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LOWER URINARY TRACT SYMPTOMS & VOIDING DYSFUNCTION (J SANDHU, SECTION EDITOR)

Management of Overactive Bladder Symptoms After Radical Prostatectomy

Benoit Peyronnet[1] · Benjamin M. Brucker[2]

Abstract

Purpose of Review Post-prostatectomy overactive bladder (OAB) is a common and challenging condition to manage. The aim of the present report was to review the recent evidences regarding OAB symptoms that develop in men after prostatectomy and how to manage them.

Recent Findings The prevalence of OAB after radical prostatectomy may range from 15.2 to 37.8%. Recent studies have highlighted the role of the urethrogenic mechanism (facilitation of the urethrovesical reflex due to stress urinary incontinence (SUI)) in the genesis of post-prostatectomy OAB in a significant proportion of patients. Several other pathophysiological factors such as iatrogenic decentralization of the bladder, defunctionalized bladder due to severe SUI, detrusor underactivity, or bladder outlet obstruction might be involved. The evaluation should aim to identify the underlying mechanism to tailor the treatment, which could range from SUI surgery, to fixing a urethral stricture, improving bladder emptying or using the conventional spectrum of OAB therapies. There is a paucity of data for OAB therapies specific to post-prostatectomy patients, with the exception of solifenacin, tolterodine, and botulinum toxin. There is currently no data on how preoperative management or surgical technique may prevent post-prostatectomy OAB.

Keywords (MeSH) · Urinary bladder · Overactive · Prostatic neoplasms · Urinary incontinence · Radical prostatectomy

Introduction

Prostate cancer (PCa) is the most commonly diagnosed male cancer and the second leading cause of death from cancer in male patients in the USA and Europe [1]. While active surveillance keeps gaining wider acceptance, radical prostatectomy remains the most commonly used active treatment for patients with clinically localized PCa [2, 3]. In spite of the widespread adoption of minimally invasive approaches over the past decade, radical prostatectomy remains associated with two side effects in a significant subset of patients: erectile dysfunction and urinary incontinence [4, 5]. While the stress urinary incontinence (SUI) component is predominant in most post-prostatectomy urinary incontinence [6], de novo overactive bladder (OAB) symptoms, with or without urgency urinary incontinence, have recently been shown to affect up to 37.8% of male patients after radical prostatectomy [7•]. Despite the exact mechanisms underlying the relationship between the OAB symptoms and radical prostatectomy are not fully elucidated, surgical excision of the prostate potentially adds anatomical and psychological factors to the complex and multifactorial pathophysiology of OAB. Its management may be challenging, owing to the frequent co-occurrence of SUI, to the emotional stress inherent to cancer treatment, and to the risk of further deterioration if additional radiation therapy is needed. The aim of the present report was to review the recent evidences regarding post-prostatectomy OAB and its management.

This article is part of the Topical Collection on *Lower Urinary Tract Symptoms & Voiding Dysfunction*

✉ Benoit Peyronnet
peyronnetbenoit@hotmail.fr

[1] Department of Urology, University of Rennes, Service d'Urologie, 2 rue Henri Le Guilloux, 35000 Rennes, France

[2] Department of Urology, New York University, New York, NY, USA

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Methods

A literature search was conducted in June 2018 using the MedLine and Embase databases, screening for randomized controlled trials (RCTs), prospective and retrospective series, animal model studies, and reviews on the management of overactive bladder symptoms after radical prostatectomy. The search strategy included the following terms "overactive bladder," "urgency," "frequency," "storage symptoms," "nocturia," "radical prostatectomy" that were used alone or in combination. Only articles published in English and deemed relevant were included in this review.

Results

Epidemiology

While voiding symptoms tend to improve after radical prostatectomy owing to the removal of the main anatomical bladder outlet resistance, a reciprocal worsening in storage symptoms has been observed in some studies [8•, 9, 10], despite there is conflicting evidence on this subject [11]. According to the few epidemiological data available, the prevalence of OAB after radical prostatectomy may range from 15.2 to 37.8% [7•, 9] and could be up to twice higher in patients receiving additional radiation therapy [8•]. Urgency has been suggested to be the primary cause of post-prostatectomy incontinence in up to a third of patients with incontinence after prostatectomy [12]. Likewise stress urinary incontinence (SUI), storage lower urinary tract symptoms (LUTS) observed in the early postoperative period can improve up to 12 months after radical prostatectomy [13]. According to a recent systematic review, the prevalence of detrusor overactivity (DO) during urodynamics following radical prostatectomy would range from 3 to 63%, preoperative DO being the main risk factor of uninhibited detrusor contractions on post-prostatectomy urodynamics [14•]. However, the clinical relevance of this urodynamic finding might be called into question in a significant proportion of patients in that clinical setting (see below).

