CONSERVATIVE MANAGEMENT OF POST-RADICAL PROSTATECTOMY INCONTINENCE

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Summary.- Radical prostatectomy is currently the mainstay of treatment for localized prostate cancer. Although there is evidence that the evolution in surgical technique with the introduction of laparoscopic and robot-assisted radical prostatectomy has resulted in an improvement of functional outcomes, a significant percentage of patients are still bothered by post-prostatectomy incontinence. However, the majority of patients will find improvement in their continence status from conservative measures and a small cohort will require more invasive therapeutic options. Conservative treatment includes pelvic floor muscle training with or without biofeedback techniques and pharmacotherapy. There is evidence that immediate initiation of physiotherapy after surgery will help in early restoration of continence, while additional benefit can be provided from pharmacotherapy mainly from duloxetine. The present review aims to provide an update on the epidemiology of post-prostatectomy incontinence, identify risk factors for incontinence after surgery and suggest current trends for conservative treatment.


Resumen.- La prostatectomía radical es actualmente uno de los tratamientos estándar para el cáncer de próstata localizado. Aunque no existe evidencia de que la evolución en la técnica quirúrgica, con la introducción de la prostatectomía radical laparoscópica asistida por robot, haya dado lugar a una mejora en los resultados funcionales, un porcentaje significativo de pacientes padecen la secuela de la incontinencia posterior a la prostatectomía. Aún así, la mayoría de los pacientes encuentra mejoría en su estado de continencia con relación a las medidas conservadoras y una pequeña cohorte requerirá opciones terapéuticas más invasivas. El tratamiento conservador incluye rehabilitación muscular del suelo pélvico con o sin técnicas de “biofeedback” y farmacoterapia. Existen pruebas de que el inicio inmediato de la fisioterapia después de la cirugía ayudará en el restablecimiento precoz de la continencia, mientras que la farmacoterapia puede proporcionar un beneficio adicional, principalmente la duloxetina. La presente revisión tiene como objetivo proporcionar información...
INTRODUCTION

Malignancies of the genitourinary tract are currently diagnosed more frequently than ever. Prostate cancer (PCa) is the most common cancer afflicting men in the Western World (1) and the second leading cause of cancer death in men, only preceded by lung cancer (2,3). The incidence of PCa in European countries has been increasing lately, mainly as a result of the wider implementation of screening, and is higher in men living in Western and Central Europe (4).

Prostate cancer is traditionally diagnosed in people of older age, is not usually upfront lethal, and therefore the vast majority of prostate cancer patients live many years with their disease. Current estimation is that there are nearly 2.8 million men living with a history of prostate cancer in the United States (5).

Contemporary treatment options for a patient diagnosed with localized PCa include active surveillance, radiation therapy and radical prostatectomy (RP), depending on cancer stage, patient comorbidity, age, and personal preferences. More than one-half (57%) of men aged younger than 65 years are currently treated with radical prostatectomy (RP), either open or minimally invasive (lap, robotic). Patients aged 65 to 74 years commonly undergo radiation therapy (42%), although radical prostatectomy (33%) is also often used.

With regard to survival, currently more than 90% of all prostate cancers are diagnosed in the local or regional stages, for which the 5-year relative survival rate approaches 100%. Over the past 25 years, the 5-year relative survival rate for all stages combined has increased from 68.3% to 99.9%. The 10-year and 15-year relative survival rates are 97.8% and 91.4%, respectively (5).

It is obvious that available treatment options for localized prostate cancer will likely cure the majority of patients from the disease. This coupled with the fact that the average life expectancy in the Western World is increasing will result in a vast patient population of prostate cancer survivors with problems related more to the received therapeutic surgical or medical interventions rather than the malignancy itself.

With regard to RP as a treatment of curative intent for PCa, studies have repeatedly shown that urinary incontinence (UI) rather than sexual function is the consequence with the worse effect on patients’ quality of life (6).

