

ing UC recovery (Table 1) [60,63-69]. In a 21-study meta-analysis, typical data showed a significant advantage associated with the PR in terms of postoperative UC at different time intervals (e.g., 3, 7, 30, and 90 days after catheter removal), but not at later follow-ups [70]. In another recent meta-analysis, PR-treated patients demonstrated significantly improved UC recovery rates at 1–4, 28–42, 90, 180, and 360 days following catheter removal [63]. The original technique reported by Rocco et al [62] was a 2-layer/2-step, in which reconstruction was performed in two layers. Afterwards, some PR surgical variations have been suggested. A recent RCT examined the usefulness of a 3-layer/2-step RARP technique being carried out using peritoneum, in comparison with the standard RARP technique [64]; 48 patients were subdivided into 2 groups, being treated with either the standard or the 3-layer technique. Four weeks after surgery, UC rates were higher in the experimental (57%) vs. the standard RARP group (26%).

### 10) Combined anterior and posterior reconstruction

In an extensive prospective trial, Tan et al [71] reported significant advantage for a complete reconstruction (CR) approach as compared with both AR and standard approaches. These results were confirmed in 2 RCTs showing better outcomes for the CR compared to a standard technique (26.5%–65% vs. 7.1%–33%) at 1-month follow-up (Table 1) [60,67]. Conversely, in a RARP series comparing patients treated with either CR, AR, or PR, no significant difference was observed at 1-month follow-up [68]. In their meta-analysis, Ficarra et al [40] showed a meaningful favour for CR at both 1- and 3 months after RARP, although no difference was detected 6 months after surgery. A novel CR approach was proposed by Porpiglia et al [72]: they reinforced the anastomosis using three posterior and two anterior tissue's layers, in order to re-establish the peri-urethral tissue's anatomy. Results were encouraging, with UC rates of 94.4%, and 98.0% at 12, and 24 weeks post-RARP, respectively. Based on the results of the RCTs [60,67-69], it seems that CR is associated with better UC outcomes 1 and 3 months after RARP, whereas long-term outcomes are scarcely supported by solid evidence.

### 11) Comparison of open vs. robotic radical prostatectomy

Although the robotic technique has allowed the surgeon to face a more detailed anatomical perspective, recent data would not seem to support RARP-superiority. Indeed, while previous series have shown a RARP-associated shorter time-to-UC-recovery [5], recent randomized and prospective studies did not confirm those findings. The first RCT comparing RARP vs. ORP failed to observe any benefit of one procedure over another in terms of UC recovery at 6 and 12 weeks [73]. The eventual update on mid-term functional outcomes at 6, 12, and 24 months confirmed such a trend [74]. Specifically, UC scores based on the Expanded Prostate Cancer Index Composite did not differ significantly between RARP and ORP at 6 (88.68 vs. 88.45), 12 (90.76 vs. 91.53) and 24 months post-RP (91.33 vs. 90.86) [69]. Herlemann et al [75] compared 755 RARP vs. 1,138 ORP patients and found better UC outcomes for ORP 1 year post-surgery but not beyond. Similarly, Ranasinghe et al [76] analyzed data from 10 online cancer support groups comparing 5,157 RARP vs. 579 ORP, and reported no differences in UC outcomes. Finally, Haese et al [77] failed to show any clinically significant improvement in terms of UC rates at 1-year assessment after RARP.

## 5. Postoperative setting

### 1) Role of postoperative length of catheterization

A number of studies [78-81] have associated a longer duration of postoperative catheterization with worst UC outcomes, with this conclusion resulting from non-randomized, potentially biased studies. Hence no definitive conclusions can be drawn regarding this issue.

### 2) Diagnostic work-up

History should identify possible features of urgency- or mixed-type UI and should include a bladder diary consisting in frequency of micturition; number of UI episodes; voided volumes; and 24-hour urinary output collection of related data. Validated tools, such as the OAB questionnaire, are considered reliable and useful to evaluate postoperative UC [82]. Due to its replicability, the 24-hour pad test is the most accurate to quantify UI [83]. A urinalysis test should also be performed in order to rule out any infection. Although its routinal adoption is considered controversial [84], urodynamic

investigation had been habitually used in the past to assess DO in candidates for corrective treatment.



### 3) Conservative strategies

Conservative care should be appraised before moving to invasive options; in this context patients should be examined on a regular basis to evaluate the improvements. Indeed, UI status can last for more than 1 year after RP [85]. Fluid intake reduction, timed voiding and reduction of bladder irritants (*e.g.*, coffee, hot spices) have been associated with improvement of post-RP urinary symptoms and UC [86].

