (PFMT) (n = 6 studies) and administration of oral medications (solifenacin) (n = 2 studies). PFMT appeared to increase UC rates and to accelerate time to achieve UC in the early postoperative period. Similarly, solifenacin provided higher rates of UC recovery and contributed to a certain degree of symptomatic relief. There was a great variability regarding NSI features and data reporting among studies. Major limitations were the small sample sizes and the short follow-up.

Conclusion  Postoperative NSI to manage UI after RARP include PFMT and solifenacin administration. Both seem to modestly improve early UC recovery. Nonetheless, evidence supporting their routinely use is still weak and lacks appropriate follow-up to evaluate possible benefits on long-term UC recovery.

Introduction

Radical prostatectomy (RP), together with radiotherapy, represents the gold standard of care for patients with intermediate- to high-risk clinically localized prostate cancer (PCa). Minimally invasive approaches have demonstrated non-inferior functional outcomes compared with open surgery and have a good safety profile. In this context,
Postoperative Non-Surgical Interventions to Improve Urinary Continence After Robot-Assisted Radical Prostatectomy: A Systematic Review

Abbreviations

NSI non-surgical interventions
PCa prostate cancer
PFMT pelvic floor muscle training
RARP robot-assisted radical prostatectomy
RCT randomized controlled trial
RP radical prostatectomy
UC urinary continence
UI urinary incontinence

The population of interest consisted of patients who had undergone RARP for PCa (P). Postoperative NSI for the management of post-RARP UI were the evaluated interventions (I). A no-NSI comparator was considered mandatory for the specific purpose of the current review (C). The primary aim was to evaluate the impact of NSI strategies in UC recovery after RARP in terms of UC rate and/or time to achieve UC. Secondary aims were to identify patient compliance with these treatments, risk factors associated with UI, and correlation between UC restoration and sexual activity recovery (O).

The treatment options of interest included postoperative non-surgical strategies to manage UI and to improve UC recovery. Stress, urgency, and mixed UI were taken into consideration, and UC was defined according to validated questionnaires.

**Literature Search**

A systematic web search was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines on April 19, 2021, through the Ovid platform with no time restrictions, using Allied and Complementary Medicine (AMED), Embase, and MEDLINE databases. The terms “continence” and “incontinence” were pooled together with the Boolean operator “OR.” The terms “RARP” and “robot radical prostatectomy” were pooled together with the Boolean operator “AND.” The web search was supplemented by a manual search (authors consultation and references of included articles). Two authors (L.C. and G.M.) independently screened all items. Disagreements were resolved through discussion or by consultation with a third and senior author (R.S.S.). Only full-text publications in English were considered.

We included all randomized controlled trials (RCTs) and prospective and retrospective series without restrictions. We excluded studies not providing (1) details on UI rate before and after RARP; (2) details on NSI; (3) continence rates after surgery; (4) appropriate definitions to categorize type and severity of UI including either the number of pads used/day or pre-defined validated questionnaires. Case reports, editorials, letters, reviews, and meeting abstracts were excluded.

Risk of bias and study quality were assessed according to European Association of Urology recommendations for performing systematic reviews and meta-analysis[15]. The Cochrane Risk of Bias assessment tool was used for RCTs and the quality appraisal tool for case series using a modified Delphi technique for retrospective studies[16] (Table 1).

**Results**

Figure 1 details the literature search strategy and the included/excluded studies. Of 2758 identified abstracts,
we included 8 studies (3 RCTs, 3 prospective single-arm trials, and 2 retrospective series) reporting results of UC recovery following postoperative NSI of 1146 patients who had undergone RARP for PCa. Overall, 2 NSI strategies to improve UC recovery after RARP were found: pelvic floor muscle training (PFMT) (n = 6 studies) and solifenacin oral administration (n = 2 studies). Only 1 RCT was a multicenter study [17]. Population sizes ranged between 39 and 623 patients. Among the studies on PFMT efficacy, 4 out of 6 had a control group [18–21]. More precisely, the study by Sayilan et al. compared PFMT with no intervention [20], while the other included studies compared modified PFMT strategy, including ultrasound-guided, biofeedback and visual-feedback PFMT, with the conventional one [18,19,21]. Among the studies on solifenacin oral administration safety and efficacy, Liss and colleagues conducted a single-arm prospective clinical trial [22], while Bianco et al. performed a multicenter RCT with a placebo arm as control group [17].