Pathophysiology of post-prostatectomy incontinence RP, the most widely used treatment for localized CaP is the most prevalent cause of UI in men. Postoperative incontinence is one of the most feared complications of RP with a major impact on quality of life. The most common type of incontinence following RP is stress urinary incontinence (SIU) followed by urge incontinence, mixed incontinence and overflow incontinence usually due to an anastomotic stricture. Climacturia or Orgasm-Associated Incontinence (OAI) is a specific type of SUI that affects 20-40% of potent men after RP. OAI is characterized by inadvertent urine leakage during orgasm due to the relaxation of the external urethral sphincter and is unrelated to the type of prostatectomy performed (open vs laparoscopic) (7-9).

Post-prostatectomy incontinence (PPI) may be the result of a number of mechanisms acting alone or in synergy; sphincter deficiency, bladder instability, nerve damage, bladder neck contracture and stenosis of vesicourethral anastomosis. Urodynamic studies in patients after RP have shown that PPI is associated with intrinsic sphincter deficiency (ISD) in more than 90% of patients. Bladder dysfunction may coexist but is rarely the only cause of PPI. Symptoms of stress urinary incontinence accurately predict the finding of intrinsic sphincter deficiency (ISD) on urodynamics (10,11).

Continence in males is maintained through the action of two sphincteric mechanisms. The proximal continence mechanism or pre-prostatic sphincter is comprised by the smooth muscle fibers of the bladder neck and provides resting continence. The distal sphincteric mechanism or rhabdosphincter is “built” by both striated and smooth muscle fibers that run for about 2cm from the verumontanum to the bulbular urethra and is responsible for maintaining resting tone and providing voluntary control of voiding in coordination with the striated skeletal muscles of the pelvis (12).

RP causes injury to the muscle fibers of the proximal sphincteric mechanism. That results in intrinsic
sphincter deficiency (ISD), an urodynamic finding that is present in about 90% of patients (13,14). ISD usually presents clinically as post-prostatectomy stress urinary incontinence. SIU is however not the sole finding in PPI. Symptoms of overactive bladder (urgency and urge incontinence) due to detrusor overactivity and decreased bladder compliance may prevail especially during the first year after RP but are gradually limited thereafter (15,16).

Although RP causes some degree of injury to both the innervation and the fibers of the striated external sphincter, under normal circumstances continence in these patients continues to be maintained through the action of the distal sphincter. In cases however of a sudden increase in intra-abdominal pressure and subsequent rise in bladder pressure the compromised external sphincter is not able to resist the rise in pressure resulting in urine leakage (17).

A parameter that has been held responsible by some authors for PPI is the functional urethral length available after prostatectomy. Studies have shown that functional urethral length (FUL) is decreasing post-operatively and attribute PPI to the reduced urethral length (16); while others have proposed that maximal urethral closure pressure is more important than urethral length itself (14). In any case taking care to maintain adequate urethral length during surgery without compromising the oncologic aspects of the intervention is advisable in order to preserve postoperative continence.

There is convincing evidence however that FUL may be the culprit in climacturia. A recent study using video-urodynamics to evaluate the cause of climacturia in patients after RP revealed that functional urethral length (FUL) was significantly lower in the climacturia group and time to recovery of continence recovery was significantly longer (9).

**Prevalence of PPI**

Post-prostatectomy incontinence is a distinct form of male UI. The prevalence of PPI is difficult to be estimated since a standardized definition of post-prostatectomy continence is lacking. The use of a variety of terms to define post-prostatectomy incontinence and grade its severity (eg; no leakage at all, no pads but loss of a few drops of urine, one safety pad per day) amongst different studies is creating biases and confusion with regard to the true incidence and severity of PPI. Considering that pad-free patients experience a better quality of life compared to patients that still need to use a security pad peer day clarifying the definition of post-prostatectomy continence status is crucial (18). Current estimation is that the rate of UI after RP ranges within 5-48% (19); a variation largely dependent on the severity of incontinence and whether the assessment of UI was made by the physician or was reported by the patient (20-22). With regard to patient’s expectations from surgery relevant to the functional recovery of continence it is interesting and probably alarming to notice that almost 1 out of 2 was expecting a better post-prostatectomy continence status (23). This observation underlines the need for utilizing preoperative patient counseling with regard to the risks and management of PPI (24).