#### (1) Pelvic floor muscle exercise

The most established conservative option for dealing with post-RP UI is PFME. However, drawing a definitive conclusion about the advantage of PFME for surgery-related UI may be difficult due to the conflicting results provided by current evidences. In this context, there is large heterogeneity between trials regarding both PFME content/delivery (*e.g.*, biofeedback, muscles targeted, and time of commencement of the training)

and UC definition (*e.g.*, 1 hour pad test, 24 hour pad test, International Consultation on Incontinence Questionnaire (ICIQ), bladder diary, and number of pads/d) (Table 2) [34]. Over the past decade, several RCTs have been conducted to evaluate the effectiveness of PFME. Whilst some RCTs supported the benefits of PFME, a recent meta-analysis including 45 RCTs [87] did not support PFME as first line rehabilitative approach for UC recovery after RP. It is here suggested that the approach of deconstructing the details of PFME protocols, as described in a recent review by Hall et al [34], can aid in getting a better understanding of the usefulness of this strategy. In their analysis, preoperative PFME, use of biofeedback, and UC defined as no leakage were features associated with successful patient outcomes. We aim at this point to summarize the most recent RCTs on this topic. In a recent RCT, UC outcomes were evaluated in 60 patients after RP, 30 received PFME whilst the 30 controls did not receive any treatment [88]. The number of pads used during the first and in the six months after surgery was significantly lower in the experimental *vs.* the control group [88]. Another

**Table 2.** Outcomes of pelvic floor muscle exercise after RP in relation to specific trial's features [34]

Trial feature	Total number of patient	Trial's number	Cumulative analysis of findings (RR, 95% CI)
Preoperative PFME	PFME: 165 Control: 166	5	0.76 (0.63–0.92)
Postoperative PFME only	PFME: 664 Control: 658	10	0.90 (0.79–1.02)
PFME only	PFME: 457 Control: 462	5	0.94 (0.88–1.00)
PFME+BFB	PFME: 372 Control: 362	10	0.73 (0.58–0.91)
Instructions focused on anal region only	PFME: 190 Control: 197	5	0.64 (0.38–1.08)
Instructions involved urethral and anal region	PFME: 626 Control: 617	9	0.90 (0.86–0.96)
Control group received no PFME instructions	PFME: 514 Control: 512	7	0.85 (0.72–0.99)
Control group received some PFME instructions	PFME: 315 Control: 312	8	0.84 (0.70–1.00)
Included all men postoperatively	PFME: 509 Control: 500	11	0.84 (0.74–0.94)
Included only men with post-RP UI	PFME: 320 Control: 324	4	0.82 (0.57–1.17)
Continence definition- no loss of urine allowed	PFME: 374 Control: 369	7	0.85 (0.72–0.99)
Continence definition- some loss of urine allowed	PFME: 455 Control: 455	8	0.82 (0.67–1.00)

RP: radical prostatectomy, RR: risk ratio, CI: confidence interval, PFME: pelvic floor muscle exercise, BFB: biofeedback, UI: urinary incontinence.

RCT allocated 97 men undergoing RP to a control group (n=47) in which a limited rehabilitation was performed, or to a PFME group (n=50) [89]. In the experimental group, interventions started 5 weeks before and were sustained for a 12-week period after RP. Controls showed a slower UC-recovery and encountered significantly extra urinary leakage, as quantified by one-day pad weight, *vs.* the experimental group.

#### (2) Pharmacological treatment

DO may be a contributing factor to post-RP UI [90], hence the attempt to improve UC with antimuscarinics. Over the last few years, several studies investigated their efficacy on post-RP OAB symptoms. One small RCT (n=27) found a significant decrease in urge UI with tolterodine 2 mg in comparison with no treatment in the early period after catheter removal [91]. Additionally, two large RCTs demonstrated earlier return to continence with solifenacin [92,93]. Two RCTs showed a significant effect of duloxetine, an antidepressant, in improving SUI after RP [94,95]. Although off-label in many European countries, duloxetine is currently recommended by the European Association Guidelines panel as an effective drug for postoperative SUI, although its side effects should be adequately explained to the patient [96]. Gandaglia et al [97] prospectively assessed a large cohort of RP patients, finding that those who were taking phosphodiesterase type 5 inhibitors (PDE5Is) presented with better UC recovery rates as compared with those left untreated. Conversely, other studies failed to show any benefits after PDE5Is in RP patients [98].

#### 4) Surgical treatments

Surgical therapy for post-RP SUI is an option for patients with unsatisfactory improvements after conservative management (Table 3).