Overall, NSI duration of treatments ranged from 1 to 3 months after surgery. Primary endpoints were UC recovery rate and time to UC in the majority of the studies. Follow-up periods ranged from 1 month to 9 months, with most of studies reporting 3 months post bladder catheter removal urinary outcomes.
Reported rates of UC varied between a minimum of 29.1% at 3 months in patients treated with solifenacin[17] to a maximum of 100% at 6 months in patients who have performed PFMT[21].

Overall, 3 out of 5 studies comparing NSI group with a control group showed a statistically significant advantage of NSI in UC recovery rate[17,20,21] whereas 2 studies did not find significant differences among groups within the follow-up period[18,19]. Regarding the time to achieve UC after RARP, PFMT has shown to decrease time to UC recovery in 2 studies with mean time ranging from 32 to 75±100 days[18,21]. Similarly, in the study by Liss et al., mean time to achieve UC was 95 days in patients treated with solifenacin[22].

Tables 2A, 2B, 3A, and 3B show patient characteristics and general information for the included studies.

Among studies reporting urinary outcomes after PFMT, we found 100% adherence to treatment: no patient with complete follow-up dropped out the exercises for any reason. The rate of adherence to NSI among patients receiving pharmacological treatment was 85% to 100%, demonstrating its good tolerability and safety profile. Overall, 2 studies reported post-RARP UI risk factors[21,23] and 1 reported data on patients’ sexual activity recovery[19].

Tables 4A and 4B show secondary outcomes of the current systematic review.

**Studies on Pelvic Floor Muscle Training**

Yoshida et al. conducted a prospective cohort study of 116 men undergoing RARP to examine whether transperineal ultrasound-guided PFMT promoted early UC recovery after surgery[16]. Overall, 36 men received US-guided PFMT (interventional group), and 80 received only verbal instructions for PFMT (control group). Continence was defined as time in days needed to require a small pad (20g) per day by patient self-report. Mean time for UC recovery was significantly shorter in the intervention group than in the control group (75±100 versus 121.8±132 days; P = 0.037). Moreover, UC rates were higher in the intervention group at 30 days (52.8% versus 35.4%; P = 0.081); however, at 9 months no statistically significant differences were found between the 2 groups in terms of continence status (P = 0.558).

Oh et al. performed an RCT with 84 patients who had undergone RARP to investigate the effectiveness of an extracorporeal biofeedback device (Anykegel) for PFMT on UC recovery[19]. Overall, 42 patients received biofeedback PFMT using the Anykegel device, and 42 patients received PFMT with only oral and written instructions. UC was defined as a loss of 0 g of urine on a 24-hour pad test. In addition, patients were also asked to complete the International Prostatic Symptoms Score (IPSS) with QoL and International Index of Erectile Function (IIEF) questionnaires to identify differences from the baseline during the follow-up period (secondary outcomes). The follow-up duration of the study was 3 months, with control visits at 1, 2, and 3 months after catheter removal. In the intervention group, the authors found a statistically significant smaller volume of urine loss at 1 month than in the control group (71 g versus 120.8 g; P = 0.028). However, at 2 and 3 months no differences were reported between the 2 groups. Likewise, the rate of continent patients was similar between the intervention and control groups throughout the study follow-up. At the end of the study, 67.5% and 61.9% of patients were continent, in the intervention and control groups, respectively. Similarly, no differences were found among groups in terms of IPPS, QoL, and IIEF, despite the intervention group demonstrating a favorable change from the baseline to the 1-month follow-up visit in IPSS score.

Sayilan and colleagues conducted an RCT to determine the effect of PFMT after RARP in UC recovery[20]. The 30 patients of the intervention group were taught to perform Kegel exercises 3 times a day for 6 months after surgery, while the control group of 30 patients did
### TABLE 2A.
General features of included studies on PFMT to improve UC recovery after RARP