PPI rates are also influenced by the time after RP that continence status is sought and reported. In the majority of cases, continence is progressively restored within months to years after surgery. By and large, more than 80% of patients will be completely dry at 2 years, 20% will need 1 pad per day and less than 2% will need more than 2 pads per day (25-28). From the patient’s perspective, continence status and related bother were restored to pre-operative levels in 1 years time for 55% and 77% of patients respectively (29).

The surgical technique of RP is another important variable influencing the rates of PPI. Following the principles of anatomic RP popularized by Walsh (30) relevant to the preservation of the neurovascular bundles and sparing of the bladder neck, earlier return to continence has been achieved for many patients (22,31). The advent of minimally invasive RP, either pure laparoscopic or robot-assisted, has resulted in certain modifications in the surgical technique with positive repercussion on the incidence of PPI, (32-34) although the incidence of severe incontinence remains largely unaffected (35).

**Risk factors for PPI**

Risk factors that have been proposed to be associated with PPI include age at time of surgery, Body Mass Index (BMI), prostate volume and disease stage, baseline continence status (36), surgical technique, surgeon experience (37), previous radiation. A recent analysis of parameters which delay the recovery of urine control identified advanced age and certain comorbidities (major depression, lower extremity circulatory disease, smoking) as predictors of worse outcomes after RP (38).

Advanced age at prostatectomy as a risk factor for PPI has been incriminated by several studies (24,36,38-41). According to Catalona, the risk of incontinence doubles for every 10 years (39). Kundu et al showed that men under 50 have a significantly better continence rate following RP compared to men over 70 (40). Mohamad and colleagues
P. Sountoulides, I. Vakalopoulos, D. Kikidakis, et al.
corroborated that increasing age is associated with an increased risk of UI and future AUS implantation (41). Finally Nilsson et al reported that advanced age at surgery was associated with a 3-fold long-term risk of incontinence (42).

Several studies have suggested the association of increased body weight with PPI (24,43-45). Obesity with BMI >30 was reported as a risk factor with an incontinence rate of 25.8% vs 8.7% in BMI <30 (44), although in other studies BMI was not associated with continence outcomes (42). Pick et al also identified IIEF-5 score and BMI as significant independent predictors of continence in multivariable analysis (45).

**Surgical technique**

There is little doubt that excision of the bladder neck during prostatectomy damages the proximal sphincteric mechanism. In order to ameliorate this phenomenon and preserve continence techniques including mucosal eversion and intussusception of the bladder neck have been used. There are studies showing that bladder neck preservation techniques might help enhance restoration of continence and avoidance of bladder neck contractures (46-48), although a contradictory opinion has been expressed by others (49). In a multivariate analysis of several factors, Sakai et al identified bladder-neck preservation (BNP) to be the only independent predictor of return to continence at 1 and 3 months (50).

Baseline prostate volume as well as a short membranous urethra are considered predictors of recovery of urinary function after radical prostatectomy. Patients with prostate volume greater than 50 ml on transrectal ultrasound had a slower recovery of continence rates of continence and worse urinary function scores 6 months and 1 year after radical prostatectomy (51).

Increased prostate volume may also affect postoperative continence by increasing the length of excised urethra. In a study by van Randenborgh et al it was shown that patients who had adequate urethral length preserved showed better continence rates and also earlier return to continence (52).

The literature relating to nerve sparing surgery is conflicting and does not offer strong evidence in support that nerve sparing RP is associated with improvement in continence outcomes. Some authors believe that nerve sparing has no significant impact by itself (45), while others did find a benefit in bilateral nerve sparing (24,28,48,53). The positive effect of local hypothermia during robotic-assisted laparoscopic prostatectomy (RALP) using a rectal cooling balloon in order to attenuate inflammation and enhance the restoration of continence has been demonstrated by Ahlering and colleagues (54,55).

Anastomotic strictures are definitely associated with PPI. Anastomotic strictures, although relatively rare following radical prostatectomy, have a negative effect on the restoration of continence. Patients that develop postoperative stricture are more 4 times more likely to experience incontinence according to a retrospective study by Park et al (56).

