

Chapter 8

Adjunctive Measures and New Therapies to Optimize Early Return of Urinary Continence

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Introduction

In the era of robotically assisted laparoscopic prostatectomy despite the powerful visualization, refined surgical techniques, minimal blood loss, and multiple nerve-sparing and reconstructive bladder neck techniques, urinary incontinence still creates a significant burden on patients and their treating physicians. Chapter 5 focuses on the preoperative, intraoperative, and postoperative technical and surgical skills and modifications that may improve urinary continence in the early and late post-prostatectomy period. In this chapter, we review the literature on nonsurgical interventions that may improve urinary continence in the short near term. Return of urinary continence as reported in the literature varies considerably, depending on surgeon expertise, definition, surgical volume (of both the surgeon and the hospital/medical center), and whether or not the outcome is patient or surgeon reported. Furthermore, the incidence of urinary incontinence experienced by men prior to prostatectomy is generally not recorded and not well known. For instance, Johnson and Ouslander reported 15–30% of men over age 65 had urinary incontinence to some degree before undergoing radical prostatectomy [1].

Predictors of Urinary Continence Following Prostatectomy

For the past 50 years, urologists have been investigating risk factors that could predict urinary continence outcomes following radical prostatectomy. Knowledge of these risk factors may help surgeons counsel patients more appropriately preoperatively and

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consider earlier and more aggressive interventions. Kumar et al. retrospectively analyzed their prospective collected data on 3362 patients with 1-year follow-up who have undergone robotic-assisted radical prostatectomy stratifying them to six groups: Group I, age more than 70; Group II, BMI 35 and over; Group III, prior bladder neck procedures; Group IV, prostate weight equal to or more than 80 g; Group V, salvage prostatectomy; and finally Group VI, with none of the above risk factors. Interestingly, the authors demonstrated that selected risk factors such as age, prostate weight, BMI, and prior bladder neck procedures only adversely affected the time to return to continence not the continence rate. Nevertheless, salvage prostatectomy patients showed to have a significantly lower continence rates in addition to delayed in mean time to return to continence [2].

In another smaller study with a shorter follow-up of 1 month from Canada, 327 patients who had undergone robotic-assisted radical prostatectomy were prospectively evaluated for predictors of early continence. The authors investigated prostate-specific antigen, prostate weight, International Prostate Symptom Score (IPSS), Sexual Health Inventory for Men (SHIM) score, and type of nerve sparing performed as potential contributing risk factors in early continence. Advanced age and IPSS scores were independent predictors of early continence following robotic radical prostatectomy in this limited patient population suggesting that significant lower urinary tract symptoms can negatively affect the path to continence postsurgery [3].

Other investigators have created a predictive model of urinary continence recovery after radical prostatectomy that incorporates magnetic resonance imaging data (membranous urethral length) and clinical contributors (age, BMI, and American Society of Anesthesiologists score) [4]. In a large group studied by Holm et al., 844 patients were prospectively evaluated for patients' ratings and risk factors for urinary continence following 12 months follow-up. The authors reported a considerable variation in reporting continence depending on the definition applied for urinary incontinence. They also reported that age more than 65, not working, sexual dysfunction, and preoperative urinary incontinence were strong predictors for postprostatectomy incontinence [5].

These risk stratifications not only can be used to counsel patients preoperatively appropriately for their continence expectations following prostatectomy but also encourage early intervention in the high-risk group.

Pathophysiology of Lower Urinary Tract Symptoms

In order to understand what adjunctive measures may influence the path to continence, we need to understand how the pelvic floor, urethral anatomy, and function change following radical prostatectomy. Chapter 1 reviews the anatomy, muscles, fascia, innervations, and supporting structures involved in male continence. However, our understanding of long-term changes that occur in the pelvic floor and urethral sphincter over a period of time is more limited. Hacad et al. evaluated pelvic floor electromyography (EMG)

before, at 1, 3, and 6 months following radical retropubic prostatectomy. In this small group of 38 men, 18 (47.7%) patients suffered from urinary incontinence 6 months postoperatively and surface EMG showed significant changes in fast contraction amplitude, rest amplitude following fast contraction, and in 10 second sustained contraction amplitude possibly as a result of nerve changes to the external urethral sphincter suggesting a whole new urethral sphincter functionality or condition following radical retropubic prostatectomy procedure [6]. In another elegant prospective study by Catarin et al., 44 patients were evaluated and they were able to show that pudenda-anal and pudenda-urethral reflexes were basically unchanged 6 months following nerve-sparing prostatectomy confirming unchanged sensory and motor pudendal innervations to the pelvic region. However, 34 (77.3%) of the patients demonstrated significant autonomic denervation of the membranous urethral mucosa which was associated with urinary incontinence [7].