Pathophysiology

In order to manage post-prostatectomy OAB appropriately, it is essential to understand the underpinning pathophysiological mechanisms involved. The multifactorial nature of OAB pathophysiology has been increasingly recognized over the past two decades [15]. Despite the exact mechanisms underlying the relationship between OAB and radical prostatectomy are not fully elucidated, surgical excision of the prostate likely add several cofactors to the complex and multifactorial pathophysiology of OAB.

Detrusor Overactivity

Historically thought to be the only driver of OAB symptoms [16], DO has then been reported to be lacking in over 50% of patients with OAB supporting the idea of diverse possible mechanisms underlying the symptoms of OAB [17]. Uninhibited detrusor contractions (and impaired compliance) have been shown to be highly prevalent on urodynamics performed after radical prostatectomy [14•] and are usually attributed to partial decentralization of the bladder resulting from intraoperative iatrogenic injury to the pelvic nerves [18]. However, data on the clinical relevance of post-prostatectomy DO and on its true implication as a causative factor of urinary incontinence and storage LUTS are contradictory [12, 18]. Detrusor overactivity and impaired bladder compliance in patients with severe post-prostatectomy SUI have been postulated to be artifactual, resulting from supraphysiologic filling of chronically under filled bladder during urodynamics.

The Urethrogenic Mechanism

Intrinsic sphincter deficiency (ISD) is commonly observed after radical prostatectomy as a result of iatrogenic damage of the muscle fibers and/or the nerve supply intraoperatively [19]. While ISD is largely established as the main causative factor of post-prostatectomy SUI, this defect in urethral tone might also be a cause of OAB and DO. In the early twentieth century, Barrington described various component reflexes of micturition in cats [20]. The second of theses reflexes was evoked by running water through the urethra and resulted in a strong bladder contraction mediated through pudendal and pelvic afferent and efferent signals [20]. Using an animal model, Jung et al. found that activation of urethral afferents by urethral perfusion could modulate the micturition reflex and thus hypothesized that entry of urine into the proximal urethra in patients with stress urinary incontinence (SUI) may stimulate urethral afferents, inducing and/or increasing DO [21]. Their findings were confirmed a few years later in healthy human volunteers with the hypothesis of an urethrovesical reflex [22–25]. Over the past few years, there has been increasing evidence of the role of this urethrogenic mechanism in post-prostatectomy OAB. In a recent study, Mastukawa et al. found that low maximum urethral closure pressure (MUCP) at baseline and greater decrease in MUCP postoperatively were strong predictors of de novo post-prostatectomy OAB reinforcing the idea that this urethral mechanism might contribute to the pathophysiology of storage LUTS after radical prostatectomy [7•]. Performing magnetic resonance imaging (MRI) after radical prostatectomy, Haga et al. found that urinary pooling, defined as the presence of urine inside the membranous urethra at rest, was strongly associated with de novo urgency likely through stimulation of urethral afferents facilitating the micturition reflex [26••].

Defunctionalized Bladder

In case of severe SUI, constant leakage may result in chronically under filled "defunctionalized" bladder. As seen in patients with end-stage renal disease with low urine output, patients with severe post-prostatectomy SUI might develop artifactual DO, impaired compliance or bladder hypersensitivity generating urgency [27]. In analogy with what is observed after kidney transplantation, those bladder dysfunctions have been shown to resolve in many cases after surgical correction of SUI restoring the physiological cycles of bladder storage and voiding [28•].

