

# Urology

## RESEARCH REVIEW™

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Issue 1 – 2020

### In this issue:

- Chronic kidney disease associated with severe COVID-19
- COVID-19 and bacillus Calmette-Guérin
- Impact of bariatric surgery on urinary incontinence
- Bladder and rectal cancer after brachytherapy for localised prostate cancer
- Functional outcomes of artificial urinary sphincter implantation
- Long-term oncological outcomes of open, robotic, and laparoscopic radical cystectomy
- Ultrasound-guided subcostal transversus abdominis plane block
- Cxbladder monitoring in previously treated bladder cancer
- Coffee consumption and risk of bladder cancer
- Simultaneous transurethral resection of bladder cancer and prostate

#### Abbreviations used in this issue

CI = confidence interval

COVID-19 = Coronavirus disease 2019

LUTS = lower urinary tract symptoms

NMIBC = non-muscle invasive bladder cancer

OR = odds ratio

## Welcome to the latest Issue of Urology Research Review.

As COVID-19 continues to dominate, the identification of predictive factors for severe infection is essential. We start this issue with a study suggesting that patients with chronic kidney disease have a 3-fold increased risk of developing severe COVID-19 infection. Following on, we learn of a potentially protective effect of bacillus Calmette-Guérin vaccination, with countries with a BCG vaccination programme exhibiting much lower incidences of COVID-19 than those without. Other topics covered in this issue include the impact of bariatric surgery on urinary incontinence, functional outcomes of artificial urinary sphincter implantation, long-term oncological outcomes of open, robotic, and laparoscopic radical cystectomy, and coffee consumption and the risk of bladder cancer.

I hope you enjoy reading this issue and look forward to any comments and feedback.

Kind regards,

**Andrew Kennedy-Smith**

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### Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection

**Authors:** Henry BM et al.

**Summary:** This meta-analysis examined the association between chronic kidney disease (CKD) and COVID-19 infection severity. In total, 4 Chinese studies including 1389 patients were included in the analysis among whom 273 (19.7%) patients had severe COVID-19 infection. No single study identified CKD as a significant clinical predictor of severe COVID-19; however, pooled analysis revealed an association of CKD with severe COVID-19 (OR 3.03; 95% CI 1.09-8.47).

**Comment:** I expect a deluge of COVID-19 literature will appear across clinical and microbiological literature in the coming months. The initial urology correspondence predominantly relates to system reorganisations to cope with the massive change in demands on hospitals and clinical staff. Given we've thus far been spared the awful circumstances in parts of the world we read about in the news, I'm hopeful this advice will be less applicable to our circumstance. This was one of a few of these early articles that may still be pertinent to NZ urologists. Pneumonia-related mortality rate in CKD patients is several times higher than in the general population and COVID-related pneumonia is no exception. The article references data from China from the start of this year. The report doesn't distinguish patients based on cause of CKD, whether CKD from medical causes is more of a risk than CKD of surgical origin. I read this as a caution and guide in selection of patients for elective surgery, particularly as we emerge from Level 4 lock-down and resume more usual practice. It suggests we should delay surgical interventions in otherwise stable patients with CKD, including patients waiting for renal transplantation.

**Reference:** *Int Urol Nephrol.* 2020;Mar 28 [Epub ahead of print]

[Abstract](#)



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## COVID-19 and bacillus Calmette-Guérin: What is the link?

**Authors:** Hegarty PK et al.

**Summary:** This study used European Centre for Disease Prevention and Control data on the number of cases and fatalities of COVID-19 in 179 countries on March 22, 2020 and compared the data by countries with a current whole-population bacillus Calmette-Guérin (BCG) vaccination programme. Overall, COVID-19 incidence on March 22 2020 was 4.5 per million population, with a fatality rate of 0.22 per million. The daily incidence of COVID-19 in countries with a BCG vaccination programme was 0.8 per million versus 34.8 per million in countries without such a programme. Crude case fatality rates were 4.1% versus 5.1% in countries with versus without a BCG vaccination programme.

