Management of erectile dysfunction and LUTS/ incontinence: the two most common, long-term side effects of prostate cancer treatment

Valentin Shabataev, MD, Seyed Hossein Saadat, MD, Dean S. Elterman, MD

Division of Urology, University Health Network, University of Toronto, Toronto, Ontario, Canada

SHABATAEV V, SAADAT SH, ELTERMAN DS. Management of erectile dysfunction and LUTS/ incontinence: the two most common, long-term side effects of prostate cancer treatment. *Can J Urol* 2020;27(Suppl 1):17-24.

The two major long-term concerns associated with different options for the management of prostate cancer, (including surgery, radiotherapy, brachytherapy, cryotherapy, HIFU, etc.) include difficulties with lower urinary tract symptoms (LUTS) and/or erectile dysfunction.

LUTS can be in the form of stress urinary incontinence (SUI), urge urinary incontinence (UUI), frequency/ urgency, and/or voiding difficulties. While surgery is mostly associated with SUI and radiation mostly results in UUI, there can be an overlap. Incontinence rates after cryotherapy and high intensity focused ultrasound (HIFU) are generally very low. Voiding difficulties can also happen after the above-mentioned options.

Treatment of SUI can start with pelvic floor muscle exercises (PFME), penile clamps or urethral plugs. If these

fail to provide satisfactory results the surgical options could include: urethral bulking agents, male slings, and artificial urinary sphincter (AUS). Surgical options are usually not recommended during the first 6-12 months after radical prostatectomy.

Management of frequency, urgency and/or UUI can also be started with lifestyle modifications and PFME. Oral agents (anticholinergics and β3-agonists) are also considered before proceeding to third line options, such as Botox injection or sacral neuromodulation.

The treatment options for ED resulting from the treatment of prostate cancer can include oral PDE5-I as the first line, local therapy as the second (such as MUSE, intracavernosal injections, and perhaps low intensity shock wave therapy) and finally surgery as the third line. Standard questionnaires and patient reported outcome measurement tools should be used for the assessment of LUTS and erectile dysfunction prior and after initiation of treatment to guide the management.

Key Words: LUTS, incontinence, prostate cancer, management

Introduction

Management of prostate cancer continues to evolve towards ever more favorable oncologic outcomes. In this context, the patients' quality of life has become of primary importance as part of their cancer survivorship. Regardless of the treatment modality chosen for prostate cancer (radical prostatectomy, brachytherapy, external radiation therapy, high intensity focused ultrasound (HIFU), cryotherapy, etc.), two main complications following treatment include bothersome lower urinary tract symptoms (LUTS) and erectile dysfunction.

Address correspondence to Dr. Dean Elterman, Division of Urology, Toronto Western Hospital, 399 Bathurst Street, Main Pavilion, Room 8-317, Toronto ON M5T 2S8 Canada

Urinary incontinence

Although it is generally believed that new techniques for nerve-sparing radical prostatectomy (RP) have helped to reduce the incidence of post-prostatectomy urinary incontinence, the reported incontinence rates are widely different and may reach figures as high as 69%, depending on definitions and questionnaires used.[1,2] The widely accepted definition of post-prostatectomy incontinence (PPI) is a persistent stress urinary incontinence (SUI) over 1 year after prostatic surgery, assuming conservative therapy failure.[3] Having said that, SUI is not the only type of incontinence after RP and patients can also experience urge urinary incontinence (UUI). According to latest reports, 29% of patients experience storage symptoms after RP and 6% report urgency urinary incontinence.[4]

The etiology of post-prostatectomy incontinence (PPI) can be multifactorial. These include mechanisms that affect sphincteric function or those that affect bladder function (resulting in impaired bladder compliance, detrusor over- or underactivity). Among these two, sphincter insufficiency is assumed to be the most important reason for incontinence after RP, resulting in SUI.[5,6] Many factors such as age or history of transurethral resection of the prostate (TURP), can influence the continence rate after RP.[2]

Radiotherapy (RT) can also damage bladder wall function through impairment of blood circulation due to endarteritis within the detrusor with subsequent apoptosis and ultimately tissue loss.[7] These differences in pathophysiology are reflected in clinical features of LUTS following radiotherapy. In other words, while RP mostly causes SUI (starting in the early period after the operation), urinary symptoms following RT usually manifest as overactive bladder symptoms such as frequency, urgency or urge urinary incontinence (UUI). Brachytherapy can also cause LUTS. One large study of 2461 men after brachytherapy with or without external radiation showed that during 6.4 years of follow up, the incidence of UUI was about three times the incidence of SUI.[8] Patients who have received RT can also experience bladder outlet obstruction with symptoms such as hesitancy, weak urinary stream and intermittency. These can progress until 5 years after external radiotherapy or brachytherapy.[7,9] Later complications of RT can include urethral strictures, leading to urinary retention, and hematuria due to radiation cystitis.