Detrusor Underactivity

Detrusor underactivity is defined by the International Continence Society (ICS) as a voiding contraction of reduced strength and/or duration, leading to prolonged or incomplete bladder emptying [29]. Detrusor underactivity, could affect over 40% of male patients after radical prostatectomy, mostly due to denervation injury during the surgical procedure [30•]. While underactive bladder is considered as the clinical correlate of the urodynamic observation of detrusor underactivity, the symptoms of detrusor underactivity has been shown to commonly overlap those of OAB, urgency having been reported as the more common symptoms in patients with urodynamically proven detrusor underactivity (seen in over 50% of patients) [31]. The occurrence of urinary urgency in patients with detrusor underactivity could be attributed to urinary tract infections due to chronic urinary retention, to the impact of such retention on urinary microbiota or to the impaired bladder sensation of patients with detrusor underactivity with shorter "warning" interval between first sensation of bladder filling and leakage [32]. Hence detrusor underactivity could contribute to post-prostatectomy OAB and should be sought in the pretherapeutic evaluation of these patients.

Bladder Outlet Obstruction

The two main causes of bladder outlet obstruction (BOO) following radical prostatectomy are bladder neck contracture and urethral stricture [33]. The cumulative incidence of BOO after radical prostatectomy has been shown to be as high as 20.3% at 10 years in large population-based study [34•]. Bladder outlet obstruction is a well-established factor of OAB symptoms, either via incomplete bladder emptying or by causing myogenic DO (progressive damage to smooth detrusor muscle cells due to chronic BOO with histological changes in to the bladder wall promoting spontaneous myogenic contractions) [35]. Thus, symptoms suggestive of BOO in patients with post-prostatectomy OAB should prompt further investigations aiming to detect urethral stricture or bladder neck contracture (see below).

Other Pathophysiological Cofactors

Metabolic syndrome is a common risk factor of both OAB and prostate cancer [36] and is then a comorbidity commonly observed in patients with post-prostatectomy OAB [37]. Metabolic syndrome could then contribute to OAB pathophysiology in a significant proportion of patients with prostate cancer [37]. Despite this factor is not specific to the post-prostatectomy setting, it should be taken into account when planning treatment as, based on available literature, treatments targeting the metabolic syndrome itself may be regarded as the most effective treatment options for OAB in these patients with cure rates of urge incontinence up to 19% and 79% for weight loss program and bariatric surgery respectively [38, 39], whereas conventional OAB treatments have been shown to bring poor outcomes in such patients [37].

Up to 40% of patients undergoing radical prostatectomy may experience psychological distress over the course of their prostate cancer management [40]. While the impact of OAB symptoms on quality of life may predispose affected individuals to anxiety and depressions, it has now been clearly demonstrated that there is a bidirectional relationship between anxiety/depression and OAB, with common biological mechanisms underlying these associations and resulting in co-occurrence of both conditions (e.g., serotonin depletion, central sensitization, decrease in corticotropin-releasing factor) [41]. Affective disorders might thus be a significant pathophysiological cofactor (not only a consequence) in some patients with post-prostatectomy OAB that should be addressed in order to achieve satisfactory outcomes.

Finally, the use of radiation therapy after radical prostatectomy (either adjuvant or salvage) has been shown to worsen storage LUTS [8•, 10] and to promote more complex features of lower urinary tract dysfunction (e.g., low bladder compliance, recalcitrant bladder neck contracture) [42]. Response to OAB treatments may also differ in irradiated vs non-irradiated patients.

Evaluation prior to therapy

A management algorithm is proposed in Fig. 1. Considering the relatively scant evidence and guidelines on post-prostatectomy OAB, this algorithm largely reflects authors' opinion and is an outline of how to think about managing these complex patients. The aim of the initial workup is to identify factors that could impact treatment decision making, mainly: mixed urinary incontinence, "treatable" pathophysiological cofactors (metabolic syndrome and affective disorders), bladder outlet obstruction, detrusor underactivity and history. Clinicians should also carefully consider any history of pelvic radiation therapy as it is known to affect treatment outcomes and risk of complications and will therefore influence patients' counseling.