A summarization of the risk factors for incontinence after RP is presented in Table I.

Relevant to the surgical technique, there have been recent studies comparing RALP over RRP in terms of earlier recovery of urinary function and continence. These prospective studies showed that RALP provides improved continence rates at 1 year and also enhances time to recovery of continence (57,58). However and since there are other publications showing no effect of the robot on continence rates (59,60) this issue remains to be resolved in future studies.

<table>
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<tr>
<th><strong>Table I. Risk factors for PPI.</strong></th>
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<tr>
<td><strong>Patient Risk Factors</strong></td>
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<tr>
<td>Advanced age at prostatectomy</td>
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<tr>
<td>Increased BMI</td>
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<tr>
<td>Increased prostate volume</td>
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<tr>
<td>Poor baseline continence status</td>
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<td>Comorbidities (smoking, depression etc)</td>
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<tr>
<td><strong>Surgical Risk Factors</strong></td>
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<tr>
<td>Non-Nerve sparing technique</td>
</tr>
<tr>
<td>Short membranous urethra length</td>
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<tr>
<td>Post-prostatectomy anastomotic stricture</td>
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<tr>
<td>Not preservation of the bladder neck</td>
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<tr>
<td>Less experienced surgeon</td>
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<td>Salvage prostatectomy-previous radiation</td>
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Patient evaluation—basic diagnostic work up

A universally accepted, meaningful, and validated tool for the measurement of PPI is lacking. Patient evaluation according to guidelines should include:

a) a detailed medical history (surgical note, adjuvant radiotherapy, past medical history-neurologic disease, surgery, medications);

b) an objective assessment of symptoms and symptom severity (IPPS, IIEF, UCLA-PCI, Incontinence Quality of Life (I-QoL), voiding diary, 24-h pad test);

c) a physical examination (palpable bladder, DRE, penis, urethral meatus, complete neurologic examination);

d) laboratory tests (urine analysis and culture, PSA, creatinine) and

e) ancillary diagnostic tests (ultrasonography for post-void residual urine measurement, uroflowmetry, flexible cystoscopy and f) urodynamics.

Although several questionnaires exist for the evaluation of incontinence, none is specific for the assessment of post-prostatectomy incontinence (61,62). The grade and severity of UI can be determined using a combination of a standardized pad tests and urodynamic findings (61). Although the 24-hour pad test is more accurate, the standardized 1-hour pad test is more widely used due to feasibility reasons. The use of less than 2 pads per day combined with less than 250 gr of urine in the 24 hour pad test discriminate moderate from severe incontinence. Urodynamic parameters that are important in grading the presence and severity of incontinence include the Valsalva Leak Point Pressure (VLPP) and Maximum Urethral Closure Pressure (MUCP).

Urethrocystoscopy and urodynamics may provide valuable additional information and should be mandatory in cases where conservative management has failed and an invasive treatment option for PPI is contemplated. Urethroscopy is useful in order to rule out the presence of urethral stenosis, Anastomotic stricture, stone, bladder tumor or foreign body (suture, surgical clips). Filling the bladder during cystoscopy may also aid in the rough evaluation of bladder capacity and compliance. Urodynamics should be performed as a multichannel examination for complete evaluation of the condition in order to guide therapeutic decisions. Nitti et al in their landmark study identified sphincteric dysfunction (90% of cases-60% as the sole finding) and bladder dysfunction (45% of cases-3% as the sole finding) as the most frequent urodynamic findings in PPI (63).

Conservative management

Although conservative management is greatly utilized in the management of PPI there is no hard evidence for treatment recommendations. Following initial evaluation of the patient using symptom severity and quality of life impact assessment (questionnaires), physical examination, imaging and laboratory tests one should keep in mind the following;

a) continence status following RP will continue to change for more than 1 year following surgery;

b) a trial of conservative therapy is indicated in the early post-operative period before moving to more invasive options;

c) the patients need to be reassured and followed with regular visits to assess the degree of improvement;

d) in a subgroup of patients with additional symptoms of overactive bladder a trial of antimuscarinics during the first 6-12 months following RP (64);

e) no randomized controlled trials exist to compare currently used noninvasive treatments for PPI.