Incontinence rates after cryotherapy and high intensity focused ultrasound (HIFU) are generally low and mostly depend on the volume of ablation (focal versus whole gland ablation). According to the report from the national Cryo On-Line Database (COLD) registry which contained information on 5853 patients, the rate of urinary incontinence after cryotherapy is 1.6% for focal ablation and 3.1 for whole gland ablation.[10] Similar degree of incontinence after HIFU was reported by several studies.[11,12]

Treatment of urinary incontinence depends on its clinical appearance (SUI versus UUI and OAB symptoms), regardless of prostate cancer treatment modality. The treatment options for SUI can be generally divided into two categories of conservative versus surgical options. Conservative methods such as pelvic floor muscle exercises, pad use, penile clamps or urethral plugs are considered the first line of treatment. If these fail to provide satisfactory results the surgical options could include: urethral bulking agents, male slings, and artificial urinary sphincter (AUS). Surgical options are usually not recommended during the first 6-12 months after RP, to allow for spontaneous recovery and maximum improvement of continence. Following the initial period, repeated assessment of incontinence severity helps to make a decision and to choose a certain type of surgical option. While urethral bulking agents and sling operations are suitable for mild to moderate cases of SUI, the AUS is recommended for more severe incontinence. Both pelvic floor muscle exercises and pharmacotherapy can be considered for overactive bladder (OAB) symptoms including UUI.

Pelvic floor muscle exercise

Pelvic floor muscle training (PFMT) is defined as "any program of repeated voluntary PFM contractions taught by a health-care professional." It is well understood by urologists that PFMT improves urethral stability and increases urethral closure pressure, which in turn helps with the improvement of SUI. Interestingly this is a treatment modality that can also improve OAB symptoms, including UUI, by inhibiting involuntary detrusor contractions (IBC). Patients may undergo office biofeedback or be referred to a physiotherapist who specializes in the pelvic floor. After providing appropriate instructions, patients can continue with PFME without any medical assistance. Unfortunately not everyone responds to PFMT.[13] According to the recent Cochrane report of 2736 patients treated by PFME for post-prostatectomy incontinence, there was only moderate evidence for an overall benefit from PFMEs compared with the control group.[14] Another interesting conclusion was obtained in a recent meta-analysis of PFME programs. The relative risk of continence in the PFME group versus control group was 2.16 at 3 months postoperatively. While at 12 months postoperatively this rate was reduced to 1.23. This indicates that PFME during the first year only helps to reach the maximum possible improvements faster.[15]

Penile compression device (penile clamp) for SUI

During the first 6-12 months after RP, or in patients who are not willing to have another surgery for correction of their SUI, or those who are not fit for additional operations penile compression devices are suitable options. They are available in different designs and sizes and can be purchased anonymously. The clamp is placed around the penis and mechanically compresses the urethra. Use of penile clamps help

to reduce the Incontinence Impact Questionnaire scores.[16] Although none of them completely eliminated urine loss, the devices are well tolerated and improve patients' confidence and tolerance of physical activity. However, complications such as pain, urethral erosion, obstruction, and edema have been reported with long term use.[17] These devices should be used only in men who have normal penile skin and who have sufficient cognitive function and dexterity to open and close the device. Also, the patients have to be instructed to remove the clamp in regular (2-3 hourly) intervals to empty the bladder and restore blood flow in the penis.[16] An alternative containment strategy includes the use of condom catheters. A specially designed condom with inner adhesive may be rolled onto a flaccid penis and the open end can drain into tubing connected to a leg bag.