<table>
<thead>
<tr>
<th>Authors</th>
<th>Accrual, year</th>
<th>Center</th>
<th>Study type</th>
<th>Intervention</th>
<th>Duration of treatment</th>
<th>Primary endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoshida et al.</td>
<td>2018</td>
<td>Japan</td>
<td>Prospective cohort study</td>
<td>US-guided PFMT vs. verbal-PFMT</td>
<td>Preoperatively and 1 month after RARP</td>
<td>Time to UC recovery</td>
</tr>
<tr>
<td>Oh et al.</td>
<td>2020</td>
<td>Korea</td>
<td>RCT</td>
<td>Biofeedback-PFMT vs. verbal-PFMT</td>
<td>3 month after RARP</td>
<td>Time to UC recovery</td>
</tr>
<tr>
<td>Sayilan et al.</td>
<td>2018</td>
<td>Turkey</td>
<td>RCT</td>
<td>PFMT vs. no intervention</td>
<td>Preoperatively to 6 months after RARP</td>
<td>Self-reported UC recovery at 6 months</td>
</tr>
<tr>
<td>Pan et al.</td>
<td>2019</td>
<td>Taiwan</td>
<td>Prospective</td>
<td>Resistance band PFMT</td>
<td>3 month after RARP</td>
<td>Improvement in UC recovery, QoL, anxiety and depression after RARP</td>
</tr>
<tr>
<td>Manley et al.</td>
<td>2016</td>
<td>Australia</td>
<td>Retrospective</td>
<td>PFMT</td>
<td>Preoperatively to 1 month after RARP</td>
<td>PFM stength</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>2021</td>
<td>Korea</td>
<td>Retrospective</td>
<td>Visual feedback PFMT vs conventional PFMT</td>
<td>1 month</td>
<td>Time to UC recovery</td>
</tr>
</tbody>
</table>

### TABLE 2B.
General features of included studies on solifenacin administration to improve UC recovery after RARP

<table>
<thead>
<tr>
<th>Authors</th>
<th>Accrual, year</th>
<th>Center</th>
<th>Study type</th>
<th>Intervention</th>
<th>Duration of treatment</th>
<th>Primary endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liss et al.</td>
<td>2014</td>
<td>United States</td>
<td>Prospective clinical trial</td>
<td>Solifenacin 5mg daily</td>
<td>3 months</td>
<td>Safety and 3 months UC recovery</td>
</tr>
<tr>
<td>Bianco F. et al.</td>
<td>2015</td>
<td>United States</td>
<td>RCT</td>
<td>Solifenacin vs. placebo</td>
<td>3 months</td>
<td>Time to UC recovery</td>
</tr>
</tbody>
</table>
## Table 2A.
General features of included studies on PFMT to improve UC recovery after RARP

<table>
<thead>
<tr>
<th>Authors</th>
<th>Accrual, year</th>
<th>Center</th>
<th>Study type</th>
<th>Intervention</th>
<th>Duration of treatment</th>
<th>Primary endpoint</th>
<th>Exclusion criteria</th>
<th>n of patients</th>
<th>UC rate (% pts)</th>
<th>Mean time to UC recovery</th>
<th>Definition of UC</th>
<th>Questionnaires / urodynamic evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoshida et al. 2018</td>
<td>Japan</td>
<td>Prospective cohort study</td>
<td>US-guided PFMT vs. verbal-PFMT</td>
<td>Preoperatively and 1 month after RARP</td>
<td>Time to UC recovery</td>
<td>Severe mental disease or cognitive impairment, neurological disorder affecting urinary tract, inability to understand Japanese</td>
<td>36 vs. 80</td>
<td>88.9% vs. 84.7% at 9 months ($P = 0.558$)</td>
<td>75±100 vs. 121.8±132 days ($P = 0.037$)</td>
<td>1 small pad (20g)/day</td>
<td>None / None</td>
<td></td>
</tr>
<tr>
<td>Oh et al. 2020</td>
<td>Korea</td>
<td>RCT</td>
<td>Biofeedback-PFMT vs. verbal-PFMT</td>
<td>3 month after RARP</td>
<td>Time to UC recovery</td>
<td>Neurologic deficiency, previous pelvic radiation therapy or urological surgery, total incontinence at catheter removal</td>
<td>42 vs. 42</td>
<td>67.5% vs. 61.9% at 3 months ($P = 0.649$)</td>
<td>not reported</td>
<td>loss of 0g on a 24h pad test</td>
<td>IPSS, IIEF-5 / None</td>
<td></td>
</tr>
<tr>
<td>Sayilan et al. 2018</td>
<td>Turkey</td>
<td>RCT</td>
<td>PFMT vs. no intervention</td>
<td>Preoperatively to 6 months after RARP</td>
<td>Self-reported UC recovery at 6 months</td>
<td>Urinary incontinence before RARP, BMI&gt;30, age&lt;30 or &gt;75 years, absence of elementary school level of education</td>
<td>30 vs. 30</td>
<td>50% vs. 3.3% at 6 months ($P = 0.001$)</td>
<td>not reported</td>
<td>ICIQ-UI score of zero</td>
<td>ICIQ-SF / None</td>
<td></td>
</tr>
<tr>
<td>Pan et al. 2019</td>
<td>Taiwan</td>
<td>Prospective</td>
<td>Resistance band PFMT</td>
<td>3 month after RARP</td>
<td>Improvement in UC recovery, QoL, anxiety and depression after RARP</td>
<td>age &lt; 40 years, patients uncapable of verbal communication or of getting out of bed and moving without assistance, UI before surgery, UTI before surgery, patients not able to lie in supine position</td>
<td>43</td>
<td>34.9% at 3 months</td>
<td>not reported</td>
<td>Using Urinary Incontinence Scale after RP (UISRP)</td>
<td>UISRP, IIQ, HADS / None</td>
<td></td>
</tr>
<tr>
<td>Manley et al. 2016</td>
<td>Australia</td>
<td>Retrospective</td>
<td>PFMT</td>
<td>Preoperatively to 1 month after RARP</td>
<td>PFM strength</td>
<td>The requirement of no continence aids</td>
<td>98</td>
<td>49.4% at 1 month</td>
<td>not reported</td>
<td>The requirement of no continence aids</td>
<td>None / None</td>
<td></td>
</tr>
<tr>
<td>Kim et al. 2021</td>
<td>Korea</td>
<td>Retrospective</td>
<td>Visual feedback PFMT vs conventional PFMT</td>
<td>1 month</td>
<td>Time to UC recovery</td>
<td>Previous pelvic RT, poor compliance due to psychiatric or medical problems, previous prostate surgery, &lt; 3 months FU</td>
<td>41 vs. 42</td>
<td>100% vs. 88.1% at 6 months ($P = 0.023$)</td>
<td>32.4 vs. 95.3 days ($P&lt;0.001$)</td>
<td>Cessation of pad use</td>
<td>None / None</td>
<td></td>
</tr>
</tbody>
</table>