Many experts believe that main contributing factor to urinary incontinence post-prostatectomy is due to urethral sphincter incompetency [8] possibly due to multiple etiologies but mainly nerve damage [9]. In addition, bladder dysfunction and lower urinary tract symptoms (LUTS) have been attributed to indirectly affect continence in this group of patients. Changes in geometric bladder anatomy, location, inflammation, and neuroplasticity can also contribute to detrusor dysfunction following radical prostatectomy procedure.

Haga et al. used magnetic resonance imaging postprostatectomy to show urinary pooling in the urethra as a possible explanation for inducing urgency [10]. Porena et al. reviewed literature and reported a de novo detrusor overactivity of 2–77%, decreased bladder compliance in 8–39%, impaired detrusor contractility in 29–61% of patients [11]. Multiple studies in the literature have also shown an association between detrusor overactivity and urinary incontinence following radical prostatectomy [12, 13]. Urodynamic evaluation immediately following RARP in 87 patients showed a decrease in cystometric capacity (from 341 to 250 ml) and a decrease in maximal urethral closure pressure (from 84.6 to 35.6 cmH₂O). In addition, 75 (86%) of the patients demonstrated an abdominal leak point pressure of 47.7 cmH₂O [14]. Hammer and Huland showed significant bladder and sphincter changes after radical prostatectomy. They found decreases in bladder capacity, bladder compliance, and an increase in bladder instability [15]. However, Asnat et al. found the primary cause of postprostatectomy incontinence is sphincteric in nature, affecting 88% of men. In fact, it was the only cause of incontinence in 32.5% of men [16]. Nonetheless, detrusor instability was identified in 33.7% but was the primary cause of incontinence in only 7.2% [17]. Giannantoni et al. carried out a well-designed study involving 49 patients. They evaluated these patients just before surgery, 1 and 8 months postoperatively. These authors found detrusor overactivity was present in 55% of patients before surgery and persisted with little change in 1 and 8 months postoperatively. Furthermore, 28.6% of the patients developed hypocontractility, possibly due to transient bladder denervation at the time of surgery. Additionally, at 1 month 18.4% of the men and at 6 months 10.2% of the men had de novo and continued decrease in compliance of their bladders [18].

These data suggest there is more to postprostatectomy incontinence than just urethral competency, thus providing other target areas for intervention. So, what can we do in an adjuvant or near term fashion to get our patients continent, and to do so in as short a period of time as possible? The area of adjuvant management is checkered with anecdotal surgeon-specific notions, ideas, and surgical techniques. There are many small, nonrandomized single surgeon trials and larger, well-done trials with equivocal results. Despite the distinct lack of clearly superior results, there are things we can do that may help, and we shall review these options in this chapter. Adjuvant therapies fall into basically four categories: pharmacological, physical in the form of pelvic floor exercises, surgical (male urethral sling, artificial urinary sphincter), and investigational such as stem cells. In this chapter, we will provide detailed reviews of current literature and valuable insights into each of the above categories.

Pharmacological Intervention

Some pharmacological agents have been evaluated postprostatectomy to potentially improve overall incontinence in patients. Tolterodine, vardenafil, tadalafil, solifenacin, and duloxetine have been proposed to address the lower urinary tract dysfunction and the bladder stability and thus improve the overall continence rate.

Anticholinergic Medications

It appears that since bladder dysfunction has some role in postoperative incontinence, anticholinergics or other medications that improve overactive bladder symptoms may impact the recovery to urinary continence. Many if not most urologists use anticholinergics as a part of their postoperative incontinence regimen. However, not many controlled trials have been carried out to evaluate the benefits of these medications. Liss et al., in an early pilot study, evaluated the usefulness of solifenacin in patients undergoing Robotic Prostatectomy by a single surgeon. They hypothesized that return of continence at greater than 3 months was in large part due to detrusor overactivity and/or dysfunction. Forty men were enrolled and “appeared” to benefit [19]. This trial led to a large, multicenter randomized double-blinded study of the anticholinergic, solifenacin, in men undergoing Robotic Prostatectomy. This well-designed study had a phase-in time of from 7 to 21 days after catheter removal, to allow a washout period for those on preoperative anticholinergics and also to exclude those who achieved complete urinary control in this early period. Patients were randomized one to one to solifenacin or a placebo. Patients were also given a smart phone-like device called a PDA (Diary Pro, Invivo Data/eResearch Technology, Inc., Philadelphia, Pennsylvania) which evaluated daily pad use and

