BLADDER

The Urinary Microbiome in Postmenopausal Women with Recurrent Urinary Tract Infections

Monique H Vaughan, Jialiang Mao, Lisa A Karstens, Li Ma, **Cindy L Amundsen**, Kenneth E Schmader, **Nazema Y Siddiqui**

The etiology of postmenopausal recurrent urinary tract infection (UTI) is not completely known, but the urinary microbiome is thought to be implicated. We compared the urinary microbiome in menopausal women with recurrent UTIs to age-matched controls, both in the absence of acute infection. This study preformed a cross-sectional analysis of baseline data from 64 women enrolled in a longitudinal cohort study. All women were using topically applied vaginal estrogen. Women >55 years of age from the following groups were enrolled: 1) recurrent UTIs on daily antibiotic prophylaxis, 2) recurrent UTIs not on antibiotic prophylaxis and 3) age-matched controls without recurrent UTIs. Catheterized urine samples were collected at least 4 weeks after last treatment for UTI and at least 6 weeks after initiation of vaginal estrogen. Samples were evaluated using expanded quantitative urine culture (EQUC) and 16S rRNA gene sequencing. With EQUC, there were no significant differences in median numbers of microbial species isolated among groups (p=0.96), even when considering Lactobacilli (p=0.72). However, there were trends toward different Lactobacillus species between groups. With 16S rRNA sequencing, the majority of urine samples contained Lactobacilli, with nonsignificant trends in relative abundance of Lactobacilli among groups. Using a Bayesian analysis, we identified significant differences in anaerobic taxa associated with phenotypic groups. Most of these differences centered on Bacteroidales and the family Prevotellaceae, although differences were also noted in Actinobacteria and certain genera of Clostridiales. Associations between anaerobes within the urinary microbiome and postmenopausal recurrent UTI warrants further investigation.

Associations between urinary 3-indoxyl sulfate, a gut microbiome-derived biomarker, and patient outcomes after intensive care unit admission

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3-indoxyl sulfate (3-IS) is an indole metabolism byproduct produced by commensal gut bacteria and excreted in the urine; low urinary 3-IS has been associated with increased mortality in bone marrow transplant recipients. This study investigated urinary 3-IS and patient outcomes in the ICU. Prospective study that collected urine samples, rectal swabs, and clinical data on 78 adult ICU patients at admission and again 72 h later. Urine was analyzed for 3-IS by mass spectrometry. Median urinary 3-IS levels were 17.1 µmol/mmol creatinine (IQR 9.5 to 26.2) at admission and 15.6 (IQR 4.2 to 30.7) 72 h later. 22% of patients had low 3-IS (≤6.9 µmol/mmol) on ICU admission and 28% after 72 h. Low 3-IS at 72 h was associated with fewer ICU-free days (22.5 low versus 26 high, p = 0.03) and with death during one year of follow-up (36% low versus 9% high 3-IS, p < 0.01); there was no detectable difference in 30-day mortality (18% low versus 5% high, p = 0.07). Low urinary 3-IS level 72 h after ICU admission was associated with fewer ICU-free days and with increased one-year but not 30-day mortality. Further studies should investigate urinary 3-IS as an ICU biomarker.

Efficacy of vibegron, a novel β3-adrenoreceptor agonist, for lower urinary tract dysfunction in mice with spinal cord injury

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The study aim was to investigate the effect of vibegron, a new clinically approved β3-adrenoceptor agonist in lower urinary tract dysfunction in mice with spinal cord injury. Investigators performed cystometry under awake conditions in 4-week spinal cord injury female mice. Two weeks after spinal cord injury, saline or vibegron (30 mg/kg) was orally administered for 2 weeks prior to the urodynamic study. Investigators removed L6-S1 dorsal root ganglia from the saline- or vibegron-treated spinal cord injury mice as well as from saline-treated normal (spinal intact) mice to evaluate the levels of transient receptor potential cation channel subfamily V member 1, transient receptor potential cation channel subfamily A member 1, activating transcription factor 3, and inducible nitric oxide synthase transcripts using real-time polymerase chain reaction. Vibegron improves spinal cord injury-induced detrusor overactivity in addition to significantly reducing C-fiber afferent receptors such as transient receptor potential cation channel subfamily V member 1, transient receptor potential cation channel subfamily A member 1, and inflammatory cytokines/markers, such as activating transcription factor 3 and inducible nitric oxide synthase, in spinal cord injury mice. Thus, vibegron might be effective in the treatment of storage lower urinary tract dysfunction induced by C-fiber afferent activation after spinal cord injury.