## Table 2B.
General features of included studies on solifenacin administration to improve UC recovery after RARP

<table>
<thead>
<tr>
<th>Authors</th>
<th>Accrual, year</th>
<th>Center</th>
<th>Study type</th>
<th>Intervention</th>
<th>Duration of treatment</th>
<th>Primary endpoint</th>
<th>Exclusion criteria</th>
<th>n of patients</th>
<th>UC rate (% pts)</th>
<th>Mean time to UC recovery</th>
<th>Definition of UC</th>
<th>Questionnaires / urodynamic evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liss et al. 2014</td>
<td>United States</td>
<td>Prospective clinical trial</td>
<td>Solifenacin 5mg daily</td>
<td>3 months Safety and 3 months UC recovery</td>
<td>95 (61–202) days</td>
<td>0 pads/ day</td>
<td>&lt; 3 pads/day</td>
<td>39</td>
<td>53.8% at 3 months</td>
<td>95 (61–202) days</td>
<td>AUA symptom score / Yes</td>
<td></td>
</tr>
<tr>
<td>Bianco F. et al. 2015</td>
<td>United States</td>
<td>RCT</td>
<td>Solifenacin vs. placebo</td>
<td>3 months Time to UC recovery</td>
<td>not reported</td>
<td>&lt; 2 pads/day or 1 dry safety pad/day</td>
<td>313 vs. 310</td>
<td>29.1% vs. 21.4% at 3 months ($P = 0.04$)</td>
<td>not reported</td>
<td>0 pads/ day or 1 dry safety pad/day</td>
<td>None / None</td>
<td></td>
</tr>
</tbody>
</table>

*SIUJ.ORG*
TABLE 3A.
Patient baseline and pathological features (PFMT cohorts)