drug intake. The PDA alerted patients every evening until the necessary information was entered. The primary endpoint was a time to complete urinary control at 3 months from first dose of study drug. Over 1000 patients were screened and 640 were randomized. Although there was no statistical difference in time to continence, 29% of the solifenacin group versus 21% of the placebo group achieved complete continence, $P=0.04$. In addition, pads per day usage in the treatment group decreased by 3.2 pads per day versus 2.9 in the controlled group, $P=0.03$. Adverse events, such as constipation, were the same for both groups but, as expected, dry mouth was more common in the treatment group, 6.1% versus 0.6%. Although the primary endpoint of the time to return of continence was not achieved, important secondary endpoints were. Namely, 99/313 solifenacin versus 66/309 placebo achieved continence during this 3-month study and pad usage decreased by a statistically significant margin in favor of the treatment arm. Limitations of this study include: no urodynamics testing was carried out preoperatively or postoperatively, the digital PDA used to record progress may have had an associated placebo effect, and that longer term follow-up up to 12 months was not designed in the study. Nonetheless, this study underscores potential benefits of anticholinergics in this patient population [20].

Alpha Agonists

As the bladder neck, trigone, and the membranous urethra are rich in alpha receptors, many urologists have over time used the alpha stimulating agents such as ephedrine and pseudoephedrine hydrochloride to help speed postprostatectomy incontinence recovery. The hope has been that by stimulating alpha receptors, a better closure of the bladder neck and sphincter can be achieved, resulting in greater resistance to flow and improved continence. Few clinical trials however have been carried out and reported. Furthermore, most of these drugs have a side effect profile (hypertension and CNS effects) that limits their usefulness and tolerability.

Radley et al. studied the usefulness of methoxamine, an α_1 adrenoceptor selective agonist in women with stress urinary incontinence. This small trial was a double-blinded crossover study giving the women placebo or methoxamine IV and measuring urethral pressures. Although statistical significance was not achieved, at the highest dose there was a definitive increase in maximum urethral pressure. Unfortunately, there was a significant increase in systolic blood pressure and decrease in pulse rate. Furthermore, all the subjects reported piloerection (“goose-flesh”), cold extremities, and headaches. The modest gain in urethral pressure was more that outweighed by the side effect profile [21].

In summary, alpha agonists may have a role to play, albeit a small one? Use of these drugs should be considered with care and patients need to be aware of potential toxicities and monitored accordingly.

Other Pharmaceutical Agents

Duloxetine

Duloxetine is a serotonin/norepinephrine reuptake inhibitor which has long been used in women with stress urinary incontinence. Cornu et al. in a randomized, placebo-controlled trial randomized 16 patients to 3 months of duloxetine 80 mg for three months versus 15 patients randomized to placebo. Treatment group reported significant improvement in multiple urinary questionnaires including QOL suggesting duloxetine may be a potential pharmacological intervention in postprostatectomy incontinence [22]. Filocamo et al. reported a more comprehensive and larger trial by randomizing 112 patients to PFMT plus duloxetine versus PFMT and placebo for 16 weeks. Authors reported a significantly improved in I-QOL scores and significant decrease in IEF scores. Authors also reported a discontinuation rate due to adverse events of about 15.2% with nausea being the most common side effect [23]. Serra et al. evaluated a group of 68 men who were over a year out from radical prostatectomy and had persistent stress urinary incontinence. The median duration of treatment was approximately 6 months. Seventy-four percent of patients had a significant decrease in their International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI-SF) and 57% experienced a significant decrease in pad use. However, 25% of the patients stopped taking the drug due to side effects such as mild extremity trembling, fatigue, and dry mouth [24].

Phosphodiesterase Type 5 Inhibitors (PDE5-I)

PDE5-I are known to positively affect postprostatectomy erectile dysfunctions and play an important role in potency rehabilitation postoperatively. Recent data suggests the PDE5-I can concurrently improve lower urinary tract symptoms in benign prostatic hyperplasia. Gacci et al. evaluated the role of vardenafil in continence recovery following nerve-sparing radical prostatectomy. Thirty-nine patients were randomized and double blinded to vardenafil on demand, vardenafil nightly, and placebo. Authors demonstrated that nightly vardenafil can improve postprostatectomy incontinence when compared to controls but the time to recovery is not affected by it [25]. Some investigators were also able to demonstrate a positive effect of PDE5-I on postprostatectomy incontinence [26] [27], versus others have not shown any benefit [28].

