38th Annual European Association of Urology (EAU) Congress 2023 Conference Review™

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In this review:

Abbreviations used in this review:

AI = artificial intelligence; **AUC** = area under the curve; **ERBT** = *en block* resection of bladder tumour; **HR** = hazard ratio; **IIEF** = International Index of Erectile Function; **IRP** = intrarenal pressure; **MSHQ** = Male Sexual Health Questionnaire; **NAC** = neoadjuvant chemotherapy; **NICE** = The National Institute for Health & Care Excellence (UK); **(N)MIBC** = (non-) muscle-invasive bladder cancer; **PROM** = patient-reported outcome measure; **PSMA** = prostate-specific membrane antigen; **QOL** = quality of life; **RCT** = randomised control trial; **RR** = risk ratio; **SR** = standard resection.

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Welcome to our review of the 2023 European Association of Urology (EAU) Conference held in Milan, Italy.

This year, specialists and medical professionals gathered from around the world at the 38th Annual EAU Congress to critically assess the very latest innovations and key developments in the field of urological research. A number of presentations highlighted the efficacy of technology in improving the detection and prediction of disease, including an Australian trial which demonstrated the superiority of PSMA PET-CT vs. conventional imaging in detecting nodal and distant metastasis in prostate cancer, a novel medical device, VisioCyt® that uses AI to detect low- and high-grade urothelial bladder tumours with significantly higher sensitivity than standard cytology, and a machine learning-based model which improves the prediction of postoperative disease-free survival in renal cell carcinoma compared to traditional scoring systems. A final highlight includes a serum analysis which identified novel prognostic biomarkers and proteomic clusters with distinct survival outcomes in MIBC.

We trust you will enjoy this conference review and find it of clinical value, and we look forward to receiving your comments and feedback

Best regards,

Professor Nathan Lawrentschuk

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Baseline PSMA PET-CT is prognostic for treatment failure in men with intermediate-to-high risk prostate cancer

Speaker: Dr Veeru Kasivisvanathan (Melbourne, Australia)

Summary: This presentation described outcomes from 54 months follow-up of the proPSMA RCT, showing that prostate-specific membrane antigen (PSMA) PET-CT nodal staging at baseline is prognostic in identifying men with intermediate-high risk prostate cancer who are at higher risk of treatment failure. In the trial, 251 men underwent PSMA PET-CT as first- or second-line imaging, and were treated with radiotherapy ± androgen deprivation, or curative-intent surgery. During follow-up, 19% of patients experienced biochemical failure, 23% underwent salvage therapy and 5% developed distant metastatic disease. Those with N0M0 disease had a longer period of freedom from treatment failure than N1M0 (HR 2.1; 95% CI 1.2—3.7; p=0.01), and at 3 years a greater proportion of patients with N0M0 continued to be free from treatment failure than N1M0 (70% vs. 46%, respectively).

Comment: The celebrated proPSMA trial from Australia demonstrated that PSMA PET-CT has superior accuracy to conventional imaging for detection of nodal and distant metastatic disease. PSMA PET-CT nodal staging is more prognostic than conventional imaging (CT and bone scan) for medium-term oncologic outcomes in men with intermediate-high risk prostate cancer without distant metastases. Among 251 patients, those with N1M0 had a higher risk of treatment failure than those with N0M0, with a hazard ratio of 2.1 and a significant p value of 0.01. At 3 years, 70% of N0M0 patients remained free from treatment failure, compared to 46% of N1M0 patients. CT and bone scan-defined N1M0 was not prognostic. This demonstrates PSMA as a remarkable prognostic tool - not just a diagnostic one. As time passes, the undoubted utility of PSMA imaging will continue to thrive and grow.

Abstract A1237

Artificial intelligence to improve cytology performance in bladder urothelial carcinoma diagnosis

Speaker: Prof. Thierry Lebret (Suresnes, France)

Summary: In this French, multicentre prospective trial, VISIOCYT1, the company VitaDX developed a medical device to improve the variability and low sensitivity of cytology, particularly in low-grade urothelial tumours of the bladder. VisioCyt® identifies tumour cells in smears of urine samples through AI algorithms and whole-slide digitalisation. Among a total of 319 patients (170 with NMIBC; 149 controls), VisioCyt® had higher overall sensitivity than standard cytology (80.9% vs. 45.9%; p<0.0001), as well as higher sensitivity in detecting low-grade (66.7% vs. 26.1%; p<.0001) and high-grade tumours (93.7% vs. 62.8%; p<.0001) at a specificity of 61.8%.