Pharmacotherapy

Although it is generally believed that urinary incontinence after RP is a result of damage to the urinary sphincter mechanism and no medications have proven to restore this function, there is evidence of additional lower urinary tract disorders, which may play at least a small part in incontinence. Those include impaired compliance and detrusor overactivity (DO).[18] The rationale of pharmacotherapy is based on improving these disorders. Antimuscarinic drugs, β3 agonists and duloxetine have been proposed as medical treatments for these scenarios.[19]

Antimuscarinic and β3 agonists medication, are known as the second-line treatment for DO after PFMT, and may also be used in mixed urinary incontinence. The literature search identified a limited number of studies regarding the use of antimuscarinic medications after prostate cancer treatment; however, one can assume these medications to be also effective in treating OAB symptoms after prostate cancer treatment. The largest randomized double-blind study was in 640 patients. Patients were randomized to solifenacin 5 mg daily or placebo for 12 weeks in an early post-prostatectomy period. In results, the continence rate was 29% in the treatment group versus 21% in the placebo group.[20] Mirabegron (Myrbetriq) is a β3 agonist, with efficacy similar to antimuscarinics but with fewer side effects. There is no data available on its use in the post-prostate cancer population.

Duloxetine is a serotonin and norepinephrine reuptake inhibitor with influence on Onuf's nucleus in the sacral spinal cord. It provides stimulation of the pudendal nerve, increasing tonus of urethral sphincter and relaxing the detrusor muscle. Duloxetine has been mostly studied in treatment of female stress incontinence. According to most studies where duloxetine was investigated as a treatment option for post RP incontinence during the first 12 months, continence rates were similar to PFME or showed minimal additional effect. The most common reported side effects of duloxetine are fatigue, dry mouth, nausea, and constipation with controversial reports about discontinuation rates.[19]

In conclusion, there is not enough evidence to recommend the use of these medications as a standard treatment of post-prostate cancer treatment incontinence.

Surgical treatment (for SUI, frequency/urgency, and/or UUI)

When conservative treatment fails, surgery is still the treatment of choice, although there is no accepted guideline on when surgical treatment should be performed. Currently artificial urinary sphincter (AUS) is considered as the gold standard treatment for patients suffering from post-prostate cancer treatment incontinence. This is based on multiple studies showing acceptable long-term success rates among the other options. Other options, such as bulking agents and male slings can be applied as less invasive alternatives in selected patients. The most important factor for choosing among these surgical options is the severity of incontinence. In order to determine the degree of incontinence, some authors suggest using pad weight test, so-called 24 h pad test, to determine the degree of incontinence. To make the right decision about surgical treatment options, it has been generally accepted to divide the incontinence into mild (< 100 gm/24 hours), moderate (100-400 gm/24 hours) and severe (> 400 gm/24 hours). However, variation in activity level can lead to significant differences in 24 hour pad weights from one day to another and that is why many physicians refused the test and continue to rely on the patient's description of pad number and wetness.[21] Indeed, the size and type of pad and frequency of pad exchanging may be variable, but this information, received from the patient, helps to recognize his perception of the severity of incontinence. For example, if a patient uses several large pads or diapers, which are always wet, that may indicate severe incontinence. In contrast, wearing one or a few small pads per day can be classified as mild or mild-moderate incontinence.[22]

In a recent US national database study of 1246 patients who were operated upon due to SUI, it was shown that 34.9% of patients received an AUS, 36.4% were treated with urethral slings, and 28.7% received a urethral bulking agent.[23]

To date, the AMS 800 is the most commonly used artificial urinary sphincter (Boston Scientific, Marlborough, MA, USA). This AUS is made up of three parts: urethral cuff which wraps around the urethra to control the flow of urine; a pump which is placed in the scrotum and helps to move fluid into or away from the urethral cuff; and a balloon or reservoir which holds the fluid when the urethral cuff is deflated, which is placed beneath abdominal muscles. Reported continence rates vary between different studies from 55% to 86%.[1] These disparities resulted from lack of universal definition of treatment success as well as a different number of patients with negative predictive features such as radiation or cryotherapy as an etiology of incontinence.[24,25] Despite high rates of patient satisfaction, it has a risk of unique AUS complications including the risk of infection (up to 16%), urethral erosion (up to 13 %) and mechanical failure (up to 6.3%).[1,26,27] The second common AUS device ZSI 375, recently introduced in clinical practice, has reported a similar success rate.[28] But in contrast to AMS 800 it does not have the balloon (reservoir) and therefore does not require an additional abdominal incision. For that reason it has a lower risk of mechanical failures (3.4%).[28]

In the last decades, synthetic mesh male slings (MS) for SUI have become more popular due to its lower cost, less invasiveness and due to the fact that they do not require mechanical manipulation while voiding. The success rate varies from 50% to 90%[29-32] according to the definition of continence and type of device. Even though this outcome seems similar to the success rate of AUS, it has to be kept in mind that MS study cohorts have been different from AUS cohorts. Most urologists concluded that in order to improve the outcomes, careful patient selection is obligatory. The proper candidate should have a mild to moderate degree of SUI, adequate detrusor contraction with no history of radiation treatment in the pelvic area.[33]

