Urology Research Review™

Making Education Easy

Issue 62 - 2023

In this issue:

Abbreviations used in this issue:

BPH = benign prostatic hyperplasia; **CI** = confidence interval; **CKD** = chronic kidney disease; **EAU** = European Association of Urology; **HR** = hazard ratio; **IPSS** = International Prostatic Symptom Score; **LUTS** = lower urinary tract symptoms; **PSA** = prostate-specific antigen; **PVR** = post-void residual volume; **UTI** = urinary tract infection.

Welcome to Issue 62 of Urology Research Review.

A French open-label, superiority trial has shown that prostatic artery embolisation provides more urinary and sexual symptoms benefit than medical treatment out to 24 months in patients with BPH, but further studies are needed to assess its true benefits. In a US single-centre, randomised, non-inferiority clinical trial, expedited post-surgical activity was found to result in non-inferior anatomic and symptomatic outcomes versus standard activity restrictions after pelvic organ prolapse surgery. Other topics covered in this issue include kidney ultrasonography after first febrile urinary tract infection in children, 10-year follow-up after radical cystectomy and orthotopic neobladder, temporary bulbar urethral stent placement after internal urethrotomy, optimal stenting duration after ureteroscopy and stone intervention, early versus delayed transurethral surgery in acute urinary retention, and Holmium laser versus cold knife urethrotomy for short segment urethral stricture.

We hope you find our selection of articles for this review interesting and welcome your feedback.

Kind Regards,

Professor Eric Chung

eric.chung@researchreview.com.au

Prostatic artery embolisation versus medical treatment in patients with benign prostatic hyperplasia (PARTEM): A randomised, multicentre, open-label, phase 3, superiority trial

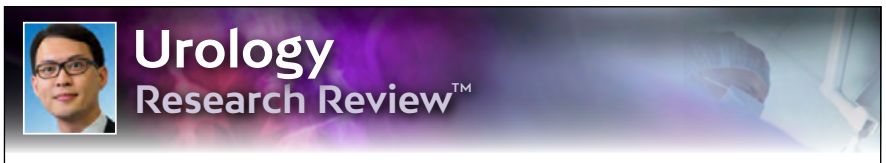
Authors: Sapoval M et al.

Summary: This French randomised, open-label, superiority trial compared symptom improvement after prostatic artery embolisation (PAE) versus medical treatment (oral dutasteride/tamsulosin hydrochloride) in 87 patients with symptomatic benign BPH. After 9 months, the change in International Prostatic Symptom Score (IPSS) was greater after PAE (-10.0; 95% CI -11.8 to -8.3) than with medical therapy (-5.7; 95% CI -7.5 to -3.8) with a difference of -4.4 (95% CI -6.9 to -1.9; p = 0.0008); 15-question International Index of Erectile Function score change was 8.2 (95% CI 2.9-13.5) versus -2.8 (95% CI -8.4 to 2.8). There were no treatment-related adverse events nor hospitalisation. Invasive prostate retreatment was required in five PAE and 18 medical treatment recipients.

Comment: There is considerable interest and controversy at the same time about the role of PAE in treating BPH/male LUTS. While this PARTEM trial appears to meet its primary endpoint of clinically significant superior reduction of IPSS after PAE compared to combined medical treatment in patients with BPH >50 mL who failed to improve after single alpha-blocker therapy, there are many limitations that need to be addressed further in detail. There is a clear inherent bias in this open-label, non-blinded trial and PAE is not compared to contemporary surgical treatments for BPH/male LUTS. Furthermore, the relatively short duration of follow-up of 9 months may not be adequate to determine the long-term benefits of PAE. Full efficacy in the medical therapy group could have been hampered by an insufficient duration of treatment and poor adherence to medication. Hence, PAE is unlikely to be adopted by the urological community at this stage as a new standard of care, especially if the patients are fit to undergo more effective surgical treatments or prefer other less invasive and more "controlled" BPH/male LUTS surgery.

