Post-Prostatectomy Stress Urinary Incontinence: What Treatment for Which Patient?

Jerzy Gajewski,1* Marcus J. Drake,2 and Matthias Oelke3,4

1Department of Urology, Dalhousie University, Halifax, Canada
2Bristol Urological Institute, Southmead Hospital, Bristol, UK
3Department of Urology, Hannover Medical School, Hannover, Germany
4Department of Urology, Academic Medical Center, University of Amsterdam, the Netherlands

Key words: artificial urinary sphincter; pelvic floor rehabilitation; physiotherapy; post-prostatectomy incontinence; prevention; slings; stress urinary incontinence

INTRODUCTION

Stress urinary incontinence (SUI) is the predominant form of post-prostatectomy incontinence (PPI) but mixed urinary incontinence is common. Incidence of PPI varies between centers and how much time has elapsed after prostatectomy. Some recent figures put PPI at 4–8%; however, in the past reported incidence was as high as 30%, reflecting both recent improvements in surgical techniques and differences in reporting. In one report, the difference between physicians and patients in reporting PPI was high (21% vs. 97%, respectively). Both subjective and objective reports have been published, but comparison is hindered by lack of standardization of evaluation.

THE NEED FOR STANDARDIZATION: ASSESSMENT TOOLS AND LAPESED TIME

Agreement regarding terminology will aid scientific research into PPI, with consequent prospects of improved clinical management. This is necessary at a surprisingly basic level, including formal definition of PPI and standardized tools relating to severity and quality of life impact. The standardization should include:

- Defining person reporting
  - Health provider (doctor, nurse ...).
  - Patient, family, patient’s care giver.
  - Independent evaluator.
- Standardizing subjective reporting by developing patient questionnaires and physician evaluation forms
- Standardize objective instruments for evaluation severity of the incontinence
  - Pad test.
  - Urodynamics.
  - Other.
- Agreeing outcome measures

© 2010 Wiley-Liss, Inc.
planning interventional treatment of PPI would be most appropriate? Consensus currently points to a year, but hard evidence is lacking.

MANAGEMENT OF POST-PROSTATECTOMY INCONTINENCE

PPI is an iatrogenic condition, in which three key facets need further emphasis:

Prevention

Several reports describe modifications of key maneuvers during RP, though comparisons are unreliable as randomization and standardized reporting are lacking. Imaging is generally used before RP, and developments to delineate tumor extension, anatomical position of nerves and vessels continue, which give an opportunity to define facets relevant to PPI. Urodynamics is less widely used before surgery. Song et al.9 performed pelvic magnetic resonance imaging (MRI), pelvic ultrasound and urodynamics in 94 patients before RP. The only predictive urodynamic factor was "continence zone area." From the imaging tests, pelvic diaphragm thickness and ratio of levator ani thickness to prostate volume were independent factors for predicting continence recovery. The authors concluded that the degree of pelvic floor development determines recovery of continence 3 months after surgery. However, extrapolating 3-month findings to 12 months is uncertain, and gives no indication on preventing PPI.

Imaging and urodynamics study can be useful before RP to evaluate function of the lower urinary tract (LUT) and to better inform patients on possible outcome. Presence of detrusor overactivity may predict more urgency urinary incontinence after RP, but it does not predict sphincter dysfunction.

Pelvic Floor Rehabilitation or Continence Protection

Pelvic floor muscle exercises (PFME) have a well-established role in clinical management of PPI, and are advocated in most guidance, in view of the comparatively low risk of adverse effects, presumed efficacy and benefit of involving the patient in their own management. They are usually recommended as a key aspect during post-operative rehabilitation. Inevitably, the derivation of evidence to underpin the role of PFME in this context is hampered by key limitations, such as the selection of outcome measures, the protracted time-frame over which the exercises have to be undertaken, uncertainty regarding patient compliance with exercise regimes, the range of confounding factors, and the recognition that symptom improvement arises spontaneously in some patients.