The MS can be divided into adjustable or non-adjustable types which in turn divided into several subtypes determined by fixation mechanism and anatomical position.[33] The adjustable MS can be easily modified to elevate the urethral compression if incontinence does not resolve. With this rationale, it has at least a theoretical advantage over non-adjustable MS. However, no significant differences have been observed in the clinical outcomes or patient satisfaction rates when comparing these devices.[29,30]

At the present time, the AdVance XP sling (Boston Scientific, Marlborough, MA, USA) is the most frequently worldwide used retro-urethral trans-obturator sling which consists of a polypropylene mesh that is placed under the membranous urethra through a trans-obturator approach.[33] The concept of the urethral sling is to reposition the bulbar urethra by a distance of 3-4 cm which produces additional functional resistance to the posterior urethra and provides support for the external sphincter complex.[34]

The overall complication rate for the AdVance sling was reported at 12.3%. Major early postoperative complications include transient urinary retention requiring temporary re-catheterization (2.7%-15.1%), local infection (1.7%-6.4%) and perineal pain (4%-17%). Late complications are mesh erosions (1.9%-12.8%) into bladder or urethra that are most commonly found in patients who have received radiation therapy.[35]

Another type of inflatable continence devices called ProACT consists of two silicone balloons on the proximal end and a titanium port in the distal end. The two balloons are implanted just below the bladder neck, one on each side, through a trans-cutaneous access in the perineal area under fluoroscopy or trans-rectal ultrasound guide. The balloons can be inflated or deflated to compress the urethral lumen just below the bladder neck.[33] The technical ease of insertion and the lack of circumferential urethral dissection are proposed advantages of ProACT device. Despite the initial high cure rate, more than a third of patients were dissatisfied with the surgical outcome in the long term. In one long term study, it has been found that only 45% of patients remained satisfied with ProACT device at a median follow up of 57 months.[36] However, given its minimally invasive nature, this device may provide some benefit for additional improvement of continence in case of persistent or recurrent incontinence after sling implantation. Common complications of ProACT device include balloon migration, pain, infection, and recurrent incontinence.

Several types of bulking agents have been proposed for SUI, such as macroplastique, collagen, bulkamide hydrogel and dextranomer/hyaluronic acid copolymer. In the case of post–prostate cancer treatment incontinence, they are injected submucosally in the anastomosis region in an attempt to enhance coaptation of the urethra.[19] In general, these agents have been shown to have low and short lasting effects and recommended in very certain scenarios. One of these indications is recurrent or persistent incontinence after male sling operations. In this case, 80% of men required no further treatment for PPI. Given its low invasive nature, only low-grade complications were reported in 10% of patients.[37]

Surgical options for the management of OAB symptoms could include botox injection or sacral neuromodulation. The details of these options are out of scope of this article.

Erectile dysfunction

Erectile dysfunction (ED) after treatment of prostate cancer is a significant quality of life problem for patients and their healthcare providers.

One of the "gold standard" treatment options for localized prostate cancer is RP, which has established long term oncologic benefits.[38] ED is a common side effect of the surgery, and given the trend towards being younger at the time of diagnosis and treatment with excellent survival rates, ED becomes a primary concern after RP for many men. The literature reports have a wide variation in erectile function recovery (EFR) rate following RP. In one previous meta-analysis of 22 relevant studies, the rate of EFR ranged from 25% to 78% in an 18 month follow up period after RP. Open RP and traditional laparoscopic RP had similar EFR (57% versus 58%), while robot-assisted RP resulted in a higher EFR rate, 73% compared with these other approaches. Patients < 60 years old had a higher EFR rate than patients ≥ 60 years, with EFR being 77% versus 61% respectively.[39] In a more recent study, the authors used more strict definitions of ED and assessed the number of patients who returned to having baseline erections after RP during 24 months without the use of any medications for ED and compared the results before and after RP. They found that only 22% of patients returned to their baseline erectile function (EF) without the use of medication. Of note, only 4% of men who were ≥ 60 years of age with functional erections prior to surgery achieved their baseline EF without the use of medication.[40]