Reference: Lancet 2023;31:100672

Abstract



Independent commentary by Professor Eric Chung

Professor Eric Chung is a consultant urological surgeon at the Andro Urology Centre for Sexual, Urinary and Reproductive Excellence and holds academic appointments at the University of Queensland (Brisbane) and Macquarie University Hospital (Sydney). He is the Leader of male LUTS and Past Chair of Andrology section in the Urological Society of Australia and New Zealand (USANZ), the Secretary-General for the Asia Pacific Society of Sexual Medicine (APSSM) and Chairperson for the Prostate Cancer Survivorship committee at the International Consultation on Sexual Medicine (ICSM). He has been invited to speak and operate at many international meetings and has authored more than 100 peer-reviewed papers and book chapters.

Standard restrictions vs expedited activity after pelvic organ prolapse surgery: A randomized clinical trial

Authors: O'Shea M et al.

Summary: This US single-centre, randomised, noninferiority clinical trial assessed whether expedited post-surgical activity results in noninferior anatomic and symptomatic outcomes versus standard activity restrictions after pelvic organ prolapse (POP) surgery. After 3 months, noninferior anatomic and symptomatic prolapse outcomes were observed. The mean maximum anatomic POP support loss (SL_{max}; the most distal point of pelvic organ support loss according to the Pelvic Organ Prolapse Quantification System) was -1.7 cm in the expedited group and -1.5 cm in the activity restriction group. After adjustment for baseline SL_{max}, mean maximum support loss was 0.18 cm higher in the expedited activity group (95% CI; -0.68 to 0.33). The coprimary outcome mean Pelvic Organ Prolapse Distress Inventory (POPDI) symptom score was 23.7 versus 25.7 points. After baseline adjustment, mean POPDI scores were 5.79 points lower in the expedited activity group (95% CI -20.41 to 8.84).

Comment: POP surgery is often complex since it can involve surgery across multiple vaginal compartments, and the surgical method is often chosen based on the surgeon's clinical judgment since no single procedure can improve all prolapse symptoms. In this randomised, non-inferiority clinical trial of patients undergoing vaginal or laparoscopic apical reconstructive surgery for POP, the findings supported non-inferior anatomic and symptomatic prolapse outcomes in terms of POPDI symptom scores in women who had postoperatively expedited activity when compared to standard restrictions. This study raises two important points, namely; (1) a surgeon's technical expertise plays an important role in overall success, and (2) both surgical approaches correct underlying problems where negative perceptions are reduced when prolapse symptoms are eliminated. Further details on the actual resumption of normal functional activity and restoration of sexual function are key aspects that were not fully addressed in this study but are equally important to the patients.

Reference: JAMA Surg. 2023;158(8):797-805
Abstract

Kidney ultrasonography after first febrile urinary tract infection in children: A systematic review and meta-analysis

Authors: Yang S et al.

Summary: This systematic review and meta-analysis was conducted to assess the prevalence of urinary tract abnormalities identified during kidney ultrasonography after the first febrile urinary tract infection (UTI) based on 29 studies including a total of 9170 children (median 60% male). Prevalence of abnormalities was 22.1% (95% CI 16.8-27.9) across all ages and 21.9% (95% CI 14.7-30.1) in patients <24 months of age. Prevalence of clinically important abnormalities was 3.1% (95% CI 0.3-8.1) across all ages and 4.5% (95% CI 0.5-12.0) in those aged <24 months. There was a bias due to study recruitment that was associated with a higher prevalence of abnormalities. The most common findings were hydronephrosis, pelviectasis, and dilated ureter with urinary tract obstruction in 0.4% (95% CI 0.1-0.8); surgical intervention occurred in 1.4% (95% CI 0.5-2.7) of cases.

Comment: UTI remains one of the most common infectious diseases in the paediatric population and represents a major cause of antibiotic consumption and hospitalisation in children. Considering the ongoing controversies on the management of paediatric UTI, this article serves to provide evidence on the clinical utility of renal tract ultrasound in children with first febrile UTI. In this systematic review and meta-analysis, one in four to five children with first febrile UTI will have a urinary tract abnormality detected on kidney ultrasonography, and one in 32 will have an abnormality that changes clinical management. In the workup of children with UTI, clinicians should judiciously utilise imaging studies to minimise exposure of children to radiation effects. Renal tract ultrasound may not be a sensitive study to localise the infection or to detect a duplicated collecting system or vesicoureteric reflux, but it can be useful to detect renal scarring and upper tract dilation. While the actual clinical utility of renal tract ultrasound in children with first febrile UTI remains debatable, it is cheap, safe, and potentially limits the need for more invasive voiding cystourethrography.