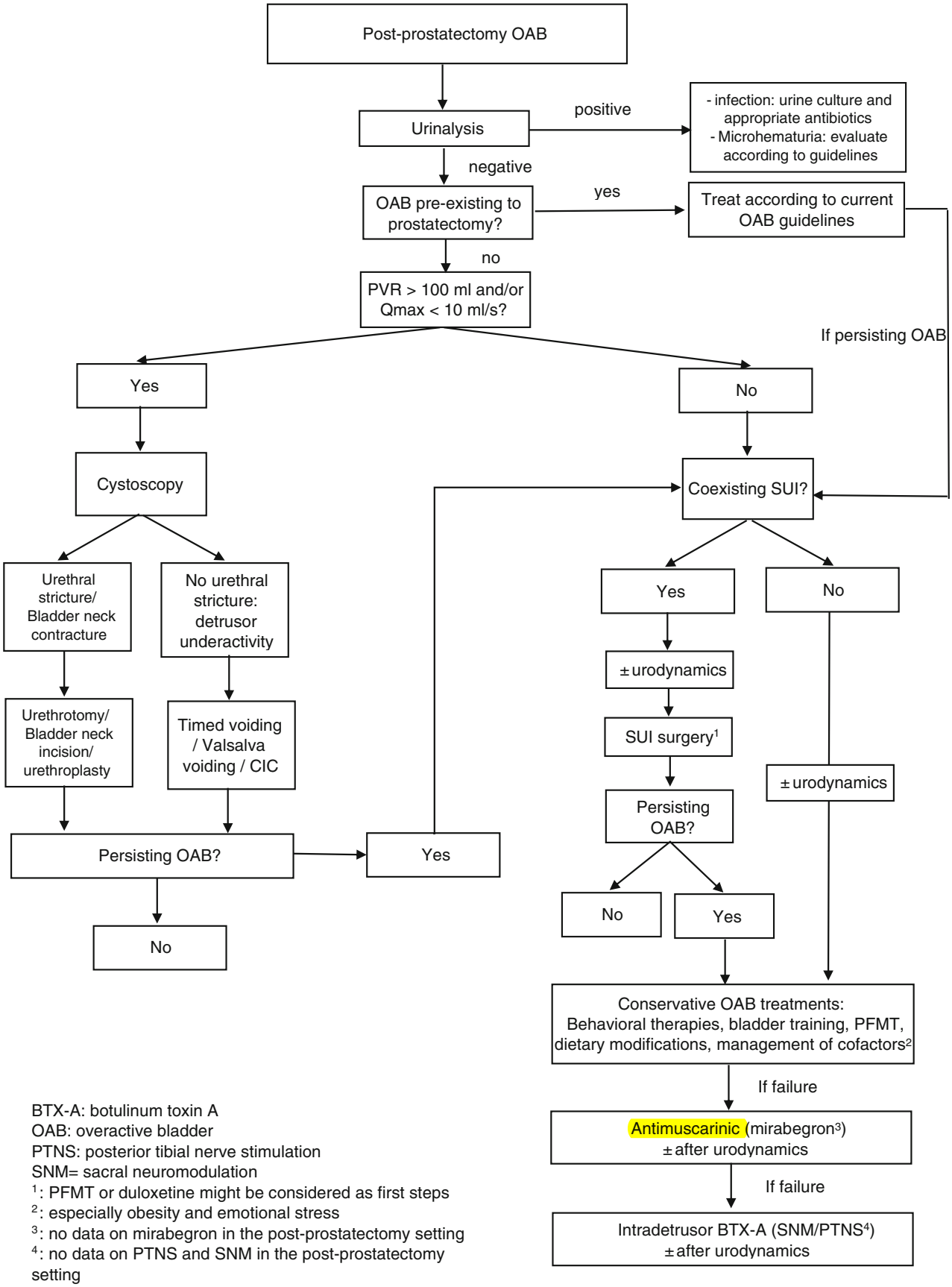

Fig. 1 Management algorithm for post-prostatectomy OAB

Clinical Assessment

A thorough medical history and physical examination is paramount in the management of storage LUTS after radical prostatectomy. Indeed, medical history could seek specifically for the aforementioned pathophysiological cofactors such as metabolic syndrome (especially obesity), affective disorders, and history of radiation therapy. An uroflowmetry and a post-void residual (PVR) measurement may help identifying detrusor underactivity or bladder outlet obstruction, which might be reasonable to treat upfront as this could be sufficient to improve storage LUTS but also because this could compromise the results of further treatment (increased risk of retention after SUI surgery, botulinum toxin, etc). During the physical examination, a cough stress test should be performed to rule out the presence of SUI. If SUI is present, pad test may help quantifying its severity. As for any OAB patients, urinalysis is recommended to rule out urinary tract infection and hematuria and voiding diaries help objectifying and quantifying symptoms and ruling out excessive fluid intake. Questionnaires can be used to measure the severity of symptoms and their changes over time, and to assess their impact on quality of life. Clinicians should also pay attention to coexisting bowel dysfunction and assess sexual function.