Non invasive management includes lifestyle modifications, pelvic floor muscle training (PFMT) and pharmacotherapy.

Lifestyle modifications

Lifestyle interventions such as smoking cessation, body weight adjustment, reduction in fluid intake especially before bedtime and avoidance of bladder irritants (coffee, alcohol, hot spices) are recommended by the majority of physicians. A recent trial showed that behavioral therapy may have a positive effect on incontinence frequency and LUTS in men with incontinence persisting for over 1 year after RP (65). Again, there are no solid clinical data in support of these recommendations. The effect of lifestyle interventions remains undetermined as no trials involving these interventions are identified (66).

Physiotherapy—Pelvic floor muscle training (PFMT)

Pelvic floor exercises were introduced by Kegel in 1951 in an attempt to enhance urinary control by increasing urethral resistance (67). These exercises aim at providing increased support
for the detrusor muscle and urethral sphincter by strengthening the pelvic floor musculature. Although the duration and the number of contractions performed per day have not been standardized, patients are generally taught to contract and relax their pelvic floor muscles and to repeat these exercises daily for a few months. The exercises are usually performed in sets of 10 contractions of the sphincter muscles lasting 2-10 seconds each and followed by 2-10 seconds of muscular relaxation depending on individual ability (68). These exercises can be repeated also in different positions: sitting, standing, squatting, and going up and down stairs. A physical therapist is usually involved and patients are trained by various methods, including verbal explanations, palpation, and visualization of the contraction at the base of the penis using a mirror. The exercises are then continued unsupervised with the aid of written information and telephone support in a home-based program specifically developed for each patient (69). Patients are instructed to identify the movements and body positions that could cause incontinence and encouraged to practice PFMT contraction before any effort or activity that might trigger incontinence (sneezing, coughing, or lifting a weight). They are also asked to keep a voiding diary recording the number and severity of any episodes of urine leakage and share this information with the physical therapist in order to evaluate their progress and reinforce the beneficial effects of training.

According to current recommendations preoperative or early postoperative PFMT, preferably supervised, is considered beneficial in hastening the return of continence after RP (19,64). Van Kampen et al using a pelvic floor re-education program involving active pelvic floor muscle exercises and biofeedback noted that differences between treatment and control groups in the percentage of incontinent patients remained highest in the first 4 months and then decreased from 31% at 1 month to 14.4% at 1 year (70).

Filocamo et al in a prospective trial studied 300 post-prostatectomy patients randomized to either PFMT or no intervention immediately after catheter removal. The PFMT group showed a significantly improved continence rate when compared with the control group (19% vs 8% after 1 month and 94.6% vs 65% after 6 months). Incontinence in the untreated group was 12.1% versus 1.3% for the PFMT group at 1 year with improvement being evident even from the first month of treatment (71).

With regard to the optimal timing of PFMT, starting PFMT and biofeedback preoperatively is advocated by many based on the results of relevant studies although there is lack of consistent evidence in support of this. Burgio et al in a prospective randomized trial found that patients started on preoperative PFMT regained continence more quickly and suffered less risk of severe incontinence in the long-term (6 months) (72). Another study showed significantly improved continence rates at 3-months for patients on preoperative PFMT (59.3%) compared to patients that initiated PFMT postoperative (37.3%) (73). A recent prospective study evaluated the efficacy of preoperative biofeedback session, combined with postoperative pelvic floor muscle training, and assisted sessions on a monthly basis in facilitating time to continence and reducing incontinence rates after RP. The authors were able to demonstrate the effectiveness of this low-intensity program in the number of incontinence episodes per week and the number of pads per week (74). Again, although there is no objective data (66), expert opinion favors initiation of PFMT immediately after catheter removal in order to reduce the continence recovery time (19).

PFMT is considered helpful even in men with persisting SUI more than 1 year after RP (65).

On the other hand, there are studies that have created uncertainty about whether or not PFMT leads to earlier recovery of continence (75-78). Parekh et al were not able to demonstrate any benefit from PFMT for patients with severe incontinence although return to continence was enhanced by PFMT (75).

