

BLADDER

[Foundational science and mechanistic insights for a shared disease model: an expert consensus: Developed by the AUGS Basic Science Subcommittee and IUGA Special Interest Group](#)

Alperin M, Abramowitch S, Alarab M, Bortolini M, Brown B, Burnett LA, Connell KA, Damaser M, de Vita R, Gargett CE, Guess MK, Guler Z, Jorge RN, Kelley RS, Kibschull M, Miller K, Moalli PA, Mysorekar IU, Routzong MR, Shynlova O, Swenson CW, Therriault MA, Northington GM

Pelvic floor disorders (PFDs) are complex conditions that impact millions of women worldwide. It is estimated that PFDs will affect approximately 30%–50% of women older than 50 years and incur a 20% lifetime risk of undergoing at least 1 surgical procedure to repair either pelvic organ prolapse (POP) or stress urinary incontinence (SUI) by age 80 years [1]. The surgical costs alone are estimated to exceed \$10 billion annually [1,2,3,4,5,6], and this does not account for the cost of nonsurgical and conservative treatments. Although a large body of epidemiological literature provides important information regarding the risk factors for PFDs, the pathogenesis of POP and SUI continues to be poorly understood. Consequently, POP and SUI are associated with significant health care expenditure primarily due to lack of preventive measures, high failure rate of available interventions, and the need for retreatments. The overarching goal of the e-book is to synthesize and interpret the available mechanistic data and to build a shared disease model of 2 PFDs—POP and SUI—that will serve to (1) further our understanding of the pathogenesis of these PFDs, (2) recognize important knowledge gaps and pinpoint research priorities, (3) identify novel targets for interventions, and (4) facilitate economically viable cross-disciplinary research initiatives.

[Subtyping of common complex diseases and disorders by integrating heterogeneous data. Identifying clusters among women with lower urinary tract symptoms in the LURN study](#)

Andreev VP, Helmuth ME, Liu G, Smith AR, Merion RM, Yang CC, Cameron AP, Jelovsek JE, Amundsen CL, Helfand BT, Bradley CS, DeLancey JOL, Griffith JW, Glaser AP, Gillespie BW, Clemens JQ, Lai HH

We present a methodology for subtyping of persons with a common clinical symptom complex by integrating heterogeneous continuous and categorical data. We illustrate it by clustering women with lower urinary tract symptoms (LUTS), who represent a heterogeneous cohort with overlapping symptoms and multifactorial etiology. Data collected in the Symptoms of Lower Urinary Tract Dysfunction Research Network (LURN), a multi-center observational study, included self-reported urinary and non-urinary symptoms, bladder diaries, and physical examination data for 545 women. Heterogeneity in these multidimensional data required thorough and non-trivial preprocessing, including scaling by controls and weighting to mitigate data redundancy, while the various data types (continuous and categorical) required novel methodology using a weighted Tanimoto indices approach. Five clusters of women with LUTS were identified using the developed methodology. None of the clusters could be characterized by a single symptom, but rather by a distinct combination of symptoms with various levels of severity. Targeted proteomics of serum samples demonstrated that differentially abundant proteins and affected pathways are different across the clusters. The clinical relevance of the identified clusters is discussed and compared with the current conventional approaches to the evaluation of LUTS patients. The rationale and thought process are described for the selection of procedures for data preprocessing, clustering, and cluster evaluation.

PROSTATE

[PSA density is associated with BPH cellular composition](#)

Jia L, Strand DW, Goueli RS, Gahan JC, Roehrborn CG, Mauck RJ

Current AUA guidelines recommend 5 alpha reductase inhibitor (5ARI) treatment for patients with obstructive benign prostatic hyperplasia (BPH) that display prostate volume ≥ 30 cc and total prostate specific antigen (PSA) ≥ 1.5 ng/ml. However, BPH is highly pleomorphic and response to 5ARIs is highly variable. An understanding of cellular composition based on a noninvasive PSA density test could lead to improved clinical decision making. The histological composition of 307 BPH specimens was scored by a pathologist for stromo-glandular content and associated with total PSA, prostate volume, PSA density and other clinical variables using univariate and multivariate linear regression. The percentage of glandular composition in prostates of 5ARI-naïve men was positively and independently associated with PSA and PSA density. It was determined through statistical modeling that a PSA density ≤ 0.05 ng/ml² associated with a glandular composition of $\leq 30\%$ with 76% sensitivity. The conclusion shows that PSA density could provide a decisive variable for estimating BPH cellular content and may eventually improve selection of patients for 5ARI treatment. Further work is needed to demonstrate that patients with higher glandular content are more responsive to 5ARI treatment.

STONES

[The duration of stone disease and the impact of a stone event on patients' quality of life](#)

Raizenne B, Deyirmendjian C, Bechis SK, Sur RL, Nakada SY, Antonelli JA, Streeper N, Sivalingam S, Viprakasit D, Averch TD, Landman J, Chi T, Pais VM Jr, Chew BH, Bird V, Andonian S, Canvasser NE, Harper JD, Penniston KL, Bhojani N.

With a 5-year stone recurrence rate of 30-50%, kidney stone formers are subject to significant morbidity which negatively impacts their Health Related

Quality of Life (HRQOL). We sought to determine the impact of age of kidney stone onset, duration of stone disease, and kidney stone event (surgery or stone passage) on patients' individual HRQOL by querying the validated and prospectively collected Wisconsin Stone Quality of Life (WISQOL) database. Cross-sectional data were obtained from a total of 2,438 kidney stone formers from 14 institutions in North America who completed the WISQOL questionnaire from 2014 to 2019. The 28-question survey has a 1-5 point scale for each item (total score range 0-140). Multivariable linear regression models assessed the impact of age of kidney stone onset, duration of stone disease and time since most recent surgery or stone passage on HRQOL. Our study demonstrates that older age of onset, longer duration of disease, increase time from most recent surgery or stone passage were independent predictors of better HRQOL in kidney stone formers. Results of future studies that focus on optimizing stone related modifiable risk factors to decrease the amount of recurrent stone episodes and thus the need for recurrent surgeries will be essential.

history of kidney stones, whereas beverages, fruits and vegetables contributed net alkali.

-Jennifer Allmaras, MPH and Muen Wang 7/5/2022

Email cairibu@urology.wisc.edu to feature your newly published research in next month's communique

[Primary Contributors to Dietary Acid Load in Patients with Urolithiasis](#)

Betz MV, Penniston KL

In susceptible individuals, high dietary acid load may contribute to the formation of certain types of kidney stones via lowering urine pH and citrate excretion. The objective of this study was to determine the contribution of dietary acid from food groups in people with urolithiasis. Patients with calcium urolithiasis (n=83) who completed food records were used for this retrospective analysis. Descriptive statistics were calculated for nutrients, Potential Renal Acid Load (PRAL) and estimated Net Endogenous Acid Production (NEAPest). Pearson's correlations were calculated between PRAL and NEAPest with each nutrient. For individuals with urolithiasis promoted by acidic urine and/or low urine citrate, dietary patterns with a high dietary acid load may contribute to recurrence risk. Meat and grains were the major contributors to dietary acid load in this cohort of patients with a