Reference: JAMA Pediatr. 2023;177(8):764-773
Abstract

Voiding and renal function 10 years after radical cystectomy and orthotopic neobladder in women

Authors: Zahran MH et al.

Summary: This retrospective (1995-2011) study assessed long-term voiding and renal function changes after radical cystectomy and orthotopic neobladder surgery in 195 women with bladder cancer without disease recurrence. Over a median follow-up of 98 months (95 patients had >10 years of follow-up), daytime continence was maintained in 87% of patients, night-time continence in 69% of patients and chronic urine retention (CUR) in 27% of patients; among those with >10 years of follow-up, the proportions were 86%, 70%, and 33%, respectively. Renal function deterioration events occurred in 74 patients and CKD stage III-V in 80 patients. Predictors of renal function deterioration were age (HR 1.41; 95% CI 1.06-1.89; p = 0.02) and serous-lined extramural tunnel diversion (HR 0.43; 95% CI 0.19-0.86; p = 0.02). In patients with >10 years of follow-up, renal function deteriorated in 46 (49%) patients and CKD stage III-V developed in 40 (42%) patients.

Comment: For women with bladder cancer who need surgery, the choice of urinary diversion is likely dictated by the patient's preferences, oncological factors, surgeon's expertise, surgical risks, and desired postoperative functional outcomes. Without a doubt, radical cystectomy with ileal conduit remains the most popular and common surgery regardless of the patient's age. However, it is well known that ileal conduit is associated with a significant burden of long-term complications, including impaired renal function, UTIs, and parastomal hernia. On the other hand, orthotopic neobladder has been shown to offer better quality of life and can minimise potential metabolic complications. In this long-term study, women surviving more than 10 years after radical cystectomy and orthotopic neobladder maintained acceptable continence status, apart from having a higher hypercontinence rate, although renal function appeared to deteriorate in nearly half of them. In recent times, many studies increasingly supported the benefits of organ-sparing treatment options for well selected women with bladder cancer. These treatment options together with patient satisfaction rate in the longer term require further validation and emphasis should be placed on refining counselling tailored to patient preference and long-term management.

Reference: BJU Int. 2023;132(3):291-297
Abstract

Feasibility and outcomes of temporary bulbar urethral stent placement after internal urethrotomy in the largest multicenter series

Authors: Sedigh O et al.

Summary: This multicentre retrospective analysis of bulbar urethral stenting procedures (n = 149) assessed complications and outcomes after direct vision internal urethrotomy (DVIU) with a cold knife or laser with stents removed ≥6 months unless complications required earlier removal. Overall, 49% of patients experienced complications, most frequently discomfort (23.8%), stress incontinence (17.5%), and stent dislocation (9.8%). Approximately 85% of adverse events were Clavien-Dindo grade <3. At a median follow-up of 38.2 months, the overall success rate was 76.9%, and the success rate was lower if the stent was removed before 6 months (53.3% vs 79.7%; p = 0.026).

Comment: Urethral stents have long been used to treat urethral stricture by preserving luminal patency but can be associated with stent encrustation and infection. The invention of temporary urethral stents can provide a safer choice and could complement the effectiveness of DVIU. In this multicentre series, temporary urethral stents were shown to have an overall success rate of 76.9% at a median follow-up of 38.2 months with reasonable complications such as discomfort, stress incontinence, and stent dislocation. For the last 30 years, urethral stents have been developed to increase the efficacy of minimally invasive treatment for urethral strictures and traumatic urethral rupture. Various pertinent factors such as the length of urethral stricture, type of stent, and stent indwelling period, coupled with a complete removal of fibrotic scar tissue are important factors to consider for stable placement of the stent and to encourage regeneration of normal urethra to prevent the recurrence of stricture.

Reference: Eur Urol. 2023;84(3):313-320
Abstract

Summary paper on the 2023 European Association of Urology guidelines on the management of non-neurogenic male lower urinary tract symptoms

Authors: Gravas S et al.