Current Understanding and Future Perspectives of Interstitial Cystitis/Bladder Pain Syndrome

Tomohiro Ueda, Philip M Hanno, Ryoichi Saito, Jane M Meijlink, **Naoki Yoshimura**

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic disease characterized by suprapubic pain and lower urinary tract symptoms. Clinical trials in all-inclusive populations of IC/BPS patients without phenotyping in the last decade have mainly failed to discover new therapeutic modalities of IC/BPS. Thus, phenotyping IC/BPS, aimed at identifying bladder-centric and/or bladder-beyond pathologies, including cystoscopic observation of Hunner or non-Hunner lesions of the bladder mucosa, is particularly important for the future of IC/BPS management. Based on recent discussions at international conferences, including the International Consultation on IC, Japan, it has been proposed that Hunner-lesion IC should be separated from other non-Hunner IC/BPS because of its distinct inflammatory profiles and epithelial

denudation compared with non-Hunner IC/BPS. However, there are still no standard criteria for the diagnosis of Hunner lesions other than typical lesions, while conventional cystoscopic observations may miss atypical or small Hunner lesions. Furthermore, diagnosis of the bladder-centric phenotype of IC/BPS requires confirmation that identified mucosal lesions are truly a cause of bladder pain in IC/BPS patients. This review article discusses the current status of IC/BPS pathophysiology and diagnosis, as well as future directions of the proper diagnosis of bladder-centric IC/BPS, in which pathophysiological mechanisms other than those in inflammatory pathways, such as angiogenic and immunogenic abnormalities, could also be involved in both Hunner-lesion IC and non-Hunner IC/BPS. It is hoped that this new paradigm in the pathophysiological evaluation and diagnosis of IC/BPS could lead to pathology-based phenotyping and new treatments for this heterogeneous disease.

Antifibrosis treatment by inhibition of VEGF, FGF, and PDGF receptors improves bladder wall remodeling and detrusor overactivity in association with modulation of C-fiber afferent activity in mice with spinal cord injury

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Spinal cord injury (SCI) above the sacral level causes bladder dysfunction and remodeling with fibrosis. This study examined the antifibrotic effects using nintedanib, an inhibitor of vascular endothelial growth factor, fibroblast growth factor, and platelet-derived growth factor receptors, on detrusor overactivity (DO) and bladder fibrosis, as well as the modulation mechanisms of C-fiber afferent pathways. Thirty female C57BL/6 mice were divided into group A (spinal intact), group B (SCI with vehicle), and group C (SCI with nintedanib). At 2 weeks after SCI, vehicle or 50 mg/kg nintedanib was administered subcutaneously for 2 weeks. Then, cystometry was conducted, followed by RT-PCR measurements of fibrosis-related molecules, muscarinic, β-adrenergic, TRP and purinergic receptors in the bladder or L6-S1 dorsal root ganglia (DRG). Trichrome stain and Western blot analysis of transforming growth factor-beta and fibronectin were performed in the bladder. TRPV1 expression in L6 DRG was measured by immunohistochemistry. In cystometry, intercontraction intervals, nonvoiding contractions, voided volume, and voiding efficiency were significantly improved in group C versus group B. RT-PCR, Western blotting, and trichrome staining revealed the fibrotic changes in the bladder of group B, which was improved in group C. Increased messenger RNA levels of TRPV1, TRPA1, P2X2, and P2X3 in DRG of group B were significantly decreased in group C. TRPV1 immunoreactivity in DRG was increased in group B, but decreased in group C.