<table>
<thead>
<tr>
<th>Authors</th>
<th>n of patients</th>
<th>Age (years)</th>
<th>BMI (Kg/m²)</th>
<th>PSA (ng/mL)</th>
<th>Prostate volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoshida et al.</td>
<td>36 vs. 80</td>
<td>66.5 (±6.2) vs. 66.6 (±5.8)</td>
<td>24.4 (±3.2) vs. 24 (±2.9)</td>
<td>11.3 (±11.8) vs. 10.3 (±8.5)</td>
<td>48.3 (±15.7) vs. 47.6 (±20.4)</td>
</tr>
<tr>
<td>Oh et al.</td>
<td>40 vs. 42</td>
<td>67.5 (±6.9) vs. 65.9 (±6.8)</td>
<td>24.8 (±2.6) vs. 24.6 (±2.7)</td>
<td>19.7 (±28.1) vs. 15 (±16.3)</td>
<td>33.7 (±10.6) vs. 36.9 (±11.9)</td>
</tr>
<tr>
<td>Sayilan et al.</td>
<td>30 vs. 30</td>
<td>63 (±8.61) vs. 59.93 (±6.98)</td>
<td>26.4 vs. 25.8</td>
<td>– – –</td>
<td>– – –</td>
</tr>
<tr>
<td>Pan et al.</td>
<td>43</td>
<td>65</td>
<td>25</td>
<td>9.7</td>
<td>47</td>
</tr>
<tr>
<td>Manley et al.</td>
<td>98</td>
<td>64 (49 - 77)</td>
<td>–</td>
<td>5.2 (4.5 - 7.1)</td>
<td>– –</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>41 vs. 42</td>
<td>68.4 (±5.98) vs. 67.7 (±4.9)</td>
<td>–</td>
<td>45.4 (±78.7) vs. 16.8 (±20.5)</td>
<td>33.8 (±15.2) vs. 36.2 (±13.8)</td>
</tr>
</tbody>
</table>

TABLE 3B.
Patient baseline and pathological features (solifenacin cohorts)

<table>
<thead>
<tr>
<th>Authors</th>
<th>n of patients</th>
<th>Age (years)</th>
<th>BMI (Kg/m²)</th>
<th>PSA (ng/mL)</th>
<th>Prostate volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liss et al.</td>
<td>39</td>
<td>65 (57–70)</td>
<td>25.9 (24.6–28.7)</td>
<td>5.8 (4.1–7.4)</td>
<td>51 (43–65)</td>
</tr>
<tr>
<td>Bianco et al.</td>
<td>313 vs. 310</td>
<td>60.5 vs. 61.2</td>
<td>28.4 vs. 28.66</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

not receive any instruction for PFMT. UC was defined as International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) score of 0. The primary outcome of this study was the patients’ self-reported UC recovery at 6 months after bladder catheter removal, and the secondary outcomes were the score of incontinence scale and the number of pads/week used. The follow-up schedule consisted of interviews at 10 days and 1, 3, and 6 months after catheter removal. The authors found a significant difference between the 2 groups in pads/week at 1 and 6 months after surgery ($P < 0.01$); likewise, ICIQ-SF scores were higher in the control group than in the intervention group at 3 and 6 months, but there were no differences at 10 days and 1 month. At 6 months after surgery, 50% of patients in the intervention group, but only 3.3% of patients in the control group, reported the use of 0 pads/week. Pan et al. conducted a pre-experimental single-group study in 43 men undergoing RARP in order to examine the effects of resistance band PFMT (modified PFMT) on patients’ UC recovery, life impact, anxiety and depression after surgery [24]. Patients were evaluated at 2 weeks, 1, 2, and 3 months after catheter removal via the Urinary Incontinence Scale after Radical Prostatectomy (UISRP), Incontinence Impact Questionnaire (IIQ), Hospital Anxiety and Depression Scale (HADS). Authors showed that UI severity significantly decreased with the study period; at 2 weeks 88.4% of patients suffered from any degree of UI versus 65.1% at 3 months.

In a retrospective study, Manley et al. evaluated the effect of PFMT in improving pelvic floor strength and UC recovery [23]. A trained pelvic floor physiotherapist gave a daily PFMT program to each man undergoing RARP and graded patient pelvic floor muscle strength (PFMS) before and 4 days and 4 weeks after catheter removal. UC was defined as the requirement for no pads, and it was assessed at the 4-week control visit. Complete data were available for 98 patients, and the majority of them increased their pelvic floor strength during the study period. Preoperatively, PFMS was strong in 79% of patients, moderate in 12%, and weak in 9%; postoperatively, the majority of those with previous moderate and weak PFMS improved to strong PFMS; younger age
was the only predictor of PFMS improvement. Overall, at 4 weeks after catheter removal 49.4% of patients were incontinent, and PFMS correlated with UI ($P < 0.01$); however, preoperatively PFMS was not associated with UC rate after RARP. Older men with baseline moderate and weak PFMS were more likely to experience UI at 4 weeks after RARP ($P = 0.07$).