**Comment:** One of the potential pitfalls in an emergency is error and pseudoscience. In the rush to contribute and publish, and enthusiasm for some good news, the rigours of scientific scrutiny may be sidelined, and the error may take quite some time to erase. But there is also the exciting possibility of the unexpected coming to light. Something that might otherwise not have been explored or been buried under investigational bureaucracy. And here is both a teasing sweetener and a practical comment on BCG, which we know well. Whilst in daily use in our departments, the exact mechanisms of action aren't completely familiar. At least to all of us. And so, I read with interest that BCG vaccination has demonstrated immune memory and enhanced protection against a number of infections unrelated to tuberculosis, including influenza. Specifically, with regard to COVID-19, the mortality rates are higher in countries without BCG vaccination, suggesting relative protection from this vaccine. The authors offer some practical guidance on BCG treatments for NMIBC during the pandemic: that the risks of interrupting treatment are likely lower than the risks to the patient of bringing them into hospital to receive the weekly treatment. And finally, there's the observation that whether or not BCG is demonstrated to truly be partly protective against COVID-19, we might see shortages (again) of our BCG supplies as this agent is requisitioned for the fight against COVID-19. With potentially poorer overall outcomes, if the efficacy against COVID-19 is minimal and patients with NMIBC are denied what we know to be an effective treatment.

**Reference:** *European Urol Oncol.* 2020 [Epub ahead of print]  
[Abstract](#)

## The impact of bariatric surgery on urinary incontinence: A systematic review and meta-analysis

**Authors:** Lee Y et al.

**Summary:** This meta-analysis of 33 cohort studies examined the effect of bariatric surgery on 2910 obese patients with urinary incontinence (UI) using Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) methodology. While the quality of evidence was very low for all outcomes, bariatric surgery appeared to improve or resolve UI in 56% (95% CI 48-63) of patients; it also relieved stress UI in 47% (95% CI 34-60) and urgency UI in 53% (95% CI 32-73) of patients. Bariatric surgery also decreased Urogenital Distress Inventory scores by 13.4 points (95% CI 7.2-19.6), International Consultation on Incontinence Questionnaire scores by 4.0 points (95% CI 2.3-5.7), and Incontinence Impact Questionnaire scores by 5.3 points (95% CI 3.9-6.6), all  $p < 0.001$ . New-onset or worsening UI occurred in 3% of patients.

**Comment:** Having contributed to the literature on this, together with Drs Luke and Stubbs et al., I'm a bit interested in this topic. Our paper, specifically rather relevant to this review, was not included in this analysis and references, leaving me either dismayed or dismissive. But noting these authors' conclusions, that the "quality of evidence is very low", I'm not surprised. And Dr Lee et al., have added another low-quality paper to the subject. But pride aside, the message is important: obesity is associated with LUTS, weight loss is associated with improvement in LUTS, and probably bariatric surgery with its immediate impact on the metabolic syndrome, prior to weight loss, is associated with improvement in LUTS. By inference, conventional urology surgery or management in obese patients is unlikely to achieve results similar to surgery/management in non-obese patients. Go cautiously with the anti-Barbie patient.

**Reference:** *BJU Int.* 2019;124(6):917-934  
[Abstract](#)

## Long-term incidence of secondary bladder and rectal cancer in patients treated with brachytherapy for localized prostate cancer: A large-scale population-based analysis

**Authors:** Mazzone E et al.

**Summary:** This analysis of data from patients with prostate cancer ( $n = 318,058$ ) from the US Surveillance, Epidemiology and End Results (SEER) database (1988-2015) assessed the incidence and trends of secondary bladder and rectal cancer after brachytherapy ( $n = 55,566$ ) compared to radical prostatectomy (RP). Propensity score-matched 20-year secondary bladder cancer incidence was 6.0% after brachytherapy versus 2.4% after RP ( $p < 0.001$ ); 20-year secondary rectal cancer incidences were 1.1% versus 0.5% ( $p < 0.001$ ), respectively. Multivariate competing-risks regression models indicated brachytherapy has higher secondary bladder (HR 1.58;  $p < 0.001$ ) and rectal (HR 1.59;  $p < 0.001$ ) cancer rates than RP. Temporal trends suggested decreasing secondary 5-year bladder and rectal cancer rates in more recently diagnosed cohorts (1988-1996 vs 1997-2005 vs 2006-2015).