Urodynamics

The role of urodynamic testing in the initial workup of OAB and post-prostatectomy incontinence remains largely debated [43, 44]. In addition, the clinical relevance of detrusor overactivity or impaired bladder compliance on post-prostatectomy urodynamics in that specific setting might be questioned (see above). Urodynamics might help diagnosing detrusor underactivity or sphincter incompetence (low MUCP or abdominal leak point pressure) [44]. However, it remains unclear whether urodynamics impact treatment decision-making for post-prostatectomy OAB nor if it predicts therapeutic outcomes accurately [44]. While the use of urodynamic seems reasonable before invasive surgical procedures, after failed surgical treatment or in case of risk factors (e.g., history of radiation therapy), the choice to perform urodynamics in patients with OAB following radical prostatectomy in other situation depend upon patient's and physician's preferences. An argument to use it in routinely is that post-prostatectomy OAB are always complex situations and urodynamics may provide a better understanding and help in patients' counseling.

Cystoscopy

The role of cystoscopy in the initial assessment of patients with OAB is very heterogeneous from on guidelines to another [43, 45]. In the specific setting of OAB after radical prostatectomy, cystoscopy seems highly desirable especially in case of voiding symptoms, low maximum urinary flow or high PVR to rule out anastomotic stricture or bladder neck contracture, or in case of hematuria especially in irradiated patients to rule out secondary malignancy and/or radiation cystitis.

Other

The functional urologist should ensure that the patient undergo regular prostate-specific antigen (PSA) assessment as part of an appropriate oncological follow-up. Renal and bladder ultrasound may be performed at physician's discretion or in case of coexisting hematuria, high PVR of high-risk urodynamic features.

Treating the Bladder Outlet

In cases where coexisting SUI is present, often treating the SUI component is the first step, or is considered after initial treatment for OAB are unsuccessful. This decision on sequencing depends on severity of SUI, degree of bother of each component of incontinence, patients' attitude to surgical intervention, etc. Treating the stress component first may be most judicious in the post-prostatectomy setting, as it has reasonable chance to improve or cure OAB symptoms. It can address the urethrogenic mechanism for post-prostatectomy OAB and prevents the "defunctionalized bladder" phenomenon. Further, in case of very low outlet resistance, even small amplitude uninhibited detrusor contraction might result in leakage making "cure" of urgency incontinence very difficult. One concern about treating the outlet is that in a subgroup of patients, when performing obstructive outlet surgeries for SUI, OAB symptoms can worsen or become more bothersome. Studies having assessed the impact of SUI treatments on post-prostatectomy OAB are summarized in Table 1.

In case where urethral stricture and/or bladder neck contracture are demonstrated, it is usually recommended to treat it as a first step [51]. Here, the intentional obstruction may be contributing to the OAB symptoms and in some case may affect the success of OAB treatment. When relieving obstruction, careful counseling and expectation about outcomes are critical.

Conservative and medical treatments

Pelvic Floor Muscle Training/Biofeedback

Numerous studies have demonstrated the effectiveness of pelvic floor muscle training (PFMT) and biofeedback in patients with post-prostatectomy SUI [52]. One could hypothesize that PFMT and biofeedback may improve the urgency component in patients with mixed urinary incontinence after radical

Table 1 Studies reporting the impact of SUI treatments on OAB symptoms in post-prostatectomy patients

Study	Patients (n)	Study design	Intervention	Assessment of OAB symptoms	Main findings
Tienforti 2012 [46•]	32	Randomized controlled trial	PFMT + biofeedback	ICIQ-OAB score	Significant improvement of OAB at 3 and 6 months after RP compared to home Kegel
Lai 2011 [47•]	34	Retrospective series	Artificial urinary sphincter AMS-800	subjective	Resolution of OAB in 29% of patients
Yiou 2016 [48]	40	Prospective series	TOMS sling	USP OAB subscore	Significant improvement of OAB at 6 and 12 months
Sacco 2018 [49]	44	Prospective series	TiLOOP sling	OABq score	Non-significant improvement of OAB at the latest follow-up ($p = 0.11$)
Yiou 2016 [50]	20	Prospective series	Adjustable Continence Therapy (proACT)	USP OAB subscore	Significant improvement of OAB at 1 year