Kim et al. performed another retrospective study to determine the benefit of PFMT with visual biofeedback compared with conventional PFMT in improving UC recovery after RARP[21]. Forty-one patients formed the intervention group in which PFMT was performed with visual biofeedback under the supervision of a physiotherapist, while 42 patients in the control group performed Kegel exercises at home after only verbal instructions were given by the treating urologist. UC was defined as the cessation of urinary pad use. The follow-up schedule consisted of outpatient office visits at 1 week and at 1, 3, and 6 months after catheter removal. Overall, UC rates were 18.1%, 49.4%, 77.1%, and 94% at 1 week and 1, 3, and 6 months, respectively. In the intervention group, the rates of UC restoration were higher at 1 ($P = 0.037$), 3 ($P < 0.001$), and 6 ($P = 0.023$) months than in the control group. Likewise, the mean time to achieve UC was shorter in the exercise group (32.4 versus 95.3 days, $P < 0.001$). At multivariate analysis, patients < 65 years old were found to have no benefit from the exercises while patients ≥ 65 years old benefited significantly from PFMT, thus suggesting that PFMT with biofeedback is an effective treatment for promoting early UC recovery and that it is more effective in elderly patients.

Studies on Oral Medical Treatment (Solifenacin)

Liss and colleagues performed an exploratory investigator-initiated phase 1 clinical trial to assess safety and efficacy of solifenacin (Vesicare) in men with UI after RARP[22]. The authors hypothesized that anticholinergic agents can reduce UI because of their effect in reducing detrusor overactivity. Men using ≥ 3 pads/day 7 days after catheter removal were enrolled in the study and were prescribed a daily dose of 5mg solifenacin for 3 months. Continence was defined as the
usage of 0 pads/day; moreover, AUA and QoL symptom scores were submitted preoperatively and 3 months after surgery to measure the effectiveness of the treatment. Complete data were available for 39 patients. Overall, 6 patients withdrew from the study because of side effects or adverse events, and 16 men achieved UI before 90 days of treatment. At 3 months, 21 patients (53.8%) were fully continent with a median time to achieve UI of 95 days. The AUA symptom score improved during the study period, but the QoL score worsened.

Bianco et al. conducted a multicentric double-blind RCT evaluating the efficacy and safety profile of solifenacin versus placebo in UC recovery in men who had undergone RARP and were still incontinent 7 to 21 days after catheter removal[17]. Patients requiring 2 to 10 pads/day for 7 consecutive days were enrolled in the study and randomized 1:1 to solifenacin 5 mg daily versus placebo during the 12-week study period. Continence was defined as zero pads/day or a dry security pad for 3 consecutive days, and QoL was assessed.

### TABLE 4A.
Secondary outcomes of the systematic review (PFMT cohorts)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Intervention</th>
<th>Duration of treatment</th>
<th>n of patients</th>
<th>Patient adherence to treatment, %</th>
<th>UI risk factors</th>
<th>Erectile dysfunction rate</th>
<th>Sexual activity recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yoshida et al.</td>
<td>US-guided PFMT vs. verbal-PFMT</td>
<td>Preoperatively and 1 month after RARP</td>
<td>36 vs. 80</td>
<td>100</td>
<td>not reported</td>
<td>not reported</td>
<td>not reported</td>
</tr>
<tr>
<td>Oh et al.</td>
<td>Biofeedback-PFMT vs. verbal-PFMT</td>
<td>3 month after RARP</td>
<td>42 vs. 42</td>
<td>100</td>
<td>not reported</td>
<td>not reported</td>
<td>No differences in IIEF-5 scores among the 2 groups</td>
</tr>
<tr>
<td>Sayilan et al.</td>
<td>PFMT vs. no intervention</td>
<td>Preoperatively to 6 months after RARP</td>
<td>30 vs. 30</td>
<td>100</td>
<td>not reported</td>
<td>not reported</td>
<td>not reported</td>
</tr>
<tr>
<td>Pan et al.</td>
<td>Resistance band PFMT</td>
<td>3 month after RARP</td>
<td>43</td>
<td>100</td>
<td>not reported</td>
<td>not reported</td>
<td>not reported</td>
</tr>
<tr>
<td>Manley et al.</td>
<td>PFMT vs. no intervention</td>
<td>Preoperatively to 1 month after RARP</td>
<td>98</td>
<td>100</td>
<td>age</td>
<td>not reported</td>
<td>not reported</td>
</tr>
<tr>
<td>Kim et al.</td>
<td>Visual feedback PFMT vs. conventional PFMT</td>
<td>1 month</td>
<td>41 vs. 42</td>
<td>100</td>
<td>Gleason score, PSA, PFMT</td>
<td>not reported</td>
<td>not reported</td>
</tr>
</tbody>
</table>