Comment: Artificial intelligence, or AI, has had significant publicity in language sectors - but it is in imaging where it thrives. It is completely logical that AI should be able to assist with cytology in the diagnosis of urothelial cancer. The new AI technique being presented here has the fancy name of VisioCyt®. Its sensitivity was evaluated in a prospective, multicentre clinical trial involving 319 patients with NMIBC and control patients with negative urinary cytology and cystoscopy. AI showed a significantly higher sensitivity than standard cytology (80.9% vs. 45.9%; p<0.0001) with a higher sensitivity for both low grade (66.7% vs. 26.1%) and high grade (93.7% vs. 62.8%) tumours. The specificity of AI was 61.8% but could not be compared with that of standard cytology due to the trial design. The real feature here is how poorly standard cytology performed, which is why many urologists have removed it from their armoury. Low-grade results are understandable, but high-grade accuracy of only around 2/3 is probably at the lower end of what is generally quoted; however, it is likely a reasonable figure. More data are needed and more algorithms will arise – only then will cytology have its faith restored.

Abstract A0592

Transurethral *en bloc* resection versus standard resection of bladder tumour

Speaker: Dr Yuen Chun Jeremy Teoh (Hong Kong)

Summary: EB-StaR was a multi-centre phase 3 trial which randomised 276 eligible patients with NMIBC tumours ≤3cm to undergo either *en bloc* resection of bladder tumours (ERBT; n=143) or standard resection (SR; n=133). Patients in the ERBT group had a significantly longer mean operative time (33.4 vs. 24.7 mins; p<0.001) and significantly lower 1-year recurrence (primary outcome; 28.5% vs. 38.1%; p=0.007) than those treated with SR. ERBT patients also had numerically lower progression, however this did not reach statistical significance (0% vs. 2.6%; p=0.065). There were no significant between-group differences in residual disease, 30-day complications, hospital stays, post-operative mitomycin C installation, detrusor muscle sampling, obturator reflex or upstaging of disease upon transurethral resection.

Comment: The EB-StaR study compared *en bloc* resection of bladder tumours (ERBT) and standard resection (SR) in treating NMIBC patients. A total of 276 histologically confirmed NMIBC patients were randomised, and the 1-year recurrence rate was significantly lower in the ERBT group compared to the SR group (28.5% vs. 38.1%; p=0.007). The ERBT group had a longer operative time but similar outcomes in terms of detrusor muscle sampling rates, complications, and disease upstaging. In patients with NMIBC of ≤ 3cm, ERBT resulted in a significant reduction in 1-year recurrence rate when compared to SR. With bladder cancer there are only a few manoeuvres that have pushed the treatment forward in the past few decades. A complete resection appears feasible and helpful. Presumably it means we have fewer cells to seed the bladder at its simplest form. This is where the postoperative management needs to be clear: water for irrigation or intravesical chemotherapy also have roles. Should we adopt this technique immediately as is what happens when new chemotherapeutics come out? Undoubtedly it probably will not, and questions will arise: Is it easy to learn? Do we believe the data? How do we get larger specimens out? …Time will tell.

Abstract A0707

Global variation in the quality of multiparametric Magnetic Resonance Imaging of the prostate from the PRIMEtrial (the glimpse study)

Speaker: Dr Alexander Ng (London, Great Britain)

Summary: Data from the international, prospective PRIME trial were used to evaluate global variation in the quality of prostate multi-parametric MRI, and to explore the impact of modifications on diagnostic quality. A total of 391 scans were analysed from 71 different scanners, which were evaluated by two blinded radiologists and graded in terms of diagnostic quality using the PI-QUAL scoring system, from 1 (all sequences below minimum standard) to 5 (optimal diagnostic quality and fully compliant with recommendations). PI-QUAL scores of 3, 4 and 5 were recorded for 13%, 55% and 32% of scanners, respectively. While all scanners reached adequate diagnostic quality for T2-WI and DWI MRI sequences, only 82% were adequate for DCE sequences. Scanners with PI-QUAL <5 were provided with basic modifications to improve MRI quality and invited to submit a new set of images. Following this, a greater proportion of scanners achieved PI-QUAL than at initial review (87% vs. 32%).