Time-dependent progression of neurogenic lower urinary tract dysfunction after spinal cord injury in the mouse model

Tetsuichi Saito, Daisuke Gotoh, Naoki Wada, **Pradeep Tyagi**, Tomonori Minagawa, Teruyuki Ogawa, Osamu Ishizuka, **Naoki Yoshimura**

This study evaluated the time-course changes in bladder and external urinary sphincter (EUS) activity and the expression of mechanosensitive channels in lumbosacral dorsal root ganglia (DRG) after spinal cord injury (SCI). Female C57BL/6N mice in the SCI group underwent transection of the Th8/9 spinal cord. Spinal intact mice and SCI mice at 2, 4, and 6 wk post-SCI were evaluated by single-filling cystometry and EUS-electromyography (EMG). In another set of mice, the bladder and L6-S1 DRG were harvested for protein and mRNA analyses. In SCI mice, nonvoiding contractions were confirmed at 2 wk post-SCI and did not increase over time to 6 wk. In 2-wk SCI mice, EUS-EMG measurements revealed detrusor sphincter dyssynergia, but periodic EMG reductions during bladder contraction were hardly observed. At 4 wk, SCI mice showed increases of EMG activity reduction time with increased voiding efficiency. At 6 wk, SCI mice exhibited a further increase in EMG reduction time. RT-PCR of L6-S1 DRG showed increased mRNA levels of transient receptor potential vanilloid 1 and acid-sensing ion channels (ASIC1-ASIC3) in SCI mice with a decrease of ASIC2 and ASIC3 at 6 wk compared with 4 wk, whereas Piezo2 showed a slow increase at 6 wk. Protein assay showed SCI-induced overexpression of bladder brain-derived neurotrophic factor with a time-dependent decrease post-SCI. These results indicate that detrusor overactivity is established in the early phase, whereas detrusor sphincter dyssynergia is completed later at 4 wk with an improvement at 6 wk post-SCI, and that mechanosensitive channels may be involved in the time-dependent changes. This is the first paper to evaluate the time-course changes of bladder dysfunction associated with mechanosensitive channels in a mouse model.

Adult female urinary incontinence guidelines: a systematic review of evaluation guidelines across clinical specialties

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The study's aim was to systematically review evaluation guidelines of uncomplicated urinary incontinence (UI) in community-dwelling adult women to assess guidance available to the full range of providers treating UI. Systematic literature search of eight bibliographic databases were performed. We included UI evaluation guidelines written for medical providers in English after January 1, 2008. Exclusion criteria included guidelines for children, men, institutionalized women, peripartum- and neurologic-related UI. A quantitative scoring system included assessed components and associated recommendation level and clarity. UI evaluation guidelines varied in level of comprehensiveness, detail, and clarity. This variability may lead to inconsistent evaluations in the work-up of UI, contributing to missed opportunities for individualized care.

KIDNEY

Familial Aggregation of CKD: Gene or Environment?

Lucrezia Carlassara, Francesca Zanoni, **Ali G. Gharav**

Nephrologists often see patients who have a family history of chronic kidney disease (CKD), but the clinical utility of this information is not always clear. Alongside comorbid conditions (such as diabetes, hypertension, and hypercholesterolemia) and constitutive parameters (such as age, ethnicity, and sex), a positive family history of CKD has gained greater attention as a major risk factor for CKD and is predictive of a positive genetic diagnosis. In recent years, nephrologists also increasingly use genetic testing in medical care, and patients frequently inquire about genetic kidney disease and the risk of disease transmission to their offspring. The identification of genetic risk factors for CKD has the potential to improve early detection and also increase our understanding of the pathogenesis of disease. However, several questions remain unanswered, such as, what is the magnitude of risk imparted by a positive family history of CKD? To what extent can family history of CKD be explained by shared genetic factors versus environmental triggers? How can we best use the family history information to improve risk stratification of CKD and its sequelae?

Iron deficiency exacerbates cisplatin- or rhabdomyolysis-induced acute kidney injury through promoting iron-catalyzed oxidative damage

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Iron deficiency is the most common micronutrient deficiency worldwide. While iron deficiency is known to suppress embryonic organogenesis, its effect on the adult organ in the context of clinically relevant damage has not been considered. Here we report that iron deficiency is a risk factor for nephrotoxic intrinsic acute kidney injury of the nephron (iAKI). Iron deficiency exacerbated cisplatin-induced iAKI by markedly increasing non-heme catalytic iron and Nox4 protein which together catalyze production of hydroxyl radicals followed by protein and DNA oxidation, apoptosis and ferroptosis. Crosstalk between non-heme catalytic iron/Nox4 and downstream oxidative damage generated a mutual amplification cycle that facilitated rapid progression of cisplatin-induced iAKI. Iron deficiency also exacerbated a second model of iAKI, rhabdomyolysis, via increasing catalytic heme-iron. Heme-iron induced lipid peroxidation and DNA oxidation by interacting with Nox4-independent mechanisms, promoting p53/p21 activity and cellular senescence. Our data suggests that correcting iron deficiency and/or targeting specific catalytic iron species are strategies to mitigate iAKI in a wide range of patients with diverse forms of kidney injury.