#### (1) Male slings

Male slings (MS) are considered a feasible alternative to artificial urinary sphincter (AUS) in a number of cases of mild to moderate post-RP UI [96]. Different types of slings are available, and all of them are meant to appropriately reposition the urethra. A clear advantage over AUS is that slings do not require patient's manual dexterity and they are also cheaper [99]. Overall, slings are classified into adjustable and non-adjustable types. Furthermore, depending on the method of insertion, slings can be divided into retropubic and transobturator categories. Currently, there is a range of adjustable MS commercially available; therefore, it is difficult to express an opinion regarding the superiority of one MS against another, due to significant heterogeneity of the available data and lack of long-term follow-up RCTs. In a recent meta-analysis [100], the recovery rate for the fixed slings varied between 8.3% and 87%. Although the overall complication rates were assessed in only a minority of studies, they were significantly more frequent for adjustable *vs.* fixed slings. In both the fixed and the adjustable varieties, pain was regarded as the commonest issue, followed by urinary retention for fixed slings, and infection for adjustable slings [100]. In considering the complications associated with this surgery, it is important to identify their possible predictors. Among them, a history of previous pelvic radiotherapy, an increased UI severity, obesity, and previous UI surgery were all considered crucial to estimate the likelihood of complications [100]. Men failing sling treatment can eventually undergo salvage AUS placement [101].

#### (2) Artificial urinary sphincter

The AUS, with the most popular being the AMS800, is based on a pressure-regulating balloon located in the pre-vesical space and connected to an inflatable cuff which acts as an all-round urethral compression device, hence regulating urine passage. The control unit

**Table 3.** Outcomes of AUS and slings for urinary incontinence after radical prostatectomy [4]

Surgical procedure	Number of trial	Overall number of patient	Continence outcome
AUS	16	991	59%–96% (0–1 pad/d)
Slings			
InVance	15	677	16%–87% (cured)
Advance	4	416	9%–74% (cured)
Others (Remeex, Argus, TOMS)	16	903	17%–79% (cured)

AUS: artificial urinary sphincter.

of this system is placed in the scrotum, allowing the patient to void the bladder. The AUS remains the most established surgery for dealing with post-RP UI, presenting with the largest body of evidence and reporting long-term success ranging from 20% to 89%, hence being currently regarded as the best available option for patients suffering from moderate to severe UI [102]. However, due to the relatively high costs, the non-negligible complication rates and the requirement for appropriate manual dexterity, the AUS may represent an unfeasible option for every single case with post-RP UI [99]. Another possible drawback is that occasional revisions may be required in some patients, with revision and explantation rates varying considerably in the range of 8% to 45% [4,102]. A large retrospective single-institution study found a 5.5% rate of device infection [103]; prompt device removal is the standard management of this complication [4]. Urethral erosion occurs in up to 8.5% (3.3%–27.8%) of implants [104]. As with any device, its components are susceptible to malfunction; the survival expectation of the AUS drops over time, with a 68-month median overall device's longevity [103].

## 5) Alternative options

### (1) Urethral bulking agents

Urethral bulking is a minimally invasive option based on increasing the juxtaposition of the tissues in both the internal and external sphincters. Several different agents (*e.g.*, collagen, teflon, silicone, autologous tissues, hyaluronic acid) have been used. In a recent meta-analysis of 25 studies, the success rates varied widely from 13% to 100% [105]. Due to poor clinical evidence base, further research is required and this approach should therefore be considered when other more established treatments are contraindicated.

### (2) Adjustable balloons

The Pro-Act system depends upon the compression force which is provided by two balloons that are located bilaterally to the BN. Adjustable balloons appear to be a valid alternative for patients with mild to moderate post-RP UI; however only small case series evaluated its outcomes in post-surgical setting. A recent retrospective single-institution study [106] focusing on 143 patients who received a post-RP Pro-Act implantation showed that, after a median follow-up of 56 months, 64% of patients showed levels of improvement, with

daily pad use reduced by  $\geq 50\%$ , and 45% of patients either did not wear any pad or used only one “security” pad per day. The treatment was considered safe, as 90.2% patients showed no complications.

### (3) Intravesical onabotulinum toxin A injections

This treatment had been approved for OAB in 2014, following the results of several RCTs. However, there are limited data relating to their use in the post-RP population. In a retrospective series of 11 patients with post-RP OAB, Habashy et al [107] observed a resolution of urgency-UI in 45% after onabotulinum toxin A intradetrusorial injection. Further clinical trials should be carried out to shed more light on the usefulness of this approach.

## CONCLUSIONS

RP remains a major cause of UI in men; therefore, during the preoperative assessment patients must be counselled concerning the risk of post-RP UI. Patient's individual features should be well kept in mind, with the aim of better assessing the individual risk of UI. Over the last decade, the advances of surgical technique opened the way to the progress of multiple intraoperative techniques to improve UC outcomes after RP. PFME and pharmacotherapy are reasonable conservative approaches for post-RP UI, even if success rates using these techniques have been inconsistent. Several surgical procedures are currently available to treat post-RP UI. Out of these, AUS showed the longest record of safety and efficacy for patients with moderate to severe UI. MS are an alternative approach, with intermediate data supporting their efficacy. Other less popular options, such as injectable agents or adjustable balloons, should only be considered when more established options are contra-indicated. Further randomized trials should be carried out to compare the different options, and innovation in the field should continue to refine current techniques and produce novel, and possibly more effective, treatment approaches.

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