Realistic delivery of a trial to determine optimal PFME regimes is challenging. Thus, the current status of PFME in treating PPI is based on a broad consensus of clinical efficacy and safety, with a relatively weak evidence base.10 Furthermore, there is no great certainty that the area will be accorded sufficient priority to warrant the substantial investment that would be needed to deliver a research program of adequate scientific rigor and statistical power. This is a frustrating situation, as at least five areas warrant particular research focus; how best to deliver PFME training for patients, the role of adjunctive approaches (e.g. biofeedback, electrical stimulation, and others), the timing of initiating PFME, the duration of conservative therapy and the mechanism of action.

In general, current publications appear to signify that more intensive and/or specialized input in PFME training achieves some advantage in continence rates. Due consideration has to be given to the inherent weakness that this type of research is generally undertaken by specialists, who are the very people advocating intensive supervised protocols and adjunctive measures.

Timing of PFME initiation warrants further scrutiny. Advantages of preoperative commencement should include easier training (in view of lower discomfort levels and better training environment), and might facilitate compliance with PFME in the post-operative phase. It might also increase muscle bulk in the bladder outlet complex, which may predict better continence outcomes.9 Nonetheless, these advantages are not confirmed, and pre-operative training may bring insufficient benefit to warrant the investment, given that continence is retained in the majority of patients. Furthermore, patients may regard the issue of continence as subordinate to the need for cancer cure, impairing compliance—particularly if the interval between diagnosis and surgery is short. Motivation is likely to be enhanced where patients identify that they are affected with continence problems subsequent to surgery. In these patients, support and training in PFME provides an important contribution to adjusting to their altered situation—a laudable approach to management for which, again, it is difficult to envisage deriving a robust evidence base. In this group, most clinicians will assert that PFME is advantageous compared with no intervention. One reported marker of likely incontinence duration is volume of leakage on initial catheter removal post-operatively,11 which may facilitate determining PFME regime and help with patient motivation.

Markers to signify that PFME has limited prospect of helping at all would be a considerable benefit for decision making. In women with SUI, absence of voluntary pelvic floor contraction can be taken to signify that response to PFME without some form of adjunctive treatment is not going to succeed. While the same may apply in PPI, it is conceivable that neuropaxia may have occurred during surgery in a proportion of patients, and that attempted use of the muscle groups supplied by the affected nerves may facilitate their functional restoration. Thus, unlike in women, absence of pelvic floor contraction in PPI cannot be assumed to be a poor prognostic marker.

Ultimately, there are two key issues respecting conservative approaches to PPI. Firstly, can overall benefits of improved continence rates on long-term follow up be demonstrated? Secondly, can earlier recovery of continence be achieved? The medical profession tends to focus on the first, but many patients understandably regard the second as important.

Treatment of Post-Prostatectomy Incontinence

Much of the current treatment choice in clinical practice depends on patient's or surgeon's preference and may be biased by open or hidden commercial activities of producers, patient groups, or publication activities of single centers. No general recommendations exist on who the most suitable candidate for which treatment is. Until now, only a few randomized-controlled trials (RCTs) have been published.

Pharmacological treatment—drugs. Trials have been conducted with y-adrenoceptor agonists (ephedrine, phenylpropanolamine, midodrine), y2-adrenoceptor agonist (clenbuterol), and serotonin—noradrenaline reuptake inhibitors (imipramine,
duloxetine). All drugs claim to raise urethral pressure by increasing striated sphincter contraction. One would expect these drugs to work only in patients where the urethral sphincter retains some residual activity; however, this is not established. Most drug trials used small numbers of patients, studied mixed populations (men and women, SUI and mixed incontinence), seldom used placebo or comparison arms for judgment of spontaneous regression, and some even did not define the PPI mechanism urodynamically. Phenytoinpropamide was withdrawn from the US market because of the increased risk of hemorrhagic strokes in women and should also be abandoned in men. Although licensed in Japan for the treatment of SUI, the mode of action of clonidine, a bronchodilator, remains obscure.