Comment: This study of the PRIME study aims to assess whether bi-parametric MRI (T2W & DWI) is non-inferior to multi-parametric MRI (T2W, DWI and DCE) in the diagnosis of clinically significant prostate cancer. As a sub-study, reporting variation has been examined. Variation in reporting and interpretation of MRI scans to help diagnose prostate cancer remains a serious issue. Part of the problem is a lack of "*closing the loop*" whereby radiologists and urologists sit together and review where they were right and wrong with whole-mount radical prostatectomy specimens. This trial, unsurprisingly, confirms variation remains an issue even between experienced centres. Is it a training or quality control issue, or both? As urologists we need to get better at interpreting studies ourselves to account for this variation. We mastered what we need from computed tomography, and we will undoubtedly master MRI of the prostate, but we have to work at it and be willing to set aside the time to do it.

Abstract A0970

Timing of symptomatic venous thromboembolism after surgery

Speaker: Prof. Kari Tikkinen (Helsinki, Finland)

Summary: This was a systematic review with meta-analysis which assessed the timing of postoperative venous thromboembolism events in 1,864,875 patients across 22 clinical studies (11 general surgery studies, 4 urologic, 2 orthopaedic, 5 mixed). Pooled analysis found that 47.1% of venous thromboembolism events took place in the first week following surgery, while 16.9%, 15.8% and 10.1% took place in the second, third and fourth weeks, respectively, with comparable timings between studies. There were no studies in the analysis which provided data on venous thromboembolism events up to 90 days following surgery.

Comment: Prevention of venous thromboembolism remains a challenge that dictates a careful balance between precipitating haemorrhage, yet preventing morbidity and even death. Mechanical preventative devices are now well-entrenched, as are stockings and early mobility. Pharmacologic prevention remains unresolved: preoperative, on induction, during procedure or postoperatively, and when? Certainly, the standard is to continue pharmacologic intervention for 21-28 days following surgery. This paper helps us to understand when symptomatic thromboembolic events occur (deep vein thrombosis, pulmonary emboli and even stroke). Of course, the common mantra is that the embolus starts intraoperatively, so the earlier the prophylaxis the better. Interestingly in this trial, nearly half of the symptomatic venous thromboembolic events in the first four weeks occurred during the first postoperative week, yet a substantial number of events occurred several weeks after surgery. The duration of postoperative thromboprophylaxis probably should be pushed to 28 days, unless other papers contradict this finding.

Abstract A1009

A comprehensive overview of patient reported outcomes

Speaker: Mr Sebastiaan Remmers (Rotterdam, The Netherlands)

Summary: These results from PIONEER, an international Big Data Consortium on prostate cancer led by the EAU, describe the ways in which patient-reported outcomes (PROMs) are assessed in men with prostate cancer. The questionnaires used to measure PROMs were EORTC QLQ-C30, EORTC PR-25 and EPIC-26. A total of five datasets were included, primarily comprising low-risk patients. Across all datasets, all QOL-related domains (sexual function, urinary function, bowel function, cancer-related QOL) were affected by active treatment. There was heterogeneity between studies in terms of treatment effect and length of follow-up, however the domain most affected by active treatment in both short- and long-term outcomes was sexual function. It was noted that the results indicate a need for standardising the collection of PROMs to improve patient care.

Comment: PROMS, or patient-reported outcomes, are certainly the new benchmark for ascertaining a treatment's impact and success, and rightly so – alongside oncologic outcomes and nominal side-effects, it is ultimately the patient's perspective of their treatment that should be our other 'ultimate' goal. The devil is always in the detail: what is collected, by whom, and when. Prostate cancer is the obvious choice, as there are many treatments and many different outcomes. Patients often base their treatments upon what their outcomes will be – yes, they want cure but with minimal impact on what is most important to them. PROMS will continue to be the best measure, and we should be benchmarking ourselves against similar treatments locally and globally, but then understand the differences to improve outcomes.