The introduction of robotic surgery has led to further evolution of the RP technique. This allows for more precise identification of the periprostatic fascia, thus providing a higher degree of preservation of the periprostatic neurovascular tissue. While most studies have shown a higher EFR rate in robotic surgery, a recent study from a high-volume center, has shown that EFR has not changed over the last decade. With the recovery rates during the last decade being 27% and 34% at 1 and 2 year post-RP respectively.[41]

The second common type of prostate cancer treatment is radiation therapy (RT), which can be external or internal (brachytherapy) radiation with different modalities and radiation dose rates. In contrast to radical prostatectomy, where ED is evident soon after the operation, radiation-based treatments lead to slowly declining EF over 1 to 3 years. Survival rates of prostate cancer patients are high and within 3-5 years of completing treatment, approximately one-half of these patients will develop ED.[42] There are several new techniques for external RT that allow for the delivery of higher doses of radiation with better

cancer control rates and fewer side effects, such as intensity-modulated radiation therapy (IMRT) or stereotactic radiation therapy. However, according to several reports, EFR rates were not much different from rates following different types of external RT or brachytherapy.[42,43]

In brief, erection is achieved through five phases: initial filling, partial erection, full erection, rigid erection, and return to flaccid state. Psychological or physical sexual stimulation leads to smooth muscle relaxation of the arteries, which allows an increase in blood flow to the corpora cavernosa. Full erection occurs when full rigidity is obtained. During a return to a flaccid state, muscle contractions result in the increased venous outflow and decreasing penile length and girth.[44] Supposed mechanisms of ED after RP or RT rely on neuronal and vascular damage, which can lead to ED through smooth muscle atrophy of the corpora cavernosa, similar to other muscles that atrophy when they are unused.[42] Both in-vitro and in-vivo studies support the theory that penile hypoxia results in collagen accumulation, smooth-muscle apoptosis and ultimately cavernosal fibrosis. Finally, these changes within the corpus cavernosum contribute to venous leakage and permanent ED, even if the normal function of the nerves return.[45]

Ablative therapy (whole gland or focal) was introduced with the hope of avoiding some of the adverse effects of radical therapy including ED, bladder or bowel dysfunction and urinary incontinence. Ablative therapies refer to a group of minimally invasive modalities, which aim for either total, subtotal or focal ablation (or destruction) of the prostate gland. Currently, apart from cryotherapy and HIFU, which have been investigated within the context of clinical trials, none of the others have been used in daily practice.[46] Currently, ED rates after ablative therapy is not interpretable, as many studies within the existing literature either use their own definitions of ED or use no definition at all.[47] Cryotherapy was one of the first ablative techniques to be introduced. It induces cell lysis by cooling tissues down to –40°C. Autonomic dysfunction occurs if the nearby neurovascular tissue reaches 20°C, which may explain the high rates of ED observed after cryotherapy. With HIFU, focused ultrasound energy results in tissue ablation via thermal coagulation, necrosis, and acoustic cavitation. It has the potential of more precise ablation than cryotherapy but many men report ED nevertheless.[48]

In a study that compared cryotherapy with HIFU in cases of whole gland ablation in patients with good pretreatment EF, there was a significant fall in International Index of Erectile Function (IIEF-5) in

both groups at 6 months. The fall from baseline was statistically greater for whole gland cryotherapy than whole gland HIFU at all time follow up points. There was a minimal improvement from the initial fall in IIEF-5 during the 24 months for both modalities.[12] On the other hand, focal ablation has a less detrimental effect on EF.[49] Interestingly, in one non-randomized comparative study, the whole gland HIFU was found to be associated with better EF than both focal and whole gland cryotherapy.[12] In a recent meta-analysis of ablative therapy outcomes, five cryotherapy studies and only two HIFU studies provided information on ED. In cases of cryotherapy, the data showed a lower rate of ED compared to those receiving RP at 1 year, but the difference was not statistically significant. However, analysis of the above mentioned HIFU studies showed a statistically less ED following HIFU comparing to RP.[46]

The treatment options for ED in post-prostate cancer treatment patients are not different from the options for common ED. Traditional three lines of recommended treatment can be applied in most cases. These include oral therapy as the first line, local therapy as second and operative treatment as the third line.[50]

Integral to the discussion on ED treatment is an understanding of how EF is assessed. Although several validated questionnaires have been developed specifically to assess the EF after prostate cancer treatment, regular International Index of Erectile, Function (IIEF) test and its variation are possible and effective to use for a quick assessment both before and after treatment, due to their simplicity and familiarity to general care practitioners. IIEF-5, also named Sexual Health Inventory For Men (SHIM) is an abbreviated version of the IIEF consisting of 5 questions, which is easier to implement in the clinical setting than the full version of the IIEF.[51] Generally, a score > 21 is considered to represent a normal EF.