Serotonin–noradrenaline reuptake inhibitors are antidepressant drugs with contractile effects on the external urethral sphincter. Evidence with imipramine is limited to one study investigating only 19 men with PPI (Oxford evidence level 2b). Duloxetine (Yentreve™, Eli Lilly, Indianapolis, IN, USA) was approved for the treatment of female SUI in most European countries but has not been licensed for male SUI. It is also not approved in North America for either indication. Four trials have investigated the efficacy of duloxetine in male SUI; one RCT (Oxford evidence level 1b) and three case series (Oxford evidence level 4). All trials demonstrated significant reductions of SUI episodes or pad weight in 50–80% of patients. Incontinence is likely to reappear after drug withdrawal. The RCT showed that duloxetine in combination with PFME is significantly more efficacious compared to PFME alone. However, patients with PFME alone were significantly more improved after drug withdrawal 1 month later. Whether the continence drop in the duloxetine treatment arm was due to coincidence, lesser motivation for physiotherapy during active treatment, related to drug effects on the urethral sphincter, or a rebound effect of the antidepressant characteristics of duloxetine causing a depressive mood and a negative attitude towards continence judgment is unknown.

Well conducted, multi-center RCTs with long-term follow-up would be needed to adequately judge drug (duloxetine) treatment, but there is no agreement whether such trials are warranted. If conducted, these trials should include men who are urodynamically confirmed SUI and a placebo arm. Adverse events have to be documented to adequately balance between treatment benefit and side effects. Such trials would be expensive.

Bulking agents. The injection of artificial or autologous material in the urethra, sphincter or bladder neck aims to increase coaptation of the urethral mucosa by bulking. Several agents have been developed; collagen, silicone, and carbon particles have been tested in men. Limited data are available for the latest bulking agents. Most results originate from case series or cohort studies (Oxford evidence level 4/2b). One RCT comparing silicone with the artificial urinary sphincter (AUS) has been published (Oxford evidence level 1b). Single-center trials with collagen showed initial improvement rates between 36% and 69% but continence was achieved in only a minority of patients (4–20%). Deterioration of efficacy over time was documented and re-injections are needed to restore improvement. It is uncertain whether injections, either at outset or when repeated, might limit potential for subsequent use of alternative treatment modalities. Three trials have been published which compared the efficacy of bulking agents (collagen or silicone) with other treatment options. Patients in a cohort trial treated either with collagen or the bone-anchored tape (InVance™, American Medical Systems, Minnetonka, MN, USA) had significantly higher success rates after the tape at 4 years (76% vs. 30%). Two other cohort studies demonstrated significantly higher success rates for the AUS (AMS 800™) compared to collagen injections (75% vs. 20%). Men with high-grade incontinence benefit significantly more from the AUS (62% vs. 91%). Problems with present bulking agents include particle migration, allergic reaction, or infection. Although the procedure seems to be easy to perform and patients are initially satisfied, results are of short durability. The present evidence does not appear to warrant additional research, and the overall strategy of bulking agents may have limited scope in PPI.

A variant on the bulking concept is the Adjustable Continence Therapy for the Prostate (ProACT™, Uromedica, Plymouth, MN, USA). Each balloon is connected with a port allowing volume adjustment according to the individual situation. Single- or multi-center case series documented improvement in 60–90% of patients. Volume adjustment was necessary in up to 88% of patients; supplementary filling of the balloons was needed three times on average. A two center cohort trial compared the ProACT™ system with the bone-anchored tape and showed equivalent overall efficacy. It is still too early to conclude if this treatment will be widely accepted in clinical practice. Additional RCTs comparing adjustable balloons to AUS with long-term follow-up would be beneficial.

Slings—Tapes

Slings consist of homologous, heterologous, or alloplastic material and may be adjustable or non-adjustable. Implantation of homologous material requires harvesting a considerable amount of fascia, which is associated with prolonged operation time and increased morbidity. Evidence suggests that alloplastic material produces better continence results. It remains mostly unknown what the mechanisms underlying restoration of continence are. Theoretically, tapes and slings could act by permanent urethral compression, a hammock type mechanism causing urethral compression only during abdominal pressure increase, elongation of the functional urethral length, or re-positioning of the proximal urethral into the abdominal cavity for increase of pressure transmission during physical activity. Potential complications (e.g., urethral erosion, lower or upper urinary tract deterioration) need to be considered if bladder outlet obstruction is elicited. The Ad Vance™ transobturator tape increases urethral closure pressure and membranous urethral length without significantly affecting maximum urinary flow rate, detrusor voiding pressure, or post void residual urine. However, these results need to be confirmed independently. Obviously, large long-term follow-up RCTs comparing tapes to AUS are necessary to evaluate clinical application of this concept.