Abstract A0496

Development of an individual postoperative prediction model for kidney cancer recurrence using machine learning (UroCCR study 120)

Speaker: Mrs Gaelle Margue (Bordeaux, France)

Summary: These researchers sought to develop a machine learning-based model to individually predict the postoperative risk of recurrence in renal cell carcinoma. A cohort of 3255 patients (mean tumour size 4cm; 71% clear cell renal cell carcinoma) undergoing surgery for localised/locally advanced renal cell carcinoma were identified from the French database UroCCR. There was a median follow-up of 25 months. Locoregional recurrence occurred in 3.6% of patients, metastatic progression in 7%, and 2.4% died. A Cox PH model including 18 variables provided improved disease-free survival prediction compared with the SSIGN and UISS and scoring systems (C-index 0.75 vs. 0.72 vs. 0.61), with an AUC of 0.71 at 5 years.

Comment: AI has largely replaced the term 'machine learning' as the new buzz phrase. Are they the same? Not necessarily. Do they wish to achieve the same aims? Potentially. Nomograms that are easy to use are indeed useful. The Memorial Sloan Kettering post nephrectomy accessible computerised nomogram has remained a staple for many clinicians worldwide. However, it is based on older data, and it cannot account for subtle individual differences. Machine learning has the power to look at more factors and may have the capability of displacing older nomograms. However, the differences in how renal cell carcinomas behave and the additional therapies will make keeping up tricky, but possible.

Abstract A0473

Independent commentary by Professor Nathan Lawrentschuk.

Nathan has appointments at the University of Melbourne, Department of Surgery as a full Professor and is Director of Urology at the Royal Melbourne Hospital. He is the founding Director of the EJ Whitten Prostate Cancer Research Centre at Epworth Hospital, Melbourne. Nathan is also a consultant uro-oncologist at the Department of Surgical Oncology at Peter MacCallum Cancer Centre. Nathan has written over 500 peer-reviewed full journal article publications and 15 book chapters and reviews for over 30 scientific journals.

Nathan is the BJUI USANZ supplement Editor and is on the editorial board of Nature Reviews Urology. He is also previous Vice-Chairman of WUOF (World Urologic Oncology Foundation) and remains active in many international meetings.

The Stockholm3 prostate cancer screening trial (STHLM3)

Speaker: Ms Chiara Micoli (Solna, Sweden)

Summary: This was an interim analysis of mortality results after 6.5 years of follow-up from the population-based STHLM3 screening trial, which used the Stockholm3 prediction model (based on polygenic risk score, blood biomarkers, clinical variables) with a single prostate-specific antigen (PSA) to detect prostate cancer (Gleason score ≥7) in men aged 50-70 years in Sweden. Researchers compared rates of cancer-specific and all-cause mortality in men who were randomly invited to and participated in STHLM3 (n=58,909) with men who were not (n=70,287). At a follow-up of 6.5 years, men in the invited group had an increased risk of prostate cancer diagnosis (RR 1.21; 98% CI 1.15—1.29). Prostate cancer deaths occurred in 91 men invited to STHLM3 and 51 men not invited (RR 0.76; 98% CI 0.50—1.14), and deaths relating to any cause occurred in 7784 vs. 3189 (RR 1.03; 98% CI 0.98—1.08). It was noted that longer-term follow-up is currently underway.

Comment: It wouldn't be urology without new aspects related to prostate cancer screening. The Swedes are at it again, this time with Stockholm3 (STHLM3) in the mix. According to the UK NICE Guidelines "*STHLM3 helps predict risk of prostate cancer in people aged 45 to 74 years with PSA of at least 1.5 ng/mL and no previous diagnosis of prostate cancer. STHLM3 combines protein biomarkers, genetic markers and clinical data with an algorithm to help identify prostate cancer.*" This current paper concluded cautiously that the test has a potential effect on reducing prostate cancer mortality by a single intensive screening intervention using PSA and STHLM3 in combination against the costs of increasing prostate cancer incidence. Of course, longer-term follow-up is needed and is indeed underway. In their study, a PSA >3ng/mL is confirmed as the ideal screening cut-off. The cost-effectiveness of MRI vs. STHLM3 will also need to be explored as an alternative.