Kidney injury biomarkers during exposure to tenofovir-based preexposure prophylaxis

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We previously reported a higher incidence of non-albumin proteinuria and a small but significant decline in estimated glomerular filtration rate (eGFR) among HIV-negative adults randomized to emtricitabine/tenofovir disoproxil fumarate preexposure prophylaxis (FTC/TDF PrEP) versus placebo. In a nested case--control study among participants randomized to FTC/TDF PrEP, established kidney injury biomarkers measured at 12 months were not significantly different between participants who subsequently experienced one of these kidney endpoints and randomly selected controls who did not.

PROSTATE

Single-cell analysis of mouse and human prostate reveals novel fibroblasts with specialized distribution and microenvironment interactions

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Stromal-epithelial interactions are critical to the morphogenesis, differentiation, and homeostasis of the prostate, but the molecular identity and anatomy of discrete stromal cell types is poorly understood. Using single-cell RNA sequencing, we identified and validated the in situ localization of three smooth muscle subtypes (prostate smooth muscle, pericytes, and vascular smooth muscle) and two novel fibroblast subtypes in human prostate. Peri-epithelial fibroblasts (APOD+) wrap around epithelial structures, whereas interstitial fibroblasts (C7+) are interspersed in extracellular matrix. In contrast, the mouse displayed three fibroblast subtypes with distinct proximal-distal and lobe-specific distribution patterns. Statistical analysis of mouse and human fibroblasts showed transcriptional correlation between mouse prostate (C3+) and urethral (Lgr5+) fibroblasts and the human interstitial fibroblast subtype. Both urethral fibroblasts (Lgr5+) and ductal fibroblasts (Wnt2+) in the mouse contribute to a proximal Wnt/Tgfb signaling niche that is absent in human prostate. Instead, human peri-epithelial fibroblasts express secreted WNT inhibitors SFRPs and DKK1, which could serve as a buffer against stromal WNT ligands by creating a localized signaling niche around individual prostate glands. We also identified proximal-distal fibroblast density differences in human prostate that could amplify stromal signaling around proximal prostate ducts. In human benign prostatic hyperplasia, fibroblast subtypes upregulate critical immunoregulatory pathways and show distinct distributions in stromal and glandular phenotypes. A detailed taxonomy of leukocytes in benign prostatic hyperplasia reveals an influx of myeloid dendritic cells, T cells and B cells, resembling a mucosal inflammatory disorder. A receptor-ligand interaction analysis of all cell types revealed a central role for fibroblasts in growth factor, morphogen, and chemokine signaling to endothelia, epithelia, and leukocytes. These data are foundational to the development of new therapeutic targets in benign prostatic hyperplasia.

A neuroanatomical mechanism linking perinatal TCDD exposure to lower urinary tract dysfunction in adulthood

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Benign Prostatic Hyperplasia / Lower Urinary Tract Dysfunction (BPH/LUTD) is a classic disease of aging which affects nearly all men. Symptoms typically present in the fifth or sixth decade and progressively worsen over the remainder of life. Here, we identify a surprising origin of this disease that traces back to the intrauterine environment of the developing male, challenging existing paradigms about when this disease process begins. We delivered a single bolus dose of a widespread environmental contaminant, present in the serum of most Americans (2,3,7,8 tetrachlorodibenzo-p-dioxin, TCDD, 1 µg/kg), and representative of a broader class of environmental contaminants, to pregnant mice and observed an increase in the abundance of a neurotrophic factor, artemin, in the developing mouse prostate. Artemin is required for noradrenergic axon recruitment across multiple tissues and TCDD rapidly increases prostatic noradrenergic axon density in the male fetus. The hyperinnervation does not resolve, but rather persists into adulthood, when it is coupled to autonomic hyperactivity of prostatic smooth muscle and abnormal urinary function, including increased urinary frequency, a bothersome symptom in men. We offer new evidence that prostate neuroanatomical development is malleable and that intrauterine chemical exposures can permanently reprogram prostate neuromuscular function to cause male LUTD in adulthood.