PFMT, pelvic floor muscle training; RP, radical prostatectomy; USP, urinary symptom profile

prostatectomy. However, data to support this hypothesis are scarce with only one randomized controlled study, with a small sample size, showed an improvement of OAB symptoms (as assessed by the ICIQ-OAB score) with biofeedback 3 and 6 months after radical prostatectomy [46•]. Despite limited evidences to support it, these conservative treatment options could be trialed, especially in the early postoperative period and in patients with mild or moderate incontinence.

Duloxetine

Duloxetine is a serotonin reuptake inhibitor that acts in the Onuf's nucleus raising the activity of pudendal motor neurons [53•]. This results in increased striated urethral sphincter tone and detrusor relaxation [53•]. Duloxetine has been shown to improve post-prostatectomy SUI in two small randomized controlled trials [53•, 54]. Neither of these studies assessed the impact of duloxetine on storage LUTS [53•, 54]. However, duloxetine has been reported in a randomized controlled trial of female OAB patients to significantly improve frequency and urgency [55]. As a result, duloxetine is recommended by the European Association Guidelines panel as the only drug effective for improvement of both stress and urgency urinary incontinence and might then be an interesting option in selected post-prostatectomy patients with OAB and SUI [56]. However, this would be off label use of duloxetine in the USA, as it is not approved for either indication by the FDA.

Other Non-surgical Treatment of SUI

Despite not specifically studied in the setting of post-prostatectomy mixed urinary incontinence, other non-surgical treatments of SUI such as penile clamp, condom catheters, or pads could be regarded as options in a small subset of patients with persistent SUI after other conservative measures and reluctant or too frail to undergo surgery.

Surgical treatment

SUI surgery

As improvement of urinary symptoms has been demonstrated up to 12 months after radical prostatectomy, one may delay any invasive surgical treatment until this timepoint [13]. Few series have assessed the impact of SUI surgery on post-prostatectomy OAB symptoms. In a series of 34 patients with mixed post-prostatectomy urinary incontinence, Lai et al. observed a resolution of OAB symptoms in 29% of patients after artificial urinary sphincter implantation [47•]. Two series have evaluated the impact on OAB symptoms of male slings for post-prostatectomy incontinence on OAB symptoms [48, 49]. In the first one, Yiou et al. reported a significant improvement of the Urinary Symptom Profile (USP) OAB subscore at 6 and 12 months after TOMS sling implantation [48]. In the second study, Sacco et al. found a trend towards improved OABq score at the latest follow-up after TiLOOP sling implantation [49]. Finally, in a series of 20 male patients with failed slings who underwent subsequent adjustable continence therapy (proACT) implantation, a significant improvement of USP OAB subscore was noted 1 year after proACT implantation [50].

In summary, despite evidence limited to single-center case series, the current literature suggests that some patients with mixed incontinence after radical prostatectomy may experience improvement, or resolution, of their OAB symptoms after SUI surgery. These data and the underpinning rationale (urethrogenic mechanism, etc) should be weighed against the risk of persistent or de novo OAB postoperatively. No predictive factors have been identified to help in patient selection and the choice to elect SUI surgery as a first step in these patients depends upon clinician's judgment.

Surgical treatment of urethral stricture and bladder neck contracture

When urethral stricture is identified during the workup, its treatment should be considered in many cases as the first step. One rationale for this is from several series having demonstrated that effective treatment of urethral stricture improves OAB symptoms [57, 58]. These series are not specific to post-prostatectomy men but if the OAB symptoms are secondary to the stricture the extrapolation may be reasonable. Another reason for treatment is that untreated BOO is going to potentially compromise the outcomes of several OAB treatments that could be used (e.g., antimuscarinics, botulinum toxin) by increasing the risk of urinary retention. On the other hand, treating the urethral stricture might worsen or cause SUI, especially in irradiated patients and in those who already have SUI. This should be discussed with patients and some may favor OAB medications as a first step, or urethral dilation and CIC, to avoid this risk of de novo/worsened SUI. The therapeutic options for urethral stricture and bladder neck contracture depend upon stricture location and severity and range from urethral dilation to internal urethrotomy, open reconstruction or urethroplasty [51].