Abstract A0890

Human in vivo ureteroscopic intrarenal pressure

Speaker: Dr Stefanie Croghan (Dublin, Ireland)

Summary: In vivo intrarenal pressure (IRP) was measured in 100 consecutive patients (56 male; mean age 57.2 years) undergoing elective ureteroscopy (94% for urolithiasis) in this multi-centre analysis. Mean baseline IRP was 23.75 cmH_20. There was variability in the IRP depending on the pressure recording system: Semi-rigid ureteroscopy (6.5-7.5Fr ureteroscope) was used in 30% with mean IRP 53.77 cmH_20. Flexible ureterorenoscopy (9.1-10Fr instrument) was used in 93%; without a ureteral access sheath this provided a mean IRP of 51.83cmH_20. Flexible ureterorenoscopy (with 11/13Fr ureteral access sheath) provided mean IRPs of 40.92cmH_20 (gravity irrigation); 58.51cmH_20 (pressurised irrigation at 100mmHg); 63.26cmH_20 (pressurised irrigation at 150mmHg) and 108.41cmH_20 (pressurised irrigation at 200mmHg). A total of four patients (4%) were readmitted with pyrexia, and these patients had a significantly higher mean procedural IRP than controls (120.25 vs. 56.15, respectively; p<0.001).

Comment: Intrarenal pressure has long been known to be a factor in urosepsis following ureterorenoscopy. Defining the pressures has been possible in the study setting but not commercially available. Irrigation regulating systems are also available but again lacked the pressure-reading capabilities. What this paper demonstrated is that pressures do vary and can become extremely high during a case. However, indeed other factors such as ureteroscope size, use of an access sheath, stone burden as well as length of procedure and visualisation will always come into play. What can be concluded is that it may be feasible to measure pressures with warning alarms to temper enthusiasm for more irrigation. Will it translate into better outcomes? Much more work is required and again costs vs. outcomes studies will be required.

Abstract A0786

Erectile and ejaculatory function after Rezūm water vapour thermal therapy at 12- and 24-months follow-up

Speaker: Dr Dean Elterman (Toronto, Canada)

Summary: The change in sexual function and bother score (MSHQ), and erectile function (IIEF) from baseline to 12 and 24 months were assessed in men who underwent outpatient Rezūm water vapour thermal therapy for benign prostatic hyperplasia. Men who had a baseline MSHQ bother score ≥3 (indicating they were moderately bothered) experienced a greater decline in 12-month MSHQ ($p<0.001$) and 24-month MSHQ ($p<0.001$) than those who scored <3. Men who had a baseline MSHQ function score ≥9 also experienced a greater decline in 12-month MSHQ ($p=0.002$) and 24-month MSHQ ($p=0.009$). Compared to men with baseline IIEF function <54, those with baseline IIEF function ≥54 experienced a greater decline in 12-month IIEF ($p<0.001$) and 24-month IIEF (mean difference -7.94), however this did not reach statistical significance ($p=0.07$).

Comment: Benign prostatic hyperplasia treatment is generally all-in or medication. Less morbid and more minimally invasive treatments have come and gone over the years. More importantly, the portfolio of options does need alternatives to medication that can be done quickly, and efficiently, with efficacy and few side effects. Men in general do not like taking medications and medications have side-effects. Many minimally invasive treatments have come and gone by not being able to deliver on these aspects. Will steam treatment buck the trend? These data out of Toronto suggest that at least ten important sexual side effects may be kept in check, particularly around erectile dysfunction and ejaculation. This is important for counselling and indeed offering alternatives to alpha blockers. As the data matures, conversations may be had: Do you want a tablet for 5-10 years, or a minimally invasive treatment instead? The trials are underway and hopefully this will become a real question with a reasonable answer.