Summary: This publication presented a summary of the EAU 2023 guidelines on the management of male LUTS developed using a Delphi technique consensus approach. Assessment of LUTS in men should be practical, based on a medical history and physical examination and using validated symptom scores, urine test, uroflowmetry, postvoid urine residual, frequency-volume charts for nocturia or predominately storage symptoms. PSA testing should be conducted if prostate cancer would change the treatment plan. Urodynamics should be conducted in selected patients and men with mild symptoms are candidates for watchful waiting. Medical treatments depend on assessment findings, predominant symptoms, ability of treatment to change findings, and expectations about the speed of onset, efficacy, side effects, and disease progression. Behavioural modification should be offered prior to or with medical treatment. Surgery should be reserved for men with absolute indications, and patients who fail, or prefer not to receive, medical therapy. Surgical management includes resection, enucleation, vaporisation, and alternative ablative and non-ablative techniques, with the choice of technique dependent on patient characteristics, expectations, and preferences; surgeon expertise; and availability of modalities.

Comment: Male LUTS are shown to adversely impact the overall quality of life and are becoming a major problem with the ageing population. With the advent of evidence-based medicine, several clinical practice guidelines have been developed to help manage LUTS with minor conflicting and inconsistent statements. This summary of recommendations on the EAU 2023 guidelines on the management of male non-neurogenic LUTS showed the need to be practical and to tailor the diagnostic assessment and treatment strategies based on the patient's needs and preferences while balancing the surgeon's expertise and availability of local resources. Urologists should rightly maintain a healthy scepticism about the reliability and applicability of scientific guidelines. After all, guidelines are there to provide guidance, it is by no means the be-all and end-all. Attention should focus beyond the prostate as the sole cause of male LUTS and incorporate management to evaluate the entire urinary tract as well as multiple system comorbidities. Therefore, prostate surgery alone does not necessarily provide adequate management in male LUTS, and multi/cross-disciplinary collaborations are often required, especially in the setting of older patients with multiple comorbidities.

Reference: Eur Urol. 2023;84(2):207-222
Abstract

What is the optimal stenting duration after ureteroscopy and stone intervention? Impact of dwell time on postoperative emergency department visits

Authors: Ghani KR et al.

Summary: This study used Michigan Urological Surgery Improvement Collaborative registry data to assess stent dwell time after ureteroscopy for stone intervention and its association with postoperative emergency department visits based on 4437 procedures including 1690 (38%) with stents with extraction strings. Median stent dwell time was lower in patients with a string (5 vs 9 days) and frequency of string use was higher in younger patients, or with patients with smaller stones, or renal stone location. Probability of an emergency department visit was higher in patients with strings when dwell times were <5 days ($p < 0.01$) but not after 5 days.

Comment: Ureteral stent placement allows for more accessible elective ureteral instrumentation and relief of urinary obstruction. However, it is unknown whether post-ureteroscopy stenting improves stone-free rate or minimises ureteric obstruction since stent-related morbidity such as stent irritation is not uncommon. Stent-on-a-string has been advocated as an invaluable solution to avoid the need for another procedure (to remove the stent) and provides a better cost-efficacy outcome. In this single-centre study, it was reported that stents with string were used more commonly in younger patients, those with smaller stones or renal stone locations. However, its use was associated with a higher probability of an emergency department visit than without a stent. There is no consensus regarding the optimal duration of postoperative stenting, and the decision to stent the patient is likely to be dependent on several factors such as day surgery, the patient's previous experience, the surgeon's comfort, and other surgical factors. Nonetheless, there are scenarios where routine post-ureteroscopy stent placement is advisable; suspected ureteric injury or stricture, solitary kidney, and patients with renal impairment.

Reference: J Urol. 2023;210(3):472-480
Abstract

Early vs delayed transurethral surgery in acute urinary retention: Does timing make a difference?

Authors: Frendl DM et al.