A recent large study from Leuven evaluated 180 men randomized to either the “experimental” group (initiating PFMT 3 weeks before surgery and continuing after surgery) or the control group (starting PFMT after catheter removal). Results showed that no additional benefit was achieved for patients in the experimental group with regard to time to recovery of continence or severity of leakage (measured by the 1-hour pad test) (79).

An updated Cochrane Database review on the subject corroborated the uncertainty regarding the efficacy of PFMT. Despite the fact that the majority of studies were of poor to moderate quality, analysis of 8 trials of conservative treatment of men after radical prostatectomy revealed no evidence that pelvic floor muscle training with or without biofeedback was better than control for men with urinary incontinence after radical prostatectomy (e.g. 57% with urinary incontinence versus 62% in the control group) (66).

An argument however in favor of a trial of PFMT in all patients with PPI before endeavoring into more invasive treatment options is that these exercises are harmful and likely to be beneficial for some patients (68).
Biofeedback

Biofeedback can be used as an adjunct to PFMT in order to assist patients in exercising their pelvic floor muscles, using visual or auditory feedback through the use of electrical external or internal devices, or verbal feedback from a therapist. Results from studies concerning the efficacy of additional biofeedback training are somewhat contradictory. There are studies comparing PFMT plus biofeedback versus controls that have demonstrated significant improvements in the severity of incontinence, voiding symptoms and pelvic floor muscle strength compared to no therapy. Ribeiro et al showed that at 1 year post-RP, 96% of patients in the treatment group versus 75% in the control group were continent with an absolute risk reduction of 21.2% (78).

Burgio et al studied the efficacy of the use of preoperative biofeedback-assisted behavioral training with regard to the duration and severity of post-prostatectomy incontinence. The study demonstrated a significant improvement in continence (defined as 3 consecutive weekly 1-day dairies showing no leakage or a completed 7-day diary with no leakage) with PFMT plus biofeedback versus controls at 6 months (72).

However, in other studies PFMT with biofeedback made no difference (65,69,80). According to the EAU guidelines, additional biofeedback therapy should be individually decided based upon patient and physician preference (64).

Electrical stimulation

Electrical stimulation is a more sophisticated form of biofeedback used for pelvic floor muscle rehabilitation involving stimulation of levatorani muscles using painless electrical current. When the pelvic floor muscles are stimulated by these small electrical currents, the levatorani muscles and urinary sphincter contract and urinary leakage is inhibited (81). Electrical stimulation can be used together with biofeedback and PFMT especially for patients who are unable to sufficiently contract their pelvic muscles (70). The beneficial effects of electrical stimulation for PPI have been demonstrated in recent studies (82,83).

Mariotti et al, in a prospective randomized study, demonstrated that patients treated with electrical stimulation and biofeedback were continent after a mean time of 8 weeks, whereas those who only performed PFMT after verbal instruction needed an average of 13.88 weeks to regain continence (83).

However, several other studies were not able to provide evidence in support that electrical stimulation is of benefit compared to PFMT alone (65,80). According to the latest EAU guidelines it is currently not judged as beneficial (64).

Other options

Extracorporeal magnetic innervations more commonly called magnetic stimulation (MSTIM) therapy may have a beneficial effect in the first 1-2 months of conservative post-prostatectomy incontinence treatment (84). However, evidence-based data are missing, and there is no current recommendation in the guidelines for extracorporeal magnetic innervation therapy(64).

Climacturia can be bothersome or embarrassing for almost 50% of potent men after RP. Although several strategies have been proposed for the prevention of this event, none have been systematically studied to date and there fore evidence of their effectiveness for improving sexual health and recovery is limited (85). Simple, non-invasive preventive measures that have been proposed include the use of condom, penile loop and urination before intercourse (8).

The application of a penile variable tension loop for prevention of climacturia has been recently evaluated in a prospective observational study. The study showed that the use of the penile loop can result in a significant decrease in the frequency and volume of climacturia and also relieve the distress associated with climacturia for both patients and their partners. The authors concluded that with the use of the penile loop climacturia resolves completely in half the patients, and occurs occasionally or rarely in the remainder (86).