The prostaglandin pathway is activated in patients who fail medical therapy for benign prostatic hyperplasia with lower urinary tract symptoms

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Little is known about how benign prostatic hyperplasia (BPH) develops and why patients respond differently to medical therapy designed to reduce lower urinary tract symptoms (LUTS). Medical therapies for BPH/LUTS are not effective in many patients. The reasons for nonresponse or loss of therapeutic response in the remaining patients over time are unknown. A better understanding of why patients fail to respond to medical therapy may have a major impact on developing new approaches for the medical treatment of BPH/LUTS. Prostaglandins (PG) act on G-protein-coupled receptors (GPCRs), where PGE2 and PGF2 elicit smooth muscle contraction. Therefore, we measured PG levels in the prostate tissue of BPH/LUTS patients to assess the possibility that this signaling pathway might explain the failure of medical therapy in BPH/LUTS patients. All PGs were significantly elevated in TZ tissues from S-BPH patients (n = 36) compared to I-BPH patients (n = 15), regardless of the treatment subgroups. In S-BPH versus I-BPH, mRNA for PG synthetic enzymes COX1 and COX2 were significantly elevated. In addition, mRNA for enzymes that convert the precursor PGH2 to metabolite PGs were variable: PTGIS (which generates PGI2) and PTGDS (PGD2) were significantly elevated; nonsignificant increases were observed for PTGES (PGE2), AKR1C3 (PGF2α), and TBxAS1 (TxA2). Within the I-BPH group, men responding to α-blockers for symptoms of BPH but requiring prostatectomy for PCa did not show elevated levels of COX1, COX2, or PGs. By immunohistochemistry, COX1 was predominantly observed in the prostatic stroma while COX2 was present in scattered luminal cells of isolated prostatic glands in S-BPH. PGE2 and PGF2α induced contraction of bladder smooth muscle in an in vitro assay.

The rising worldwide impact of benign prostatic hyperplasia

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To describe the trend in the impact of lower urinary tract symptoms attributed to benign prostatic hyperplasia (LUTS/BPH) on a global scale using the Global Burden of Disease (GBD) database. Using the GBD database, worldwide data aggregated from registries and health systems from 1990 to 2017 were filtered for LUTS/BPH diagnoses. Calculation of years lived with disability (YLD) were compared with other urological diseases. YLD were calculated by a standardized method using assigned disability weights. The GBD-defined sociodemographic index (SDI) was used to assess impact of LUTS/BPH by global SDI quintile. Lower urinary tract symptoms attributed to benign prostatic hyperplasia exert a rapidly rising human burden far exceeding other urological diseases. As the population ages and men in a lower SDI enjoy increased life expectancy and decreased competing mortalities, a continually accelerating wave of LUTS/BPH can be forecast. These epidemiological trends have serious implications for the future allocation of resources and the global urological workforce.

Cluster analysis of men undergoing surgery for BPH/LUTS reveals prominent roles of both bladder outlet obstruction and diminished bladder contractility

Andrew J Schneider, **Matthew Grimes**, Will Lyon, Amanda Kemper, Sijian Wang, **Wade Bushman**

Lower urinary tract symptoms (LUTS) in aging men are commonly attributed to bladder outlet obstruction from benign prostatic hyperplasia (BPH) but BPH/LUTS often reflects a confluence of many factors. We performed a hierarchical cluster analysis using four objective patient characteristics (age, HTN, DM, and BMI), and five pre-operative urodynamic variables (volume at first uninhibited detrusor contraction, number of uninhibited contractions, Bladder Outlet Obstruction Index (BOOI), Bladder Contractility Index (BCI) and Bladder Power at Qmax) to identify meaningful subgroups within a cohort of 94 men undergoing surgery for

BPH/LUTS. Two meaningful subgroups (clusters) were identified. Significant differences between the two clusters included Prostate Volume (95 vs 53 cc; p-value = 0.001), BOOI (mean 70 vs 49; p-value = 0.001), BCI (mean 129 vs 83; p-value <0.001), Power (689 vs 236; p-value <0.001), Qmax (8.3 vs 4.9 cc/sec; p-value <0.001) and post-void residual (106 vs 250 cc; p-value = 0.001). One cluster is distinguished by larger prostate volume, greater outlet resistance and better bladder contractility. The other is distinguished by smaller prostate volume, lower outlet resistance and worse bladder contractility. Remarkably, the second cluster exhibited greater impairment of urine flow and bladder emptying. Surgery improved flow and emptying for patients in both clusters. These findings reveal important roles for both outlet obstruction and diminished detrusor function in development of diminished urine flow and impaired bladder emptying in patients with BPH/LUTS.