Treating the bladder

In patients with minimal or no coexisting SUI and no BOO, "conventional" OAB treatments should be offered. This treatment paradigm is utilized despite the vast majority of OAB treatments having little to no post-prostatectomy specific data. The only exception could be patients with detrusor underactivity with high PVR in whom optimizing bladder emptying may improve storage LUTS.

Conservative treatment

As mentioned above, detrusor underactivity is common after radical prostatectomy and often manifests itself as OAB symptoms [30–32]. In case where detrusor underactivity is diagnosed during the initial workup, its management should be considered before pursuing OAB therapies as it might be sufficient to relieve storage LUTS and if not addressed initially may act as a confounding factor. Valsalva voiding and/or timed voiding might be suggested in selected patients, but in case of high or symptomatic PVR, clean-intermittent catheterization remains the gold standard [59].

In patients without coexisting SUI or voiding dysfunction, conservative OAB therapies should also be used as the initial step of post-prostatectomy OAB management, despite the lack of evidence of their efficacy on storage LUTS after radical prostatectomy. As mentioned about the only data comes from one randomized trial showing an improvement of OAB symptoms with biofeedback 3 and 6 months after radical prostatectomy [46•]. Other behavioral interventions, more focused on controlling urgency, may involve bladder training, dietary modifications (reduce caffeine, alcohol, and other bladder irritants) and management of constipation based on the low risk and success in other populations [52, 60]. The management of metabolic syndrome and affective disorders, both highly prevalent in post-prostatectomy patients, could contribute to improve OAB symptoms in these patients [52, 60].

Medical treatment

As is usually the case for any patients with OAB, medical treatment should be offered to patients refractory to behavioral interventions.

Anticholinergics

Anticholinergics are one of the two therapeutic classes approved and recommended for the treatment of OAB [43, 56]. Over the past few years, several studies have aimed to assess the efficacy of anticholinergics on post-prostatectomy OAB symptoms. The studies having assessed the efficacy of OAB treatments for storage LUTS after radical prostatectomy are summarized in Table 2. Two prospective cohort studies evaluated solifenacin, one showing significant improvement of storage LUTS (as assessed by IPSS subscores) [61] and one reporting unchanged storage LUTS (as assessed by IPSS subscores) [62]. One small randomized controlled trial (n = 27) found significantly greater decrease in urgency incontinence (as assessed by the IPSS subscore) with tolterodine 2 mg than with no treatment at 1, 15, and 30 days after catheter removal post-prostatectomy [63]. Additionally, two large randomized controlled trials, demonstrated earlier return to continence after radical prostatectomy with solifenacin despite not meeting their primary endpoints [66, 67•]. It should be noted that these studies did not specifically assess the impact of antimuscarinics on OAB symptoms. Overall, there is some evidence, despite limited, supporting the use of antimuscarinics in patients with OAB symptoms after radical prostatectomy.

Beta-3 agonists

Mirabegron has been the first (and still the only) $\beta_3$adrenoceptor agonists approved by the FDA and EMA in 2012 after the publications of four large phase 3 RCTs (three vs. placebo and one vs. tolterodine) [68]. This new therapeutic class has rapidly gained popularity among physicians and patients because it largely lacks the side effect of dry mouth and generally are considered to be safe; specifically, the phase 3 studies have not identified a risk for blood pressure or heart rate increases [69]. Mirabegron could be regarded as an attractive option for patient with OAB symptoms after radical

Table 2 Studies having assessed OAB treatments in patients with storage LUTS after radical prostatectomy

Study	Patients (*n*)	Study design	Intervention	Assessment of OAB symptoms	Main findings
Yang 2016 [61]	40	Phase 1 prospective cohort study	Solifenacin 5 mg once daily	IPSS subscore	Significant improvement of urgency, frequency and nocturia at 3 and 6 months
Liss 2014 [62]	40	Prospective series	Solifenacin 5 mg once daily	IPSS subscore	No improvement in any storage LUTS at 3 months
Mitropoulos 2006 [63]	27	Randomized controlled trial	Tolterodine 2 mg once daily	IPSS subscore	Significant improvement of urgency incontinence 1, 15 and 30 days after catheter removal
Honda 2016 [64]	44	Retrospective series	Tadalafil	OABSS	Greater improvement of OAB at 6 months than patients not taking tadalafil
Habashy 2015 [65]	11	Retrospective series	Intradetrusor onabotulinum toxin A	Subjective	Resolution of urgency incontinence in 45% of patients

IPSS, International Prostate Symptom Score

prostatectomy. However, it should be noted that no studies to date have evaluated its safety and efficacy in the post-prostatectomy setting.