**Comment:** Oh brachy wherefore art thou going? And shouldn't you be going there quicker? This is a SEER database review, patients treated with curative intent with either (low dose) brachytherapy +/- external beam boost compared to patients having RP. And it shows that radiation causes cancers, which is well recognised. But as a study, it has all the challenges of retrospective comparison of non-randomised groups. And potentially the observed increased risk of bladder and rectal cancer may be from pre-existing factors that aren't apparent from the database review. But the fact remains: radiation causes cancers.

**Reference:** *BJU Int.* 2019;124(6):1006-1013  
[Abstract](#)

### Independent commentary by Mr Andrew Kennedy-Smith FRACS, MB BCH



Andrew is a full-time consultant urologist at Wellington Hospital, with commitments in both private and public urology practice. He grew up in Zimbabwe and South Africa, undertook his specialist surgical and urological training in New Zealand and Australia, and Fellowship training in Cardiff, Wales and Paris, France. His interests include general adult urology, laparoscopic and minimally invasive urologic surgery, surgical management of kidney cancer, kidney transplantation, evaluation and treatment of urinary incontinence and prolapse, laparoscopic pelvic floor reconstruction and urology prosthesis surgery.

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## Functional outcomes of artificial urinary sphincter implantation with distal bulbar double cuff in men with and without a history of external beam radiotherapy

**Authors:** Maurer V et al.

**Summary:** This study (2009-2015) assessed functional outcomes and complication rates of artificial urinary sphincter (AUS) implants with a distal bulbar double cuff in 150 men with stress UI, 73 of whom had a history of external beam radiotherapy. Over a median follow-up of 24 months, social continence was achieved by 94.8% and objective continence by 84.3% of all AUS implant recipients. There were no differences in continence rates (social continence 100% vs 90.2%; objective continence 87% vs 82%), explantation rates, implant durability, or complication rates between radiotherapy and non-radiotherapy groups.

**Comment:** This is a carefully collected and well-presented study. But the devil is in the study detail (and not in the AUS): although the database was set up prior to this study, and the data faithfully entered into their database at the time of surgery and follow up, the study itself is not prospective and is retrospective in its analysis. Unfortunately, their radiotherapy cohort is bundled together, and there is no information on the indications for radiotherapy, the field or the dose: Are the outcomes the same for patients having radical radiotherapy as for those having adjuvant, or salvage? Is the sequencing of radiotherapy and surgery important?

Alas too, their median follow-up period is not defined, with their AUS survival outcomes presented as a Kaplan-Meier. The authors acknowledge the “vast body of literature outlining higher complication and revision rates of AUS devices in high-risk patients with a previous history of radiotherapy” but suggest their data refutes this. And it seems their explantation and revision rates are indeed similar between their non-radiotherapy patients and their prior radiotherapy patients (with the above caveats). Only their rates for radiotherapy-naïve AUS survival are only as good as others report on radiotherapy-AUS survival, suggesting they’ve had bad luck with their non-radiotherapy AUS patients.

**Reference:** *BJU Int.* 2019;124(6):1040–1046

[Abstract](#)

## Long-term oncological outcomes from an early phase randomised controlled three-arm trial of open, robotic, and laparoscopic radical cystectomy (CORAL)

**Authors:** Khan MS et al.

**Summary:** This study reviewed 5-year oncological outcomes in 60 patients with muscle-invasive bladder cancer (n = 38) or high-risk non-muscle-invasive bladder cancer (n = 21) who previously took part in the CORAL trial of open radical cystectomy (ORC), robotic-assisted radical cystectomy (RARC), or laparoscopic radical cystectomy (LRC). After 5-years, the recurrence-free survival rates did not significantly differ between groups (ORC 60% vs RARC 58% vs LRC 71%); there were also no significant differences in 5-year cancer-specific survival rates (64% vs 68% vs 69%) or overall survival rates (55% vs 65% vs 61%).