Non-adjustable slings or tapes. Sling or tapes without the possibility of post-operative adjustment are implanted via a perineal incision and are either anchored to the pubic bone with screws (InVance™, AMS) or guided through the obturator membrane (transobturator tapes; e.g., AdVance™, AMS), where the tape remains in position due to the rough surface; fibrotic stabilization will occur within the next months. It remains to be investigated how much tension of the tape is necessary to achieve continence and how long stabilization takes.

For the bone-anchored system, intermediate-term results with a mean follow-up of 28–48 months were published as...
Adjustable slings. Adjustable slings are implanted via perineal and suprapubic incisions. Two adjustable devices have been marketed, the Remoex® (Neomedic, Neomedic Int., Barcelona, Spain) and the Argus® (Albyn Medical Smart Medical Group, Navarra, Spain), both capable of increased or decreased tape tension according to the individual situation. Short- and intermediate-term results of the Remoex® sling have been published in single- or multi-center case series (Oxford evidence level 4) for a total of 75 male patients,44 with dry or improved rates of 67–84% after a mean follow-up of 18–32 months. Readjustment of the sling tension was necessary in 44% of the patients after a mean time of 5 months. The Argus® sling was investigated in one prospective multi-center trial (Oxford level 4) of 48 patients, with mean follow-up of 7.5 months; cure of incontinence was reported in 73% and improvement in 10% of patients.45 After a mean follow-up of 45 months, continence or improvement was shown in 66% and 13% respectively.46

Artificial Urinary Sphincter (AUS)

The AUS (AMS 800®TMT, AMS) is the oldest and most investigated continence system. Other treatment modalities should be compared against AUS, though allowing for the effect of incontinence severity on treatment selection and outcome. Single-center case series (Oxford evidence level 4) with long-term follow-up of up to 15 years demonstrated treatment success in 70–90%.46,47 A cohort study (Oxford evidence level 2b) comparing InVanceTM with collagen injections reported a higher success rate for the bone-anchored tape.25 Transobturator tapes (e.g., AdvanceTM, AMS) were introduced to the market in 2007. Placement of the tape can be either outside-in or inside-out.29 Only short-term data have been published as single-center case series (Oxford evidence level 4). These trials reported success rates of 70–77% after a follow-up ≤ 12 months.46,47

CONCLUSIONS

Despite numerous clinical interventions, published literature reports outcomes of limited numbers of patients and quality of evidence is weak. On the current evidence base it is not possible to answer which treatment is suitable for which patient, and good quality research with adequate follow-up duration has to be regarded as a priority.

Independent regulatory bodies ideally should steer and approve continence devices in the future. Results of devices produced by other companies cannot be simply extrapolated from well-investigated systems. Competitive pricing and marketing strategies should not distract the medical profession from the ultimate goal of effective and safe long-term management. Ultimately, large-scale registries (similar to the Austrian TVT database)75 may be the most realistic approach gathering real-life data and avoiding publication bias derived from specialized or high-volume continence centers.

RESEARCH PROPOSALS

There is a considerable amount of progress needed to improve the situation for men with PPI.

1. A formal definition of PPI accepted and in widespread use.
2. Standardized tools for use at baseline and follow-up, and agreed outcome measures.
3. Evaluation of the clinical utility of prophylactic or therapeutic PFME regimes? In particular, is the additional cost of intensive protocols, specialized supervision or adjunctive measures justified by the purported improvement in continence rates?
4. Randomized-controlled trials to evaluate efficacy of all treatment modalities, using appropriate comparator arms, sustained over an adequate duration of follow-up.
5. Consensus driven, evidence-based PPI management pathways for different patient groups and incontinence severity.

REFERENCES