Summary: This retrospective (2002-16) cohort analysis used data from the New York Statewide Planning and Research Cooperative System to compare outcomes of early versus delayed transurethral surgery (primary ambulatory transurethral resection or photoselective vaporization of the prostate), for BPH after acute urinary retention compared to men without preoperative acute retention. In 17,474 patients, 10% had preoperative acute retention with a median time to surgery of 2.4 months, of whom 37% had a ≥6 month delay before surgery. Ten-year cumulative treatment failure rate was 17.2% in catheter-naive men and 34.0% in those with ≥2 pre-catheterisations, and 32.9% in those with a ≥6 months delay to surgery. Higher rates of treatment failure were associated with delays of <6 months (sub-distribution HR [SHR] 1.49; $p < 0.001$) and ≥6 months (SHR 2.11; $p < 0.001$) from catheterisation to surgery versus catheter-naive men

Comment: While pharmacological management has significant demonstrable benefits, surgery for BPH may confer greater absolute reductions in the long-term risk of catheterisation for acute urinary retention. Men who experience an episode of acute urinary retention are at a 20% increased risk of undergoing repeat catheterisation, coinciding with a roughly 20% reduction in the rate of surgery in this same high-risk group. Furthermore, progressive detrusor muscle failure in patients with urinary retention may lead to lower surgical success rates and make earlier surgical intervention in patients with less severe symptoms more beneficial. These days, many patients progress to surgery at an older age despite medical treatment, with acute urinary retention becoming a more common indication for surgery. There is an incremental association between the risk of surgical BPH treatment failure with an increasing number of catheterisation events and increasing delays to surgery after requiring Foley catheter placement. If an acute retention episode can be predicted and avoided in patients without any other underlying pathology contributing to bladder dysfunction, it may be beneficial to consider BPH surgery before progressing to retention. For men who progress to urinary retention requiring a catheter, delaying definitive BPH surgery can have quality-of-life implications and increase the risk of overall health complications.

Reference: J Urol. 2023;210(3):492-499
Abstract

The PINNACLE study: A double-blind, randomized, sham-controlled study evaluating the Optilume BPH catheter system for the treatment of lower urinary tract symptoms secondary to benign prostatic hyperplasia

Authors: Kaplan SA et al.

Summary: The prospective, randomised, double-blind, sham-controlled PINNACLE study assessed the Optilume BPH Catheter System versus a sham surgical procedure in 148 men with symptomatic BPH. After 1 year, Optilume BPH recipients had a reduction in IPSS of 11.5 points versus a reduction of 8.0 points at 3 months in sham recipients. Flow rate was also improved by 10.3 mL/s (125%) from baseline to 1 year.

Comment: The Optilume BPH Catheter System is a minimally invasive paclitaxel-coated dilation system and the first minimally invasive surgical treatment (MIST) device with a dual mechanical and pharmacological mechanism of action. Early experience with paclitaxel-coated balloons showed it to be generally safe and effective, and it can significantly reduce the rate of stricture recurrence in men with urethral strictures. The proposed mechanism of action is inferred from the established action of paclitaxel in the prevention of smooth muscle cell growth, but direct mechanistic evidence is lacking. The PINNACLE randomised, double-blind, sham-controlled clinical study showed that treatment with Optilume BPH leads to better symptom relief (improvement in IPSS scores) and objective measures (maximum flow [Q_{max}] and post-void residual volume [PVR]). While the actual symptom improvement seen with Optilume BPH may be comparable to that reported for other MISTs in similar patient populations, the longer-term data and cost-comparative analysis are not clear and require further validation.

Reference: J Urol. 2023;210(3):500-509
Abstract

One treatment with onabotulinumtoxinA relieves symptoms of overactive bladder in patients refractory to one or more oral medications

Authors: Farrelly E et al.

Summary: This exploratory *post hoc* analysis of data from the prospective observational GRACE study assessed whether treatment history impacts the effect of treatment with onabotulinumtoxinA (onabotA) in patients with overactive bladder (OAB). Compared to baseline, reductions in urinary incontinence, urgency, micturition, and nocturia occurred after 1 week and were sustained at 12 weeks, regardless of prior oral medications. After 12 weeks, the mean change from baseline urinary incontinence episodes/day for those with a treatment history of only 1 anticholinergic was -2.4 ($p \leq 0.001$), ≥1 anticholinergic -2.4 ($p \leq 0.001$); 1 β-3 -3.3 ($p < 0.05$), and ≥1 anticholinergic and ≥1 β-3 -3.2 ($p \leq 0.001$). Pad and liner use were decreased at 12 weeks across all treatment history groups. Reductions in diaper use varied, with less reduction in patients with ≥1 anticholinergic, ≥1 anticholinergic and 1 β-3 ($p < 0.05$) or with only 1 anticholinergic ($p < 0.05$). Overall, a total of 253 of 288 (88%) patients reported improvements on the treatment benefit scale after 12 weeks, regardless of type and number of prior oral medications. Among patients who received ≥1 dose (n = 504), 57 adverse events occurred in 38 (7.5%) patients (9 [1.8%] serious), urinary retention occurred in five (1.0%) patients (1 [0.2%] severe), and symptomatic UTI occurred in two (0.4%) patients.

