New CAIRIBU GU Basic Science, Clinical/Translational, and Population Health Research Jan. 2023

BLADDER

Bladder Mucosal Cystitis Cystica
Lesions are Tertiary Lymphoid
Tissues that Correlate with Recurrent
UTI Frequency in Postmenopausal
Women

Ligon MM, Liang B, Lenger SM, Parameswaran P, Sutcliffe S, Lowder JL, Mysorekar IU

A retrospective, observational cohort of women with rUTIs that underwent cystoscopy (n=138) from 2015 to 2018 were identified using electronic medical records. CC status was abstracted from cystoscopy reports and correlations were identified by logistic regression. UTI-free survival time associated with CC was evaluated by Cox proportional hazards regression. Exact logistic regression was used to identify factors associated with changes to CC lesions on repeat cystoscopy. Biopsies of CC lesions were examined by routine histology and immunofluorescence. 53 patients (38%) had CC on cystoscopy. CC was associated with postmenopausal status (odds ratio [OR] [95% confidence interval [CI]]: 5.53 [1.39-37.21]), pelvic floor myofascial pain (PFMP; 6.82 [1.78-45.04]), having ≥4 UTIs in the past year (2.28 [1.04-5.09]), and a shorter time to next UTI (hazard ratio: 1.54 [1.01-2.35]). 42 patients (82%) demonstrated improvement resolution of lesions. 10/11 (91%) biopsied CC lesions were tertiary lymphoid tissue with germinal centers and resembled follicular cystitis (FC). The conclusion showed CC lesions were associated with postmenopausal status, PFMP, and number of UTIs in the prior year and predicted worse rUTI outcomes. CC lesions are tertiary lymphoid tissue/FC that may improve or resolve over time with treatment. Identifying CC in rUTI patients may be useful in informing future UTI risk and tailoring appropriate treatment strategies.

Collaborating for the advancement of interdisciplinary research in benign urology (CAIRIBU): outcomes, effectiveness, and future directions of annual CAIRIBU meetings

Penniston KL, Allmaras JM

The 5th annual CAIRIBU Meeting (CAIRIBU = Collaborating for the Advancement of Interdisciplinary Research in Benign Urology) was held November 29-December 2, 2022 in Bethesda, MD and organized by the CAIRIBU (U24) Interactions Core. Altogether, nearly 100 individuals participated, representing U54 Urology OBrien Centers, P20 Urology Centers, and K12 Urology Career Development Programs currently and previously funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Several NIDDK Program Officers participated in the meeting, including those representing the NIDDK Central Repository and several urologic research consortia. The science presented during scientific and poster sessions represented the various areas of research among CAIRIBU and CAIRIBU-affiliated investigators. They included non-malignant prostate and lower urinary tract dysfunction; urinary tract microbes and infection; bladder function and physiology; neurourology in the lower urinary tract; and obstructions and calculi in the urinary tract. A primary objective of the CAIRIBU Interactions Core is to develop metrics for evaluating collaborative research initiatives. This requires understanding engagement within the CAIRIBU Community and whether it leads to cross-disciplinary interactions and collaborative research products and resources. The annual CAIRIBU meeting is one window through which the outcomes and direction of the CAIRIBU Community may be observed.

Compound 48/80 increases murine bladder wall compliance independent of mast cells

Saxena P, Broemer E, Herrera GM, Mingin GC, Roccabianca S, Tykocki NR

A balance between stiffness and compliance is essential to normal bladder function, and changes in the mechanical properties of the bladder wall occur in many bladder pathologies. These changes are often associated with the release of basic secretagogues that in turn drive the release of inflammatory mediators from mast cells. Mast cell

degranulation by basic secretagogues is thought to occur by activating an orphan receptor, Mas-related G protein-coupled receptor B2 (Mrgprb2). We explored the effects of the putative mast cell degranulator and Mrgprb2 agonist Compound 48/80 on urinary bladder wall mechanical compliance, smooth muscle contractility, and urodynamics, and if these effects were mast cell dependent. In wild-type mice, Mrgprb2 receptor mRNA was expressed in both the urothelium and smooth muscle layers. Intravesical instillation of Compound 48/80 decreased intermicturition interval and void volume, indicative of bladder overactivity. Compound 48/80 also increased bladder compliance while simultaneously increasing the amplitude and leading slope of transient pressure events during ex vivo filling and these effects were inhibited by the Mrgprb2 antagonist QWF. Surprisingly, all effects of Compound 48/80 persisted in mast cell-deficient mice, suggesting these effects were independent of mast cells. These findings suggest that Compound 48/80 degrades extracellular matrix and increases urinary bladder smooth muscle excitability through activation of Mrgprb2 receptors located outside of mast cells. Thus, the pharmacology and physiology of Mrgprb2 in the urinary bladder is of potential interest and importance in terms of treating lower urinary tract dysfunction.