Abstract A0002

Proteomic profiling of muscle invasive bladder cancer treated with neoadjuvant chemotherapy

Speaker: Mr Moritz Johannes Reike (Vancouver, Canada)

Summary: These researchers attempted to identify markers of response to chemotherapy in the proteome of patients with MIBC treated with neoadjuvant chemotherapy (NAC) followed by radical cystectomy. A total of 107 eligible patients provided pre-NAC tissue specimens, in which residual tumour was present in 62%. Across all samples, 9769 unique samples were evaluated, revealing 4 clusters (confirmed by immunohistochemistry), with unique biology and survival outcomes, but comparable responses by pathologic stage: Cluster 1 (luminal profile; high metabolic activity), cluster 2 (high nuclear processes activity), cluster 3 (basal characteristics; high immune infiltration) and cluster 4 (stromal signature; high immune infiltration). Cluster 3 was associated with poorer survival outcomes ($p<0.01$). In pre-NAC tissue, MAPK9 and MTIF3 were identified as novel favourable markers, while DVL2 and NES were identified as unfavourable. Markers for NAC resistance included AZGP1 and ORM1. In resistant tumours from post-NAC samples, two clusters were detected: post-NAC cluster 1 had worse outcomes with enrichment for nuclear processes, however post-NAC cluster 2 showed enrichment for immune pathways. Chemoresistance mechanisms were suggested by clonal heterogeneity in pre- and post-NAC matched tumours.

Comment: Liquid biopsy has been a fashionable term for a few years, but little tangible progress has been made. Bladder cancer is an ideal one for such an analysis, particularly if it could be done via urine in the future. Serum still seems to be the go-to and this study described four pre-NAC and two post-NAC proteomic clusters with distinct biology and survival outcomes, alongside novel prognostic biomarkers. The future work for this research will include the validation of these clusters by immunohistochemistry in larger independent MIBC cohorts. A non-NAC cohort using pre-NAC tissue will be used to confirm the prognostic vs. predictive relevance of these findings. Ideally, a combination of both tissue analysis and liquid biopsy analysis would be available. Then, it may be possible to profile the different genomics, transcriptomics, proteomics and metabolomics layers to generate models that broaden our understanding of disease development, but also make us more capable in identifying novel biomarkers. This study appears an important addition to understanding the complexity of MIBC.

Abstract A1163

Similar artefact susceptibility for water- and air-filled urodynamic systems

Speaker: Mrs Madlen Marie Elisabeth Kasten (Zurich, Switzerland)

Summary: This non-inferiority RCT compared pressure measurements between patients randomly assigned to urodynamic investigation via a water-filled system (WFS; n=244) or an air-filled system (AFS; n=246). Artefact susceptibility was the primary endpoint, evaluated by a modified Bristol UTraQ quality scoring system (0-18, higher scores indicative of better quality). Overall, the WFS and AFS had median quality scores of 14.5 and 15.5, respectively. AFS was found to be non-inferior to WFS according to the pre-specified non-inferiority margin of -2 ($p<0.001$). Common artefacts in the WFS and AFS groups included repeated rectal contractions (57% vs. 68%; $p=0.015$), poor pressure during empty bladder cough test (38% vs. 4%; $p<0.001$) and detrusor resting pressure outside of the physiological range when bladder was empty (16% vs. 42%; $p<0.001$). At the commencement of urodynamic investigation, AFS provided higher overall resting pressures. The time for urodynamic investigation was comparable between groups ($p=0.913$), as were rates of AEs ($p>0.18$), however a significantly higher proportion of patients reported pain following AFS ($p=0.014$).

Comment: Water or air? This has been debated in urodynamic circles for years. The research results demonstrated that air-filled systems are non-inferior to water-filled systems regarding overall quality of urodynamic traces. However, both measurement systems have particular pitfalls that need to be known for problem solving during urodynamic investigation and require awareness for accurate interpretation of urodynamic studies. Certainly, both air and water measurement systems have been recognised to have limitations. Ultimately, it is pattern recognition and interpretation that are more relevant in the definition of the disease of the patient. What this study indicates is that air or water, it likely doesn't matter. We have contrasting and conflicting evidence in the literature about the prognostic role of this test concerning different voiding dysfunction. Now we need to move forward to perhaps use AI to help interpret the more difficult studies, and relate them to outcomes.

Abstract A0693