An active pelvic floor rehabilitation program consisting of active pelvic PFM exercises, electromyography biofeedback for strength and endurance, and electrical stimulation has shown encouraging results with regard to improvement in erectile function, continence and resolution of climacturia in a cases series of 3 men following RP (87).

Pharmacotherapy

As has been previously commented, patients suffering from symptoms of urgency and urge incontinence following RP should be optimally managed with a course of anticholinergics (64). However for genuine stress UI following RP there is currently no approved pharmacologic therapy. Duloxetine, a centrally acting, dual serotonin (5-HT)
and noradrenalin reuptake inhibitor, effective for the treatment of female SUI, (88,89) has been recently evaluated for off label use in men.

Studies have shown significant effectiveness for duloxetine. Duloxetine was tested in a prospective trial of 31 patients randomized to either the drug or placebo for 3 months. A mean reduction in Incontinence Episodes Frequency (IEF) of 52.2% was achieved after 12 weeks with 80mg of duloxetinedaily with significant improvement seen as early as 8 weeks. This reduction in the frequency of incontinence had a positive impact on quality of life outcomes, also evaluated in the study. The most common side effects reported, fatigue (50% vs 13% for placebo), insomnia (25% vs 20%), loss of libido (19% vs 7%), constipation, nausea, diarrhea and dry mouth usually resolved with time (90).

In another study a significant synergistic effect of adding duloxetine in combination with PFMT was demonstrated (91).

Fink et al evaluated the potential efficacy of duloxetine in 49 men with PPI that had failed a trial of PFMT. Duloxetine was administered in a dose of 40 mg twice daily. The authors reported a decrease in pad use (from 3.3 to 1.5 per day) with 14 patients rendered pad-free. The majority of patients reported mild and temporary side effects, with 41% of patients assessing symptoms as either moderate or severe (92).

Duloxetine was also evaluated in a prospective observational study from Spain where 68 patients with over 1 year of untreated PPI were subscribed duloxetine (30-60 mg/day) for 9 months. A significant improvement in symptoms and number of pads used was evident even at 3-months while at the end of the follow-up period, 74% and 57% of the patients sustained a significant symptom improvement and a decrease in the number of daily pads used. Side effects were reported by almost half of the patients with a significant 25% of patients stopping the drug due to side effects (93).

In conclusion, duloxetine is currently not approved for the treatment of post-prostatectomy incontinence, and should only be prescribed as an off-label therapy. Results have shown some efficacy even in cases that have failed PFMT, however this improvement comes with the price of increased risk of side effects.

A schematic overview of the management of PPI is shown in Figure 1.

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**Figure 1. Management overview of post-radical prostatectomy incontinence.**

Conservative management of PPI

- SUI
  - PFMT +/- biofeedback
  - Pharmacotherapy (duloxetin)
  - Anticholinergics

PPI= post-prostatectomy incontinence, SUI=stress urinary incontinence, OAB=overactive bladder, PFMT= pelvic floor muscle training.
CONCLUSIONS

Urinary incontinence can be a trouble some complication of radical prostatectomy. Surgical trauma to the urinary sphincter results in sphincter deficiency which manifests as stress urinary incontinence and adversely impacts quality of life. Preoperative counseling of patients is key in establishing realistic expectations from surgery with regard to postoperative continence status. Efforts and care should be taken in order to prevent this complication from happening, with encouraging results reported with the utilization of laparoscopic and robotic technology in radical prostatectomy. The evaluation of PPI should rule out other possible causes of postoperative incontinence (anastomotic stricture, overactive bladder) that need to be addressed. Patients with PPI stress incontinence should be motivated towards a conservative therapeutic algorithm including pelvic floor muscle exercises even before surgery. The addition of biofeedback and electrical stimulation techniques might augment the therapeutic benefit of pelvic floor muscle rehabilitation. Although preliminary studies have shown some efficacy for drug treatment with duloxetine, the high rate of adverse effects is limiting their usage.

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