Given pathophysiology of ED, the treatment strategy aims to improve oxygenation of cavernosal tissue and prevent structural changes by providing better blood supply. Thus, it has been proposed that using pharmacological or mechanical treatment for ED before, during and after prostate cancer treatment will improve blood supply and prevent cavernosal fibrosis. This concept, also named as "penile rehabilitation" or "erectile function rehabilitation", has been developed to specifically treat ED following radical prostatectomy, but can be applied to other prostate cancer treatment approaches too. Despite this, no official definition or widely accepted treatment plan has been established.[45]

A variety of treatment regimens have been introduced as penile rehabilitation strategies using PDE5i. According to the American Urological Association

(AUA) meta-analyses that compared several penile rehabilitation regimens, including PDE5i and placebo among men who had RP indicate no difference in rates of restored EF between groups. In addition, early administration of PDE5i does not improve later responses to these medications compared to early administration of placebo.

A new useful algorithm to care for sexual dysfunction following prostate cancer treatment was recently developed by Canadian men's sexual health experts and published in Canadian Urological Association journal in December 2018.[52] This algorithm was based on a complex approach, which may be tailored to the individual patient (and partner) presentation. The baseline recommendations for all patients are attempts to perform a regular sexual activity (at least once a week) and involve the sexual partner in the treatment process. The algorithm divides into three sections. The first section includes recommendations for using PDE5i, ICI, MUSE or VED. Choosing certain conservative options depends on the type of prostate cancer treatment received (radiation versus surgery with different levels of cavernous nerve sparing), followed by the desired level of invasiveness (a mechanical device, medication or intracavernous injection).[52] Surgical options including rigid or inflatable penile prosthesis, are recommended as the final treatment line. These are usually not recommended during the early post-surgical phases to allow for natural recovery.[50]

The second section of the algorithm provides treatment recommendations according to time: pre- or post-prostate cancer treatment and according to patient goals for erectile recovery (long term versus short term). The third section of the algorithm is based on providing patients with an expected erection recovery timeline. This is intended to help patients realize the real time of the recovery process. Thus, even using pharmaceutical mechanical tools for ED after RP, some early recovery of mild to moderate erection is expected within 4 months after the operation in less than 10% of patients.[52]

Conclusion

In conclusion, similar to common ED, management of post-prostate cancer treatment ED can be initiated by general physicians by starting oral therapy and referring the patient to the urologist in refractory cases for a second and third line therapy. In such model, general physicians, using the algorithm suggested by Canadian men's sexual health experts, can start the "rehabilitation treatment" and, given longstanding relationships with the patient they can provide an important therapeutic impact that eventually improves clinical results. □

References

1. Kretschmer A, Nitti V. Surgical treatment of male postprostatectomy incontinence: current concepts. *Eur Urol Focus* 2017;3(4-5):364-376.

2. Tienza A, Robles JE, Hevia M et al. Prevalence analysis of urinary incontinence after radical prostatectomy and influential preoperative factors in a single institution influential preoperative factors in a single institution. *Aging Male* 2018; 21(1):24-30.

3. Caremel R, Corcos J. Incontinence after radical prostatectomy: anything new in its management? *Can Urol Assoc J* 2014;8(5-6): 202-212.

4. Hosier GW, Tennankore KK, Himmelman JG, Gajewski J, Cox AR. Overactive bladder and storage lower urinary tract symptoms following radical prostatectomy. *Urology* 2016;94: 193-197.

5. Singla AK. Male incontinence: pathophysiology and management. *Indian J Urol* 2007;23(2):174-179.

6. Majoros A, Bach D, Keszthelyi A, Hamvas A, Romics I. Urinary incontinence and voiding dysfunction after radical retropubic prostatectomy (prospective urodynamic study). *Neurourol Urodyn* 2006;15(1):2-7.

7. Biers S, Sievert K, Thiruchelvam N. Overactive bladder syndrome and lower urinary tract symptoms after prostate cancer treatment. *Curr Opin Urol* 2017;27(3):307–313.

8. Leapman MS, Stone NN, Mock S, Stock RG, Hall SJ. Urinary incontinence following prostate brachytherapy. *Urology* 2016; 95:151-157.