<u>Current research and future</u> <u>directions in non-malignant urologic</u> <u>research - proceedings of the annual</u> <u>CAIRIBU meeting</u>

Popovics P, Penniston KL

The Annual Collaborating for the Advancement of Interdisciplinary Research (CAIRIBU) Meeting in 2022 highlighted basic, translational, and clinical non-malignant urology research within five main areas affecting the urinary tract: urinary dysfunction due to prostate disease, microbes and infection, bladder function and physiology, neurology and neuromuscular influences and calculi and obstruction. In this paper, we summarize main findings and future

directions outlined by CAIRIBU-affiliated scientists who presented as part of the scientificsessions.

Strategies for Difficult Fluoroscopic Landmarking During Neuromodulation Lead Placement Luchristt D, Amundsen C

Fluoroscopic guidance is a key tool used

in combination with sensory and motor testing to ensure optimal sacral neuromodulation lead placement. The objectives of this video are to briefly review bony landmarks for fluoroscopic imaging and provide strategies to overcome common obstacles during fluoroscopic mapping for sacral neuromodulation lead placement. We provide an overview of normal fluoroscopic landmarks for both AP and lateral fluoroscopic i maging during sacral neuromodulation lead placement, along with a series of 6 non-ideal examples. Strategies for overcoming barriers to identification of bony anatomy on fluoroscopy are provided in the context of these examples. While appropriate patient preparation and positioning are important to optimize fluoroscopic guidance during sacral neuromodulation lead placement, patient anatomy and other factors often obscure or distort expected anatomic landmarks. We approach demonstrate our overcoming common fluoroscopic obstacles and provide strategies for improvement of operative efficiency. These strategies can be combined with other intra operative information such as tactile feedback, additional fluoroscopic views, and intraoperative complex nerve mapping to help optimize sacral neuromodulation lead placement and improve operative efficiency.

KIDNEY

Serum myo-inositol and valine metabolomic-based improve estimated glomerular filtration rate among kidney transplant recipients Meeusen JW, Stämmler F, Dasari S, Schiffer E, Lieske JC

Close monitoring of glomerular filtration rate (GFR) is essential for the management of patients post kidney transplantation. Measured GFR (mGFR), the gold standard, is not readily accessible in most centers. Furthermore. the performance of new estimated GFR (eGFR) equations based upon creatinine and/or cystatin C have not been validated in kidney transplant patients. Here we evaluate a recently published eGFR equation using cystatin C, creatinine, myo-inositol and valine as measured by nuclear magnetic resonance (eGFRNMR). Residual sera was obtained from a cohort of patients with clinically ordered iothalamate renal clearance mGFR (n = 602). Kidney transplant recipients accounted for 220 (37%) of participants. The 2021 CKD-EPI eGFRcr and eGFRcr-cys have similar bias, P15, and agreement while eGFRNMR more closely matched mGFR with the strongest improvement among kidney transplant recipients.

PROSTATE

White's operation: the history of 19th century attempts to treat prostate disease with castration

Nicholson TM, Best SL, Ricke EA, Timms BG, Ricke

To understand the roots of 19th century hormonal treatments for BPH in the career of J. William White, a prominent surgeon scientist at the University of Pennsylvania. We reviewed primary and secondary literature available in PUBMED, the University of Pennsylvania Archives, and internet resources. In 1893, Dr. White presented a series of experiments demonstrating atrophy of the canine prostate following castration and advocated for this procedure in men suffering from prostatic hypertrophy. This approach was adopted by many of White's contemporaries. In 1895, White presented findings from 111 patients and reported improvement of urinary symptoms in three quarters of these patients. Improvements in surgical techniques for prostatectomy have predominantly eliminated castration as a clinical procedure for BPH treatment. These early experiments demonstrated the critical dependence of the prostate on testicular androgens and were the basis for subsequent hormonal therapies for BPH. In conclusion, the bold

experiments of late 19th century surgeons paved the way for our contemporary understanding of the important role of sex steroid hormones in BPH.