Stem Cell Therapy

In the early to mid-1990s, many investigators identified bone marrow stromal cells capable of differentiating into numerous cell lines. Caplan, in 1991, defined these as “mesenchymal” “stem cells” [29]. This definition has since been refined by the International

Society for Cell Therapy as “multipotent stromal cells” [30]. Since that discovery, well over 5000 publications have appeared in peer-reviewed literature regarding stem cells. The potential urologic opportunities for the use of these cells have also increased dramatically. The regenerative capabilities offered by stem cells have been exploited by plastic surgeons in the treatment of mastectomy defects [31] and facial defects due to trauma [32]. This regenerative option has generated much interest and enthusiasm in urologists for the potential of treating urinary incontinence and impotence.

In a comprehensive review of stem cell therapy, Damaser describes stem cells as “unique population of cells with three defining characteristics: (1) ability to self-renew; (2) multipotent differentiation potential; and (3) clonogenicity, or the ability to form clonal cell populations derived from a single stem cell.” These characteristics are important in the ability of stem cells to affect repair of injured tissues, in this case the urinary rhabdosphincter [33]. Stem cells are able to be derived from a number of sources: embryonic stems cells (ESCs) and mesenchymal stem cells (MSCs), which include: placental or amniotic fluid stem cells (AFPSCs), muscle-derived stem cells (MDSC), adipose-derived stem cells (ADSC), bone-marrow-derived stem cells, and even urinary-derived stem cells (USC). The mechanism of action of stem cells is their ability to migrate to sites of acute and chronic injury where they facilitate healing. The ability of stem cells for multipotential differentiation and proliferation is felt to be the mechanism for return of urinary rhabdosphincter recovery through an increase in muscle and neuronal volume. Furthermore, it is also felt that stem cells secrete bioactive factors that have additional therapeutic benefits and are perhaps more responsible for the large, overall therapeutic effects, as stem cells do not remain long in injured tissues.

As the science of stem cells and their multipotential use in any number of diseases has improved and gained clinical traction, their use in stress urinary incontinence has grown as well. Many researchers and investigators believe that the future management of stress urinary incontinence will be by stem cell injections into the rhabdosphincter. Zhao et al., in a surgically created incontinent rat model, using adipose-derived stem cells (ADSC) with nerve growth factor, demonstrated a significant increase in rhabdosphincter muscle and ganglia and return of continence in urethral pressure profile measurements to preop levels compared to controls [34]. In another rat study by Lin et al., the animals were subjected to stretch/traumatic injury in the urethra and had their ovaries removed to simulate postmenopausal women. Animals were randomized to three groups: direct injection of ADSC to rhabdosphincter, ADSC injection into the tail vein, and a controlled group. The rats were sacrificed 4 weeks later. The results showed that 80% of the control group had abnormal voiding function whereas only 33% of the two treatment groups had this finding [35]. Kim et al. carried out bilateral pudendal nerve dissection and 2 weeks later had periurethral injection of muscle-derived stem cells. The results again showed that the treated animals’ leak point pressures and urethral closure pressures were similar to animals subjected to sham surgery [36]. Finally, Chermansky et al., after inducing stress incontinence in female rats by midurethral cauterization, treated the animals 1 week after injury with injection of muscle-derived stem cells into the midurethra. The treated animals had significant

increases in leak point pressure compared to controls, and with histologic evidence of muscle-derived stem cell integration into the urethral musculature [37].

Human trials in stress urinary incontinence have been ongoing for a number of years. Carr et al. reported on a patient population of 38 women with stress urinary incontinence who underwent muscle-derived stem cell injections into the sphincter. The women were also offered a second injection 3 months later. Ninety percent of the treated women had over a 50 % decrease in pad weight and only 50 % reported leaks. Adverse events were essentially absent [38]. Gotoh treated 11 men with persistent stress urinary incontinence 1 year after prostate surgery and demonstrated a 60 % decrease in urinary leakage volume on pads weighed by the patients. One of the 11 achieved complete return of urinary control. Functional urethral leak and urethral closing pressures were also increased compared to pretreatment levels. No adverse events were reported [39]. Currently, there is a large multicenter ongoing trial phase 3 trial in the United States with muscle-derived stem cells in women with stress urinary incontinence and a phase 1, 2 trial using muscle-derived stem cell in postprostatectomy incontinence (ClinicalTrials.gov Identifier: NCT01893138 and NCT02291432).