### TABLE 4B.
Secondary outcomes of the systematic review (solifenacin cohorts)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Intervention</th>
<th>Duration of treatment</th>
<th>n of patients</th>
<th>Patient adherence to treatment, %</th>
<th>UI risk factors</th>
<th>Erectile dysfunction rate</th>
<th>Sexual activity recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liss et al.</td>
<td>Solifenacin 5 mg daily</td>
<td>3 months</td>
<td>39</td>
<td>85%</td>
<td>not reported</td>
<td>not reported</td>
<td>not reported</td>
</tr>
<tr>
<td>Bianco et al.</td>
<td>Solifenacin vs. placebo</td>
<td>3 months</td>
<td>313 vs. 310</td>
<td>100%</td>
<td>not reported</td>
<td>not reported</td>
<td>not reported</td>
</tr>
</tbody>
</table>
Postoperative Non-Surgical Interventions to Improve Urinary Continence After Robot-Assisted Radical Prostatectomy: A Systematic Review

by AUA symptom score and ICIQ-SF questionnaires. Overall, 623 patients completed the study and no differences in time to achieve UC were found between the 2 groups (P = 0.17). However, UC rate by the end of the observation period was 29% versus 21% (P = 0.04) in the intervention and control group, respectively. Moreover, patients in both groups had a statistically significant decrease in the number of pads/day from baseline to the end of the study that was greater in the solifenacin arm at 12 weeks (P = 0.01). QoL measures significantly improved by the end of the study (P < 0.001) without differences between groups. Among patients on solifenacin, 33.2% reported at least 1 adverse event, dry mouth being the most common.

Discussion

We performed a systematic review investigating postoperative NSI role in early UC recovery after RARP. Our interest was motivated by the need for conservative interventions to manage mild UI in order to improve patient satisfaction and QoL in the early postoperative period[25]. In this context, it is important to underline that surgery (eg, male slings) is not always recommended for patients who experience post-RARP UI[26]. Overall, we focused our research on NSI carried out only in patients who have undergone RARP because of the wide availability of the robotic prostatectomy procedure and its technical advantages that can lead to optimal functional outcomes[27,28]. Several findings are of interest. To date, PFMT and orally administered solifenacin have been proposed as the only available NSI to improve UC recovery after RARP. These NSI are carried out in the early postoperative period with a limited duration of treatment of 1 to 6 months, theoretically in all patients submitted to RARP. Recently, Marchioni et al. reviewed 6 articles, concluding that PFMT has the advantage of shortening the time to recovery of UC, while the use of solifenacin does not offer any significant advantages in post-RARP UI management[10].

Studies included in our systematic review showed a possible association between PFMT and oral solifenacin administration and an early improvement in urinary functional outcomes after RARP. Yoshida et al. found that the mean time for UC recovery was significantly shorter in the intervention group (ultrasound-guided PFMT) than in the control group (conventional PFMT) (75±100 versus 121.8±132 days; P = 0.037). Moreover, UC rates were higher in the intervention group at 30 days (52.8% versus 35.4%; P = 0.08); however, at 9 months no statistically significant differences were found between the 2 groups in terms of continence status (88.9% versus 84.7%, P = 0.558)[18]. Oh et al. found similar UC rates at 3 months in the intervention and control groups (67.5% and 61.9%, respectively; P = 0.649)[19]. Sayilan et al. found a significant difference in pads/day at 1 and 6 months after surgery between PFMT and no-NSI cohorts (P < 0.01); at 6 months after surgery, 50% of patients in the intervention group but only 3.3% of patients in the control group reported the use of 0 pads/day[20]. Kim et al. found that in the interventional group (visual-feedback PFMT) the rates of UC restoration were higher at 1 (P = 0.037), 3 (P < 0.001), and 6 (P = 0.023) months than in the control group (conventional PFMT). Likewise, the mean time to achieve UC was shorter in intervention group (32.4 versus 95.3 days; P < 0.001)[21]. Pan et al. and Manley et al. reported UC rates of 34.9% at 3 months and 49.4% at 1 month after bladder catheter removal, respectively[23,24]. Regarding solifenacin administration, Liss et al. reported that at 3 months, 21 patients (53.8%) were fully continent with a median time to achieve UC of 95 days[22] while Bianco et al. reported 3 months UC rate of 29% versus 21% (P = 0.04) in the intervention group and placebo group, respectively; however, no differences in time to achieve UC was found between the 2 groups (P = 0.17)[17]. Of note, among included studies, only Bianco et al. provided level 1B clinical evidence supporting the use of NSI (solifenacin) to improve UC recovery after RARP[17]. Nevertheless, Liss et al. failed to demonstrate an obvious benefit of solifenacin administration in urinary outcomes except a potential symptomatic relief[22]. Previously, other oral medications such as duloxetine showed a good efficacy profile in the UI following RP[29]. However, to the best of our knowledge, there are no studies exploring post-RARP duloxetine administration since current evidence is available only for open or laparoscopic RP[30].