9. Ferrer M, Guedea F, Suárez JF et al. Quality of life impact of treatments for localized prostate cancer: cohort study with a 5 year follow-up. *Radiother Oncol* 2013;108(2):306-313.

10. Ward JF, Jones JS. Focal cryotherapy for localized prostate cancer: a report from the national Cryo On-Line Database (COLD) Registry. *BJU Int* 2012;109(11):1648-1654.

11. Uchida T, Tomonaga T, Kim H et al. Improved outcomes with advancements in high intensity focused ultrasound devices for the treatment of localized prostate cancer. *J Urol* 2015;193(1):|103-110.

12. Liu YY, Chiang PH. Comparisons of oncological and functional outcomes between primary whole-gland cryoablation and high intensity focused ultrasound for localized prostate cancer. *Ann Surg Oncol* 2016;23(1):328-334.

13. Siegel AL. Pelvic floor muscle training in males: practical applications. *Urology* 2014;84(1):1-7.

14. Anderson CA, Omar MI, Campbell SE et al. Conservative management for postprostatectomy urinary incontinence. *Cochrane Database Syst Rev* 2015;1:CD001843.

15. Fernandez RA, García-Hermoso A, Solera-Martinez M. Improvement of continence rate with pelvic floor muscle training post-prostatectomy: a meta-analysis of randomized controlled trials. *Urol Int* 2015;94(2):125-132.

16. Barnard J, Westenberg AM. The penile clamp: medieval pain or makeshift gain? *Neurourol Urodyn* 2015;34(2):116:115–116.

17. Kalra S, Srinivas PR, Manikandan R, Dorairajan LN. Urethral diverticulum: a potential hazard of penile clamp application for male urinary incontinence. *BMJ Case Rep* 2015;2015:bcr2015209957.

18. Ventimiglia B, Sigona M, Di Dio A, Puglisi T, Costantino G. Urinary incontinence and neuropathy after radical prostatectomy: diagnosis and treatment. *Urologia* 2015;82(1):42-45.

19. Løvvik A, Müller S, Patel HR. Pharmacological treatment of post-prostatectomy incontinence: what is the evidence? *Drugs Aging* 2016;33(8):535-544.

20. Bianco FJ, Albala DM, Belkoff LH et al. Placebo control, phase 4, multicenter study evaluating urinary continence after robotic assisted radical prostatectomy. *J Urol* 2015;193(4):1305-1310.

21. Malik RD, Cohn JA, Chung DE, Bales GT. Assessing variability of the 24-hour pad weight test in men with post-prostatectomy incontinence. *Int Braz J Urol* 2016;42(2):327-333.

22. Syan R, Nitti VW. Post-prostatectomy Incontinence Initial Evaluation. In: Sandhu J. (eds) Urinary Dysfunction in Prostate Cancer. Springer Cham. 2016

23. Chughtai B, Sedrakyan A, Isaacs AJ et al. National study of utilization of male incontinence procedures. *Neurourol Urodyn* 2016;35(1):74-80.

24. Miller AR, Linder BJ, Rangel LJ, Yang DY, Elliott DS. The impact of incontinence etiology on artificial urinary sphincter outcomes. *Investig Clin Urol* 2017;58(4):241-246.

25. Husch T, Kretschmer A, Thomsen F et al. Risk factors for failure of male slings and artificial urinary sphincters: results from a large middle European cohort study. *Urol Int* 2017;99(1):14-21.

26. Ravier E, Fassi-Fehri H, Crouzet S, Gelet A, Abid N, Martin X. Complications after artificial urinary sphincter implantation in patients with or without prior radiotherapy. *BJU Int* 2015;115(2):300-307.

27. Loh-Doyle JC, Hartman N, Nazemi A et al. (2018) Mechanical failure rates of artificial urinary sphincter components: is the 3.5-cm urethral cuff at higher risk? *Neurourol Urodyn* 2019;38(1):187-192.

28. Ostrowski I, Blewniewski M, Neugart F et al. Multicentre experience with ZSI 375 artificial urinary sphincter for the treatment of stress urinary incontinence in men. *Urologia* 2017;84(3):148-152.

29. Seweryn J, Bauer W, Ponholzer A, Schramek P. Initial experience and results with a new adjustable transobturator male system for the treatment of stress urinary incontinence. *J Urol* 2012;187(3):956-961.

30. Cornel EB. Argus-T adjustable male sling: the influence of surgical technique on complications and short-term efficacy. *Urol Int* 2016;96(2):164-170.