Although stem cells derived from any source are not yet ready for clinical use in men with stress urinary incontinence after radical retropubic prostatectomy, the future appears to hold promise. Nonetheless, ethical and regulatory issues remain of concern and may present hurdles to widespread clinical adoption [40]. The early ethical concerns surrounding the use of fetal embryonic stem cells have by and large been resolved by the development of so many other sources for multipotent stem cells. Nonetheless, the recent classification of stem cells as a “drug” places them under the purview of the FDA and now regulatory hurdles may enhance or impede the science and usefulness of these agents. Finally, the fears of the development of secondary cancers or causing early recurrences/failures of cancers if stem cells are released into the operative field to and in early functional recovery are very real. Well-structured trials need to be carried out to address these questions and the questions of which (if any) of the currently available products might be best used in men undergoing prostatectomy. Nonetheless, the future of stem cells use in our patients undergoing prostatectomy appears bright.

Conservative Management

The value of various conservative interventions to improve continence postprostatectomy is an area of debate with conflicting data. The recommended timing of when to initiate intervention and or education is not clear either. Burgio and his colleagues prospectively randomized 125 men undergoing radical prostatectomy to preoperative biofeedback-assisted behavioral training plus daily home exercises versus a usual control care (postoperative Kegel exercises). Authors found that patients with preoperative training had a significantly shorter time to continence and decreased the severity of urine leak [41].

PFPT with or Without Biofeedback

Pelvic Floor Physical Therapy refers to any technique that causes targeted and repetitive and contractile activity in specific pelvic floor muscles with the hope of training these muscle groups to actively contribute to coaptation of urethral sphincter when the intra-abdominal pressure is increased. Biofeedback also refers to auditory or visual cues to the patient during contractions to provide feedback on the quality and effectiveness of the exercise. Biofeedback can be obtained by sophisticated equipment or electromyography versus a simple feedback from the trainer by digital rectal examination. The effects of pelvic floor physical therapy on urinary incontinence recovery still stay controversial in the literature. Ribeiro et al. evaluated the long-term effects of early postoperative biofeedback-pelvic floor muscle training in 73 males who were undergoing radical prostatectomy with a 12 months follow-up. They randomized 36 patients to biofeedback-pelvic floor muscle training once a week for 3 months and a control group of 37 patients. At 12 months 25 patients in the treatment group and 21 patients in the control group were continent ($p=0.028$). In addition, it appeared that biofeedback-pelvic floor muscle therapy overall significantly improved the severity of incontinence, lower urinary tract symptoms, and quality of life of the treatment group that lasted 12 months following the procedure [42]. Different trainings and delivery method of pelvic floor muscle training (PFMT) to the patients have been evaluated and the literature has inconsistent data. For instance, Moore et al. in a multicenter randomized trial stratified 205 patients to weekly therapist-guided PFMT versus standardized verbal and written instructions and demonstrated no significant differences between groups at 8, 12, 28, and 52 weeks [43]. These data may suggest a less-intense, standard therapy may be as effective but less costly for the system. On the contrary some experts believe that intensive prolonged and early initiation of PFMT can improve continence that persists in the first 12 months [44]. A recent and comprehensive Cochrane review on eight trials showed that there is no evidence to support PFPT with or without biofeedback to be more effective than control for patients up to 12 months following radical prostatectomy [45].

Authors caution us with the significant variations in the patients, interventions, data, and outcome measures, but overall it appeared that patients' continence improved over time regardless of intervention.

Some experts have suggested and questioned that possibly initiating preoperative PFPT may improve continence outcomes [46, 47]. In a meta-analysis to evaluate preoperative intervention with PFPT, Wang et al. included five studies but reported insufficient data to report any benefit in quality of life or continence benefits with preprostatectomy PFPT [48].

Electrical Stimulation and Extracorporeal Magnetic Innervation

Data on electrical stimulation either used alone or in conjunction with behavioral therapy or physical therapy is conflicting in the literature. Electrical stimulation is thought to stimulate the striated urethral sphincter and thus increase its contractility.