STONES

Should we treat asymptomatic concurrent contralateral renal stones? A longitudinal analysis

Shuang Li, Scott Quarrier, Emily C Serrell, **Kristina L Penniston**, Stephen Y Nakada

The objective is to explore the need for future surgery among patients treated for asymptomatic concurrent contralateral stones versus those that were not. Upon IRB approval, we retrospectively reviewed records of patients who underwent stone surgeries (SWL, URS, PCNL) from 2009 to 2018. Patients were included if they were greater than 18 years old, had a minimum follow-up of 2 years, and had pre-operative imaging. Patients were divided into three groups: bilateral surgery, ipsilateral surgery with, and without asymptomatic concurrent contralateral stones. Cox regression was used to analyze patients' need for future surgery while controlling demographic and comorbid characteristics. Of the 1666 patients included, 51.9% were men. They were 59.7 ± 15 years and had a BMI of 31.3 ± 8.2 kg/m2. During the follow-up of 5.2 ± 2.2 years (range 2-11 years), patients who had bilateral surgery and patients who had ipsilateral surgery without treatment of the asymptomatic concurrent contralateral stones had no difference in the need for future surgery (41.7% vs. 43%, p = 0.585). When stratified by stone size, patients with contralateral stones > 6 mm were more likely to require future surgical treatment than those treated bilaterally (p < 0.001). Our study demonstrates that treating asymptomatic concurrent contralateral stones does not lower the need for future surgical interventions. However, asymptomatic concurrent contralateral stones > 6 mm may portend earlier need for treatment. Therefore, bilateral treatment should be considered at presentation.

Clinical Impact of the Institution of Moses Technology on Efficiency During Retrograde Ureteroscopy for Stone Disease: Single Center Experience

Margaret Knoedler, Shuang Li, Sara L Best, Sean P Hedican, **Kristina L Penniston**, Stephen Y Nakada

The study objective was to evaluate the clinical benefits of Moses technology compared to the regular mode with the Lumenis® Pulse™ P120H holmium laser during ureteroscopy for stone disease. An IRB approved database of patients with urolithiasis was analyzed for ureteroscopies from 1/2020 - 12/2020 at an outpatient surgery center. Patients who underwent ureteroscopy with the Lumenis® Pulse™ P120H holmium laser system with the Moses or regular mode were included. Patient characteristics and stone parameters were collected. Operative room parameters were compared including procedural time, fragmentation/dusting time, lasing time and total energy used. Complication rates and stone free rates were also analyzed. Univariate analysis and MANCOVA controlling for cumulative stone size were performed. Patients with staged procedures were excluded. Of 197 surgical cases, 176 met inclusion criteria. Moses was utilized in 110 cases and regular mode in 66. There was no difference in cumulative stone size between Moses and regular modes (11.8±7.9 vs 11.6±9.2 mm, p=0.901). Procedural time (43.5±32.1 vs 39.8±24.6 min, p=0.436), fragmentation/dusting time (20.5±25.3 vs 17.1±16.1 min, p=0.430), lasing time (7.5±11.1 vs 6.7±7.9 min, p=0.570) and total energy used (5.1±6.7 vs 3.8±4.8 kJ, p=0.093) were also similar. Complications (6.4% vs 6.1%, p=0.936) and stone free rates (61.6% vs 73.5%, p=0.163) did not differ.