31. Friedl A, Muhistadt S, Zachoval R et al. Long-term outcome of the adjustable transobturator male system (ATOMS): results of a European multicentre study. *BJU Int* 2017;119(5):785-792.

32. Bauer RM, Grabbert MT, Klehr B et al. 36-month data for the AdVance XP ® male sling: results of a prospective multicentre study. *BJU Int* 119(4):626-630.

33. Chung E. Contemporary surgical devices for male stress urinary incontinence: a review of technological advances in current continence surgery. *Transl Androl Urol* 2017;6(Suppl2):S112–S121.

34. Rehder P, Gozzi C. Transobturator sling suspension for male urinary incontinence including post-radical prostatectomy. *Eur Urol* 2007;52(3):860-866.

35. Crivellaro S, Morlacco A, Bodo G et al. Systematic review of surgical treatment of post radical prostatectomy stress urinary incontinence. *Neurourol Urodyn* 2016;35(8):875-881.

36. Venturino L, Dalpiaz O, Pummer K, Primus G. Adjustable continence balloons in men: adjustments do not translate into long-term continence. *Urology* 2015;85(6):1448-1452.

37. Chung A, Lynch W, McCammon K. Outcomes of periurethral bulking agent injection for treatment of postprostatectomy. *Eur Urol Suppl* 2018;17(2):e1655.

38. Eastham JA, Scardino PT, Kattan MW. Predicting an optimal outcome after radical prostatectomy: the trifecta nomogram. *J Urol* 2008;179(6):2207-2211.

39. Tal R, Alphs HH, Krebs P, Nelson CJ, Mulhall JP. Erectile function recovery rate after radical prostatectomy: A meta-analysis. *J Sex Med* 2009;6(9):2538-2546.

40. Nelson CJ, Scardino PT, Eastham JA, Mulhall JP. Back to baseline: erectile function recovery after radical prostatectomy from the patients' perspective. *J Sex Med* 2013;10(6):1636-1643.

41. Capogrosso P, Vertosick EA, Benfante NE et al. Are we improving erectile function recovery after radical prostatectomy? Analysis of patients treated over the last decade. *Eur Urol* 2019;75(2):221-228.

42. Mahmood J, Shamah AA, Creed TM et al. Radiation-induced erectile dysfunction: Recent advances and future directions. *Adv Radiat Oncol* 2016;1(3):161-169.

43. Abdullah E, Idris A, Saparon A. Papr reduction using scs-slm technique in stfbc mimo-ofdm. *ARPN J Eng Appl Sci* 2017;12(10): 3218-3221.

44. Dean RC, Lue TF. Physiology of penile erection and pathophysiology of erectile dysfunction. *Urol Clin North Am* 2005; 32(4):32:379-395.

45. Sopko NA, Burnett AL. Erection rehabilitation following prostatectomy-current strategies and future directions. *Nat Rev Urol* 2016;13(4):216-225.

46. Ramsay CR, Adewuyi TE, Gray J et al. Ablative therapy for people with localised prostate cancer: A systematic review and economic evaluation. *Health Technol Assess* 2015;19(49):1-490.

47. Postema AW, De Reijke TM, Ukimura O et al. Standardization of definitions in focal therapy of prostate cancer: report from a Delphi consensus project. *World J Urol* 2016;34(10):34:1373-1382.

48. Faure Walker NA, Norris JM, Shah TT et al. A comparison of time taken to return to baseline erectile function following focal and whole gland ablative therapies for localized prostate cancer: A systematic review. *Urol Oncol* 2018;36(2):67-76.

49. Li LY, Lin Z, Yang M, Gao X, Xia TL, Ding T. Comparison of penile size and erectile function after high-intensity focused ultrasound and targeted cryoablation for localized prostate cancer: a prospective pilot study. *J Sex Med* 2010;7(9):3135-3142.

50. Bella AJ, Lee JC, Carrier S, Benard F, Brock GB. 2015 CUA Practice guidelines for erectile dysfunction. *Can Urol Assoc J* 2015;9(l-2)23-29.

51. Cappelleri JC, Rosen RC. The Sexual Health Inventory for Men (SHIM): A 5-year review of research and clinical experience. *Int J Impot Res* 2005;17(4):307-319.

52. Elterman DS, Petrella AR, Asseldonk B. Van et al. Canadian consensus algorithm for erectile rehabilitation following prostate cancer treatment. *Can Urol Assoc J* 2018; epub ahead of print.