The electrical stimulation to the pelvic floor can either be delivered through noninvasive anal probes or surface electrodes as Transcutaneous Electrical Nerve Stimulation (TENS) similar to the one's used in overactive bladder. Goode et al. in a prospective randomized control trial evaluated the role of biofeedback in patients with persistence urinary incontinence 12 months following surgery. Two-hundred and eight patients 1–17 years following their prostatectomy were stratified to three groups. Group one which included 8 weeks of behavioral therapy with pelvic floor muscle training; group 2 which included the behavioral therapy plus in office, dual-channel electromyography biofeedback in addition to daily home pelvic floor electrical stimulation; group 3 served as a delayed treatment group and a control group. The authors showed that 8 weeks of behavioral therapy compared to controls improved continence episodes whereas adding pelvic floor electrical stimulation did not increase the efficacy [49]. On the contrary, Yamanishi et al. used electrical stimulation in 56 men with severe postprostatectomy incontinence with all patients receiving concurrent pelvic floor muscle training preoperatively and throughout the recovery. Twenty-six patients were randomized to the treatment group and 30 to sham. Authors reported an improvement in amount of leakage, the International Consultation on Incontinence Questionnaire in the active group at 1 month but not at 12 months [50]. Early use of combination pelvic floor electrical stimulation and biofeedback has also shown to be effective in early recovery of urinary incontinence postprostatectomy [51].

Extra-corporeal magnetic innervation (ExMI) which stimulates pelvic floor contractions through using a magnetic field on a chair has also been proposed to improve stress and urge urinary incontinence [52]. In a small series with a short follow-up, Yokoyama and colleagues compared ExMI to functional electrical stimulation (FES) and found that these two therapies only offered an earlier return to urinary continence in 1 month compared to controls. However, at 6 months follow-up 24 h pad test was similar between the treatment groups and the controls [53]. Another smaller study examined penile vibratory stimulation (PVS) in 64 patients following radical prostatectomy. Authors reported 90% continence in the treatment group and 94.7% in the control group after 12 months demonstrating no documented benefit from using PVS [54].

Life Style Changes

Life style changes would include time voiding, fluid management, and overall changes that would promote weight loss, smoking cessation, healthy diet, and exercise. Currently, there are no strong evidence that life style changes will have a direct positive affect on postprostatectomy incontinence [45].

Acupuncture

In a small Chinese study, 109 patients were stratified to PFPT with or without electrical acupuncture. At a short follow-up of 6 weeks patients with combined PFPT and electrical acupuncture had better urinary continence outcome.

However, the results were not long lasting and both groups had similar outcomes at 16 weeks [55].

Pilates and Concentration Therapy

In hopes to improve effectiveness of PFPT, treating physicians have explored adjunctive methods to PFPT. Pilates includes stretching and core stability exercises that focus on pelvic floor, body alignment, and trunk muscles. In addition, these exercises are performed in coordination of deep breathing and focus on intra-abdominal pressures. Pedriali et al. randomized 85 patients to three groups of G1: Pilates, G2: Pilates and PFPT, G3: control group. Both treatment groups performed ten weekly sessions. Authors reported no statistically significant difference between the two treatment groups in regards to daily pad use, 24 h pad test, ICIQ-SF scores. The authors concluded that Pilates exercises can be as effective as PFPT in postprostatectomy incontinence and it may even contribute to higher continence rates when compared to controls in short term [56]. Concentration therapy is very varied among practitioner and the data can be conflicting, never the less a small Thai study compared PFPT with or without concentration therapy and reported some benefits [57]. Authors of this chapter believe that these data need to be replicated in larger randomized trials with standardized continence measurements before general recommendation or use.

Compression Devices (Penile Clamps)

External devices have long been used in urology to control the urinary leak. Penile clamps have evolved to become easier to use, disposable, and only compressing on the ventral side [58, 59]. Condom catheters have also been used in significant incontinence especially in the neurogenic bladder setting or for overnight control.

Late Intervention

Surgical interventions: Like balloon adjustable implants, bulking agents, slings, and artificial urinary sphincter (AUS) are the last resort if all other adjunctive measures fail.

Conclusion

In conclusion based on the review of the literature, there is a paucity of level 1 evidence in adjunctive measures to improve urinary continence in the early and late period following radical prostatectomy. Future prospective studies in large group of patients with longer follow-up are needed to evaluate each intervention in more

detail. In addition, we need to understand the anatomical and functional changes that follow radical prostatectomy in each patient with higher degree of precision to be able to individualize our recommendations and treatments.

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