Comment: Oral OAB medications are associated with variable clinical efficacy, poor adherence, and side effects. Second-line therapies such as Botox injection and neuromodulation are considered after first-line therapy has failed to provide relief, although some patients may need to take ongoing oral medications. This exploratory *post hoc* GRACE study analysis found that regardless of the type and number of previous oral OAB medications, up to 88% of patients reported clinical improvements with mean urinary incontinence, urgency, micturition, nocturia, and incontinence product use decreased after treatment with onabotA alone. While there were few differences in baselines or outcomes based on prior treatment history; these results may be due to differences in baseline severity rather than true improvements. Limitations to this analysis include the small sample size of each group, the observational nature of this study, the lack of randomisation and a comparator group, as well as the lack of information on the sequence of prior medications, reasons for switching between oral medications, and reasons for discontinuing oral medications. Since outcomes in patients were generally similar among patients who had taken 1 compared to >1 oral OAB medication, patients and clinicians may want to consider earlier treatment with onabotA if oral medications fail to provide adequate symptom relief. Delays in progressing to advanced OAB therapies are often related to cycling through multiple oral medications for OAB. Studies such as this shed light on the potential benefits of treatment with onabotA after one or more oral medications fail to provide adequate symptomatic relief in patients with OAB.

Reference: Neurourol Urodyn. 2023;42(6):1203-1213
Abstract

Holmium laser versus cold knife visual internal urethrotomy for management of short segment urethral stricture: A prospective randomized clinical trial

Authors: Ali MM et al.

Summary: This prospective randomised study examined the safety and efficacy of holmium laser versus Sachse cold knife visual internal urethrotomy (VIU) in the management of short segment urethral stricture in 66 male patients. Mean values of IPSS, PVR and Q_{max} improved in the groups. There was no significant difference between groups in mean values of IPSS, PVR and Q_{max} during follow-up at 1, 3, and 6 months; however, at the end of 1 year there was a difference in the mean IPSS, PVR and Q_{max} due to higher recurrence rate in the cold knife group. The overall complication rate was lower with the holmium laser ($p = 0.014$).

Comment: Different treatment modalities have been tried for the management of urethral strictures ranging from simple non-invasive techniques to one-stage or more urethroplasty depending on its length, location, depth of scar and extension of spongiofibrosis. Different kinds of laser energy and technology have been used to treat urethral strictures with varying degrees of success rates. In this prospective, randomised study, holmium laser VIU was found to be as effective and safe as short-segment urethral stricture as the cold knife DVIU but had a lower overall complication rate ($p = 0.01$). Two main principles that should be kept in mind when treating urethral stricture to minimise the risk of recurrence are complete removal of fibrotic tissues and avoidance of injury to healthy tissues. Hence, urethroplasty remains the most effective and definitive treatment option for urethral stricture by removing all the scarred and fibrotic tissues, which are the cornerstones in preventing recurrence. Nonetheless, urologists depend on DVIU for its ease, simplicity, minimal invasiveness, shorter convalescence, and time to catheter removal.

Reference: World J Urol. 2023;41(7):1897-1904
Abstract

Research Reviews are prepared with an independent commentary from relevant specialists. To become a reviewer please email geoff@researchreview.com.au.
Research Review Australia Pty Ltd is an independent Australian publisher. Research Review receives funding from a variety of sources including Government depts., health product companies, insurers and other organisations with an interest in health. Journal content is created independently of sponsor companies with assistance from leading local specialists. **Privacy Policy:** Research Review will record your email details on a secure database and will not release them to anyone without your prior approval. Research Review and you have the right to inspect, update or delete your details at any time. **Disclaimer:** This publication is not intended as a replacement for regular medical education but to assist in the process. The reviews are a summarised interpretation of the published study and reflect the opinion of the writer rather than those of the research group or scientific journal. It is suggested readers review the full trial data before forming a final conclusion on its merits.
Research Review publications are intended for Australian health professionals.