A variability in UC definition exists among studies reporting functional outcomes after prostatectomy, thus making difficult a standardized interpretation of the results[31]. In the literature, UC is mainly defined as the use of no pad or the use of 1 safety pad/day, and 5 out of 8 reviewed studies adopted this method. In this context, Kuehhas et al. recommend adding the use of validated questionnaires to assess UC after prostatectomy[32]; however, in 4 studies of the current systematic review, the authors did not distribute questionnaires to patients[17,18,21,23]. In general, a comprehensive evaluation of both subjective and objective functional outcomes combined with assessment of satisfaction has not been conducted systematically. Yoshida et al. defined UC as the need to require a small pad (20g) per day by patient self-report[18]; Oh et al. used a loss of 0 g of urine on a 24-hour pad test to define UC[19]; Sayilan et al. and Pan et al. used validated questionnaires to score UI[20,24]; in the remaining studies UC was defined as no need of urinary pad usage[17,21–23].
Importantly, among included studies only data on early urinary function outcomes are reported. Therefore, follow-up is inadequate to evaluate medium- and long-term continence recovery rates in patients who performed PFMT or have been treated with solifenacin.

Several studies reported the natural history of urinary function in men who have undergone RARP and found that UC rates increase up to 90% to 95% especially during the first year after surgery, thus demonstrating a spontaneous improvement in UC rate with time [33–35]. Even though mild UI can spontaneously improve in the first year after surgery, we believe that conservative strategies to accelerate this process should be taken into account by urologists to ameliorate patients’ QoL in the early postoperative period.

Of note, we miss 2 of our secondary aims because of data insufficiency: to identify risk factors associated with UI after RARP and to find a correlation between postoperative UC and sexual activity recovery in patients enrolled to NSI. Regrettably, the studies included in our review did not analyze the association among patient related characteristics such as age, BMI and comorbidities, PCa features and surgical variables that may impact on post-RARP UC before surgery given that UI is a multifactorial condition[36]. However, we found high compliance to PFMT and solifenacin administration, thus suggesting the feasibility of these interventions to manage UI.

From a research perspective our work highlights the gaps we should fill to improve evidence on NSI to manage mild UI after RARP. First, further multicenter randomized studies are needed, including large population studies comparing NSI—even PFMT in combination with solifenacin—with no postoperative intervention with longer follow-up. Second, UI should be defined as the use of 0 pads/day or 1 safety pad/day and validated questionnaires should be submitted to patients. Third, UI risk factors and sexual activity recovery might be reported to globally assess patients’ functional outcomes.

The study has several limitations. First, there was great variability in the assessment and data reporting of UI and UC recovery among studies, thus making comparison between results difficult. Moreover, some studies did not use a control group against which to compare NSI. Second, all studies reported short-term follow-up functional outcomes, with the majority of them reporting results only to 3 months. Third, the sample sizes of the studies were generally small and heterogeneous in terms of comorbidities and PCa features. Fourth, the different PFMT schedules used in the studies could influence patient outcomes. For these reasons we were not able to perform a meta-analysis of the 8 selected studies in order to integrate their results.

Conclusions
Early postoperative NSI—including PFMT and oral administration of solifenacin—to manage UI after RARP may improve UC recovery. Moreover, both interventions are safe and well tolerated, with high patient adherence to treatment. However, clinical evidence supporting their routine use is still weak. Further multicenter prospective studies with longer follow-up, adequate number of patients, and standardized functional outcomes assessment are needed to confirm the efficacy of the NSI on UC recovery after RARP.
References