STONES

Pulse-modulated Holmium:YAG Laser vs the Thulium Fiber Laser for Renal and Ureteral Stones: A Singlecenter Prospective Randomized Clinical Trial

Haas CR. Knoedler MA. Li S. Gralnek DR. Best SL Penniston KL, Nakada SY

We sought to compare the clinical effectiveness of the pulse-modulated (holmium:yttrium-aluminumgarnet) laser and the thulium laser fiber for ureteroscopic stone management in a randomized clinical trial. The primary outcome was the ureteroscope time required to adequately fragment stones to 1 mm or less. Secondary outcomes were stone-free rate, complications, subjective surgeon measurement of laser performance, patient related stone quality of life outcomes, measurements of laser efficiency. An Institutional Review Board-approved randomized clinical trial was conducted to randomize patients to outpatient treatment with either the Moses 2.0 or thulium laser fiber in a 1:1 manner after stratification into groups based on the maximal diameter of treated stone (3-9.9 mm or 10-20 mm). Patient, stone, and operative parameters were compared using the appropriate categorical/continuous and parametric/nonparametric statistical tests (SPSS 25). This randomized clinical trial suggests no significant clinical advantage of one laser technology over the other. Surgeon and institutional preference are the best approach when selecting one or the other.

Risk Factors for Increased Stent-Associated Symptoms Following Ureteroscopy for Urinary Stones: Results from STENTS

Harper JD, Desai AC, Maalouf NM, Yang H, Antonelli JA, Tasian GE, Lai HH, Reese PP, Curatolo M, Kirkali Z, Al-Khalidi HR, Wessells H, Scales CD The STudy to Enhance uNderstanding of sTent-associated Symptoms (STENTS) sought to identify risk factors for pain and urinary symptoms, as well as how these symptoms interfere with daily activities after ureteroscopy for stone treatment. This prospective observational cohort study enrolled patients aged ≥12 years undergoing ureteroscopy with ureteral stent for stone treatment at 4 clinical centers. Participants reported symptoms at baseline; on postoperative days (POD) 1, 3, 5; at stent removal; and day 30 poststent removal. Outcomes of pain intensity, pain interference, urinary symptoms, and bother were captured with multiple instruments. Multivariable analyses using mixed-effects linear regression models were identified characteristics associated with increased stent-associated symptoms (SAS). In this multicenter cohort, interference persisted even as pain intensity decreased. Patient factors (e.g., age, depression) rather than surgical factors were associated with symptom intensity. These findings provide a foundation for patient-centered care and highlight potential targets for efforts to mitigate the burden of SAS.

whether reducing flare frequency even without reducing mean pain intensity may be important to patients). We used screening visit and weekly run-in period data from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Symptom Patterns Study to investigate associations between flare frequency and multiple measures of illness impact and health care seeking activity, independent of typical nonflare and overall pelvic pain levels. Our findings suggest that flare frequency and possibly other flare characteristics may be worth considering as additional outcome measures in urological chronic pelvic pain syndrome research to support the development of new preventive and therapeutic flare strategies.

PATIENT-CENTERED RESEARCH

Associations Between Urological Chronic Pelvic Pain Syndrome
Symptom Flares, Illness Impact, and Health Care Seeking Activity: Findings
From the Multidisciplinary Approach to the Study of Chronic Pelvic Pain
Symptom Patterns Study

Sutcliffe S, Newcomb C, Bradley CS, **Clemens JQ**, Erickson B, Gupta P, **Lai HH**, Naliboff B, Strachan E, Stephens-Shields A

studies interstitial Most on cystitis/bladder pain syndrome and chronic prostatitis/chronic pelvic pain syndrome use typical or average levels of pelvic pain or urological symptom intensity as their outcome, as both are associated with reduced quality of life. Symptom exacerbations or "flares" have also been found to be associated with reduced quality of life, but no studies, to our knowledge, have investigated whether these associations are independent of typical pelvic pain levels and thus might be useful additional outcome measures (or stated differently,

- Jennifer Allmaras MPH, Muen Wang, 1/30/2023

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