Other oral therapy

In a recent small non-controlled cohort studies, tadalafil was found to be moderately effective in treating de novo OAB symptoms following radical prostatectomy [64]. This is of interest as there is growing evidence of the role of phosphodiesterase inhibitors as a possible new therapeutic pathway for OAB. In the first randomized trial assessing the role of phosphodiesterase inhibitors in female patients, daily low-dose tadalafil was reported as an effective and well-tolerated treatment of OAB [70]. However, the use of phosphodiesterase type 5 inhibitors can obviously not be recommended based on such scant evidence and confirmatory studies will be necessary.

Third-line therapies

Intradetrusor injections of onabotulinum toxin A have been approved for treating OAB in 2014 based on several RCTs [71]. In a retrospective series of 11 patients with post-prostatectomy OAB, Habashy et al. observed a resolution of urgency incontinence in 45% after onabotulinum toxin A intradetrusor injections [65•]. Interestingly, in an unpublished conference abstract, Hoffman et al. reported a 0% rate of clean-intermittent catheterization in a cohort of 23 men treated with onabotulinum toxin A after radical prostatectomy suggesting an interesting safety profile in this population [72]. No study has been published on the two other third-line therapies, namely sacral neuromodulation (SNM) and posterior tibial nerve stimulation (PTNS), in the dedicated setting of post-prostatectomy OAB. However, data for these two therapies are robust in idiopathic OAB patients and they could be considered in post-prostatectomy patients paralleling the usual OAB treatment pathway [43]. Sacral neuromodulation has also been proven helpful in patients with detrusor underactivity and OAB symptoms, especially in those with impaired contractility and detrusor overactivity and could be regarded as an interesting option in this selected population [73].

Prevention of post-prostatectomy OAB

Several studies have aimed at assessing the impact of various steps of radical prostatectomy surgical techniques (bladder neck dissection, open vs minimally invasive approaches, neurovascular bundle preservation, etc) on postoperative sexual function and continence status [6]. Despite this, no studies evaluated the impact of these intraoperative technical aspects specifically on the reduction of developing OAB symptoms. However, one may assume that techniques aiming at preserving vascular and neural supply (i.e., neurovascular bundles sparing) and bladder anatomy (e.g., bladder neck sparing) may diminish the risk of post-prostatectomy OAB by reducing the likelihood of bladder decentralization, urethrogenic urgency, etc., which may be mechanisms of OAB in men after prostatectomy. However, the real influence of surgical technique on post-prostatectomy OAB symptoms has yet to be determined [6].

Despite the conflicting evidence in this field, preoperative pelvic floor muscle training (PFMT) has been suggested as a possible way to minimize the risk of post-prostatectomy SUI [52, 60]. One may then assume that preoperative PFMT and bladder training might reduce the risk of OAB after radical prostatectomy. However, there is currently no data to support such hypothesis.

Conclusion

OAB can occur in up to 37.8% of patients after radical prostatectomy owing to several specific pathophysiological factors such as iatrogenic decentralization of the bladder, decreased urethral tone facilitating the urethrovesical reflex (urethrogenic mechanism), defunctionalized bladder due to severe SUI, detrusor underactivity, or bladder outlet obstruction. The work-up should aim to uncover identifiable causes and then tailor the treatment. These treatments range from SUI surgery, to fixing a urethral stricture, improving bladder emptying or using the conventional spectrum of OAB treatment (i.e. behavioral therapies, anticholinergics, botulinum toxin).

Compliance with Ethical Standards

Conflicts of Interest Benoit Peyronnet is a consultant for Allergan, Medtronic, Astellas and Boston Scientific, and an investigator for Ipsen.

Benjamin Brucker is a consultant for Allergan, Watkins Conti, Avadel, Serenity, and an investigator for Ipsen and Medtronic.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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