**Comment:** I think this is reassuring – that the technique for access neither compromises nor enhances the cancer outcomes from major cancer surgery. And it isn't too surprising. Whilst this is a database review, the database was established as a randomised prospective trial comparing open, laparoscopic and robotic access approaches, reporting in 2016 on the 30- and 90-day complications and outcomes from each of these approaches. The techniques of cystectomy differ somewhat between the 3 approaches, but within the commonly accepted variations (Bricker vs Wallace, antegrade vs retrograde dissection). In each, the ileal neo-bladder was fashioned extra-corporeally and only the cystectomy component was performed open or with one or other minimally invasive technique. I look forward to the passing of robot-hype and a return to a more critical evaluation of the techniques themselves, and adjuvant measures associated with surgery, rather than focusing on the door used to gain access.

**Reference:** *Eur Urol.* 2020;77(1):110–118

[Abstract](#)

## Perioperative analgesic effects of preemptive ultrasound-guided subcostal transversus abdominis plane (TAP) block for percutaneous nephrolithotomy

**Authors:** Özdilek A et al.

**Summary:** This study compared the perioperative analgesic effect of an ultrasound-guided, subcostal, transversus abdominis plane (TAP) block (20 mL bupivacaine 0.125% plus 10 mL lidocaine 1%) versus IV paracetamol 1 g in 79 patients undergoing percutaneous nephrolithotomy under general anaesthesia (propofol, fentanyl, rocuronium induction; sevoflurane, fentanyl, rocuronium maintenance). After 48 hours, total morphine consumption (p = 0.022) and perioperative fentanyl consumption (p < 0.001) was lower in TAP recipients.

**Comment:** This makes sense and seems simple enough. I'm a fan of local infiltration with kidney surgery and spraying it over the surgery bed at the end of laparoscopy. When we looked at the benefit of wound catheters in laparoscopic nephrectomy, we had similar findings, but small numbers and we couldn't reach significance. For a not-very painful post-operation procedure, it's difficult to demonstrate a difference in the pain scores. But less opiate will mean earlier return to normal and a shorter hospital stay. What isn't clear to me, either from this or our own work, is whether the effect and benefit from the local anaesthetic is local or from systemic absorption and a similar benefit could be achieved with an IV lignocaine infusion during surgery. Which may be simpler still.

**Reference:** *Endourol.* 2020;Mar 31 [Epub ahead of print]

[Abstract](#)



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## An evaluation of the real world use and clinical utility of the Cxbladder monitor assay in the follow-up of patients previously treated for bladder cancer

**Authors:** Koya M et al.

**Summary:** This multicentre trial audited the clinical utility of a new surveillance protocol utilising the Cxbladder Monitor (CxbM) test in 309 patients previously treated for bladder cancer. In total, 257 (83.2%) patients were classified as low-risk, while 52 (16.8%) patients were classified as high-risk; 443 CxbM tests were conducted. Among low-risk CxbM-negative patients (n = 108) during the first post-CxbM cystoscopy (at a mean of 10 months), no pathology-confirmed recurrences were observed. In 53 low-risk CxbM-positive patients, 3 recurrences were observed during cystoscopy (at a mean 2.7 months). Among 49 high-risk patients, 39 CxbM-negative patients had no pathology-confirmed recurrences. Ten high-risk CxbM-positive patients had 4 confirmed recurrences (2 high- and 2 low-grade). Median time to first cystoscopy was 12.13 months (95% CI 11.97-12.4) in CxbM-negative patients versus 1.63 months (95% CI 1.13-2.3) in CxbM-positive patients (p < 0.00001). Over 35 months of follow-up, no positive cases were missed, no patients progressed to invasive or metastatic disease, and no patients died of cancer. CxbM identified 77.8% of patients who were managed with one cystoscopy per year.