Comparison of Different Pulse Modulation Modes for Holmium:YAG Laser Lithotripsy Ablation in a Benchtop Model

Russell Stevens Terry, **Derek S Ho**, Dominick Scialabba, Patrick S Whelan, Robert Qi 6, Brian Thomas Ketterman, **Glenn M Preminger**, **Pei Zhong**, **Michael Eric Lipkin**

Manipulation of Holmium:YAG (Ho:YAG) laser parameters such as pulse energy, frequency, and duration can impact laser lithotripsy ablation efficiency. In 2017, Lumenis introduced Moses™ Technology which uses pulse modulation to enhance the delivery of energy from fiber to stone as well as to minimize stone retropulsion. Since the introduction of Moses™ Technology, other companies have brought additional pulse modulation concepts to market. The purpose of this in vitro study is to compare the pulse characteristics and stone ablation efficiency of Lumenis' Moses™ Technology with Quanta's Vapor Tunnel™. Submerged BegoStone phantoms were systematically ablated using either the Lumenis MOSES™ Pulse 120H or the Quanta Litho 100 clinical laser system. Two pulse energies (0.4J and 1J), three fiber-stone standoff distances (0.5, 1, 2mm), and all available pulse duration and modulation modes for each laser were tested in combination. Fiber speed was adjusted to scan across the stone surface at either 1 pulse/mm or 10 pulses/mm to form single pulse craters or an ablation trough, respectively. Volumes of single craters and 1 mm trough segments were imaged and quantified using optical coherence tomography (OCT). Ablation volumes decreased with decreasing pulse energy and increasing standoff distance. Statistically significant variability was seen between pulse types at every tested parameter set. Among pulse modulation modes, Moses Distance was superior at 0.5mm in all testing and at 2mm in trough testing. Vapor Tunnel was superior in 2mm single crater testing. All modulated pulses performed similarly at 1mm.

PATIENT-CENTERED RESEARCH

Development of a conceptual model of patient-reported outcomes in light chain amyloidosis: a qualitative study

Anita D'Souza, Judith Myers, Rachel Cusatis, Angela Dispenzieri, Muriel Finkel, Julie Panepinto, **Kathryn E Flynn**

Light chain (AL) amyloidosis is a plasma cell neoplasm associated with high early mortality and severe morbidity that can cause severe disability. We explored the impact of AL amyloidosis on symptoms and well-being from the perspectives of patients and health care providers who regularly care for AL patients. We intended to develop a conceptual understanding of patient-reported outcomes in AL amyloidosis to identify the context of use and concept of interest for a clinical outcome assessments tool in this disease. Patients and professionals were interviewed. The impact of AL amyloidosis on patients' life was multidimensional, with highly subjective perceptions of normality and meaning. Four major themes from patients and experts included diagnosis of AL amyloidosis, living with AL amyloidosis, symptom burden, andsocial roles. Barriers to patient-reported outcomes data collection in patients were additionally explored from experts. The themes provide a comprehensive understanding of the important experiences of symptom burden and its impact on daily life from AL amyloidosis patients' and from the perspectives of professionals who care for patients with AL amyloidosis.

GeneLiFT: A novel test to facilitate rapid screening of genetic literacy in a diverse population undergoing genetic testing

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With the broader introduction of genomic medicine in research and clinical care, an increasing number of persons are offered genetic testing. Many factors, including genetic literacy, may impact the utilization of genetic results by patients and their families. We developed a rapid, self-administered measure of genetic literacy, called Genetic Literacy Fast Test (GeneLiFT). We next evaluated the association of GeneLiFT scores with the comprehension of limitations of genomic medicine in participants undergoing genetic testing in the NIH-sponsored eMERGE III study at Columbia University Irving Medical Center, New York. All participants underwent genetic screening for variants in 74 actionable genes associated with adult-onset disorders. A diverse cohort of 724 participants completed the survey. The GeneLiFT was validated using known group differences based on education, health literacy, and numeracy, and with questions assessing genetic knowledge. GeneLiFT identified multiple standard genetics terms, that is, jargon, not recognized by more than 50% of participants (including actionability and pathogenicity). Low genetic literacy, identified in 210 participants (29%), was significantly associated with poor understanding of the limitations of genetic testing (p-values < 10-9). This association was independent of education, health literacy, and numeracy levels, highlighting the importance of directly measuring genetic literacy. Low genetic literacy was also associated with low satisfaction with the informed consent process. GeneLiFT is a practical tool for rapid assessment of genetic literacy in large studies or clinical care. GeneLiFT will allow future research to efficiently assess the role of genetic literacy on the clinical impact of genetic testing.

- Jennifer Allmaras, MPH, 7/29/2021

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