**Comment:** For many reasons, it's nice to see this in print. It's not high science, but an audit of now-established clinical practice using Cxbladder in place of some cystoscopy surveillance, without seeing adverse outcomes. It illustrates that we may moderate the invasiveness and cost of our follow-up strategies, recognising superficial bladder cancer is our most costly cancer. In the era of no-patient-contact, isn't this timely?

**Reference:** *BMC Urol.* 2020;20(1):12

[Abstract](#)

## Coffee consumption and risk of bladder cancer: A pooled analysis of 501,604 participants from 12 cohort studies in the BLadder Cancer Epidemiology and Nutritional Determinants (BLEND) international study

**Authors:** Wu EYW et al.

**Summary:** This pooled analysis sought to determine the relationship between coffee consumption and bladder cancer using data from 12 cohort studies (2601 cancer cases from 501,604 participants). The relationship between coffee consumption and bladder cancer risk had an interaction with sex (p < 0.001) and smoking (p = 0.001), so analyses were stratified by sex and smoking. After adjustment, an increased bladder cancer risk was observed in participants with high coffee consumption (>500 mL/day, >4 cups/day) versus never drinkers among current (HR 1.75; 95% CI 1.27-2.42; p = 0.002) and former male smokers (HR 1.44; 95% CI 1.12-1.85; p = 0.001). Dose-response analyses suggested that male smokers also had an increased bladder cancer risk with coffee consumption of >500 ml/day, with a 1-cup-increment risk of 1.07 (95% CI 1.06-1.08).

**Comment:** Coffee is that good, it's assumed it must be a little bit bad. But it ain't. It might cause frequency and nocturia, wakefulness and palpitations, but these are either benefits or readily worth the trade-off. If anything, this remarkable drug appears multiply beneficial; cardiovascular system, liver diseases, diabetes as well as gastrointestinal disorders. Ok the smokers have to go.

**Reference:** *Eur J Epidemiol.* 2020;Jan 10 [Epub ahead of print]

[Abstract](#)

## Assessment of the clinical efficacy of simultaneous transurethral resection of both bladder cancer and the prostate: A systematic review and meta-analysis

**Authors:** Zhou L et al.

**Summary:** This meta-analysis examined the clinical efficacy of simultaneous transurethral resection of bladder cancer and the prostate (TURBT + TURP) in NMIBC and benign prostatic hyperplasia using data from 8 studies in a total of 1032 patients. Patients that underwent TURBT + TURP had lower recurrence rates (OR 0.70; 95% CI 0.53-0.93; p = 0.01) and greater maximal urinary flow rate (Qmax; weighted mean difference 5.92; 95% CI 4.67-7.16; p < 0.001) than TURBT-only patients. Rates of recurrence at the prostatic urethra/bladder neck, bladder tumour progression, and time to recurrence did not differ between groups.

**Comment:** Patients with NMIBC sometimes have LUTS. The question then regarding the place of TURP simultaneous with TURBT is "does this man need TURP?" But why this is of some interest, is that I have wondered whether bladder outlet obstruction (BOO), and retained urine, underlies recurrent NMIBC. It would make sense, wouldn't it? If the carcinogens are in the urine, and these are retained in the bladder, the risks and rate of recurrent NMIBC must increase. Like squamous cell carcinoma and sun-exposed skin. Perhaps this in part underlies the different rates of NMIBC in men and women. So, if TURBT + TURP is safe, should this be the standard of care in men with some or any signs of BOO? There are reports that 5-alpha reductase inhibitors are protective against NMIBC, though the mechanism has not been elucidated. Well, I wonder...

**Reference:** *Aging Male.* 2020;1-12

[Abstract](#)

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